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Gait and cognition: mapping the global and discrete relationships in ageing and neurodegenerative disease.

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Key Points

- A robust relationship between gait and cognition is identified in cross sectional studies in older adults, cognitive impairment and PD
- Evidence of selective relationships between discrete gait and cognitive functions in ageing and pathology are subtle but emerging
- A longitudinal gait-cognition relationship is evident in older adults identifying gait may be more sensitive to pathological degeneration compared to cognitive outcomes
- Comprehensive measurement of gait and cognition will consolidate knowledge of specific relationships
- Gait may be a surrogate marker of cognitive impairment and cognitive decline

ABSTRACT

Recent research highlights the association of gait and cognition in older adults but a stronger understanding is needed to discern coincident pathophysiology, patterns of change, examine underlying mechanisms and aid diagnosis. This structured review mapped associations and predictors of gait and cognition in older adults with and without cognitive impairment, and Parkinson's disease. Fifty papers out of an initial yield of 22,128 were reviewed and a model of gait guided analysis and interpretation. Associations were dominated by the pace domain of gait; the most frequently studied domain. In older adults pace was identified as a predictor for cognitive decline. Where comprehensive measurement of gait was conducted, more specific pathological patterns of association were evident highlighting the importance of this approach. This review confirmed a robust association between gait and cognition and argues for a selective, comprehensive measurement approach. Results suggest gait may be a surrogate marker of cognitive impairment and cognitive decline. Understanding the specific nature of this relationship is essential for refinement of diagnostics and development of novel therapies.

Keywords: gait, cognition, ageing, Parkinson's disease, cognitive impairment

INTRODUCTION

Gait provides a marker of global health and is an important tool as a predictor for health status and survival in older adults (Hausdorff *et al.*, 2001; Studenski *et al.*, 2011). Gait is no longer regarded as purely a motor task. An extensive body of research has established that safe and effective gait requires input from higher cognitive areas (Hausdorff *et al.*, 2005). Research over the past decade has refined our understanding of the relationship between gait and cognition to reveal compensatory cognitive strategies which vary as a function of age and pathology (Hausdorff *et al.*, 2005). Cross sectional studies identify associations between gait and cognition in normal ageing and neurodegenerative disease (Yogev *et al.*, 2005; Ijmker and Lamoth, 2012; Verlinden *et al.*, 2013a; Lord *et al.*, 2014) as supported by neuroimaging studies (Holtzer *et al.*, 2014). Longitudinally, gait emerges as a strong and significant predictor of future cognitive impairment and dementia in older adults (Marquis *et al.*, 2002; Verghese *et al.*, 2007; Buracchio *et al.*, 2010; Mielke *et al.*, 2013).

Gait speed is universally used to reflect gait because of its utility and robust clinometric properties (Wade, 1992). However, due to its inherent complexity and because it is a multidimensional construct comprised of a number of discrete characteristics, gait cannot be represented by a single outcome. Although gait speed is sensitive to pathology, it is neither discriminative nor reflective of subtle and selective alterations of gait expressed in response to change in neuropathology in ageing and disease (Stolze *et al.*, 2001; Verghese *et al.*, 2007; Lord *et al.*, 2014). Selective identification of gait characteristics is therefore critical for discrimination of pathology, identifying specific features of disease progression and discerning the effect of age for detection of shared neural correlates.

To allow for selectivity and specificity a comprehensive range of gait characteristics must be assessed, although there is high covariance among gait characteristics which needs to be accounted for. In response, several groups have proposed gait models that group gait characteristics into gait domains using data reduction techniques such as principle components

analysis (Verghese *et al.*, 2007; Hollman *et al.*, 2011; Lord *et al.*, 2013; Verlinden *et al.*, 2013b). Whilst the models are comparable, there are subtle differences. For example Verghese and colleagues collated eight gait characteristics to form three domains; pace, variability and rhythm whereas Lord and colleagues obtained two further domains; asymmetry and postural control by collating 16 characteristics. Other models have produced more novel domains such as tandem and turning (Verlinden *et al.*, 2013b) allowing for inclusion of more complex motor tasks. Independent domains of gait (and the characteristics thereof) can then be hypothesised to reflect independent neuroanatomical and functional substrates. Similarly for cognition, independent assessments are grouped to examine domains (Martin *et al.*, 2013; Verlinden *et al.*, 2013a; Lord *et al.*, 2014) that are thought to represent independent neural substrates underlying cognitive functions.

Current understanding of disease pathology provides insight into potential associations of gait and cognition. For example, people with Alzheimer's disease (AD) present foremost with deficits in amnestic ability predominantly due to amyloid deposition in the entorhinal cortex and hippocampus (Braak and Braak, 1995), with concordant findings of an association between atrophy of the hippocampus and decreased gait speed and step length (Callisaya *et al.*, 2013). Similarly, people with Parkinson's disease (PD) present with executive attention deficits due to compromised fronto-striatal circuitry (Stern *et al.*, 1993; Burton *et al.*, 2004) and attention also is significantly associated with reduced gait speed and step length (Lord *et al.*, 2014). The question remains however if discrete gait domains share a different association dependent upon cognitive function? Furthermore, if the relationship between gait and cognitive variables is selective one may expect a different signature of impairments to emerge underpinned by the selective influence of pathology. A better understanding of this relationship would strengthen an understanding of the mechanisms of gait impairment, the shared neural and pathological correlates of gait and cognitive function and validate the role of gait as a surrogate biomarker of cognitive decline and pathology (Lord *et al.*, 2014; Mollenhauer *et al.*, 2014). The relationship between gait and cognition however is still an emerging are of work, largely

due to recent advances in the understanding of gait and improvement in the ability to measure its discrete characteristics. To date a comprehensive investigation of the selective association between independent gait and cognition characteristics has not been undertaken.

The purpose of this review was therefore to undertake a detailed comparison of studies exploring discrete relationships of gait and cognitive domains. For this review, studies were limited to measuring gait under single task conditions. Gait under single task conditions reflects the ability of the cognitive system to control locomotion and to compensate for motor and cognitive deficit as a consequence of ageing and pathology. Therefore it is expected that changes in cognitive function would be reflected in changes in gait performance. Although dual task paradigm studies are extensively used to examine associations of gait and cognition, inconsistent findings are reported due to methodological issues such as diverse concurrent tasks, controlling for baseline task demand and different analysis of calculating dual task interference (Rochester *et al.*, 2014). In addition to these inconsistencies, the underlying cognitive nature of dual task methodology remains unclear and does not reflect baseline cognitive influence on gait; therefore making it difficult to tease out direct underlying neural correlates.

In light of this, the aims of this review are to i) explore evidence for the associations between independent features of gait and cognitive function and ii) identify the longitudinal nature of relationships. We hypothesise that independent gait characteristics would be related to discrete cognitive functions in a specific rather than global manner and the pattern of association would be different with respect to pathology and ageing. In order to address this hypothesis we adopted a model of gait previously used in OA (Lord *et al.*, 2013)(Figure 1) and a comprehensive range of cognitive domains previously described (Emre *et al.*, 2007) to improve consistency, reduce redundancy and retain independence between gait and cognitive features respectively to ease interpretation of results. We mapped individual gait domains (or respective characteristics) to individual cognitive functions to develop a matrix from which to identify discrete relationships. Three different cohorts were included: older adults (OA); those with cognitive

impairment (CI); and people with PD, in order to explore gait-cognition associations in pathology and normal ageing. Cross-sectional and longitudinal study designs were examined to identify causality. It is hoped this review will not only to provide a clear understanding of current associations but in addition identify gaps in the literature to inform recommendations for future work.

2. METHODS

2.1 SEARCH STRATEGY

Three databases were used for the search: Medline, Psychinfo and Scopus. For each of the databases used, three separate searches were performed for the three cohorts included in the review; OA, CI and PD. In total, nine separate searches were completed. Each search used the key terms ‘Gait’, ‘Cognition’ and either ‘Parkinson’s disease’, ‘dementia’ or ‘older adults’. For each of the key terms, a list of synonyms were correlated and entered into the search (Table 1). Where possible, MESH headings were used for Medline and Psychinfo. The search was limited for papers published since 1990 to February 2014, written in English language and restricted to full journal articles only.

The initial nine searches were combined into three master databases; ‘Parkinson’s disease’, ‘Cognitive Impairment’ and ‘Older Adults’. Duplicates were then deleted and an initial title screen was performed by the reviewer (RM). After the initial title screen, the titles and abstracts were reviewed by independent reviewers (RM and JB). A review of the full text was needed in incidences where it was unclear from the abstract whether the paper was suitable for inclusion.

2.2 INCLUSION AND EXCLUSION CRITERIA

Articles were included if they assessed OA and patients with either a degree of cognitive impairment or PD completing a gait assessment under single task conditions and independently completing a minimum of one cognitive assessment. Cognitive assessments included general cognitive tests (e.g. MMSE/MOCA) as well as tests of attention, executive function, memory, language, processing speed and visuospatial skills. Articles must have completed analysis for gait assessment under single task conditions. Articles were excluded if they only completed cognitive tasks under dual task conditions or if analysis was only reported for dual task conditions. Intervention studies were excluded as well as studies focusing on falls, freezing of gait (FOG) and overall physical activity.

2.3. DATA EXTRACTION

A title and abstract screen was undertaken by two independent reviewers; RM and JB. Three separate data extraction forms were created for the three cohorts. Data from the extraction forms was then transferred into a table. Information included; participant groups, participant characteristics, study type, gait variables measured, gait analysis tool, cognitive domains tested, cognitive assessments used and main study findings. The cognitive impairment cohort included the type of cognitive impairment and for the PD cohort whether participants were ON or OFF medication.

RESULTS

3.1 SEARCH YIELD

The search strategy generated a total of 43,828 papers; after exclusion criteria were applied the search strategy generated a total of 25,487 papers. After duplicates were removed, a total number of 22,128 papers were yielded from the search. The total number of papers were compiled into three databases; OA (*n*=11609), CI (*n*=7919 and PD (*n*=2600). After the initial title

screen, the total number of papers of interest for each group were OA (*n*=168), CI (*n*=119) and PD (*n*=62).

After an abstract screen, 66 papers were eligible for data extraction (*n*=34 OA, *n*=22 CI, *n*=10 PD). 11 papers were excluded due to inability to access paper (*n*=7), duplicate findings (*n*=1) and studies which were not full journal articles (*n*=3). Data extraction was completed for a total of 55 papers; 30 for the OA cohort, 15 for the CI cohort and 10 for the PD cohort. After data extraction, 9 papers were excluded due to completing only dual task conditions (*n*=4), not associating gait and cognition (*n*=1), associating fast speed only (*n*=1), participants being too young (*n*=1, all <60 years), not completing both independent cognitive domains and gait variables (*n*=1) and focusing on cognitive reserve (*n*=1). Four papers (Dodge *et al.*, 2012; Lord *et al.*, 2014), (Kaye *et al.*, 2012) and (Xu *et al.*, 2014) have been identified since the search closed and were added to the data extraction process. The total number of papers used was 50. The search yield is demonstrated in Figure 2. All articles were originally published in the English language. Publication dates ranged from 2002 (Lord and Menz, 2002; Marquis *et al.*, 2002) to 2014 (Lord *et al.*, 2014; Xu *et al.*, 2014).

3.2 MEASUREMENT OF GAIT AND COGNITION – METHODOLOGICAL COMPARISONS

Gait measurement techniques included the use of activity monitors (Rochester *et al.*, 2004; Rochester *et al.*, 2005; Rochester *et al.*, 2008; Gillain *et al.*, 2009; Lord *et al.*, 2010; Maquet *et al.*, 2010; Ijmker and Lamoth, 2012), gait walkway systems (Holtzer *et al.*, 2006; Hollman *et al.*, 2007; van Iersel *et al.*, 2008; Beauchet *et al.*, 2012; Coelho *et al.*, 2012; Holtzer *et al.*, 2012; Muir *et al.*, 2012; Beauchet *et al.*, 2013; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*, 2013a; Lord *et al.*, 2014), optokinetic systems (Ble *et al.*, 2005; Amboni *et al.*, 2012), foot pressure sensors (Sheridan *et al.*, 2003; Allali *et al.*, 2010b), infra-red cameras (Kaye *et al.*, 2012; Wild *et al.*, 2013), timed up and go test (Donoghue *et al.*, 2012; Smulders *et al.*, 2013; Xu *et al.*, 2014), timed to walk (Fitzpatrick *et al.*, 2007; Auyeung *et al.*, 2008; Duff *et al.*, 2008; Persad *et al.*, 2008; McGough *et al.*, 2011) and 6 minute walk

distance test (Lord and Menz, 2002). A number of studies used a combination of techniques listed above (Hausdorff *et al.*, 2005; Yogev *et al.*, 2005; Lamoth *et al.*, 2011; Bramell-Risberg *et al.*, 2012). The majority of studies assessed single gait characteristics but five studies utilised gait domains (Verghese *et al.*, 2007; Amboni *et al.*, 2012; Lord *et al.*, 2013; Verlinden *et al.*, 2013a; Lord *et al.*, 2014).

