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Brain activity during dual task gait and balance in aging and age-related neurodegenerative conditions: A systematic review

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Abstract

The aims of this systematic review were to investigate (1) real-time brain activity during DT gait and balance, (2) whether changes in brain activity correlate with changes in behavioral outcomes in older adults and people with age-related neurodegenerative conditions. PubMed, PsycINFO, and Web of Science were searched from 2009 to 2019 using the keywords dual task, brain activity, gait, balance, aging, neurodegeneration, and other related search terms. A total of 15 articles were included in this review. Functional near-infrared spectroscopy and electroencephalogram measures demonstrated that older adults had higher brain activity, particularly in the prefrontal cortex (PFC), compared to young adults during dual task gait and balance. Similar neurophysiological results were observed in people with age-related neurodegenerative conditions. Few studies demonstrated a relationship between increased brain activity and better behavioral outcomes. This systematic review supports the notion that aging and age-related neurodegenerative conditions are associated with neuronal network changes, resulting in increased brain activity specifically in the PFC. Further studies are warranted to assess the relationship between increased PFC activation during dual task gait and balance and behavioral outcomes to better optimize the rehabilitation interventions.

Keywords

Brain activity; Dual task; Gait; Balance; fNIRS; EEG; Older adults; Neurodegeneration

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1. Introduction

The ability to stand or walk while simultaneously carrying out cognitive tasks is a critical skill for most daily-life activities (Plummer et al., 2015). When the demands of executing two tasks concurrently exceed cognitive capacity, performance on one or both tasks will diminish (Kelly et al., 2012). Studies have shown that the cost of performing dual task (DT) gait and balance is greater in older adults and in people with age-related neurodegenerative conditions (Li et al., 2001; McIsaac et al., 2018; Verhaeghen et al., 2003). Reduced ability to allocate sufficient attentional resources may result in increased risk of falls and loss of independence in older adults with or without age-related neurodegenerative conditions (Lajoie and Gallagher, 2004; Verghese et al., 2002; Wajda et al., 2017).

DT deficiency is operationally defined as a decrease in motor or cognitive performance (or both) when tasks are performed concurrently. The conceptual framework of DT revolves around three main theories: the bottleneck theory, the cross-talk theory, and the attentional capacity theory. The bottleneck theory is based on the notion that tasks must be processed sequentially in the brain, and not in a parallel (Pashler, 1994). The cross-talk theory postulates that tasks using the same cognitive domain and neuronal populations in the brain will not interfere with each other. However, tasks that are using separate cognitive areas will interfere when they are performed simultaneously (Navon and Miller, 1987). Lastly, based on the attentional capacity theory, humans have limited cognitive capacity. As a result, doing two tasks at the same time decreases performance on one or both (Friedman et al., 1982). Older adults and people with age-related neurodegenerative conditions may be more affected by DT deficiency due to the aging process or degeneration of the neuronal circuits, resulting in impairments in both motor and/or cognitive performances (Kelly et al., 2012).

DT deficiency is typically evaluated by the DT cost [((DT – single task (ST))/ST) * 100] on behavioral outcomes, which can either be performance on a motor or a cognitive test (Heinzel et al., 2016; Plotnik et al., 2011). However, these common endpoints have methodological limitations (ceiling/floor effect). They are not sensitive to change and they do not explain the brain activity needed to complete the tasks (Karatekin et al., 2004). DT cost assessed by behavioral outcomes only provide an indirect measure of DT deficiency. Neurophysiological measures, however, provide direct information about DT deficiency beyond what is provided by behavioral outcomes alone. Therefore, neurophysiological tools may advance our understanding of mobility deficits and falls risk before they emerge. Advances in technology enable us to quantify brain activity during actual motor and cognitive testing in real time. As part of normal aging, older adults may exhibit increased brain activity to maintain stable balance and gait (Boisgontier et al., 2013). However, in age-related neurodegenerative conditions, individuals might exhibit a disproportional increase in brain activity to compensate for impaired structural and functional brain regions. It is important to continuously monitor brain activity during DT gait and balance to determine whether attentional demand is altered and whether this alteration affect gait and balance performance in older adults and more specifically in people with age-related neurodegenerative conditions.

Functional near-infrared spectroscopy (fNIRS) and electroencephalogram (EEG) are neurophysiological tools that are commonly applied to measure neurophysiological changes during DT. These neurophysiological tools enable real-time, continuous recording of brain activity while performing natural activities such as standing and walking. Other neuroimaging technologies such as (functional) magnetic resonance imaging and positron emission tomography scanners are also valid and reliable measures of DT deficiency. However, these neuroimaging tools are typically utilized during a motor imagery task or imitated DT walking (Maidan et al., 2016b; Shine et al., 2013; Vervoort et al., 2016; Yuan et al., 2015), which limits the generalization of findings to real-time DT gait and balance. fNIRS is a non-invasive, safe, and portable neuroimaging method to measure changes in oxygenated and deoxygenated hemoglobin concentrations (HbO2 and HbR, respectively) in the brain (Irani et al., 2007). This technology can be used in any postural or mobile condition, which allows measurement of brain activity during a walking or balance task and even during DT. EEG is widely used by clinicians and researchers to measure the electrical activity of the cerebral cortex (Jeffrey W. Koubeissi and ., 2016). EEG frequency bands and event-related potentials (ERP) are direct measurements of brain activity. It is important to note that EEG is not frequently used in DT gait activities compared with fNIRS. Spatial resolution of fNIRS is better than EEG, but inferior to the spatial resolution of fMRI. This can make it difficult to distinguish neural responses from discrete but adjacent cortical areas. In addition, fNIRS and fMRI rely on hemodynamic changes which are intrinsically slower compared to electrophysiological processes recorded through EEG (Ferrari et al., 2004). Overall, EEG and fNIRS each have specific advantages regarding spatial and temporal resolution and both have been shown to provide reliable and valid data during DT balance and gait (Agbangla et al., 2017; Malcolm et al., 2019; Shaw et al., 2018).

