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Intraindividual reaction time variability, falls and gait in old age: A systematic review

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Running head: RT variability, falls and gait in old age

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## Abstract

**Objectives:** Intraindividual variability (IIV) refers to the variation in reaction time (RT) performance across a given cognitive task. As greater IIV may reflect compromise of the frontal circuitry implicated in falls and gait impairment in older adults, we conducted a systematic review of the literature relating to this issue. **Methods:** Searches were conducted of electronic databases that identified empirical investigations of IIV, falls and gait in older adult samples with a mean age of 65 years or over. Data were extracted relating to IIV measures, study population, and outcomes. **Results:** Of 433 studies initially identified, nine met inclusion criteria for IIV and falls ( $n = 5$ ), and gait ( $n = 4$ ). Representing a total of 2,810 older participants, all of the studies of IIV and falls showed that elevated variability was associated with increased risk of falling, and half of the studies of gait indicated greater IIV was related to gait impairment. **Discussion:** Across studies, IIV measures were consistently associated with falls in older persons and demonstrated some potential in relation to gait. IIV metrics may, therefore, have considerable potential in clinical contexts and supplement existing test batteries in the assessment of falls risk and gait impairment in older populations.

A major concern with aging populations around the world is their increased vulnerability to falls. A third of older adults suffer at least one fall every year and a further 50 percent experience more (Tinetti, 2003). Falls are a leading cause of fractures, traumatic brain injury and disability in old age, impacting on quality of life, as well as representing a major cost to healthcare systems. As research demonstrates that interventions targeting risk factors for falling can lead to a reduction in the number of falls, there is a pressing need to understand more of the determinants of falling in order to effectively predict and prevent such incidents in old age. In particular, it is important to develop tools that not only provide insights into the neurocognitive processes that may contribute to falls, but also have clinical potential for early detection and assessment of persons at risk of falling.

In the present review, we consider intraindividual reaction time variability (IIV) in relation to falls and gait impairment in older adults. Also referred to as within-person variability and inconsistency, this measure captures the trial-to-trial variability in reaction times (RT) across a given cognitive task, and is measured through the intraindividual RT standard deviation or derivatives thereof. The measure is thought to convey unique information about cognitive functioning beyond that offered by mean performance (e.g., Jensen, 1992). Theoretically, it is thought to reflect fluctuations in attentional or executive control mechanisms (Bunce, MacDonald, & Hultsch, 2004; Bunce, Warr, & Cochrane, 1993; West, Murphy, Armilio, Craik, & Stuss, 2002), and neurobiological disturbance (e.g., Hultsch, Strauss, Hunter, & MacDonald, 2008). Empirical work shows that IIV increases in normal aging (e.g., Hultsch, MacDonald, & Dixon, 2002), although this can be attenuated by lifestyle factors such as physical fitness (Bauermeister & Bunce, 2014). Additionally, IIV increases in neuropathological aging in respect to, for example, mild dementia (e.g., Bielak, Hultsch, Strauss, Macdonald, & Hunter, 2010; Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000), mild cognitive impairment (e.g., Christensen et al., 2005; Dixon et al., 2007) and Parkinson's disease (de Frias, Dixon, Fisher, & Camicioli, 2007).

It is well-established that older adults diagnosed with cognitive impairment are at greater risk of falling (van Dijk, Meulenberg, van de Sande, & Habbema, 1993; van Doorn et al., 2003). Recent evidence, however, suggests that even minor cognitive deficits in healthy older adults can increase the risk of falling (e.g., Gleason, Gangnon, Fischer, & Mahoney, 2009), and an expanding body of work has focused on deficits in specific cognitive domains. For example, older adults with deficits in verbal reasoning (Anstey, von Sanden, & Luszcz, 2006),

processing speed (Chen, Peronto, & Edwards, 2012; Holtzer et al., 2007) and visual-spatial ability (Liu-Ambrose, Nagamatsu, Handy, & Leghari, 2008) are all more likely to experience falls. Moreover, there is clear evidence of a relationship between executive function and falling. In a recent review (Kearney, Harwood, Gladman, Lincoln, & Masud, 2013), nine of 11 studies found a positive association between this construct and falls risk in older persons. Additionally, work shows that older adults who exhibit poorer dual-tasking ability may also be at a higher risk of falling (e.g., Beauchet et al., 2009). As the ability to switch between concurrent tasks is supported by executive control, this research also suggests that cognitive measures placing demands on executive mechanisms supported by the frontal cortex may have some potential in distinguishing fallers from nonfallers.