A variety of cognitive assessments were utilised as shown in Tables 6, 7, 8 and 9 however, several of the same assessments were used in different studies and reported as testing different cognitive domains. Therefore for clarity we've noted studies that either assessed single cognitive assessments in association with gait; (Lord and Menz, 2002; Marquis *et al.*, 2002; Sheridan *et al.*, 2003; Rochester *et al.*, 2004; Ble *et al.*, 2005; Hausdorff *et al.*, 2005; Rochester *et al.*, 2005; Yogev *et al.*, 2005; Alfaro-Acha *et al.*, 2007; Atkinson *et al.*, 2007; Fitzpatrick *et al.*, 2007; Hollman *et al.*, 2007; Inzitari *et al.*, 2007; Auyeung *et al.*, 2008; Duff *et al.*, 2008; Persad *et al.*, 2008; Rochester *et al.*, 2008; van Iersel *et al.*, 2008; Deshpande *et al.*, 2009; Gillain *et al.*, 2009; Allali *et al.*, 2010a; Atkinson *et al.*, 2010; Buracchio *et al.*, 2010; Lord *et al.*, 2010; Maquet *et al.*, 2010; Auyeung *et al.*, 2011; Lamoth *et al.*, 2011; McGough *et al.*, 2011; Beauchet *et al.*, 2012; Bramell-Risberg *et al.*, 2012; Coelho *et al.*, 2012; Donoghue *et al.*, 2012; Ijmker and Lamoth, 2012; Muir *et al.*, 2012; Taniguchi *et al.*, 2012; Beauchet *et al.*, 2013; Lord *et al.*, 2013; Smulders *et al.*, 2013; Wild *et al.*, 2013; Xu *et al.*, 2014) or grouped assessments to form domains (Holtzer *et al.*, 2006; Verghese *et al.*, 2007; Watson *et al.*, 2010; Amboni *et al.*, 2012; Dodge *et al.*, 2012; Holtzer *et al.*, 2012; Kaye *et al.*, 2012; Martin *et al.*, 2013; Verlinden *et al.*, 2013a; Lord *et al.*, 2014).

3.3 ASSOCIATIONS BETWEEN GAIT DOMAINS AND COGNITION

Associations between independent cognitive functions were explored with respect to independent gait domains (Figure 1). Individual gait characteristics were mapped onto their respective domains such that relationships are

explored with respect to broad gait domains. Where possible, studies which outlined their own domains were appropriately matched to the most relevant domain in the model used in this review as individual gait characteristic associations were mainly not reported. In addition, the strongest statistical analysis has been reported for each study (e.g. if the analysis included consideration of covariates). Tables 2, 3, 4 and 5 summarises the findings into associations for each cohort which are colour coded to show whether an association was found (green) or not (red). Tables 6, 7, 8 and 9 provide further details on each individual study. Figures 3 and 4 complete the schema map of associations for cross-sectional (Figure 3) and longitudinal studies (Figure 4).

3.3.1 PACE

Pace was the most frequently assessed gait variable in all three cohorts (Lord and Menz, 2002; Sheridan *et al.*, 2003; Rochester *et al.*, 2004; Ble *et al.*, 2005; Hausdorff *et al.*, 2005; Rochester *et al.*, 2005; Yogev *et al.*, 2005; Holtzer *et al.*, 2006; Fitzpatrick *et al.*, 2007; Hollman *et al.*, 2007; Auyeung *et al.*, 2008; Duff *et al.*, 2008; Persad *et al.*, 2008; Rochester *et al.*, 2008; van Iersel *et al.*, 2008; Deshpande *et al.*, 2009; Gillain *et al.*, 2009; Allali *et al.*, 2010b; Atkinson *et al.*, 2010; Lord *et al.*, 2010; Maquet *et al.*, 2010; Watson *et al.*, 2010; Lamoth *et al.*, 2011; McGough *et al.*, 2011; Amboni *et al.*, 2012; Beauchet *et al.*, 2012; Bramell-Risberg *et al.*, 2012; Donoghue *et al.*, 2012; Holtzer *et al.*, 2012; Ijmker and Lamoth, 2012; Kaye *et al.*, 2012; Muir *et al.*, 2012; Beauchet *et al.*, 2013; Lord *et al.*, 2013; Martin *et al.*, 2013; Smulders *et al.*, 2013; Verlinden *et al.*, 2013a; Wild *et al.*, 2013; Lord *et al.*, 2014; Xu *et al.*, 2014). In addition, a number of studies assessed specific gait characteristics that loaded onto the pace domain (Sheridan *et al.*, 2003; Rochester *et al.*, 2004; Hausdorff *et al.*, 2005; Yogev *et al.*, 2005; Holtzer *et al.*, 2006; Hollman *et al.*, 2007; van Iersel *et al.*, 2008; Gillain *et al.*, 2009; Allali *et al.*, 2010b; Maquet *et al.*, 2010; Lamoth *et al.*, 2011; Amboni *et al.*, 2012; Beauchet *et al.*, 2012; Coelho *et al.*, 2012; Holtzer *et al.*, 2012; Ijmker and Lamoth, 2012; Muir *et al.*, 2012; Beauchet *et al.*, 2013; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*, 2013a; Lord *et al.*, 2014) (Figure 1). In

OA, associations were evident between pace and attention as shown by 7 of 7 studies (Holtzer *et al.*, 2006; Duff *et al.*, 2008; Watson *et al.*, 2010; Holtzer *et al.*, 2012; Kaye *et al.*, 2012; Lord *et al.*, 2013; Martin *et al.*, 2013), executive function as shown by 8 of 12 studies (Hausdorff *et al.*, 2005; Holtzer *et al.*, 2006; Watson *et al.*, 2010; Beauchet *et al.*, 2012; Donoghue *et al.*, 2012; Holtzer *et al.*, 2012; Martin *et al.*, 2013; Verlinden *et al.*, 2013a), processing speed as shown by 5 of 6 studies (Holtzer *et al.*, 2006; Watson *et al.*, 2010; Donoghue *et al.*, 2012; Kaye *et al.*, 2012; Martin *et al.*, 2013), language as shown by 3 of 3 studies (Holtzer *et al.*, 2006; Duff *et al.*, 2008; Holtzer *et al.*, 2012) and visuospatial skills as shown by 2 of 3 studies (Duff *et al.*, 2008; Kaye *et al.*, 2012). In OA no association was evident between pace and global cognition (Hausdorff *et al.*, 2005; Fitzpatrick *et al.*, 2007; Hollman *et al.*, 2007; Irani *et al.*, 2007; Atkinson *et al.*, 2010; Bramell-Risberg *et al.*, 2012; Lord *et al.*, 2013) and pace and memory (Hausdorff *et al.*, 2005; van Iersel *et al.*, 2008; Kaye *et al.*, 2012; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*, 2013a). In the CI cohort pace was assessed in nine studies with AD participants (Sheridan *et al.*, 2003; Persad *et al.*, 2008; Gillain *et al.*, 2009; Allali *et al.*, 2010a; Maquet *et al.*, 2010; Lamoth *et al.*, 2011; Coelho *et al.*, 2012; Ijmker and Lamoth, 2012; Muir *et al.*, 2012; Beauchet *et al.*, 2013), two with FTD (Allali *et al.*, 2010a; Ijmker and Lamoth, 2012), one with CI (Auyeung *et al.*, 2008) and three with MCI (Gillain *et al.*, 2009; Muir *et al.*, 2012; Beauchet *et al.*, 2013). Slower gait speed was associated with AD (Sheridan *et al.*, 2003; Persad *et al.*, 2008; Gillain *et al.*, 2009; Maquet *et al.*, 2010; Coelho *et al.*, 2012; Ijmker and Lamoth, 2012), FTD (Allali *et al.*, 2010a; Ijmker and Lamoth, 2012) and CI (Auyeung *et al.*, 2008) but not MCI (Gillain *et al.*, 2009; Muir *et al.*, 2012; Beauchet *et al.*, 2013). In the CI cohort, an association between pace and executive function was supported by 2 of 3 studies (Persad *et al.*, 2008; McGough *et al.*, 2011). Only one study associated pace with global cognition and attention (Maquet *et al.*, 2010). In PD, an association was evident between pace and attention with 2 of 3 studies obtaining this result (Lord *et al.*, 2010; Lord *et al.*, 2014). Evidence was inconclusive for pace and executive function with 5 studies finding an association (Rochester *et al.*, 2004; Rochester *et al.*, 2005; Yogev *et al.*, 2005; Smulders *et al.*, 2013; Xu *et al.*, 2014) and 5 not (Rochester *et*

al., 2008; Lord *et al.*, 2010; Amboni *et al.*, 2012; Wild *et al.*, 2013; Lord *et al.*, 2014), pace and visuospatial with one study finding an association (Amboni *et al.*, 2012) and one study not (Lord *et al.*, 2014) and pace and memory with one study finding an association (Lord *et al.*, 2014) and one study not (Amboni *et al.*, 2012). There was no association between pace and global cognition for PD.

3.3.2 VARIABILITY

Characteristics of gait variability including step velocity variability, step length variability and step width variability (Figure 1) were comprehensively assessed in OA (van Iersel *et al.*, 2008; Holtzer *et al.*, 2012; Kaye *et al.*, 2012; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*, 2013a) but were limited in PD (Amboni *et al.*, 2012; Lord *et al.*, 2014) and were not studied in CI. In OA no consistent associations were evident with any of the cognitive domains (van Iersel *et al.*, 2008; Holtzer *et al.*, 2012; Kaye *et al.*, 2012; Lord *et al.*, 2013; Martin *et al.*, 2013). In PD only two studies explored variability and cognition (Amboni *et al.*, 2012; Lord *et al.*, 2014). One study assessed global cognition for which an association was found (Lord *et al.*, 2014). Evidence was inconclusive for visuospatial ability with one study finding an association (Amboni *et al.*, 2012) and the other study refuting these findings (Lord *et al.*, 2014). No associations were found with executive function, attention or memory in PD.

3.2.3 RHYTHM

Characteristics of rhythm including step time, step swing time and step stance time (Figure 1) were assessed throughout the three cohorts (Rochester *et al.*, 2004; Hausdorff *et al.*, 2005; Gillain *et al.*, 2009; Allali *et al.*, 2010a; Maquet *et al.*, 2010; Lamoth *et al.*, 2011; Coelho *et al.*, 2012; Holtzer *et al.*, 2012; Ijmker and Lamoth, 2012; Muir *et al.*, 2012; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*, 2013a; Wild *et al.*, 2013; Lord *et al.*, 2014). Five studies in OA assessed rhythm (Hausdorff *et al.*, 2005; Holtzer *et al.*, 2012; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*,

2013a) providing evidence for an association with processing speed (Martin *et al.*, 2013; Verlinden *et al.*, 2013a) but no other domains. Rhythm was assessed in AD (Gillain *et al.*, 2009; Maquet *et al.*, 2010; Lamoth *et al.*, 2011; Coelho *et al.*, 2012; Ijmker and Lamoth, 2012; Muir *et al.*, 2012), FTD (Ijmker and Lamoth, 2012) and MCI (Gillain *et al.*, 2009; Maquet *et al.*, 2010; Muir *et al.*, 2012) with only inconclusive evidence associating rhythm deficit in FTD (Ijmker and Lamoth, 2012) and MCI (Gillain *et al.*, 2009; Maquet *et al.*, 2010). In the CI group, only one study assessed global cognition for which an association was found (Maquet *et al.*, 2010). There was no evidence for an association between rhythm and attention (Maquet *et al.*, 2010). In PD, rhythm was measured by five studies (Rochester *et al.*, 2004; Amboni *et al.*, 2012; Wild *et al.*, 2013; Lord *et al.*, 2014) with no evidence for associations with cognition. One study which sub-grouped motor phenotype (Lord *et al.*, 2014) associated rhythm and executive function in the postural instability/gait difficulty (PIGD) phenotype only.

3.3.4 ASYMMETRY

Asymmetry was the least frequently tested gait variable with characteristics of step time asymmetry, step swing asymmetry and step stance asymmetry (Lord *et al.*, 2013; Lord *et al.*, 2014) assessed in OA and PD only (Figure 1). There were no associations with cognition.