Gait and balance are under control of higher-order cognitive processes which leads to involvement of widespread cortical areas (Jacobs and Horak, 2007; Slobounov et al., 2005). Studies have indicated that pre-frontal cortex (PFC) has a crucial role in human balance and gait (Mihara et al., 2008; S. Stuart et al., 2018). According to the scaffolding theory of aging and cognition, increased activation in PFC and structures related to executive functioning with aging and age-related neurodegenerative conditions is an indicator of an adaptive brain that engages with compensatory activity in order to maintain performance in spite of declining neural structures and functions (Park and Reuter-Lorenz, 2009). In older adults, it is common to observe decreased brain functional connectivity across the default network and frontal attentional system as well as reduced integrity of white matter and grey matter compared to the healthy young adults (Andrews-Hanna et al., 2007; Sullivan and Pfefferbaum, 2006). These changes are more prominent in people with neurodegenerative conditions, resulting in overreliance on the prefrontal-striatal networks that are involved in executive function during gait and balance control (Montero-Odasso et al., 2017). Therefore, increased activation in PFC and structures related to executive functioning during DT is expected to compensate for brain functional inefficiency.

In three reviews, the neural correlates of gait and balance were evaluated in young adults (Leone et al., 2017), in people with Parkinson’s disease (S. Stuart et al., 2018), and in various populations (Herold et al., 2017). However, the literature in older adults and in people with age-related neurodegenerative conditions has yet to be compiled for

comprehensive evaluation and interpretation of real-time brain activity changes during DT gait and balance. The aims of this systematic review were to investigate (1) real-time brain activity during DT gait and balance and (2) whether changes in brain activity correlate with changes in behavioral outcomes in older adults and people with age-related neurodegenerative conditions.

2. Methods

This systematic review conforms with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria and was registered on PROSPERO as CRD42017055835 on January 23, 2017 before running the initial searches.

2.1. Data sources and searches

We searched the published literature using strategies created by a medical librarian to identify studies measuring real-time brain activity during DT gait and balance in aging and age-related neurodegenerative conditions. We searched Medline through PubMed, PsycINFO, and Web of Science from 2009 to 2019. The initial search strategy was designed for MEDLINE/PubMed using both keywords and Medical Subject Headings (MeSH). The key words described four main concepts, including a) brain mapping terms such as brain activity, cortical activity, brain imaging, neurophysiological monitoring, fNIRS, EEG; b) DT terms including neurophysiological alterations, dual-task, balance impairments, gait disturbances; c) diseases or conditions including Parkinson's disease, Alzheimer's disease, dementia, neurodegenerative diseases; and d) aged, elderly, and frail defined as 65 + years in age. All four concepts were combined to identify the relevant studies. The PubMed search strategy was then conducted in the other two databases. Studies published in languages other than English were excluded. All searches resulted in a total of 768 articles, including duplicates. Reference lists of all relevant articles and reviews were also hand-searched for additional studies.

2.2. Inclusion and exclusion criteria

Inclusion criteria: 1. Studies that used balance or gait as the primary outcome; 2. Studies that included a cognitive task simultaneously to the balance or gait task; 3. Studies that included a real-time brain activity measurement during DT gait and balance.

Exclusion criteria: 1. Studies investigating the effects of training, exercise intervention, therapy, drugs, or alcohol effects on DT; 2. Studies including assessment of brain activity before and after concurrent motor and cognitive tasks; 3. Non-English published studies.

2.3. Data extraction

Two independent reviewers (MK and SM) screened the available articles based on their titles and abstracts. After initial triage, the full-text articles were examined independently by the two reviewers. Discrepancies were solved by discussion between the two reviewers and a consensus was reached. Agreement between two reviewers (Cohen's kappa = 0.90) was strong. The flow chart (Fig. 1) describes the systematic review process.

2.4. Quality appraisal method

The National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies was used by two independent evaluators (MK, SM), to critically evaluate the methodological quality of the included studies (www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools). Interrater agreement was calculated using the kappa statistic. The kappa values were interpreted as < 0.40 poor agreement, 0.40 to 0.60 moderate agreement, and > 0.80 excellent agreement as suggested by Tooth and Ottenbacher (2004). Disagreements between the two raters were resolved through consensus discussion.

3. Results

A total of 15 articles met the inclusion criteria (Al-Yahya et al., 2018; Beurskens et al., 2014; Doi et al., 2013; Fraser et al., 2016; Holtzer et al., 2011; Holtzer et al., 2016; Maidan et al., 2019; Maidan et al., 2016a; Malcolm et al., 2015; Marusic et al., 2019; Ozdemir et al., 2016; Rosso et al., 2017; Samuel Stuart et al., 2019; Tard et al., 2016; Verghese et al., 2017). All articles selected in this review (1) utilized gait or balance as a behavioral outcome; (2) administered cognitive tasks in addition to motor tasks; and (3) used a real-time neurophysiological tool to assess DT. A summary of included articles is presented in Table 1. Among 15 unique studies, 12 studies used gait as the primary behavioral outcome measure, whereas three studies used balance or postural adjustment to assess motor control. Eight studies examined older adults without age-related neurological conditions (healthy), whereas seven studies included older adults with age-related neurodegenerative conditions. Regarding the real-time neurophysiological assessment, 11 studies utilized fNIRS, whereas four used EEG. Most studies (n = 14) were cross-sectional, whereas one study was a prospective cohort design (Verghese et al., 2017).

The results will be discussed in two main sections based on the type of neurophysiological tools applied in each study (fNIRS or EEG). The sections will be divided by the type of subjects investigated (healthy or with age-related neurodegenerative condition), and outcomes including neurophysiological results (HbO2 levels, frequency bands, or ERP) during ST and DT and behavioral results (gait, balance, or cognition).

3.1. fNIRS studies

3.1.1. Healthy older adults

3.1.1.1. Neurophysiological results.: Five studies used fNIRS to measure brain activity during DT in healthy older adults. In general, the results of the studies showed that older adults had increased PFC activation during DT compared to ST. In addition, older adults also showed higher PFC activation during DT compared to young adults. Holtzer et al. showed that HbO2 levels in the PFC increased bilaterally during DT compared to ST in both older and younger groups (Holtzer et al., 2011). However, a smaller increase in HbO2 levels was observed in older adults than young adults. Fraser et al. (2016) investigated the levels of HbO2 and HbR (deoxygenated hemoglobin) in eight different regions of the PFC, including anterior/posterior dorsolateral/ventrolateral PFC (aDLPFC, pDLPFC, aVLPFC, and pVLPFC) of left and right hemispheres. For HbO2, older and young adult groups showed

task effects (ST < DT) with increased HbO2 in the left pDLPFC (older adults) and left aVLPFC, right aDLPFC, and right pDLPFC (young adults) during DT (normal pace walk + n-back) compared to ST. For HbR, task effects (ST < DT) were observed in all eight regions in older adults and seven regions in young adults. Furthermore, during DT with 2-back test, older adults did not show any significant hemispheric differences in HbO2 and HbR levels, whereas young adults demonstrated significant differences in HbO2 and HbR levels in pDLPFC and pVLPFC (right > left).

