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REVIEW ARTICLE

Loss of gait control assessed by cognitive-motor dual-tasks: pros and cons in detecting people at risk of developing Alzheimer's and Parkinson's diseases

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Abstract Alzheimer's and Parkinson's diseases are age-related progressive neurodegenerative diseases of increasing prevalence worldwide. In the absence of curative therapy, current research is interested in prevention, by identifying subtle signs of early-stage neurodegeneration. Today, the field of behavioral neuroscience has emerged as one of the most promising areas of research on this topic. Recently, it has been shown that the exacerbation of gait disorders under dual-task conditions (i.e., simultaneous performance of cognitive and motor tasks) could be a characteristic feature of Alzheimer's and Parkinson's diseases. The cognitive-motor dual-task paradigm during walking allows to assess whether (i) executive attention is abnormally impaired in prodromal Alzheimer's disease or (ii) compensation strategies are used in order to preserve gait function when the basal ganglia system is altered in prodromal Parkinson's disease. This review aims at (i) identifying patterns of dual-task-related gait changes that are specific to Alzheimer's and Parkinson's diseases, respectively, (ii) demonstrating that these changes could potentially be used as prediagnostic markers for disease onset, (iii) reviewing pros and cons of existing dual-task studies, and (iv) proposing future directions for clinical research.

Keywords Dual-task · Gait control · Attention · Executive function · Alzheimer's disease · Parkinson's disease · Prediagnostic phase · Prodromal phase · Clinical phase

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Introduction

Alzheimer's disease (AD) and Parkinson's disease (PD) are a major public health concern as the world's population ages. Unfortunately, AD and PD are up-to-date diagnosed in the advanced stage. In the absence of curative therapy, current research is interested in prevention by identifying subtle signs of early-stage neurodegeneration. Crucially, early diagnosis would provide a critical opportunity for disease-modulating interventions targeting modifiable risk factors for AD or PD (Barnes and Yaffe 2011), or even neuroprotective therapies, which both would help delay, slow, or even prevent disease progression (i.e., more cases would remain in the mild stage rather than degrade to moderate or severe stages; Petersen 2009).

These risk factors are modifiable by making lifestyle changes (e.g., greater participation in physically and intellectually stimulating activities, social engagement, balanced diet with a high proportion of unsaturated fatty acids) and treating long-term health conditions (e.g., excessively high or low blood pressure, insufficient and/or fragmented sleep, diabetes, and midlife obesity).

From these clinical perspectives, increasing evidence supports the idea that the neuropathological process underlying AD and PD begin long before the onset of clinical symptoms as currently defined. This prodromal phase has opened new lines of research to identify the earliest markers that confirm the beginning of the disease. Behavioral neuroscience has emerged as one of the most promising areas of research on this topic. Recently, it has been shown that gait control is already affected in the prodromal phases of AD and PD (Postuma et al. 2012; Montero-Odasso et al. 2014), and thus may have the potential to serve as a new prodromal marker of these diseases. Prodromal markers represent "signatures" of an ongoing pathological process before the presence of typical symptoms allowing the clinical diagnosis (Heinzel et al. 2016). The loss of gait control is commonly evaluated by dual-task walking paradigms, during which the subject performs a cognitive (attention-demanding) task while walking, to assess any modifications compared to the reference (i.e., single-task condition), in either the cognitive or the walking subtasks ("dual-task cost"; Woollacott and Shumway-Cook 2002; McIsaac et al. 2015). At the onset of mild cognitive impairment (MCI, which may in some cases represent the prodromal phase of AD), this method has been widely used to assess whether or not executive attention functions (i.e., refers to higher cognitive processes used to allocate attention among different tasks performed simultaneously) are abnormally impaired. Such cognitive dysfunctions (i.e., predominantly inhibitory control) are considered today as a predictor of AD (Balota et al. 2010; Harrington et al. 2013; Seo et al. 2016). In the prodromal phase of PD, the dual-task paradigm is used to exhaust compensation strategies aimed at preserving the motor function when the basal ganglia system is altered (Chen et al. 2013; Lerche et al. 2014). Collectively, previous evidence that dual-task conditions significantly affect patients in the prodromal phases of AD and PD with respect to healthy controls might offer a rationale for the use of this paradigm as a screening tool for the risk of developing AD and PD. This background leads to the heart of this review. Thus, our purposes were fourfold (i) to identify patterns of dual-task-related gait changes that are specific to AD and PD, respectively, (ii) to demonstrate that these changes could potentially be used as prodromal markers for clinical disease onset, (iii) to review pros and cons of existing dual-task studies, and (iv) to propose future directions for clinical research.

Changes in gait control under single-task condition in Alzheimer's disease

Clinical phase of Alzheimer's disease

AD, the primary cause of irreversible dementia among elderly people, is a progressive neurodegenerative disease characterized by the presence of amyloid beta plaques and neurofibrillary tangles (Ballard et al. 2011; Ittner and Götz 2011) together with synaptic reduction, neuronal death, and atrophy (Braak and Braak 1991; Terry et al. 1991). In addition to these classical neuropathological markers, some studies have shown a disease burden in the motor cortex equivalent to the entorhinal cortex, hippocampus, and the association areas of the frontal and parietal lobes (Suvà et al. 1999). Behaviorally, patients with early AD have mainly severe episodic and working memories impairments, deficits in language, and semantic knowledge. Also, they fail tasks requiring relatively complex brain communication, such as under dual-task conditions; these tasks depending substantially on executive attention control (Nordahl et al. 2006; Mayda et al. 2011). Interestingly, cognitive impairment in AD, specifically executive attention control deficits, and the hyperexcitability of the motor cortex affect gait (van Iersel et al. 2004; Sheridan and Hausdorff 2007; Beauchet et al. 2008; Coelho et al. 2012). Overall, AD patients present a lower gait speed (Verghese et al. 2007; Rucco et al. 2017), shorter stride length (Coelho et al. 2012; Rucco et al. 2017) and cadence (Sheridan and Hausdorff 2007), and greater stride time variability (Beauchet et al. 2008, 2014). Stride length variability has rarely been studied but appear to be increased compared to healthy older adults (van Iersel et al. 2004; Coelho et al. 2012). According to Beauchet et al. (2008), stride time variability is a fine marker of gait control, thus, highlighting that gait in AD should not be considered as a simple automatic motor behavior, but one requiring "high-level cognitive

functions," particularly executive attention control (Allali et al. 2007).

Prodromal phase of Alzheimer's disease

Converging evidence suggests that executive attention control, predominantly inhibitory control, changes before episodic memory impairment, which is the clinical hallmark of early AD (Harrington et al. 2013). Importantly, such changes could predict AD (Balota et al. 2010). Neuropathological findings suggest that extracellular amyloid could appear first in the basal isocortex including the entorhinal cortex and only later in the hippocampus (Harrington et al. 2013). As mentioned earlier, deficits in executive attention control may be responsible for gait disorders. Interestingly, this association also exists in the prodromal phase of AD and may predict older adults at risk of developing dementia. In fact, longitudinal studies that examined baseline gait disorders and the risk of dementia have shown that gait slowing appears 12 years before the onset of MCI and precedes a decline in cognitive function (Buracchio et al. 2010; Mielke et al. 2013). The Oregon Brain Aging study supports this view and found that a longer time to complete a 30-ft (15-m) walk at baseline was an independent predictor of cognitive impairment over a 6-year period of follow-up (Marquis et al. 2002). In addition to these findings, the 5-year longitudinal study conducted by Verghese et al. (2007) showed that changes in both rhythm (i.e., cadence, swing time, stance time, and double support time) and variability (i.e., stride length variability and swing time variability) domains of gait predicted decline in both executive attention control and episodic memory. The latter two were in turn shown to be associated with an increased risk for cognitive decline and dementia (Marquis et al. 2002; Verghese et al. 2007). Recently, during a median follow-up of 2.7 years, Taniguchi et al. (2012) found that shorter stride length was an independent predictor of cognitive decline in a general population of older adults and could be a better predictor than gait slowing.