3.3.5 POSTURAL CONTROL

Postural control characteristics of step width and step length asymmetry (Figure 1) were assessed by a total of seven studies (van Iersel *et al.*, 2008; Amboni *et al.*, 2012; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*, 2013a; Lord *et al.*, 2014) throughout the cohorts. In OA one study assessed postural control and visuospatial function, and reported a significant association (Martin *et al.*, 2013). Evidence was inconclusive in OA for an association with executive function, attention and processing speed with 2 of 4 studies (Lord *et al.*, 2013; Martin *et al.*, 2013), 1 of 2 studies (Martin *et al.*, 2013) and 1 of 2 (Martin *et al.*, 2013) studies observing associations

respectively. No association was evident in OA for postural control for global cognition (Lord *et al.*, 2013) and memory (van Iersel *et al.*, 2008; Lord *et al.*, 2013; Martin *et al.*, 2013; Verlinden *et al.*, 2013a). There was no evidence for associations in the CI cohort. Two studies observed postural control in PD (Amboni *et al.*, 2012; Lord *et al.*, 2014) with inconclusive evidence for associations with memory (Lord *et al.*, 2014) and visuospatial (Amboni *et al.*, 2012). In PD there were no associations with global cognition (Amboni *et al.*, 2012; Lord *et al.*, 2014), executive function (Amboni *et al.*, 2012; Lord *et al.*, 2014) or attention (Lord *et al.*, 2014).

3.4 LONGITUDINAL STUDIES OF THE GAIT-COGNITION RELATIONSHIP

Twelve studies investigated longitudinal relationships between gait and cognition (Marquis *et al.*, 2002; Alfaro-Acha *et al.*, 2007; Atkinson *et al.*, 2007; Inzitari *et al.*, 2007; Verghese *et al.*, 2007; Deshpande *et al.*, 2009; Atkinson *et al.*, 2010; Buracchio *et al.*, 2010; Watson *et al.*, 2010; Auyeung *et al.*, 2011; Dodge *et al.*, 2012; Taniguchi *et al.*, 2012). Eleven studies assessed healthy OA at baseline (Marquis *et al.*, 2002; Alfaro-Acha *et al.*, 2007; Atkinson *et al.*, 2007; Inzitari *et al.*, 2007; Verghese *et al.*, 2007; Deshpande *et al.*, 2009; Atkinson *et al.*, 2010; Buracchio *et al.*, 2010; Watson *et al.*, 2010; Auyeung *et al.*, 2011; Taniguchi *et al.*, 2012). One study observed three cohorts at different stages of MCI (Dodge *et al.*, 2012). 9 of the 12 studies assessed gait as a predictor for cognitive decline (Marquis *et al.*, 2002; Alfaro-Acha *et al.*, 2007; Inzitari *et al.*, 2007; Verghese *et al.*, 2007; Auyeung *et al.*, 2008; Deshpande *et al.*, 2009; Buracchio *et al.*, 2010; Dodge *et al.*, 2012; Taniguchi *et al.*, 2012), 2 of 12 assessed cognition as a predictor for gait decline (Atkinson *et al.*, 2007; Watson *et al.*, 2010) and 1 of 12 studied the decline of gait and cognition simultaneously (Atkinson *et al.*, 2010).

3.4.1 GAIT AS A PREDICTOR FOR COGNITIVE DECLINE

All nine studies assessing gait as a predictor measured pace. Evidence was strong for pace as a predictor for global cognition as shown by 7 of 9 studies (Marquis *et al.*, 2002; Alfaro-Acha *et al.*, 2007; Verghese *et al.*, 2007; Buracchio *et al.*, 2010; Auyeung *et al.*, 2011; Dodge *et al.*, 2012; Taniguchi *et al.*, 2012) with two studies refuting these findings (Deshpande *et al.*, 2009; Atkinson *et al.*, 2010).Two studies observed cognitive domains (Inzitari *et al.*, 2007; Verghese *et al.*, 2007). Pace predicted a decline in executive function (Verghese *et al.*, 2007) and processing speed (Inzitari *et al.*, 2007). Evidence was inconclusive for decline in attention with one study finding this (Inzitari *et al.*, 2007) and one not (Verghese *et al.*, 2007). Pace was not found to be a predictor of memory decline (Verghese *et al.*, 2007). One study assessed variability of gait (Verghese *et al.*, 2007) which predicted dementia onset but not domains of global cognition, attention, executive function or memory. Two studies assessed rhythm of gait (Verghese *et al.*, 2007; Taniguchi *et al.*, 2012). An association between rhythm and decline in memory was identified by one study (Verghese *et al.*, 2007). Evidence was inconclusive for rhythm as a predictor of global cognitive decline (Verghese *et al.*, 2007; Taniguchi *et al.*, 2012) with one study identifying rhythm as a risk factor for dementia onset (Verghese *et al.*, 2007) . No links were found between rhythm and decline in executive function or attention (Verghese *et al.*, 2007).

3.4.2 COGNITION AS A PREDICTOR FOR GAIT DECLINE

All three studies assessed pace only. Evidence suggested that global cognition (Atkinson *et al.*, 2007; Watson *et al.*, 2010), executive function (Atkinson *et al.*, 2007; Watson *et al.*, 2010) and memory (Watson *et al.*, 2010) predicted a decline in pace. There were no evidence for processing speed (Watson *et al.*, 2010) or attention (Watson *et al.*, 2010) as predictors of decline in pace.

4. DISCUSSION

To our knowledge this is the first structured review to summarise the relationship between single task gait and cognition in older adults with and without cognitive impairment, and in PD. Key findings from this structured review are that for all groups the pace domain of gait (driven predominantly by gait speed) is associated with a broad range of cognitive functions but also selectively associated with executive attention. Gait speed is also a strong predictor of cognitive decline in OA, however there is also some evidence of reverse causality. Other relationships are emerging but restricted by a limited scope of gait and cognitive outcomes as well as methodological inconsistencies. Results from this study partly confirm our hypotheses. Independent gait characteristics relate to discrete cognitive functions and the pattern of association varies as a function of pathology and age. This specificity will help inform our understanding of co-incident pathology and shared neural networks, and help identify the pattern of change for each over time. In all three groups the pace domain of gait was also associated almost universally with cognitive measures. Although less discrete, this sensitivity provides a basis for understanding the broader relationship between gait and cognition, and provides a platform for more specific inquiry.

4.1 GAIT AND COGNITION: A GLOBAL RELATIONSHIP

This review identified a broad range of cognitive correlates for gait. Of all gait characteristics measured, those from the pace domain (particularly gait speed) yielded the strongest relationships. Reasons for this are twofold. With one exception, gait speed was universally measured in all studies which increased the likelihood of chance findings and dominated the results. Secondly, of the 16 gait characteristics reflected in the gait model, gait speed is the most sensitive and least specific metric. It reflects global gait impairment but does not inform about the underlying cause of that impairment. Gait speed may be considered ‘the final common expression’ of gait, and associations with cognition are therefore likely to be more evident for this global measure.

4.2 GAIT AND COGNITION: A SELECTIVE RELATIONSHIP

A number of studies adopted a broader approach to measurement where selective associations became evident (Verghese *et al.*, 2007; Verlinden *et al.*, 2013a; Lord *et al.*, 2014). Assessments were particularly limited in pathological cohorts and in addition, sample sizes tended to be small, albeit with some exceptions (Rochester *et al.*, 2008; McGough *et al.*, 2011; Amboni *et al.*, 2012; Smulders *et al.*, 2013; Lord *et al.*, 2014). Despite limitations, subtle emergent associations have been mapped that appear specific to pathology which are discussed below. These findings contribute to our understanding of underlying pathology and the mechanisms that underpin cognitive and gait functions with respect to that pathology. What is evident is that common neural substrates for gait and cognition emerge which may differ according to age and pathology. This knowledge will ultimately lead to refinement of diagnostics and development of novel therapeutics.

Evidence associating pace with attention and executive function (considered here as the executive attention domain (Perry and Hodges, 1999; Woodruff-Pak and Papka, 1999; Emre *et al.*, 2007; Wild *et al.*, 2013)) was demonstrated in all three groups. This was most evident in OA as demonstrated by large number of high quality studies. In disease cohorts this association was not as strong, due to a smaller number of studies which were more varied in quality and therefore must be interpreted with more caution. Lesion (Wilkins *et al.*, 1987) and imaging studies (Collette *et al.*, 2006) implicate the prefrontal cortex (PFc) as the site for executive attention which initiates purposeful, goal directed behaviours essential to daily living (Criado *et al.*, 1997; Perry and Hodges, 1999) . In addition, the PFc drives executive attention processes during locomotion to modulate gait (Malouin *et al.*, 2003; Koenraadt *et al.*, 2014). In normal ageing, executive attention declines (Gunning-Dixon and Raz, 2000; Grieve *et al.*, 2007) with more pronounced deficits occurring in neurological disorders including PD (Emre, 2003) and AD (Perry and Hodges, 1999). Decline in PFc function is associated with increased white matter lesions in older adults and pathology (Bartzokis *et al.*, 2003; Resnick *et al.*, 2003) resulting in deficits in velocity and step length of gait (Nadkarni *et al.*, 2009; de Laat *et al.*, 2012). An important caveat to interpretation of imaging data is that not all brain

structures potentially implicated in gait and cognitive processing are imaged, and this may lead to an incomplete view. The notion of shared cognitive and gait neural substrates is supported elsewhere. For example, in PD, dopaminergic neuronal loss of the substantia nigra impacts on the PFc via a complex network of neuronal pathways and connections (Gotham *et al.*, 1988). This loss attenuates cognitive resource in people with PD, which in turn compromises the ability to cognitively compensate for gait deficit (Yogev-Seligmann *et al.*, 2008). Other neurotransmitters are implicated in this relationship. For example, acetyl-choline (Ach) mediates attentional processes of the PFc (Yarnall *et al.*, 2011) which is associated with a slower gait speed (Rochester *et al.*, 2012). Preliminary results report beneficial effects of Rivastigmine, an acetylcholinesterase inhibitor, on reducing step time variability in people with PD (Henderson *et al.*, 2015), considered a proxy of falls. Thus, age-related degeneration in white matter may elicit an associated decline in pace and executive attention, predominantly due to cholinergic burden. This burden may be exacerbated in disease such as dementia and PD. Development of cognitive enhancement therapies is likely to expand as our understanding of the effect of cognitive processes on gait becomes more refined.

Specific to PD pathology but not dementia, postural control and variability were both associated with cognition. Postural control is an essential component of gait, and similarly to pace, cortical networks are used to modulate postural control (Kelly *et al.*, 2015) via activation of executive-attention networks (Lord *et al.*, 2013; Martin *et al.*, 2013). The ability to regulate postural control is compromised by white matter pathology in these and other cortical networks (de Laat *et al.*, 2011; Rosano *et al.*, 2012). Executive-attention also mediates visuo-spatial function which is critical to postural control (Suarez *et al.*, 2011). This association of visuo-spatial function was noted in older adults (Martin *et al.*, 2013), although this was reported only in one study. However previous literature has identified an association of visual performance and measures of balance in older people (Brach *et al.*, 2008). This relationship may be exacerbated, in people with PD with freezing of gait (FOG), who perform worse on tests of visuospatial ability

compared to non-FOG (Cowie *et al.*, 2010) possibly due to decreased grey matter in posterior cortical areas (Tessitore *et al.*, 2012). Evidence of association for postural control and memory was contradictory for the two studies that examined these features (Amboni *et al.*, 2012; Lord *et al.*, 2014). Both studies used valid tests as recognised by the PDD movement disorder task force (Dubois *et al.*, 2007), Lords' study showed an association used working memory (forward digit span) (Lord *et al.*, 2014) in contrast to Amboni's study which did not show an association used the Rey Auditory Verbal Learning Test (RAVLT) (Amboni *et al.*, 2012). Important to note is the association in Lord's study was driven by the PIGD phenotype (Lord *et al.*, 2014), which further sensitised results. Associations for global cognition and visuospatial ability with variability were also evident for people with PD but once again were contradictory. A positive association was found with global cognition using the MoCA (Lord *et al.*, 2014) but not the MMSE (Amboni *et al.*, 2012) essentially because the MoCA is a more sensitive test of cognition in those with PD (Zadikoff *et al.*, 2008). Similarly for visuospatial outcomes, an association was found when a rigorous visuospatial assessment battery was used, thus optimising neural correlates (Lord *et al.*, 2014). However, once again these results were in the FOG cohort. The same results were not replicated in OA suggesting the relationship is mediated by visuospatial difficulties in PD and not normal ageing. However, the data emerges from a small number of studies and, although promising, will need to be explored in future research.

