

Dual tasking in Parkinson's disease: should we train hazardous behavior?

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Carolien Strouwen¹, Esther ALM Molenaar², Liesbeth Münks¹, Samyra HJ Keus², Bastiaan R Bloem³, Lynn Rochester⁴ and Alice Nieuwboer*¹

¹KU Leuven – University of Leuven, Department of Rehabilitation Sciences, Faculty of Kinesiology and Rehabilitation, Tervuursevest 101 bus 1501, 3001 Leuven, Belgium ²Radboud University Medical Center, Niimegen Centre for Evidence Based Practice, Department of Neurology, Niimegen, the Netherlands ³Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, Department of Neurology, Nijmegen, the Netherlands ⁴Institute for Ageing and Health. Clinical Ageing Research Unit, Newcastle University, Campus for Ageing and Vitality, Newcastle upon Tvne, UK *Author for correspondence: Tel : +32 1632 9119 Alice.Nieuwboer@faber.kuleuven.be

Dual-task (DT) circumstances aggravate gait disorders in Parkinson's disease (PD) and are associated with an increased risk of falling and reduced functional mobility. Clinical rehabilitation guidelines for PD consider DT interventions as potentially hazardous and recommend avoiding them in daily life. The current article challenges this notion and addresses the necessity of implementing DT training in PD. First, underlying reasons for DT interference in PD and current theoretical models are discussed. Subsequently, different training approaches to tackle DT difficulties are put forward. Finally, the effectiveness and limitations of DT training in PD are reviewed. We conclude that there is a need for DT interventions in PD and recommend randomized, power-based studies to further test their efficacy.

Keywords: cognition • dual task • dual-task training • falls • Parkinson's disease • rehabilitation

Parkinson's disease (PD) is a neurodegenerative disorder of the basal ganglia in which the production of dopamine is reduced, leading to nonmotor and motor impairments and loss of automaticity [1,2]. Loss of automaticity implies that patients find it difficult to maintain movement amplitude, rhythm and posture without consciously attending to the required activity [2]. Brain imaging studies demonstrated the need for higher levels of conscious processing in PD by showing higher activations in the fronto-striatal circuit during automatic task performance [3,4]. An often used paradigm to test the level of automaticity is the dual-task (DT) paradigm [5]. Dual tasking can be defined as the simultaneous execution of two tasks, which have distinct goals and often involve motor and/or cognitive task sets [6]. An often-used measure to express the amount of performance deterioration from single-task (ST) to DT conditions is DT interference [7]. Because of the pathophysiology of PD, it is not surprising that several studies demonstrated that gait and balance disorders deteriorate under DT conditions in PD compared with healthy age-matched controls [8-10]. DT interference in PD expresses itself most frequently as reductions in gait velocity and stride length and increases in asymmetry and

variability [10]. However, the extent of DT difficulties in these studies varied and was determined by differential task demands and severity of the disease [8-10]. Interestingly, it was shown in '*de novo*' PD, that is, patients who are newly diagnosed, that DT interference was comparable with that of age-matched controls when task difficulty was matched to the individual's baseline cognitive level [11].

Different clinical signs can manifest themselves in people with PD influencing DT performance. One of the most disabling gait problems in PD is freezing of gait (FOG), which is characterized by episodes of lack of forward progression despite having the intention to walk [12]. Up to 79.2% of PD patients the advanced disease stage reported in FOG [13] and 38.2% of patients indicated this symptom to be present even when ONmedication [14]. FOG frequency increases when dual tasking [8], suggesting that patients who freeze have greater loss of automaticity than those who do not [15]. Moreover, FOG was identified as an independent predictor of falling [16]. PD patients have a high prevalence of falls irrespective of FOG, ranging from 15.2% [9.3-21.1%] in Hoehn & Yahr stage 1 to 58.3% [38.6-78.1%] in stage 4 [17]. Associations between DT difficulties and falling

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were shown [16] although this was not substantiated in a large cohort of early to mid-stage PD patients [18].