Marusic et al. (2019) utilized fNIRS to assess a postural-cognitive DT. For the hemodynamic changes, HbO2 levels in the PFC significantly increased from quiet standing to postural ST (tandem stance), but no change was observed from postural ST to DT in both groups. The study also found no significant effects of aging on HbO2 levels throughout all task conditions including quiet standing, STs (cognitive task or postural control), and DT. In summary, most fNIRS studies showed that older adults had increased PFC activation during DT compared to ST. Older adults also showed higher PFC activation during DT compared to young adults. However, Beurskens et al. (2014) reported contradicting results demonstrating decreased PFC activation in older adults during DT compared to ST, which may be related to reduced brain activity in older adults. Marusic et al. (2019) reported no changes in PFC activation from ST to DT.

3.1.1.2. Behavioral results.: In general, healthy older adults showed poorer or similar performances in motor and/or cognitive tasks compared to young adults. Older adults demonstrated poorer accuracy on both 1-back and 2-back tests compared to young adults. In addition, older adults showed poorer accuracy during n-back tests during DT (normal pace walk + n-back) compared to young adults (Fraser et al., 2016). Holtzer et al. (2016) showed slower gait velocity in healthy older adults during DT (normal pace walk + verbal fluency) compared with ST (normal pace walk). Similar results were found by Maidan et al. (2016b).

Postural balance in older adults during DT was compared with young adults (Rosso et al., 2017). An auditory choice reaction task (CRT), clicking a right or left button depending on the frequency (high or low) of the given sound cue, was administered while participants were standing on a dynamic posturography platform. Older adults showed longer response time during ST2 (auditory choice reaction task) and DT (postural balance task + auditory choice reaction task) compared to young adults. However, no significant group difference was observed between ST1 (postural balance task) and DT. Similar study by Marusic et al. (2019) found that changes in postural control (center of pressure sway path) were not different across tasks (ST and DT) and groups (older and young adults). For the cognitive performance, older adults were significantly worse on both ST (cognitive task only) and DT than younger adults. No significant difference in cognitive performance from ST to DT was found in older adults.

Samuel Stuart et al. (2019) reported no significant differences in gait characteristics between tasks (ST (normal pace walk) and DT (normal pace walk + digit vigilance task)) or groups (older and young), except a slower preferred treadmill speed during ST and DT in older adults compared with young adults. Lastly, the study by Beurskens et al. (2014) measured step duration, step length, and number of steps between older and young adults. The study

consisted of one ST (normal pace walk) and two DTs (DT1: normal pace walk + checking the boxes on a piece of paper with a pen for 30 s; DT2: normal pace walk + verbal letter fluency task). Compared with young adults, older adults showed greater DT cost in step duration, step length, and number of steps during DT2 compared to ST. Also, older adults showed greater DT cost in step duration during DT1 compared to DT2. In summary, healthy older adults showed poorer or similar performances in motor and/or cognitive tasks compared to young adults.

3.1.2. Older adults with age-related neurodegenerative conditions

3.1.2.1. Neurophysiological results.: Five fNIRS studies investigated older adults with age-related neurodegenerative conditions such as mild cognitive impairment (Doi et al., 2013), neurological gait abnormalities (Holtzer et al., 2016), PD (Al-Yahya et al., 2018), and severe neurological conditions with gait impairment (Verghese et al., 2017).

Study conducted by Holtzer et al. (2016) investigated non-demented older adults with neurological gait abnormalities. The study found that central neurological gait abnormalities induced attenuated changes in the HbO2 level during DT (normal pace walk (ST1) + verbal fluency task (ST2)), compared to STs (ST1 and ST2). Maidan et al. (2016b) and Al-Yahya et al. (2018) assessed older adults with PD during DT walking conditions. Older adults with PD showed a non-significant increasing trend in HbO2 levels during DT compared to ST, whereas healthy older adults showed a significant increase in HbO2 levels during DT compared to ST (Maidan et al., 2016b). Another study found increased HbO2 levels in older adults with mild cognitive impairment while performing DT compared to ST (Doi et al., 2013). In addition, older adults with PD demonstrated increased PFC and M1 activation under DT walking compared to ST (Al-Yahya et al., 2018). These results may suggest that during ST brain stem and spinal circuits automatically initiate and maintain a gait pattern without substantial need for executive control. Automaticity refers to the ability of the nervous system to successfully control gait and balance activities with minimal use of executive and attentional resources (Clark, 2015). However, with DT older adults with PD may need to use their cognitive resources for motor planning or gait deficit compensation. Overall, most studies found increased levels of HbO2 in PFC among older adults with age-related neurodegenerative conditions while performing DT.

3.1.2.2. Behavioral results.: Most studies used a normal pace walk as ST. Regardless of the age-related neurodegenerative condition, older adults showed decreased gait velocity during DT (verbal letter fluency or serial 3's subtraction) compared to ST. Doi et al. (2013) demonstrated that older adults with mild cognitive impairment had slower gait velocity during DT (normal pace walk + verbal letter fluency) compared to ST (normal pace walk). Similarly, Verghese et al. (2017) demonstrated a DT effect in community-dwelling older adults without cognitive and gait abnormalities, showing slower gait velocity during DT (normal pace walk + verbal letter fluency) compared with ST (normal pace walk). Older adults with PD showed reduced performance in stride length, gait velocity, step time, and step time variability compared with healthy older adults (Maidan et al., 2016a).

3.2. EEG studies

3.2.1. Healthy older adults

3.2.1.1. Neurophysiological results.: Two studies used EEG to measure brain activity during DT in healthy young adults. Malcolm et al. (2015) studied DT gait in healthy older and young adults using a response inhibition task (Go/No-Go) during normal pace walk. In this study, event-related potentials (ERP) were recorded using EEG. During DT, older adults had limited ERP modulation showing a delayed and reduced P300 amplitude, whereas young adults showed ERP modulations at early (reduced N200 amplitude) and later (earlier P300 latency) stages as motor load increased during DT. These findings suggest that older adults may exhibit less flexibility in allocation of cognitive resources during multiple tasks.

