Functional parameters indicative of Mild Cognitive Impairment: a Systematic Review using Instrumented Kinematic Assessment

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Abstract

Background People with mild cognitive impairment (MCI) experience alterations of functional parameters, such as impaired balance or gait. The current systematic review set out to investigate whether functional objective performance may predict a future risk of MCI; to compare functional objective parameters in people with MCI and a control group; and to assess changes in these parameters after different physical activity interventions.

Methods A systematic review of relevant literature was conducted. Literature were searched in PubMed, AMED, CINAHL, EMBASE, PEDro and Web of Science as well as grey literature databases. Cohort studies and Randomized Controlled Trials (RCTs) were included. Quality of reviewed studies were assessed independently by reviewers using quality assessment checklists. Results Seventeen studies met inclusion criteria including people with MCI.

Results from RCTs suggested that gait speed, gait variability and balance may be improved by different physical activity interventions. Cohort studies showed that gait speed,especially in Dual Task (DT) conditions, was the parameter impaired in people with MCI in comparison with a Control Gorup. Furthermore, cohort studies suggested that gait variability could be a predictor of MCI. However, RCTs showed an unclear risk of bias and all studies included in this systematic review reported a low quality of evidence.

Conclusions Studies suggest that gait variability may predict incident MCI, moreover different gait parameters, especially during DT conditions, could be impaired in MCI. These parameters could be improved by some physical activity interventions. Further studies are required to refute our findings.

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Background

From 1990 to 2016 the global healthy life expectancy increased by an average of 6.24 years and with that, morbidity and chronic individual diseases also increased [1-4]. In addition, with people living longer the number of people affected by dementia is increasing [5]. Thus, while dementias affected around 46.8 million people worldwide in 2016 [5], it is expected that in 2050 there will be 115-135 million people suffering from dementia [6, 7]. There is an increase in the interest of mild cognitive impairment (MCI), defined as a clinical stage accounting for cognitive impairment that often precedes dementia [5, 8-17], and whose prevalence in adults of ≥65 years old is 10-20%, increasing this prevalence with age [5,8].

Diagnosis criteria of MCI generally accepted reported that patients with MCI were characterized by an objective impairment of cognition that is often not severe enough to interfere with activities of daily living (ADL), instrumental activities of daily living (IADL) or in social or occupational functioning [5, 8, 10-14, 17-21]. In the same way, Petersen [11] determined that individuals with MCI presented very mild degrees of functional impairment that is difficult to distinguish from the functional problems of cognitively healthy

individuals of the same age. However, people with MCI may have problems in functional tasks [5] and it has been reported that these patients present the alteration of functional parameters, such as mobility, muscle strength, balance, gait dysfunction, or increased risk of falls [8, 22-26]. Decreased gait speed also have been suggested as the mainly altered parameter in older populations [23-25, 27-32] which may be a marker for the preclinical stages of dementia [23, 30-33]. Thus, Doi et al. [34], Eggermont et al. [35] and Deshpande et al. [36] reported that decreased gait speed could be indicative of MCI. Veronese et al. [30] showed an association between decreased gait speed and low performance in the Short Physical Performance Battery (SPPB) and cognitive decline.

Using some functional tests, such as Timed Up Go (TUG), Hand Grip Strength Test (HGST), Sit to Stand Test (STS), or Walking Speed Test (WST), the existence of an association between physical fitness and MCI has been demonstrated [22, 30, 37, 38]. Moreover, Mirelman et al. [39] showed that although there were no differences between people with MCI and cognitively healthy individuals in the overall performance of a functional test, patients with MCI could have functional alterations only identifiable through a kinematic analysis conducted in their case with an inertial sensor. Furthermore, Bahureksa et al. [40] revealed that Kinematic gait parameters such as velocity, stride length, and stride time discriminated best between MCI and cognitively healthy individuals under single task (ST) conditions, increasing discriminative power of gait variables under dual task assessment. Balance parameters such as anterior-posterior and medio-lateral sway position also were identified as significant discriminators [40].

Currently, no drug has been shown to be effective for MCI [8, 17, 18, 41]. Moreover, the overwhelming majority of the focus of treatments are aimed at reducing cardiovascular risk factors and preventing stroke. The combination of aerobic exercise, balance training, cognitive training, the Mediterranean diet and social commitment can help reduce the risk of further cognitive impaiment and may improve cognition, mobility, balance and Quality of life [8, 17, 18, 41-43]. Knowing objective functional parameters that could be impaired in patients with MCI or which could indicate if a person is at risk of mild cognitive impairment is essential to help detect MCI and to develop physical activity interventions that improve functional performance [37]. Kinematic measurements are frequently used by physicians and researchers to quantify normal and pathological movements [44]. Considering this, the main objectives of this systematic review were (1) to examine if functional kinematic parameters may predict a future risk of MCI; (2) to compare these functional objective parameters in people with MCI and a control group; (3) to assess longitudinal changes in these parameters after different physical activity interventions. The secondary objectives were (1) to assess the risk of bias of the included studies using The Newcastle-Ottawa Quality Assessment Scale (NOS) and The Cochrane Collaboration's tool; (2) to assess the level of evidence per outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

Methods

This systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [45]. The PRISMA checklist for this trial is available as supporting document (see online supplementary appendix A). The systematic review protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO: CRD42019119180).

Data sources and search strategy

A systematic search was performed by two independent reviewers (IJ-FA and A-CV) from inception to January, 14th 2019 using optimised search strategies in the following electronic databases: PubMed, AMED, CINAHL, EMBASE, PEDro, Web of Science. An update of the search strategy was carried out in February 2020. A sensitive search strategy using relevant search terms that were developed from Medical Subject Headings (MeSH), and keywords from other similar studies were used: 'mild cognitive impaiment' (MeSH Terms), 'kinetics' (MeSH Terms), 'acceleromet*' (MeSH Terms), 'walking speed' (MeSH Terms), 'Kinematic', 'Kinematic analysis', 'Timed Up and Go', 'TUG', 'gait speed', 'gait speed test' , 'walking speed test', 'short physical performance battery', 'SPPB', 'six minute walk test', '6 minute walk test', 'sit to stand test', 'single leg stance test', 'one leg stance test', 'functional reach test', 'romberg test' and 'functional task´. The complete search strategy report with all search terms is shown online in supplementary appendix B. The grey literature databases, such as New York Academy of Medicine Grey Literature Report, Grey Literature in Health Research and Open Grey were explored to detect any relevant unpublished data. References were exported, and duplicates were removed using citation management software (Mendeley desktop V.1.19.2).

Eligibility criteria

Only studies published in full-text papers were included. Abstracts in conference proceedings, poster presentations, notes or letters to the editor were excluded because they had insufficient detail to be evaluated. Each study had to meet the following inclusion criteria:

1. Cohort studies examining the relationship between functional kinematic parameters obtained by instrumented analysis (e.g., electronic walkways, wearable sensors, camera systems…) and incident MCI or comparing these functional objective paremeters between confirmed MCI and a Control Group formed by cognitively healthy individuals or people with Alzheimer Disease.
2. RCTs assessing longitudinal changes in functional objective parameters after different physical activity interventions.
3. Studies that included people with MCI diagnosed by a specialist or which used validated diagnostic criteria (e.g., Petersen's et al. [11, 12, 14-16], Winblad et al. [13]), supported by a score of 0.5 on the Clinical Dementia Rating (CDR)) [46], < 26 on the Montreal Cognitive Assessment (MoCa) [47, 48], or > 24 Mini-Mental State Examination (MMSE) [48, 49], that permited to confirm the diagnosis of MCI.
4. Studies recruiting participants from any setting (general population, primary, secondary or tertiary care).