Collectively, the abovementioned findings are consistent with the view that the loss of cognitive and motor functions observed in the prodromal phase of AD may share common underlying neuropathological mechanisms, namely, an executive attention control deficit. According to Buchman and Bennett (2011), the fact that several non-cognitive symptoms, such as gait disorders, predict the subsequent development of AD, suggests that non-cognitive behaviors may serve as phenotypic markers of prodromal AD. Likewise, Beauchet et al. (2014) suggested that there might be a motor phenotype of cognitive performance decline, which could be used to improve the prediction of dementia, particularly in AD. Currently, such a view is mainly explored using dual-task-walking paradigms. This approach is very advantageous compared to others, because it reveals subtle age- and disease-related abnormalities in gait control, which are masked by internal factors such as compensation mechanisms underlying cognitive reserve, and thus difficult to detect using either conventional neuropsychological tests or single-task walking assessment (Muir et al. 2012; Perrochon and Kemoun 2014; Perrochon et al. 2013, 2015).

Changes in gait control under single-task condition in Parkinson's disease

Clinical phase of Parkinson's disease

PD is a chronic neurodegenerative disease caused by progressive and profound loss of nigrostriatal dopaminergic neurons projecting to the striatum and the presence of Lewy bodies in the central, peripheral, and autonomic nervous systems (Jellinger 2012). Clinically, PD is characterized by the emergence of at least two cardinal motor features, including bradykinesia (i.e., slowness of movement) and either rigidity, tremor, gait disorders, or postural instability (Tolosa et al. 2006; Massano and Bhatia 2012). Overall, gait disorders appear in early in PD. They are characterized by (i) decreases in gait speed, stride length, and arm swing amplitude (Lewek et al. 2010; Volpe et al. 2017) and (ii) increases in cadence, double support time, arm swing amplitude, swing time asymmetry (Yogev et al. 2007), and variability in stride time and swing time (Baltadjieva et al. 2006; Mirek et al. 2007; Svehlík et al. 2009; Lewek et al. 2010; Volpe et al. 2017). From a behavioral point of view, the gait showing results from the inability of PD patients to generate sufficient stride length and arm swing amplitude (i.e., gait hypokinesia) even though cadence control remains intact (Morris et al. 1994; Hausdorff 2009), whereas the increased variability in temporal parameters from an alteration of the internal cueing mechanism needed to walk in a rhythmic fashion (Sheridan and Flowers 1990; Morris et al. 1994; Ebersbach et al. 1999; Schaafsma

et al. 2003). From a neuropathological point of view, the causes of these gait disorders may result from (i) dopaminergic striatal deficit (Wu et al. 2015), (ii) excessive inhibition of the mesopontine locomotion center by the basal ganglia (Sterling et al. 2015), and (iii) cortical cholinergic denervation (Bohnen et al. 2013; Müller et al. 2015).

Prodromal phase of Parkinson's disease

Positron emission tomography data revealed that clinical symptoms of Parkinsonism could develop after 70–80% of striatal dopamine is depleted, corresponding to 30–50% cell death of dopaminergic neurons (Fearnley and Lees 1991; Stoessl 2007; Postuma et al. 2012). The duration of this phase prior to diagnosis of PD is still in debate (Gaenslen et al. 2011) and has been estimated to last many years, with an average of 5 years (Morrish et al. 1998; Postuma et al. 2012), or even decades (Marek and Jennings 2009). To date, several motor and non-motor symptoms characterize this prodromal phase. While prodromal non-motor symptoms (e.g., mood disorders and olfaction) are largely explored, motor symptoms, on the other hand, remain poorly studied. However, because PD is currently diagnosed by its motor features, it is reasonable to speculate that subtle changes in the motor function will be present before the appearance of the cardinal motor signs required for diagnosis (Mirelman et al. 2016). In line with this view, Postuma et al. (2012) suggested that the stage when idiopathic rapid eye movement (REM) sleep behavior disorder (i.e., characterized by vivid, often-fearful dreams, and loss of normal muscle atonia during rapid eye movement sleep) (Olson et al. 2000) is diagnosed may provide a window to better understand prodromal motor symptoms. Accordingly, motor skills of 78 patients with idiopathic REM sleep behavior disorder, as assessed by the Unified Parkinson Disease Rating Scale, the Purdue Pegboard Test, the Alternate Tap Test, and the Timed Up and Go Test, became abnormal ~4.5 years before the diagnosis of PD (Postuma et al. 2012). Specifically, voice and face akinesia seem to be the first signs to appear (estimated prodromal interval: 9.8 years), followed by rigidity (4.4 years), gait abnormalities (4.4 years), and limb bradykinesia (4.2 years). As regards gait changes, these findings suggest that patients with early PD should present subtle gait disorders (Panyakaew and Bhidayasiri 2013; Mirelman et al. 2016). Yet, they are not detectable under undisturbed walking conditions (i.e., self-selected comfortable speed under single-task condition) in the prodromal phase. This is perhaps due to satisfactory motor system mechanisms compensating the slowly progressive nigrostriatal dopamine depletion within and outside the basal ganglia (Buhmann et al. 2005; Maetzler and Hausdorff 2012; Bezard and Fernagut 2014). Unfortunately, the exact compensatory mechanisms underlying gait disorders in the prodromal phase of PD remain unclear. Previous studies examining manual motor performance proposed the following mechanisms: (i) an increased activity in lateral premotor and parietal areas as well as in the anterior cingulate cortex to counterbalance defective striatofrontal motor circuits (Samuel et al. 1997; Sabatini et al. 2000; Buhmann et al. 2005), (ii) an increase in corticostriatal excitatory input to the basal ganglia (Wu et al. 2015), and (iii) the use of extrastriatal areas, such as executive attention control and more "'voluntary" brain activity efforts to execute movements usually performed automatically in healthy people (Wu et al. 2015).

Although the above studies did not examine gait, the findings are consistent with the possibility of changes in the neural networks underlying control of gross motor skills such as gait, and perhaps also in the recruitment of compensatory processes (or cognitive strategy use), which might themselves depend on the individual's cognitive reserve (Stern 2009). The challenge remains about how to capture these gait disorders despite compensatory capabilities? An intriguing possibility, which has recently been envisioned by very few studies (Lerche et al. 2014; Mirelman et al. 2011, 2016), is that dual-task walking may serve as a new, sensitive prodromal marker of PD.