In PD, difficulties with dual tasking are likely to be exacerbated by nonmotor symptoms, most notably by cognitive dysfunction. Mild cognitive impairment most frequently expresses itself in the domains of executive function and attention [19,20]. Here, the term executive function is used as an umbrella term encompassing several cognitive abilities that control goaldirected behavior [21]. These include task switching, appropriately inhibiting and generating responses and updating working memory contents, all of which are necessary for optimal functioning in daily life [21,22]. Especially nonroutine actions that need conscious attentional control are coordinated by executive functions [21]. In PD, disruption of the dopamine network, and more specifically the fronto-striatal circuits, has been shown to be associated with deficits in executive function [22]. Dopaminergic pharmacotherapy partly restores these functions, especially in early disease [20]. As the fronto-striatal circuit together with the mesocortical and fronto-parietal networks are thought to compensate for automaticity loss [22], it is not surprising that several studies indicated executive dysfunction to be associated with greater DT interference in PD [9,23].

In sum, dual tasking is problematic in PD, dependent on patients' motor and cognitive abilities and crucially related to fall risk and freezing, albeit not unequivocally. Hence, the scope of the current article is to better understand the complexity of dual tasking to delineate the DT training potential in the PD population. First, the most commonly adopted theoretical models of dual tasking will be summarized. Second, key considerations for DT training approaches will be discussed. Third, an overview will be given of effect studies concerning DT training in PD. Finally, we will discuss how future studies can move the field forward with regard to improving DT performance in PD.

Theoretical models of dual tasking

DT interference, in general, has been extensively studied and has been underpinned by a number of theoretical models [24], which have their roots in classical capacity theories. The bottleneck model states that when two tasks are performed simultaneously using the same neural processor/network, a bottleneck is created causing one of the two tasks to be delayed until the processor/network is available again [25]. According to this theory, it is not possible to perform two tasks at the same time when these tasks use similar neural networks in the brain. The capacity-sharing theory, on the other hand, contends that it is possible to perform two tasks in parallel using the same processor/network. However, this processor/network is thought to have a restricted amount of available capacity and a delay may occur when tasks exceed it [26]. Both the bottleneck model and the capacity-sharing theory assume that DT limitations are attributed to the central stage of processing (i.e., conscious response selection). Task performance, however, also depends on the perception of environmental stimuli prior to task execution (i.e., perception stage of processing) and on task execution itself (i.e., motor stage of processing) [27]. A third model, the EPIC model (executive processing and interactive control), assumes that either sequential (in analogy with the bottleneck model) or parallel (in analogy with the capacity-sharing theory) processing is possible, not only at the central stage but at any of the processing stages [27]. Finally, the more recent multiple resource model proposes that resource competition occurs at multiple dimensions [28] and, as such, fits better with multitasking inherent to everyday functional activities. This model postulates that successful multitasking depends on the capacity to simultaneously rely on multiple brain resources necessary to run the different components of the tasks [28]. Dual tasks with a greater resource overlap would thus induce greater interference, particularly when more generic (i.e., prefrontal and fronto-parietal brain regions) rather than specific brain networks are involved in the task [7]. Based on the models described above, however, it is unclear whether a structural limitation or a strategic postponement of processing stages is the main cause for difficulties with dual tasking.

Dual-task processing difficulties

Recently, the notion of structural limitation was supported by Watanabe et al. [29], who showed that DT interference is already present at the level of single-neuron activity in the lateral prefrontal cortex of monkeys trained to perform a simultaneous memory and attention task. Unlike during ST, prefrontal neuron activity lost the ability to fire in a task-specific manner during DT, confirming overloaded recruitment of overlapping neural populations as underlying interference [29]. Informationprocessing, however, could still be flexibly allocated and reallocated among the two tasks [29]. Clinical studies in PD support this finding by showing that changing task prioritization consciously, that is, allocating attention to one task specifically, led to differences in task performance [30]. Next to structural limitations, attention thus seems to be a mediating factor determining the level of DT interference. In older people, fronto-parietal circuits showed greater activation during DT compared with ST performance, illustrating that top-down attention was needed [7,22]. As fronto-striatal circuits may be hyperactive during ST performance of previously well-learned tasks [31,32], flexible internetwork compensation may be hampered in PD. Brain imaging studies confirmed increased brain activity during dual tasking in PD compared to healthy controls [33].

