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

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Abstract

Background

Subjects 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 confirmed MCI people with a control group; and to assess longitudinal changes in these parameters after different physical 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

Fifteen studies met inclusion criteria including mild cognitive impairment people. Results from RCTs suggested that gait speed, gait variability and balance may be improved by different physical interventions. Cohort studies showed that gait speed, gait variability and gait symmetry, especially in Dual Task (DT) conditions, were parameters impaired in confirmed MCI patients in comparison with a Control Group. 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 had a low quality of evidence.

Conclusions

Existing 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 interventions. Further studies are required to refute our findings.

Background

From 1990 to 2016 the global healthy life expectancy increased by an average of 6.24 years [1-3]. As life expectancy increases in a population, the presence of disability adjusted life years and morbidity
has increased considerably, largely because the frequency of chronic individual diseases increases with age [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].

Mild cognitive impairment constitutes a significant risk factor for the development of future dementia [5, 8-11]. Key risk factors for MCI include age, subjective memory complaints, clinical factors such as the presence of diabetes or an APOE allele, suffering a stroke or neuropsychiatric disorders such as depression [5, 8, 12, 17-19]. The rates of progression from MCI to dementia normally vary between 12-40% [5, 8, 10, 11], compared to 1-2% in the cognitively normal elderly population [11]. Subjects with MCI also experience higher mortality than cognitively normal subjects of the same age [10].

The diagnosis criteria of MCI generally accepted are: (1) Complaints or subjective cognitive concern, preferably corroborated by an informant. (2) Objective evidence of cognitive impairment or decrease in cognitive function that is abnormal for age, and that can occur in any of the different cognitive domains: memory, executive function, attention, language or visuospatial skills. (3) Objective cognitive impairment that is not serious enough to classify as dementia. (4) Activities or functional capacities preserved [8, 10-14, 17, 20, 21].

In terms of functional status, patients with MCI are 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]. 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 normal individuals of the same age. However, individuals with MCI may have problems in functional tasks [5] and it has been reported that these subjects present the alteration of functional parameters, such as mobility, muscle strength, balance, gait dysfunction, or increased risk of falls [8, 22-26], with
decreased gait speed being suggested as being the main parameter altered in older individuals [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 the decrease in gait speed could be indicative of MCI. Veronese et al. [30] showed an association between the reduction of physical performance across multiple objective functional tests and cognitive decline, with decreased gait speed and low performance in the Short Physical Performance Battery (SPPB) the main indicators of 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 subjects with MCI and healthy subjects in the overall performance of a functional test, subjects with MCI could have functional alterations only identifiable through a kinematic analysis conducted in their case with an inertial sensor. Furthermore, a Meta-analysis using an instrumented assessment and conducted by Bahureksa et al. [40], revealed that gait parameters such as velocity, stride length, and stride time discriminated best between MCI and healthy controls under single task 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. Thus, instrumented functional assessment could provide a critical opportunity for MCI diagnosis and tailored intervention targeting functional impairment [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 impairment and may improve cognition, mobility, balance and Quality of life [8, 17, 18, 411-43]. Knowing objective functional parameters that could be impaired in mild cognitive impairment patients or which could indicate if a person is at risk of mild cognitive impairment is essential to help detect MCI and to develop physical 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 confirmed MCI people with a control group; (3) to assess longitudinal changes in these parameters after different 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).

Patient and public involvement
Patients and or public were not involved.

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. 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 impairment’ (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 parameters between confirmed MCI and a Control Group formed by Healthy people or Alzheimer Disease people.

2. RCTs assessing longitudinal changes in functional objective parameters after different physical therapies or interventions.

3. Studies that included adults 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 permitted 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 analysis.

3. Studies exploring the relationship between functional kinematic parameters and older healthy adults 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 conduct a kinematic instrumented analysis.