Changes in gait control under dual-task condition in Alzheimer's disease

Clinical phase of Alzheimer's disease

In the clinical phase of AD, all studies showed that dual-task-related gait changes are larger in AD patients than in healthy controls. Such disorders include decreases in gait speed (Camicioli et al. 1997; Sheridan et al. 2003; Cocchini et al. 2004; Pettersson et al. 2007; Maquet et al. 2010; Coelho et al. 2012; Muir et al. 2012; Rucco et al. 2017), cadence (Coelho et al. 2012; Rucco et al. 2017), stride length, and increases in stride

width (Rucco et al. 2017), double support time (Muir et al. 2012; Rucco et al. 2017), swing time, stance time (Rucco et al. 2017), stride time (Muir et al. 2012), stride length asymmetry (Maquet et al. 2010), stride length variability (Rucco et al. 2017), stride time variability (Sheridan et al. 2003; Muir et al. 2012), stance time variability, swing time variability, and stride width variability (Rucco et al. 2017). In most studies, the authors analyzed dual-task-related changes in gait but not in cognitive performance. The few studies that also did the latter showed a decline in the two domains (Cocchini et al. 2004; Coelho et al. 2012; Ijmker and Lamoth 2012). From a neuropathological point of view, dual-task-related gait changes in AD could reflect metabolic changes in cells of the associative cortices and hippocampal complex (Rolls and Grabenhorst 2008). The study of Marshall et al. (2007) suggests that the reduction in glucose consumption and perfusion in the cingulate gyrus and orbitofrontal cortex may also explain the difficulty of patients with AD to perform dual-task walking.

Prodromal phase of Alzheimer's disease

In the prodromal phase of AD, dual-task-related gait changes are larger in MCI patients than in healthy controls, and greater dual-task complexity further worsens gait performance. The gait disorders reported in MCI patients include (i) decreases in gait speed (Pettersson et al. 2007; Maquet et al. 2010; Montero-Odasso et al. 2009a; Montero-Odasso et al. 2012; Muir et al. 2012; Doi et al. 2014; Tseng et al. 2014; Tarnanas et al. 2015) and stride length (Montero-Odasso et al. 2009b; Maquet et al. 2010) and (ii) increases in stride time (Muir et al. 2012), swing time (Boripuntakul et al. 2014), stride length variability (Boripuntakul et al. 2014), double support time variability (Montero-Odasso et al. 2009b), and stride time variability (Camicioli et al. 2006; Allali et al. 2007; Montero-Odasso et al. 2009b; Muir et al. 2012; Ijmker and Lamoth 2012; Montero-Odasso et al. 2014). From a neuropathological point of view, dual-task-related gait changes were interpreted as resulting from impairments in working memory and executive attention control (Maquet et al. 2010), both altering the ability of patients to execute more than one task at a time. Another interpretation proposed by Montero-Odasso et al. (2009a) is the limitation of attentional resources (the "central capacity-sharing model of dual-task performance"; Tombu and Jolicoeur 2003), which could account for dual-task interference in gait among people with MCI. Hence, it is likely that both explanations of dual-task interference during gait are relevant.

In contradiction with the above results, two studies (Pettersson et al. 2005; Nascimbeni et al. 2015) have reported no dual-task walking effect. This counterintuitive finding is likely due to either the gait assessment method (i.e., use of clinical performance-based measures, such as Timed Up and Go Test, Tinetti Gait Test, instead of instrumental gait analysis), the choice of the secondary cognitive task (i.e., type and complexity), the selection criteria for the control group (e.g., in Pettersson et al. 2005: people complaining of subjective cognitive impairment), the large heterogeneity of the MCI group, and/or the low sample size. Furthermore, it is reasonable to assume that part of these MCI patients will not evolve to dementia, but rather remain cognitively stable or even revert to normal during follow-up. It is hypothesized that dual-task walking could have the potential to improve the power of discrimination between MCI converters and non-converters. In a longitudinal study, comparing MCI patients who developed AD to those who remained stable, Gillain et al. (2016) provided first evidence supporting this view. Specifically, the authors showed that MCI converters deteriorated their gait speed and gait variability under dual-task conditions more than non-converters. Other longitudinal studies recruiting both healthy older adults and MCI patients are needed to confirm these findings. Besides, such studies are important to determine the threshold of change under dual-task walking that would differentiate healthy compensation mechanisms from pathological ones.

Table 1 summarizes the findings of dual-task-related gait changes in AD and MCI patients.

Changes in gait control under dual-task condition in Parkinson's disease

Clinical phase of Parkinson's disease

In the clinical phase of PD, dual-task-related gait changes are larger in PD patients than in healthy controls. Such disorders include (i) decreases in gait speed (Fuller et al. 2013; Wild et al. 2013; Stegemöller et al. 2014; Strouwen et al. 2016), stride length (O'Shea et al. 2002; Rochester et al. 2004; Plotnik et al. 2011; Tseng et al.

Table 1 Summary of dual-task testing protocols in the prodromal and clinical phases of Alzheimer's disease

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
Camicioli et al. 1997	EAD (n = 15) HOA (n = 43)	Verbal fluency task	Walking 30 ft at usual pace	Not indicated	Not measured	Time to walk 30 ft Cadence	Repeated measures ANOVA	↓ time to walk 30 ft in EAD compared to HOA
Sheridan et al. 2003	EAD (n = 28)	Forward digit span task	Walking 50 ft at usual pace	Foot switches placed inside the shoe (i.e., at the ankle)	Not measured	Gait speed, Stride time variability	Wilcoxon signed-rank test	↑ stride time variability, ↓ gait speed
Cocchini et al. 2004	EAD (n = 15) HOA (n = 15)	Verbal fluency task Digit span task	Walking 11 m at usual pace	Not indicated	Number of words verbally enumerated Percentage of digits correctly recalled	The distance covered by each participant in 30 s	Not indicated	- When task difficulty was not titrated, EAD walked a shorter distance than HOA - When task difficulty was titrated, group difference disappeared - Decreased cognitive performance in EAD compared to HOA
Pettersson et al. 2005	NCI (n = 33) MCI (n = 59) EAD (n = 22) HOA (n = 26)	Verbal fluency task	Walking 10 m at usual pace	Not indicated	Not measured	Time to walk 10 m	Two-way factorial ANCOVA	↓ time to walk 10 m in EAD compared to HOA
Camicioli et al. 2006	EAD (n = 42)	Forward digit span task	Walking 15 m at usual and fast paces	GAITRite® system	Not measured	Gait speed Cadence Stride time Stride length Swing time Double support time	Repeated measures ANOVA	↑ stride time, ↑ swing time, ↑ swing time variability, ↓ cadence
Pettersson et al. 2007	AD (n = 6) MCI (n = 6) HOA (n = 25)	Verbal fluency task	Walking 10 m at usual pace	Stopwatch	Not measured	Gait speed	Difference in mean between single- and dual-task walking	↓ gait speed in EAD compared to MCI and HOA
Allali et al. 2007	AD, VaD, mixed AD/VaD	Forward and backward counting	Walking 10 m at usual pace	GAITRite® system	Number of figures	Stride time Stride time variability	Dual-task cost[a] for each parameter	↑ stride time variability

Table 1 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
	(*n* = 16)				verbally enumerated			- No difference in cognitive performance
Montero-Odasso et al. 2009a	MCI (*n* = 55)	Serial substraction task Verbal fluency task	Walking 10 m at usual pace	Stopwatch	Not measured	Gait speed	Difference in time between single and dual-task walking	↓ gait speed
Montero-Odasso et al. 2009b	MCI (*n* = 11)	Serial substraction task (from 100)	Walking 6 m at usual pace	GAITRite® system	Not measured	Gait speed Stride length Stride time Double support time Gait variability for all parameters	Paired *t* test	↓ gait speed, ↑ stride time variability, ↑ stride time, ↑ double support time
Maquet et al. 2010	MCI (*n* = 14) MAD (*n* = 6) HOA (*n* = 14)	Serial substraction task	Walking 45 m at usual pace	Locometrix® Electrical photocells	Not measured	Gait speed Stride frequency Stride length Stride symmetry Number of stops	Difference in mean between single- and dual-task walking	↓ gait speed in MAD and MCI compared to HOA
Ijmker and Lamoth 2012	AD and FTD (*n* = 15) YOA (*n* = 12) HOA (*n* = 14)	Phonemic fluency task (letters: "R," "G," and "P")	Walking for 3 min at a self-selected pace up and down a 10 m long course	Ambulant accelerometer	Number of words verbally enumerated	Gait speed Stride time Stride time variability	Wilcoxon signed-rank test	↑ stride time variability and - Decreased cognitive performance in FTD and AD compared to YOA and HOA
Muir et al. 2012	AD (*n* = 23) MCI (*n* = 29) HOA (*n* = 22)	Verbal fluency task Serial substraction task (by ones and sevens)	Walking 6 m at usual pace	GAITRite® system	Not measured	Gait speed Stride time variability	Dual-task cost[b] for each parameter	↑ stride time, ↑ stride time variability, ↓ gait speed in AD and MCI compared to HOA
	MAD (*n* = 23)			Digital camera		Cadence		↓ cadence,

