Cognitive training interventions for dementia and mild cognitive impairment in Parkinson's disease

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[Intervention Review]

Cognitive training interventions for dementia and mild cognitive impairment in Parkinson's disease

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ABSTRACT

Background

Approximately 60% to 80% of people with Parkinson's disease (PD) experience cognitive impairment that impacts on their quality of life. Cognitive decline is a core feature of the disease and can often present before the onset of motor symptoms. Cognitive training may be a useful non-pharmacological intervention that could help to maintain or improve cognition and quality of life for people with PD dementia (PDD) or PD-related mild cognitive impairment (PD-MCI).

Objectives

To determine whether cognitive training (targeting single or multiple domains) improves cognition in people with PDD and PD-MCI or other clearly defined forms of cognitive impairment in people with PD.

Search methods

We searched the Cochrane Dementia and Cognitive Improvement Group Trials Register (8 August 2019), the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL, and PsycINFO. We searched reference lists and trial registers, searched relevant reviews in the area and conference proceedings. We also contacted experts for clarifications on data and ongoing trials.

Selection criteria

We included randomised controlled trials where the participants had PDD or PD-MCI, and where the intervention was intended to train general or specific areas of cognitive function, targeting either a single domain or multiple domains of cognition, and was compared to a control condition. Multicomponent interventions that also included motor or other elements were considered eligible.

Data collection and analysis

Two review authors independently screened titles, abstracts, and full-text articles for inclusion in the review. Two review authors also independently undertook extraction of data and assessment of methodological quality. We used GRADE methods to assess the overall quality of the evidence.

Main results

Seven studies with a total of 225 participants met the inclusion criteria for this review. All seven studies compared the effects of a cognitive training intervention to a control intervention at the end of treatment periods lasting four to eight weeks. Six studies included people with PD living in the community. These six studies recruited people with single-domain (executive) or multiple-domain mild cognitive impairment in PD. Four of these studies identified participants with MCI using established diagnostic criteria, and two included both people with PD-MCI and people with PD who were not cognitively impaired. One study recruited people with a diagnosis of PD dementia who were living in long-term care settings. The cognitive training intervention in three studies targeted a single cognitive domain, whilst in four studies multiple domains of cognitive function were targeted. The comparison groups either received no intervention or took part in recreational activities (sports, music, arts), speech or language exercises, computerised motor therapy, or motor rehabilitation combined with recreational activity.

We found no clear evidence that cognitive training improved global cognition. Although cognitive training was associated with higher scores on global cognition at the end of treatment, the result was imprecise and not statistically significant (6 trials, 178 participants, standardised mean difference (SMD) 0.28, 95% confidence interval (CI) −0.03 to 0.59; low-certainty evidence). There was no evidence of a difference at the end of treatment between cognitive training and control interventions on executive function (5 trials, 112 participants; SMD 0.10, 95% CI −0.28 to 0.48; low-certainty evidence) or visual processing (3 trials, 64 participants; SMD 0.30, 95% CI −0.21 to 0.81; low-certainty evidence). The evidence favoured the cognitive training group on attention (5 trials, 160 participants; SMD 0.36, 95% CI 0.03 to 0.68; low-certainty evidence) and verbal memory (5 trials, 160 participants; SMD 0.37, 95% CI 0.04 to 0.69; low-certainty evidence), but these effects were less certain in sensitivity analyses that excluded a study in which only a minority of the sample were cognitively impaired. There was no evidence of differences between treatment and control groups in activities of daily living (3 trials, 67 participants; SMD 0.03, 95% CI −0.47 to 0.53; low-certainty evidence) or quality of life (5 trials, 147 participants; SMD −0.01, 95% CI −0.35 to 0.33; low-certainty evidence). There was very little information on adverse events. We considered the certainty of the evidence for all outcomes to be low due to risk of bias in the included studies and imprecision of the results.

We identified six ongoing trials recruiting participants with PD-MCI, but no ongoing trials of cognitive training for people with PDD.

Authors' conclusions

This review found no evidence that people with PD-MCI or PDD who receive cognitive training for four to eight weeks experience any important cognitive improvements at the end of training. However, this conclusion was based on a small number of studies with few participants, limitations of study design and execution, and imprecise results. There is a need for more robust, adequately powered studies of cognitive training before conclusions can be drawn about the effectiveness of cognitive training for people with PDD and PD-MCI. Studies should use formal criteria to diagnose cognitive impairments, and there is a particular need for more studies testing the efficacy of cognitive training in people with PDD.

PLAIN LANGUAGE SUMMARY

Cognitive training interventions for dementia and mild cognitive impairment in Parkinson's disease

Review question

We wanted to know whether cognitive training interventions are effective in improving cognition (thinking) in people with Parkinson's disease dementia or mild cognitive impairment.

Background

Approximately 60% to 80% of people with Parkinson's disease (PD) develop some degree of cognitive impairment, meaning that they may have difficulties with thinking and reasoning, memory, language, or perception. If these difficulties are severe enough to affect the person's ability to carry out daily activities, then the person is said to have Parkinson's disease dementia (PDD). If someone has cognitive problems but their daily activities are not significantly affected, then he or she is said to have mild cognitive impairment in Parkinson's disease (PD-MCI). Cognitive training involves practising cognitive skills such as memory, attention, and language through specific tasks. It may be able to help people with PDD or PD-MCI maintain better cognitive skills.

What we did

This review examined whether cognitive training is effective in improving outcomes such as overall cognitive skills ('global cognition'), memory, attention, or ability to carry out daily activities in people with PD and either dementia or MCI. We searched the medical literature for research studies that compared people receiving a cognitive training intervention to those not receiving the intervention (a 'control group'). We only included studies in which the decision about whether or not someone received the cognitive training intervention was made randomly; such studies are called randomised controlled clinical trials and are considered to be the fairest method to test whether or not a treatment is effective. We did not examine other types of studies.

What we found

We found seven studies that randomly allocated a total of 225 participants to cognitive training or to a control group. Treatment lasted from four to eight weeks. All the cognitive training interventions were delivered by computer. The control groups received either no intervention or a control intervention such as language or motor exercises or participation in recreational activities. We found no difference between people who received cognitive training and people in the control groups in global cognition shortly after treatment ended. There was no convincing evidence of benefit in specific cognitive skills and no benefit shown in activities of daily living or quality of life. However, these findings were based on a small number of participants in a small number of studies. The overall certainty of the evidence was low, meaning that the results of further research could differ from the results of this review.

Conclusion

We found no good evidence that cognitive training is helpful for people with Parkinson's disease and dementia or MCI. The included studies were small and had flaws that may have affected the findings. The certainty of the results was low, and further studies are needed before we can be confident whether or not cognitive training is effective for this group of people.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Cognitive training compared to control intervention for cognition in PDD and PD-MCI

Cognitive training compared to control intervention for cognition in PDD and PD-MCI

Patient or population: cognition in PDD and PD-MCI
Setting: community and long-term care
Intervention: cognitive training
Comparison: control intervention (no intervention, participating in recreational activities, receiving speech or language exercises, computerised motor therapy, or motor rehabilitation combined with recreational activity)

Outcomes	SMD (95% CI) meta-analysis	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Global cognition post-treatment Assessed with: MMSE, CERAD Follow-up: range 4 weeks to 8 weeks	SMD 0.28 higher (0.03 lower to 0.59 higher)	178 (6 RCTs)	⊕⊕⊖⊖ LOW [1,2]	A higher score is indicative of improved cognition.
Executive function post-treatment Assessed with: Trail Making Test B, Stockings of Cambridge Follow-up: range 4 weeks to 6 weeks	SMD 0.1 higher (0.28 lower to 0.48 higher)	112 (5 RCTs)	⊕⊕⊖⊖ LOW [1,2]	A higher score is indicative of improved executive function.
Attention post-treatment Assessed with: Stroop Task and Brief Test of Attention Follow-up: range 4 weeks to 6 weeks	SMD 0.36 higher (0.03 higher to 0.68 higher)	160 (5 RCTs)	⊕⊕⊖⊖ LOW [1,2]	A higher score is indicative of improved attention.
Verbal memory post-treatment Assessed with: WMS Logical Memory test, Selective Reminding Test, Hopkins Verbal Learning Test-Revised, Verbal short-term memory DemTect Follow-up: range 4 weeks to 6 weeks	SMD 0.37 higher (0.04 higher to 0.69 higher)	160 (5 RCTs)	⊕⊕⊖⊖ LOW [1,2]	A higher score is indicative of improved memory.
Visual processing post-treatment Assessed with: Judgement Line Orientation Test Follow-up: range 4 weeks to 6 weeks	SMD 0.3 higher (0.21 lower to 0.81 higher)	64 (3 RCTs)	⊕⊕⊖⊖ LOW [1,2]	A higher score is indicative of improved visual processing.
Activities of daily living post-treatment Assessed with: Barthel Index, Unified Parkinson's Disease Rating Scale, Cognitive Difficulties Scale Follow-up: range 4 weeks to 8 weeks	SMD 0.03 higher (0.47 lower to 0.53 higher)	67 (3 RCTs)	⊕⊕⊖⊖ LOW [1,2]	A higher score is indicative of improved activities of daily living.
Quality of life post-treatment Assessed with: Parkinson's Disease Questionnaire, QUALIDEM Follow-up: range 4 weeks to 8 weeks	SMD 0.01 lower (0.35 lower to 0.33 higher)	147 (5 RCTs)	⊕⊕⊖⊖ LOW [1,2]	A higher score is indicative of improved quality of life.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **RCT:** randomised controlled trial; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

