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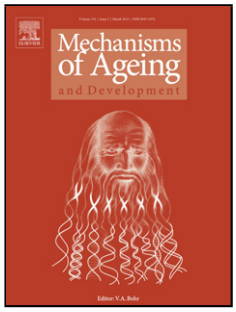

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The Use of Motor Cognitive Dual-Task Quantitative Assessment on Subjects with Mild Cognitive Impairment: A systematic Review

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Abstract

Dementia and Alzheimer's Disease (AD) represent a health emergency. The identification of valid and noninvasive markers to identify people with Mild Cognitive Impairment (MCI) is profoundly advocated.

This review outlines the use of quantitative Motor and Cognitive Dual-Task (MCDT) on MCI, by technologies aid. We describe the framework and the most valuable researches, displaying the adopted protocols, and the available technologies. PubMed Central, Web of Science, and Scopus were inspected between January 2010 and May 2020. 1939 articles were found in the initial quest. Exclusion criteria allowed the selection of the most relevant papers; 38 papers were included. The articles, regarding four technological solutions "wearable sensors", "personal devices", "optokinetic systems", and "electronic walkways", are organized into three categories: "Quantitative MCDT", "MCDT Inspired by Neuropsychological Test", and "MCDT for MCI Stimulation".

MCDT might furnish clinical landmarks, supplying aid for disease stratication, risk prediction, and intervention optimization. Such protocols could foster the use of data mining and machine learning techniques. Notwithstanding, there is still a need to standardize and harmonize such protocols.

Keywords: Motor-Cognitive Interference, Motor Control, Dementia

Introduction

Due to the rapid global aging, people affected by dementia will triple worldwide in the next 30 years [Prince et al. (2015) Cova et al. (2017)]. Furthermore, the circumstances are exacerbated by the fact that no effective curative treatments have been identified so far, which may be partially due to the inclusion, in intervention studies, of patients with overt cognitive impairment [Petersen (2009)]. Nowadays, the identification of subjects with a higher risk of incident dementia generally occurs when they already present an advanced stage of a pathological process. Therefore, the need to accurately intercept such a trajectory, as early as possible, justifies the increasing efforts to identify reliable predictors of the disease [Grande et al. (2018)]. Thus, the identification of clinically valid, inexpensive, and non-invasive markers is highly advocated [Montero-Odasso et al. (2018)]. In this framework, the Mild Cognitive Impairment (MCI) represents a promising clinical signature, it is, in fact, a 10-fold risk condition of progressing to dementia [Petersen (2011)], and, interestingly, even if the clinical hallmark of MCI is primarily cognitive impairment, several studies found that also gait dysfunctions can occur in this type of subjects. Then, the possibility to use gait characteristics as reliable information regarding the cognitive subject's status is an emerging research point.

Either the recent interest growth in neuroscience and the technical progress of quantitative motor assessment tools have fostered this research field. Thus motor activity is now used to gather information about the physical and cognitive patients' health. Human motor activity is the outcome of a widespread and complex network, which involves cortical and sub-cortical structures, and that requires the functioning of several cognitive domains, indeed. Hence, the coordinated activity of several brain cortices is necessary for the human movement: Motor (M1), premotor (PMA), and supplementary motor areas (SMA), as well as the action of the prefrontal cortex (PFC), dorsolateral prefrontal

cortex (DLPFC), and the parietal cortices, which regulate the higher-order aspect of motor behavior and gait. The frontal cortices produce complex motor responses integrating the multiple sensory inputs, including proprioceptive information, with environment constraints [Beauchet et al. (2008)]. On the other hand, the motor cortices support the integration of such information, generating a global motor control message [Graziano et al. (2002)], while the posterior parietal cortex provides visuomotor transformation able to control the movement and cope with the environment [Pizzamiglio et al. (2018)]. The activity of subcortical regions, such as dorsal-basal ganglia and thalamus is also required. These areas, by the inter-playing with the supplementary motor areas, modulate the walking speed and the stride length [Takakusaki (2017)]. Eventually, the brainstem, supervised by the cerebellum, basal ganglia, and motor cortex, regulates the gait initiation and the gait cadence through its projections to the spinal cord. While, the cerebellum exerts its control by comparing actual movements with the indented ones [Drew et al. (2008), Mori et al. (1992)].

Aging affects either motor and cognitive systems, perturbing the smooth functioning of the motor-cognitive interface. With aging, the mass and quality of muscles decline, the sensory functions decrease, and the cortical and spinal circuits controlling posture and gait show maladaptive reorganization. Besides, the physiological age-related cognitive decline may affect motor ability. Elderly subjects show reduced step lengths and gait speed, lower stepping frequency, and greater step-to-step variability. These abnormalities, barely detectable in single motor tasks, are exacerbated and unmasked using the Motor and Cognitive Dual-Task (MCDT) approach. The MCDT is a "brain-stress test" [Montero-Odasso et al. (2017)] developed to evaluate the functioning of the motor-cognitive interface. This technique provides for the simultaneous performance of a cognitive task (counting backward, or verbal fluency) and a motor task (walking). Nevertheless, the different combinations of motor tasks and cognitive exercises can be utilized [McIsaac et al. (2015), Wollesen et al. (2019)]. The intriguing point is to observe how such an effort would affect motor performance, disturbing its correct execution. The rationale behind this approach is

that cognition is an embodied proprieties. Therefore, movements would require cognitive supplies (attention, memory, and the involvement of executive functions) for its functioning [Koziol et al. (2012)]. The performance of dual-task requires more cognitive resources, reflected by a higher brain activation in the prefrontal cortex if compared with single-tasking [Bayot et al. (2018), Kahya et al. (2019)]. For these reasons, MCDT can be considered as a window on the brain - and cognitive - process, and, through the calculation of the Dual-Task Cost (DTC), it also helps to isolate the cognitive control component of movement and provides insights into the mechanisms of control [Montero-Odasso et al. (2014)]. Several neurocognitive theories have been developed to explain such phenomenon, among which the *Capacity Sharing Theory* and the *Limited Capacity Model*, which provided a theoretical explanation of motor-cognitive interaction: the performance of a motor task at the same time as a cognitive one can overload the neural-networks standing for these tasks, producing an atypical motor performance [Tombu & Jolicœur (2003)]. Interestingly, the adoption of this approach went beyond the early detection of Alzheimer's Disease (AD) and dementia. The quantitative motor assessment has been applied on studies on healthy adults [Sunderaraman et al. (2019)], lower limb amputee people [Petrini et al. (2019)], presence of peripheral neuropathy in diabetics patients [Paul et al. (2009)], stroke patients [Curuk et al. (2019)], subject with Parkinson's Disease (PD) [Yang et al. (2019)], and even on children with intellectual disability [Kachouri et al. (2019)].

Motor abnormalities in MCI, measured through the DTC magnitude, are also a hallmark increased falls risk and incident frailty syndrome [Beauchet et al. (2009), Montero-Odasso et al. (2009)]. Therefore, the Motor Cognitive Risk (MCR) label is increasingly adopted to describe patients reporting subjective cognitive impairment and gait abnormalities [Hausdorff & Buchman (2013)]. Hence, researches recommend the assessment of the motor-cognitive interface in the clinical setting, stating that such a paradigm could be valuable in the process of early diagnosis of dementia and/or frailty syndrome [Auvinet et al. (2017)].

In conclusion, early dementia screening is crucial to provide an opportunity for secondary prevention, as well as planning for future care, safety concerns, and financial and legal arrangements. The study of the motor-cognitive interface is offering new diagnostic tools, as the MCDT to identify frail people and to distinguish among different dementia [De Cock et al. (2019)], but is also re-shaping the clinical landscape offering new diagnostic solutions, such as the MCR. Thus, this review aim at collecting and summarizing the most outstanding works in the field of quantitative motor assessment by the use of MCDT on MCI subjects.

Methods

Data Sources

An electronic database search was performed for the period from May 2019 until May 2020 using the U.S. National Library of Medicine (PubMed®), Web of Science (ISI®), and Scopus® databases to identify articles concerning the use of quantitative analysis of movement in MCDT protocol for MCI clinic. According to the PRISMA statement [Moher et al. (2015)], an additional manual search was performed (e.g., through citations of articles included in this review).

Search Terms

Specifically, the search queries included the following terms: ("swing time" OR "stance time" OR cadence OR stride OR MCDT OR "motor-cognitive dual task" OR walking OR gait) AND (CIND OR "cognitive impairment no dementia" OR "age-associated memory decline" OR "age-associated memory impairment" OR MCI OR "Mild Cognitive Impairment"). The terms research was performed regarding titles and/or abstracts.

Study Selection Process

Only original, full-text articles published in English, within January 2010 and May 2020, which addressed the aforementioned topic, were included in this review. First duplicated documents were manually identified and excluded;

thereafter, items were excluded if: (1) they were an abstract, a letter, a review article, or a chapter from a book; (2) they were not written in the English language; (3) were from years prior to 2010.

Each author independently screened the articles that were excluded with reason if: (1) they did not encompass any type of technological methods for kinematics evaluation (electronic walkways, wearable sensors, optical systems, and/or personal devices); (2) they did not manage MCI subjects; (3) they did not refer to MCDT approach; (4) they did not appear suitable for this review after regarding of title and abstract; or (5) they were not full access. In addition, (6) if multiple articles written by same authors had similar content, more recent articles have been selected. Disagreements on the inclusion/exclusion and classification of the articles were solved through meetings and discussion.

Finlly, the selected articles, fully evaluated and included, were classified into three groups based on whether (1) their application were the movement assessment for early diagnosis and clinical characterization; (2) the use of novel technological solution of quantitative movement evaluation for the enhancement of standard neuropsychological tests; (3) the use of MCDT protocols for cognitive and motor stimulation of MCI subjects.

Data Abstraction

Data were abstracted from each selected articles, as reported in Tables 1,2,3. For each article information about the study characteristics (MCI diagnostic criteria, sample size, demographic data, and sample composition) were reported. Furthermore, Inclusion/Exclusion criteria for experimental subjects were listed, as well as the totality of neuropsychological battery used and the entire Motor and MCDT protocol took into account. Lastly, a list of motor parameters extracted and analyzed have been included.

Results

Application Overview

Obtained in the research were 403 references from PubMedCentral®, 790 references from Web of Science®, and 746 references from Scopus®. After removing duplicated items, 1158 refereces were screened. Thereafter 347 articles were fully evaluated. 38 papers were included in this review (Figure 1).