For participants with cognitive impairment and dementia an association emerged between cognitive function and the rhythm domain of gait, possibly mediated by the hippocampus which is affected by cognitive decline and FTD (Fellgiebel *et al.*, 2004; Franceschi *et al.*, 2005). The hippocampus plays an important role in motor and gait tasks (Bland and Oddie, 2001; Paylor *et al.*, 2001; Malouin *et al.*, 2003), and is key to effective spatial navigation (Epstein, 2008). However, this data should be interpreted cautiously because AD and FTD groups were combined, and this may have confounded results. More surprisingly, rhythm was also associated with executive function in PIGD phenotype of PD (Lord *et al.*, 2014). People with

PD who present with the PIGD phenotype deteriorate at a faster rate in both gait and cognitive function and are at a higher risk of developing dementia than those with the tremor-dominant phenotype (Burn *et al.*, 2006) making the association more sensitive. Unexpectedly, rhythm was also associated with processing speed in older adults (Martin *et al.*, 2013; Verlinden *et al.*, 2013a). The authors suggested this may be linked to the velocity aspect of rhythm and to the timing nature of cognitive assessments (Martin *et al.*, 2013; Verlinden *et al.*, 2013a). In addition, cognitive tests of processing speed may overlap with executive-attentional elements (Donoghue *et al.*, 2012) which may well have contributed to this association. Although rhythm is considered a 'rudimentary' characteristic of gait (Lord *et al.*, 2013) controlled by subcortical brain regions including the brain stem and spinal cord (Taniguchi *et al.*, 2012), in response to pathology and ageing it may become more cortically mediated.

We did not find any reported associations between the asymmetry domain of gait and cognition, although only four studies assessed asymmetry across all cohorts (Gillain *et al.*, 2009; Maquet *et al.*, 2010; Lord *et al.*, 2013; Lord *et al.*, 2014). Asymmetry comprises both spatial and temporal features of gait. Spatial asymmetry is more likely to be associated with cognitive function given its relationship with step length which, as evidenced by this review, is frontally mediated (Martin *et al.*, 2013). In contrast, temporal features of asymmetry are driven subcortically (Barrière *et al.*, 2008) and cognitive correlates are therefore less likely. However, the single study in early PD that examined these features separately did not find a relationship between spatial asymmetry and cognition. Although spatial asymmetry was significantly worse in PD compared to controls, the threshold for cognitive deficit to provide a signal with asymmetry was not reached.

4.3 GAIT AS A PREDICTOR OF COGNITIVE DECLINE

This review provides robust evidence of the capacity of gait to predict cognitive decline, with a number of large, community based studies in older adults supporting this view (Table 5). Risk of developing vascular dementia

or decline in executive attention is predicted by impairment in the pace domain of gait (Gootjes *et al.*, 2004; Verghese *et al.*, 2007) signalling that gait is sensitive to early changes in WMH. This finding is also evident in older adults (Nadkarni *et al.*, 2009) suggesting sensitivity of gait to more subtle cognitive burden. Studies that take a nuanced approach have found specific associations (Verghese *et al.*, 2007). For example, Verghese and colleagues reported that change over time in gait rhythm was a predictor of memory decline and risk of future dementia in healthy older adults (Verghese *et al.*, 2007) which may reflect early pathology in the hippocampus (Braak and Braak, 1997).

The question of reverse causality however cannot be ignored. Several studies (although smaller in number) report that cognition was predictive of decline in the pace domain of gait (Atkinson *et al.*, 2007; Watson *et al.*, 2010). These findings further indicate the intricate relationship between gait and cognition and argue for a comprehensive and sensitive battery of testing for both in order to tease out their relative burden and temporal course. Figure 5 explores this complexity in more detail. It is plausible, for example, for cognitive and gait deficit to co-inside in response to ageing and the time course of decline to occur in parallel or for one to precede the other (Tabbarah *et al.*, 2002; Gale *et al.*, 2014)(Figure 5, concept 1 & 2). By contrast, this is less likely to be the case for pathology where different pathophysiological substrates define the initial magnitude and direction of change, and their putative course (Figure 5, concept 4). In the absence of data we are left to speculate and future research will examine these questions in greater depth and discern these complex processes. No longitudinal studies on the relationship between gait and cognition have been conducted in PD, and the field is open at this stage to interpretation. Based on current evidence (Lord *et al.*, 2014), we speculate that for people with PD, decline in cognition and development of dementia will be predicted by frontal and pre-frontal mechanisms that manifest as deficits in the pace domain of gait (Figure 5, concept 3 & 4).

The time course of the relationships between gait and cognition is likely to be variable and disease-specific, although there is limited evidence to support

this. Most cross sectional studies in established AD report an association with pace but not rhythm (Sheridan *et al.*, 2003; Gillain *et al.*, 2009; Allali *et al.*, 2010a; Maquet *et al.*, 2010; Coelho *et al.*, 2012; Ijmker and Lamoth, 2012; Muir *et al.*, 2012) suggesting as disease progresses cortical influences on gait may become more dominant (Braak and Braak, 1995). One longitudinal study supported an association between early change in gait variability and global cognitive decline, similar to cross sectional findings (Verlinden *et al.*, 2013a; Lord *et al.*, 2014). However, further work is required to examine these features.

4.4 RECOMMENDATIONS AND FUTURE WORK

The key recommendation from this review is that future studies need to incorporate comprehensive batteries of gait and cognition in order to robustly identify associations. Use of standardised protocols will ensure consistency and aid interpretation. Advances in technology via use of validated body worn senses mean that gait can now be measured in home and community environments rather than the laboratory (Godfrey *et al.*, 2014). Not only do sensors provide a simple and cost-effective method of data collection, their use also facilitates measurement in naturalistic environments which reflect habitual gait patterns. The cognitive correlates of naturalistic gait may be different what we have reported here (Hagler *et al.*, 2010) and this is an exciting field of future research.

Limitations to this review include use of a model of gait we were familiar with to structure our analysis. We may have found more associations if we had included more gait characteristics or used a different model. However, we were confident in selecting the model because it has been validated in PD and older adults, and it allowed for a more structured and robust interpretation. Nevertheless, it is important to recognise the interdependence of both gait characteristics (and therefore gait domains), and cognitive functions which also overlap. This has the potential to obfuscate findings and challenge interpretation. Secondly, a quality assessment tool was not used within this structured review which may have limited interpretation. Early on our review process clearly indicated predominance of measurement for the pace domain of gait to the exclusion of other domains. We felt this would bias results if a full systematic review with grading for study quality had been

undertaken. Our findings highlight the need for a more robust methodological approach in this field, which warrants further investigation. Finally, dual task conditions were not reviewed here because we were interested in habitual gait performance. Also, dual task protocols vary widely and findings are inconsistent (Kelly *et al.*, 2015). Methodological issues include diversity of concurrent tasks, inadequate control of baseline task demand, and a varied approach to calculating and interpreting dual task interference (Rochester *et al.*, 2014). However, not including dual task studies may have attenuated findings. Studies report an increase in gait variability (Hollman *et al.*, 2007), rhythm (Yogev *et al.*, 2005) and asymmetry (Yogev *et al.*, 2007) in OA and PD under dual task conditions, reflecting an inability to compensate cognitively for gait deficit. Selective associations with cognitive outcomes have been reported, but it is beyond the scope of this review to comment on these.

In conclusion, this review has systematically examined and reported on a large number of studies concerning the relationship between gait and cognition which is firmly established. Future research will consolidate findings and procure a more nuanced understanding of this important relationship.

Conflicts of Interest

No conflicts of interest are declared

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Figure Captions

Figure 1: Model of gait proposed by Lord et al, 2013 for older adults. Domains include; Pace, Rhythm, Variability, Asymmetry and postural control.

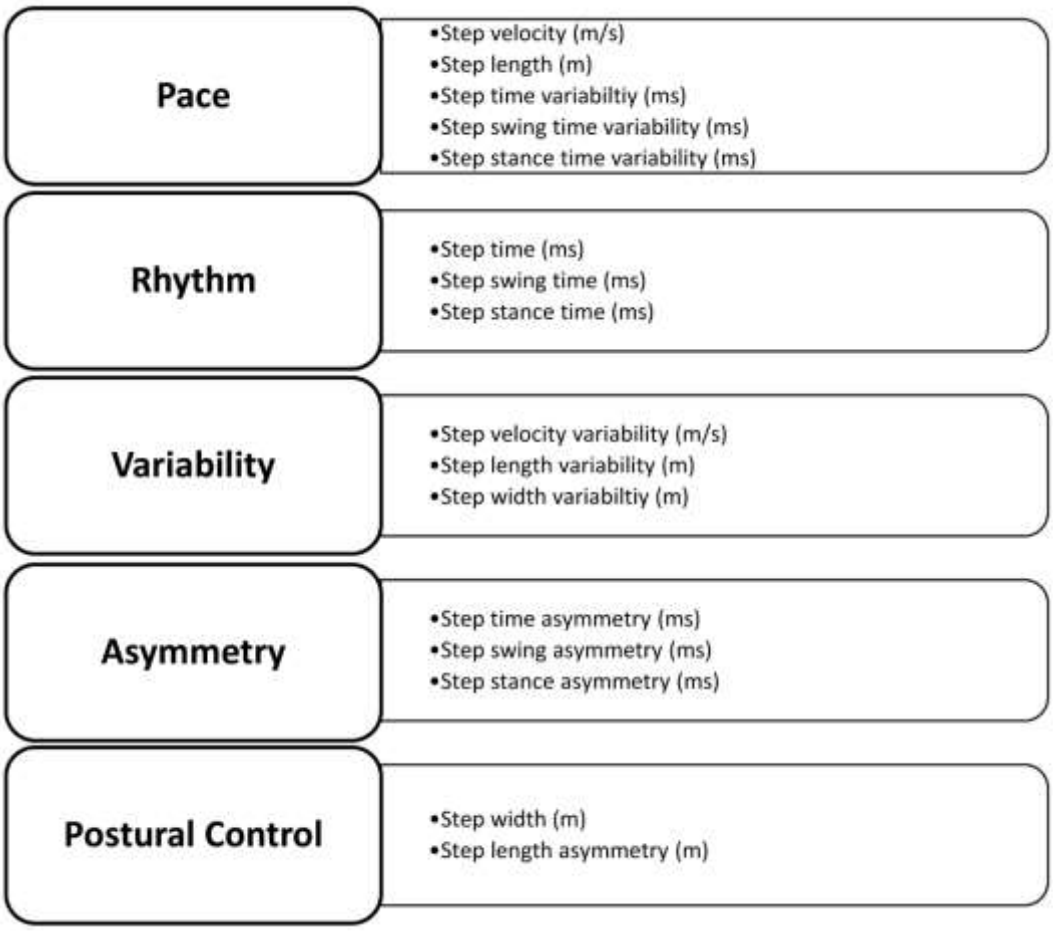


Figure 2: Prisma diagram presenting the search yield for the structured review. Information for exclusion reasons post abstract screen can be found in Results 3.1.

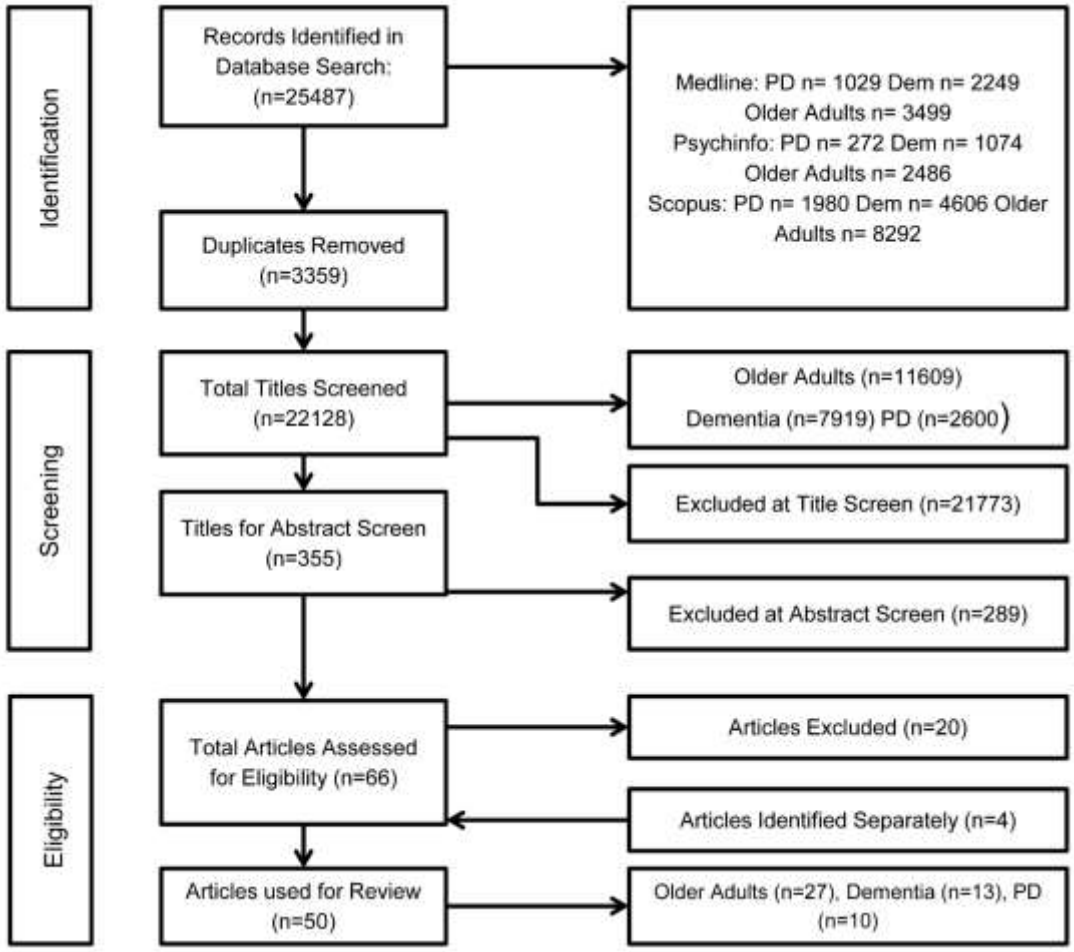


Figure 3: Map of cross sectional associations between gait and cognitive domains in older adults (OA, solid line), cognitive impairment (CI, dashed line), Parkinson's disease (PD, dotted line).