Another study examined balance in both young and older adults (Ozdemir et al., 2016). They investigated standing balance during four different DT conditions using two cognitive tasks (non-challenging (1-back) and challenging (2-back)) and two surface platforms (non-challenging (fixed surface) and challenging (sway surface)). Thus, four DT conditions were '1-back + fixed', '1-back + sway', '2-back + fixed', and '2-back + sway'. Cortical activity modulations using EEG band frequencies revealed differences between older and younger individuals in DT. Delta bands decreased in the frontal, central-frontal, central, central-parietal, and parietal regions when older adults engaged in a challenging postural control task with DT ('1-back + sway' and '2-back + sway'), compared with young adults. Theta band activity was smaller during DT with a challenging cognitive task ('2-back + fixed' and '2-back + sway') in the frontal and central-frontal regions in older adults compared to young adults. In other words, theta bands are more responsive to cognitive tasks. The smaller theta band activation in the older adult group compared to the young adult group may represent less activation of neural correlates relating high-level cognitive computations. Alpha bands were more activated over central-parietal and parietal cortices in both older and young adult groups when performing challenging postural control DTs (1-back + sway and 2-back + sway). Gamma bands increased over frontal, central-parietal, and parietal regions in older adults during DT with challenging postural control conditions ('1-back + sway' and '2-back + sway'). This suggests that gamma bands are associated with more increased attention to postural tasks in older adults. No significant changes were observed in beta bands across any ST and DT conditions.

Maidan et al. (2019) investigated ERP during DT, with a special focus on P300 amplitude and latency. The study used an auditory oddball test in standing position (ST) and during normal pace walk (DT). P300 latency during DT was significantly longer in older adults compared to young adults. Also, both groups showed longer P300 latency during DT compared to ST. P300 amplitude was similar within each group and between the two groups during DT, which contradicts a previous finding from Malcolm et al. (2015). This contradiction may be due to the use of different cognitive task (auditory oddball vs. Go/No-Go).

3.2.1.2. Behavioral results.: In general, older adults showed slower response time, stride time, and impaired postural control compared to the young adults during DT. Ozdemir et al. (2016) found that during STs (balance only task on fixed or sway platform) and DTs with a

non-challenging cognitive task (1-back), postural control performance was similar between young and older adult groups. However, postural control performance in older adults became considerably worse when performing DTs with a challenging cognitive task (2-back) compared with young adults on both surface conditions. Although older adults showed no difference in postural performance during DTs with a non-challenging cognitive task (1-back) compared with young adults, older adults showed decreased accuracy in '1-back + sway'. This suggests that older adults have less cognitive capacity compared to young adults during the challenging postural control performance. Alternatively, older adults may allocate more cognitive resources for postural control, resulting in decreased performance in the non-challenging cognitive task (1-back).

3.2.2. Older adults with age-related neurodegenerative conditions

3.2.2.1. Neurophysiological results.: Two studies used EEG to measure brain activity during DT in older adults with age-related neurodegenerative conditions. A study by Tard et al. (2016) examined changes in cortical activities due to modulated attention during motor preparation in older adults with PD. During DT (attention + motor preparation), EEG results showed that theta and alpha bands increased over 500 ms followed by S1 in all three groups (freezing of gait, non-freezing of gait, and healthy older adults), which implied an event-related synchronization of the brain. Older adults with PD without freezing of gait and healthy older groups showed decreased beta bands during DT, which reflected an event-related desynchronization of the brain. Older adults with PD with freezing of gait had different EEG patterns, showing prolonged event-related synchronization and no generation of event-related desynchronization during DT. The results suggest that older adults with PD with freezing of gait have a relatively intact function to discriminate stimuli because they showed changes in EEG patterns (greater modulation in the beta band) after the target sound though it was prolonged. However, their attention-motor preparation coupling is impaired since the beta band did not decrease (no event-related desynchronization).

Another EEG study by Maidan et al. (2019) investigated older adults with PD. In this study, participants performed an auditory oddball test while standing (ST) and during normal pace walk (DT). P300 ERP latency in older adults with PD was longer than that in young adults during DT. However, there was no difference in P300 latency between older adults with PD and healthy older adults during DT. P300 amplitude during ST was not different across older adults with PD and healthy older and young adult groups. However, older adults with PD demonstrated a lower P300 amplitude during DT, which indicates older adults with PD may have a lack of attentional resources, compared with healthy older and young adults, especially when the cognitive demand is greater such as DT.

3.2.2.2. Behavioral results.: Motor performance, including inappropriate postural adjustment, inappropriate anticipatory postural adjustment, and step speed, was worse in older adults with PD than healthy controls (Tard et al., 2016). Similarly, motor performance outcomes also distinguished between PD with and without freezing of gait. In addition, older adults with PD showed worse gait performance including slower gait velocity, stride, and step regularity during DT compared with young adults (Maidan et al., 2019). Cognitive

performance measured immediately after ST and DT in older adults with PD was also worse than healthy young adults and older adults.

3.2.2.3. Correlation between neurophysiological and behavioral outcomes.: Only two studies investigated the correlation between neurophysiological and behavioral outcomes. One study found a strong inverse relationship between Stroop interference and HbO2 levels in the left inferior frontal gyrus in older adults with mild cognitive impairment (Doi et al., 2013) whereas another study found increased HbO2 levels with increased gait speed in people with PD (Maidan et al., 2016a).

3.3. Methodological quality

The methodological quality for each included study is reported in Table 2. The agreement between the quality raters was Cohen's kappa = 0.98, indicating excellent agreement. Fourteen studies were designed as an observational study whereas only one study was a prospective cohort study. Hypotheses and study design were reported for all studies, and all of them included a clear definition for identifying the target population. In all studies, independent and dependent variables included in the analyses were reliable, valid, and implemented consistently across all the participants. Very few studies controlled for confounding variables in the statistical analyses and only one study reported sample size justification in their methods section.

4. Discussion

The objectives of this systematic review were to investigate the real-time brain activity during DT gait and balance and the correlation between changes in brain activity and behavioral outcomes in older adults and in people with age-related neurodegenerative conditions. A total of 15 articles were included using real-time neurophysiological tools (fNIRS and EEG) to measure brain activity during DT gait and balance. Walking while performing a cognitive task was the most common paradigm to measure the brain activity during DT. Gait velocity and postural sway were the most commonly reported behavioral outcomes in the included studies. In general, studies demonstrated higher brain activity during DT compared to ST in PFC and structures related to executive functioning in older adults and in people with age-related neurodegenerative conditions. Few studies demonstrated relationship between increased brain activity and better behavioral performance. These results suggest that with aging and/or neurodegeneration, individuals are less efficient in performing two tasks simultaneously and therefore recruit alternative neural resources predominantly from the PFC to compensate for the activity.