Thus, residual neural capacity [7] depends on structural limitations, on the one hand, and on the level of automaticity versus cognitive processing required for task execution on the other [34].

Brain mechanisms of dual-task training

In young adults, it was shown that DT learning was related to a decrease in activity in fronto-parietal networks and to an increase in striatal activity, confirming a shift from cognitive to automatic DT execution [32]. After practice, young adults were able to perform two tasks concurrently without any interference, showing that residual capacity increased sufficiently [32,34]. Although practice improved DT performance also in the elderly, interference was never completely absent, probably



because of an age-related reduction of residual capacity [7]. Wu & Hallett [33] showed that PD patients, unlike controls, were only able to perform an easy but not a difficult DT after 20 min of practice. Brain imaging showed that PD patients activated several (pre)frontal, premotor, parietal, temporal and occipital regions together with cerebellar and thalamic areas to a much larger extent during DT processing than healthy controls [33]. Brain scans after practice showed that brain activity became more efficient in both groups, but much more so in healthy controls [33]. Interestingly, in addition to brain regions involved in ST execution, extra brain areas were found to be active during DT performance in both healthy elderly and PD. These DT-specific activations included the precuneus, dorsolateral prefrontal cortex and various cerebellar regions [3,33,35]. As such, practice could be assumed to improve DT coordination and increase efficiency in these DT integration areas [36].

Considerations for different approaches to dual-task learning in PD

The previous section underpins that DT performance may be improved by learning, not only in younger and older adults but also in PD. In general, motor learning studies suggest that not only intensity but also exact practice conditions are critical in determining whether practice-related improvement leads to long-term consolidation [37]. Promoting cognitive processes similar to those required for retrieval of the learned skill and cognitively challenging the learner were also shown to enhance retention and transfer of learning [37]. In PD, it was found that, typically, automaticity, considered a hallmark of consolidation, was reduced [33,38] and that learning was highly dependent on cognitive status [39].

Similar to older adults, different models for DT training in people with PD may be proposed [40,41]. Consecutive task training [41] implies that separate ST training will make the performance of each task faster and improve DT performance indirectly. This is in line with the bottleneck theory, which states that improvement in DT performance can only occur by shortening the time period at each processing stage and thus by shortening the time it takes to perform both tasks consecutively [42]. In addition, the capacity-sharing and multiple resource models may explain more efficient DT performance through consecutive training by enlargement of the available capacity through enhanced ST performance, on the one hand, and by improving reallocation of resources between the two tasks, on the other [42]. ST practice can be assumed to lead to needing less brain capacity, resulting in less overlap when tasks are executed simultaneously. Indeed, brain imaging studies in PD of short-term ST practice have shown that premotor cortex, supplementary motor area and right postcentral gyrus were less activated after training and that functional connectivity between cerebellar regions and motor-cognitive areas increased [35]. In addition, learning-related shifts toward increased striatal activation were found in both healthy controls and PD [4]. However, PD patients showed decreased connectivity from striatum to motor execution networks when asked to re-attend to the learned task, indicating a shift back from automatic to conscious processing [4]. In addition, ST gait training, for example, treadmill training and cueing strategies, was demonstrated to be effective in many studies [43,44]. Recent work also showed potential for cognitive ST training [45,46]. In conclusion, as both motor and cognitive functions benefit from consecutive practice in PD, combined performance may improve as well.

Second, integrated task training [41] assumes that concurrent DT practice will increase the efficiency of shared neural resources and as such improve DT performance. Both the capacity-sharing and the multiple resource models, which state that practice can enlarge the available capacity or improve its reallocation between the two tasks, support this view [42]. Also the EPIC model, in which improvements after training are thought to occur due to better task-scheduling, integration and more efficient processing at any of these stages [42], is in line with this training mode. Moreover, according to the principles of motor learning, integrated training resembles the desired outcome most and as such argues in favor of this form of practice [37]. Brain imaging studies after DT training in young adults showed that pre-post decreases of neural activity in frontal and parietal regions were correlated to the behavioral changes seen after training [32,34,47]. Transfer of learning to daily life situations may be facilitated by such integrated practice [48]. In balanceimpaired older adults, both consecutive and integrated training modes led to improvements of gait speed, balance and cognitive performance under DT conditions [41]. The integrated training program, however, resulted in better retention and greater improvements in cognitive outcomes than in consecutive training [41]. Evidence on integrated task training efficacy in PD can be found in TABLE 1 and will be discussed in the next paragraph.