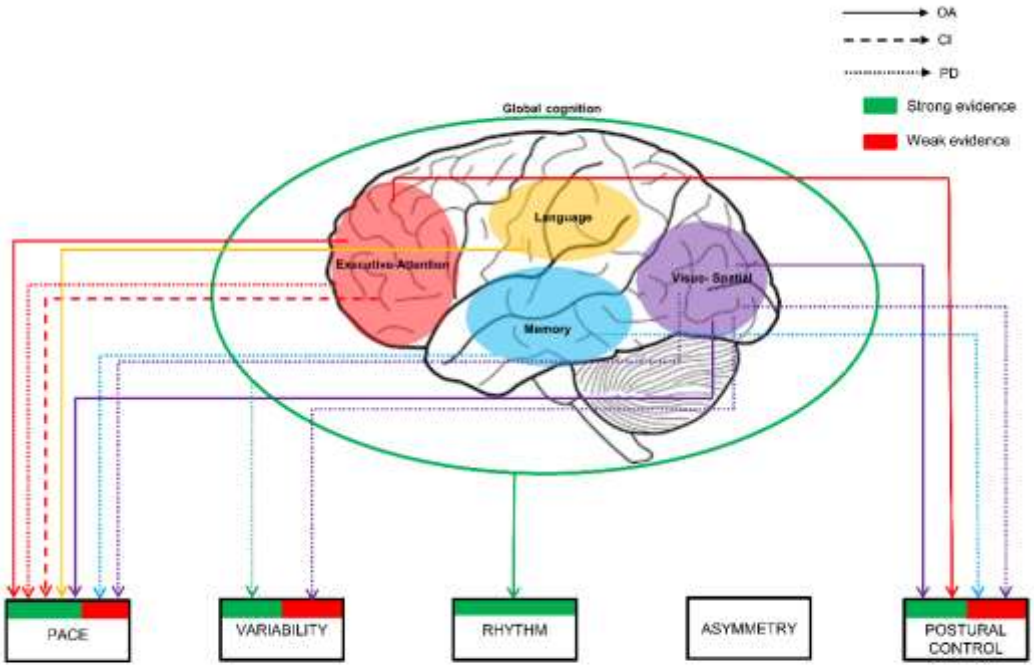


Figure 4: Map of associations between cognitive domains and gait domains longitudinally in older adults.

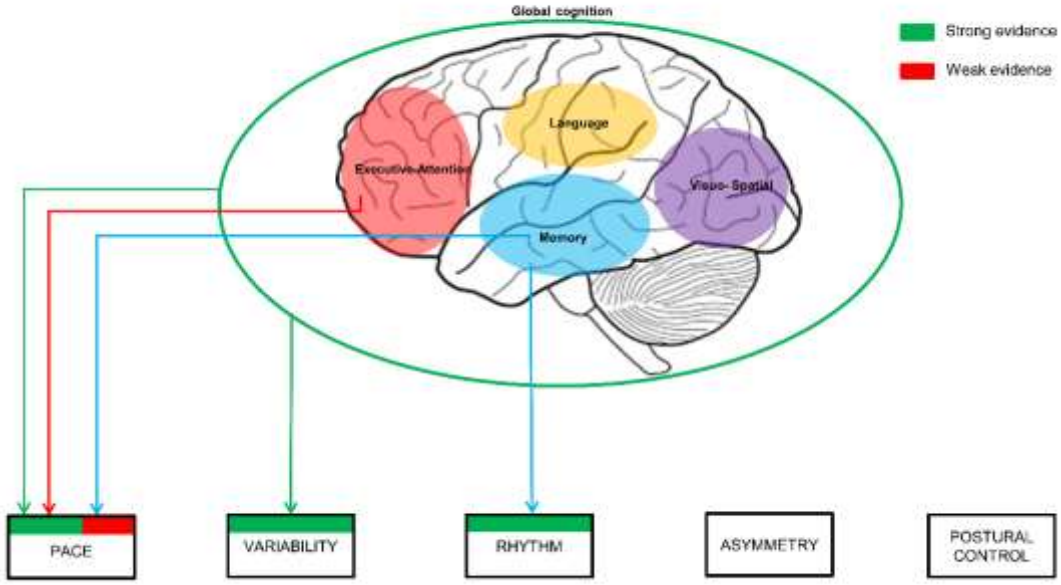
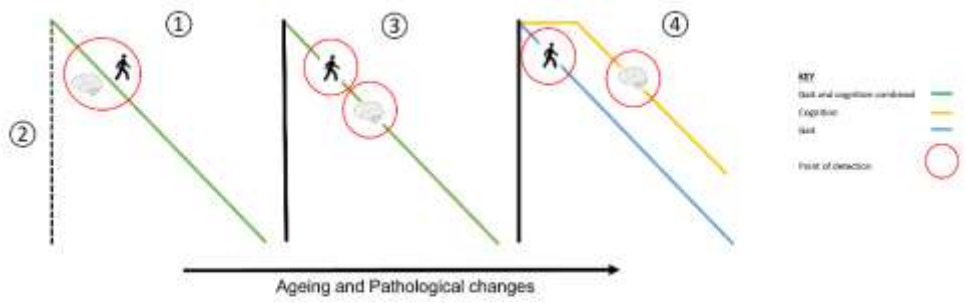


Figure 5: Hypothesised relationship of cognitive decline with respect to the temporal course of decline in gait and cognition in ageing and neurodegenerative disease. ①Gait and cognition decline concurrently, this may occur in normal ageing – and explains evidence for reverse causality (Tabbarah *et al.*, 2002). ②The temporal nature of decline with age is unknown, it is unclear therefore if gait and cognition decline together or if one precedes the other in normal ageing (Gale *et al.*, 2014). ③ Neural substrate (pathological change) underpins decline in cognition, but gait proves a more sensitive metric of cognitive change (due to role of cognition in gait) than global cognitive measures which are in common use. ④ Common neural substrate with a different temporal course (pathology affects motor function prior to cognitive function), gait therefore declines prior to cognition.



① Gait and cognition decline concurrently, this may occur in normal ageing – and explains evidence for reverse causality (Tabbarah *et al.*, 2002)
② The temporal nature of decline with age is unknown, it is unclear therefore if gait and cognition decline together or if one precedes the other in normal ageing (Gale *et al.*, 2014)
③ Neural substrate (pathological change) underpins decline in cognition, but gait proves a more sensitive metric of cognitive change (due to role of cognition in gait) than global cognitive measures which are in common use.
④ Common neural substrate with a different temporal course (pathology affects motor function prior to cognitive function), gait therefore declines prior to cognition

Table 1: Key terms search table used for structured search. Table includes the three databases used, the individual terms for each cohort and MESH headings where applicable.

	Medline	**Psychinfo**	**Scopus**
Gait	MESH Headings: Gait, locomotion, walking, Keywords: symmetry, asymmetry, frequency, variability, pace, rhythm, speed, velocity, step	MESH Headings: Gait, locomotion, walking Keywords; symmetry, asymmetry, base of support, frequency, variability, speed/velocity, stance	Keyword Search: Gait OR locomotion OR walking OR symmetry OR asymmetry OR frequency OR variability OR speed OR velocity OR stance OR step OR swing OR stride OR "double limb"
Cognition	MESH Headings: Cognition, cognition disorders, memory, neuropsychological tests, attention, executive function, reaction time, psychomotor performance Keywords; Processing speed, visuospatial, verbal fluency	MESH Headings; cognition, cognitive ability (tick spatial ability, verbal ability, cognitive assessment, cognitive impairment, cognitive processing speed, executive function, metacognition) Memory, Attention, visuospatial ability, verbal fluency, reaction time Keywords; psychomotor performance	Keyword Search: Cognition* OR "global intelligence" OR cognitive* OR memory OR attention OR "executive function" OR "processing speed" OR psychomotor OR visuospatial OR "verbal fluency" OR "reaction time"
Cohort	**PD:** MESH: Parkinson's disease	**PD:** MESH: Parkinson's disease	**PD:** Parkinson*
	Dementia: MESH: Dementia (explode), Alzheimer's disease,	**Dementia:** MESH: Dementia (explode dementia-cognitive impairment, Alzheimer's disease, dementia with lewy bodies, vascular dementia)	**Dementia:** Alzheimer*, "lewy body", dementia, "frontal lobe dementia", "intellectual impairment"
	Older Adults: Seniors, older*, aging, elderly*	**Older Adults:** Seniors, older*, aging, elderly*	**Older Adults:** Older* OR elderly* OR Seniors OR aging

Table 2: Colour correlation table to display gait and cognitive correlations in older adults. Green indicates an association was found, red indicates no association found. [1]Beauchet *et al.* (2012); [2]Ble *et al.* (2005); [3]Bramell-Risberg *et al.* (2012); [4]Donoghue *et al.* (2012); [5]Duff *et al.* (2008); [6]Fitzpatrick *et al.* (2007); [7]Hausdorff *et al.* (2005); [8]Hollman *et al.* (2007); [9]Holtzer *et al.* (2006); [10]Holtzer *et al.* (2012); [11]Kaye *et al.* (2012); [12]Lord and Menz (2002); [13]Lord *et al.* (2013); [14]Martin *et al.* (2013); [15] van Iersel *et al.* (2008); [16]Verlinden *et al.* (2013). From longitudinal studies: [17]Alfaro-Acha *et al.* (2007); [18]Atkinson *et al.* (2010); [19]Deshpande *et al.* (2009); [20]Watson *et al.* (2010). * Referred executive function and attention as 'Executive Attention'. ɬ speed of executive attention

Domain/Factor	Global cognition	Executive function	Attention	Visuospatial	Memory	Language	Processing Speed
Pace *Step Velocity (m/s)* *Step Length (m)* *Step Time Variability (ms)* *Step Swing Time Variability (ms)* *Step Stance Time Variability (ms)*	4 5 17 19 20 3 6 7 8 11 12 13 18	1 4 7 9* 10* 14* 16 20 2 11 13 15	5 9* 11 13 10* 14* 20	5 11 14	4 5 9 10 20 7 11 13 14 15 16	5 9 10	4 9ɬ 11 14 20 16
Variability *Step Velocity Variability (m/s)* *Step Length Variability (m)* *Step Width Variability (m)*	11 13	10* 11 13 14* 15 16	10* 11 13 14*	14	10 11 13 14 15 16	10	11 14 16
Rhythm *Step Time (ms)* *Step Swing Time (ms)* *Step Stance Time (ms)*	7 13	10* 7 13 14* 16	10* 13 14*	14	10 7 13 14 16	10	14 16
Asymmetry *Step Time Asymmetry (ms)* *Step Swing Asymmetry (ms)* *Step Stance Asymmetry (ms)*	13	13	13		13		
Postural Control *Step Width (m)* *Step Length Asymmetry (m)*	13	13 14* 15 16	14* 13	14	13 14 15 16		14 16