---

[1]Downgraded one point due to risk of bias (all studies have at least two domains at unclear risk of bias with none of the studies at low risk of bias in all domains).
[2]Downgraded one point for imprecision due to small sample size (< 400 participants) and wide confidence intervals.
PDD: Parkinson's disease dementia
PD-MCI: Parkinson's Disease–Mild Cognitive Impairment
MMSE: Mini-Mental State Examination
CERAD: Consortium to Establish a Registry for Alzheimer's Disease test battery
WMS: Wechsler Memory Scale

BACKGROUND

Parkinson's disease (PD) is a common neurodegenerative disorder characterised by motor features such as resting tremor, rigidity, bradykinesia, and postural instability (Hughes 1992). It is now widely accepted that in addition to the motor symptoms, cognitive impairment is a core feature of the disease and should be considered when managing symptoms (Meireles 2012). Cognitive impairment in PD increases in frequency over time, but is already common in the early stages of the disease (Dubois 1997), and may even be present prior to the onset of motor symptoms (Pont-Sunyer 2015). Longitudinal studies show that people with Parkinson's disease have a three to six times higher risk of developing dementia than the general population without PD (Aarsland 2001). Cognitive impairment negatively affects patient quality of life (Leroi 2012a; Schrag 2000), and increases the risk of developing psychosis (Aarsland 2007; Giladi 2000). Once PD dementia (PDD) develops, the risk of requiring long-term care increases (Vossius 2011), with substantially higher healthcare costs compared to people living with PD but no dementia (Aarsland 2000).

Current pharmacological treatments include the cholinesterase inhibitors rivastigmine and donepezil. These may reduce some of the direct effects of the disease, including cognitive symptoms (Emre 2004; Ravina 2005; Rolinski 2012), but may be associated with adverse effects (Cutson 1995; van Laar 2011). Memantine is also used. It has a small clinical benefit, is generally safe and well-tolerated (Leroi 2009; McShane 2019), and may prolong survival (Leroi 2014; Stubendorff 2014). However, clinical responses to drug treatments can vary (Cutson 1995; van Laar 2011). Given the limited number of treatment options and the negative impact of cognitive symptoms in PD, there may be a therapeutic role for non-pharmacological interventions that target cognitive symptoms. Despite numerous cognition-based interventions such as cognitive training being investigated in dementia due to Alzheimer's disease (AD) and in mild cognitive impairment (MCI) (Bahar-Fuchs 2019; Neely 2009; Rojas 2013), less research has focused on the efficacy of cognition-based interventions in people with cognitive impairment in PD.

Description of the condition

Parkinson's disease is a neurodegenerative disorder affecting approximately 1% to 2% of people aged 60 years and over (de Rijk 2000). Although widely regarded as a motor disorder, it is frequently associated with dementia (Emre 2003; Levy 2002b), which may be a distinct syndrome (Aarsland 2001; Buter 2008). Population-based studies show that point prevalence of PDD is close to 30%, with dementia incidence rates four to six times higher than in otherwise healthy older people (Emre 2007; Hely 2008). Estimates vary, but the incidence rate of dementia per 1000 persons-per year amongst people with PD is around 30 (Williams-Gray 2007), with a cumulative prevalence rate up to 80% (Buter 2008; Hely 2008). The rate of cognitive decline can be represented as an average of a one-point decrease per year on the Mini-Mental State Examination (MMSE) (Aarsland 2004). Key risk factors for developing dementia are older age, male sex, more severe stage of parkinsonism, presence of depression, and cognitive symptoms severe enough to meet criteria for MCI (Dubois 2007; Emre 2007; Marinus 2018). PDD is associated with high levels of disability, impaired quality of life, and greater burden of care (Bassett 2005; Leroi 2012a; Vatter 2018). The clinical features of PDD are similar to those in dementia with Lewy bodies (DLB), with both typically involving progressive executive dysfunction, difficulties with visuo-spatial tasks, and memory impairment Lippa 2007. DLB is diagnosed when cognitive impairment precedes parkinsonian motor signs or is evident within one year from its onset, whereas in PDD, cognitive impairment develops within the context of a well-established PD diagnosis Emre 2007.

The Movement Disorder Society (MDS) has proposed clinical diagnostic criteria for possible and probable PDD (Emre 2007), providing practical guidance for clinicians and researchers Dubois 2007. These include: (i) a diagnosis of Parkinson's disease according to the Queen Square Brain Bank criteria (Hughes 1992); and (ii) development of motor symptoms prior to dementia onset (McKeith 2002). Dementia is defined as: (a) impairment in at least two cognitive domains, representing a decline from premorbid functioning; and (b) cognitive deficits severe enough to impair daily life, independent of impairment in PD-related motor symptoms (Dubois 2007). The cognitive profile of PDD is distinct from that of AD, characterised primarily by impairments in attention, executive, and visuo-spatial functions, but fewer impairments in language compared to AD (Bronnick 2007; Emre 2003). Memory impairment also differs (Aretouli 2010), with greater deficits in retrieval and fewer difficulties with encoding (Aarsland 2003b; Jacobs 1995). A further clinical feature distinguishing PDD from AD is cognitive fluctuations, which are more frequent in PDD (Galvin 2006). Neuropsychiatric symptoms differ between the two populations, with visual hallucinations and sleep disorders occurring more often in PDD (Aarsland 2001).

Lewy body-type degeneration is considered to be the main pathology (Halliday 2014; Irwin 2012); however, cortical changes typical of AD and frontal atrophy may also be present (Lashley 2008; Sabbagh 2009). Neurochemically, cholinergic deficits are also found in PDD as well as in AD. This provides the rationale for the use of cholinesterase inhibitors in PDD (Aarsland 2003a; Emre 2004; Leroi 2004; Reading 2001), which may improve cognition and activities of daily living (Rolinski 2012).

Cognitive impairment severe enough to meet criteria for mild cognitive impairment is frequent in Parkinson's disease (Aarsland 2010), and increases the risk of developing PDD (Pedersen 2013). The term 'Parkinson's disease with mild cognitive impairment' (PD-MCI) has been proposed by the Movement Disorder Society Task Force alongside consensus-derived clinical diagnostic criteria that remain to be validated (Litvan 2012). PD-MCI criteria include the following:

- subjective report of cognitive problems by the patient or carer;
- performance at least 1.5 standard deviations (SDs) below the age-corrected mean score in one cognitive domain;
- no impairments in activities of daily living that can be attributed to cognitive impairment.

Approximately 50% of people with PD have mild cognitive impairment (Aarsland 2010; Janvin 2005), with more than 40% presenting with PD-MCI at time of diagnosis (Aarsland 2010; Yarnall 2014). PD-MCI primarily affects memory, visuo-spatial, and executive functions and may be a transitional state between normal ageing and dementia (Backman 2005). There may also be a subtype of PD-MCI that is non-progressive and does not convert to dementia (Williams-Gray 2007), although the majority of individuals with PD-MCI progress to PDD over time (Caviness 2007; Janvin 2006;

Williams-Gray 2009). As with PDD, PD-MCI is associated with older age at disease onset, being male, experiencing depression, and having severe motor symptoms (Aarsland 2010).

Description of the intervention

For the purposes of this review, we systematically reviewed cognitive training interventions in people with PDD and PD-MCI. Cognition-based interventions differ from other non-pharmacological interventions in that they specifically aim to enhance cognition, as opposed to other behavioural or functional outcomes, either directly or indirectly. Given that terminology describing these interventions can be confusing, in this review we followed the classification of Bahar-Fuchs 2019, dividing these interventions into three types:

1. cognitive stimulation;
2. cognitive training;
3. cognitive rehabilitation.

Interventions that involve non-specific stimulation of cognitive and social functioning, engaging patients in general activities and discussions are termed 'cognitive stimulation' approaches, whereas 'cognitive training' interventions use guided practice on standardised paper and pencil or computerised tasks to target specific areas of cognition (single or multiple domains). 'Cognitive rehabilitation' uses individualised approaches to target restrictions in everyday life and improve functioning in relation to individualised goals. Interventions may also use mixed approaches, combining elements across cognition-based approaches or by adding additional physical or motor components. In this review we included studies of cognitive training targeting either a single cognitive domain or multiple cognitive domains.

Depending on the protocol used, cognitive training targets a single or multiple cognitive domains, for example memory, executive, attention, and visuo-spatial functions, and is delivered face-to-face or remotely, with sessions lasting from 30 minutes to an hour. Tasks may vary in complexity, and may be individually tailored (taking into account baseline cognitive performance or level of cognitive impairment) (Calleo 2012). Standardised programmes have been developed, as well as multimodal interventions, incorporating training in everyday activities and practising daily tasks using mnemonics, planning, and memory training. Interventions may take place in various settings (outpatient clinics, hospital settings, person's own home), on an individual or group basis, using either paper and pencil or multimedia computer software.