Third, hybrid task practice consists of mixed consecutive and integrated task training and has the advantage that both task automatization (according to the bottleneck and capacitysharing theories) and task integration (according to the EPIC model) are addressed. So far, only two studies have been performed suggesting that this method was effective in obtaining DT benefits in older adults [40,48].

In summary, all of the above training approaches offer a potential framework for achieving DT improvements in PD. Applying the principles of motor learning [37], we put forward that practicing both tasks at the same time (i.e., integrated task training) will be most effective in reaching the desired DT outcomes in PD. However, specific subgroups, that is, people with falling, FOG or MCI, may be at higher risk for adverse events. In these subgroups, integrated task training may be hazardous. Therefore, we propose that consecutive task training is a safer training model, which may be able to improve DT performance provided that both tasks are practiced. Finally, hybrid task practice may be the superior option for patients who are at risk for falls or FOG or who only very occasionally experience such events, offering the best compromise between safety issues and training effectiveness. In the next paragraph, we will critically examine the currently available evidence on DT training in PD.

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	Ref.	[55]	[51]	[52]	[53]	[57]	[54]	L: Late
	Results after intervention	Gait speed ↑ (DT) Cadence ↑ (DT) Retention after 3 weeks	Step length \uparrow (DT) Gait speed \uparrow (DT) Step length CoV \downarrow (DT)	Gait speed f(trained + untrained) Gait variability U(trained + untrained) DT interference ((trained) Retention after 30 days	Gait speed \uparrow (ST + DT) Stride length \uparrow (ST + DT) Stride time \downarrow (ST + DT) Gait variability \downarrow (DT) Retention at follow-up at 4 weeks (ST + DT) Endurance \uparrow 31% less mistakes on serial 3 subtraction task	Young: COP velocity↑ Heel height variability↑ Other groups: No effect	In all cueing conditions: gait speed \uparrow (ST + DT) step length \uparrow (ST + DT) Transfer of walking speed (DT) and step length (ST + DT) to non-cued task Retention after 6 weeks (cued + uncued)	practice; ITT: Integrated task practice;
:on's disease.	Intervention details	10-m walks at 'fast-as- possible' pace combined with cognitive, manual and triple tasks	Improving step length while concurrently performing working memory language and counting tasks Variable priority	Walking in combination with cognitive tasks Variable priority	Progressive intensive treadmill training with virtual obstacles Progression by increase of difficulty VR and increase in walking time	Postural control task with cognitive task	Cueing training: Auditory, visual or somatosensory cues chosen by patient Early group: training after test 1 Late group: training after test 2	Hoehn and Yahr scale; HTT: Hybrid task
ning effect in Parkins	Intervention dose (min, frequency, weeks) – category	30, 1, 3 ITT	20, 1, - ITT	30, 3, 4 ITT	45, 3, 6 ITT	Acquisition: 21 trials 48-h retention: 9 trials 1-week retention: 9 trials	30, 3, 3 ITT	Dual task; E: Early group; H&Y: H
dual-task trai	Design (or level of evidence)	Pre-post design Uncontrolled	Pre-post design Uncontrolled	Pre-post design Uncontrolled	Repeated measures design based on retrospective control group without VR- treadmill training	Pre-post design Controlled	Cross-over trial Control period without training	icient of variation; DT: CVR: Virtual reality.
g a beneficial	Secondary task	Cognitive Motor	Cognitive Motor	Cognitive	Cognitive Motor	Cognitive	Motor	pressure; CoV: Coeff ask: T: Training group
s showin	Primary task	Walking	Walking	Walking	Walking	Postural control	Walking	OP: Center of
verview of studie	Population (number, age, H&Y)	5, 61.0 ± 8.0, II–III	20, 68.5 ± 11.3, II–III	7, 63.8 ± 8.4, II–III	20, 67.1 ± 6.5, II–III	PD: 7, 68.7, I–III Elderly: 7, 70.5, - Young: 10, 25.5, -	153, E: 67.5 and L: 69.0, IL-IV	effects; C: Control group; C Jutes: PD: Parkinson's diseas
Table 1. O	Study (year)	Canning CG <i>et al.</i> (2008)	Brauer SG <i>et al.</i> (2010)	Yogev- Seligmann G et <i>al.</i> (2012)	Mirelman A <i>et al.</i> (2011)	Foreman KB <i>et al.</i> (2013)	Rochester L <i>et al.</i> (2010)	1/1: Significant