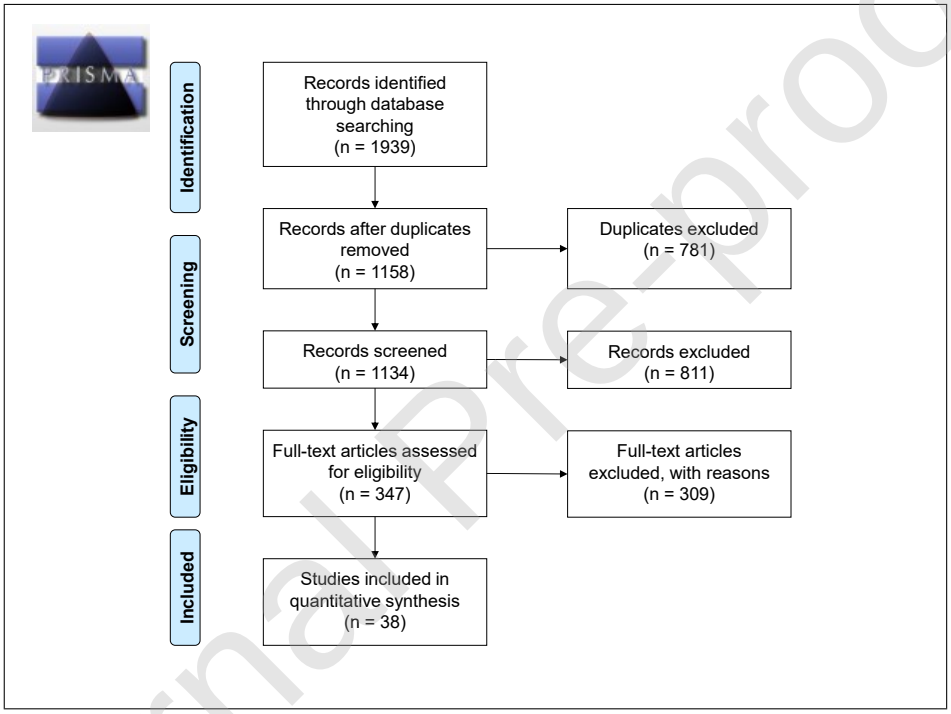

Figure 1: Research methodology for review process following PRISMA guidelines.

Analysis Method

Thirty-eight papers were selected according to the aforementioned methods and classified on the basis of three main application areas: "Quantitative Motor and Cognitive Dual-Task Approach" (82% of the papers), "Motor and Cognitive Dual-Task Inspired by Neuropsychological Test" (13% of the papers), "Motor

and Cognitive Dual-Task for MCI Stimulation" (5% of the papers), (see figure 2.C).

Reported Results

Regarding the technologies used in these works, most of the studies (53%) has adopted different types of electronic walkway for the gait analysis, while roughly a third of the studies (34%) has utilized wearable sensor in order to evaluate kinematics parameters. Alternatively, either optokinetic systems (8%) and personal devices (5%) have been used (see figure 2.B).

Of the 38 fully evaluated papers, 11 (29%) were published in 2019, while 24 (63%) were published over the past 4 years. This result confirms the increasing interest for the use of quantitative MCDT assessment with people with MCI (see Figure 2.A).

All 38 papers are illustrated in detail in Tables 1,2,3. In addition, a brief summary of the data included in this paragraph is included in Figure 2.

Application

The following section encompasses all the paper reviewed. The total amount of the research included have been organized in three categories, respectively: "Quantitative Motor and Cognitive Dual-Task Approach", "Motor and Cognitive Dual-Task Inspired by Neuropsychological Test", "Motor and Cognitive Dual-Task for MCI Stimulation". The first one concerns the use of MCDT as an assessment tool, and is itself formed by three subsections concerning the technology used (electronic walkways, wearable sensors, and other technologies); the second group of papers provides an overview of revised neuropsychological tools that combine physical activity and cognitive performance; and, in conclusion, the third section aims at applying the MCDT paradigm to stimulate the subjects comprehensively. The paper are here listed and described. Information relatively to: experimental design, technology used, type of patients enrolled, parameters extracted, and result gathered are detailed.

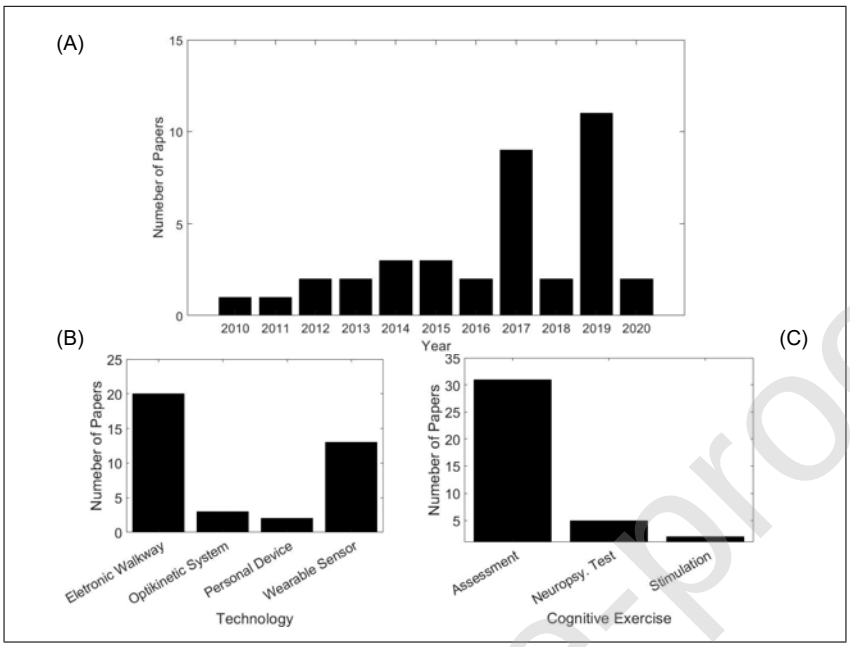

Figure 2: (A) Publication trend per year; (B) Paper distribution per technologies used; (C) Paper distribution per aim.

Quantitative Motor and Cognitive Dual-Task Approach

This subsection refers to the possibility to use new technologies to make the MCDT approach more precise and quantitative. That represents the most addressed topic, the 82% of the total amount of articles reviewed are encompasses here. Furthermore, roughly half of them (45%) has been published within the previous three years. This section encompasses all the papers that have addressed the topic of quantitative MCDT assessment for MCI, from 2010 to 2020, and represent the amplest section in this literature review.

As aforementioned this section is organized in three main part, for the sake of clarity we decided to display the works on the topic on the basis of the technology took into account.

The use of Electronic Walkways in MCDT Assessment for MCI subjects

The seventeen following articles address the usage of electronic walkways in the field of MCDT assessment for people with MCI. Nowadays, electronic walkways represent a gold standard device for gait analysis, therefore they are the most widespread technology.

One of the first work about the use of electronic walkways in MCDT with MCI subjects is the research conducted by Muir et al. Through the aid of an electronic walkway, the authors assessed MCI and AD subjects using single motor task and several MCDT (see Table 1). The authors mainly examined two dimensions of human gait: velocity and variability, seen as stride time variability. The authors reported that gait velocity is an informative parameter evaluating MCDT performances, it shows, indeed, a significant decreasing from single-task paradigm to MCDT approach for each group of subjects: MCI, AD, and Healthy Older Adults(HOA). Furthermore, the DTC referring to gait velocity is higher for clinical subjects compared to HOA (25% and 27% versus 9% for naming animals, and 35% and 39% versus 15% for counting backwards by 7). Notwithstanding, this parameter seems capable of distinguish cognitively impaired subjects from healthy elderly, but it is not reliable to discriminate MCI subjects from AD under the MCDT approach. Similarly, the stride time variability increase for each group from single-task to MCDT, but if the increase is marginal for HOA, on the other hand is statistically significant for MCI and AD. Moreover, the authors report that the confront of stride time variability during MCDT is informative in discriminate HOA from MCI and AD, but not in finding differences between the latter two categories [Muir et al. (2012)]. Likewise, Boripuntakul et al. compared a group of MCI to healthy elderly using the MCDT approach. The authors were interested in the analysis of gait initiation (GI), therefore all the parameters reported concern the first and the second step. The authors report that adding the cognitive load (the transition from single-task to MCDT) had a similar effect on all parameters in MCI and HOA. For which concerns the mean spatiotemporal parameters, the authors report a

greater swing and step times, and a shorter step length and reduced step width under the MCDT condition for both groups. Instead, the variability analysis of the subjects shows an increasing of swing time, step time, step length, and step width in the passage from single task to MCDT condition. Significant difference were accounted between MCI and HOA, only under the MCDT condition, both for step length and width [Boripuntakul et al. (2014)].

One of the most important contributions in this field has given by Montero-Odasso et al. The authors assessed differences between amnesic MCI and healthy older subjects. In the first work, the authors report statistically significant differences, within group (MCI and HOA), in the mean values of gait parameters (gait velocity, stride time, and stride time variability) across the different walking test condition (usal gait, naming animals, counting backwards by 7). Differences between groups were also found in each walking test condition for the same parameters. Moreover, the magnitude of increased gait variability across tasks was greater for MCI (2.68%-9.84%) than the control group (1.86%-3.74%), showing a between group significant difference. In addition significant interaction effect was found between cognitive status and walking condition in favor of MCI group, demostrating that gait varibility increased as complexity of gait task increased [Montero-Odasso et al. (2012)]. Thereafter the authors compared non-amnestic MCI (na-MCI) and amnestic MCI (a-MCI), using the same MCDT approach. Results report a decreased gait velocity in a-MCI group if compared with na-MCI. Statistically difference were attested under MCDT condition, namely counting backwards by 1 and naming animals. Interestingly no significant differences were accounted by the counting backwards by 7. For what concern the stride time variabilty, a-MCI showed an increasing of such parameters, if compared with na-MCI, both for usual gait and for counting backwards by 1. As predictable, a-MCI suffered an higher DTC, with significant differences in all three velocity DTC. Moreover, such metrics resulted to be related with performance in delayed recall, a measure of episodic memory, in all MCI participants [Montero-Odasso et al. (2014)]. Afterward, the authors considered the opportunity to use MCDT to assess the risk of MCI develop-

ing dementia. The authors stated that MCI who progressed to dementia have beforehand shown significantly lower MCDT velocity and higher DTC. The authors found that all MCDT conditions were able to predict incident dementia, interestingly, except for the counting backwards by 7. Moreover, the increasing of DTC in gait velocity counting backwards and naming animals were both associated with dementia progression. In addition, stratification of sample into quartiles of MCDT velocity showed that participants in the lowest quartile ha the highest risk of progression to dementia. The authors suggest that MCDT would be associated with the risk of developing dementia. High DTC, while counting backward and naming animals, was associated respectively with an increased risk by 3.8 and 2.4 fold. Moreover, they added that even single-task seems to own inherent predictive power, although not statistically significant. That revealing the unique of MCDT in the clinical encounter [Montero-Odasso et al. (2017)].