How the intervention might work

Cognition-based interventions in people with cognitive impairment of any aetiology (e.g. neurodegenerative disorders, traumatic brain injury, stroke), have been guided theoretically by restorative or compensatory approaches; these involve respectively either improving specific cognitive functions or using contextualised perspectives in which training is adapted to accommodate cognitive impairment (Ylvisaker 2002). For example, people engage in specific tasks that target one or more areas of cognitive function through guided practice (Bahar-Fuchs 2019). These types of interventions have been associated with improvements in memory in healthy older people and people with non-PD-related mild cognitive impairment, although they have not been shown to outperform active control interventions (Lampit 2014; Martin 2011). Generalisation of effects to other outcomes such as activities of daily living is still limited in both cognitively healthy older people and in people with mild cognitive impairment (Kelly 2014; Reijnders 2007).

In line with restorative approaches, cognitive training strengthens neural networks of attentional and control processes via neuroplasticity, as a result of experience or environmental stimulation (Raz 2006; Shaw 1994). Cognitive training may enhance frontal lobe function by activating mechanisms of brain plasticity (Boller 2004). Animal and human studies have shown that sensory systems in the cerebral cortex can improve through learning and practising tasks and that brain changes in cortical areas mediate cognitive improvements (Buonomano 1998; Gilbert 2001). Training in specific tasks increases grey matter volume (Driemeyer 2008). Cognitive training exercises increase memory-related activation in several brain areas in people with non-PD-related mild cognitive impairment such as memory-related hippocampal function (Belleville 2011; Hampstead 2012), consistent with the notion that cognitive training may encourage neuroplasticity of the brain.

Why it is important to do this review

Whilst treatment for motor symptoms in PD has improved considerably, treatment of cognitive symptoms remains limited. In clinical practice, PDD is often under-recognised and not optimally managed. The effects of drug treatments on symptoms are modest (Aarsland 2009; Emre 2010; Horstink 2006; Leroi 2009; Rolinski 2012), and no disease-modifying therapy is available. Polypharmacy, high medical comorbidity, and the side effect profile of the drugs all contribute to problems with tolerability of cholinesterase inhibitors, limiting access to evidence-based treatments for some people with PDD and PD-MCI (Rolinski 2012).

Cognitive impairment in the context of Parkinson's disease increases morbidity and mortality and experiences of neuropsychiatric symptoms (Buter 2008; Hughes 1992; Leroi 2012b), and is a marker of rapid functional decline (Hely 1995). Cognitive decline decreases patient quality of life (Leroi 2012a; Levy 2002a), and increases carer burden (Leroi 2012b), therefore any interventions that alleviate cognitive symptoms have the potential to reduce disability and improve quality of life for people with PDD and their carers.

Although cognitive training may be useful in improving cognitive outcomes in PDD, its effectiveness has not been systematically reviewed. It is important to describe the effects of these interventions in this population separately from others with dementia, as cognitive deficits are different to those observed in other dementias, and therefore interventions may need to be tailored to the cognitive domains commonly affected in PD. Since many people with PD present with MCI at the time of diagnosis (Smith 1999), identifying cognitive training approaches that can help manage cognitive symptoms in PD-MCI would be very useful clinically. The current review aims to benefit clinical practice by identifying whether cognitive training interventions improve cognitive function in people with PDD and PD-MCI, and to make recommendations for future research.

OBJECTIVES

Primary objective

To determine whether cognitive training (targeting single or multiple domains) improves cognition in people with PDD and PD-MCI or other clearly defined forms of cognitive impairment in people with PD.

Secondary objectives

To determine the effect of cognitive training on quality of life, activities of daily living, neuropsychiatric symptoms, adverse events, carer quality of life, and carer burden.

METHODS

Criteria for considering studies for this review

Types of studies

We included studies that fulfilled the following criteria:

- were randomised controlled trials (RCTs), including cluster-randomised trials;
- included a control or comparison group receiving no specific cognitive intervention.

Types of participants

People of any age, from any setting (e.g. home, community, long-term care, or rehabilitation settings), diagnosed with PDD (Emre 2007), or people with PD-MCI (Litvan 2012). We included studies that used the criteria for MCI proposed by Petersen 1999 or similar criteria.

Types of interventions

We included studies that reported a comparison between a cognitive training intervention and a control intervention. Cognitive training was defined as any intervention that targeted cognition (single or multiple cognitive domains) using a cognitive training approach involving guided practice (Bahar-Fuchs 2019; Davis 2001). Cognitive training interventions could be of any intensity, duration, or frequency, conducted on an individual or group basis, with or without the involvement of carers. We did not exclude trials on the basis of the language used to describe the intervention in the trial paper. Cognitive training interventions meeting criteria for inclusion in this review could also be described as 'memory therapy' or 'cognitive therapy', 'cognitive groups', 'cognitive training or retraining', 'cognitive support', or 'cognitive stimulation'.

Eligible control conditions could include no treatment (usual care), a waiting list for cognitive training, or an active control condition in which the comparison group engaged in non-specific activity (i.e. an attention control, controlling for effects of staff attention or social contact). 'Usual care' refers to what would usually be provided to people with cognitive impairment in Parkinson's disease in the setting in which the study was conducted (including medication, day care, and support, but no specific structured cognitive training intervention). Multicomponent interventions were considered eligible as long as one component was a clearly defined cognitive training intervention. We imposed no restrictions regarding additional physical or motor components. We excluded treatments identified as exercise, music, art, befriending, or bibliotherapy.

Types of outcome measures

We included studies that reported a cognitive outcome or outcomes, measured by a standardised test or any test that has acceptable psychometric properties.

Primary outcomes

Measures of cognitive function: global cognition, executive function, attention, memory (specifically verbal memory), and visual processing.

Secondary outcomes

- Measures of function (e.g. activities of daily living)
- Measures of quality of life
- Measures of neuropsychiatric symptoms including depression, anxiety, and apathy assessed by a validated rating scale
- Measures of carer outcomes including quality of life, experience of carer burden, well-being, or mood
- Adverse effects (e.g. on mood, awareness of cognitive difficulties)

We included studies assessing outcomes during or immediately after the intervention period.

Search methods for identification of studies

Electronic searches

We searched ALOIS (alois.medsci.ox.ac.uk/), the Cochrane Dementia and Cognitive Improvement Group's Specialised Register, on 8 August 2019. ALOIS is maintained by the Information Specialists of the Cochrane Dementia and Cognitive Improvement Group and contains studies in the areas of dementia (prevention and treatment), mild cognitive impairment, and cognitive improvement. The studies are identified from:

- monthly searches of a number of major healthcare databases: MEDLINE, Embase, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, and LILACS (Latin American and Caribbean Health Science Information database);
- monthly searches of a number of trial registers: ISRCTN, UMIN (Japan's trial register), and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (which covers the US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov, ISRCTN, the Chinese Clinical Trials Register, the German Clinical Trials Register, the Iranian Registry of Clinical Trials, and the Netherlands National Trials Register, plus others);
- quarterly search of the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library;
- six-monthly searches of a number of grey literature sources from ISI Web of Science Core Collection.

To view a list of all sources searched for ALOIS see 'About ALOIS' on the ALOIS website. Details of the search strategies used for the retrieval of reports of trials from the healthcare databases, CENTRAL, and conference proceedings can be viewed in the 'Methods used in reviews' section within the editorial information about the Dementia and Cognitive Improvement Group. We

performed additional searches in many of the sources listed above to cover the time frame from the last searches performed for ALOIS to ensure that the search for the review was as up-to-date and comprehensive as possible. We also searched relevant reviews in the area and conference proceedings.

The search strategies used are described in Appendix 1. We have run five separate searches to date, the latest one on 8 August 2019.

Searching other resources

We contacted corresponding authors of identified ongoing trials for additional references and unpublished data. We scanned the reference lists of identified publications for additional trials, and all review papers related to cognitive training interventions in cognitive impairment in PD, PDD, and PD-MCI.

Data collection and analysis

Selection of studies

Two review authors (VO, KM) independently assessed the titles and abstracts of records identified by the search for potential eligibility. Any disagreements were resolved by discussion with a third review author (IL). We excluded studies that did not meet the inclusion criteria and obtained full-text copies of those references deemed potentially relevant. We documented reasons for the exclusion of studies. Where necessary, we requested additional information from the original study authors, specifically for ongoing trials and studies reporting mixed data on people with PD with or without cognitive impairment. We repeatedly contacted authors to request further information and were successful in one instance.

Data extraction and management

We extracted information about methods, participants, interventions, outcomes, and results as described below for all studies meeting the inclusion criteria, ongoing studies, and studies awaiting classification.