Given the theoretical link that IIV has with both executive processes and empirical work showing greater IIV with age-related neurobiological disturbance, there is good reason to expect an association not only with falls, but also gait, in old age. This is supported by work showing that white matter hyperintensities (WMH: microscopic white matter lesions identified through structural MRI), particularly in the frontal lobes, are associated with both risk of falling in the elderly (Zheng, Delbaere, Close, Sachdev, & Lord, 2011) and also impaired gait, balance and stepping performance (Zheng et al., 2012). Importantly, IIV has been found to predict frontal WMH burden both in midlife (Bunce et al., 2010; Bunce et al., 2013) and in early old age (Bunce et al., 2007). Together, this research suggests that examining the potential of IIV to predict falls in older persons may provide valuable neurocognitive insights into a major worldwide health concern. Critical analysis of the literature may reveal that greater IIV is a risk factor for falls, and as such the measure may have considerable potential in clinical contexts.

We therefore conducted a systematic review of the literature to assess the extent to which IIV and falls were related in old age. Additionally, as there is an association between gait and falls (e.g., Ambrose, Paul, & Hausdorff, 2013), we also considered whether IIV was related to gait. Gait control is supported by frontal circuitry that is also implicated in executive control (e.g., Parihar, Mahoney, & Verghese, 2013) and IIV. Age-related or neuropathological deterioration of this circuitry may result in executive control deficits, elevated IIV and gait impairment. Given the potential overlap in these frontal mechanisms, we therefore expected evidence of an additional association between IIV and gait in older adults.

## Method

For inclusion in the systematic review, studies were required to examine the association between IIV and either falls, gait speed or gait variability in a population of older adults. Studies which only measured the number of errors or percentage of correct responses from a given cognitive task, or mean reaction time, were excluded, as were studies investigating IIV in populations exhibiting a neurological condition (e.g., stroke, head injury). The exception was investigations of Parkinson's disease (PD) which were included because gait abnormalities, a key characteristic of PD, make this group particularly vulnerable to falls. Consistent with other systematic reviews in the area (e.g., Beauchet et al., 2009; Kearney et al., 2013), only investigations of samples with a mean age of 65 years or over were considered for inclusion.

The electronic databases Embase, Medline, PsycINFO and Web of Science were used to search for relevant literature until April 2014. The terms 'fall\*' and 'gait' were combined with all known variations of the term IIV: 'intraindividual variability', 'within person variability', 'reaction time variability', 'RT variability', 'reaction time inconsistency' and 'RT inconsistency'. The terms 'sustained attention' and 'impaired attention' were also included as possible variations. Reference lists of investigations identified, as well as key articles and review papers in the area, were inspected for further studies that may not have been found by searches of the above databases. Figure 1 presents a flow diagram of the study selection process.

Figure 1 about here

## Results

Of the 433 studies that were initially identified by the electronic and hand searches, 87 full articles were obtained for detailed analysis. Seventy-eight of these did not meet the criteria and were excluded. In consequence, nine studies were identified for inclusion in the review (see Table 1). These studies assessed a total of 2,536 community dwelling older adults, 60 geriatric outpatients and 214 PD patients who met inclusion criteria for this review. The majority of recruited participants were 65 years or older, and in all cases, the mean age was above 70. One study (O'Halloran et al., 2011), however, also included individuals aged between 60 and 65 while another (O'Halloran, Finucane, Savva, Robertson, & Kenny, 2014)

recruited participants as young as 50. Data from those aged 50-64 were analysed separately to those over 65 though, and will not be considered here. All but one study (Allcock et al., 2009) excluded participants with possible cognitive impairment, determined in most cases by Mini-Mental State Examination cut-offs between  $<15$  and  $<26$ .