De Cock et al. presented other seminal contributions to understand how to use the MCDT approach during standard cognitive screening. The authors expanded the number of selectable gait variables to broaden the opportunity to detect MCI. The authors refer that gait velocity at usual pace, as well under MCDT conditions (naming animals and counting backwards) differs from HOA, MCI and demented subjects. Other parameters, as mean step length and swing time variability differed across the dementia stages, increasing as cognition decreases. On the other hand, the authors report that there was no significant differences between groups, if step width variability were took into account. Interestingly, several DTC (velocity, mean step length, and swing time variability) for naming animal, and not for counting backwards by 2, were significant different among the cognitive stages [De Cock et al. (2017)]. Recently, the authors proposed to use spatiotemporal gait characteristics for dementia profiling. The authors, in a follow-up study (31-41 months), observed that the DTC for step width, during a counting backwards task was greater in patients which would evolve in AD or Fronto-Temporal Dementia (FTD) respect to those remaining stable as MCI overtime. The authors attested also differences between MCI

which remained stable in contrast to whose are at risk to develop vascular dementia or Levy Body Dementia (LBD). The velocity, normalized velocity, and normalized steps per meters under MCDT condition, particularly naming animals, have been associated with these subjects, indeed. Moreover, the authors state that the most suggesting gait parameters to indicate differences between MCI which develop AD or FTD in the future, from those which develop vascular dementia or LBD, seemed the usual pace gait characteristics. Particularly, authors attested a decreasing in gait velocity and normalized velocity, and an arising of normalized step per meters in subjects who would have developed vascular dementia or LBD [De Cock et al. (2019)]. The authors state that these findings should be taken into account to develop a uniform test protocol for routine clinical screening. An article published by Goyal et al. investigated how the nature of a secondary task, motor or cognitive, affects subjects' gait in a dual-task protocol, even if the use of motor-motor paradigms is still controversial [McIsaac et al. (2015)]. The authors found evidence of differences in gait performance between MCI and HOA subjects, even in a single task. Furthermore, the gait of both MCI and healthy subjects was affected by both the procedures (motor-motor and motor-cognitive). Generally, MCI subjects walked slower than HOA participants, and shown a increased cadence and, therefore, a diminished step and stride length. Moreover, motor-motor task and MCDT heavily affects MCI gait in all parameters, and that trend is also reflected by the computation of DTC. Is worth to report that, in some cases (step and stride length) significant differences have been founded also between motor-motor task and MCDT, proving that the combination of cognitive and motor task requires much more effort than just the augmentation of motor complexity [Goyal et al. (2019)].

Similarly, Hunter et al. were interested in understanding how different auxiliary tasks, motor or cognitive, could affect the gait of the subjects. The authors found evidence of MCI gait was affected by both secondary tasks. Notwithstanding, they influenced gait velocity and DTC differently. The choice of the secondary task performed, in terms of nature and content, is essential in the

authors' opinion. This because different tasks challenge different cognitive domains. Therefore, some subjects may be proficient with serial subtractions by sevens yet compromised with a semantic memory task. Thus the authors proposed a framework to guide clinicians in choosing tools to progressively increase the cognitive challenge to ensure that patients are working at or close to the capacity to uncover deficits. Similarly to the aforementioned works, the authors reports significant changing in gait velocity and DTC between groups (MCI and HOA), along with the increasing difficulty of motor task (walking), motor-motor task (walking while carrying a glass full of water), MCDT (walking and counting backwards or naming animals), and "MCDT + motor task" (walking while counting backwards or naming animals, and at the same time carrying a glass full of water). Moreover, on the basis of within groups statistical differences on these gait metrics (velocity and DTC), the authors were able to stratified the exercises in three complexity levels for HOA, and five levels MCI people. Thus, defining a taxonomy for expanded MCDT in HOA and MCI [Hunter et al. (2018)].

Naidu et al. proposed a remarkable application of MCDT, in which the authors try finding differences in gait parameters between MCI subjects and Depressed people. Three groups of subjects were analyzed, MCI subjects, people with a diagnosis of late-life depression (LLD), and a control group. The authors found evidence suggesting that both LLD and MCI have a clinically significant effect due to dual-task, but to different sizes. Interestingly, the gait velocity at the baseline did not differed from one group to another. On the contrary, MCDT (naming animals) velocity was able to differentiate MCI people from HOA, while was not informative in distinguishing LLD from MCI or even LLD from HOA. The most important data is related to the DTC of gait velocity, respectively 12% for LLD subjects, 22% for MCI patients, and 2% for the controls. The comparison among these values report statistically significant difference, therefore it seems that the computation of such a metrics would be useful to highlight varying degrees of similar underlying neuropathological changes that could influence executive functions and cognition-mobility interaction, and that are shared by

LLD and MCI subjects [Naidu et al. (2019)].

So far, we reviewed researches concerning standard MCDT, namely walking while performing a secondary task. Differently, Pieruccini-Faria et al. assessed the MCI ability to negotiate with obstacles. The authors found evidence that MCI performed fewer anticipatory gait adjustments when approaching an obstacle. Particularly, the authors report that even if there is an overall effect of MCDT gait velocity, both for HOA and MCI, if late gait phase (the part of gait in which adjustments for obstacle negotiation should occur) were took into account, only HOA show modification (both for gait velocity and step length variability). On the other hand, MCI did not show any kind of interaction between cognitive effort, due to a MCDT, and motor adjustments in the late phase of the gait. The authors state that executive function impairment may play a role in this phenomena and could cause an improper assessment of environmental hazards [Pieruccini-Faria et al. (2019)]. This study expands the concept suggested by Montero-Odasso that gait problems in MCI increase if frontotemporal brain networks were overstimulated [Montero-Odasso et al. (2014), Montero-Odasso et al. (2017)]. The authors affirm that cognitive deficits affect not only the capability of walking but also the ability to estimate balance hazards when navigating.

Neuroimaging is another tool recently adopted in combination with quantitative MCDT methods to assess the motor-cognitive interface. Anneweiler et al. observed a relationship between the decrement of gait velocity and a higher level of choline/creatine in MCI subjects. Also, these subjects showed a smaller primary motor cortex volume. Otherwise, a greater CoV seems to be associated with lower N-acetyl aspartate/creatine and with a smaller primary motor cortex volume.

Similarly, Sakurai et al. analyzed changes in entorhinal cortex volume associated with DTC in different groups of MCI. The authors compared a group of amnestic MCI single domains (a-MCI-sd) to a group of amnestic MCI multiple domains (a-MCI-md). Notably, the a-MCI-md represents a population with a higher risk of developing dementia. The authors found evidence of a lower vol-

ume of the left entorhinal cortex associated with slower dual-task gait velocity in all MCDT conditions and a higher DTC cost in counting backwards by 1 and by 7 [Sakurai et al. (2018)].

A singular work is a recent paper by Snir et al. The authors assessed forty-three MCI subjects using standardized assessment of cognitive domains, gait performance (ST and DT), and white matter integrity (WMI), using a 3 Tesla diffusion tensor imaging (DTI). Authors have examined either macro-structural imaging characteristics (white and gray matter), and micro-structural WMI parameters, and they try associating them with falls and gait performances. Authors report that multiple white matter (WM) tracts, encompassing corpus callosum, forceps minor, and left inferior fronto-occipital fasciculus, were significantly associated with lower dual-task gait performance. Therefore, the authors' conclusion highlights the requirement to analyze also WM tracts and their integrity, particularly those involved in executive and visuospatial functions [Snir et al. (2019)].

Differently, Crockett et al. investigated connectivity changes in the default mode network (DMN) and supplementary motor area (SMA) associated with MCDT performance in MCI. The authors reported a significant correlation between mean DMN functional connectivity and DTC. Furthermore, the mean functional connectivity resting state between DMN-SMA networks correlated significantly with gait speed, as well as postural sway under the eyes open floor condition [Crockett et al. (2017)].

Another application of the quantitative MCDT for MCI subjects is the gain that such procedures would furnish evaluating the effectiveness of pharmacological and non-pharmacological trials. Gschwind et al. discussed the benefits of Ginko Biloba Special Extract LI-1370 (GBE) on cognitive and motor performances in a sample composed of MCI. The authors state that MCDT represents a reliable tool for the assessment of the GBE's effect.. A possible explanation of such benefits could be related to the impact on memory performance, which is associated with gait rhythm and, which, in turn, directly affects the rhythmic component of counting [Gschwind et al. (2017)].

In conclusion, Montero-Odasso et al. addressed the effect of donepezil on gait

and balance in MCI subjects. The authors found evidence that the donepezil does not affect single task gait performance after six months of trial. Notwithstanding, they observed a trend for the group treated with donepezil, who improved MCDT gait velocity (counting backwards by 1 and by 7, and also naming animals), and in the respective DTC (counting backwards by 1 and by 7). Furthermore, they report also a trend of decreasing of gait variability in the experimental group. The authors report that cholinesterase inhibitors may improve gait performance by cognitive enhancement and also by non-cognitive-mediated pathways. Cognitive functions and neural control of gait share brain cortical networks and neurotransmitters. One of them is acetylcholine that has a critical role in cognitive functions and in controlling gait and balance. Therefore, the authors' idea is that reducing its loss in MCI may improve attention and subsequently gait performance under dual-tasking [Montero-Odasso et al. (2019)].

The use of Wearable Sensors in MCDT Assessment for MCI subjects

The nine following articles address the use of wearable sensors in MCDT protocol for the assessment of people with MCI.

Moquet et al. assessed, through the aid of wearable sensors, differences among healthy older adults, MCI, and AD. They reported that under the dual-task condition the gait velocity among all the groups were different. Moreover, MCI subjects shown decreased gait stride frequency if compared to healthy controls. On the contrary, MCI subjects shown more regularity in walking and less errors in the cognitive part (namely, counting backwards) of the task if compared with AD subjects. Interestingly, studying how the MCDT influence performance within groups, is worth to report that MCI performances were heavily disrupted by the adding of a secondary cognitive task, even more than the AD performances. In fact, only the stride frequency parameters changed from single to dual-tasking in AD subjects, whereas the velocity of gait, the stride frequency, the stride length and the symmetry of walking were affected in MCI subjects under MCDT condition [Maquet et al. (2010)]. Koenig et al. presented

analogous research, in which they compared healthy controls to MCI and AD subjects. The authors reported that dual tasking negatively affected the gait velocity of all the participants, and also, they found differences between the single-task and MCDT condition between healthy elderly and clinical subjects, both MCI and AD. Not only gait velocity differed between single and dual task conditions, but also the cadence of the gait. In fact, all participants showed a decrease of gait cadence in the MCDT condition, and this difference was even more strong concerning the clinical groups. On the contrary, the step variance remain constant also under the MCDT condition. Conclusively, the authors suggested that changes in gait induced by MCDT could be too subtle to be identified by a wrist-worn actigraph [König et al. (2017)].

Differently, Doi et al. compared MCI subjects with and without white matter loss (WML). The authors found evidence that WML was associated with trunk stability for MCI during the MCDT. In fact, significant statistical differences were founded in all gait variables under normal walking and MCDT condition between groups. Moreover, the subjects that showed an higher level of WML showed also a significant decrease of gait velocity and harmonic ratio under both the conditions [Doi et al. (2015)].