5. Studies written in English or Spanish.

The exclusion criteria were as follows:

1. All studies not including a longitudinal design (e.g cross-sectional studies).
2. Studies that included the relationship between functional parameters and incident MCI but did not include a kinematic instrumented analysis.
3. Studies exploring the relationship between functional kinematic parameters and cognitively healthy individuals or people with other neurologic diseases different from MCI.
4. Studies examining the relationship between MCI and other different kinematic parameters such as graphomotor functions, handwriting process variables, etc.
5. Studies that evaluated the relationship between functional kinematic parameters and brain structures in patients with MCI.
6. Studies that did not include validated diagnostic criteria of MCI, did not specify how those patients with MCI were diagnosis or used a diagnosis based on a MMSE score of less than 24, which could be indicative of a greater dementia than the MCI [48-52].

Study selection

All studies identified by the search strategy were screened using the eligibility criteria previously specified. Two independent reviewers (IJ-FA and A-CV) carried out the first stage, which involved the screening of titles and abstracts to identify potentially relevant records. If the reviewers were unable to determine a study's eligibility based on title and abstract, the full text was retrieved. In this first stage, the two reviewers also excluded those documents that were not full-text papers. The same reviewers undertook the second stage, screening those articles that met all inclusion criteria. A short checklist was carried out to the present review in order to guide the selection of relevant studies (see online supplementary appendix C).

Data extraction

Two independent reviewers (IJ-FA and A-CV) extracted the following relevant data from each study: study details (first author, year of publication), study design, length of follow up, sample size and characteristics of participants (mean age, gender), functional assessment or test used to assess functional variables, physical activity intervention, instrument used to kinematic analysis and the methods used to diagnose or assess mild cognitive impairment.

Quality assessment

Two independent reviewers (IJ-FA and A-CV) assessed the risk of bias of the included longitudinal studies using Newcastle Ottawa Scale (NOS) [53]. The NOS is a reliable and valid tool for assessing the quality of non-randomized studies [53] and assigns up to a maximum of nine points for the least risk of bias in three domains: selection of study groups (four points); comparability of groups (two points); and

ascertainment of exposure and outcomes (three points). The risk of bias of the included RCTs was assessed using The Cochrane Collaboration's tool [54]. The Cochrane Collaboration's tool includes seven domain or sources of risk or bias assessment: random sequence generation, allocation concealment, selective reporting, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and other bias. For each domain, the risk is categorized as "low risk", "high risk" or "unclear risk". To assess the overall quality and the strength of the evidence per outcome, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used [55]. In brief, the GRADE classification was carried out according to the presence, or not, of the following identified factors: (i) study design, (ii) risk of bias, (iii) inconsistency of results (iv) indirectness (v) imprecision, and (vi) other considerations (e.g. reporting bias). Two researchers (IJFA and ACV) judged whether these factors were present for each outcome. The GRADE system was applied when each outcome was informed at least by two studies with the same design. The quality of the evidence based on the GRADE criteria is classified as: (1) high (further research is unlikely to change our confidence in the estimate of effect and there are no known or suspected reporting biases); (2) moderate (further research is likely to have an important effect on our confidence in the estimate of effect and might change the estimate); (3) low (further research is likely to have an important effect on our confidence in the estimate of effect and is likely to change the estimate); or (4) very low (we are uncertain about the estimate) [55].

Data synthesis and analysis

It was planned to conduct a meta-analysis of functional kinematic parameters such as gait, balance, posture or mobility, that could be indicative of mild cognitive impairment. However, due to an observed heterogeneity across studies in the type of design, methods of functional assessment, instruments used to conduct a kinemtaic analysis, duration of follow-up, statistical analysis, interventions and data presentation, the statistical pooling of results was deemed not appropriate. Therefore, a meta-analysis of results was not conducted, and a descriptive quantitative analysis was carried out. For this reason, a narrative synthesis of the most relevant summary measure and the main change from baseline was reported.

Results

Study characteristics

A total of 2,239 citations were identified through electronic databases, with 0 additional studies identified through Grey Literature sources. 1157 titles and abstracts were screened, and 277 full-text papers were assessed. The number of studies retrieved from each database and the number of studies excluded in each screening phase are shown in Figure 1. The full reference of excluded studies in the second stage (n= 260) is reported online in supplementary appendix D**.** The conflict of interests of included studies are shown online in suppelementary appendix E. Of these, 17 studies (six RCTs, one pilot RCT study, one pilot cohort study, eight cohort studies and a reliability study) with a total of 478 participants with MCI and 1540 cognitively healthy individuals at baseline, were included in this review. The characteristics of the

included RCTs and the main results are reported in Table 1. The results of cohort studies which compared functional objective paremeters between confirmed MCI and a Control Group are reported in Table 2. The characteristics of cohort studies examining the relationship between functional kinematic parameters obtained by instrumented analysis and incident MCI are showed in Table 3. Functional kinematic parameters were obtained by wearable sensors, tri-axial accelerometers, digital balance platform, motion and contact sensors, cameras and electronic walkways such as the GAITRite (see Table 4). The most frequently used diagnosis criteria of MCI were Petersen criteria (n= 7, 41%) and the combination of the CDR (n= 9, 53%) and MMSE (n= 11, 65%) (see Table 5).

Functional Objective Parameters after physical activity interventions

RCTs showed that Gait speed, Cadence, Stride Length, Smoothness of trunk movement in the vertical direction could be improved by aerobic exercises (60% of aged predicted maximal heart rate), specially when aerobic exercises is performed alongside cognitive exercises or others physical exercises such as muscle strength training, postural balance retraining, or gait training [56, 57, 62]. Stride time and the total time to perform the TUG also could be decreased by the same interventions [56, 57]. Balance training also may decreased the center of mass sway in anterior-posterior and medial-lateral directions [58].

Functional Objective Parameters predicting MCI or discriminating MCI patients from a Control Group

Cohort studies suggested that a decreased gait speed in ST condition and, specially, in DT conditions (counting backwards) was the parameter that best discriminated people with MCI from cognitively healthy individuals [63, 67, 68]. Larger variance in the median gait speed also could discriminate people with MCI from cognitively healthy individuals [64, 67]. However, the total time to perform the TUG and the different subtask of the TUG, was the parameter which best discriminated people with MCI from patients with Alzheimer disease instead of the gait speed, because people with MCI took lower time in performing the TUG [65].

On the other hand, cohort studies showed that larger gait variability, trajectories of weekly gait speed or larger variance of gait speed could predict an incident MCI [70, 71]. Decreased Cadence and Walk-Regularity also were associated with an incident MCI [73].

Methodological quality

The methodological quality assessment of RCTs included is shown online in supplementary Table 6, while the methodological quality assessment of included prospective non-randomized longitudinal studies is presented online in supplementary Table 7. The quality of the evidence based on the GRADE criteria is shown online in supplementary Table 8.

Discussion

Statement of principal findings and Comparision with others studies

The objective of this study was to review the current state of knowledge on the presence of functional Kinematic parameters which may predict a future risk of MCI, could discriminate people with MCI from a control group and could even be improved after different physical activity interventions. To our knowledge, this is the first systematic review that provides a comprehensive overview of longitudinal studies (RCTs and cohort studies) using objective instrumented kinematic assessment of functional task as outcome measures or as parameters which could be impaired in people with MCI or may predict an incident MCI. Furthermore, most of the studies included in this review were published after 2015, which indicates the novelty of the topic [57-63, 65, 68, 70-73].