Table 1. O	verview of studi	es showing	g a beneficial	dual-task traii	ning effect in Parkin	son's disease (cont.).		
Study (year)	Population (number, age, H&Y)	Primary task	Secondary task	Design (or level of evidence)	Intervention dose (min, frequency, weeks) – category	Intervention details	Results after intervention	ef.
Conradsson D et al. (2015)	100 (T: 51; C: 49), T: 72.9 ± 6.0 and C: 73.6 ± 5.3, II–III	Balance Walking	Cognitive	Randomized controlled trial	60, 3, 10 HTT	Balance training focused on several balance components with the progressive introduction of dual-task exercises starting from week 3	Training group: [56 Mini-BESTest ↑ (ST) Gait speed ↑ (ST) Step length ↑ (ST) Cognitive task ↑ (DT) Control group: No effect	56]
↑/↓: Significant ∈ group; min: Min	effects; C: Control group; utes; PD: Parkinson's disea	COP: Center of p ase; ST: Single tas	sk; T: Training group;	icient of variation; DT: ; VR: Virtual reality.	Dual task; E: Early group; H&Y:	Hoehn and Yahr scale; HTT: Hybrid task	practice; ITT: Integrated task practice; L: Late	ate

Efficacy of dual-task training in PD

Currently, the most often cited recommendation in PD evidencebased rehabilitation guidelines is to avoid DT situations and divide complex tasks in easier subcomponents [49]. The most recent European guideline provides a more graded view, stating that in Hoehn and Yahr stages 2 and 3 DT training may be safe and effective [50]. Evidence on DT training in PD is still limited. TABLE 1 shows seven studies addressing the efficacy and feasibility of such interventions. Methodologically five out of seven studies had uncontrolled designs. Six out of seven studies looked at the effect of integrated task practice, whereas one study could be categorized as hybrid task practice. Interestingly, no evidence on consecutive task practice was found. Most studies showed increased gait speed and step length during DT conditions after training [51-56]. One study, in which DT stance was trained in a single session, showed negative results [57]. The RESCUE-trial [44,54], a large randomized controlled trial on cued exercise in PD, showed sustained reductions of DT interference after ST and DT cued gait training without increasing fall risk. However, effects may have been cue related and were not placebo-controlled. A recent pilot study [53] investigated the effect of a virtual reality (VR) augmented treadmill training in comparison to a traditional treadmill intervention in PD. The VR-enriched training induced greater improvement, particularly on DT and cognitive outcomes. Retention effects ranged from 30 days to 6 weeks after training [52,53]. Yogev et al. [52] investigated gait training in combination with several cognitive tasks and demonstrated improvements in DT gait not only for the trained but also for the untrained tasks. This transfer effect was also found after only 20 min of DT training [51]. A randomized controlled trial assessing the effect of a 10-week DT balance training program based on the hybrid training model only showed positive results for DT cognitive performance, but not for DT gait and balance performance [56]. Together, these results advocate that integrated and hybrid DT training may have positive effects on both motor and cognitive functioning without increasing fall risk in PD. However, conclusions should be drawn cautiously as five of the seven studies were open-label studies, including less than 20 patients [51-57]. Further research is thus needed to explore which of the training approaches is most effective in reaching DT benefits.