Table 1 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
Coelho et al. 2012		Serial substraction task (from 20)	Walking 8 m at usual pace	Passive marker to the fifth right metatarsus	Number of errors	Stride length Gait speed	Repeated measures ANOVA	↓ gait speed, ↓ stride length - MAD made more errors
Montero-Odasso et al. 2012	MCI (n = 43) HOA (n = 25)	Serial substraction task (from 100) Semantic fluency task	Walking 6 m at usual pace	GAITRite® system	Not measured	Gait speed Stride time Stride time variability	Repeated measures ANOVA	↑ stride time variability, ↓ gait speed in MCI compared to HOA (all the more with increasing task complexity)
Boripuntakul et al. 2014	MCI (n = 30) HOA (n = 30)	Serial substraction task (by threes from 20 or 50)	Gait initiation (first and second stride) Walking at usual pace	GAITRite® system	Not measured	Swing time Stride time Stride length Stride width Gait variability for all parameters	Repeated measures ANOVA	↑ swing time, ↑ stride length variability for the first and second stride gait initiation in MCI compared to HOA
Tseng et al. 2014	a-MCI (n = 16) HOA (n = 10)	Phonemic fluency task (letter "C") 5-digit backward span task Serial substraction task (by sevens) 3-item delayed recall task	Walking 10 m at usual pace	Not indicated	1 point for each word correctly recited 1 point for each digit in the right order 1 point for each correct subtraction	Gait speed	Repeated measures ANOVA	↓ gait speed in a-MCI compared to HOA - Decreased cognitive performance in a-MCI compared to HOA
Montero-Odasso et al., 2014	a-MCI (n = 42) na-MCI (n = 22) HOA (n = 35)	- Serial substraction task (by ones from 100) - Verbal fluency task	- Walking at usual pace	- GAITRite® system	- Not measured	- Stride time variability - Gait speed	- Dual-task cost[2] for each parameter	↑ stride time variability, ↓ gait speed in a-MCI compared to HOA and na-MCI
Doi et al. 2014	a-MCI (n = 191)	Serial substraction	Walking 11 m at usual pace	Horizontal walkway	Not measured	Gait speed	Repeated measures ANOVA	↓ gait speed in both a-MCI and na-MCI compared to HOA

Table 1 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
	na-MCI (n = 198) HOA (n = 35)	task (from 100)						
Nascimbeni et al. 2015	MCI (n = 13) HOA (n = 10)	Serial substraction task (by ones from 378 or 283) Verbal fluency task Short story recall task	Walking at usual pace back and forth over a distance of 12 m	Footswitches based on force sensitive resistors placed on the first and fifth metatarsal heads and the posterior part of heel Stopwatch	Number of correctly produced digits Number of correctly produced items Number of correctly recalled items	Stride time Stride time variability Double support time Gait speed	Repeated measures ANOVA	↓ gait speed, ↑ stride time, ↑ stride time variability, ↑ double support time in both groups - Performance decreased on serial substraction and improved on short story recall in both groups
Tarnanas et al. 2015	EAD (n = 86) Na-MCI (n = 65) HOA (n = 76)	Serial substraction task (by ones from 100) Verbal fluency task	Walking at usual pace over a distance of 10 m	GAITRite® system	Not measured	Gait speed Stride time variability	Difference in mean between single- and dual-task walking	↓ gait speed, ↑ stride time variability in EAD and na-MCI compared to HOA
Gillain et al. 2016	MCI (n = 13)	Serial substraction task (from 50)	Walking at usual pace	Locometrix®	Not measured	Gait speed Stride time variability Stride length Cadence	Difference in mean between single- and dual-task walking	↓ gait speed, ↑ stride time variability in MCI who developed AD
Rucco et al. 2017	AD (n = 22) FTD (n = 23) HOA (n = 20)	Serial substraction task (by sevens from 100)	Walking at usual pace over a distance of 10 m	Stereo-photogram-metric system	Not measured	Gait speed Cadence Stride length Stride time Stride width Stance time Swing time Double support time	Difference in mean between single- and dual-task walking	↓ gait speed, ↓ cadence, ↑ double support time, ↑ stance time variability, ↑ swing time variability, ↑ stride length variability, ↑ stride width variability in AD and FTD compared to HOA

Table 1 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
						Gait variability for all parameters		

NCI subjects with no cognitive impairment, *EAD* early Alzheimer's disease, *AD* Alzheimer's disease, *MAD* mild Alzheimer's disease, *FTD* frontal temporal dementia, *MCI* mild cognitive impairment, *a-MCI* amnesic mild cognitive impairment, *na-MCI* non-amnesic mild cognitive impairment, *HOA* healthy older adults, *YOA* younger older adults, *VaD* vascular dementia, ↑ increased, ↓ decreased

[a] Gait DTC = [(dual-task gait performance − single-task gait performance)/(dual-task gait performance + single-task gait performance)/2] × 100

[b] DTC = [(single-task value − dual-task value)/single-task value] × 100

2012; Panyakaew and Bhidayasiri 2013; Kelly and Shumway-Cook 2014; Stegemöller et al. 2014), bilateral gait coordination (i.e., the generation of left-right antiphase stepping), and swing time (Plotnik et al. 2009; 2011; Tseng et al. 2012; Vervoort et al. 2016) and (ii) increases in stride time (Panyakaew and Bhidayasiri 2013; Stegemöller et al. 2014), cadence (Rochester et al. 2014), stance time (Wild et al. 2013), stride width (Stegemöller et al. 2014), stride length asymmetry (Rochester et al. 2014; Vervoort et al. 2016), swing time variability (Stegemöller et al. 2014), stride time variability, and stride length variability (Hausdorff et al. 2003; Yogev et al. 2007; Plotnik et al. 2009, 2011; Yogev-Seligmann et al. 2012; Rochester et al. 2014; Stegemöller et al. 2014). Decreases in arm swing amplitude and increases in both arm swing asymmetry and arm swing variability have also been documented (Mirelman et al. 2016). The few studies that have examined dual-task-related changes in both gait and cognitive performance showed a decline in the two domains (O'Shea et al. 2002; Yogev et al. 2005).