On the one hand, Cohort studies showed that decreased gait speed in ST condition and, specially, in DT conditions (counting backwards) and larger variance in the median gait speed were the parameters that best discriminated people with MCI from cognitively healthy individuals [63, 64, 67, 68]. These results were in line with some studies that identified a reduced gait speed in people with MCI in comparison with cognitively healthy individuals [25-27, 29, 34, 35]. Bahureksa et al. [40] also revealed that a decreased gait speed could discriminate best people with MCI from cognitively healthy individuals under ST conditions. However, Bahureksa et al. [40] identified others kinematic parameters which may discriminate people with MCI from cognitively healthy individuals such as larger stride length, fewer stride time and larger coefficient of variation of these parameters. Verghese et al. [29] also reported decreased cadence and stride length, larger temporal gait kinematic parameters such as swing phase, stance phase, double support phase and swing time variability, in people with MCI in comparison with cognitively healthy controls. Larger gait variability, above all in DT conditions (counting backwards and naming animals), also seem to be associated with MCI [26]. Furthermore, another systematic review [74] demonstrated slower gait speed, largest variance of gait speed, less level of general activity and more variable day-today pattern of activity in patients with MCI than in cognitively healthy individuals.

On the other hand, cohort studies showed that larger gait variability, trajectories of weekly gait speed or larger variance of gait speed could predict an incident MCI [70, 71]. Decreased cadence and walk-regularity also were associated with an incident MCI [73]. Slower gait speed was slightly associated with incident MCI risk [70] in the present systematic review. However, in most studies a slow gait speed seem to be the main parameter which could predict a future MCI and may be useful in the early detection of MCI [24, 28, 30-33, 36]. Larger time to stand up and sit down 5 times in a chair, worse balance in three balance test such as tandem, semitandem and side-by-side stand positions and poor SPPB performance also could predict the onset of cognitive impairment [28, 30]. Slow gait pace and larger variability also may predict a future risk of cognitive decline and dementia [75]. Other studies also showed that stride time variability in dual task may be a sensitive indicator of cognitive change [26, 76].

In our systematic review, RCTs suggested gait speed, stride length, stride time, balance and the time to perform the TUG may be improved by aerobic exercises (60% of aged predicted maximal heart rate), specially when aerobic exercises is performed alongside cognitive exercises or others physical exercises such as muscle strength training, postural balance retraining, or gait training [56-58, 61]. Nevertheless,

sample sizes were small in most of included studies [56-59, 61,62], the quality and the strength of evidence per outcome was low and the risk of bias was substantial to draw firm conclusions.

Other study showed a limited evidence on intervention effects on stride time variability [77] although this parameter seems to be a important predictor of MCI [58, 61, 63]. It has been demonstrated in other RCTs that the combination of aerobic exercise, balance training and cognitive training could help reduce the risk of further cognitive impairment and may improve cognition, mobility, balance and Quality of life [41, 43]. Furthermore, some Systematic Reviews and Meta-analysis formed by Randomized Controlled Trials also showed that exercise, specifically aerobic and resistance (strength) exercises, join cognitive training could improve cognitive function, activities in daily living and mood [78-81].

Strengths and weaknesses of the study

The strengths of this systematic review included the use of a pre-specified protocol registered on PROSPERO, the PRISMA checklist, the NOS and The Cochrane Collaboration's tool to determine the risk of bias of each study and the GRADE system to evaluate the overall quality and the strength of the evidence per outcome. Furthermore, another strength of this review is that we performed a systematic review using studies only which provided a validated diagnostic criteria of MCI. There are several limitations that should be mentioned. First, despite this review was designed to be comprehensive with a robust search strategy, using a long variety of MeSH terms, and searching in other sources (grey literature), it is possible that some studies were not identified. Second, the lack of uniformity among the study design (e.g. walking distance, variables measured, differents instruments used in kinematic analysis) should be taken into account when interpreting the results. In the literature, it has been demonstrated that participant walking strategy changes with walking distance, resulting in a significant effect on gait variability [82], so walking distance could be highly relevant in order to measure gait variability as a marker for MCI. Furthermore, studies did not report the reliability or validity data of the instruments used in kinematic analysis. Third, reported bias were found in several included studies, especially in clinical trials where the risk of bias in most domains was “unclear”. Moreover, the quality and the strength of evidence per outcome was low. This could also limit the findings of the present systematic review.

Implications for clinical practice

Our results showed that, overall, kinematic gait parameters could be impaired and may predict an incident MCI. This is an important step forward in developing a clinically validated approach for measuring MCI related functional deficits which could predict a future risk of MCI and could even help its early diagnosis, although further studies are required in order to validate the findings of this review. Findings of this systematic review also could be useful for promoting specific interventions aiming reverse early functional changes associated with MCI, since RCTs included in this systematic reviews have demonstrated that physical activity interventions could improve some functional objective parameters.

Implications for further research

Despite the promising results of the present study, some flaws observed in most of the included studies in this review should be resolved. Hence, there are some recommendations to guide future research: (i) studies should use the same instrument to perform the kinematic analysis which would allow a better comparison of data between studies; (ii) these instruments should be valid and reliable as established in the Cosmin taxonomy; (iii) RCTs and Cohort studies with high quality of evidence should be conducted since studies included in this systematic review often showed an unclear risk of bias and a low quality of evidence; (iv) Clinical trials which use functional objective parameters as outcome measures of physical activity interventions in MCI also should be conducted.

Conclusion

Decreased gait speed in ST condition and, specially, in DT conditions and larger variance in the median gait speed are the parameters that best could discriminate people with MCI from cognitively healthy individuals. Slower gait speed, larger gait variability, trajectories of weekly gait speed, larger variance of gait and poor performance of some functional test may predict an incident MCI or could even help its early diagnosis. Some functional objective parameters such as gait speed, stride length, stride time, balance and the time to perform the TUG also may be improved by aerobic exercises when aerobic exercises is performed alongside cognitive exercises or others physical exercises such as muscle strength training, postural balance retraining, or gait training. Nevertheless, further RCTs and cohort studies with high methodological quality are required to confirm our findings, since some studies of this systematic review showed an unclear risk of bias and a low quality of evidence.

Abbreviations

MCI: Mild Cognitive Impairment; **AMED**: The Allied and Complementary Medicine Database; **CINAHL**: Cumulative Index to Nursing and Allied Health Literature; **PEDro**: Physiotherapy Evidence Database; **RCTs**: Randomized Controlled Trials; **DT**: Dual Task conditions; **ADL**: Activities of Daily Living; **IADL**: Instrumental Activities of Daily Living; **SPPB**: Short Physical Performance Battery; **TUG**: Timed Up and Go Test; **HGST**: Hand Grip Strength Test; **STS**: Sit-To Stand Test; **WST**: Walking Speed Test; **ST**: Single Task condition; **NOS**: Newcastle-Ottawa Quality Assessment Scale; **GRADE**: Grading of Recommendations Assessment,Development and Evaluation; **PRISMA**: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **PROSPERO**: International Prospective Register of Systematic Reviews; **MeSH**: Medical Subject Headings; **CDR**: Clinical Dementia Rating; **MoCA**: Montreal Cognitive Assessment; **MMSE**: Mini-Mental State Examination.

Declarations

Ethics approval and consent to participate

Not aplicable-this manuscript does not report on or involve the use of any animal or human data or tissue.

Consent for publication

Not aplicable-this manuscript does not contain data from any individual person.

Availability of data and materials

Not aplicable – this manuscript does not contain any data.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

IJ-FA and A-CV contributed to the conception of this study. IJ-FA and A-CV were involved in the selection of the included studies. IJ-FA, A-CV, B-S, LM-PB, MR-BL and R-GH were involved in the writing and in the review of the manuscript, so all authors have read and approved the manuscript.