Table 1 about here

Of the nine studies identified in total, five included the number of falls as a primary outcome measure. Falls assessment periods ranged from 6 to 12 months retrospectively with all studies using participant self-reports at interview. Two studies (Allcock et al., 2009; Mirelman et al., 2012) also collected prospective data (for 12 and 66 months, respectively) using falls diaries that were returned by participants on a monthly basis. Three of the nine studies included gait speed as a primary outcome although the way this was measured differed. Whereas two studies (O'Halloran et al., 2014; Holtzer et al., 2013) had participants walk in a straight line, in another (de Frias et al., 2007) participants were instructed to walk 15 feet, turn, and walk back. One study (Holtzer et al., 2013) measured gait under both single and dual-task conditions, the latter requiring participants to count backwards in 7s while they walked. Finally, one study (O'Halloran et al., 2014) recorded gait for the purpose of calculating frailty status, so the measure of gait speed used in their analysis was a binary classification (low or normal). Whereas the above investigations measured gait speed, one study (Sukits et al., 2014) included measures of temporal and spatial (step length) gait variability.

All studies included at least one measure of IIV although these differed by the task administered, ranging from psychomotor tests (e.g., choice reaction time task) to tests of specific cognitive domains (e.g., Flanker task which assesses response inhibition). They also differed according to the way the variability measure was computed (see Table 1); five of the nine studies calculated the raw standard deviation of RTs (raw SD) whereas the others used the coefficient of variation (CV) or intraindividual standard deviation (ISD). The CV adjusts the raw intraindividual SD by intraindividual mean RT, and the ISD statistically removes potential artefacts from the variability measure such as effects relating to time-on-task and task condition. In addition to the raw SD, two studies (O'Halloran et al., 2014; O'Halloran et al., 2011) analyzed RT data using a fast Fourier transformation (e.g., Johnson et al., 2007) to produce a further measure of moment-to-moment variability (referred to as fast frequency variability: FFV).

### *IIV and falls*

All five studies that measured falls (two prospectively) found a significant association suggesting greater variability in fallers in respect to at least one IIV measure. One study compared fallers and healthy adults on three cognitive tasks, finding that fallers had higher raw SDs on all tasks after adjusting for age, education, gender and computer experience (Hausdorff et al., 2006). Similarly, another investigation (Reelick et al., 2011) compared the performance of recurrent fallers against non-recurrent fallers (who were defined as having zero or 1 fall in the previous 6 months) on a choice reaction time task, reporting significantly greater IIV in recurrent fallers. A further study also considered different faller types, finding that raw SD was significantly greater for single and recurrent fallers compared to non-fallers (O'Halloran et al., 2011).

Three studies used regression analyses to assess whether IIV was a potential risk factor for falling. One study in PD patients found that the summed CV for three cognitive tasks was significantly associated with falls frequency over a 12 month follow up period (Allcock et al., 2009). This association remained significant after adjusting for scores on the Unified Parkinson's Disease Rating Scale (Fahn, Elton, & Committee, 1987), a five-stage assessment that determines the severity of the disease. Another found that IIV on an inhibition task significantly predicted the rate of falls over 66 months after taking into account age, gender, years of education, BMI, history of falls and grip force (Mirelman et al., 2012). Finally, one study reported that FFV on a sustained attention task, but not raw SD, was significantly higher in fallers relative to non-fallers after controlling for age and gender (O'Halloran et al., 2011).