Conversely, Gillain et al. were interested in understanding which variable between gait speed and gait variability was more reliable to define the risk of MCI subjects in developing dementia. Two groups of MCI were compared: MCI, who developed dementia within five years from MCI diagnosis (MCI+), and MCI, who do not (MCI-). All the MCI subjects have shown better performances in a single-task if compared with MCDT. Notwithstanding, The MCI+ shown the lower velocity of gait (both in single and MCDT) and less gait symmetry in MCDT, than the MCI-. Moreover, the regularity of the gait was lower in MCI+ that in MCI-, but in this case, the difference was not statistically significant [Gillain et al. (2016)].

Matinez-Ramirez et al. studied the possibility of using MCDT for the identification of frail subjects with and without MCI. The authors reported that, if on one side, MCDT seems to be a reliable method for discriminate frail patients

from controls (statistical differences among several gait parameters, such as gait velocity, step and stride regularity and step time variability), on the other hand, the approach was not able to spot cognitive impairment in frail subjects. The only differece accounted concerned the stride regularity between fMCI and MCI. The authors suggested that the absence of differences may indicate that frailness and MCI were distinct entities within the same spectrum. The authors state that naming animals could determine a cognitive effort able to influence motor function more than counting backward by one. The authors suggest that the arithmetical task could be more mechanical, while the verbal dual-task represents an improvised performance [Martínez-Ramírez et al. (2016)].

Another crucial work is the research of Auvinet et al., in which the authors aimed at identifying MCI's motor phenotype using the MCDT approach. The authors studied the kinematics performance of several type of clinical subjects, among which: MCI, subjects with central nervous system pathology, subjects with musculoskeletal disease, or also vestibular disease. First of all, the authors demonstrated that MCI subjects, along with the subjects with central nervous system pathology, showed an higher level of DTC for each walking variables compared to the other groups. Moreover, they identified three motor phenotypes using DTC, for stride frequency and stride regularity. These subjects did not differ from white matter hyperintensities, but with an increased Scheltens score from the first to the third motor phenotype [Auvinet et al. (2017)].

Breakthrough works by Toosizadeh et al. and Ehsani et al. addressed a brand new approach in the field of quantitative MCDT for MCI assessment, namely the opportunity to use upper-extremity functioning (UEF) as a reliable MCDT parameter. Particularly, Toosizadeh et al. aimed at distinguishing healthy controls, MCI, and AD using UEF rather than standard walking MCDT. The authors measured several parameters related to the elbow flexion, among which information about the agility, flexibility and variability of the gesture. Particularly, the flexion number and the sensor-based motion variability parameters, within the normal pace elbow flexion, showed a significant between-group differences. Afterwards, cognitive indexes were developed using multivariate ordinal

logistic models to predict the cognitive status of the subjects using the parameters. The authors reported that the UEF task owns sensitivity and specificity of 0.82 and 0.72 respectively; therefore it may become a rapid tool for cognitive screening. The ratio underlying the research is that muscle strength, reflexive performance, and dynamic balance deficits could excessively influence the ability of walking, whereas elbow flexion is a less musculoskeletal demanding task, which may be more suitable for cognitive assessment [Toosizadeh et al. (2019)].
The work of Ehsani et al. moves a step further in the direction of using UEF in the MCDT approach. A within ANOVA model adjusted with demographic information, UEF dual-task parameters, including speed and range-of-motion variability were significantly higher by 52%, among cognitively impaired impaired participant ($p<0.01$). Logistic models with these UEF parameters plus age predicted cognitive status with sensitivity, specificity, and area under curve (AUC) of 71%, 81% and 0.77 for UEF counting backwards 1. The corresponding values for UEF counting backwards by 3 were, instead, 91%, 73% and 0.81 respectively. The authors state that this work attested the pertinence of using the UEF (the counting backwards by 3) to detect cognitive impairment in older adults, Additionally, the UEF was superior to gait as the motor task component of dual-task [Ehsani et al. (2019)].
Differently from the study listed so far, Liao et al. utilize the MCDT approach neither to identify motor phenotypes in MCI subjects nor to assess their risk of developing dementia, but rather to assess the efficacy of a virtual reality-based physical and cognitive training on MCI subjects. The authors reported that both MCI and HOA showed significant improvements in single-task and in the motor performances of MCDT. However, only the group that used the VR showed improvements in the cognitive part of the MCDT and relatively to the DTC of cadence. Moreover, the VR group showed more improvements than the traditional physical-cognitive training in cognitive performance, such as Trailing-Making Test, and DTC of cadence with borderline significance [Liao et al. (2019)].

Other technologies used in MCDT Assessment for MCI subjects

Here are reported the works in which neither wearable sensors nor electronic walkways were involved in the quantitative MCDT assessment of MCI subjects. Amboni et al. proposed a work in which they aim at differentiating gait patterns in PD-MCI, PD subjects, and controls using an optokinetic system. The authors found evidence that PD-MCIs display specific gait features, as reduced step length and swing time and impairment of dynamic stability if compared to the other groups. The authors affirm that levodopa treatment partially addressed these symptoms, and also that these gait alterations were present both in off and on treatment state respect to PD subjects and controls. These findings support evidence that cognitive loading exerts a detrimental effect on gait performance in PD patients, the magnitude of which is related to the underlying cognitive dysfunction [Amboni et al. (2012)]. Similarly, Charette at al., used a optitrack system to differentiate MCI from HC. Authors adopted a unusual methodology to assess gait performance durign DT, they asked the subjects to approach and descend a 5-step staircase while a simultaneous visual Stroop test was administered. Authors reported the presence of subtle, but significant, differences in movement fluidity and in the cognitive side of MCDT, particularly during the approaching and the transition to descent phases. MCI group also tended to use more the handrails if compared to HC [Charette et al. (2020)]. On the other hand, de Oliveira Silva et al., performed the gait analysis, through the TUG test, of three groups of subjects (HC, MCI, and AD) with a videogrammetry using a low-cost video-camera. Authors report that gait parameters, particularly velocity, captured with the videogrammetry, can be useful to discriminate among HC, MCI and AD subjects, both in single and dual-task [de Oliveira Silva et al. (2020)].

Kikkert et al., using an iPod, aimed at identifying prototypic gait characteristics in MCI, AD, and healthy elderly. The authors built a multivariate model, using Partial Least Square-Discriminant Analysis (PLS-DA). This model, for single tasking, explained the 63% of gait variance in MCI gait. Moreover, the

discrimination of geriatrics patients with and without cognitive impairment was poor, with 57% (single-task) and 64% MCDT of the patients misclassified. The authors state that, while geriatric patients versus HOA walked slower, and less regular they found no differences in gait between geriatrics patients with and without cognitive impairment. The authors affirm that the effects of multiple comorbidities, in such subjects, possibly causes a so-said floor effect. The authors stated, therefore, that the diagnostic power of their method was inadequate due to the sample characteristics. Hence, gait did not deteriorate further, even if tested using the MCDT condition [Kikkert et al. (2017)]. Similarly, Serra-Año et al. assessed HC and two groups of subjects suffering from AD (mildly and severe impaired) through two mobility tests, under ST and DT conditions. Such performances were registered using the Android device's embedded sensors. Firstly, they evaluated the subjects' postural control, further the sit-to-stand, the turning and sit power, and the total time required to complete the TUG test were measured. Authors' finding indicate that AD subjects present impairment in key functional abilities such walk, stay still, turn and sitting, or sit to stand, either at mild or severe stage [Serra-Añó et al. (2019)].

Table 1: | MCDT for Assessment.

Reference	**Study Characteristics (MCI Criteria, number, mean age, %female [if reported]).**	**Inclusion/Exclusion Criteria**	**Neuropsychological Assessment**	**Instrumental Assessment**	**Motor Parameters**
Maquet et al., 2010	**Criteria**: Petersen 2001, Winblad 2004. **Subjects**: HC (14, 74y, 50%), MCI (14, 73y, 50%). AD (6, 74y, 50%).	**Inclusion Criteria**: MCI diagnosis and MMSE >24; **Exclusion Criteria**: mental Retardation, less than 4 y education, brain trauma, epilepsy, cancer, depression, any major systematic disease, any substance abuse, drugs that affect brain function.	**Screening**: MMSE; **Global Cognition**: Mattis Scale; **Memory**: FCSRT **Visual abilities**: ROCF **Attention**: TAP	**Instrument**: Locométrix; tri-axial accelerometer. **Position**: trunk, L3-L4 spinous proces **Acquisition Frequency**: 50 Hz. **Walking Length**: 45 m (no buffer); **Tasks**: walking at usual pace; DT walking: - counting backwards.	Velocity, Stride Freq., Stride Length, Symmetry, Regularity, Stops,