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Not Applicable.

References

1. Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, Abdulkader RS, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100): 1260–344.

2. Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, Aboyans V, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100): 1151–210.
3. Wang H, Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, et al. Global, regional, and national under-5 mortality, adult mortality, age-specific mortality, and life expectancy, 1970-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100): 1084–150.
4. Hoffman C, Rice D, Sung HY. Persons with chronic conditions: their prevalence and costs. JAMA. 1996;276: 1473–1479.6.
5. Cornelis E, Gorus E, Beyer I, Bautmans I, De Vriendt P. Early diagnosis of mild cognitive impairment and mild dementia through basic and instrumental activities of daily living: Development of a new evaluation tool. PLoS Med. 2017;14(3): 1–22.
6. Ferretti-Rebustini RE de L, Balbinotti MAA, Jacob-Filho W, Rebustini F, Suemoto CK, Pasqualucci CAG, et al. Validity of the Katz Index to assess activities of daily living by informants in neuropathological studies. Rev Esc Enferm USP. 2015;49(6): 946–52.
7. Limongi F, Siviero P, Noale M, Gesmundo A, Crepaldi G, Maggi S. Prevalence and conversion to dementia of Mild Cognitive Impairment in an elderly Italian population. Aging Clin Exp Res. 2017;29(3): 361–70.
8. Langa K, Levine D. The Diagnosis and Management of Mild Cognitive Impairment: A Clinical Review. J Am Med Assoc. 2014;312(23): 2551–61.
9. Brodaty H, Aerts L, Crawford JD, Heffernan M, Kochan NA, Reppermund S, et al. Operationalizing the Diagnostic Criteria for Mild Cognitive Impairment: The Salience of Objective Measures in Predicting Incident Dementia. Am J Geriatr Psychiatry. 2017;25(5): 485–97.
10. Roberts R KD. Classification and Epidemiology of MCI. Clin Geriatr Med. 2013 Novemb;29(4): 1–19.
11. Petersen RC. Mild cognitive impairment as a diagnostic entity. Jourrnal Intern Med. 2004;256(9): 183–94.
12. Petersen RC, Caracciolo B, Brayne C, Gauthier S, Jelic V, Fratiglioni L. Mild cognitive impairment: A concept in evolution. J Intern Med. 2014;275(3): 214–28.
13. Winblad B, Palmer K, Kivipelto M, Jelic V, Fratiglioni L, Wahlund L-O, et al. Mild cognitive impairment–beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. J Intern Med. 2004;256(3): 240–6.
14. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: Clinical characterization and outcome. Arch Neurol. 1999;56(3): 303–8.
15. Petersen RC, Doody R, Kurz A, Mohs RC, Morris JC, Rabins PV, et al. Current concepts in mild cognitive impairment. Arch Neurol 58: 1985–1992.
16. Petersen R, Morris J. Mild cognitive impairment as a clinical entity and treatment target. Arch Neurol. 2005;62(7): 1160–3.

17. Sachs-Ericsson N, Blazer DG. The new DSM-5 diagnosis of mild neurocognitive disorder and its relation to research in mild cognitive impairment. Aging Ment Heal. 2015;19(1): 2–12.
18. Lin JS, O'Connor E, Rossom RC, Perdue LA, Eckstrom E. Screening for Cognitive Impairment in Older Adults: A Systematic Review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013;(107): 1–403.
19. Risk of dementia and mild cognitive impairment in older people with subjective memorycomplaints: meta-analysis. Mitchell AJ, Beaumont H, Ferguson D, Yadegarfar M, Stubbs B. Acta Psychiatr Scand. 2014 Dec;130(6): 439-51
20. Petersen RC, Knopman DS, Boeve BF, Yonas E, Ivnik RJ, Smith GE, et al. Mild cognitive impairment: Ten years later. Arch Neurol. 2009;66(12): 1447–55.
21. Portet F. Mild cognitive impairment (MCI) in medical practice: a critical review of the concept and new diagnostic procedure. Report of the MCI Working Group of the European Consortium on Alzheimer's Disease. J Neurol Neurosurg Psychiatry [Internet]. 2006[cited 2019 Jan 21];77(6): 714–8. Available from: http://jnnp.bmj.com/cgi/doi/10.1136/jnnp.2005.085332
22. Lee SH, Han JH, Jin YY, Lee IH, Hong HR, Kang HS. Poor physical fitness is independently associated with mild cognitive impairment in elderly Koreans. Biol Sport. 2016;33(1): 57–62.
23. Waite LM, Grayson DA, Piguet O, Creasey H, Bennett HP, Broe GA. Gait slowing as a predictor of incident dementia: 6-Year longitudinal data from the Sydney Older Persons Study. J Neurol Sci. 2005;229–230: 89–93.
24. Buracchio T, Dodge H, Howieson D, Wasserman D, Kaye J. The trajectory of gait speed preceding MCI. Arch Neurol. 2011;67(8): 980–6.
25. Tseng B, Cullum C, Zhang R. Older Adults with Amnestic Mild Cognitive Impairment Exhibit Exacerbated Gait Slowing under Dual-Task Challenges. Curr Alzheimer Res [Internet]. 2014[cited 2019 Feb 12];11(5): 494–500. Available from:http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1567-2050&volume=11&issue=5&spage=494
26. Montero-Odasso M, Muir SW, Speechley M. Dual-task complexity affects gait in people with mild cognitive impairment: The interplay between gait variability, dual tasking, and risk of falls. Arch Phys Med Rehabil. 2012;93(2): 293–9.
27. Gillain S, Warzee E, Lekeu F, Wojtasik V, Maquet D, Croisier JL, et al. The value of instrumental gait analysis in elderly healthy, MCI or Alzheimer's disease subjects and a comparison with other clinical tests used in single and dual-task conditions. Ann Phys Rehabil Med. 2009;52(6): 453–74.
28. Aggarwal NT, Wilson RS, Beck TL, Bienias JL, Bennett DA. Motor dysfunction in mild cognitive impairment and the risk of incident Alzheimer disease. Arch Neurol. 2006;63(12): 1763–9.
29. Verghese J, Robbins M, Holtzer R, Zimmerman M, Wang C, Xue X, et al. Gait Dysfunction in Mild Cognitive Impairment Syndromes. J Am Geriatr Soc. 2009;56(7): 1244–51.
30. Veronese N, Stubbs B, Trevisan C, Bolzetta F, Rui M De, Solmi M, et al. What physical performance measures predict incident cognitive decline among intact older adults? A 4.4 year follow up study. Exp Gerontol. 2016;81: 110–8.