In contradiction with these findings, two studies (Kelly and Shumway-Cook 2014; Rochester et al. 2014) found that certain aspects of gait, namely gait speed, stride length, stride length variability, and stride time variability, were unexpectedly unaffected under dual-task conditions. This may be due to the use of an auditory Stroop task (Kelly and Shumway-Cook 2014) and an auditory Wechsler Forward Digit Span task (Rochester et al. 2014) as secondary tasks. Indeed, the auditory modality may provide beneficial cueing effects on gait rhythm through compensatory cerebellar-parieto-premotor pathways or by facilitating task prioritization and/or executive attention control (Rochester et al. 2008). Overall, PD patients were less able than healthy controls to use a "posture first" strategy (i.e., prioritizing walking over other concurrent tasks). In fact, some patients may give inappropriate prioritization to the concurrent attention-demanding task, thus, sacrificing attention resources needed for gait by using a "posture second" strategy (Bloem et al. 2006). Evidence for this strategy use was observed in several studies in which explicit instructions regarding task prioritization were not given (Yogev-Seligmann et al. 2010). Hence, one could posit that the auditory cueing provided by the cognitive task improve walking automaticity, and thus reduce the attentional demands of gait control.

From a neuropathological point of view, theoretical mechanisms that could explain dual-task-related gait changes in clinical PD are (i) a reduced movement

automaticity (i.e., the ability to perform a skilled movement without conscious or executive control or attention directed toward the movement) and the need for increased reliance on cognitive resources to control gait because of basal ganglia dysfunction (Wu et al. 2004; Poldrack et al. 2005), (ii) dopamine-mediated dysfunction of the basal ganglia (Middleton and Strick 2000), and (iii) presence of non-dopaminergic pathology, such as serotonin, norepinephrine (noradrenaline), or acetylcholine (Leverenz et al. 2009). Recently, Nieuwhof et al. (2016) suggest that altered functioning of the prefrontal cortex may also contribute to difficulties in dual-task walking. These mechanisms are not mutually exclusive but might overlap with one another.

Prodromal phase of Parkinson's disease

There exist three studies that have examined dual-task-related gait changes in the prodromal phase of PD (Lerche et al. 2014; Mirelman et al. 2011, 2016). All of them have reported dual-task interference during gait. Specifically, two cross-sectional studies conducted by Mirelman et al. (2011, 2016) have shown decreases in arm swing amplitude and axial rotation smoothens and increases in arm swing variability, arm swing asymmetry (Mirelman et al. 2016), and stride time variability (Mirelman et al. 2011) in LRRK2 G2019S mutation carriers without a clinical diagnosis of PD. The third study by Lerche et al. (2014) has demonstrated dual-task decrement in gait speed in patients with mild parkinsonian signs to the same extent as non-demented patients with PD. From a neuropathological point of view, the authors suggested that impairment of movement automaticity because of early basal ganglia dysfunction and cognitive inflexibility might explain these changes in gait under dual-task conditions.

Table 2 summarizes the findings of dual-task-related gait changes in patients with PD, mild parkinsonian signs, and LRRK2-G2019S mutation carriers without a clinical diagnosis of PD.

Summary of methodological issues of dual-task studies

Currently, a comparison between dual-task studies in the clinical and prodromal phases of both AD and PD is made difficult because of the variety of all aspects of the protocols. Cognitive tasks used include the following: auditory Stroop task; serial subtraction by ones, threes, and sevens from a given number (e.g., 100 and 283); working memory task (i.e., listening to strings of digits while walking and repeating them back and letter 2-back task); short story recall memory task; 3-item delayed recall episodic memory task; and semantic fluency (i.e., naming animals and reciting male or female names) or phonemic fluency (i.e., letters F, A, S, R, G, P, and C) tasks. Gait tasks used include walking at a comfortable, self-selected pace or at a maximum pace over varying distances (6, 8, 9, 10, 11, 15, 12, 25, and 45 m), walking backward, or walking 3 min). Instruments that have been used to assess both gait parameters (gait speed, stride time, stride length, stride height, stride width, double support time, stride frequency, symmetry, regularity, and gait variability) and cognitive performance (number of correct responses, reaction time, error rate, and accuracy) include treadmill, GAITRite®, stopwatch, Locometrix®, and motion capture system. Other sources of variability are the choice of the clinical population (MCI subtypes, different stages of AD: from moderate to severe), sample size, medication, and statistical approach (i.e., repeated ANOVA, paired Student *t* test, specific dual-task cost formulas). Tables 1 and 2 summarize the different dual-task testing protocols and findings in both the clinical and prodromal phases of AD and PD.

Discussion

To our knowledge, this is the first review that provides a comprehensive overview of dual-task-related gait changes that are specific to AD and PD (Table 3).

Dual-task-related gait changes in AD at the clinical stage The pace (i.e., gait speed, stride length, stride time variability, swing time variability, stance time variability, and double support time), rhythm (i.e., stride time, stance time, swing time, and cadence), variability (stride length variability and stride width variability), and postural control (i.e., stride width and stride length asymmetry) domains of gait showed to be consistently sensitive to dual-task interference in AD. Unfortunately, the exact neuropathological mechanisms underlying changes in each domain of gait are still unknown. Yet, based on neuropsychological studies, changes in the pace domain could be related to impairments in either executive attention control (Sheridan et al. 2003; Maquet et al.

Table 2 Summary of dual-task testing protocols in the prodromal and clinical phases of Parkinson's disease

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
O'Shea et al. 2002	PD (n = 15) HOA (n = 15)	Coin transference Serial substraction task (by threes from 125 or 250)	Walking 10 m at usual pace	Footswitches based on force sensitive resistors placed on the hallux and the first, second, and fourth metatarsal heads	Not measured	Gait speed Stride length Cadence Double support time	Paired t test	↑ double support time, ↓ stride length, ↓ gait speed, ↓ cadence in PD (with either a motor or cognitive secondary task)
Hausdorff et al. 2003	PD (n = 10)	Serial substraction task (by threes from 200, 193, and 186)	Walking 20 m at usual pace	Footswitches based on force sensitive resistors	Not measured	Stride time Stride time variability	Wilcoxon signed-rank test	↑ stride time variability
Yogev et al. 2005	PD (n = 30) HOA (n = 28)	Serial substraction task (by sevens from 500) Listening through ear phones to a text	Walking 20 m at usual pace	Footswitches based on force sensitive resistors	Not measured	Stride time Swing time Stride time variability	Repeated measures ANOVA	↑ stride time variability in PD compared to HOA
Plotnik et al. 2009	PD (n = 21) HOA (n = 13)	Serial substraction task (by sevens)	Walking at usual pace for 2 min	Footswitches based on force sensitive resistors	Not measured	Gait speed Stride time variability Swing time variability Stride time asymmetry Left-right stepping coordination	Repeated measures ANOVA	↓ left-right stepping coordination, ↑ swing time variability, ↑ stride time variability in PD compared to HOA
Plotnik et al. 2011	PD (n = 30)	Serial substraction task (by threes and sevens)	Walking 80 m at usual pace	Footswitches based on force sensitive resistors	Not measured	Gait speed Stride length Stride time variability Swing time variability Swing time asymmetry Left-right stepping	Paired t test	↓ left-right stepping coordination, ↓ stride length, ↓ gait speed, ↑ swing time asymmetry, ↑ swing time variability - Gait changes are more pronounced with concomitant serial subtraction task by sevens