- Participants: Characteristics of the sample (age, diagnostic criteria, severity of cognitive impairment, and exclusion criteria).
- Methods: Data were extracted on methodologies used for randomisation, blinding, and participant dropout.
- Interventions: Duration, intensity, type, and frequency of cognitive training and control interventions.
- Outcomes: Primary outcomes included measures of cognition. Secondary outcomes were activities of daily living, quality of life, and adverse events. Secondary outcome measures for carers were quality of life, experience of carer burden, carer well-being or mood.
- Results: Where data were available, we collected the number of participants on whom the outcome was measured in each group, means and SDs. We used change from baseline scores for all of the analyses reported and calculated the change scores manually. Calculations of the SD of change scores were based on an assumption that the correlation between measurements at baseline and those at subsequent time points is zero. This method overestimates the SD of the change from baseline, but is considered preferable in a meta-analysis to take a conservative approach. For one study (three analyses) (Folkerts 2018), we used median scores of outcomes and calculated the SD from the interquartile range.

Assessment of risk of bias in included studies

We used Cochrane's tool for assessing risk of bias to evaluate the methodological quality of the included studies (Higgins 2011). The tool addresses six specific domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other sources of bias. Two review authors (VO, KM) independently assessed each domain, resolving any differences by discussion with a third review author (IL). In cases where no information was available to make a judgement, this is explicitly stated.

Measures of treatment effect

All outcomes were continuous, and a variety of different scales contributed data to each meta-analysis, therefore we used the standardised mean difference (SMD) as the measure of treatment effect.

Unit of analysis issues

Where trials had multiple treatment groups, we combined all relevant experimental groups into a single group and all relevant control groups into a single control group. We did not identify any cluster-RCTs.

Dealing with missing data

We reported the number of participants included in the final analysis as a proportion of all participants in the study.

Assessment of heterogeneity

We used the I^2 statistic to assess heterogeneity amongst studies. We defined substantial heterogeneity as an I^2 of more than 50%. We observed no or minimal heterogeneity in all of our analyses ($I^2 \leq 1\%$).

Assessment of reporting biases

We only identified seven RCTs and pooled data from a maximum of six studies in total, therefore we did not use a funnel plot to assess for publication bias (Egger 1997).

Data synthesis

Had data permitted, we would had performed separate analyses on PDD and PD-MCI and analysed cognitive training interventions separately from multicomponent interventions. We did conduct analyses by cognitive domain: specifically, we separately analysed effects of cognitive training on global cognition, executive function, attention, verbal memory, and visual processing ability.

Subgroup analysis and investigation of heterogeneity

We had planned to conduct subgroup analyses comparing the effects of cognitive training versus active or passive control conditions, and comparing the effects of single-domain versus multiple-domain cognitive training interventions. However, there were too few studies and participants to permit any meaningful subgroup analyses..

Sensitivity analysis

We conducted sensitivity analyses excluding studies where fewer than 50% of participants had PD dementia, mild cognitive impairment, or other form of clinically significant cognitive decline as verified by a neuropsychological test.

Summary of findings and assessment of the certainty of the evidence

We used the GRADE approach to assess the certainty of the evidence for the included studies reporting on the treatment effect of cognitive training in PD-MCI and PDD compared to a control condition for a total of seven outcomes (Guyatt 2011). We used risk of bias, imprecision, inconsistency, indirectness, and publication bias to rate the overall certainty of the evidence. We have presented key findings of the review in the Summary of findings for the main comparison, which includes ratings of the certainty of evidence for all outcomes.

RESULTS

Description of studies

Results of the search

We identified a total of 3849 results via the electronic searching and five articles via other sources. After a first assessment of the search results performed by the Cochrane Dementia and Cognitive Improvement Group Information Specialists, 456 results remained for evaluation (first search: 126 results, four studies identified via handsearch; second search: 21 results, one study identified by handsearch; third search: 54 results; fourth search: 165 results; fifth search: 85 results). We screened a total of 63 full-text articles for eligibility, of which 47 were excluded with reasons; seven studies met the inclusion criteria (Alloni 2018; Cerasa 2014; Costa 2014; Folkerts 2018; Lawrence 2018; París 2011; Petrelli 2014); six studies are ongoing (NCT03582670; ACTRN12618000999235; NCT02225314; NCT03285347; NCT02525367; van de Weijer 2016); and three studies are awaiting classification until further information is obtained (NCT01647698; NCT01646333; NCT02920632); (see Figure 1).

Figure 1. Study flow diagram.

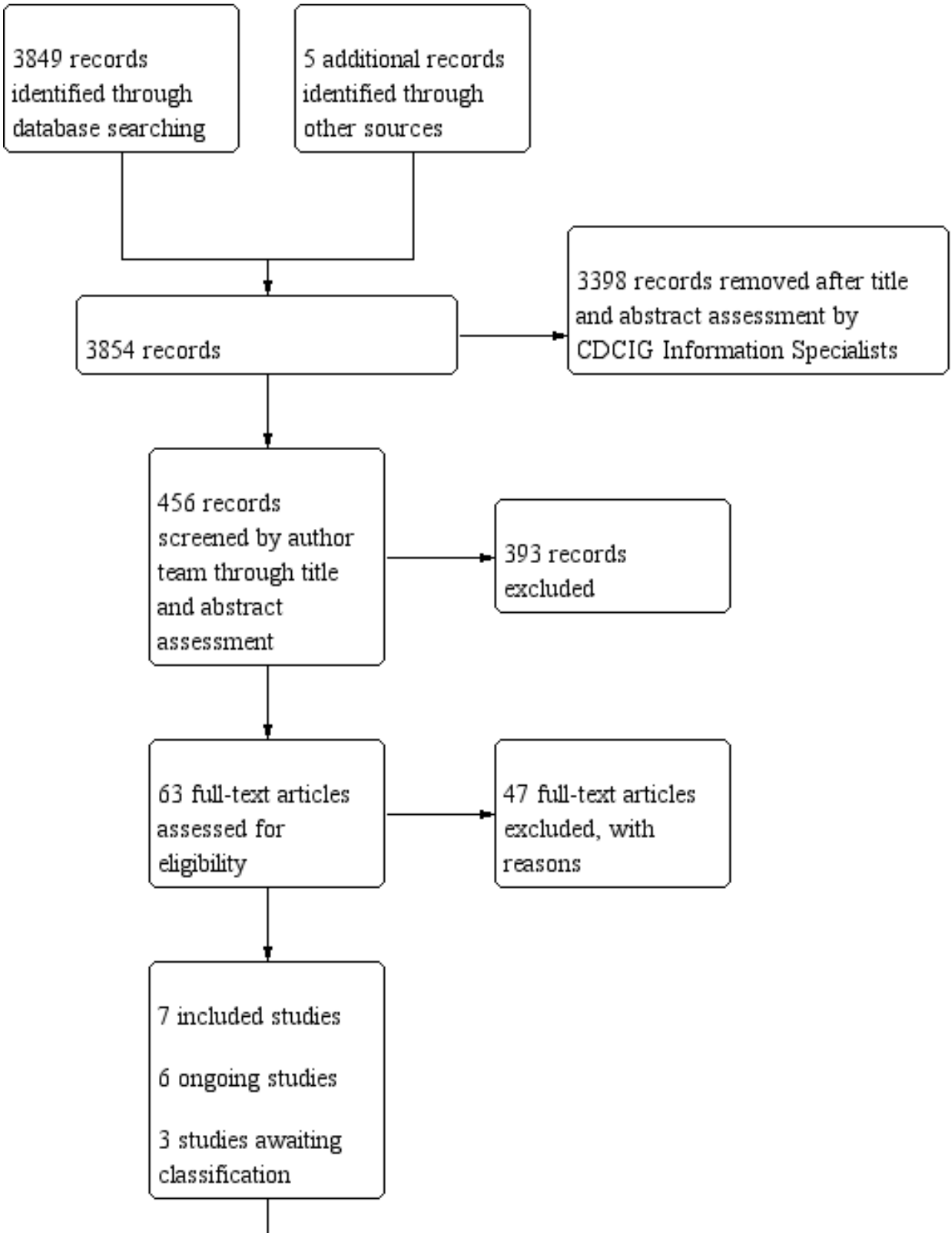
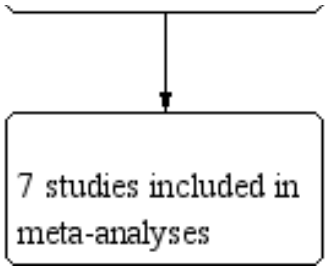


Figure 1. (Continued)



Included studies

See Characteristics of included studies.

Of the seven studies meeting the inclusion criteria (Alloni 2018; Cerasa 2014; Costa 2014; Folkerts 2018; Lawrence 2018; París 2011; Petrelli 2014), all studies except Costa 2014 contributed to the analysis of effects of cognitive training on global cognition. Five studies contributed to the analysis of effects of cognitive training on executive function (Alloni 2018; Cerasa 2014; Costa 2014; Lawrence 2018; París 2011). Five studies contributed to the analysis of effects on attention and verbal memory (Alloni 2018; Cerasa 2014; Lawrence 2018; París 2011; Petrelli 2014). Three studies contributed to analyses of visual processing ability (Cerasa 2014; Lawrence 2018; París 2011). Three studies contributed to the analysis of activities of daily living (Folkerts 2018; Lawrence 2018; París 2011), and five studies contributed to the analyses of effects of cognitive training on quality of life (Cerasa 2014; Folkerts 2018; Lawrence 2018; París 2011; Petrelli 2014).