Based on the Compensation-Related Utilization of Neural Circuits Hypothesis (CRUNCH) model, older adults and people with age-related neurodegenerative conditions recruit neuronal networks from both hemispheres to compensate for declines in functional efficiency (Reuter-Lorenz and Cappell, 2008). CRUNCH states that in aging or neurodegeneration, the brain recruits compensatory neural resources when solving a task to maintain similar performance of a younger brain. In older adults and in people with age-related neurodegenerative conditions, the brain may increase the activity in a certain neural network to compensate for declining processing efficiency in that same network. In addition,

compensation might be achieved by increased activity in other, yet connected networks. Thus, increasing the activity in a certain or alternative network may reflect compensation for reduced neural processing. Another explanation of the compensation derives from the scaffolding theory of aging and cognition. This theory states that increased PFC activation with age and age-related neurodegenerative conditions is an indicator of an adaptive brain that engages with compensatory activity to maintain the performance as a result of declining neural functions and structure (Park and Reuter-Lorenz, 2009). The results of this systematic review support these two theories. Most studies demonstrated that older adults had increased brain activity compared to young adults (Malcolm et al., 2015; Ozdemir et al., 2016; Rosso et al., 2017; Samuel Stuart et al., 2019). Studies with fNIRS provided that older adults had increased activation in the PFC during DT activities compared to the ST (Al-Yahya et al., 2018; Holtzer et al., 2011; Holtzer et al., 2016; Verghese et al., 2017). Similar results were observed in several populations including PD (Al-Yahya et al., 2018), PD with freezing of gait (Tard et al., 2016) and mild cognitive impairment (Doi et al., 2013).

Interestingly, three studies found decreased HbO2 levels in the PFC during DT in older adults and in people with neurodegenerative conditions compared to their controls (Beurskens et al., 2014; Fraser et al., 2016; Maidan et al., 2016a). This might be explained in two ways. First, although fNIRS is sensitive to movement artifacts and valid to measure neurophysiological response of the brain during gait and balance (Vitorio et al., 2017), it only measures oxygenated and deoxygenated hemoglobin (HbO2/HbR) levels in the specific area of the brain. In this systematic review, most of the studies used the PFC region as the area of interest whereas only one study (Samuel Stuart et al., 2019) used whole brain fNIRS. It is possible that older adults and people with age-related neurodegenerative conditions recruit additional areas beyond the PFC to compensate during DT. Second, older adults and people with age-related neurodegenerative conditions might show decreased HbO2 levels when the cognitive demand of the DT paradigm exceeds the available cognitive resources. When this conflict between cognitive demand and cognitive resources occurs, participants may disengage from the task, resulting in less brain activity and decreased behavioral performance. Reflecting an inverted U-shaped pattern, at low levels of cognitive demand, older adults and people with age-related neurodegenerative conditions need to exhibit more brain activity compared to young adults in order to maintain task performance (Grady, 2012). However, at high levels of cognitive demand, this compensatory mechanism is no longer effective leading to reduced brain activity due to decreased attention to the task (Vermeij et al., 2014). Therefore, it is important to consider both behavioral and brain activity outcomes to interpret the results of DT studies.

In addition, one study found a decreased hemispheric difference in PFC activation during DT in older adults compared to the young adults during treadmill walking with a 2-back test (Fraser et al., 2016). According to the Hemispheric Asymmetry Reduction in Older Adults (HAROLD) model, older adults exhibit neurofunctional changes which are characterized by a reduction in functional hemispheric lateralization (Cabeza, 2002). A possible explanation could be that older adults use additional neural networks to compensate for functional inefficiency to maintain similar behavioral performance compared to young adults. However, future research is needed to demonstrate this phenomenon in people with age-related neurodegenerative conditions during DT gait and balance conditions.

EEG studies demonstrated prolonged ERP in P300 topography during DT in people with PD (Maidan et al., 2019) and in people with PD who have freezing of gait (Tard et al., 2016). Evidence suggests that increased ERP in the P300 topography links with recruiting frontal neural circuits as a compensatory activity in aging and in age-related neurodegenerative conditions (van Dinteren et al., 2018). However, the results of the EEG studies should be carefully interpreted because of the heterogeneity of the outcome measurements across the studies (brain wave activity or ERPs). In addition, due to the small number of studies using EEG, it remains unclear which EEG metric best reflects the neurophysiological changes during DT and shows the strongest correlation with aging and the neurodegeneration process. Future research should investigate a combined EEG and fNIRS approaches to have a robust measurement during DT gait and balance. Using fNIRS as a guide to EEG source localization will eventually advance spatial resolution.

Coupling of behavioral and neurophysiological findings is paramount to advance our understanding of brain-behavior interactions. The behavioral outcomes consistently showed that older adults or people with neurodegenerative conditions had decreased motor performance measured by gait velocity (Doi et al., 2013; Holtzer et al., 2011; Holtzer et al., 2016; Maidan et al., 2019; Maidan et al., 2016a; Verghese et al., 2017), step duration (Beurskens et al., 2014), postural sway (Ozdemir et al., 2016; Rosso et al., 2017; Tard et al., 2016), and decreased performance on the cognitive task (Fraser et al., 2016; Malcolm et al., 2015) from ST to DT conditions. Similar performance decrements were observed when comparing the behavioral outcomes between older adults and young adults as well as between people with age-related neurodegenerative conditions and older adults. People with age-related neurodegenerative conditions had a disproportional decrease in their motor performance from ST to DT conditions (Maidan et al., 2016b; Tard et al., 2016). In this systematic review, few studies investigated the relationship between behavioral and neurophysiological findings. One study found a strong inverse relationship between Stroop interference and HbO2 levels in the left inferior frontal gyrus in older adults with mild cognitive impairment (Doi et al., 2013) whereas another study found increased HbO2 levels with increased gait speed in people with PD (Maidan et al., 2016a). Future studies are needed to investigate the association between neurophysiological and behavioral outcomes to better understand the brain-behavior relationship in older adults and in people with age-related neurodegenerative conditions.

This systematic review has several limitations. First, the DT paradigms were different in almost all studies which made it harder to interpret the findings. It is recommended to build a consensus to find the most applicable DT paradigm and standardize the testing protocol to better interpret the effect of increased DT cost on behavioral and neurophysiological outcomes in older adults and in people with age-related neurodegenerative conditions. Another limitation was the heterogeneity of the outcome measures that were obtained from the neurophysiological tools across the studies. Therefore, it is not surprising to observe inconsistent findings regarding the region and volume of brain activity during DT gait and balance across the studies. In addition, a limited number of studies using EEG with different outcome parameters led to difficulties interpreting which EEG parameter is most sensitive to measure brain activity during DT in older adults and in people with age-related with

neurodegenerative conditions. Future studies are needed to standardize behavioral and neurophysiological outcomes in DT gait and balance studies.