Table 2 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
						coordination		
Mirelman et al. 2011	LRRK2 ($n = 25$) HOA ($n = 27$)	Serial substraction task (by sevens)	Walking 20 m at usual and maximal pace	Accelerometer	Not measured	Gait speed Stride time Stride length Stride time variability	Paired *t* test	↑ stride time variability in LRRK2 compared to HOA at both paces
Tseng et al. 2012	PD ($n = 30$) HOA ($n = 28$)	Serial substraction task (from 100)	Walking forward and backward 6 m at usual pace	GAITRite® system	Not measured	Gait speed Stride length - Stride time Double support time Gait variability for each	Paired *t* test	↓ gait speed, ↓ swing time, ↓ stride length, in both walking directions in PD compared to HOA
Yogev-Seligmann et al. 2012	PD ($n = 18$) HOA ($n = 15$)	Verbal fluency task	Walking 30 m at usual pace	Ambulatory recorder Footswitches based on force sensitive resistors	Not measured	Stride time Swing time Stride time variability Gait speed Swing time variability	Repeated measures ANOVA	↓ gait speed, ↑ stride time variability, ↑ swing time variability, in both groups
Fuller et al. 2013	PD ($n = 154$)	Phonemic fluency (letters: "F", "A", and "S")	Walking 15 m at usual pace	Not indicated	Number of words verbally enumerated	Gait speed	Hierarchical regression	↓ gait speed - Decreased cognitive performance
Panyakaew and Bhidayasiri 2013	PD ($n = 21$) HOA ($n = 21$)	Serial substraction task (by threes from 200)	Walking 7.82 m at usual pace	GAITRite® system	Not measured	Gait speed Cadence Stride length Stride time Swing time Double support time Stride width Gait variability for each parameter	Paired *t* test	↑ cadence, ↑ stride width, ↓ swing time, ↑ stride time in PD compared to HOA
	PD ($n = 18$)					Stride length		↑ cadence,

Table 2 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
Wild et al. 2013	HOA (n = 18)	Serial substraction task (by sevens from 500) Text comprehension task Phoneme counting task	Walking 9 m at usual pace	Kinemetric with a fixed camera	Total correct serial subtractions Percent of correct responses (text comprehension) Percent of total phonemes	Cadence Swing time Stance time	Gait DTC formula[a]	↓ swing time, ↓ stance time in PD compared to HOA - Decreased cognitive performance in PD in all conditions compared to HOA
Yogev-Seligmann et al. 2012	PD (n = 18) YA (n = 21) HOA (n = 15)	Verbal fluency task	Walking 30 m at usual pace	Ambulatory recorder Footswitches based on force sensitive resistors Accelerometer located on posterior distal part of the shin above the malleoli	Number of words verbally enumerated	Gait speed Stride time Stride time variability	Repeated measures ANOVA	↓ gait speed, ↑ stride time, ↑ stride time variability in PD compared to YA and HOA
Rochester et al. 2014	PD (n = 44) HOA (n = 55)	Working memory task (participants listened to strings of digits and repeated them back)	alking for 2 min at usual pace	GAITRite® system	Error rate	Gait speed Stride length Stride time Stride width variability Stride time variability Stride width variability Stance time asymmetry	Gait DTC formula[b]	↓ gait speed, ↑ stride length, ↑ stride time, ↑ stride width Variability, ↑ stride time variability, ↑ stride width variability, ↑ stance time asymmetry in both HOA and PD
Kelly and Shumway-Cook 2014	PD (n = 11) HOA (n = 12)	Auditory Stroop task	Usual-base and narrow-base walking over a distance of 8.8 m	Motion capture system (Qualisys)	Response latency Response accuracy	Stride length Stride width Cadence Stride width variability Stride time variability	Repeated measures ANOVA	↓ gait speed in PD compared to HOA - Decreased cognitive performance in PD compared to HOA

Table 2 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
						Center of mass		
Lerche et al. 2014	PD (n = 27) MPS (n = 73) HOA (n = 892)	Box-checking task Serial substraction task (by sevens)	Walking 20 m at usual and maximal paces	Accelerometer	Not measured	Gait speed	Gait DTC formula[c]	↓ gait speed in both conditions
Stegemöller et al. 2014	PD (n = 35)	Serial substraction task (by threes)	Walking 12 m at usual pace	Motion capture system	Not measured	Gait speed Stride time Stride length Stride width Swing time Variability for each parameter	Repeated measures ANOVA	↓ gait speed, ↑ stride length, ↑ stride time, ↑ stride width, ↑ variability for each parameter
Strouwen et al. 2016	PD (n = 121)	Serial substraction task Auditory Stroop task Mobile phone task	Walking 10 m at usual pace	GAITRite® system	Reaction time Number of errors	Gait speed	Regression models	↓ gait speed - A strong correlation between gait speed and cognitive flexibility
Vervoort et al. 2016	PD (n = 73) HOA (n = 20)	Auditory Stroop task	Walking 6 m at usual pace	Motion capture system (Vicon)	Reaction time (average and variability)	Gait speed Stride length Stride width Stride time Stance time Swing time Double support time Gait variability for each gait parameter	MANOVA	↑ stance time, ↑ stride length asymmetry, ↓ swing time in PD compared to HOA - Decreased cognitive performance in PD compared to HOA - A strong correlation between gait speed and cognitive flexibility
Mirelman et al. 2016	PD (n = 194) LRRK2 (n = 122) HOA (n = 64)	Serial substraction task (by threes)	Walking 15 m at usual pace	Lightweight body-fixed sensor Velcro straps		Arm swing amplitude Arm swing variability Arm swing asymmetry	Paired t test	↑ stride time variability, ↑ arm swing variability, ↑ arm swing asymmetry, ↓ axial rotation smoothness in LRRK2 compared to HOA

Table 2 (continued)

Studies	Populations	Cognitive tasks	Gait tasks	Instruments	Cognitive parameters	Gait parameters	Dual-task cost analysis	Dual-task findings
						Stride time variability Axial rotation smoothness		

HOA healthy older adults, *YA* younger adults, *PD* Parkinson's disease, *LRRK2* carriers of the LRRK2-G2019S mutation, *MPS* mild Parkinsonian signs in older adults, *IRBD* patients with REM idiopathic behavioral disorder, ↑ increased, ↓ decreased

[a] Gait DTC = [(single-task gait performance − dual-task gait performance)/single-task gait performance × 100

[b] Gait DTC = dual-task gait performance − single-task gait performance

[c] Gait DTC = (1 − dual-task speed/single-task speed) × 100

2010; Coelho et al. 2012) or global cognitive functions (Coelho et al. 2012). Based on the study of Nakamura et al. (1996), decreased regional cerebral blood flow in the frontal lobe may also contribute to changes in the pace domain (particularly, stride time variability). Other studies suggested that atrophy in the hippocampus and entorhinal cortex, which are two key regions responsible for the sequential ordering of movement (Smith and Milner 1981) may explain changes in both the variability and rhythm domains of gait under dual-task conditions (Morris et al. 2016). From a clinical point of view, dual-task paradigms have been used to distinguish fallers from non-fallers among AD patients. For example, Reelick et al. (2011) showed that only stride length variability discriminate significantly between the faller groups in the dual-task, and not the single-task, condition. Furthermore, if clinicians are seeking further information on attention and executive functions of their patients, dual-task gait paradigms might be of value to explore the attentional requirement of balance during locomotion (Amboni et al. 2013; Menant et al. 2014).