7. 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, instrument used to kinematic analysis and the methods used to diagnose or
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-randomised 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 kinematic 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 1,929 citations were identified through electronic databases, with 0 additional studies identified through Grey Literature sources. Ninety hundred and seventy titles and abstracts were screened, and 240 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= 225) is reported online in supplementary appendix D. The conflict of interests of included studies are shown online in supplementary appendix E. Of these, 15 studies (five RCTs, one pilot RCT study, one pilot cohort study, seven cohort studies and a reliability study) with a total of 444 participants with MCI and 291 healthy people 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 parameters 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 mild cognitive impairment 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, 47%) and the combination of the CDR (n= 9, 60%) and MMSE (n= 10, 67%) (see Table 5).

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**

The objective of this study was to review the current state of knowledge on the presence of functional Kinematic parameters that may be impaired in mild cognitive impairment during the performance of functional tasks. Moreover, this systematic review hoped to investigate if these functional objective parameters could be improved by different physical 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 mild cognitive impairment patients 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 [57-62, 64, 67, 69-71]. Therefore, we are still in an exploratory stage regarding the use of kinematic parameters in the detection of functional impairment related to mild cognitive impairment or as outcome measures in RCTs. The present review included fifteen studies. On the one hand, Cohort studies showed that the coefficient of variation in the median walking speed, day-to-day pattern, gait speed, gait variability as well as gait symmetry, specially in Dual Task conditions, were parameters which could be impaired in MCI Patients [62, 63, 66-68]. Furthermore, these prospective longitudinal studies suggested that gait variability, the coefficient of variation of the walking speed and trajectories of weekly walking speed may be significant predictors of MCI, whereas gait speed was not associated with incident MCI risk [69-71]. On the other hand, RCTs suggested gait speed, stride length, stride time, balance and the time to perform the TUG may be improved after some physical interventions [56-58, 61]. Nevertheless, the quality and the strength of evidence per outcome was low and the risk of bias was substantial to draw firm conclusions.

**Comparision with other studies**
The present systematic review establish that gait speed, especially on the dual task conditions [62, 67, 68], was significantly reduced in subjects with mild cognitive impairment. These results were in line with some studies that have identified reduced gait speed as a predictor of preclinical stages of dementia or mild cognitive impairment [23-25, 29, 30, 33-36]. Within the kinematic analysis of the walking speed, the coefficient of variation in the median walking speed, gait speed, gait variability as well as gait symmetry, specially in Dual Task conditions, were parameters which may be impaired in MCI Patients [62, 63, 66-68] according to included studies of the present systematic review.

Moreover, the coefficient of variation of the walking speed, trajectories of weekly walking speed and gait variability might be a significant predictor of MCI [69-71]. This statement is in accordance with a previous 5 years of follow-up prospective study which determined that gait pace and variability may predict a future risk of cognitive decline and dementia in initially non-demented older adults [72]. Other studies also showed that stride time variability in dual task may be a sensitive indicator of cognitive change [26, 73]. Furthermore, Bahureksa et al. [40], in a systematic review and meta-analysis, also revealed that gait parameters such as velocity (p<0.01), stride length (p<0.01), stride time (p=0.02) and coefficient of variation (p<0.01), could discriminate best between MCI and healthy controls under single task conditions. Another systematic review [74] also demonstrated that physical activity in home or everyday life activities monitored by sensor technologies in home, were parameters indicative of MCI. Finally, it is important to underline our studies included different walking distances and different kinematic instruments. In the literature, it has been demonstrated that participant walking strategy changes with walking distance, resulting in a significant effect on gait variability [75], so walking distance could be highly relevant in order to measure gait variability as a marker for MCI. Randomized Controlled Trials included in this systematic review showed that gait speed, stride length, stride time, balance, specially the center of mass sway in anterior-posterior and medial-lateral directions, and the time to perform the TUG may be improved after some physical interventios [56-58, 61]. Nevertheless, there is still room for improvement in current interventions. For instance, there is limited evidence on intervention effects on stride time variability [76] although this parameter seems to be a important predictor of MCI [58, 61, 62]. 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 Trial showed that exercise, specifically aerobic and resistance (strength) exercises, join cognitive training could improve cognitive function, activities in daily living and mood [77-80]. However, It has not been identified others Systematic Reviews that assess changes in functional objective parameters after physical interventions and It has not been found either RCTs which use Kinematic parameters as outcome measures, so It would be necessary more clinical trials using these parameters as outcome measures.