31. Mielke MM, Roberts RO, Savica R, Cha R, Drubach DI, Christianson T, et al. Assessing the Temporal Relationship Between Cognition and Gait: Slow Gait Predicts Cognitive Decline in the Mayo Clinic Study of Aging. J Gerontol Med Sci. 2013;68(8): 929–37.
32. Ojagbemi A, Este CD, Verdes E, Chatterji S, Gureje O. Gait & Posture Gait speed and cognitive decline over 2 years in the Ibadan study of aging. Gait Posture. 2015;41(2): 736–40.
33. Verghese J, Wang C, Lipton RB, Holtzer R, Xue X. Quantitative gait dysfunction and risk of cognitive decline and dementia. J Neurol Neurosurg Psychiatry. 2007;78(9): 929–35.
34. Doi T, Shimada H, Park H, Makizako H, Tsutsumimoto K, Uemura K, et al. Cognitive function and falling among older adults with mild cognitive impairment and slow gait. Geriatr Gerontol Int. 2015;15(8): 1073–8.
35. Laura H. Eggermont, PhD, Brandon E. Gavett, PhD, Karin M. Volkers, MSc, Christiaan G. Blankevoort, MSc, Erik J. Scherder, PhD, Angela L. Jefferson, PhD, et al. Lower-Extremity Function in Cognitively Healthy Aging, Mild Cognitive Impairment, and Alzheimer's Disease. Retrieved Sept. 2007;91(4): 584–8.
36. Deshpande N, Metter EJ, Bandinelli S, Guralnik J, Ferrucci L. Gait speed under varied challenges and cognitive decline in older persons: A prospective study. Age Ageing. 2009;38(5): 509–14.
37. Narazaki K, Matsuo E, Honda T, Nofuji Y, Yonemoto K, Kumagai S. Physical fitness measures as potential markers of low cognitive function in Japanese community-dwelling older adults without apparent cognitive problems. J Sport Sci Med. 2014;13(3):590–6.
38. Ansai JH, Andrade LP De, Nakagawa TH, Assis F, Vale C. Differences in Timed Up and Go Subtasks Between Older People With Mild Cognitive Impairment and Mild Alzheimer's Disease. Motor Control. 2018;1–12.
39. Anat Mirelman, Aner Weiss, Aron S. Buchman, David A. Bennett, Nir Giladi JMH. Association Between Performance on Timed Up and Go Subtasks and Mild Cognitive Impairment: Further Insights into the Links Between Cognitive and Motor Function. J Am Geriatr Soc. 2014;62(4): 673–8.
40. Bahureksa L, Najafi B, Saleh A, Sabbagh M, Coon D, Mohler J, et al. The Impact of Mild Cognitive Impairment on Gait and Balance: a Systematic Review and Meta-Analysis of Studies using Instrumented Assessment. Gerontology. 2017;28(2): 180–7.
41. Han JW, Lee H, Hong JW, Kim K, Kim T, Byun HJ, et al. Multimodal Cognitive Enhancement Therapy for Patients with Mild Cognitive Impairment and Mild Dementia: A Multi- Center, Randomized, Controlled, Double-Blind, Crossover Trial. J Alzheimer's Dis. 2017;55(2): 787–96.
42. Panza GA, Taylor BA, Macdonald H V., Johnson BT, Zaleski AL, Livingston J, et al. Can Exercise Improve Cognitive Symptoms of Alzheimer's Disease? A Meta-Analysis. J Am Geriatr Soc. 2018 Mar;66(3): 487-495.
43. Hagovská M, Olekszyová Z. Impact of the combination of cognitive and balance training on gait, fear and risk of falling and quality of life in seniors with mild cognitive impairment. Geriatr Gerontol Int. 2016 Sep;16(9): 1043–50.

44. Cuesta-Vargas AI, Galán-Mercant A, Williams JM. The use of inertial sensors system for human motion analysis. Phys Ther Rev. 2010;15(6): 462–73.
45. Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gotzsche, P.C., Ioannidis, J.P., Clarke, M., Devereaux, P.J., Kleijnen, J., Moher, D., 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 339, b2700.
46. Morris JC (1993) The clinical dementia rating (CDR): current version and scoring rules. Neurology 43:2412–2414.
47. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc, 2005, 53: 695–699.
48. Ciesielska N, Sokołowski R, Mazur E, Podhorecka M, Polak-Szabela A, Kędziora-Kornatowska K. Is the Montreal Cognitive Assessment (MoCA) test better suited than the Mini-Mental State Examination (MMSE) in mild cognitive impairment (MCI) detection among people aged over 60? Meta-analysis. Psychiatr Pol. 2016 Oct 31;50(5): 1039–52.
49. Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the state of patients for the clinician. J Psychiatry Res. 1975;12: 189–198.
50. Tombaugh TN, McIntyre NJ. The Mini-Mental State Examination: A Comprehensive Review. J Am Geriatr Soc. 1992;40: 922–35.
51. Mitchell AJ. A meta-analysis of the accuracy of the mini-mental state examination in the detection of dementia and mild cognitive impairment. J Psychiatr Res. 2009;43(4): 411–31.
52. Cacho J, Benito-León J, García-García R, Fernández-Calvo B, Vicente-Villardón JL, Mitchell AJ. Does the combination of the MMSE and clock drawing test (mini-clock) improve the detection of mild Alzheimer's disease and mild cognitive impairment? J Alzheimer's Dis. 2010;22(3): 889–96.
53. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. *The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses* [Internet]. 2009 [cited 2019 Feb 19]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
54. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343: d5928.
55. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. BMJ. 2004;328: 1490 doi:10.1136/bmj.328.7454.1490[PMC free article] [PubMed]
56. Doi T, Makizako H, Shimada H, Yoshida D, Tsutsumimoto K, Sawa R, et al. Effects of multicomponent exercise on spatial–temporal gait parameters among the elderly with amnestic mild cognitive impairment (aMCI): Preliminary results from a randomized controlled trial (RCT). Arch Gerontol Geriatr [Internet]. 2013 Jan [cited 2019 Mar 13];56(1): 104–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0167494312002002
57. Laure Combourieu Donnezan, Alexandra Perrot, Sylvie Belleville FB, Gilles Kemoun. Effects of simultaneous aerobic and cognitive training on executive functions, cardiovascular fitness and

functional abilities in older adults with mild cognitive impairment. Ment Health Phys Act. 2018;15: 78–87. doi: 10.1016/j.mhpa.2018.06.001.

58. Schwenk M, Sabbagh M, Lin I, Morgan P, Grewal GS, Mohler J, et al. Sensor-based balance training with motion feedback in people with mild cognitive impairment. J Rehabil Res Dev. 2016;53(6): 945–58.
59. Fogarty JN, Murphy KJ, McFarlane B, Montero-Odasso M, Wells J, Troyer AK, et al. Taoist Tai Chi® and Memory Intervention for Individuals with Mild Cognitive Impairment. J Aging Phys Act. 2016 Apr;24(2): 169–80.
60. Seongryu Bae, Sangyoon Lee SL, Songee Jung, Keitaro Makino, Kazuhiro Harada K, Harada, Yohei Shinkai, Ippei Chiba HS. The effect of a multicomponent intervention to promote community activity on cognitive function in older adults with mild cognitive impairment: A randomized controlled trial. Complement Ther Med. 2018;42: 164–9.
61. Delbroek T, Vermeylen W, Spildooren J. The effect of cognitive-motor dual task training with the biorescue force platform on cognition, balance and dual task performance in institutionalized older adults: a randomized controlled trial. J Phys Ther Sci. 2017;29(7): 1137–43.
62. Liao Y-Y, Chen I-H, Lin Y-J, Chen Y, Hsu W-C. Effects of Virtual Reality-Based Physical and Cognitive Training on Executive Function and Dual-Task Gait Performance in Older Adults With Mild Cognitive Impairment: A Randomized Control Trial. Front Aging Neurosci. 2019;11:162.
63. Gillain S, Dramé M, Lekeu F, Wojtasik V, Ricour C, Croisier J-L, et al. Gait speed or gait variability, which one to use as a marker of risk to develop Alzheimer disease? A pilot study. Aging Clin Exp Res [Internet]. 2015 Apr 16 [cited 2019 Mar 19];28(2): 249–55. Available from: http://link.springer.com/10.1007/s40520-015-0392-6
64. Tamara L. Hayes, Francena Abendroth, Andre Adami, Misha Pavel, Tracy A. Zitzelberger JAK. Unobtrusive assessment of activity patterns associated with mild cognitive impairment. Alzheimer's Dement. 2008;4(6): 395–405.
65. Ansai JH, Andrade LP de, Nakagawa TH, Rebelatto JR. Performances on the Timed Up and Go Test and subtasks between fallers and non-fallers in older adults with cognitive impairment. Arq Neuropsiquiatr. 2018 Jun;76(6): 381–6.
66. Pfeiffer E. A Short Portable Mental Status Questionnaire for the Assessment of Organic Brain Deficit in Elderly Patients. J Am Geriatr Soc. 1975;23(10): 433–41.
67. Dodge HH, Mattek NC, Austin D, Hayes TL, Kaye JA. In-home walking speeds and variability trajectories associated with mild cognitive impairment. Neurology. 2012 Jun 12;78(24): 1946–52.
68. Pieruccini-Faria F, Sarquis-Adamson Y, Montero-Odasso M. Mild Cognitive Impairment Affects Obstacle Negotiation in Older Adults: Results from "gait and Brain Study." Gerontology. 2018 Oct 12;p: 1–10.
69. Manuel Montero-Odasso, Alvaro Casas KTH, Patricia Bilski, Iris Gutmanis JLW and MJB. Quantitative gait analysis under dual-task in older people with mild cognitive impairment: A reliability study. J Neuroeng Rehabil. 2009;6: 35.