Dual-task-related gait changes in PD at the clinical stage The rhythm (i.e., cadence, stride time, and stance time), asymmetry (i.e., stride time asymmetry), postural control (i.e., stride width and stride length asymmetry), pace (i.e., gait speed, stride length, stride time variability, swing time variability, and double support time variability), and variability (i.e., stride length variability and stride width variability) domains of gait, but also arm swing parameters (i.e., arm swing amplitude, arm swing variability, and arm swing asymmetry) showed to be consistently sensitive to dual-task interference in PD. Biomechanically, gait slowing is mainly due to reduced stride length. The reason for reduced stride length has not yet been fully elucidated, although it has been suggested that gait hypokinesia could reflect a difficulty in activating the locomotor control system (i.e., inadequate contribution to cortical motor set by the basal ganglia (Hausdorff 2009). PD patients typically increased their cadence to compensate for reduced stride length (Morris et al. 1994). Concerning the other pace parameters, some studies showed that increases in stride time variability and swing time variability are likely due to the inability to generate "internal cues" in the supplementary motor areas, a necessary step in the creation of a normal sequenced movement (Yogev et al. 2005) According to Blin et al. (1990), deficits in muscle strength, of which the exact neuropathological

Table 3 Dual-task-related gait changes in the prodromal and clinical phases of Alzheimer's and Parkinson's diseases, including six domains of spatiotemporal gait parameters inspired from Hollman et al. 2011 and Lord et al. 2013 (pace, rhythm, phases, asymmetry, variability, and postural control), and arm swing parameters inspired from Mirelman et al. 2016 (amplitude, variability, and asymmetry)

Gait domains	Clinical phase		Prodromal phase	
	AD	PD	AD	PD
Pace	↓ gait speed ↓ stride length ↑ stride time variability ↑ swing time variability ↑ stance time variability	↓ gait speed ↓ stride length ↑ stride time variability ↑ swing time variability	↓ gait speed ↓ stride length ↑ stride time variability ↑ double support time variability	↓ gait speed ↑ stride time variability
Rhythm	↓ cadence ↑ swing time ↑ stance time ↑ stride time	↑ cadence ↓ swing time ↑ stance time ↑ stride time	↑ swing time ↑ stride time	–
Phases	↑ double support time	↑ double support time	↑ double support time	–
Asymmetry	–	↑ stride time asymmetry	–	–
Variability	↑ stride length variability ↑ stride width variability	↑ stride length variability ↑ stride width variability	↑ stride length variability	
Postural control	↑ stride width ↑ stride length asymmetry	↑ stride width ↑ stride length asymmetry	–	–
Arm swing parameters	–	↓ arm swing amplitude ↑ arm swing asymmetry ↑ arm swing variability	–	↓ arm swing amplitude ↑ arm swing asymmetry ↑ arm swing variability

AD Alzheimer's disease, *PD* Parkinson's disease, ↑ increased, ↓ decreased

mechanisms may come from central activation impairments (Stevens-Lapsley et al. 2012), may also explain changes in the pace domain. Beyond motor explanation, Yogev et al. (2005) suggest that deficits in executive attention control may also contribute to these changes among PD patients.

Decreased arm swing amplitude of the more affected body side is frequently reported in the literature. Such parameter seems to be related to both rigidity (Kwon et al. 2014) and dopamine-mediated dysfunction of the basal ganglia (Wu et al. 2015). Also, it mechanically induces a reduction in both bilateral arm coordination and arm swing symmetry (Lewek et al. 2010; Huang et al. 2012) as well as greater arm swing variability (Mirelman et al. 2016). From a neuropathological point of view, these changes in arm swing parameters appear to be linked to the asymmetric process of nigrostriatal dopaminergic denervation (Lewek et al. 2010; Huang et al. 2012). In an effort to clarify the origin of dual-task-related gait changes in PD, Lord et al. (2010) have suggested that some gait domains are levodopa-sensitive and others are levodopa-resistant. In support of this view, Hausdorff (2009) showed that temporal gait variability is independent of dopaminergic pathways, and that both spatial gait variability and arm swing parameters are dependent of dopaminergic pathways (Lord et al. 2010). Hence, such findings suggest that the latter have potential utility to predict gait dysfunction related to PD (Lord et al. 2010). As for AD, dual-task-related gait changes in the clinical phase of PD is clinically relevant to detect patients at risk of falls. Also, some studies have shown that dual-task walking performance was associated with gait quality (Kelly et al. 2012), freezing (Spildooren et al. 2010), disease severity, and disability (Fuller et al. 2013).

Dual-task-related gait changes: comparison between AD and PD at the clinical stage Even though the neuropathological origin of dual-task-related gait changes is different between the two diseases, the corresponding gait patterns display some similarities, particularly in the pace, rhythm, postural control, and variability domains of gait. Mechanistically, similar dual-task-related gait changes between AD and PD are likely due to a limited attentional capacity (serial bottleneck theory; Pashler 1984, 1994) resulting from more brain damage that prevents patients to share their attentional resources and perform both tasks simultaneously (capacity sharing theory; Tombu and Jolicoeur 2003). In addition, dysfunction in executive attention, anxiety, and depression, which are known to have negative effects on cognition and motor performance, may also be another common factor (Hausdorff et al. 2003; Beurskens and Bock 2012). Despite this commonality, gait parameters between the two patient groups have never been directly compared. Thus, the question arises as to whether the dual-task walking paradigm is sensitive enough to characterize specific spatiotemporal gait profiles of AD and PD, respectively. Such a question has not yet been addressed in the literature. Nonetheless, our review suggests that the rhythm (i.e., cadence), pace (i.e., stride length and stride time variability), and variability (i.e., stride length variability) domains of gait as well as arm swing parameters (i.e., arm swing amplitude, arm swing asymmetry, and arm swing variability) could differentiate these two diseases. Specifically, we suggest that cadence and arm swing parameters would be more altered in PD, whereas stride length, stride time variability, and stride length variability would be more altered in AD (Table 3). Further studies comparing patients with AD, PD, and healthy controls are needed to confirm this proposal.

The second result that clearly emerges from this review is that dual-task-related gait changes could potentially be used as prodromal markers for clinical disease onset.

Added value of the dual-task paradigm in the prediction of AD and PD Both PD and AD share a long prediagnostic phase in which gait control under dual-task conditions is already altered. The dual-task walking paradigm showed benefit either (i) to explore the involvement of cortical level in gait control (Beauchet et al. 2014), thus, allowing to assess whether or not executive attention control is abnormally impaired, as in prodromal AD or (ii) to exhaust compensation strategies aimed at preserving motor function when the basal ganglia system is altered, as in prodromal PD. Taking together, it is understandable that dual-task walking may be a useful tool to reveal deficits unseen during single-task walking, and therefore be a particularly sensitive predictor of AD and PD. Given that the neuropathological profile of PD differs from AD, the question arises as to whether the dual-task walking paradigm is sensitive enough to identify disease-specific gait patterns during the prediagnostic phase. To our knowledge, this question has not been addressed in the literature. Currently, decreased gait speed is one of the most reported gait parameters in the literature for both diseases. Despite the relevance of such a finding, gait slowing could not be considered as a specific parameter for either disease, as it also occurs in healthy aging. From a neuropathological point of view, gait slowing may be primarily due to neuropathological mechanisms that are common to normal aging and neurodegenerative diseases, especially increased prion-inflammatory makers and vascular burden (Valkanova and Ebmeier 2017). In the next sections, we identified dual-task-related changes in other parameters than gait speed that could be specific to AD and PD at the prodromal stage.