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Muir et al., 2011	**Criteria**: Winblad 2004. **Subjects**: HC (22, 71y, 88%), MCI (29, 74y, 59%). AD (23, 76y, 61%).	**Inclusion Criteria**: recent diagnosis of MCI or AD, aged >65 years old, independent gait. **Exclusion Criteria**: inability to understand English, fall in the previous year, Parkinsonism, any neurological disorder, muscoloskeletal disorder, use of psychotropic drugs, major depression.	**Screening**: MMSE; MoCA; CDR.	**Instrument**: Electronic Walkway (GAITRite). **Walking Length**: 6 m (no buffer); **Tasks**: walking at usual pace; DT walking: - counting backwards by 1. - counting backwards by 7. - animal naming.	Velocity, Stride Time, Stride Time Var, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Amboni et al., 2012	**Criteria**: Caviness 2007. **Subjects**: HC (20, 64y, 50%), PD-MCI (19, 65y, 84%). PD (24, 64y, 83%).	**Inclusion Criteria**: PD diagnosis	**Screening**: MMSE; **Global Cognition**: 10 Point Clock Test. **Memory**: 15 Rey's Words. **Ex. Functions**: Phonemic Fluency; FAB; Stroop Test. **Visuospatial**: Spatial Span; Constructive Apraxia; PM 47.	**Instrument**: Optokinetic System (Qualisys). **Acquisition Frequency**: 240 Hz. **Walking Length**: *not reported*; **Tasks**: walking at usual pace; DT walking: - counting backwards by 7. - carrying 2 glass filled.	Step Lenght, Stance Phase, Swing Phase, S/D Support T R, Cadence, Velocity, Step Lenght Var, Swing Time Var.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Montero-Odasso et al., 2012	**Criteria**: Winblad 2004. **Subjects**: HC (25, 72y, 88%), a-MCI (43, 75y, 56%).	**Inclusion Criteria**: recent diagnosis of MCI, >65 y old, able to walk **Exclusion Criteria**: inability to understand English, parkinsonism neurologic disorder muscoloskeletal disorders, knee or hip replacement, use of psychotropic drugs, major depression.	**Screening**: MMSE; MoCA; CDR. **Memory**: Costumized test.	**Instrument**: Electronic Walkway (GAITRite). **Walking Length**: 6 m (no buffer). **Tasks**: walking at usual pace; DT walking: - counting backwards by 7. - naming animals.	Velocity, Stride Time, Stride Time Var, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Annweiler et al., 2013	**Criteria**: Petersen 1999. **Subjects**: MCI (20, 76y, 30%).	**Inclusion Criteria**: diagnosis of MCI, **Exclusion Criteria**: diagnosis of a terminal illness, life expectancy ¡12 months, pending nursing home placement, arthroplasty within 6 months, inability to walk, use of walking aids, dementia.	**Screening**: MMSE; MoCA.	**Instrument**: Electronic Walkway (GAITRite). **Walking Length**: 6 m (no buffer). **Acquisition Frequency**: 60 Hz. **Tasks**: walking at usual pace; DT walking: - counting backwards by 7.	Velocity, Stride Time Var, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Boripuntakul et al., 2013	**Criteria**: Petersen 2001. **Subjects**: HC (30, 71y, 66%), MCI (14, 71y, 66%).	**Inclusion Criteria**: being able to walk for at least 10 m, being able to follow instructions. **Exclusion Criteria**: neurological conditions, acute and/or chronic disease, depressive symptoms, uncorrected visual impairments, uncorrected hearing impairments, alcohol use ¡6 hours before testing, taking drugs that affect gait.	**Screening**: MMSE, MOCA; **Memory**: Logical Memory; **Attention**: Digit Span; **Ex. Function**: TMT (A-B); **Language**: Animal Fluency; **Visualspatial**: Block Design.	**Instrument**: 1) Electronic Walkway (GAITRite). **Walking Length**: 6 m (no buffer). **Instrument**: 2) Costumized footswitch system **Acquisition Frequency**: 100 Hz. **Tasks**: walking at usual pace; DT walking: - counting backwards by 3.	Swing Time, Swing Time Var., Step Time, Step Time Var., Step Length, Step Length Var., Step Width, Step Width Var.

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Montero-Odasso et al., 2014	**Criteria**: Petersen 1999. **Subjects**: HC (35, 70y, 83%), a-MCI (42, 77y, 43%). na-MCI (22, 74y, 64%).	**Inclusion Criteria**: age > 65 years old, ability to walk independently. **Exclusion Criteria**: No English proefficiency, Parkinsonis, Neurologic Diseases, Knee-Hip replacement, Muscoloskeletal Dis, Major Depression, Use of Psychotropics.	**Screening**: MMSE, MOCA; **Memory**: Rey AVLT; **Attention**: Digit Span; **Ex. Function**: TMT (A-B); **Working Memory**: Letters-Numbers seq.; **Language**: BNT.	**Instrument**: Electronic Walkway (GAITRite). **Walking Length**: 6 m (no buffer). **Tasks**: walking at usual pace; DT walking: - naming animals; - counting backwards by 7.	Velocity, Stride Time Var., DTC.

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Doi et al., 2015	**Criteria**: Petersen 2001/2004. **Subjects**: WML MCI (109, 76y, 47%), no-WML MCI (451, 72y, 46%).	**Inclusion Criteria**: willing participate, autonomy. **Exclusion Criteria**: uncorrected visual impairment, neurologic pathology, orthopedic surgery, depression, drugs that influence gait.	**Screening**: MMSE, **Global Cognition**: NCGG-4D.	**Instrument**: MVP-RF8 (accelerometer and gyroscope). **Position**: 1) trunk, L3 spinous process; 2) right heel. **Acquisition Frequency**: 200 Hz; **Walking lenght**: 11 m (2 m buffer). **Task**: walking at usual pace; DT walking: - counting backward by 1.	Velocity ST, Velocity DT.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Gillain et al., 2015	**Criteria**: Petersen 2001. **Subjects**: MCI conv. (9, 74y, 44%); MCI no conv. (4, 70y, 50%).	**Exclusion Criteria**: cerebrovascular disease, parkinson, depression, connective tissue disease, heart pacemaker, severe vision impairment, severe hearing impairment, depressive, contradiction of exe. by a doctor.	**Screening**: MMSE, **Global Cognition**: Mattis. **Memory**: Grober & Bushke.	**Instrument**: Locométrix (accelerometer), **Position**: trunk, L3-L4 spinous process; **Acquisition Frequency**: 50 Hz; **Walking lenght**: 50 m (10 m buffer). **Task**: walking at usual pace; DT walking: - counting backward by 1.	Velocity, Regularity, - Symmetry.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Martinez-Ramirez et al., 2016	**Criteria**: Winblad 2004. **Subjects**: HC (10, 88y, 60%); MCI (11, 92y, 73%); Frail (20, 93y, 70%).	**Exclusion Criteria**: presence of dementia, disability, inability to walk independently.	**Screening**: CDR, **Global Cognition**: CERAD. **Ex. Function**: TMT (A,B).	**Instrument**: Orientation Tracker MTx, **Position**: trunk, L3 spinous process; **Walking lenght**: 7 m (2 m buffer). **Task**: walking at usual pace; DT walking: - naming animals, - counting backward by 1.	Velocity, Step Regularity, Stride Regularity, Step Time Var.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Auvinet et al., 2017	**Criteria**: Gait Instability Network. **Subjects**: MCI (24,*not rep.*, 14%).	**Exclusion Criteria**: lack of French, education ¡4 y, institutionalization, acute medical condition, hospitalization within 6 months, depression,	**Screening**: MMSE.	**Instrument**: Locométrix accelerometer. **Position**: trunk, L3-L4 spinous process; **Acquisition FrequencY**: 50 Hz. **Walking lenght**: 30 m (no buffer). **Task**: walking at usual pace; DT walking: - counting backward by 1.	Velocity, Stride Frequency, Stride Regularity DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Crockett et al., 2017	**Criteria**: Aggarwal 2006. **Subjects**: MCI (40, 76.6y, 53%).	**Inclusion Criteria**: >60 years; MoCA >26/30; had SMC; MMSE 24/30; ADL 6/8; right hand dominant; living independently; visual acuity 20/40. **Exclusion Criteria**: neurodegenerative disease, stroke, dementia, psychiatric condition, peripheral neuropathy, musculoskeletal disease, psychotropic medication, carotid sinus sensitivity, living in a nursing home, were ineligible for (MRI).	**Screening**: MMSE, MoCA.	**Instrument**: Electronic Walkway (GAITRite). **Walking Lenght**: 4 m (2 m buffer); **Task**: walking at usual pace; DT walking: - counting backward by 7.	Velocity, DTC.

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
De Cock et al., 2017	**Criteria**: Albert 2011. **Subjects**: HC (78, 75y, 54%), MCI (140, 79y, 63%), mild AD (222, 81y, 55%), moderate AD (96, 83y, 74%).	**Exclusion Criteria**: dementia, unable to walk 10 meters, living at home.	**Screening**: MMSE, ACE-R. **Global Cognition**: WAIS-IV	**Instrument**: Electronic Walkway (GAITRite). **Walking Lenght**: 6 m (no buffer); **Task**: walking at usual pace; walking at fast pace; walking at slow pace; DT walking: - naming animals, - counting backward by 2.	Velocity, Normalized Velocity, Step Length, Swing Time Var, DTC.

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Gschwind et al., 2017	**Criteria**: Winblad 2004. **Subjects**: MCI EG (25, 67.8y, 60%), MCI CG (25, 69.2y, 40%).	**Inclusion Criteria**: Aged 50–85 years, German-speaking, Completed elementary school, gait velocity of >10% DT vs ST, no dementia, MCI diagnosis. **Exclusion Criteria**: antipsychotic treatment, warfarin-like treatment, diagnosed psychiatric disorders, impaired gait, neurologic disorders, took part to a clinical trial within 2 months, use of a walking aid, habitual gait velocity ¡100 cm/s.	*Not reported*	**Instrument**: Electronic Walkway (GAITRite). **Walking Lenght**: 10 m (no buffer); **Task**: walking at usual pace; DT walking: - naming animals, - counting backward by 2.	Velocity, Cadence, Stride Time Var., Base of Support.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Kikkert et al., 2017	**Criteria**: Papegaaij 2014. **Subjects**: MCI (29, *not rep.*), AD (10, *not rep.*), Unimp. Patients (31, *not rep.*), Older Control (25, *not rep.*).	**Inclusion Criteria**: age 65 or older. **Exclusion Criteria**: inability to walk, neurodegenerative disorders, inability to speak Dutch, mobility disability, limiting leg functioning.	**Screening**: MMSE. **Global Cognition**: Clock Drawing test. **Memory**: 7-min Screen. **Language**: Animal Fluency. **Ex. Function**: Benton's test, Enhanced Cue Recall.	**Instrument**: IPod touch G4. **Position**: Trunk, L3 spinous process; **Walking Lenght**: 3 min on 10 m platform; **Task**: walking at usual pace; DT walking: - phonetic fluency.	Velocity, Acc. Amplitude Var., Index of Harmonicity, Cross-Sample Entropy, Step Regularity, Stride Regularity, Symmetry Multi-Scale Sample Entropy, Trunk Acceleration, Stride Frequency Var.,

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Koening et al., 2017	**Criteria**: Petersen 1999. **Subjects**: HC (22, 73y, 75%), MCI (24, 75y, 67%), AD (23, 77y, 48%).	**Inclusion Criteria**: MCI diagnosis. **Exclusion Criteria**: history of head trauma, history of lower limb surgery, arthritis, obesity, use of benzodiazepines, use of antipsychotics, psychotic, aberrant motor activity.	**Screening**: MMSE. **Ex. Function**: FAB, TMT (A, B).	**Instrument**: CE-marked accelerometer prototype. **Position**: Wirst. **Walking Lenght**: 20 m (no buffer). **Task**: walking at usual pace; DT walking: - counting backwards by 1.	Velocity, Cadence, Step Var.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Montero-Odasso et al., 2017	**Criteria**: Petersen 1999. **Subjects**: MCI (85, 75y, 51%), MCI Conv.(27, 79y, 43%).	**Inclusion Criteria**: age 65 years and older, able to walk 10m, MCI diagnosis. **Exclusion Criteria**: lack of English proficiency, parkinsonism, neurologic disorder, musculoskeletal disorders, use of neuroleptics, benzodiazepines, depression.	**Screening**: MMSE, MoCA. **Ex. Function**: TMT (A, B). **Memory**: RAVLT. **Language**: BNT. **Attention**: Digit Span. **WM**. Letter-Number Test.	**Instrument**: Electronic Walkway (GAITRite). **Walking Lenght**: 6 m (2 buffer). **Task**: walking at usual pace; DT walking: - counting backwards by 1. - counting backwards by 7. - naming animals.	Velocity, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Hunter et al., 2018	**Criteria**: Petersen 2001. **Subjects**: HC (41, 72 y, 80%), MCI (41, 76 y, 56%).	**Inclusion Criteria**: diagnosis of MCI, aged >65 years, independent ambulators. **Exclusion Criteria**: lack of English proficiency, Parkinsonism, neurologic disorder, musculoskeletal disorders, knee/hip replacement affecting gait, use of psychotropics, depression.	**Screening**: MoCA, CDR.	**Instrument**: Electronic Walkway (GAITRite). **Walking Lenght**: 6 m (2 buffer). **Task**: walking at usual pace; DT walking: - counting backwards by 1. - counting backwards by 7. - naming animals. - carrying a glass. - 1 serial and carrying a glass. - 7 serial and carrying a glass.	Velocity, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Pieruccini-Faria et al., 2018	**Criteria**: Petersen 2001. **Subjects**: HC (27, 72y, 33%), MCI (52, 74y, 29%).	**Inclusion Criteria**: > 65 years old, ability of walking 10 m. **Exclusion Criteria**: visual problems not corrected, motor issues due to a stroke, neurodegenerative disease joint osteoarthritis, severe pain affecting gait.	**Screening**: MoCA, CDR; **Ex. Functions**: TMT (A-B), FAB; **Attention**: Digit Span. **Memory**: RAVL; **Language**: BNT.	**Instrument**: Electronic Walkway (Zeno). **Walking Length**: 6 m (no buffer). **Task**: walking at usual pace; DT walking: - counting backwards by 1, (both with and without an obstacle).	Velocity, Step Length Var, DTC.