Table 3: Colour correlation table to display cognitive and gait correlations in the cognitive impairment cohort. Green indicates an association was found, red indicates no association found. [1]Allali *et al.* (2010); [2]Auyeung *et al.* (2008); [3]Beauchet *et al.* (2013); [4]Coelho *et al.* (2012); [5]Gillain *et al.* (2009); [6]Ijmker and Lamoth (2012); [7]Lamoth *et al.* (2011); [8]Maquet *et al.* (2010); [9]McGough *et al.* (2011), [10]Muir *et al.* (2012); [11]Persad *et al.* (2008); [12]Sheridan *et al.* (2003).*results found for those with dementia as well as healthy controls; analysed as whole cohort.** MCI group only. *** Had AD or MCI with executive function impairment

Domain/Factor	AD[1]	FTD[1]	CI	Global Cognition	Executive Function	Attention	Visuospatial	Memory	Language	Processing speed
Pace *Step Velocity (m/s)* *Step Length (m)* *Step Time Variability (ms)* *Step Swing Time Variability (ms)* *Step Stance Time Variability (ms)*	4 5 6 8 11 12 1 3 7 10	1 6	2 3 5 10	8**	9 11*** 12	8**				
Variability *Step Velocity Variability (m/s)* *Step Length Variability (m)* *Step Width Variability (m)*										
Rhythm *Step Time (ms)* *Step Swing Time (ms)* *Step Stance Time (ms)*	6 4 5 7 8 10	6	5 8 10	8**		8**				
Asymmetry *Step Time Asymmetry (ms)* *Step Swing Asymmetry (ms)* *Step Stance Asymmetry (ms)*										
Postural Control *Step Width (m)* *Step Length Asymmetry (m)*	5 8		5 8	8**		8**				

Table 4. Colour correlation table to display cognitive and gait correlations in Parkinson's disease. Green indicates an association was found, red indicates no association found. [1]Amboni *et al.* (2012); [2]Lord *et al.* (2010); [3]Lord *et al.* (2014); [4]Rochester *et al.* (2004); [5]Rochester *et al.* (2005); [6]Rochester *et al.* (2008);

Domain/Factor	Global Cognition	Executive Function	Attention	Visuospatial	Memory	Language	Processing speed
Pace *Step velocity (m/s)* *Step Length (m)* *Step Time Variability (ms)* *Step Swing Time Variability (ms)* *Step Stance Time Variability (ms)*	3 4 9	4 5 7 9 10 1 2 3 6 8**	2 3 8**	1 3	3 1		
Variability *Step Velocity Variability (m/s)* *Step Length Variability (m)* *Step Width Variability (m)*	3	1 3	3	1 3	1 3		
Rhythm *Step Time (ms)* *Step Swing Time (ms)* *Step Stance Time (ms)*	3 4	3* 1 4 8**	3 8**	1 3	1 3		
Asymmetry *Step Time Asymmetry (ms)* *Step Swing Asymmetry (ms)* *Step Stance Asymmetry (ms)*	3	3	3	3	3		
Postural Control *Step Width (m)* *Step Length Asymmetry (m)*	3	1 3	3	1 3	3 1		

[7]Smulders *et al.* (2013); [8]Wild *et al.* (2013); [9]Xu *et al.* (2014); [10]Yogev *et al.* (2005). *PIGD (postural and gait instability disorder) phenotype only. ** Executive Function and attention classified as one domain.

Table 5. Colour correlation table to display cognitive and gait correlations from longitudinal studies. Green indicates an association was found, red indicates no association found. [1]Buracchio *et al.* (2010); [2]Dodge *et al.* (2012); [3]Alfaro-Acha *et al.* (2007); [4]Atkinson *et al.* (2007); [5]Atkinson *et al.* (2010); [6]Auyeung *et al.* (2011); [7]Deshpande *et al.* (2009); [8]Inzitari *et al.* (2007); [9]Marquis *et al.* (2002); [10]Taniguchi *et al.* (2012); [11]Verghese *et al.* (2007); [12]Watson *et al.* (2010). No circle outline= gait as predictor, black circle outline= cognition as a predictor. *= seen at baseline but not longitudinal. **= associated with the onset of dementia. †= classified as na-MCI where there was an impairment in any domain other than memory but particular domain not specified. ł gait speed enhanced prediction model.

Domain/Factor	Global cognition	Executive Function	Attention	Visuospatial	Memory	Language	Processing Speed
Pace *Step Velocity (m/s)* *Step Length (m)* *Step Time Variability (ms)* *Step Swing Time Variability (ms)* *Step Stance Time Variability (ms)*	1 2† 3 4 6 9ł 10 11 12 5 5 7*	4 11 12	8 11 12*		12 11		8 12*
Variability *Step Velocity Variability (m/s)* *Step Length Variability (m)* *Step Width Variability (m)*	11**	11	11		11		
Rhythm *Step Time (ms)* *Step Swing Time (ms)* *Step Stance Time (ms)*	11** 10	11	11		11		
Asymmetry *Step Time Asymmetry (ms)* *Step Swing Asymmetry (ms)* *Step Stance Asymmetry (ms)*							
Postural Control *Step Width (m)* *Step Length Asymmetry (m)*							

Table 6. Main characteristics of the studies assessing cross-sectional gait and cognitive domains in older adults. Abbreviations as follows; 3MSE, modified mini mental state examination; CDR, cognitive drug research battery; CRT, choice reaction time; CTT, colour trails test; DV, digit vigilance; FCSRT, free and cued selective reminding test; LDST, letter digit substitution test; MMSE, mini mental examination; MoCA, Montreal cognitive assessment; PAL, paired associate learning; PRM, pattern recognition memory; SART, sustained attention response task; SRM, spatial recognition memory; SRT, simple reaction time; TMT, trail making test; TUG, timed up and go; WAIS, Wechsler adult intelligence scale.

Study	Participant Characteristics	Gait Variables Measured	Gait Analysis Tool	Cognitive Domains Associated	Main Findings
1. Beauchet *et al.* (2012)	**Older Adults** (n=78) Age; 69.9±0.9	Stride Time Variability (*%CV*)	SMTEC Gait Walkway (10m + 2m pre and post)	Executive Function (*Digit Span Test, TMT A & B, Stroop Colour Word Test*)	↑Stride time variability correlated with ↓ executive function.
2. Ble *et al.* (2005)	**Older Adults** (n=926) Age; 74.6±6.7, 44% M, MMSE 25.5±2.8, Education 5.6±3.3	Gait Velocity (m/sec)	Photocells (4m)	Executive Function (*TMT A & B*)	No correlation found after adjusting for variables.
3.Bramell-Risberg *et al.* (2012)	**Older Adults** (n=2115) split into 3 groups depending on word recall score: **Cases** (0/3) ; Age 75.8±10.2, **Intermediate** (1/3) Age 71.8±9.5, **Controls** (2-3/3) Age 69.0±9.1	Gait Velocity (*m/sec*)	TUG (3m, turn, 3m), Time to Walk Test (15m, turn, 15m)	Global Cognition (*MMSE- 3 word delayed recall subsection*)	No correlation found at usual pace walking.
4.Donoghue *et al.* (2012)	**Older Adults** (n=4998) Age: 62, 54%F, MMSE 29	Gait Velocity (*s*)	TUG (3m, turn, 3m)	Global Cognition (*MMSE, MOCA*), Executive Function (*CTT, Clock drawing, Cube drawing, SART, Word fluency, Letter fluency*), Processing Speed (*CTT, CRT, SART*)	↓TUG correlated with ↓ global cognition, EF, memory and processing speed.
5.Duff *et al.* (2008)	Older Adults (n=675) Age; 73.2±5.8, 288M & 387F	Gait Velocity (*s, split into 3 groups: <14 secs, 14-17s, >17s*)	Time to Walk Test (25ft, turn, 25ft)	Attention, Language, Visuospatial and Memory (*Repeatable Battery for the Assessment of Neuropsychological Status Domains*)	↓Velocity was associated with ↓ global RBANS score as well as each RBANS domain.
6.Fitzpatrick *et al.* (2007)	Older Adults (n=3070) Age; 78.6±3.3, 53.9% M,	Gait Velocity (*m/s*)	Time to Walk Test (15ft)	Global Cognition (*3MSE*)	No correlation was found between gait velocity and global cognition.
7.Hausdorff *et al.* (2005)	Older Adults (n=43) Age; 71.9±6.4, 22W & 21M, MMSE 29.0±1.1, Education 13.7±2.1	Gait Velocity (*m/s),* Stride Time (*s*), Stride time Variability (*%CV*)	Force-sensitive Sensors, Time to Walk (10m + 7.5m pre/post)	Global Cognition (MMSE), Executive Function (Stroop Test), Verbal Memory (*Verbal Memory Test*)	↑ Stride time variability but not stride time correlated with ↓ executive function after adjusting for covariates.
8.Hollman *et al.* (2007)	**Older Adults** (n=20), Age 81±5, 7M & 13W **Middle Aged adults** (n=20) age 48±5, 9M & 11W **Younger Adults** (n=20) age 25±3,	Gait Velocity (*cm/s*), Stride Time Variability (*%CV*)	GaitRite 80Hz (8.3m + 1m pre/post walkway)	Global cognition (*Short Test of Mental Status*)	No correlation found under ST conditions

	9M & 11W				
9.Holtzer *et al.* (2006)	**Older Adults** (n=186) Age; 78.00±4.50, 43.4%M, Education 14.30±3.30	Gait Velocity (*cm/s*), Step Length (*cm*), Stride Length (*cm*), Stride Length Variability (*%CV*), Double Support time (*s*)	GaitRite (12ft), including 3ft pre/post walkway)	Factor analysis domains: Verbal IQ (*Information, vocabulary, digit span, Boston naming test, FAS*). Attention/Executive speed (*Block design, Digit Symbol, TMT A & B*). Memory (*Category Fluency*, *FCSRT*)	Only correlated gait velocity. All cognitive domains were associated.
10.Holtzer *et al.* (2012)	**Older Adults** (N=671) Age; 79±5.2, 60%F, Education 13.8±3.5	Gait Velocity (*cm/s*), Stride Length (*cm*), Stride length Variability (*%CV*), Cadence (*Steps/min*)	GaitRite (12ft including 3ft pre/post walkway)	Executive Attention, Memory, Verbal IQ (*Battery Included: Vocabulary, Information, Digit Span, Digit Symbol, Block Design, WAIS, FCSRT, total free recall, Boston Naming Test, letter fluency, category fluency, TMT A and B*)	All domains associated with pace. Memory and executive attention correlated with cadence. Executive attention was correlated with stride length variability.
11.Kaye *et al.* (2012)	**Older Adults** (n=76) Age; 85.9±4.9, 86%F, MMSE 28.3±1.7, Education 15.5±2.5	Gait Velocity (*cm/s*), Gait Velocity (*%CV*), Mean Number walks/day, Number walks/ day (*%CV*)	Passive Infra-red motion sensor fixed in-home (Avg 500 walks per month)	Global Cognition (*MMSE*), Executive Function (*TMT-B, Category Fluency*), Working Memory (*Letter-number sequencing*), Attention/Processing Speed (*Digit Span Forward, Digit Symbol, TMT-A*), Memory (*Logical Memory II, Visual Reproduction II, Word-List Recall*), Visuospatial (*Picture Completion, Block Design*)	↑Attention, processing speed and visuospatial scores associated with mean ↑ walking velocity.
12.Lord and Menz (2002)	**Older Adults** (n=515) Age; 79.5±6.4, 76M & 439F	Gait Distance (*m*)	6 Minute Walk Test	Global Cognition (*MMSE*)	No correlation was found between gait velocity and global cognition.
13.Lord *et al.* (2013)	**Older Adults** (n=189) Age; 69.5±7.6, 79M & 110F, MMSE 29.3±1.0	16 Gait Variables into 5 domains: *Pace* (step velocity m/s), mean step length m, swing time variability ms), *Rhythm* (step time ms, swing time ms, stance time ms), *Variability* (step velocity variability m.s-1, step length variability m, step time variability ms, stance time variability ms), *Asymmetry* (swing time asymmetry ms, step time asymmetry ms, stance time asymmetry ms), *Postural Control* (step length asymmetry m, step width m, step width variability m)	GaitRite (7m), 2min walk around 25m circuit	Global Cognition (*MMSE*), Power of Attention (*CDR; SRT, CRT, DV*), Memory (*PRM, SRM*), Executive Function (*One Touch Stocking of Cambridge*)	↑Executive function correlated ↑postural control. ↑Attention correlated with ↑pace.
14.Martin *et al.* (2013)	**Older Adults** (n=422) Age; 72.0±7.0, 238M & 184F, GDS 2.05±2.3	Gait Velocity (*cm/s*), Step Time (ms *CV%*), Step Length (*cm, CV%*), Support Base (*cm, CV%*), Double Support Phase (*ms, CV%)*	GaitRite (4.6m, + 2m pre/post walkway)	Executive/Attention (*Controlled word association test, category fluency, stoop test, digit span*), Processing Speed (*Symbol Search, Digit Symbol Coding*), Visuospatial Ability (*Rey Complex Figure*	Executive /Attention correlated with velocity, step length, step time variability, double support time, double support time variability.