5. Conclusion

This systematic review demonstrated that, in general, older adults and people with age-related neurodegenerative conditions had increased brain activity during DT, specifically in the PFC, while performing gait and balance activities. In addition, small number of studies reported better behavioral performance with increased brain activity. Induced DT cost during gait and balance is clinically important since it is linked to loss of independence and increased risk of falls. Further studies are warranted to assess the relationship between increased PFC activation during DT and behavioral outcomes to better optimize rehabilitation interventions to improve independence and to decrease fall risk.

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Appendix A

Search strategy presented in User Query Format:

(Brain mapping[Mesh] OR Neuroimaging[Mesh] OR Neurophysiological monitoring[mesh] OR Neurofeedback[Mesh] OR Magnetoencephalography[mesh] OR electroencephalography[mesh] OR “Brain activity”[tiab] OR “brain activities”[tiab] OR “neural activity”[tiab] OR “Neural activities”[tiab] OR “Subcortical activity ”[tiab] OR “Subcortical activities”[tiab] OR “Cortical activity”[tiab] OR “Cortical activities”[tiab] OR Neuromonitoring[TIAB] OR “Brainstem monitoring”[tiab] OR “brain stem monitoring” [tiab] OR “cerebral monitoring”[tiab] OR “Neuroimaging”[tiab] OR “Neurophysiological monitoring”[tiab] OR “Neurofeedback”[tiab] OR “brain imaging”[tiab] OR “brain mapping”[tiab] OR functional magnetic resonance imaging[tiab] OR fMRI[tiab] OR functional Near Infrared Spectroscopy[tiab] OR fNIRS[tiab] OR MEG[tiab] OR Magnetoencephalography[tiab] OR EEG[tiab] OR electroencephalography[tiab]) AND (cognitive-motor interference[tiab] OR motor-cognitive interference[tiab] OR cognitive-motor interaction[tiab] OR motor-cognitive interaction[tiab] OR Dual-task[tiab] OR balance[tiab] OR Gait[tiab] OR walking[tiab] OR postural ability[tiab] OR gait[mesh] OR walking[mesh] OR postural balance[mesh] OR gait disorders, neurologic[mesh] OR neurophysiological alterations[tiab]) AND (Parkinson disease[Mesh] OR parkinsonism[tw] OR parkinsonian disorders[mesh] OR parkinsonian disorders[tiab] OR Alzheimer disease[mesh] OR Alzheimer disease[tiab] OR dementia[mesh] OR dementia[tiab] OR cognitive dysfunction[mesh] OR mild cognitive impairment[tiab] OR neurodegenerative diseases[mesh] OR neurodegenerative diseases[tiab]) AND (Aged[mesh] OR aged[tiab] OR frail elderly[mesh] OR frail*[tiab] OR elderly[tiab]) Sort by: Relevance Filters: Aged: 65 + years; 80 and over: 80 + years.

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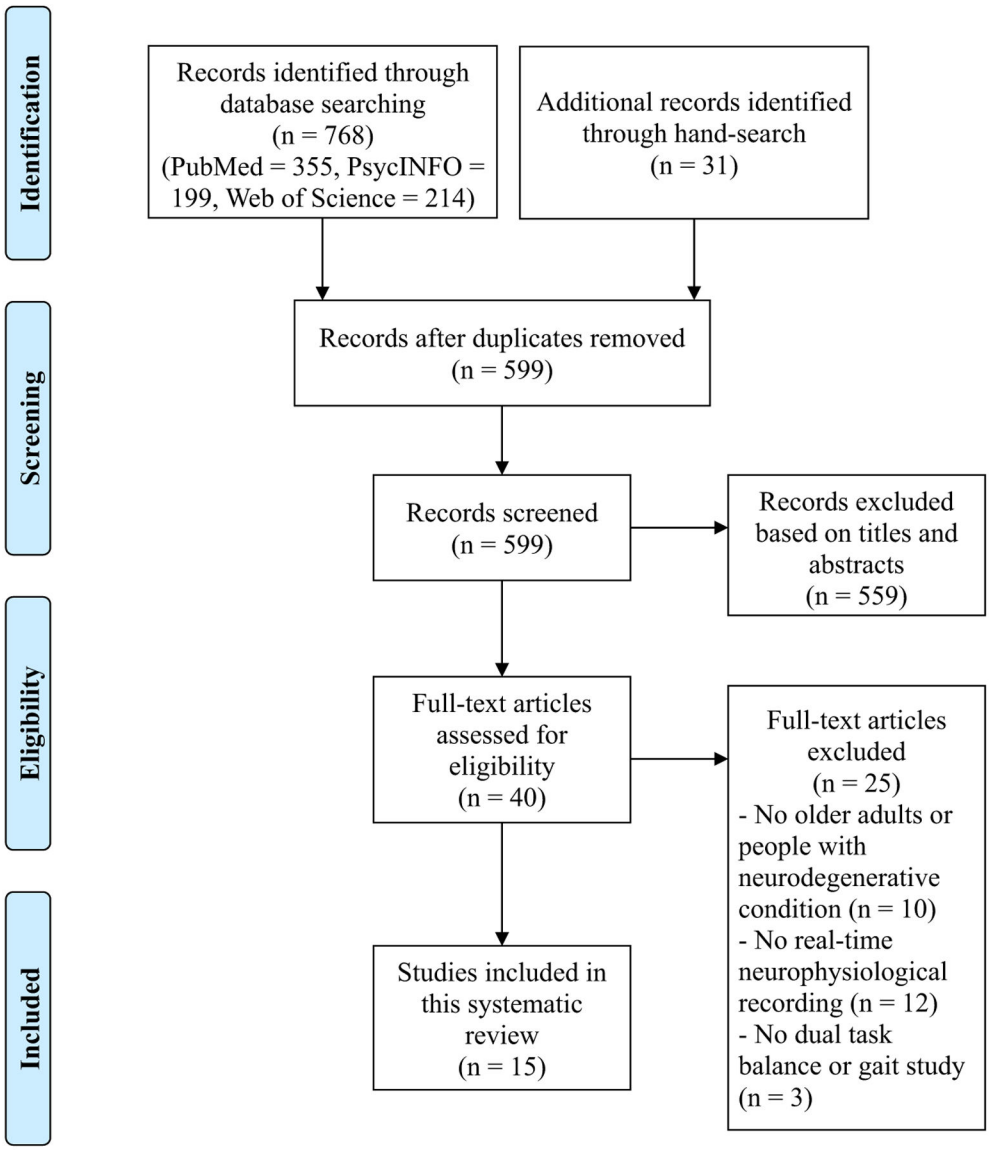

Fig. 1.
PRISMA flow chart of search and retrieval process.