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Naidu et al., 2019	**Criteria**: Winbald 2004. **Subjects**: HC (23, 69y, 65%). MCI (23, 69y, 65%). LLD (23, 69y, 65%).	**Inclusion Criteria**: Age 60 to 85, Able to read, Able to communicate in English, No hearing Issues, Able to sit for 30-45 m, Able to walk 10 m, No diagnoses of psychiatric illnesses, No dementia, No psychotropic use, No depression. **Exclusion Criteria**: Parkinsonism, neurological disorder, A major medication change, Infarction (within 12 months), stroke (within 12 months), TIA (within 12 months), Head trauma, Gait impairments.	**Screening**: MoCA, MMSE.	**Instrument**: Electronic Walkway (Zeno). **Walking Length**: 6 m (2 m buffer). **Task**: walking at usual pace; DT walking: - naming animals.	Velocity, DTC.

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
De Cock et al., 2019	**Criteria**: NIA-AA. **Subjects**: 71 HC, 122 MCI (CDR= 0.5), 168 Mild Dementia, 54 Moderate Dementia, 18 Severe Dementia	**Inclusion Criteria**: refusing to participate, ¡ 50 years old, severely demented (MMSE ¡ 10), unable to walk without help, living in a nursing home **Exclusion Criteria**: physical frailty, orthopedic prostheses pacemaker gait speed slower than 60 cm/s, swing time variability >30, cycle time variability >1	**Screening**: MMSE.	**Instrument**: Electronic Walkway (GAITRite). **Walking Length**: 6 m (no buffer). **Task**: walking at usual pace; walking at fast pace; walk at slowest pace; DT walking: - counting backwards by 2, - naming animals.	Velocity, Cadence, Step Width, Step Width Var., Swing Time, Number of Steps, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Ehsani et al., 2019	**Criteria**: Arbirtary chosen. **Subjects**: 79 HC (MoCA>20). 21 MCI (MoCA¡20),	**Inclusion Criteria**: > 65 years old, **Exclusion Criteria**: Stroke, Parkinson, Amputation, Major mobility disorders, Upper-extremity disorders.	**Screening**: MoCA,	**Instrument**: BioSensics LLC, gyroscope. **UEF Position**: biceps, wrist. **Gait Position**: Shins. **Acquisition frequency**: 100 Hz **UEF Task**: Normal pace (60 s); DT UEF: - counting backwards by 1 (20 s), - counting backwards by 3 (20 s), **Gait Task**: Normal pace (25 steps), DT Gait: - counting backwards by 1, - counting backwards by 3.	**UEF:** Velocity, Range of Motion, Power, Rise Time, Speed Reduction, Flexion Number, Speed Var., Range of Motion Var. **Gait:** Stride Velocity, Stride Time, Stride Length, Double Support, Stride Velocity Var., Stride Time Var., Stride Length Var.

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Liao et al., 2019	**Criteria**: Arbirtary chosen. **Subjects**: MCI (34, 74y, 68%).	**Inclusion Criteria**: > 65 years and over; able to walk 10 m; MoCA ¡26; Self-reported memory complaints; Ability to perform ADLs. **Exclusion Criteria**: Dementia; Life expectancy ¡ 3 months; Neurological disease; Orthopedic disease; education level ¡6 years.	**Screening**: MoCA, MMSE.	**Instrument**: GAIT Up system. **Position**: Feet. **Acquisition frequency**: *Not reported.* **Walking Lenght**: *Not reported.* **Gait Task**: Normal pace, DT Gait: - counting backwards by 2, - carrying a glass of water.	Velocity, Stride Length, Cadence, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Sakurai et al., 2019	**Criteria**: Windblad 2004, Petersen 2011. **Subjects**: 21 HC; 15 aMCI-sd; 4 aMCI-md.	**Inclusion Criteria**: MCI Diagnosis 3T magnetic resonance imaging . **Exclusion Criteria**: Terminal illness, pending nursing home placement, joint arthroplasty within 6 months, inability to walk 10 m, diagnosis of dementia.	**Screening**: MoCA, MMSE. **Ex. Functions**: TMT (A,B). **Memory**: RAVLT	**Instrument**: Electronic Walkway (GAITRite) **Walking Lenght**: 6 m (2 m buffer). **Task**: Normal pace, DT Gait: - counting backwards by 1, - counting backwards by 7, - naming animals.	Velocity, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Goyal et al., 2019	**Criteria**: *Not reported.* **Subjects**: HC (8, 73y, 62.5%); MCI (8, 78y, 75%).	**Inclusion Criteria**: Objective memory decline, preserved general intellectual function, normal or corrected vision, ability to stand and walk, ability to understand instructions. **Exclusion Criteria**: Neurological impairment, any kind of pain, inability to perform the exp. tasks, and clinical dementia.	**Screening**: MMSE.	**Instrument**: Electronic Walkway (GAITRite). **Walking Lenght**: 6 m (2 m buffer). **Task**: Normal pace, DT Gait: - reciting alphabet skipping two letters, - carrying a glass of water.	Velocity, Cadence, Step Length, Stride Length, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Toosizadeh et al., 2019	**Criteria**: NIA-AA. **Subjects**: HC (35 84y, 63%), MCI (34, 84y, 53%). AD (22, 84y, 50%).	**Inclusion Criteria**: > 65 years old, ability to understand instructions, English language proficiency. **Exclusion Criteria**: diseases with severe motor deficits; severe speech disorders; severe upper-extremity disorders.	**Screening**: MoCA, MMSE.	**Instrument**: BioSensics LLC, gyroscope. **Position**: biceps, wrist. **Acquisition frequency**: 100 Hz **UEF Task**: Normal pace (60 s); DT UEF: - counting backwards by 1 (20 s), - counting backwards by 3 (20 s),	Velocity, Rise Time, Flexion Number, Range of Movement, Speed Variability, Range of Movement Var., Flexion Var.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Montero-Odasso et al., 2019	**Criteria**: Windblad 2004. **Subjects**: MCI Donepezil (31, 74y, 48%); MCI Placebo (29, 77y, 41%).	**Inclusion Criteria**: > 65 years of age, able to walk 10 m, MCI diagnosis. **Exclusion Criteria**: lack of English proficiency, parkinsonism, neurological diagnosis, musculoskeletal disorder, low body weight (¡45 kg), diagnosis of Alzheimer, use of herbal preparations, history of substance abuse, anticholinergic agents, major depression, history of liver diseases, bradycardia, sick-sinus syndrome, previous allergy to donepezil, obstructive pulmonary disease, asthma and history of seizures.	**Screening**: MoCA, MMSE. **Ex. Functions**: Digit Span Test, TMT (A, B). **Working Memory**: Digit Span, Letter-number sequence. **Memory**: RAVLT; **Language**: BNT.	**Instrument**: Electronic Walkway (GAITRite). **Length**: 6 m (no buffer). **Task**: normal pace, DT gait: - counting backwards by 1, - counting backwards by 7, - naming animals.	Velocity, Gait Var, DTC.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Serra-Añó et al., 2019	**Criteria**: revised NINCDS-ADRDA 2007. **Subjects**: HC (22, 76y, *not rep.*); Mild AD (18, 77y, *not rep.*); Moderate AD (22, 80y, *not rep.*).	**Inclusion Criteria**: able to walk 10 m, availability to participate. **Exclusion Criteria**: motor alterations after stroke, neurological disorders, uncorrected visual disorders, uncorrected auditory disorders,	**Screening**: CDR.	**Instrument**: Android Device FallSkip System® **Position**: posterior superior iliac crests **Acquisition frequency**: 100 Hz **Length**: 3 m + 3m (no buffer), turn & sit, stand & walk, (TUG). **Task**: normal pace, DT gait: - telling a story.	Total time Reaction time **Postural Control**: Medio-lateral displacement Antero-posterior displacement **Gait analysis**: Vertical range Medio-lateral range **Turn-Sit-Stand**: Turn-to-sit power Sit-to-stand power

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Snir et al., 2019	**Criteria**: Windblad 2004. **Subjects**: MCI (43, 75y, 42%);	**Inclusion Criteria**: able to walk independently for 10m **Exclusion Criteria**: Parkinsonism, other motor deficits, major depression, Use of neuroleptics, Use of benzodiazepines musculoskeletal disorders, joint disorders.	**Screening**: MoCA, MMSE.	**Instrument**: Electronic Walkway (GAITRite). **Length**: 6 m (2m buffer). **Task**: normal pace, DT gait: - counting backwards by 1, - counting backwards by 7, - naming animals.	Velocity.

Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Charette et al., 2020	**Criteria**: Petersen 2004. **Subjects**: HC (23, 71y, *not rep.*) MCI (11, 73y, *not rep.*);	**Inclusion Criteria**: *not reported* **Exclusion Criteria**: alcoholism, substance abuse, color blindness, physical problems, neurological problems, cardio-respiratory problems, walking speed < 1 m/s, visual acuity $< 20/30$.	**Language** BTN **Executive functions** TMT Stroop's test WSCT **Attention** TEA CCP II **Working memory** Brown Peterson Paradigm	**Instrument**: Optotrak system (3020, NDI). **Acquisition frequency**: 50 Hz **Length**: staircase of 5 steps **Task**: normal pace, DT gait: - Stroop test,	Velocity Fluidity Min. foot clearance uni/bilateral handrail use DTC

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Table 1: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
De Oliveira Silva et al., 2020	**Criteria**: ICD-10 DSM-5 **Subjects**: HC (17, 71y, 100%) MCI (23, 77y, 52%) AD (23, 78y, 61%);	**Inclusion Criteria**: ¿60 years old resident in Rio de Janeiro MCI diagnosis AD diagnosis no other mental illness **Exclusion Criteria**: illiterate elderly NYHA class III-IV psychological comorbidities physical comorbidities visual impairments auditory impairments cerebrovascular infraction electroconvulsive therapy psychotherapy severe AD	**Screening** CDR MMSE	**Instrument**: video camera (SONY HDR-CX 190). **Acquisition frequency**: 30 Hz **Length TUG**: 3 m + 3 m (no buffer) **Task**: speed pace, DT gait: - Naming animals	Step length Stride length Velocity Cadence Symmetry

Motor and Cognitive Dual-Task Inspired by Neuropsychological Test

This section encompasses five out thirty-eight articles analyzed. Three out of five belong by a single research group and addresses the topic using an electronic walkway or similar technology. Conversely, the other researches addressed the issue through the aid of wearable sensors. Hence, this section displayed the works that were interested in apply new technologies for the quantitative assessment of motor performance to standard neuropsychological tests for MCI evaluation. Describing a further step in the development of MCDT. It represents a field understudied, but still extremely wide.

Perrochon et al. addressed the topic of MCDT in the context of neuropsychological testing, using both standard electronic walkways and customized wireless tapestry with force sensors. The authors aim at assessing memory impairment of MCI through a modified version of the Corsi's test (MWCT). The authors reported that the span scores obtained on the MWCT and in the standard Corsi's test were significantly lower in the HAO than in young controls. Furthermre, they reported that the MWCT appeared more complex than the standard one, but no differences were reported comparing MCIs to healthy older people. The qualitative analysis outlined different patterns between the controls and MCI. The MCI, in fact, demonstrated a higher number of random sequence, whereas the healthy elderly subjects appeared to use the most appropriate strategy [Perrochon et al. (2014)]. Further, Perrochon et al. aim at the developing of a "Walking Trail-Making Test" (WTMT) for the early detection of MCI. A cluster analysis, on the basis of locomotor performances at the WTMT, reveled the presence of three groups of subjects: HOA, amnestic MCI, and dysexecutive MCI. The authors reported that the WTMT has high sensitivity (78%) and specificity (90%) in recognizing the dysexecutive MCI, whereas it showed still high but lesser sensitivity and specificity in identifying the beginning of this impairment [Perrochon & Kemoun (2014)]. In addition, a recent work by the same authors describes a modified version of the Stroop test called: "Stroop Walking Test". The authors state that this MCDT was able to

outline abnormalities of several gait parameters, in the comparison of cognitive impaired and non-impaired subjects. MCI group made a higher number of mistakes compared to the control group. In conclusion, the authors report that this tool can identify global cognitive impairment and decline in executive functions with high sensitivity (89%) and specificity (87%) [Perrochon et al. (2015)].

In a recent work, Zhou et al. applied the quantitative MCDT to try re-innovating the TMT neuropsychological test (iTMT) and for using that in order to identify people with a-MCI. The highest effect size for separation between groups with and without cognitive impairment was obtained using $\text{iTMT}_{\text{number-letter}}$. Pairwise comparison suggested strong effect sizes between AD and healthy, and between a-MCI and AD. Moreover, significant correlation was observed when comparing $\text{iTMT}_{\text{number-letter}}$ with MoCA and standard TMT. In addition, the authors suggest that iTMT is more sensitive tool to identify motor-cognitive impairment compared to its standard version [Zhou et al. (2017)]. Conclusively, Fiorini et al. conducted similar research in which they proposed a modified TAP sustained attentional task, in which the participants had to walk and in the meanwhile perform a cognitive demanding task. The authors, studying only the cognitive output of the test, affirm that the traditional TAP subtest presents a meaningful correlation with the proposed SmartWalk, for "correct", "error" and "omitted" responses, respecitvely (r=0.54, r=0.34, r=0.39). These results suggest that the two approaches can be comparable in assessing the auditory sustained attention, with the advantage of adding an aerobic exercise to the traditional cognitive task [Fiorini et al. (2019)].

Table 2: | MCDT Mimic Neuropsychological Test.

Reference	**Study Characteristics (MCI Criteria, number, mean age, %female [if reported]).**	**Inclusion/Exclusion Criteria**	**Neuropsychological Assessment**	**Instrumental Assessment**	**Motor Parameters**
Perrochon et al., 2014 (a)	**Criteria**: Petersen 2004. **Subjects**: YHC (15, 25y, 80%); EHC (21, 74y, 76%); MCI (15, 77y, 80%).	**Inclusion Criteria**: > 65 years old, ability to walk. **Exclusion Criteria**: lack of English, Parkinsonism, Any neurologic disorder, Knee/hip replacement affecting gait, Use of psychotropics, Major depression.	**Screening**: MMSE. **Ex. Functions**: FAB, Stroop Test, TMT (A, B). **Global Cognition**: WAIS-IV. **Memory**: Dubois's 5 Word test.	**Instrument**: Wireless tapestry with force sensors. **Dimension**: 250x300 cm. **Task**: normal pace, DT gait: - Modified Walking Corsi's Test	Velocity.

Table 2: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Perrochon et al., 2014 (b)	**Criteria**: Petersen 2004. **Subjects**: YHC (15, 25y, 80%); 11 EHC (*not specified*); MCI (15, 77y, 80%).	**Exclusion Criteria**: Parkinson, Stroke, Clinical osteoarthritis, Myopathy, Neuropathy, Depressive symptoms, Psychotrops.	**Screening**: MMSE. **Ex. Functions**: FAB, Stroop Test, TMT (A, B). **Global Cognition**: WAIS-IV. **Memory**: Dubois's 5 Word test.	**Instrument**: Electronic Walkway (GAITRite). **Length**: 8 m (3 m buffer). **Task**: normal pace, DT gait: - Walking Trail-Making Test	Velocity, Gait Frequency, Walking Cycle Time, Double Support Time.

Table 2: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Perrochon et al., 2015	**Criteria**: Petersen 2004. **Subjects**: YHC (15, 25y, 80%); EHC (21, 73.7y, 76%); MCI (15, 77y, 80%).	**Inclusion Criteria**: Ability to walk, Ability to hear the instructions, Lack of vision problems. **Exclusion Criteria**: Lack of French, Parkinsonism, Neurologic disorder, Musculoskeletal disorders, knee or hip replacement, Use of psychotropic, Major depression.	**Screening**: MMSE. **Ex. Functions**: FAB, Stroop Test, TMT (A, B). **Global Cognition**: WAIS-IV.	**Instrument**: Electronic Walkway (GAITRite). **Length**: 6 m (2 m buffer). **Instrument**: High resolution WebCam. **Acquisition Frequency**: 30 Hz **Task**: normal pace, DT gait: - Stroop Color–Word Paper–Walking Test.	Velocity, Cadence, Cycle Time, Step Length, Double Support Time, Distance.

Table 2: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Zhou et al., 2017	**Criteria**: Petersen 2004. McKhann 2011. **Subjects**: HC (11, 81, 55%); aMCI (10, 85, 50%); AD (9, 81, 22%).	**Exclusion Criteria**: Severe gait impairment, Neurological conditions, Psychiatric condition, Substance abuse, Severe visual impairment, Unwilling to participate.	**Screening**: MoCA. **Ex. Functions**: TMT (A, B).	**Instrument**: Wearable Sensor (LEGSys). **Position**: Left and Right upper and lower legs. **Acquisition Frequency**: 100 Hz **Length**: 20 m (no buffer). **Task**: normal pace, DT gait: - Counting backwards by 1	Ankle Reaching Velocity.

Table 2: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Fiorini et al., 2019	**Criteria**: Petersen 2004. McKhann 2011. **Subjects**: HC (29, 43y, 48%); MCI (20, 75y, 45%);	**Inclusion Criteria**: Diagnosis of MCI, Ability to walk 30 mins, Right foot dominance, Absence of hearing loss, Absence of depression Absence of psychopathological issues, Absence of other neuromotor impairment.	**Screening**: MODA. **Attentio**: TAP.	**Instrument**: Wearable Sensor (SesnFoot V2). **Position**: Right foot. **Acquisition Frequency**: 100 Hz **Length**: 30 minutes. **Task**: DT gait: - Walking performing TAP.	*Not Computed.*

Motor and Cognitive Dual-Task for MCI Stimulation

This section encompasses the articles that intend applying the usage of quantitative MCDT to the stimulation of MCI subjects, namely two out of thirty-eight papers. That makes this section the smallest one in this review. Despite this section represents a melting point, in which wearable sensors, fixed platform, and virtual reality were applied to the quantitative MCDT to create stimulation tools, is difficult to draw a clear picture of the achievement and aims in the topic.

The first article is a work by Schwenk et al., in which authors present a study to evaluate a sensor-based interactive balance MCDT training program for MCI. The participants performed some exercises meant to improve their balance, such as ankle point-to-point reaching tasks and virtual obstacle crossing tasks. The system developed used the data gathered from sensors to provide visual and auditory feedback during balance exercises. The authors report that, after the intervention, the experimental group shows a reduced center of mass sway if compared to control group (p=0.027-0.047), while the effect sizes were moderate to large. Furthermore, fear of falling was significantly reduced in the experimental group if compared to the control one (p=0.015), with high effect size. On the other hand, amelioration in balance and gait speed were present despite not significant if the two group were confronted. In conclusion, the intervention effect was null for stride variability and cognitive performance [Schwenk et al. (2016)].

Similarly, Delbroek et al. examined the effect of MCDT training, using the platform BioRescue, on cognition, balance, and dual-task performance in patients with MCI. A revised version of Time Up and Go (TUG), which took into account motor and cognitive performance, has been used to evaluate the effectiveness of the intervention. Differently from Schwenk et al. work, this virtual reality training showed no significant effect on MCDT performances [Delbroek et al. (2017)].

Table 3: | MCDT for Stimulation.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported]).	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Schwenk et al., 2016	**Criteria**: Petersen 2004. **Subjects**: MCI Control (10, 79, 50%); MCI Intervention (12, 78, 58%);	**Inclusion Criteria**: MCI diagnosis **Exclusion Criteria**: Severe cognitive impairment, Major mobility disorder, Parkinson, Other neurological conditions, Psychiatric condition, Current alcohol/drug abuse, Severe visual impairment, Unwillingness to participate.	**Screening**: MoCA. ADL. **Ex. Functions**: TMT(A, B).	**Instrument**: Wearable Sensor (LEGSys). **Position**: RT/LFT upper/lower legs and back. **Acquisition Frequency**: 100 Hz. **Task**: - ankle point-to point reaching tasks. -virtual obstacle crossing task.	Velocity, Stride Time Var.