Design

All seven studies were RCTs that evaluated the effects of a cognitive training intervention aimed at training one or more domains of cognitive function.

Setting

Alloni 2018, Cerasa 2014, and Costa 2014 were conducted in Italy and recruited outpatients in neurorehabilitation or academic units. Folkerts 2018 recruited residents of a PDD-specific long-term care unit in the Netherlands. The study by Lawrence 2018 was conducted in Western Australia and recruited outpatients. París 2011 was conducted in Spain and recruited outpatients from movement disorders clinics. Petrelli 2014 was conducted in Germany and recruited participants from a university hospital, an outpatient movement disorders clinic, and regional PD support groups.

Participants

Thirty-one participants were randomised in Alloni 2018; 20 in Cerasa 2014; 17 in Costa 2014; 12 in Folkerts 2018; 42 in Lawrence 2018; 33 in París 2011; and 70 in Petrelli 2014.

In the study by Alloni 2018, participants had a diagnosis of idiopathic PD (United Kingdom Parkinson's Disease Society Brain Bank (UKPDBB) criteria) (Hughes 1992), and scored ≤ 4 on the Hoehn and Yahr scale (Hoehn 1967). All participants experienced single-domain (executive) or multiple-domain mild cognitive impairment with executive involvement (Litvan 2012). People with pre-existing cognitive impairment (e.g. aphasia, neglect), severe disturbances in consciousness, psychiatric or neurological conditions, or severe motor or sensory disorders were excluded. The mean Mini-Mental State Exam (MMSE) score of participants at baseline was 25.35 (SD = 2.59).

In Cerasa 2014, participants had a clinical diagnosis of PD (UKPDBB criteria) and predominant deficits in either attention and/or information processing speed, working memory and/or executive functioning (demonstrated in at least one of the following tests: Symbol Digit Modalities Test (SDMT), Trail Making Test (TMT A–B), Paced Auditory Serial Addition Test (PASAT), digit span forward and backward, and Stroop word-colour task (ST), but no additional impairment in other cognitive domains (i.e. language, verbal and spatial long-term memory) or motor complications (i.e. levodopa-induced dyskinesias) (Hughes 1992). People with dementia (Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria), psychiatric history (assessed by structured clinical interview of the DSM-IV), vascular brain lesions, brain tumour and/or marked brain atrophy were excluded. The mean MMSE score of participants at baseline was 29.05 (SD = 1.00).

In Costa 2014, idiopathic PD was defined according to UKPDBB criteria (treated with levodopa or dopamine agonists, or both) (Hughes 1992); all participants had MCI according to Litvan 2012 criteria and performed 1.5 SD below the normative population in two tests of a neuropsychological screening battery (one of which investigated executive functioning). People with psychiatric disorders, neurological conditions other than PD, vascular brain lesions, metabolic disease, or people with significant changes in routine activities (measured by standardised tests) were excluded. The mean MMSE score of participants at baseline was 28.25 (SD = 1.60).

In the study by Folkerts 2018, all participants had PDD according to the MDS criteria (Emre 2007). Inclusion criteria were being a resident in the unit, having idiopathic PD (diagnosed by a neurologist/psychiatrist), experiencing cognitive dysfunction (MMSE score between 10 to 25), good language, vision, and hearing, and consent from a legal representative. People with a history of alcohol or drug abuse, a life-threatening illness, psychotic symptoms, or those who were bedridden were excluded. The mean MMSE score of participants at baseline was 17.83 (SD = 5.55).

In Lawrence 2018, participants were diagnosed with idiopathic PD (UKPDBB criteria) and MCI in accordance with the MDS PD-MCI level II diagnostic criteria (Hughes 1992; Litvan 2012), were on a stable response to antiparkinsonian medication, and cognitive deficits did not interfere with functional independence (Unified Parkinson's Disease Rating Scale (UPDRS-II) score less than 3). People with PDD, a recent history of brain surgery, migraine, or epilepsy were excluded. The mean MMSE score of participants at baseline was 25.66 (SD = 2.08).

In the study by París 2011, participants were diagnosed with PD (UKPDBB criteria) (Hughes 1992), with disease severity of Hoehn and Yahr stages I to III and not receiving any other cognitive, psychological, or physical treatment (Hoehn 1967). People with significant cognitive impairment (MMSE < 23), below-average premorbid intelligence (vocabulary subtest, Wechsler Adult Intelligence Scale-III (WAIS-III) typical score < 40), on cholinesterase inhibitors, or having any change in their medication were excluded. People with major depression (Geriatric Depression Scale (GDS-15) > 10), severe sensory deficits, or a psychiatric/neurological condition were excluded. Fifty per cent (14 of 28 participants) met Petersen 2005 and Artero 2006 criteria for MCI and demonstrated a decrement of more than 1.5 SDs on a cognitive test or subtest. The mean MMSE score of participants at baseline was 27.85 (SD = 1.37).

In Petrelli 2014, participants had idiopathic PD (UKPDBB criteria) (Hughes 1992). People with suspected dementia (MMSE < 25), other neurological or psychiatric diseases, or impaired hearing or sight were excluded. Twenty per cent of the sample fulfilled criteria for PD-MCI (Litvan 2011). The mean MMSE score of participants at baseline was 27.90 (SD = 1.93).

Cognitive training interventions and control comparisons

Alloni 2018 evaluated computerised cognitive training (CoRe Alloni 2015) consisting of patient-tailored exercises aimed primarily at stimulating executive function versus a control intervention incorporating motor rehabilitation combined with recreational activity. The cognitive training was individual sessions of 45 minutes 3 times a week over 4 weeks (12 sessions in total).

Cerasa 2014 investigated the effectiveness of individually tailored group computer-based attention-training (RehaCom Cerasa 2013) versus computerised motor therapy consisting of simple visuomotor co-ordination tasks. Cognitive training was 1-hour group sessions twice a week for 6 weeks (12 sessions in total).

Costa 2014 compared a cognitive training intervention aimed at practising shifting ability (prospective memory) versus simple language and respiratory exercises (Macdonald 2011). Cognitive training was delivered in 45-minute sessions, 3 times per week for 4 weeks (12 sessions in total).

Folkerts 2018 evaluated a modified version of the NEUROvitalis senseful programme, which targeted executive and visual spatial function versus treatment as usual, which incorporated a variety of non-pharmacological interventions such as sports, music, and arts open to all residents (Baller 2009; Middelstadt 2016). The intervention was delivered for 60 minutes twice weekly for 8 weeks (16 sessions in total).

Lawrence 2018 evaluated an interactive online computer-based cognitive training known as Smartbrain Pro (www.smartbrain.net) (Tárraga 2006), which aims to train several cognitive domains (attention, working memory, psychomotor speed, executive function, and visuo-spatial ability). The training was delivered in sessions of 45 minutes each, 3 times per week for 4 weeks (12 sessions in total). This was an RCT with six parallel intervention arms: standard cognitive training, tailored cognitive training, transcranial direct current stimulation (tDCS), standard cognitive training + tDCS, or tailored cognitive training + tDCS. We combined the standard cognitive training and the tailored cognitive training intervention groups and compared them to the no-intervention control group in the meta-analysis.

París 2011 evaluated the same Smartbrain Pro training, also in 45-minute sessions, 3 times per week for 4 weeks (12 sessions in total). In París 2011, participants completed additional homework exercises stimulating specific and non-specific cognitive areas. The comparator was group speech therapy.

Petrelli 2014 compared structured training using the same NEUROvitalis programme as Folkerts 2018, unstructured cognitive training using a programme called "Mentally fit", and a waiting-list control group. The interventions were delivered as group sessions of 90 minutes, twice a week for 6 weeks (12 sessions in total). We combined the structured and unstructured cognitive training groups and compared them with the waiting-list control group in the meta-analysis.

For further details see Characteristics of included studies.

Adherence

Folkerts 2018 reported the highest level of adherence (92.7%) across all studies, followed by Alloni 2018 (90%) and Cerasa 2014 (80%). In both París 2011 and Petrelli 2014, at least 88% of the sample completed over 75% of sessions. Costa 2014 and Lawrence 2018 did not provide details regarding adherence to the intervention.

Outcomes

All studies reported outcomes immediately after the intervention was finished, with two studies also reporting later follow-up: Alloni 2018 at 24 weeks and Lawrence 2018 at 12 weeks. End-of-treatment time points were: four weeks for Alloni 2018, Costa 2014, Lawrence 2018, and París 2011; six weeks for Cerasa 2014 and Petrelli 2014; and eight weeks for Folkerts 2018.