Table 1

Summary of participant characteristics, task paradigm, neurophysiological tool, behavioral outcomes, and neurophysiological outcomes of the studies included in the systematic review.

Authors (year)	Participant characteristics	Task paradigms (single (ST) and dual (DT) tasks)	Neurophysiological tool	Behavioral outcomes	Neurophysiological outcomes
Holtz er et al. (2011)	*N* = 22 (14f/8 m) (i) older adults, *n* = 11 (7f/4 m), age range = 69–88 yrs. (ii) young adults, n = 11 (7f/4m), age range = 19–29 yrs	ST: normal walk DT: walk + cognitive task (verbal letter fluency task: reciting alternate letters beginning with the letter A or B)	fNIRS	↓ gait velocity during ST and DT in older adults compared with young adults ($p < .001$) ↓ gait velocity during DT compared with ST in both groups ($p < .001$)	↑ HbO2 level in PFC in both groups during DT compared with ST ($p < .05$ in 15 out of 16 channels) ↓ HbO2 level in PFC in older adults during DT compared with young adults ($p < .05$ in 13 out of 16 channels)
Doi et al. (2013)	*N* = 16 (6f/10m) Age = 75.4 (7.2) yrs., with mild cognitive impairments	ST: normal walk DT: walk + cognitive task (verbal letter fluency)	fNIRS	↓ gait velocity during DT compared with ST (p < .001)	↑ HbO2 level in PFC during DT, compared with ST (p < .001) Correlation between HbO2 level during DT and Stroop inference (measured by Stroop test assessing executive function) (p < .05)
Beurskens et al. (2014)	*N* = 25 (i) older adults, *n* = 10, age = 71.0 (3.8) yrs. (ii) young adults, *n* = 15, age = 24.5 (3.3) yrs	ST: normal walk → cognitive task 1 (checking the boxes on the paper with a pen for 30 s) → cognitive task 2 (verbal letter fluency task) → DTI: walk + cognitive task 1 → DT2: walk + cognitive task 2	fNIRS	↑ DT cost (DT2 - ST) in step duration (p < .05), step length (p < .05), and number of steps ($p < .01$), during DT2 in older adults compared to young adults ↑ DT cost in step duration during DTI compared to DT2 in older adults (p < .05) ↓ DT cost in step duration, step length, and number of steps (all p < .001) during DT2 compared to DTI in young adults	↓ HbO2 level in PFC during DT2, but no changes in HbO2 levels during ST and DTI in older adults No changes in HbO2 level in PFC during ST, DTI, and DT2 in young adults
Malcolm et al. (2015)	*N* = 33 (17f/16 m) (i) older adults, n = 16 (9f/7 m), age = 63.9 (4.0) yrs. (ii) young adults, *n* = 17 (8f/9 m), age = 27.2 (4.6) yrs	ST1: cognitive task (Go/No-Go) in sitting ST2: normal walk DT: walk + cognitive task	EEG	↓ response time in older adults during ST1 and DT compared to young adults (p < .001) ↑ DT cost in cognitive task accuracy in older adults between ST1 and DT whereas no changes in young adults ($p = .07$; approaching significance) ↓ stride time in older adults during DT compared to young adults (p < .05)	↑ P3 amplitude: delayed and attenuated ERP during DT in older adults ERP modulations at N2 amplitude reduction and P3 latency during DT in young adults
Fraser et al. (2016)	N = 33 (24f/9 m) (i) older adults, *n* = 14 (12f/2 m), age = 66.9 (5.3) yrs. (ii) young adults, *n* = 19 (12f/7 m), age = 21.8 (1.9) yrs	ST1: normal walk ST2: cognitive task (n-back) DT: walk + cognitive task	fNIRS	↑ accuracy during 1-back in older and young adults compared to 2-back (p < .001) ↓ accuracy during ST2 and DT in older adults compared to young adults ($p = .009$)	↑ HbO2 and HbR levels in PFC in older and young adults during DT compared to ST1 No significant age effect between older and young adults in HbO2 and HbR levels during any tasks
Holtz er et al. (2016)	*N*= 236 (122f/114 m) Age = 75.5 (6.5) yrs., all nondemented (≥ 65 years) (i) healthy older adults, *n* = 167	ST1: normal walk ST2: cognitive task only (verbal letter fluency) DT: walk + cognitive task	fNIRS	↓ gait velocity during DT compared to ST1 in healthy older adults (p < .001)	Between groups, ↓ HbO2 level in older adults with neurological gait abnormalities during DT, compared to HbO2 levels during ST1 or ST2