**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, different instruments used in kinematic analysis) should be taken into account when interpreting the results. 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. Moreover, these functional objective parameters could be improved by physical
interventions in MCI patients. 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 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 interventions could improve gait speed, stride length, stride time, balance, specially the center of mass sway in AP and ML directions [56-58].

Implications for further research

Despite the promising results of the present study, some flaws observed in most of the included 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) it should be conducted RCTs and Cohort studies with high quality of evidence since studies included in this systematic review often showed an unclear risk of bias and a low quality of evidence; (iv) it would be necessary conducting more Clinical trials which use functional objective parameters as outcome measures of physical interventions in MCI

Conclusion

The coefficient of variation in the median walking speed, gait speed, gait variability as well as gait symmetry, specially in Dual Task conditions, were parameters which could be impaired in MCI patients. Furthermore, gait variability, the coefficient of variation of the walking speed and trajectories of weekly walking speed may be significant predictors of MCI. Thus, these parameters should be used as functional objective parameters which could be impaired, may predict an incident MCI or could even help its early diagnosis. Moreover, these functional objective parameters could be improved by physical interventions in MCI patients. Therefore, the use of kinematic analysis may provide objective parameters related to functionality that be indicative of MCI and which could provide a critical opportunity for early intervention before functional changes have a major impact on ADLs, fall risk, and overall independence. 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.

Declarations

**Ethics approval and consent to participate**

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

**Consent for publication**

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

**Availability of data and materials**

Not applicable – 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.

**Abbreviations**

- **MCI**: Mild Cognitive Impairment;
- **AMED**: Allied and Complementary Medecine 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;
- **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.

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Tables

| Study author and year | Study Design | Study Characteristics (groups, number of participants, mean age) | MCI Diagnostic Criteria | Instrumented Functional Assessment | Instrument |
|-----------------------|--------------|---------------------------------------------------------------|------------------------|-----------------------------------|------------|
| Doi et al. [56], 2013. | RCT.         | Intervention Group (aMCI): n=25. 75.3 years old.             | Petersen Criteria [11].| Walking at preferred speed (11 meters walkway). | Tri-axial accelerometer attached to L3 spinous. |
| Study                          | Design     | Participants | Outcome Measures                                                                 |
|-------------------------------|------------|--------------|----------------------------------------------------------------------------------|
| Donnezan et al. [57], 2018.   | RCT.       | All Groups of MCI: 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. WSC. TUG. |
| Schwenk et al. [58], 2016.    | Pilot RCT. | Two MCI Groups: 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 and a fast pace (10 meters). Wearable sensors. |
| Fogarty et al. [59], 2016.    | RCT.       | Two MCI Groups: MIP + TTC: n= 22. 71.55 years. MIP: n = 18. | Petersen Criteria [11]. MMSE > 24 [49]. Walking at usual pace in ST and DT conditions. GAITRite® Portable Walkway System. |
| Study (first author and year) | Study Design | Study Characteristics (groups, number of participants, mean age) | MCI Diagnostic Criteria | Instrumented Functional Assessment | Instrument |
|-------------------------------|--------------|---------------------------------------------------------------|------------------------|-----------------------------------|------------|
| Gillain et al. [62], 2015.    | Pilot Cohort Study. | MCI +: n = 9. 74.44 years old. | Petersen Criteria [15]. | Walking at preferred speed (40 meters) in ST | Tri-axial accelerometric (Locometrix®) |