We classified cognitive measures used in each of the studies by considering which instrument contributed most to each outcome in line with the primary outcomes set for the review and the similarity of instruments used across studies. This task involved judgement, as many of the measures in the included studies can relate to several cognitive domains. We extracted change from baseline values for all analyses and outcomes due to imbalances at baseline and small sample sizes across all studies. Details of which outcome measures contributed to each of the analyses appear below.

Primary outcome - Cognition

Global cognition

Global cognition was measured by the MMSE, Folstein 1975, in five studies (Alloni 2018; Cerasa 2014; Lawrence 2018; París 2011; Petrelli 2014); scores on the MMSE range from 0 to 30, with lower scores indicative of greater impairment in cognition. Folkerts 2018 used the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) (Welsh 1994), where higher scores indicate better performance. Three studies, Alloni 2018; París 2011; Petrelli 2014, additionally used the Montreal Cognitive Assessment (MoCA) (Nasreddine 2005), Addenbrooke's Cognitive Examination (ACE) (Mathuranath 2000), and the DemTect (Kalbe 2004), respectively, to measure global cognition. Lower scores indicate greater impairment in cognition in all instruments. Lawrence 2018 also measured cognition using the Parkinson's

disease-cognitive rating scale (Pagonabarraga 2008); higher scores indicate better performance in this scale.

In our meta-analysis of effects of cognitive training on global cognition, we used the MMSE where possible to reduce heterogeneity and make results comparable to the wider literature on cognitive-based interventions and pharmacological trials. We used an alternative only if a study had not used the MMSE. For our meta-analysis on global cognition we included the following measures.

1. MMSE for Alloni 2018, Cerasa 2014, and Lawrence 2018 (combining the two treatment arms of standard and tailored cognitive training); París 2011 and Petrelli 2014 (combining the two treatment arms of structured and unstructured cognitive training).
2. CERAD for Folkerts 2018.

Cognitive subdomains

Alloni 2018 measured executive function using the Raven's Matrices 47 test (RM47) (Raven 1988); the Weigl's Colour-Form Sorting Test (WCFT) (Weigl 1941); the Frontal Assessment Battery (FAB) (Dubois 2000); and the F-A-S Test (Spreen 1977). Attention was measured using the Attentive Matrices (Spinnler 1987); Trail Making Tests A and B (Reitan 1985); and the Stroop task (Stroop 1935). Verbal memory was measured with the verbal and digit span tests (Wechsler 2001); Rey's 15-words test (Rey-15) (Lezak 1983); and the Wechsler Memory Scale (WMS) Logical Memory test measuring immediate and delayed recall (Wechsler 1945). Spatial memory was assessed using the Corsi Block-Tapping Test and the Rey-Osterrieth Complex Figure Test (Corsi 1972; Rey 1941). Visuo-spatial ability was measured using the Rey-Osterrieth Complex Figure Copy test (Meyers 1995).

Cerasa 2014 measured executive function using the Controlled Oral Word Association Test (COWAT) (Benton 1983). Attention and working memory were measured by the Symbol Digit Modalities Test (SDMT) (Smith 2007), the Paced Auditory Serial Addition Test (PASAT) (Gronwall 1974), the digit span test (Wechsler 2001), the Trail Making Test A and B and B-A (Reitan 1985); and the Stroop task (Stroop 1935). Verbal memory was assessed using the Selective Reminding Test (Buschke 1973), spatial memory with the Rey-Osterrieth Complex Figure Test (Rey 1941), and visuo-spatial ability with the Judgment of Line Orientation (JLO) test (Benton 1994).

Costa 2014 measured executive function using tasks of phonemic, semantic and alternating (phonemic/semantic) fluency and attention with the Trail Making Test A and B (Downes 1993; Reitan 1985).

Lawrence 2018 assessed executive function with the Stockings of Cambridge (SOC) test, Robbins 1998, and the Controlled Oral Word Association Test (COWAT), Benton 1983. Attention was measured by the Letter Number Sequencing test, Wechsler 1945, and the Stroop task, Stroop 1935. Verbal memory was assessed by the Hopkins Verbal Learning Test-Revised, Brandt 2001, and the Paragraph Recall Test (PRT), Wilson 1989. Language was assessed with the Boston Naming Test (BNT), Kaplan 1983, and the Similarities Test, Wechsler 1945. Visuo-spatial ability was measured by the JLO test, Benton 1994, and the Hooper Visual Organization Test (HVOT), Hooper 1983.

París 2011 measured executive function using the Tower of London (TOL), Culberston 2001, and the F-A-S Test, Spreen 1977. Attention and working memory were measured with the Wechsler Adult Intelligence Scale (WAIS-III) Digit Span test (Wechsler 2001), the SDMT (Smith 2007), Trail Making Tests A and B (Reitan 1985), and the Stroop task (Stroop 1935). Verbal memory was assessed by the California Verbal Learning Test Revised, Delis 2000, and the WMS Logical Memory test, Wechsler 1945. Spatial memory was assessed with the Rey-Osterrieth Complex Figure Copy test, Meyers 1995, and visuo-spatial ability with the JLO test, Benton 1994.

Petrelli 2014 measured executive function with the digit span reverse test of the DemTect and verbal and semantic fluency with fluency tasks of the same instrument (Kalbe 2004). The Brief test of attention was used to measure attention (Schretlen 1996). Verbal short- and long-term memory and visual long-term memory were assessed by the DemTect (Kalbe 2004). Visuo-spatial ability was measured with the Rey-Osterrieth Complex Figure Copy test (Meyers 1995).

We thoroughly reviewed all tests to ensure there was as much overlap as possible across domains and instruments used.

For analyses addressing effects of cognitive training on executive function, we selected the following tests: Trail Making Test B for Alloni 2018, Cerasa 2014, Costa 2014, and París 2011; and Stockings of Cambridge (SOC) for Lawrence 2018 (combining the two treatment groups).

For analyses of effects on attention, we used the following tests: the Stroop task for Alloni 2018, Cerasa 2014, and Lawrence 2018 (combining the two treatment groups) and París 2011; and the Brief test of attention for Petrelli 2014 (combining the two treatment groups).

For analyses of effects on verbal memory, we used the following tests: the WMS Logical Memory test (Immediate Recall) for Alloni 2018 and París 2011; the Selective Reminding Test-long-term storage for Cerasa 2014; the Hopkins Verbal Learning Test-Revised Immediate Recall subtest for Lawrence 2018 (combining the two treatment groups); and the verbal memory test of short-term memory of the DemTect for Petrelli 2014 (combining the two treatment groups).

For analyses of effects of cognitive training on visual processing, we included studies that used the JLO test, which were Cerasa 2014, Lawrence 2018 (combining the two treatment groups), and París 2011.

Secondary outcomes

Activities of daily living

Folkerts 2018 measured ADLs using the Barthel Index (Barthel 1965), where higher scores are indicative of greater independence in activities of daily living. Lawrence 2018 used the UPDRS Part II (Goetz 2008), in which higher scores are indicative of more severe impairment. París 2011 evaluated cognitive difficulties in ADLs using the Cognitive Difficulties Scale (CDS) (McNair 1983), where higher total summed scores indicate worse cognitive complaints associated with ADLs. We combined these three studies for our analyses on effects of cognitive training on ADLs (Folkerts 2018; Lawrence 2018 (combining the two treatment groups); París 2011).

Quality of life

Four studies, Cerasa 2014; Lawrence 2018; París 2011; Petrelli 2014, used the Parkinson's Disease Questionnaire (PDQ-39) to measure quality of life (Jenkinson 1997); lower scores in this scale indicate higher quality of life. Folkerts 2018 used the QUALIDEM scale (Ettema 2007), in which higher scores are indicative of higher quality of life. We pooled data from all five of these studies to investigate the effects of cognitive training on quality of life (Cerasa 2014; Folkerts 2018; Lawrence 2018 (combining the two treatment groups); París 2011; Petrelli 2014 (combining the two treatment groups)).

Depression

Cerasa 2014 and Petrelli 2014 used the Beck Depression Inventory II to measure depressive symptoms (Beck 1996); París 2011 used the Geriatric Depression Scale (GDS) (Sheikh 1986); Folkerts 2018 used the GDS and the Cornell Scale for Depression in Dementia (CSDD) Alexopoulos 1988. Higher scores indicate more symptoms in all measures.

Other outcomes

Cerasa 2014 measured anxiety symptoms with the State-Trait Anxiety Inventory (STAI) Spielberger 1983. Folkerts 2018 measured health-related quality of life with the EQ-5D-5L EuroQoL Group 1990, and neuropsychiatric symptoms with the Neuropsychiatric Inventory (NPI) Cummings 1997. None of the studies included outcome measures for carers.

For further details see Characteristics of included studies.

Ongoing trials

We identified six ongoing trials, which on the basis of the information available meet the inclusion criteria for this review. These are described in the Characteristics of ongoing studies table.

Studies awaiting classification

We found three studies that are awaiting classification. These are all ongoing trials, but it is unclear whether or not they will meet our review inclusion criteria. For two trials, we await further information regarding the inclusion criteria of participants (whether participants meet criteria for PD-MCI). In the third trial, it is currently uncertain whether the intervention is best classified as cognitive training or cognitive rehabilitation (or possibly a combination of both of these approaches) due to limited information provided. These three trials are described in the Characteristics of studies awaiting classification table.