70. Byun S, Han JW, Kim TH, Kim K, Kim TH, Park JY, Suh SW, Seo JY, So Y, Lee KH, Lee JR, Jeong H, Jeong HG, Han K, Hong JW KK. Gait Variability Can Predict the Risk of Cognitive Decline in Cognitively Normal Older People. Dement Geriatr Cogn Disord. 2018;45(5–6): 251–61.
71. Akl A, Taati B, Mihailidis A. Autonomous Unobtrusive Detection of Mild Cognitive Impairment in Older Adults. IEEE Trans Biomed Eng. 2015 May;62(5):1383–94.
72. Akl A, Mihailidis A. Estimating in-home walking speed distributions for unobtrusive detection of mild cognitive impairment in older adults. In: 2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). IEEE; 2015. p. 5175–8.
73. Buchman A-S, Dawe R-J, Leurgans S-E, Curran T-A, Truty T, Yu L, et al. Different combinations of mobility metrics derived from a wearable sensor are associated with distinct health outcomes in older adults. J Gerontol A Biol Sci Med Sci. 2019.
74. Lussier M, Lavoie M, Giroux S, Consel C, Guay M, Macoir J, et al. Early detection of mild cognitive impairment with in-home monitoring technologies using functional measures: A systematic review. IEEE J Biomed Heal Informatics. 2018;2194(c): 1–11.
75. Verghese J, Wang C, Lipton RB, Holtzer R, Xue X. Quantitative gait dysfunction and risk of cognitive decline and dementia. J Neurol Neurosurg Psychiatry. 2007;78(9): 929–35.
76. Lamoth CJ, van Deudekom FJ, van Campen JP, Appels BA, de Vries OJ, Pijnappels M. Gait stability and variability measures show effects of impaired cognition and dual tasking in frail people. Journal of neuroengineering and rehabilitation. 2011;8: 2–2.
77. Schwenk M, Zieschang T, Englert S, Grewal G, Najafi B, Hauer K. Improvements in gait characteristics after intensive resistance and functional training in people with dementia: A randomised controlled trial. BMC geriatrics. 2014;14: 73.
78. Gomes-Osman J, Cabral DF, Morris TP, McInerney K, Cahalin LP, Rundek T, et al. Exercise for cognitive brain health in aging. Neurol Clin Pract. 2018;8(3): 257–65.
79. Karssemeijer, E.G.A.Esther, Aaronson, J.A.Justine, Bossers, W.J.Willem, Smits, T.Tara, Rikkert, M.G.M.Marcel Olde, Kessels, R.P.C.Roy, Positive effects of combined cognitive and physical exercise training on cognitive function in older adults with mild cognitive impairment or dementia: A meta-analysis. Ageing Research Reviews http://dx.doi.org/10.1016/j.arr.2017.09.003
80. Song D, Yu DSF, Li PWC, Lei Y. The effectiveness of physical exercise on cognitive and psychological outcomes in individuals with mild cognitive impairment: A systematic review and meta-analysis. Int J Nurs Stud. 2018; 79: 155–64.
81. Wang C, Yu J-T, Wang H-F, Tan C-C, Meng X-F, Tan L. Non-pharmacological interventions for patients with mild cognitive impairment: a meta-analysis of randomized controlled trials of cognition-based and exercise interventions. J Alzheimers Dis. 2014 Aug 28;42(2): 663–78.
82. Najafi B, Helbostad JL, Moe-Nilssen R, Zijlstra W, Aminian K. Does walking strategy in older people change as a function of walking distance? Gait & posture. 2009; 29:261–266.

Tables

mmary of included RCT studies involved an Instrumented Functional Assessment as

y gn	Study Characteristics (groups, number of participants, mean age)	MCI Diagnostic Criteria	Instrumented Functional Assessment	Instrument	Intervention	Data Collection (follow-up)	Main results in MCI
	Intervention Group: n= 25. 75.3 years old. Control Group: n= 25. 76.8 years old.	Petersen Criteria [11]. MMSE > 24 [49].	Walking at preferred speed (11 meters walkway).	Tri-axial accelerometer attached to the L3 spinous.	**Intervention Group:** Aerobic exercise (60% of aged predicted maximal heart rate), endurance walking, muscle strength training, postural balance retraining, and gait training (90 min, 2/ week, 6 months). **Control Group**: 2 Education classes about health promotion.	(T1) at baseline; (T2) six months.	↑Gait speed ↓Stride time and ↑Stride length in both groups***. ↑HR in VT in the Intervention group***. ↑Gait speed, stride length and HR in VT in the Intervention group vs control group**.
	PCT: n= 21. 75.2 years old. PT: n= 18. 77.1 years old. CT: n= 16. 76.3 years old. Control Group: n= 14. 79.2 years old.	Petersen Criteria [11].	Walking speed at usual pace (6 meters) in ST and DT conditions. WSC. TUG.	Electronic walkway GAITRite® (length: 4.3 meters).	**PT:** Aerobic training on bikes (60% of aged predicted maximal heart rate). **CT:** Cognitive exercises. **PCT:** Aerobic training on bikes (60% of aged predicted maximal heart rate) + cognitive exercises. **Control Group:** Maintaining their usual lifestyle.	(T1) at baseline; (T2) twelve weeks; (T3) six months.	↓Time to perform the TUG***. ↑ Gait speed**. TUG improved after PT and PCT intervention***. Gait Speed in ST and DT conditions improved after PCT training***.
	Intervention: n=12. 77.8 years old. Control: n= 10. 79.00 years old.	Petersen Criteria [11].	Balance (to stand for 30 seconds with feet close together with EO and EC. Walking at usual pace	Wearable sensors.	**Intervention:** Balance training (weight shifting and virtual obstacle crossing). Real-time visual/ audio lower-limb motion feedback provided from wearable sensors 2/week, 4 weeks).	(T1) at baseline; (T2) four weeks.	↓CoM sway in both directions (AP, ML) in the intervention with EO**.