Table 3: | Continued.

Reference	Study Characteristics (MCI Criteria, number, mean age, %female [if reported])	Inclusion/Exclusion Criteria	Neuropsychological Assessment	Instrumental Assessment	Motor Parameters
Delbroek et al., 2017	**Criteria**: Nasreddine 2005. **Subjects**: MCI (20, 87.2y, 65%);	**Inclusion Criteria**: Able to walk 10 m. 3 months lived in residential care. MCI diagnosis. **Exlcusion Criteria**: Dementia. Sensory Impairment. Motor Impairment.	**Screening**: MoCA.	**Instrument**: Platform (BioRescue). **Task**: DT: - Memory exercise. - Avoidance whilst walking	TUG Time, Turn Time, Sit-to-stand Time, turn-to-sit Time, Step time before turn.

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Discussion and Conclusions

This review aims to depict the current use of the quantitative approaches to the MCDT on MCI. We collected papers, within 2010 and 2020, which adopted electronic mats, wearable sensors, or even personal devices to assess MCI subjects and try to improve the characterization of such conditions going beyond the standard methodologies, and using a biomechanical approach.

ATN Biomarkers (amyloid-β, tau protein-related markers, and neurodegeneration) are promising to forecast incident dementia - particularly AD -, but they are not accurate enough yet. Indeed, similar degrees of neurological burden may reflect different levels of cognitive impairment. Therefore, the role of *functional markers* is growing faster. Recently, the neuropsychological classification of MCI and AD has been enriched by the employment of new methodologies since cognition is not the only area affected by dementia. So far, there has been a lack of emphasis on non-cognitive symptoms in MCI and early dementia, whereas behavioral and motor issues are prevalent [Qarni & Salardini (2019)]. As highlighted in this review paper, over the last ten years, researchers efforts identified the MCDT as the most common tool to assess the motor-cognitive interface and the interaction between these two spheres. Analyzing all the papers, it is possible identifying and grouping the barriers and opportunities within this research topic. The research community could use such results as a road-map for future studies in this field (see Table 4).

The growing interest in new technologies, above all electronic walkways and wearable inertial sensors, is permitting to enhance its use, moving toward a more quantitative approach in the dementia screening. As reported in Table 4, up to now, the scientific community studying MCDT is more oriented to non-portable technologies (Electronic Walkways and Video-based systems), whereas portable system are less spread. More intensive use of wearable sensors, or personal device, to assess motor performances, especially under DT might make such assessment more ecological, avoiding the 'Hawthorne effect', and allowing an alternative to traditional laboratory-based and clinical assessment of gait.

They may be used in the clinic, but also in free-living, opening a whole new perspective in terms of assessing mobility over extended periods of time while concurrently evaluating traditional and novel measures of quantitative measures of physical activity [Buckley et al. (2019)].

Additionally, up to now, a plethora of movement parameters have been employed for MCI detection and characterization. Particularly, velocity and standard gait/movement parameters have been mostly used (Table 4). Remarkably, only a small part of the researches took into account more complex features, such as power-related or entropy-related gait/movement parameters, or even features related to the movement harmony. Moreover, a specific metric (i.e.Dual Task Cost) has been implemented to furnish information on the effect of cognitive effort on motor performance. Future studies should include a more extensive examination of motor parameters, going beyond the traditional approaches that include standard temporal gait parameters. Furthermore, research efforts should be devoted to investigate their relation to brain structures and functional activation, thus to enhance our knowledge on Motor-Cognitive Interface and to exploit such relation to identifying the neurocognitive disease.

Furthermore, we identified two main areas where quantitative MCDT has been employed: the assessment and the differential diagnosis of MCI subjects - either using the standard MCDT approach and also mimic neuropsychological tests- and the stimulation of cognitively impaired subjects. Regarding the former application, the use of MCDT to mimic neuropsychological tests aims at the improvement of their sensitivity, the specificity, and the ecology. On the other hand, the second area is related to the possibility of providing stimulation protocols, improving both cognitive and motor functioning. This latter application represents a technological and conceptual melting point, in which wearable sensors, virtual reality, and human-computer interfaces are combined. This area is arising a great interest but, up today, represents the more complex and controversial application of quantitative MCDT.

Generally, MCDT protocol provides for a walking task and a simultaneous counting backward (by 1,2,3,7) exercise for the cognitive task. Notwithstanding,

some studies are expanding the framework and using auxiliary motor tasks in addition to the first one (carrying objects or negotiate with obstacles). Furthermore, breakthrough works are moving beyond the well-established gait analysis toward a new approach, called UEF, see Table 4. Monitoring upper-body movements is emerging as a powerful measure complementary to traditional gait analysis, even though, has been mostly applied to Parkinson's Disease [Buckley et al. (2019)]. Considering the wide choice of task combinations, the secondary task should be selected meticulously. It has to be challenging enough to have people working near their limits, but not to cause too much cognitive distress. Recently, McIsaac et al. [McIsaac et al. (2015)] state that an accepted taxonomy of dual-task is becoming indispensable, indeed. New researches on the topic ought to study how different level of cognitive and motor effort would affect each other, in this manner would be possible identify an equilibrium of motor and cognitive demand that will define a sweet-spot for the early diagnosis of MCI.

Eventually, MCDT is an impressive tool to study the Motor-Cognitive Interface. It seems to be remarkably useful in the field of neurodegenerative diseases, such as dementia. In particular, to identify the disease's early onset and to better characterize the patients' profile.

In conclusion, quantitative and objective MCDT data might furnish landmarks to clinicians, enriching the tools they could use and might supply aid for: disease stratification, risk prediction, tracking disease progression, and decision making for intervention optimization and maximizing therapeutic response. Since the breadth of tools that are used to measure motor parameters during MCDT are vast, as are the range of protocols for data collection and the outcome measures that are extracted, there is an urgent need to standardize and harmonize approaches. Moreover, following the big data framework, large cohorts through multi-center studies should be strongly encouraged. That also allows researchers to utilize data mining and machine learning techniques (support vector machines, hidden Markov models, multilayer layer perception, neural networks) to improve accurate diagnosis, disease classification, risk prediction,

and recommendations for future direction.

Table 4: | MCDT Trends, Barriers and Opportunities.

Areas	Trends, Barriers and Opportunities
Application	**Trends:** 2010-2020: Assessment (95%); Stimulation (5%). 2019-2020: Assessment (100%). **Barriers and Opportunities:** The data regarding the percentage of MCDT goals show that they have been -and are- applied mostly on the assessment, instead of the stimulation. Up to now seems particularly difficult use such a technique for subjects stimulation, also because the majority part of the researches are not longitudinal studies. The quantitative study on the effect of MCDT approaches on cognitive/motor MCI stimulation represents a quite unexplored field.
Technology	**Trends:** 2010-2020: Portable Systems (39%) Vs Non-Portable Systems (61%). 2019-2020: Portable Systems (38%) Vs Non-Portable Systems (62%). **Barriers and Opportunities:** The data regarding the percentage of technologies typology used during MCDT show that fixed system have been -and are- slightly preferred. That limits the experimental setting only to laboratory environment. The design, development and use of wearable/portable sensors would enable researchers to evaluate MCDT performances in more ecologically settings.
Dataset	**Trends:** 2010-2020: >50 (47%); 50-70 (26%); 71-100 (16%); >100 (11%). 2019-2020: >50 (38%); 50-70 (38%); 71-100 (16%); >100 (8%). **Barriers and Opportunities:** Either concerning a 10-years time span, or narrowing the search on the last 2 years, a larger part of articles took into account samples with small sizes. Only few recent studies recruited sizable samples: n>100, [see De Cock et al. (2019)]. Large pilot, along with longitudinal study, could clarify the interaction of cognitive and motor spheres, and the usefulness of MCDT paradigms.

Table 4: | Continued.

Areas	Trends, Barriers and Opportunities
Exercise	**Trends:** 2010-2020: Normal Walking (77%); Slow/Fast Walking (5%); TUG (8%); UEF (5%); Other (5%). 2019-2020: Usual pace (58%); Slow/Fast Walking (7%); TUG (14%); UEF (14%); Other (7%). **Barriers and Opportunities:** Even though we are referring to a limited number of papers, is it possible notice a growing interest in new types of motor exercise to study the Motor-Cognitive Interface. Particularly UEF [see Toosizadeh et al. (2019) and Ehsani et al. (2019)], seems to be a promising techniques.
DT Protocol	**Trends:** 2010-2020: 1 Cognitive Lvl. (47%); 2+ Cognitive Lvl. (34%); Additional Exercise & Cognitive Task(s) (18%). 2019-2020: 1 Cognitive Lvl. (38%); 2+ Cognitive Lvl. (46%); Additional Exercise & Cognitive Task(s) (15%). **Barriers and Opportunities:** It is possible to notice that in the last two years the prevalence of studies referring to different levels of cognitive load or even of combination of additional motor tasks and cognitive load is increasing. The systematic analysis of several cognitive loads is paramount to understand how the cognitive loading affects the motor performance. In addition, more ecological cognitive tasks could be useful to engage the Motor-Cognitive Interface in a daily-life manner.

Table 4: | Continued.

Areas	Trends, Barriers and Opportunities
Parameters	**Trends:** 2010-2020: Velocity (21%); DTC (11%); Other Std. Gait Param. (57%); Power-Rel. Param. (3%); Harmony-Rel. Param. (8%). 2019-2020: Velocity (17%); DTC (11%); Other Std. Gait Param. (64%); Power-Rel. Param. (5%); Harmony-Rel. Param. (3%). **Barriers and Opportunities:** Velocity and others standard gait/motor parameters (such as step variability, swing time or stride length), along with the DTC computation, represent the most widely used parameters in the field of MCTD. More complex parameters, related to power/entropy of the movement, or even harmony or fluidity have been seldom studied, even recently. The study of such parameters might enlarge the knowledge about Motor-Cognitive Interface, and enhance the sensitivity and specificity of such approaches in identify MCIs.

Author Contributions

Conceptualization, G.M. and F.C.; Data curation, G.M., L.F.; Formal Analysis, G.M. E.R.; Investigation, L.F., E.R.; Methodology, G.M., E.R.; Supervision; F.C., L.F.; Writing original draft G.M; writing review & editing E.R., L.F. All authors have read and agreed to the published version of the manuscript.

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Highlights

- Motor and Cognitive Dual-Task (MCDT) is becoming a spreading tool for dementia and Mild Cognitive Impairment (MCI) screening.
- Technological solutions can support clinicians performing MCDT protocols, objectifying the screening assessment.
- MCDT approaches deployed through technological solutions are reveled useful either for assessment and stimulation.
- Cognitive and Motor analysis combined can be reliable tools for screening, assessment, and treatment of MCI and dementia, also opening a range of future perspective, related to big data framework, machine learning techniques, and more ecologically assessment