Excluded studies

We excluded a total of 47 studies (see Characteristics of excluded studies). Further information regarding these studies appears below.

RCTs of cognitive training or other interventions in PD-MCI with no control group

Two studies evaluated cognitive training in people with PD-MCI in which there was no control comparison group (Reuter 2012; Biundo 2015). Reuter 2012 tested the effects of cognitive training (targeting attention, executive function, and memory training) versus cognitive and transfer training versus cognitive, transfer, and psychomotor training. The study by Biundo 2015 evaluated cognitive training (RehaCom; attention, concentration, planning, and memory exercises) as a stand-alone intervention versus cognitive training with non-invasive brain stimulation. Mahmoud 2018 evaluated cognitive remediation therapy versus motor imagery training for people with PD and cognitive dysfunction diagnosed by a cognitive assessment on RehaCom; in this RCT there was no control group. Vlagsma 2020 examined the effects of computerised cognitive training for attention (CogniPlus) with a cognitive rehabilitation intervention as the comparison group in people with PD and executive dysfunction. Maggio 2018 tested the effects of virtual reality cognitive rehabilitation versus standard cognitive training in people with PD and mild to moderate cognitive impairment (MMSE from 11 to 26). An onoing RCT NCT03836963 is testing effects of cognitive and memory strategy training in veterans with PD-MCI. Active comparators in this three-arm RCT are cognitive and memory training as stand-alone interventions.

Other cognition-based interventions in people with PDD and PD-MCI

Quayhagen 2000 evaluated a carer-led cognitive stimulation intervention (incorporating memory/problem solving and fluency activities) in people with AD, cardiovascular dementia, or PDD. In this study no separate data for PDD were provided, and diagnosis of PDD was not made using clinical criteria. Hindle 2016 evaluated cognitive rehabilitation in people with PDD, and Farzana 2015 the effects of a home-based cognitive stimulation intervention in people with PD and mild to moderate cognitive impairment, in which diagnosis of PDD and PD-MCI was not reported. This study employed a pre-post design. McCormick 2018 tested the feasibility and acceptability of individual cognitive stimulation therapy for people with PD-related dementias. We found one ongoing RCT NCT03335150 of cognitive rehabilitation (CogSMART-PD) for people with PD-MCI versus a support group control intervention.

Non-RCTs of cognitive training or other cognition-based interventions in people with PD-MCI

Naismith 2013 evaluated the effects of computerised cognitive training (based on individually tailored cognitive exercises) alongside education versus a waiting-list control condition in a controlled trial design (non randomised) in a mixed sample of people with PD, of which some had no cognitive impairment and some had PD-MCI. Stiver 2015 tested the efficacy of a mobile gaming engine aimed at reducing cognitive interference via a pre-post design. Kim 2016 used a pre-post design to test the effects of cognitive training (PD-CoRE) in people with PD and executive dysfunction.

Cognitive training in people with PD without dementia or MCI

We identified nine RCTs of cognitive training in people with PD where people with dementia or MCI, or both, were excluded.

Zimmermann 2014 tested the effects of computer-based cognitive training (versus a non-cognition-specific computer sports game; Nintendo Wii) in PD without cognitive impairment; Sammer 2006 examined the effects of working memory training targeting executive function (versus a control intervention) in people with PD and no cognitive impairment. Peña 2014 tested the effects of integrative structured cognitive training (REHACOP) (targeting attention, memory, processing speed, language, and executive function) versus occupational group activities in PD excluding

people with dementia. One ongoing RCT NCT01469741 investigates effects of prospective memory training in PD but no dementia.

Edwards 2013 tested the effects of a self-administered speed of information processing training excluding people with dementia, and Strouwen 2017 examined the effects of integrated versus consecutive dual task practice cognitive training aimed at increasing gait performance (in this study people with MMSE scores ≤ 24 were excluded). Pompeu 2012 evaluated the effects of a Wii-based motor and cognitive training intervention (training attention and working memory) versus balance exercise therapy, in which people with dementia were excluded (MMSE ≥ 23). Piemonte 2016 tested a declarative memory training intervention aimed at improving gait and activities of daily living in people with PD with no cognitive impairment. We found one ongoing study NCT02922530 testing effectiveness of a mobile cognitive training intervention for depression and quality of life in people with PD without cognitive impairment. Valdés 2017 examined the effects of information processing training versus a delayed control group in people with PD without dementia or MCI (MMSE ≥ 24). Fernandez-del-Olmo 2018 examined the effects of cognitive training versus cognitive training with concurrent physical exercise in people with PD without cognitive impairment. We further excluded two ongoing studies; NCT03680170 and NCT04048122; which evaluate effects of web-based working memory training versus low-dose short-term memory training in PD without cognitive impairment and the feasibility of cognitive rehabilitation (MC4PD strategy training) versus standard care for people with PD and subjective cognitive decline (MoCA < 21; primary outcome goal attainment).

Multicomponent interventions or cognitive interventions targeting other domains in people with PD without dementia or MCI

Peters 2012 is an ongoing study evaluating a multidisciplinary intervention incorporating exercise rehabilitation and cognitive and speech activities versus standard exercise in people with PD (excluding people with cognitive impairment). Monticone 2015 tested the effects of a multidisciplinary intervention incorporating task-oriented activities, cognitive-behavioural therapy, and occupational therapy (people with a MMSE < 24 were excluded). The study by Pompeu 2016 tests the effects of a physiotherapy guideline in people with PD and no dementia or MCI versus Microsoft Kinect games training (Kinect-Adventures-based training; KABT) on postural control, cognition, and quality of life. Walton 2016 evaluates the effects of a cognitive training intervention targeting executive function, processing speed, and attention, where freezing of gait is the primary outcome; cognition is not measured in this study. In an ongoing RCT ACTRN12617000634370, a cognitive-plus-exercise-enrichment intervention is compared to standard care in people with PD and no cognitive impairment. Fellman 2018 examined the effects of cognitive training on working memory versus quiz training in people with PD and no cognitive impairment; in this RCT people with dementia were excluded. Goedeken 2018 is testing the effects of encoding strategy training versus verbal rehearsal (control group) for people with PD; in this RCT people with PDD are excluded. An ongoing trial NCT01156714 investigates the effects of exercise training versus computerised memory training versus combined exercise and motor training versus a comparison control group in people with PD and no cognitive impairment. The study by Motlagh 2017 compares cognitive training for freezing of gait to a control comparison group in people with PD and no cognitive impairment.

Non-RCTs of cognitive training or other interventions targeting cognition in people with PD without dementia or MCI

Mirelman 2011 examined the feasibility of virtual reality training incorporating cognitive components in people with PD and no dementia; Disbrow 2012 tested the effects of computerised cognitive and motor training aimed at improving motor-related executive function in PD without dementia, whereas Canning 2008 examined multiple task walking training incorporating cognitive activities. Both Atias 2015 and Adamski 2016 used pre-post methodology to assess the feasibility of cognitive training in people with PD without dementia or MCI. Nombela 2011 tested the feasibility of Sudoku-based cognitive training; this study neither commented on the cognitive level of the participants nor reported whether people with cognitive impairment were excluded.

We found three studies using pre-post test methodology to evaluate the feasibility of cognitive training in people with PD and subjective cognitive complaints. Mohlman 2011 tested the feasibility of attention process training in PD and subjective cognitive complaints of working memory; Sinforiani 2004 tested the effects of cognitive training targeting multiple domains (attention, abstract reasoning, visuo-spatial abilities, and motor training) in people with PD and mild cognitive deficits (defined by neuropsychological evaluation) using pre-post methodology; people with severe cognitive impairment and dementia were excluded. An ongoing study NCT02826785 used pre-post methodology to examine the effects of cognitive training in PD; participants reported at least one problem with their daily cognitive performance (but had no dementia). Both Díez-Cirarda 2017 and Fearon 2017 employed a non-RCT design: the feasibility of cognitive training was tested in Díez-Cirarda 2017, and of a virtual reality-based intervention combining motor and cognitive training in Fearon 2017. Both studies included people with PD and no cognitive impairment.