### *IIV and gait*

Only two of the four studies that investigated gait abnormalities found evidence of a relationship with IIV. One concluded that there were no significant associations (at  $p < .01$ ) between gait speed and IIV on any of the four cognitive tasks that they assessed (de Frias et al., 2007). Likewise, nonsignificant associations between IIV on two inhibition tasks and four measures of gait variability were reported by another study (Sukits et al., 2014). In contrast to these findings, CV on an executive function task significantly predicted gait speed (Holtzer, Mahoney, & Verghese, 2014), although this association became nonsignificant after controlling for gender, age, education, disease comorbidity and clinical gait abnormalities. A



final study found that higher FFV (but not raw SD) on a sustained attention task was significantly associated with low gait speed after adjusting for age, gender, executive function, processing speed, number of chronic conditions and number of medications (O'Halloran et al., 2014).

### Discussion

This is the first systematic review to consider the relationship between neurocognitive variability and either falls or gait in older persons. Given the potential of IIV measures as a neuropsychological assessment tool, the findings are of considerable interest. First, only nine studies conducted in older populations were identified in total. All five investigations looking at IIV and falls found an association having adjusted for a range of variables including age, gender and years of education: Greater within-person variability was associated with an increased likelihood of falling. By contrast, of the four studies that looked at IIV and gait, only two reported significant associations with gait impairment.

The review provided clear evidence that older adults exhibiting greater neurocognitive variability are more likely to experience a fall. One explanation for this consistent association stems from work suggesting that IIV is an index of attentional or executive control (Bunce et al., 2004; Bunce et al., 1993; West et al., 2002), deficits in which are a risk factor for falls in the elderly (e.g., Kearney et al., 2013). It is also well established that the frontal cortex undergoes changes with age and is implicated in age-related executive control deficits, and a number of studies have reported a link between frontal brain integrity and IIV. For example, greater within-person variability has been found in patients with frontal brain damage (Stuss, Murphy, Binns, & Alexander, 2003) as well as cognitively intact older adults with smaller white matter volumes (Walhovd & Fjell, 2007). The presence of WMHs in the frontal cortex has also been associated with greater IIV in older adults (Bunce et al., 2007) and diffusion tensor MRI research has demonstrated a relationship between IIV and measures of white matter integrity (Deary et al., 2006). Against this background, the association demonstrated between IIV and falls in the reviewed studies is completely in line with our expectations.

By contrast, there was less evidence of an association between IIV and gait. This is surprising given that, as with falls, it is thought that gait and cognition share similar frontal circuitry (Parihar et al., 2013). Although there are uncertainties of the temporal relationship between cognitive and gait impairment, a recent study has provided evidence that gait slowing may

actually precede cognitive decline in older adults by several years (Mielke et al., 2013). It is possible, therefore, that the lack of a consistent association between gait and variability shown here was due to the temporal differences in aging processes captured by the respective measures. It is also possible that methodological differences between studies contributed to the heterogeneity observed in the findings. For example, sample sizes were greater in investigations reporting a positive association between IIV and gait relative to those reporting a nonsignificant association suggesting that statistical power may have been influential. Additionally, one of the studies reporting null associations with gait (de Frias et al., 2007) set alpha conservatively at the  $p < .01$  level.

As already noted, the way in which gait was measured differed between studies. For example, one of the studies that did not find an association with IIV, assessed gait variability as opposed to speed. While gait variability and speed tend to be highly correlated (e.g., Wuehr et al., 2013), it has been demonstrated that different aspects of gait are related to different cognitive domains (e.g., Verghese, Wang, Lipton, Holtzer, & Xue, 2007). For instance, a recent study demonstrated a significant association between executive function and walking speed but not variability (Verlinden, van der Geest, Hofman, & Ikram, 2014). It is possible therefore, that differing gait measures across studies differentially tapped the underlying core construct of IIV, namely executive function.

Another methodological consideration across both falls and gait studies relates to the way in which the IIV measures were computed. Four different methods were reported across the reviewed papers, with most studies only employing one of the measures. Mixed results were found in the studies that used the raw intraindividual SD, the most basic calculation which does not adjust for mean performance or other potential confounds such as time-on-task effects. By contrast, studies that assessed the CV (adjusting the intraindividual SD by the intraindividual mean RT) all reported significant associations. Positive associations were also found in investigations using a fast Fourier transformation to compute IIV. Taken together, the evidence suggests that in the main, the more sophisticated measures of IIV may possess greater sensitivity where effects exist, possibly because potential confounds have been adjusted for in computing the measure. That said, there was some evidence that studies using the more sophisticated measures of IIV also tended to have larger sample sizes. This suggests that an important area for future work is to determine the sensitivity of the respective IIV

measures relative to sample size, particularly as in clinical practice the more sophisticated measures may not be practical to compute.