				Copy Task), Memory (*Hopkins Verbal Learning Test*)	Processing speed correlated with velocity, step time, step length, DSP and DSP variability. Visuospatial correlated with DSP variability.
15.van Iersel *et al.* (2008)	**Older Adults** (n=100) Age; 80.6±4.0, 64M & 36F	Gait Velocity (*m/s*) Stride Length Variability (*%CV*), Stride Time Variability (*%CV*), Mediolateral body sway (*degrees*)	GaitRite (5.6m + 2m pre/post walkway)	Executive Function (*TMT A & B, Stroop Colour-Word Test*), Memory (*CANTAB; PAL, PRM*)	No correlation found under single task conditions
16.Verlinden *et al.* (2013)	**Older Adults** (n=1232) Age; 66.3 ±11.8, 558M & 674F, MMSE 28.0 ± 1.8	Factors; Rhythm (single support time [s], swing time [s], step time [s], stride time [s], cadence [steps/min], stance time [s]) Variability (stride length SD [cm], step length SD [cm], stride velocity SD [cm/s], stride time SD [s], step time SD [s], stance time SD [s], swing time SD [s], single support time SD [s], double support time SD [s], Phases (single support [%GC], swing [%GC], stance [%GC], double support [%GC], double support time [%GC], Pace (stride length [cm], step length [cm], velocity [cm/s]), Tandem (Sum of feet surface [fraction], sum of step distance [cm], double step [n]), Turning (turning step count [n], turning time [s]), Base of support (stride width SD [cm], stride width [cm]).	GaitRite (5.79m)	Memory (*immediate and delayed recall of 15 word verbal learning test*), Executive Function (*stroop interference, word fluency, LDST*), Information Processing Speed (*stroop reading, stroop colour naming & LDST*), Fine Motor Speed (*Purdue Pegboard Test*), Global Cognition (*average of all above test scores*)	After adjusting for covariates (including independence of cognitive domains); information processing speed correlated with rhythm, executive function associated with pace.

Table 7. Main characteristics of the studies assessing cross-sectional gait and cognitive domains in the cognitive impairment and dementia. Abbreviations as follows; AD, Alzheimer's disease; ADAS-cog, Alzheimer's disease assessment scale-cognition; CDR, cognitive drug research battery; FAB, frontal assessment battery; FCRT, free and cued recall test; FTD, fronto-temporal dementia; HC, healthy control; MCI, mild cognitive impairment; Dem, dementia; MCI-/+ EF, MCI with or without impairment in executive function; MMSE, mini mental examination; MoCA, Montreal cognitive assessment; TAP, test of attentional performance; TMT, trail making test.

Study	Participant Characteristics	Gait Variables Measured (*Units*)	Gait Analysis Tool (Distance)	Cognitive Domains Tested (*Test Used*)	Main Study Findings
1. Allali *et al.* (2010)	**HC** (*n*=22) Age 71.0±0.5, 8M & 14F **AD** (*n*=19) Age 79.3±8.4 6 6M & 13F, MMSE 19± 7 **FTD** (*n*=19) Age 66.8±9.7 10M & 9F, MMSE 26 ± 6	Stride Time (Mean & CV)	SMTEC Footswitch System (10m)	Global cognition (*MMSE, Mattis Dementia Rating Scale*), Frontal Cognition (*FCRT*)	Stride time variability was ↑ in FTD after adjusting for variables.
2. Auyeung *et al.* (2008)	**Cognitively Intact** (n=NR) M=72.18±0.11 W=71.87±0.13 **Cognitively Impaired** (n=NR) M= 76.43±0.59, W=74.64±0.26	Gait Velocity (*m/s*)	Timed to Walk Test (6m)	Global cognition (*MMSE*), Dementia Severity *(Community Screening Instrument for Dementia*)	Gait velocity correlated with CI in men and women.
3. Beauchet *et al.* (2013)	**HC** (n=44) Age 74.5±6.5 14M & 28F, MMSE 29.0±1.1 **MCI** (n=39) Age 73.6±6.1 24M & 15F, MMSE 27.8±1.4 **AD** with mild dementia (n=21) Age 79.2±5.6 12M & 21F, MMSE 25.0±2.3	Gait Velocity (*cm/s*), Stride time Variability (CV%)	GaitRite 60Hz (9.72m, + 2m pre/post walkway)	Global cognition (*MMSE*), Frontal lobe assessment (*FAB*), AD Severity (*ADAS-Cog*)	Under usual pace walking there were no differences between MCI or AD after adjusting for variables.
4. Coelho *et al.* (2012)	**Mild AD** (n=12) Age 75.7±6.8, MMSE 22.0±2.2, Education 5.5±3.0 **Moderate AD** (n=11) Age 80.1±7.5, MMSE 16.2±2.2, Education 3.5±1.1	Stride Length (*m*), Stride Speed (*m/sec*), Cadence (*Strides/sec*)	GaitRite 60Hz (8m)	Executive Function (*FAB & Clock Drawing Test*), Attention (*Symbol Search*)	Moderate AD had ↓ stride length and ↓ stride speed compared to mild AD. Did not assess EF and attention in association with ST conditions.
5. Gillain *et al.* (2009)	**HC** (n=14) Age 73.53, MMSE 28.21± 1.58, Education 13.71±3.73 **MCI** (n=14) Age 72.85, MMSE 26.71±1.68, Education 13.64±3.30 **AD** (n=6) Age 73.66, MMSE 22.83±2.14, Education 9.33±3.78	Gait Velocity (*m/s*), Stride Frequency (*Hz*), Stride Length (*m*), Stride regularity, Stride symmetry	Locometrix 3 Axis Accelerometer (30m)	Global cognition (*MMSE & Mattis*), Episodic Memory (*Graber & Buschke-version of*), Visuoconstructive/Visuospatial ability (*Rey's Complex Figure Test*), Attention (*TAP*)	Velocity and stride length were↓ in AD compared to HC. Those with MCI had ↓ stride frequency compared to HC. Associations between domains under ST conditions were unclear.
6. Ijmker and Lamoth (2012)	**HC Elderly** (n=14) Age 76.9±4.1, 12M & 2F, MMSE 28.5±1.16 **HC Younger** (n=12) Age 64.3±2.8, 9M & 3F, MMSE 29.1±0.93 **Dem** (AD and FTD, n=15) Age 81.7±6.3, 13M and 2F, MMSE 19.6±3.58	Gait velocity (*m/s*), mean stride time (*m*), stride time variability *(%CV*)	Dynaport®Ambulant Accelerometer (3 mins on 10m course)	Global cognition (*MMSE*), Processing speed (*Category Fluency*), Psychomotor Speed (*Stroop*), Executive Function (*Stroop*), Attention (*Digit Span Forward/Backward & TMT*), Working Memory (*Digit Span*)	Those with Dem had ↓ gait velocity; ↑ stride time and ↑ stride time variability compared to both HC groups. Cognitive domains associated with gait as whole cohort only so therefore not reported.
7. Lamoth *et al.* (2011)	**HC** (n=13) Age 79.38±5.55, 10M&16F, MMSE 28.23±1.09 **AD** (n=13) Age 82.62±4.29, 6M&7F, MMSE 18.00±3.54	Gait Velocity (m/sec), Stride Frequency (strides/sec), Stride Time (s), Stride Time Variability (%CV),	Timed to walk test, Dynaport® Tri-Axial Ambulant Accelerometer (160m)	Global cognition (*MMSE, 7min Screening*)	No correlations found under ST conditions.

		Phase Variability Index (%)			
8. Maquet *et al.* (2010)	**HC** (n=14) Age 74±5, 7M&7F **MCI** (n=14) Age 73±4, 7M&7F **Mild AD** (n=6) Age 74±4, 3M&3F	Gait Velocity(*ms-1*), Stride Frequency (*Hz*), Stride length (*m*), Step Asymmetry (*Sym*)	Locometrix ™ Acceleration Sensor (90m)	Global Cognition (*MMSE & Mattis*), Episodic Memory (*Grober & Buschke*), Visuoconstruction/Visuospatial Ability (*Rey's Complex Figure Test*), Attention (*TAP*)	↓gait velocity and ↓stride length in AD compared to HC and MCI. MCI s.d to controls for stride In MCI group, correlation between ↓velocity and ↓stride length and ↓cognition and ↓attention and stride frequency and global cognition.
9. McGough *et al.* (2011)	**CI** (n=201) Age; 84.6±5.7, 80.1% female, high school educated 97.5%	Gait Velocity (*m/s*)	Timed to Walk Test (2.4m)	Executive Function (*TMT-B & Stroop Word-Colour*)	↓ gait velocity associated with lower executive function score
10. Muir *et al.* (2012)	**HC** (n=22) Age 71.0±5.0, 3M &19F, MMSE 29.5±0.6, MOCA 28.2±1.5 **MCI** (n=29) Age 73.6±6.2, 12M&17F, MMSE 27.5±1.9, MOCA 23.4±2.8 **AD** (n=23) Age 77.5±5.0, 9M&14F, MMSE 24.2±2.3, MOCA 17.2±3.4	Gait Velocity (*cm/s*), Stride Time (*ms*) Stride Time Variability (*CV%*)	GaitRite (6m + 1m pre/post walkway)	Global Cognition (*MMSE, MOCA, CDR*)	No difference in gait variables under ST conditions
11. Persad *et al.* (2008)	**HC** (N=12) Age 70.0±5.8, 7M&5W, MMSE 27.8±2.2, Education 17.0±2.6 **MCI-EF** (n=14) Age 72.5±4.6, 10M&4W, MMSE 26.6±2.1, Education 16.57±3.2 **MCI+EF** (n=10) Age 75.1±6.9, 6M&4W, MMSE 25.8±2.0, Education 15.8±3.2 **AD** (n=12) Age 77.5±5.3, 9M&3W, MMSE 22.6±2.3, Education 14.8±2.9	Gait Velocity (s)	Timed to Walk Test (10m)	Executive Function (*Map Planning & Paper Folding*), Visual Short Term Attention (*Corsi Block Task & Benton Form Visual Discrimination*), Visuo-Motor (*Block-Design*), Memory (*Delayed Recall*)	Those with AD and MCI+EF had a ↓gait velocity compared to HC and MCI-EF. Walking speed correlated with EF.
12. Sheridan *et al.* (2003)	**Patients diagnosed with probable AD** (n=28) Age; 77.9±6.9, MMSE 13.8±7.9	Velocity (msec), Stride Time Variability (*%CV*)	Footswitch System (100Hz) (~500ft)	Global Cognition (*MMSE*), Executive Function (*Clox I & II, Verbal Fluency*) Dementia Severity (*CDR*)	Those with AD had ↓ gait velocity and ↑ increased stride time variability. No correlation with executive function under ST conditions

Table 8. Main characteristics of the studies assessing cross-sectional gait and cognitive domains in Parkinson's disease. Abbreviations as follows; FAB, frontal assessment battery; FOG-Q, freezing of gait questionnaire; H & Y, Hoehn & Yahr disease severity classification; HC, healthy controls; MCI; mild cognitive impairment; MCI+/MCI-, with/without mild cognitive impairment; MMSE, mini mental examination; MoCA, Montreal cognitive assessment; PD, Parkinson's disease; UPDRS, unified Parkinson's disease rating scale.