Authors (year)	Participant characteristics	Task paradigms (single (ST) and dual (DT) tasks)	Neurophysiological tool	Behavioral outcomes	Neurophysiological outcomes
	(ii) older adults with neurological gait abnormalities, *n* = 69			No main and interaction effects between neurological gait abnormality status and tasks	
Maidan et al. (2016a)	*N* = 106 (40f/66 m) (i) healthy older adults, *n* = 38 (18f/20 m), age = 70.4 (0.9) yrs. (ii) PD, *n* = 68 (22f/46 m), age = 71.6 (0.9) yrs	ST: normal walk DTI: walk + cognitive task (serial 3's subtraction) DT2: walk + obstacle negotiation	fNIRS	↓ functional performance (stride length, gait velocity, etc.) during all walking conditions in adults with PD compared with healthy older adults ($p \leq .001$)	↑ HbO2 level in PFC during ST in PD compared to healthy older adults ($p < .030$) ↑ HbO2 level in PFC during DTI only in healthy older adults compared to ST ($p < .001$) ↑ HbO2 level in PFC during obstacle negotiation in PD ($p = .001$) and in healthy older adults ($p = .053$)
Ozdemir et al. (2016)	N = 19 (10f/9 m) (i) young adults, *n* = 10 (4f/6 m), age = 26.2 (2.8) yrs. (ii) older adults, *n* = 9 (6f/3 m), age = 81.4 (6.3) yrs	ST: balance task only and/or cognitive task (n-back) only → DT: balance + cognitive task	EEG	↓ 2-back performance in balance tasks (fixed and sway platforms) in older group compared with young group ($p < .05$) ↓ balance during sway platform balance test + 2-back test in the older group compared with young group ($p < .001$)	↑ delta, theta, and gamma oscillations in frontal, central-frontal, central, and central-parietal cortices during DT (sway + 2-back) in older group compared with ST (all $p < .05$)
Tard et al. (2016)	N = 38 (1 Of/28 m) (i) PD FoG, *n* = 12 (3f/9m), age = 62.5 (5.2) yrs. (ii) PD non-FoG, *n* = 13 (3f/10m), age = 60.2 (10.2) yrs. (iii) healthy older adults, n = 13 (4f/9 m), age = 65.4 (5.8) yrs	ST1: auditory preparatory stimulus (standard or target sound) → ST2: visual imperative stimulus ("Go" sign → step initiation)	EEG	↓ motor performance (↑ inappropriate postural adjustment, ↑ inappropriate anticipatory postural adjustment, ↓ step speed) in PD FoG, compared with PD non-FoG ↓ motor performance in PD non-FoG, compared with healthy older adults	↑ low-frequency power over 500 ms following the auditory stimulus in all three groups (ERS; event-related synchronization) Then ↓ mid-range frequency power after both target and standard sounds in normal controls and non-FoG (ERD; event-related desynchronization) However, no ERD in FoG after ERS
Rosso et al. (2017)	N = 16 (9f/7 m) (i) older adults, n = 10 (7f/3 m), age range = 66–81 yrs. (ii)young adults, n = 6 (2f/4 m), age range = 22–30 yrs	ST1: postural balance task ST2: cognitive task (auditory choice reaction time) DT: balance (ST1) + cognitive task	fNIRS	↑ reaction time during ST2 and DT in older adults compared to young adults ($p < .001$ (ST2); $p = .01$ (DT)) No significant differences between ST1 and DT in both older and young adults	↑ HbO2 and HbR levels in PFC during DT in older adults compared to young adults ($p = .006$ (HbO2); $p = .02$ (HbR))
Verghese et al. (2017)	*N* = 166 (85f/81 m) Age = 75.0 (6.1) yrs.; older adults without severe neurological conditions and gait impairment	ST: normal walk → cognitive task only (verbal letter fluency) → DT: walk + cognitive task	fNIRS	↓ gait velocity during DT compared to ST	↑ HbO2 level in PFC during DT compared to ST
Maidan et al. (2019)	*N* = 31 (14f/17 m) (i) older adults, n = 10 (6f/4 m), age = 67.1 (1.7) yrs. (ii) PD, n = 10 (4f/6m), age = 60.5 (3.6) yrs. (iii) young adults, n = 11 (4f/7 m), age = 32.3 (1.8) yrs	ST: cognitive task (auditory oddball test; counting odd tones (600 Hz) among standard tones (1200 Hz)) in standing DT: walk + cognitive task	EEG	↓ gait velocity, step regularity, and stride in PD compared to young adults	Prolonged P300 (ERP component) latency during DT in PD ↓ P300 amplitude during DT only in PD
Marusic et al. (2019)	*N* = 20 (13f/7 m) (i) older adults, n = 10 (6f/4 m), age = 72.3 (3.2) yrs. (ii) young adults, n = 10 (7f/3 m), age = 22.6 (2.8) yrs	ST1: postural balance task ST2: cognitive task (serial 3's subtraction) DT: balance + cognitive task	fNIRS	↓ cognitive performance during STs and DT in older adults compared with young adults No significant difference in postural balance task	↑ HbO2 levels from baseline to ST1, but not changes from ST1 to DT No significant difference across groups

Authors (year)	Participant characteristics	Task paradigms (single (ST) and dual (DT) tasks)	Neurophysiological tool	Behavioral outcomes	Neurophysiological outcomes
Stuart et al. (2019)	*N* = 35 (18f/17 m) (i) older adults, *n* = 18 (9f/9 m), age = 72.6 (8.0) yrs. (ii) young adults, n = 17 (9f/8 m), age = 20.3 (1.2) yrs	ST: normal walk DT: walk + cognitive task (digit vigilance task: counting the number of random number X for 30 s)	fNIRS	No significant differences in gait characteristics between tasks (ST vs. DT) or groups (older vs. young)	↑ HbO2 level in motor regions of the brain during DT compared to ST in older and young groups No significant HbO2 level change in PFC during DT compared to ST in older and young groups
Al-Yahya et al. (2018)	*N* = 51 (29f/22 m) (i) PD, *n* = 29 (13f/16 m), age = 66.3 (5.9) yrs. (ii) older adults, *n* = 22, (16f, 6 m) age = 59.5 (6.8)	ST: Self-selected walking speed (SSWS) and Fast walking speed (FWS) DT: Subtracting while walking in SSWS and FWS	fNIRS	↑ step time and step time variability in older adults from ST to DT No significant changes in the PD group	↑ HbO2 level in PFC and Ml from ST to DT in both SSWS and FWS for both older adults and PD group

Age = Mean (SD or Q1–Q3).

Abbreviations: DT = dual task, EEG = electroencephalography, ERD = event-related desynchronization, ERP = event-related potential, ERS = event-related synchronization, fNIRS = functional near infrared spectroscopy, FoG = freezing of gait, HbO2 = oxygenated hemoglobin, HbR = deoxygenated hemoglobin, PD = Parkinson's disease, PFC = prefrontal cortex, ST = single task.

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Table 2

Result of methodological quality checklist.

Authors (year)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14
Holtzer et al. (2011)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Doi et al. (2013)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Beurskens et al. (2014)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Malcolm et al. (2015)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Fraser et al. (2016)	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Holtzer et al. (2016)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Maidan et al. (2016a)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Ozdemir et al. (2016)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Tard et al. (2016)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Rosso et al. (2017)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Verghese et al. (2017)	Y	Y	Y	Y	N	NA	Y	Y	Y	N	Y	NA	Y	Y
Maidan et al. (2019)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Marusic et al. (2019)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Stuart et al. (2019)	Y	Y	NA	Y	Y	NA	NA	Y	Y	N	Y	NR	NA	N
Al-Yahya et al. (2018)	Y	Y	NA	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N

Q1: Was the research question or objective in this paper clearly stated?

Q2: Was the study population clearly specified and defined?

Q3: Was the participation rate of eligible persons at least 50%?

Q4: Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?

Q5: Was a sample size justification, power description, or variance and effect estimates provided?

Q6: For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?

Q7: Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?

Q8: For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?

Q9: Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

Q10: Was the exposure(s) assessed more than once over time?

Q11: Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

Q12: Were the outcome assessors blinded to the exposure status of participants?

Q13: Was loss to follow-up after baseline 20% or less?

Q14: Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

Y: Yes; N: No; NA: Not Applicable; NR: Not Reported.