In addition to the computation of IIV, there are several other methodological issues that need to be considered. The first, concerns the type of task administered. Although IIV measures across different cognitive tasks have been found to correlate with one other (e.g., Hultsch et al., 2002), associations between IIV and other cognitive domains vary according to the complexity of the task. For example, previous findings from research on age differences in IIV have shown that age effects are greater for tasks that are more cognitively challenging (Bunce et al., 2004; Dixon et al., 2007; West et al., 2002). While there is some evidence from the reviewed papers to support this notion, this was not consistent across all studies. Further investigation is clearly needed to determine how strongly task complexity influences associations between IIV and outcomes such as falls and gait. Additionally, for one of the studies that reported a positive association, data were obtained from PD patients (Allcock et al., 2009). Although the aetiology of this group clearly differs from that of the other older groups included in the review, we do not believe that this markedly affected our overall conclusions, as the findings from this study followed the same trend as those from non-PD populations.

Despite the methodological issues raised, there remains good evidence for a link between neurocognitive variability and falls in older populations. It is important to note that some of the studies provided evidence of a dissociation between mean RT and IIV from the same task such that the latter but not the former produced significant associations with outcome (Reelick et al., 2011; Allcock et al., 2009; Hausdorff et al., 2006). This clearly suggests that in the present context, the IIV measures exhibited greater predictive utility than measures of mean performance obtained from the same task. Further empirical evidence is required to confirm the association between greater IIV and risk of falling and, in particular, there is a need for more prospective studies. Only two of the reviewed studies assessed falls prospectively and establishing the predictive utility of IIV measures in relation to future falls should be a major goal for further research. Such work may have important clinical implications especially as measures of IIV are quick to administer, with average times ranging from 51.94 seconds for 20 trials to 103.88 seconds for 40 trials (Bunce et al., 2013). They also require little training compared to other neuropsychological measures and have minimal linguistic content which limits bias arising from language or background, making

them well suited for use in ethnically diverse communities. Given the ease of administration in clinical contexts, there is good reason to consider IIV measures as a supplement to existing test batteries in falls risk.

However, further investigation is needed to establish whether a consistent association exists between IIV and gait. Here though, it should be noted that the value of using additional IIV measures to predict gait impairment in clinical contexts is less clear given that gait assessment is relatively straightforward and quick to administer. However, since baseline levels of neurocognitive variability have been found to predict declines in cognition up to five years in the future (Bielak et al., 2010), it is possible that the metric has potential for detecting risk of gait impairment earlier than standard gait assessments (although as noted earlier, uncertainty exists of the temporal relationship between cognitive and gait impairment). Additionally, as IIV is thought to be a marker of central nervous system integrity (Hendrickson, 1982), it may also be possible to use IIV measures to examine whether certain gait impairments are more attributed to central rather than peripheral causes.

The clinical potential of IIV has been demonstrated in relation to other age-related neuropathology including mild dementia (e.g., Bielak et al., 2010; Hultsch et al., 2000), mild cognitive impairment (e.g., Christensen et al., 2005; Dixon et al., 2007) and Parkinson's disease (de Frias et al., 2007). It is important therefore, that similar work is directed to falls and gait impairment in older adults both in community samples and in more vulnerable segments of the population such as older frail persons.