			and a fast pace (10 meters).		**Control:** No training.		
	MIP + TTC: n= 22. 71.55 years. MIP: n= 18. 72.61 years.	Petersen Criteria [11]. MMSE > 24 [49]. MoCA < 26 [47].	Walking at usual pace in ST and DT conditions. CTSIB with EO and EC.	GAITRite® Portable Walkway System. Digital Balance Platform.	**TTC:** Taoist Tai Chi (2/week, 90min/session, 10 weeks). **MIP:** Education about lifestyle factors that impact memory and teaching of memory strategies (8 sessions).	(T1) at baseline; (T2) ten weeks; (T3) twenty-two weeks.	No significant change between groups in gait variables, the DT cost variables, or in the amount of sway on the balance measures.
	Intervention: n= 41. 75.5 years old. Control: n= 42. 76.4 years old.	Winblad Criteria [13]. MMSE > 24 [49].	Maximum hand grip strength. Walking speed and physical activity (time spent in MVPA and step count).	Handheld dynamometer. Tri-axial accelerometer.	**Intervention:** Physical activities (walking, muscle strength training, stretching etc) + cognitive exercises + social activities (2/week, 90min, 24 weeks). **Control:** 2 Health education classes (90 mins each, during the 24-week).	(T1) at baseline; (T2) six months.	↓Time spent in MVPA after intervention in the control group**. ↓Step count after intervention in the control group**. Intervention Group kept baseline parameters.
	Intervention: n= 10. 86.9 years. Control: n= 10. 87.5 years.	MoCa < 26 [47].	TUG in ST and DT conditions.	Inertial measurement units on the ankles, wrists and sternum.	**Intervention:** Virtual reality dual-task training using the BioRescue (2/week, 18-30 mins, 6 weeks). **Control:** No training.	(T1) at baseline; (T2) six weeks.	↓Total time to perform the TUG in the intervention group during ST condition**.
	Intervention: n= 18. 75.5 years. Control: n= 16. 73.1 years.	MoCa < 26 [47].	Walking at preferred Speed in ST and DT conditions.	GAIT Up System.	**Intervention:** VR-based physical and cognitive training (60 min, 3/week, 12 weeks). **Control:** Combined physical (resistance, aerobic [50-75% heart rate] and balance exercises) and cognitive exercises.	(T1) at baseline; (T2) three months.	↑ Gait Speed and Stride Length in ST and DT conditions in VR group** ↑ Gait Speed and Cadence only in ST in Control group**

						No differences between groups*.

ive impairment. RCT: Randomized Controlled Trial. aMCI: amnestic mild cognitive impairment. MMSE: Mini-mental State Third lumbar vertebra level. HR: harmonic ratio that represent the smoothness of trunk movement. VT: vertical direction. PCT: aneous Physical and Cognitive Training. PT: Physical Training. CT: Cognitive Training. ST: single task. DT: dual task. WSC: arpet test. TUG: Timed Up an Go Test. EO: eyes open. EC: eyes closed. CoM: center of mass. AP: anterior-posterior. ML: medial- mory Intervention Program. TTC: Taoist Tai Chi. MoCA: Montreal Cognitive Assessment. CTSIB: Clinical Test of Sensory alance. MVPA: Moderate-to-Vigorous Physical Activity. VR: Virtual Reality.

creased.

05. ***$p < 0.001$.

nmary of included Cohort studies compared Instrumented Objective Functional Parameters nfirmed MCI and a Control Group.

dy sign	Study Characteristics (groups, number of participants, mean age)	MCI Diagnostic Criteria	Instrumented Functional Assessment	Instrument	Data Collection (follow-up)	Main results in MCI
t Cohort dy.	- MCI +: n = 9. 74.44 years old. - MCI -: n= 4. 70.00 years old.	Petersen Criteria [15]. CDR = 0.5 [46]. MMSE > 24 [49].	Walking at preferred speed (40 meters) in ST and DT conditions.	Tri-axial accelerometric (Locometrix®) attached to the L3.	(T1) at baseline; (T2) one year; (T3) four years.	↑Gait speed in ST and in DT in MCI- than in MCI+ **. ↑Symmetry in DT in MCI- than in MCI+ **. ↓Gait performances in DT compared to ST.
nsversal gitudinal dy ired nparison eated asure OVA)	- Healthy Group: n=7. 90 years old. - MCI: n= 7. 88.44 years old.	All: MMSE ≥ 24 [49]. Control: CDR = 0 [46]. MCI: CDR = 0.5 [46].	Activity in the home, amount of variance in activity, tracking visitors, absences from the home, and walking speed.	Motion sensors and magnetic contact sensors placed in home, and wireless contact switches.	(T1) mean of 315 days.	↑COV in the median walking speed in MCI compared with Healthy group **. ↑24-hour wavelet variance in MCI Group than Healthy Group (↑variance in the day-to-day pattern of activity)**.
gitudinal spective dy.	- AD: n= 37. 78.5 years old. - MCI: n= 38. 74.75 years old.	MCI Group: CDR = 0.5 [46]. MMSE > 24 [49]. Pfeffer [66].	TUG	Qualisys ProReflex motion analysis system with seven cameras.	(T1) at baseline; (T2) six months.	↓Total time to perform the TUG in MCI vs AD**. ↑ Gait speed in the walking forward subtask in MCI vs AD**. ↓ Time in the turn subtask in MCI vs AD**. ↑ Gait speed in the walking back subtask in MCI vs AD**. ↓ Time in the turn-to-sit subtask in MCI vs AD**.

gitudinal tent ectory del). t of ort dy.	- aMCI: n = 8. 84,5 years old. - naMCI: n = 31. 83.8 years old. - Healthy Group: n= 54. 84.9 years old.	ALL: CDR ≤ 0.5 [46]. MMSE > 24 [49]. MCI: Petersen Criteria [11].	Walking speed and its variability; total daily activity, visitors and time out of home.	Motion sensors and contact sensors fixed in the homes, and wireless contact switches.	(T1) at baseline; (T2) mean of 2.6 ± 1.0 years.	Slow speed in naMCI**. ↑or↓ baseline COV of walking speed groups in naMCI. ↓Gait Speed in MCI than in Healthy Group**.
t of a spective ort dy.	- MCI: n= 52. 73.7 years old. - Healthy Group: n= 27. 71.7 years old.	Control: - CDR = 0 [46]. - MoCA ≥ 27 [47]. MCI: - CDR = 0.5 [46]. - MoCA < 26 [47].	Walking speed in ST and DT conditions.	Electronic walkway (lenght: 6 meters) embedded with sensors.	(T1) at baseline; (T2) two years; (T3) four years; (T4) five years.	↓ Gait speed in DT conditions in MCI**. ↓Step length adjustments in DT conditions in MCI**. ↓ Gait speed in MCI**.
iability dy.	- MCI: n= 11. 76.6 years old.	Petersen Criteria [14]. CDR = 0.5 [46]. MoCA < 26 [47]. MMSE > 24 [49].	Gait performance under ST and DT conditions.	Electronic walkway (GAITRite® System. Lenght: 6 meters).	(T1) at baseline; (T2) one week.	↓Mean gait speed under DT conditions**. ↑gait variability on stride time, step time, and double support time under DT conditions**.

ve impairment. MCI +: MCI who will develop AD. MCI -: MCI who will not develop AD. CDR: Clinical Dementia Rating score. MMSE: e Examination.ST: simple task. DT: dual task. L3: Third lumbar vertebra level. ANOVA: Analysis of Variance. COV: coefficient of heimer Disease. TUG: Timed Up an Go Test. aMCI: amnestic mild cognitive impairment. naMCI: non-amnestic mild cognitive A: Montreal Cognitive Assessment. GV: Gait velocity.