Dual-task-related gait changes in AD at the prodromal stage Patients with various subtypes of MCI decrease their speed under dual-task conditions (Pettersson et al. 2007; Maquet et al. 2010; Montero-Odasso et al. 2009a, 2012; Muir et al. 2012; Doi et al. 2014; Tseng et al. 2014; Tarnanas et al. 2015). This gait slowing may result from reduced stride length and increased double support time (Bahureksa et al. 2017) and is mostly due to cerebrovascular disease (Annweiler et al. 2013). Besides, the rhythm (i.e., stride time, stance time, and cadence), pace (i.e., stride length, stride time variability, and double support time variability), and variability (i.e., stride length variability) domains of gait showed to be consistently sensitive to dual-task interference. Notably, in a recent meta-analysis including 14 studies, Bahureksa et al. (2017) found that dual-task walking highlights the sensitivity of the latter gait parameters for discriminating between MCI subtypes and healthy controls. Furthermore, it has been shown that dual-task-related gait changes could differentiate between non-amnestic and amnestic MCI (Montero-Odasso et al. 2014; Valkanova and Ebmeier 2017). Specifically, the pace domain (i.e., gait speed and stride length) was more affected in non-amnestic MCI, whereas the rhythm (i.e.,

cadence, swing time, stance time, and double support time) and variability (i.e., stride length variability and swing time variability) domains were worse in amnestic MCI (Verghese et al. 2008). Of note, Verghese et al. (2008) used another model to study the gait domains compared to the one used in our review (inspired from Hollman et al. 2011 and Lord et al. 2013).

From a neuropathological point of view, imaging studies using magnetic resonance spectroscopy in MCI patients showed that dual-task-related gait changes are associated with altered neurochemistry (i.e., lower N-acetyl aspartate/creatine) and lower volume of both the hippocampal and primary motor cortex (Annweiler et al. 2013). Specifically, stride length variability was correlated negatively with the hippocampal neurochemistry, whereas stride time variability was correlated negatively with the volume and neurochemistry of the primary motor cortex (Annweiler et al. 2013). Mechanistically, such findings suggest that dual-task-related gait changes in MCI patients likely result from impaired frontal-hippocampal circuits that are important in spatial orientation and navigation (Montero-Odasso et al. 2014). Furthermore, these results highlight the possible involvement of primary motor cortex changes in the onset of high-level gait disorders during the prodromal stage of AD (Annweiler et al. 2013). In addition to imaging data, neuropsychological studies suggest that reduced performance in episodic memory (Montero-Odasso et al. 2014), working memory, and executive attention control (Maquet et al. 2010) may alter the ability of MCI patients to execute more than one task at a time. Particularly, reduced performances in both episodic memory and executive attention control are strongly associated with stride time variability (Maquet et al. 2010; Beauchet et al. 2014; Montero-Odasso et al. 2014). Furthermore, the meta-analysis of Beauchet et al. (2014) showed that higher stride time variability was related to both MCI and dementia. Therefore, dual-task-related changes in stride time variability could be a motor signature of MCI, and thus be potentially used as a marker of cognitive decline before and during dementia, including AD (Beauchet et al. 2014). From a neuropathological point of view, such results suggest that dual-task-related gait changes in MCI do not only result from impaired frontal-hippocampal circuits but also from fronto-striatal circuits that are important in executive attention control (Montero-Odasso et al. 2014). Hence, it is likely that both explanations are relevant to explain dual-task interference in prodromal AD. Concerning the other gait domains found in the literature, the specific underlying mechanisms are unknown. Yet, other neuropsychological studies suggest that the pace domain of gait (i.e., stride length) is mainly associated with decreased performance in both visuospatial abilities and executive attention control (Maquet et al. 2010). The recent meta-analysis of Morris et al. (2016) further suggested that the variability (i.e., stride length variability) and rhythm (i.e., stride time, stance time, and cadence) domains of gait could be associated with global cognition.

Dual-task-related gait changes in PD at the prodromal stage LRRK2 G2019S mutation carriers without a clinical diagnosis of PD (i.e., likely representing a prodromal stage of PD) decrease their speed under dual-task conditions (Mirelman et al. 2011, 2016). This gait slowing results from reduced stride length, which itself is mainly due to co-contraction of proximal muscles. Besides, stride time variability and arm swing parameters (i.e., arm swing amplitude, arm swing variability, and arm swing asymmetry) are both impaired. According to Mirelman et al. (2016), the poorer performance of the mutation carriers may be consistent with initial abnormalities in the central gait network. Notably, only arm swing parameters under dual-task conditions discriminate between LRRK2 G2019S mutation carriers and healthy controls. Such findings confirm the sensitivity of dual-task walking to unmasked compensation strategies aimed at preserving the motor (gait) function when the basal ganglia system is altered. Overall, these mechanisms depend on brain regions relatively unaffected by dopamine depletion, such as the anterior striatum (Brück et al. 2006; Mounayar et al. 2007). Using fMRI in early-stage PD, Helmich et al. (2010) showed a shift in cortico-striatal connectivity from severely affected striatal regions (posterior putamen) to less affected striatal regions (anterior putamen). If these changes reflect compensation, they should also occur in the prodromal phase of PD, when a functional reorganization of cerebral circuits prevents overt clinical symptoms (Palop et al. 2006). Accordingly, asymptomatic LRRK2 G2019S mutation carriers show a reorganization of cortico-striatal circuits that mirrors findings in idiopathic PD (Helmich et al. 2015).

Future directions for clinical research

The findings of this review suggest that dual-task-related gait changes can be detected in early stages of

AD and PD and can, therefore, be a marker of these diseases. However, before its use in clinical practice, some methodological concerns need clarification. First, the majority of findings reported in this review come from transversal studies. Therefore, longitudinal studies characterizing the continuum of gait profile of AD and PD from complaints to the clinical expression of the disease are needed not only to confirm findings from transversal studies but also to identify a critical threshold for dual-task-related gait changes which would allow discriminating healthy populations from pathological ones. To our knowledge, this threshold is unknown in the literature. Methodologically, in order to propose a reliable threshold, it is imperative to take into account factors modulating the capacity to cope with a concurrent cognitive load while walking, among which, the most important are age, gender, stress, processing speed (Sleimen-Malkoun et al. 2013), and cognitive reserve (i.e., the background cognitive capacity that a subject brings to a given task; Stern 2009). Applying these methodological recommendations for the conduct of future research would likely enhance the reliability of dual-task gait assessment and its large-scale application in clinical practice.

Another matter that requires further refinement and clarification is the choice of the secondary cognitive task. Although the serial subtraction task (substracting by sevens) has been reported with the highest sensitivity to challenge dual-task walking performance (Bahureksa et al. 2017), it remains non-specific to neurodegenerative process underlying AD and PD. Furthermore, this cognitive task depends on arithmetic skills, which are very heterogeneous between individuals. In our view, a way to make better use of dual-task walking paradigms is to select a secondary cognitive task that both interferes with gait control and challenges the underlying neuropathological processes (in favor of the bottleneck model) of each disease. As such, a possible solution comes from neuropsychological findings that have recently demonstrated that patients with prodromal AD are particularly deficient in tasks requiring inhibition (i.e., Stroop task; Balota et al. 2010) and patients in prodromal PD in tasks involving cognitive flexibility (i.e., task set switching; Cools et al. 2001; Lerche et al. 2014). Importantly, these executive function components are known to interfere with gait (Maquet et al. 2010; Morris et al. 2016) and begin to decrease early in the disease course. Moreover, cognitive flexibility and inhibition depend on dopamine function in the basal ganglia (Berry et al. 2016) and entorhinal cortex (Velayudhan et al. 2013), respectively. Thus, our proposition, requiring more investigation, could open new avenues to use gait as a robust marker for prediagnostic AD and PD.

In conclusion, a growing body of evidence shows that dual-task-related gait changes may be a potential marker that could increase the likelihood of early detection of AD and PD. Longitudinal studies and new dual-task walking paradigms based on the neuropathological profile of each disease are needed to better understand the dual-task interference origins and the interaction between brain damage and gait control, notably by comparing patients from complaints to disease expression (preclinical, prodromal, and clinical) from those who will remain stable.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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