In conclusion, this review of within-person RT variability, falls and gait considered a total of nine studies. Five studies looked at IIV in relation to falls and, without exception, reported positive associations. Although there are theoretical reasons to expect an association between IIV and gait, in the four studies identified, the evidence for an association was less strong. Methodological variations between studies may underlie this finding while it is also possible that temporal differences in cognitive and gait decline prevented a consistent trend from emerging. Together, the findings suggest that greater IIV may be a risk factor for falling in old age and may also be related to gait impairment, with further work needed to determine if and how this is the case. IIV measures, therefore, may have considerable potential in clinical contexts and serve as a valid supplement to commonly-used neuropsychological measures in assessment batteries. Future research should investigate prospectively the predictive utility of

IIV in relation to falls and gait as well as other outcomes in the older population. It is important too that this research is extended beyond samples of functioning community-dwelling older adults in order to assess how relations may vary in particularly vulnerable groups such as the older frail.

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#### Author statement

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Table 1. Summary of studies IIV, falls and gait included in the review

Author, year	Participants	Test measure(s)	Outcome measure(s)	Main findings
<b>Studies measuring falls</b>				
Hausdorff et al., 2006	Community dwelling fallers (n = 18, M = 77.1 ± 4.9 years) and non-fallers (n = 25, M = 70.0 ± 6.1 years) <sup>a</sup>	Raw SD for Go-NoGo, Stroop congruent and incongruent	No. of falls 6 months prior to study	Raw SD was significantly higher for elderly fallers on all cog tasks; p < .05 for all when compared to healthy older adults
Allcock et al., 2009	PD patients (n = 164, M = 71.2 ± 7.8 years) classified as fallers (n = 103) and non-fallers (n = 61)	Composite CV for SRT, CRT-2 and Digit Vigilance	No. of falls 12 months after the study	The composite CV for all 3 tasks was significantly associated with fall frequency (p = .045); even after correcting for the severity of PD (p = .028)
Reelick et al., 2011	Geriatric outpatients Non-recurrent fallers (n = 38, M = 75.8 ± 7.2 years) and recurrent fallers (n = 22, M = 75.7 ± 5.6 years).	CV for CRT-5	No. of falls 6 months prior to study	CV was higher for recurrent fallers (p = .04) compared to non-recurrent fallers
O'Halloran et al., 2011	Community dwelling non-fallers (n = 261, M = 70.3 ± 6.4 years) and fallers (n = 197, M = 73.5 ± 7.3 years)	Raw SD and FFV for SART	No. of falls 12 months prior to study	Raw SD was higher for single (p = .046) and recurrent fallers (p = .042) compared to non-fallers; FFV was significantly associated with falls in the past year (OR 1.14, 95% CI 1.03-1.26, p < .01)
Mirelman et al., 2012	Community dwelling older adults (n = 256, M = 76.4 ± 4.5 years)	Raw SD for Go-NoGo	No. of falls 12 months prior to study and 66 months after	Raw SD was strongly associated with fall frequency over 66 months (RR 1.19, 95% CI 1.07-1.34, p = .001)
<b>Studies measuring gait</b>				
de Frias et al., 2007	Community dwelling older adults (n = 48, M = 71.5 ± 4.9 years) and PD patients (n = 50, M = 71.5 ± 4.7 years)	ISD for SRT, CRT-2, CRT-4 and CRT-8	Average cadence score (steps per second) over two 30ft trials	No associations were found at the p < .01 level between ISD for any of the 4 tasks and cadence score
O'Halloran et al., 2014	Community dwelling nonfrail, prefrail and frail older adults over 65 years of	Raw SD and FFV for SART	Average gait speed over two 16ft trials; calculated by	FFV was significantly associated in prefrail and frail groups with low gait speed