MCI: mild cognitive impairment. RCT: Randomized Controlled Trial. aMCI: amnestic mild cognitive impairment. MMSE: Mini-mental State Examination. L3: Third lumbar vertebra level. HR: harmonic ratio that represent the smoothness of trunk movement. VT: vertical direction. Cognitive Training, PT: Physical Training. CT: Cognitive Training. ST: simple task. DT: dual task. WSC: Walking Stroop Carpet test. TUG: Timed Up and Go Test. CoM: center of mass. AP: anterior-posterior. ML: medial-lateral. MIP: Memory Intervention Program. TTC: Taoist Tai Chi. MoCA: Montreal Cognitive Assessment. CTSIB: Clinical Test of Sensory Integration and Balance.
| Study          | Design Description                                                                 | Control Group                                                                 | MCI Group                                                                 | Activity and DT Conditions                                                                 | Measurement Tools |
|---------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------------------------------------------------------------------|-------------------|
| Hayes et al. [63], 2008. | Transversal and longitudinal study (paired comparison and repeated measure ANOVA) | Healthy Group: n=7, 90 years old. MCI: n=7, 88.44 years old.                        | MCI: CDR = 0.5 [46]. MMSE > 24 [49].                                         | 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. |
| Ansai et al. [64], 2018. | Longitudinal prospective study.                                                    | AD: n=37, 78.5 years old. MCI: n=38, 74.75 years old.                            | MCI Group: CDR = 0.5 [46]. MMSE > 24 [49]. Pfeffer [65].                      | TUG Qualisys ProReflex motion analysis system with seven cameras.                        |                   |
| Study | Method | Description | Participants | Outcomes | Devices |
|-------|--------|-------------|--------------|----------|---------|
| Dodge et al. [66], 2012. | Longitudinal (Latent trajectory model). Part of cohort study. | 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. |
| Pieruccini-Faria et al. [67], 2018. | Part of a prospective cohort study. | 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. |
| Montero-Odasso et al. [68], 2009. | Reliability study. | 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). |
MCI: mild cognitive impairment. MCI +: MCI who will develop AD. MCI -: MCI who will not develop AD. CDR: Clinical Dementia Rating. MMSE: Mini-mental State Examination. ST: simple task. DT: dual task. L3: Third lumbar vertebra level. ANOVA: Analysis of Variance. COV: coefficient of variation. AD: Alzheimer Disease. TUG: Timed Up and Go Test. aMCI: amnestic mild cognitive impairment. naMCI: non-amnestic mild cognitive impairment. MoCA: Montreal Cognitive Assessment.

| Table 3. Summary of included Cohort studies examined the relationship between Kinematic Functional Parameters obtained by Instrumented Analysis and MCI. |
|---|---|---|---|---|
| Study (first author and year) | Study Design | Study Characteristics (groups, number of participants, mean age) | MCI Diagnostic Criteria | Instrumented Functional Assessment | Instrument |
| Byun et al. [69], 2018. | Prospective cohort study. | Healthy: n = 91. 67.3 years old. | Not diagnosis MCI at baseline: CDR = 0 [46]. MMSE > 24 [49]. | Walking at usual pace (20 meters). | Tri-axial accelerometer (FITMETER®) at the level of the 3rd–4th lumbar vertebra. |
| Akl et al. [70], 2015. | Longitudinal study (trajectory with time window vector machines and random forests) | 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. |
| Akl et al. [71], 2015. | Longitudinal study (linear regression). | 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. |
MCI: mild cognitive impairment. CDR: Clinical Dementia Rating score. MMSE: Mini-mental State Examination. HR: Cox proportional hazard. CI: Confidence Interval. NS: Not Specified. COV: coefficient of variation.

Table 4. Instruments used in kinematic analysis.

| Instrument                                      | Papers n, % | References     |
|------------------------------------------------|-------------|----------------|
| Tri-axial accelerometer (e.g. Locometrix®, etc.) | 4, 27%      | [56, 60, 62, 69] |
| Electronic walkway (e.g. GAITRite®, etc.)      | 4, 27%      | [57, 59, 67, 68] |
| Wearable sensors                               | 1, 7%       | [58]           |
| Digital Balance Platform                       | 1, 7%       | [59]           |
| Inertial measurement units (IMUs)              | 1, 7%       | [61]           |
| Motion and contact sensors                     | 4, 27%      | [63, 66, 70, 71] |
| Qualisys ProReflex motion analysis System (cameras) | 1, 7%   | [64]           |

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