Study	Participant Characteristics	Gait Variables Measured (*Units*)	Gait Analysis Tool/ Distance Walked	Cognitive Domains Tested (*test used*)	Main Findings from Study
1. Amboni *et al.* (2012)	HC: (n=20) Age; 63.5±3.14, 10M & 10F PD-MCI: (n=24) Age; 64.08±6.44, 20M & 4F, Disease duration; 5.42±2.80 FOG-Q; 5.83±5.71 PD+MCI: (n=19) Age; 65.1±6.85, 13M & 6F, Disease duration; 5.47±2.71 FOG-Q; 7.26±6.17 *Med: On and Off*	*Factors:* *Pace* (stance phase (*s*), swing phase (s), cadence (*steps/min*), velocity (m/s) *Stability* (step length (*m*), single/double support time ratio, step length variability (*COV*), swing time variability (*COV*).	Optokinetic system (6 camera, 240Hz) 8M	Episodic memory (*Rey 15 words*), executive function (*Phonemic Fluency, FAB, Stroop II & III*), visuospatial (*spatial span, constructive apraxia, Raven's PM 47, Ten point clock test*)	The Pace 'domain' was not correlated with a cognitive domain. ↓Stability of gait strongly correlated with ↓visuospatial ability.
2. Lord *et al.* (2010)	PD: n= 29 Age; 71.3±7.4, 19M & 10F, MMSE 26.9±2.8, Disease duration; 5.8±5.5 *Med: Off*	Gait Velocity (*m/s*)	Vitaport Activity Monitor (6.5m ±1.5m)	Executive Function (*Brixton*), Attention *(Telephone Search & Lottery Task*)	Those with impaired sustained attention had ↓ gait velocity.
3. Lord *et al.* (2014)	HC: n=184, Age; 69.4±7.7, 78M & 106F, NART 116.9±7.6 PD: n=121, Age; 67.0±10.4, NART 114.9±11.0, UPDRS III 25.5±10.4, H & Y; I (28), II (72), III (21) *Med: on*	16 Gait Variables into 5 domains: *Pace* (step velocity m/s), mean step length m, swing time variability ms), *Rhythm* (step time ms, swing time ms, stance time ms), *Variability* (step velocity variability m.s-1, step length variability m, step time variability ms, stance time variability ms), *Asymmetry* (swing time asymmetry ms, step time asymmetry ms, stance time asymmetry ms), *Postural Control* (step length asymmetry m, step width m, step width variability m)	GaitRite Platinum Model (7m)	Global cognition (MoCA), Working Memory (Forward Digit Span), Power of Attention (Mean single reaction time, mean choice reaction time, mean digit vigilance), Fluctuating Attention (*Single reaction time CV, Choice reaction time CV, Digit Vigilance CV*), Executive Function (*one touch stocking, Semantic Fluency, Hayling & Brixton*), Memory (*Pattern recognition memory, spatial recognition memory, paired associate learning*), Visuospatial (*Pentagons, MoCA Item 1*)	PD & HC: those with ↑pace had ↑attention test scores. PD: ↑ postural control and better working memory, ↑gait variability associated with ↓global cognition. HC: those with ↑postural control had ↑ attention scores.
4. Rochester *et al.* (2004)	HC: (n=10) Age; 63.5±7.03, 6M & 4F, MMSE 28.90 PD: (n=20) Age; 64.6±7.96, 12M & 8F, MMSE 27.15±1.98 H&Y 2.7±0.69. Disease duration; 10.0±1.6	Gait velocity (*m/s*), step frequency (*steps/s*), step length (*m*)	Vitaport Activity Monitor (6.60±1.51m)	Global cognition (*MMSE*), Executive Function (*Hayling & Brixton*)	↓gait velocity was correlated with ↓ executive function scores.

	Med: On				
5. Rochester *et al.* (2005)	HC: (n=10) Age; 63.5±7.03, 6M & 4F, MMSE 28.90 PD: PD: (n=20) Age; 64.6±7.96, 12M & 8F, MMSE 27.15±1.98 H&Y 2.7±0.69. Disease duration; 10.0±1.6 *Med: On*	Gait Velocity (*m/s*)	Vitaport Activity Monitor (6.60±1.51m)	Executive Function (*Hayling & Brixton*)	↓gait velocity was correlated with ↓ executive function scores.
6. Rochester *et al.* (2008)	PD: (n=153). Age; 66.61±7.57, 78M & 52F, MMSE 28.30±1.77, UPDRS III; 33.05±11.28, Disease duration 8.26±4.90 *Med: On*	Gait Velocity (*m/s*)	Vitaport Activity Monitor (6m, turn, 6m)	Executive Function (*Brixton*)	No correlation was found under single task conditions.
7. Smulders *et al.* (2013)	PD: (n=232). Age; 64.4±7.9, 153M & 79F, MMSE 28.1±1.6, UPDRS III 33.4±9.1 *Med: NR*	Gait Velocity (*s*)	TUG (3m, turn, 3m)	Executive Function (*Spatial working memory, Set Shift Test, Auditory Stroop Paradigm, Phonological and Semantic Cue*)	↓Executive function correlated with ↓TUG time.
8. Wild *et al.* (2013)	HC: (n=18)Age; 69.44±1.41, 8M & 10F PD: (n=18) Age; 69.33±2.65, 8M & 10F *Med: On*	Gait velocity (*Km/h*), Mean swing time (*s*), Relative stance time (*s*)	Fixed Infra-Red Camera (8m)	Executive function/attention (*Winconsin Card Sorting Test, Stroop Colour and Word*)	No correlation was found under single task conditions.
9. Xu *et al.* (2014)	HC: (n=20) Age; 68.9 ± 4.8, 65% M, MMSE 28.7 ± 1.1, Education 12.7 ± 3.4 PD: (n=20) Age 65.9 ± 9.4, 65% M, MMSE 27.6 ± 1.6, Education 12.4 ± 2.5, Disease duration 6.0 ± 3.8, UPDRS III 26.6 ± 10.8, H & Y 1.4 ± 0.9 *Med: On*	Gait Velocity (s)	TUG (3m, turn, 3m)	Global cognition (*MMSE, Addenbrooke's*), Executive function (*TMT-A, TMT-B*)	↓ Executive function associated with ↓ pace in PD but not control.
10. Yogev *et al.* (2005)	HC: (n=28) Age; 69.8±6.3, MMSE 29.1±1.1, Education 13.7±2.1 PD: (n=30) Age; 70.9±.9, MMSE 28.1±1.6, Education 13.9±3.8, UPDRS III 17.5±8.3, H &Y 2.3±0.4 *Med: NR*	Gait velocity (*m/s*), stride time (*s*), swing time (*s*), stride time variability (*%*), swing time variability (*%*)	Timed to walk test (2 min), In-Shoe Pressure sensor (100Hz)	Executive function (*Stroop & Go-Nogo*), Memory (*Trail Recall*)	Only associated stride and swing variability with EF. Correlation was found between ↓executive function and ↑stride and swing time variability.

Table 9. Main characteristics of the studies assessing longitudinal gait and cognitive domains in older adults. Abbreviations as follows; 3MS, modified mini mental state examination; a/na MCI, amnestic/ non-amnestic mild cognitive impairment; CDR, cognitive drug research battery; EXIT 15, the executive interview; MCI, mild cognitive impairment; MMSE, mini mental examination; TMT, trail making test; WAIS, Wechsler adult intelligence scale.

Study	Participant Characteristics	Gait Variables Measured (*Units*)	Gait Analysis Tool (Distance)	Cognitive Domains Tested (*Test used*)	Main Study Findings
1. Buracchio *et al.* (2010)	**HC** (n=109) Age 79.0±8.8, 60M & 49F, MMSE 28.3±1.5, Years Education 14.5±2.7 **Converters to MCI** (n=95) Age 83.5±7.0, 37M & 58F, MMSE 28.1±1.6, Education 14.7±2.6	Gait Velocity (*m/s*)	Timed to Walk Test (30ft)	Global Cognition (*MMSE*), Dementia Rating Scale (*CDR*)	Those who converted to MCI had ↓ gait velocity up to 12.1 years prior to MCI.
2. Dodge *et al.* (2012)	**HC** (n=54) Age 84.9±4.0, 91% female, MMSE 29.0±1.3 **aMCI** (n=8) Age 84.5±2.6, 88% female, MMSE 28.3±1.2 **naMCI** (n=31) Age 83.8±6.0, 84% female, MMSE 28.1±1.6	Gait velocity (cm/s), Gait velocity variability (*%CV*)	Passive Infra-red motion sensor fixed in-home	Global Cognition (*MMSE*), Memory (*Logical Memory Delayed*), Executive Function (*Category Fluency, TMT Part B*), Attention (*WAIS Digit Symbol*), Language (*Boston Naming Test*), Visuospatial (*WAIS Revised Block Design*)	naMCI had ↓ gait velocity compared to HC and showed decline in gait velocity over time, those with naMCI had ↑ gait speed variability in the home.
3. Alfaro-Acha *et al.* (2007)	**Older Adults** (n=1218) Age; 71.7±5.7, 57.5% F, MMSE 26.5±2.9, Education 5.4±3.9	Gait Velocity (*Split into quartiles: 1; ≥9s, 2;6-8s, 3; 4-5s, 4; <4s*)	Time to Walk Test (8ft)	Global Cognition (*MMSE*)	No correlation at baseline. At 7 year follow up association between slow gait velocity and ↓cognition.
4. Atkinson *et al.* (2007)	**Older Adults** (n=2349) Age; 75.6±2.9, 52.3% F	Gait Velocity (*m/s*)	Time to Walk Test (20m)	Global Cognition (*MMSE, 3MS*), Executive Function (*Clox 1, EXIT 15*)	Greater gait velocity decline over 3 years was seen in those with lowest cognition and EF scores.
5. Atkinson *et al.* (2010)	**Older Adults** (n=1793) Age; 70.3±3.7, 3MS Score 95.1±4.4	Gait Velocity (*m/s*)	Time to Walk Test (6m)	Global Cognition (*3MS*)	Gait speed was not associated with 3MS score at baseline when adjusting for covariates. Baseline 3MS did not predict decline in gait speed (or vice versa) after adjusting for covariates.
6. Auyeung *et al.* (2011)	**Older Adults** (n=2737) M=1514 Age 71.6±4.58, MMSE 27.4±2.25 F=1223 Age 71.5±4.85 MMSE 25.8±2.80	Gait Velocity (*m/s*), Step Length (*m*), Step Number	Time to Walk Test (6m)	Global Cognition (*MMSE*)	In male subjects, stride length correlated with decline MMSE score but not gait velocity after adjusting for covariates.
7. Deshpande *et al.* (2009)	**Older Adults** (n=660) Age; 74.6±5.3, 54.2% F, Education 5.8±3.4	Gait Velocity (*m/s*)	Timed to Walk Test (7m)	Global Cognition (*MMSE*)	Baseline; those with ↓MMSE had ↓gait speed. Longitudinal; Gait velocity at fast pace only predicted decline in cognition.
8. Inzitari *et al.* (2007)	**Older Adults** (n=3075) Age; 73.6±2.9, 1491M & 1584F	Gait Velocity (m/s)	Timed to Walk Test (6m)	Global Cognition (*3MS*), Attention and Psychomotor Speed (*Digit Symbol Substitution Test*)	↑global cognition scores related to ↑ gait speed. Gait speed predicted ↓attention and ↓ psychomotor speed at 5 years. Difference in gait speed at baseline related to ↑ risk of decline in attention and

					psychomotor speed.
9. Marquis *et al.* (2002)	**Older Adults** (n=108) Age; 83.2±7.9, 40M & 68W	Gait Velocity (*s*), Step Number (excluding turn)	Timed to Walk Test (4.5m, turn, 4.5m)	Global Cognition (*MMSE*), Dementia Severity (*CDR*), Memory (*Wechsler Memory Scale*)	Time to walk aided the prediction model of onset of persistent cognitive impairment.
10. Taniguchi *et al.* (2012)	**Older Adults** (n=853) Age; 77.5±5.4, 47.3% M, MMSE 28.1±1.7, Education 8.3±2.2, GDS 4.0±2.4	Gait Velocity (*m/s*), Mean Step Length (*cm*), Step Frequency (*times/min*)	Timed to Walk Test (5m)	Global Cognition (*MMSE*)	↓Gait velocity and ↓step length associated with decline in general cognition. Step length found to be a better predictor of cognitive decline than gait speed.
11. Verghese *et al.* (2007)	**Older Adults** (n=399) Non-dementia; Age 78.9±4.7, 56.3%M, Education 13.4±3.5. **Developed Dem**; (n=33) Age 82.6±5.7, 57.6%M, Education 14.0±3.6	Pace (Gait Velocity (*cm/s*), Stride Length (*cm*)) Rhythm (Cadence (*steps/min*), Double Support (*s*), Swing Time (*s*), Stance Time (*s*)) Variability (stride length variability, swing time variability)	GaitRite(180 inches +3ft Pre/Post Walkway)	Global Cognition (*Blessed Information Memory-Concentration Test*), Memory (*Free & Cued Selective Reminding Test*), Executive Function (*Digit Symbol Substitution & Letter Fluency Test*), Attention (*Digit Span*)	Rhythm was associated ↓memory; pace was associated with ↓ executive function. Rhythm and variability associated with dementia onset. Pace of gait predicted vascular dementia.
12. Watson *et al.* (2010)	**Older Adults** (n=909) Age; 75.2±2.8, 49.4%M, Education below 12y 78.4%	Gait Velocity (m/s)	Time to Walk Test (20m)	Global Cognition (*3MS*), Memory (*Buschke Selective Reminding Test*), Executive Function (*EXIT 15*), Psychomotor Speed (*Box and Digit Copying*), Attention (*Pattern and Letter Comparison Test*)	Cross sectional; All cognitive domains correlated with gait velocity. Longitudinal; ↓ global cognition, memory and executive function associated with greater speed decline per year.