05. ***$p < 0.001$.

nmary of included Cohort studies examined the relationship between Kinematic Functional obtained by Instrumented Analysis and MCI.

ly gn	Study Characteristics (groups, number of participants, mean age)	MCI Diagnostic Criteria	Instrumented Functional Assessment	Instrument	Data Collection (follow-up)	Main results in MCI
pective rt y.	Healty: n = 91. 67.3 years old.	Not diagnosis MCI at baseline: CDR = 0 [46]. MMSE > 24 [49]. Winblad Criteria [13] for diagnosis of MCI.	Walking at usual pace (20 meters).	Tri-axial accelerometer (FITMETER®) at the level of the 3rd–4th lumbar vertebra.	(T1) at baseline; (T2) 2 years; (T3) median duration was 47.1 months.	↑Gait variability was a significant predictor of MCI (HR = 11.97, 95% CI = 1.29–111.37)***. Gait speed was slightly associated with incident MCI risk (HR = 5.04, 95% CI = 0.53–48.18) **.
itudinal y ectory time ow or hines random sts).	Older adults: n= 97. NS, 70 years old and +.	Cognitively Healthy: - CDR < 0.5 [46]. - MMSE > 24 [49]. MCI: - CDR = 0.5 [46]. - MMSE > 24 [49].	Walking speed and general activity in the home. Visitors and absences from the home.	Motion sensors and wireless contact switches placed in the home.	(T1) at baseline; (T2) one year; (T3) two years; (T4) three years.	Trajectories of weekly walking speed, COV of the walking speed, COV of the morning and evening walking speeds could detect MCI in older adults.
itudinal y ar ession).	Older adults: n= 15. NS, 70 years old and +.	Cognitively Healthy: -CDR < 0.5 [46]. MCI: -CDR = 0.5 [46].	Walking speed in home.	Motion sensors on the ceiling in areas such as a hallway or a corridor.	(T1) at baseline; (T2) one year; (T3) two years; (T4) three years.	Walking speed distributions was difference in the subjects when cognitively intact and when having MCI. Transitioning to MCI, daily activities were less distinguishable and often occurred later.

itudinal rt y.	Older adults: n= 1249. 80.0 years.	MCI: - MMSE > 24 [49].	Walking at their self-selected Speed (10 meters). TUG. Standing Posture with closed eyes.	Wearable sensor on the lower back.	(T1) at baseline; (T2) during 3.6 years.	↓ Cadence and Regularity were associated with incident MCI **. Gait Speed and Gait variability were not associated with incident MCI *.

ve impairment. CDR: Clinical Dementia Rating score. MMSE: Mini-mental State Examination. HR: Cox proportional Hazard. CI: al. NS: Not Specified. COV: coefficient of variation.

sed.

05. ***$p < 0.001$.

Table 4. Instruments used in kinematic analysis.

Instrument	Papers n, %	References
Tri-axial accelerometer (e.g. Locometrix®, etc.)	4, 23.5%	[56, 60, 63, 70]
Electronic walkway (e.g. GAITRite®, etc.)	4, 23.5%	[57, 59, 68, 69]
Wearable sensors	2, 12%	[58, 73]
Digital Balance Platform	1, 6%	[59]
Inertial measurement units (IMUs)	1, 6%	[61]
Motion and contact sensors	4, 23.5%	[64, 67, 71, 72]
Qualisys ProReflex motion analysis System (cameras)	1, 6%	[65]
GAIT Up System.	1, 6%	[62]

Table 5. Criteria for MCI diagnosis reported in studies.

Criteria	Papers n, %	References
Petersen et al.[11, 12, 14-16]	7, 41%	[56-59, 63, 67, 69]
Winblad et al. [13]	2, 12%	[60, 70]
CDR [41]	9, 53%	[63-65, 67-72]
MoCA [42]	5, 29%	[59, 61, 62, 68, 69]
MMSE [44]	11, 65%	[56, 59, 60, 63-65, 67, 69-71, 73]
Pfeiffer [60]	1, 6%	[65]

MCI: Mild Cognitive Impairment; CDR: Clinical Dementia Rating; MoCA: Montreal Cognitive Assessment; MMSE: Mini-Mental State Examination.

Figures

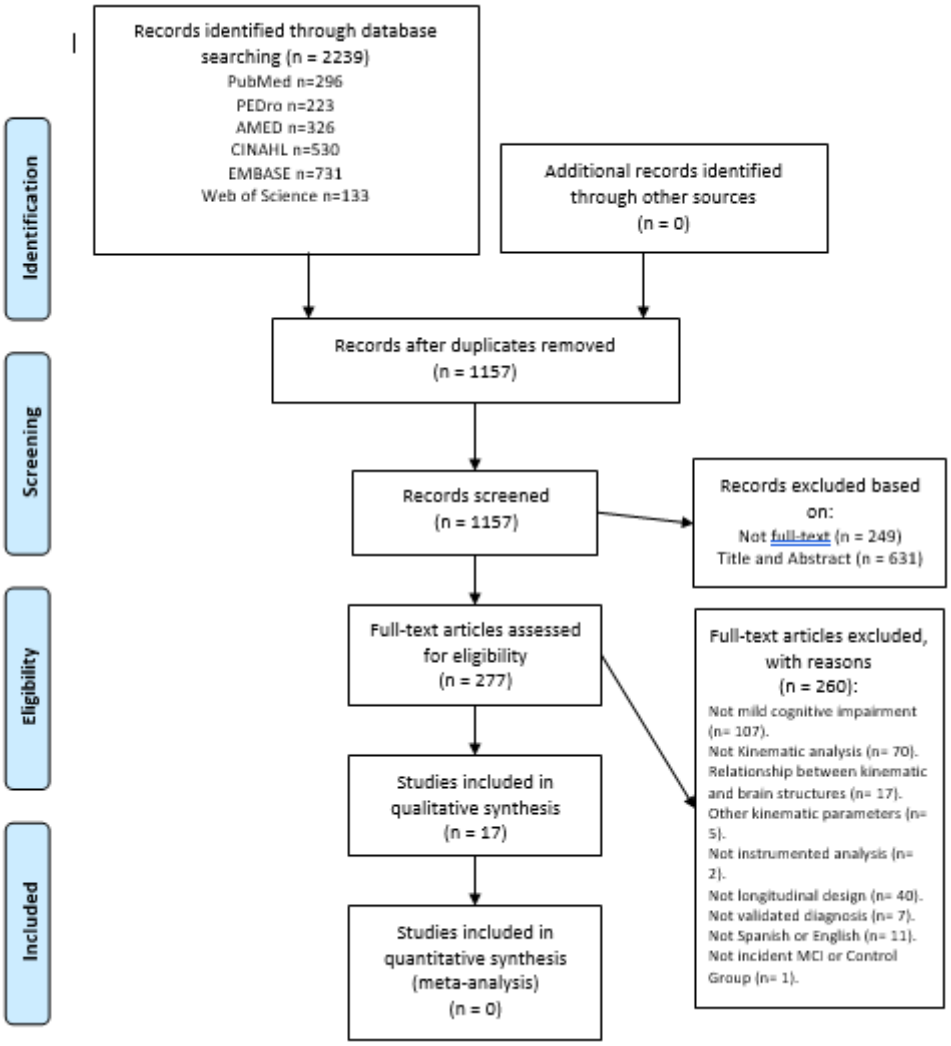

Figure 1

PRISMA Flow Diagram

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable8..docx
- SupplementaryFiles.zip
- AppendixA.PRISMAChecklist..docx
- AppendixB.SearchStrategy.docx
- SupplementaryTable7..docx
- AppendixE.Conflictofinterestofincludedstudies..docx

- AppendixD.Excludedstudiesinthesecondscreening..docx
- SupplementaryTable6..docx