Expert commentary

The literature review supports a potential beneficial effect of DT interventions in PD, despite the common advice to avoid dual tasking [49]. Although the latter advice is cautious and has face validity, it lacks an ecological rationale as dual tasking is intricately connected to functional mobility. Furthermore, DT avoid-ance may not be advisable as patients need to be aware of their DT impairment. Therefore, we recommend to incorporate DT training in rehabilitation protocols using a graded approach, tailored to each patient's individual profile. It is currently unknown to what extent integrated [41], consecutive [41] and hybrid [40,48] DT training should be applied to PD. If these training modes lead to largely the same results as in frail older adults, consecutive DT training is likely the best option for subgroups with PD who

rehabilitation.								
Study (year)	Population (number, H&Y)	Primary outcome	Secondary tasks	Design (or level of evidence)	Intervention dose (min, frequency, weeks)	Intervention details	Ref.	
Brauer SG <i>et al.</i> (2011)	60, I–IV	Step length	Cognitive Functional	Randomized controlled trial	40–60, 3, 4	Single-task training: Gait training aimed at improving step length Home program from week 2 (walking, balance, strength, postural exercises) Dual-task training: Improve step length under dual-task conditions (added cognitive or motor tasks)	[59]	
Mirelman A <i>et al.</i> (2013)	PD: 100, II–III Elderly: 100, - MCI: 100, -	Fall rate	Walking Cognitive	Randomized controlled trial	45, 3, 6	Control group: Treadmill training Intervention group: Treadmill training + virtual reality	[60]	
Strouwen C <i>et al.</i> (2014)	120, II–III	Gait speed	Cognitive Functional	Randomized controlled trial	30–40, 4, 6	Consecutive task training: Single task training of cognition Single task training of gait Functional training (avoiding dual tasks) Integrated task training: Training of gait while performing cognitive exercises Functional training (focus on dual tasks)	[61]	

Table 2. Overview of three current ongoing randomized controlled trials focusing on dual-task rehabilitation.

H&Y: Hoehn and Yahr stage; MCI: Mild cognitive impairment; min: Minutes; PD: Parkinson's disease

complain of falling and have established cognitive decline as was put forward above. Considering their faster cognitive decline, patients with the postural instability and gait difficulty subtype [58] and those at risk of falling or experiencing occasional FOG episodes [12] may gain more from hybrid task training [58]. In contrast, integrated training may be the preferred option for patients in an early disease stage who do not suffer from FOG, cognitive deficit and falling and present with a tremor-dominant subtype [58]. In these cases, integrated training may provide the best chances for consolidation of learning. On the basis of current evidence, we recommend for clinical practice to perform an extensive evaluation of the patient prior to the start of the training, the outcome of which should determine which training strategy is most suitable. To acknowledge safety concerns, DT practice should be supervised and guided by a trained physiotherapist. We also recommend that self-practice of dual tasks should be avoided, particularly in the later disease stages.

Five-year view

In 5 years, we expect to have a better understanding of the effect of DT training in PD in different clinical subgroups. Three large trials (TABLE 2) into the efficacy of DT training are currently being conducted [59–61]. The first (ACTRN12609000791235) contrasts DT gait training with ST gait training and is aimed at improving DT step length [59]. The second trial [62] is a large study into the efficacy of combining virtual reality tasks with treadmill walking versus treadmill walking alone in PD and other frail elderly and is aimed at improving fall risk [60]. The third trial, the DUALITY study, [63], compares the effect of consecutive versus integrated task training of motor and cognitive tasks in PD [61]. DT gait speed is the primary outcome of this study and falls are monitored weekly throughout a period of 24 weeks. The results of these studies will inform clinicians about the potential to consolidate and retain DT training effects and about the safety of these programs. As well, information will be gathered about which patient profile will benefit most. Finally, we expect to gain a better understanding into the neural mechanisms of DT performance in PD as a basis for new treatment strategies. For this purpose, brain imaging studies need to be conducted to refine current theoretical models and to understand how tasks of different complexity cause interference in PD to optimize applications for clinical practice. Functional brain imaging studies, preferably using methods that can be applied during ST and DT walking, such as fNIRS or EEG, may be a helpful tool for this purpose [64].

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Key issues

- Dual-task (DT) interference is an important problem in people with Parkinson's disease.
- Residual neural capacity appears to determine the extent of DT interference in Parkinson's disease.
- Consecutive, integrated and hybrid DT training approaches may be relevant for different subgroups of Parkinson's disease.
- Evidence on the efficacy of DT training is scarce and is methodologically weak.
- Integrated dual-task training needs to be considered as part of rehabilitation for Parkinson's disease to generate awareness of difficulties with dual tasking, including fall risk.

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