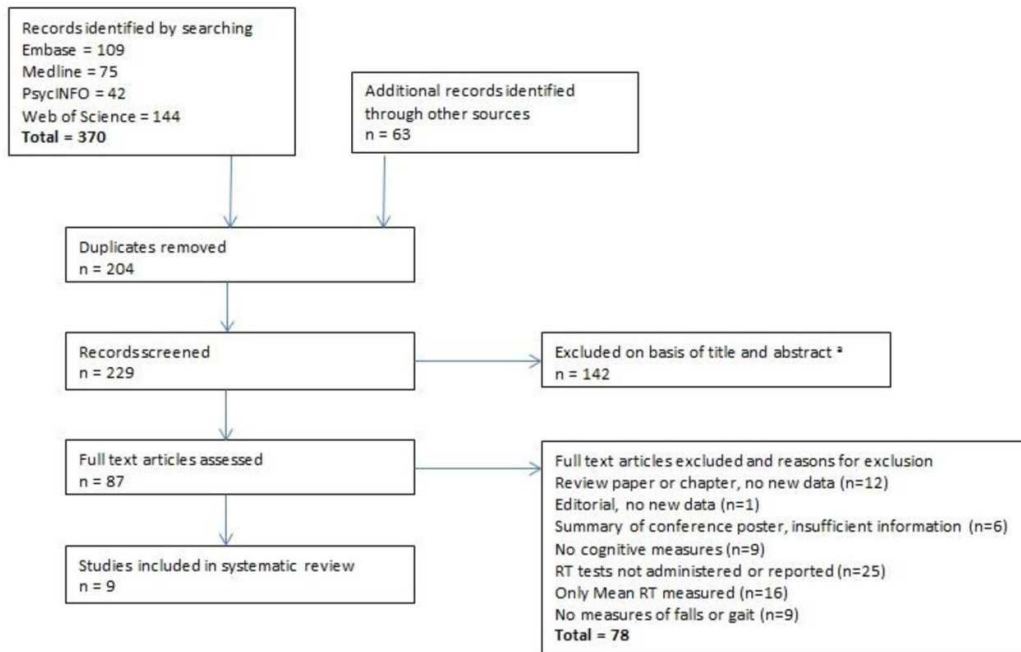
	age (n = 1,426) <sup>b</sup>		GAITRite electronic walkway	(OR 1.31, 95% CI 1.08-1.59, p < .01), but Raw SD was not
Holtzer et al., 2013	Community dwelling older adults (n = 234, M = 76.5 ± 7.2 years)	CV for Flanker task	Gait speed on a 8.5m trial, with or without dual-tasking (Serial 7s); calculated by GAITRite electronic walkway	CV was associated with gait speed (p = .079) in single task walking conditions and this effect became stronger in the dual-task walking condition (p = .007)
Sukits et al., 2014	Community dwelling older adults (n = 71, M = 75.7 ± 4.0 years)	Raw SD for Response Conflict and Perceptual Conflict tasks	4 measures of gait variability (stance time, double support time, step time, step length)	No significant associations were found between CV and any of the gait variability measures

CI = Confidence interval; CRT-2 = 2-choice Reaction Time task; CRT-4 = 4-choice Reaction Time task; ; CRT-5 = 5-choice Reaction Time task; CRT-8 = 8-choice Reaction Time task; CV = Coefficient of variation typically measured as the within-person SD/mean; FFV = fast frequency variability obtained through a Fourier transformation; ISD = Intraindividual standard deviation which partials out extraneous influences such as time-on-task effects; OR = Odds ratio; PD = Parkinson's Disease; Raw SD = Raw reaction time variability; SART = Sustained Attention to Response Task; SRT = Simple Reaction Time task

<sup>a</sup> Hausdorff et al. (2006) also included PD patients in their sample (n = 30) but only compared their performance to the healthy older adults, not the fallers.

<sup>b</sup> O'Halloran et al. (2014) divided their sample into two age groups: 50-64 years and 65+ years. Separate analyses were performed for each group and here we only consider findings from the 65+ group. No age statistics were given for the separate groups but the median age of the whole sample (n = 4,317) was 61 with an age range of 50-93.

Figure 1. Flow diagram of the study selection process



## Figure 1 note

<sup>a</sup> Numerous articles were removed at this stage because the term “intraindividual variability” (and its alternatives) captured research falling beyond the scope of this review. For example, the term was also used to describe changes in gait variables, but where no measures of neurocognitive variability were recorded, as well as capturing other behaviors such as REM sleep variation.