Risk of bias in included studies

Two review authors independently assessed risk of bias for all seven included studies (see Characteristics of included studies). None of the included studies met criteria for low risk of bias in all domains. See Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

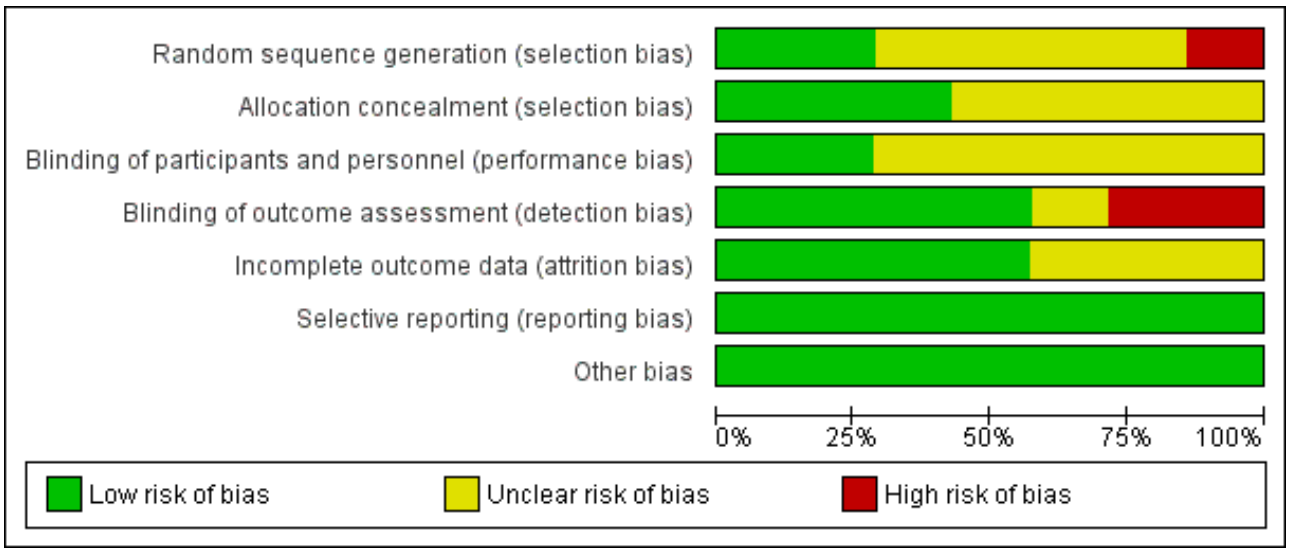
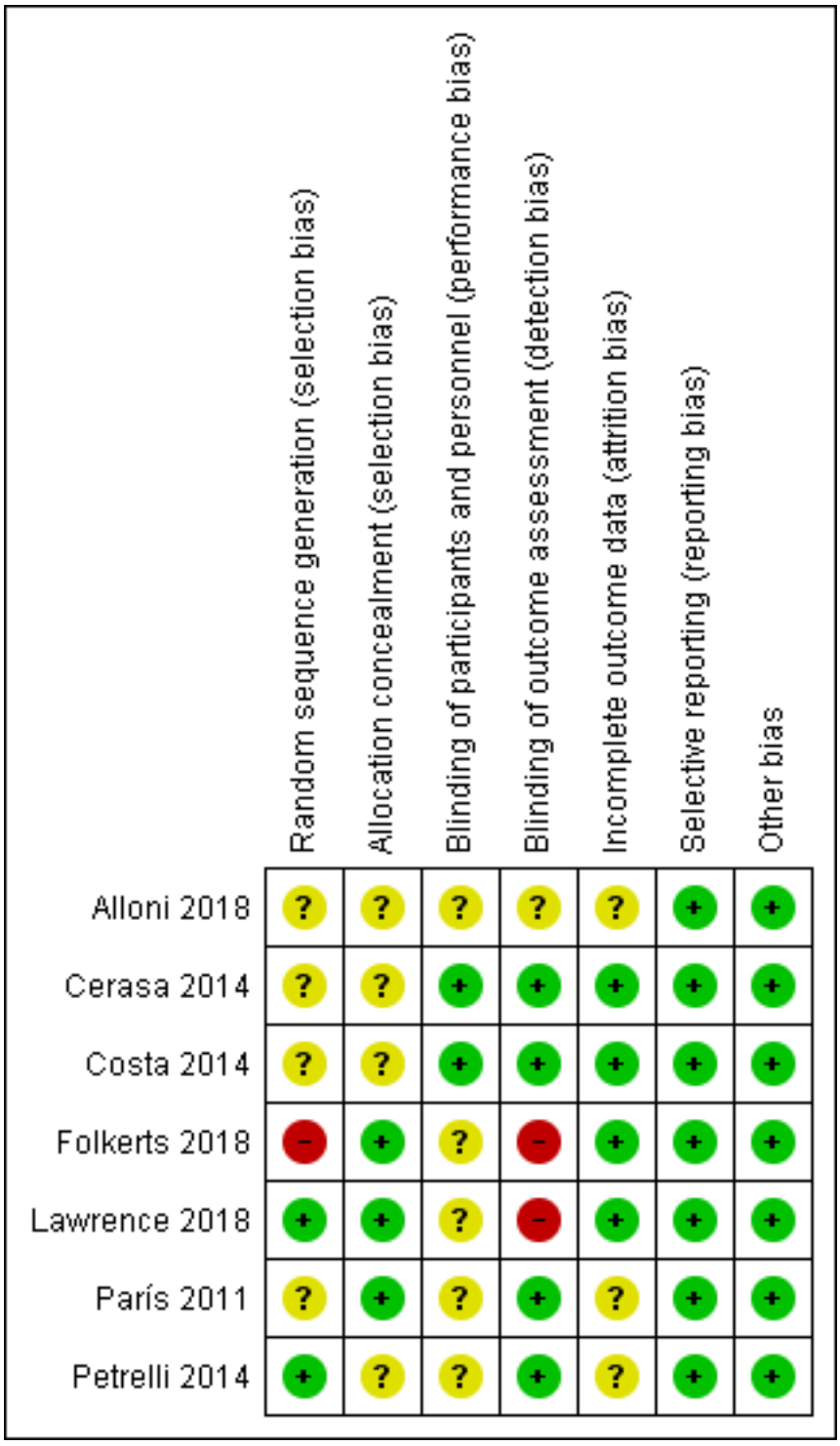


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

For the domain of random sequence generation, we considered two studies to be at low risk (Lawrence 2018; Petrelli 2014), one study at high risk (Folkerts 2018), and four studies at unclear risk of bias due to insufficient information on how the random assignment was performed (Alloni 2018; Cerasa 2014; Costa 2014; París 2011). For the allocation concealment domain, we judged three studies to be at low risk, Folkerts 2018; Lawrence 2018; París 2011, and four studies to be at unclear risk of bias, again due to insufficient detail in the published reports (Alloni 2018; Cerasa 2014; Costa 2014; Petrelli 2014).

Blinding

We judged two studies to be at low risk of performance bias; in these studies both the intervention (cognitive training) and control (sham cognitive intervention) groups were not informed about their group assignment or the rationale behind their training and could therefore be considered blind to the intervention (Cerasa 2014; Costa 2014). We considered the risk of bias for the other five studies to be unclear for this domain. We judged four studies to be at low risk, Cerasa 2014; Costa 2014; París 2011; Petrelli 2014, one study to be at unclear risk, Alloni 2018, and the remaining two studies to be at high risk of detection bias, Folkerts 2018; Lawrence 2018, because they reported that not all assessors were blind to treatment allocation or that it was not possible to blind assessors.

Incomplete outcome data

We judged three of the seven included studies to be at unclear risk of attrition bias. One of these studies reported the number of participants who did not complete the study (Alloni 2018), but not the reasons for withdrawal. Two studies reported excluding participants who completed fewer than 75% of sessions from the analyses (París 2011 Petrelli 2014). We assessed the remaining four studies as at low risk of attrition bias.

Selective reporting

We found no evidence of selective reporting in any study, therefore we classified all studies as being at low risk of bias for this domain.

Other potential sources of bias

We did not identify any other sources of bias in the included studies.

Effects of interventions

See: **Summary of findings for the main comparison** Cognitive training compared to control intervention for cognition in PDD and PD-MCI

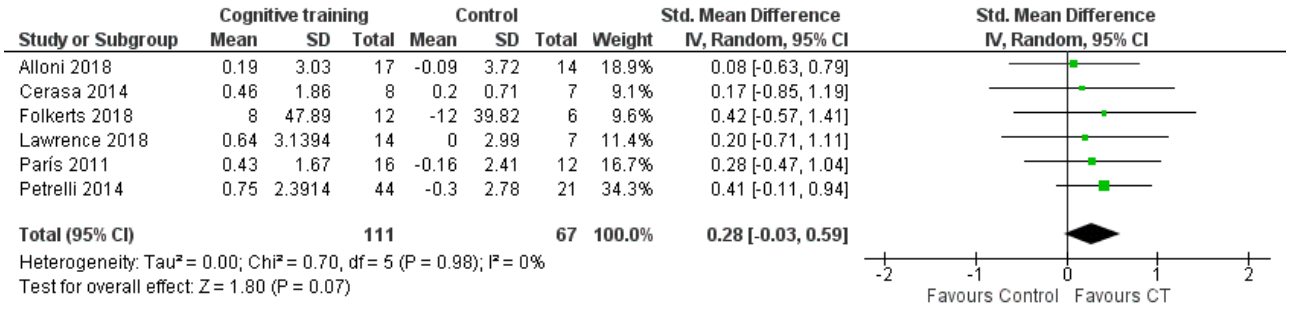
Positive results favour cognitive training for all outcomes. A summary of findings and assessment of the certainty of the evidence is presented in the Summary of findings for the main comparison.

Primary outcomes

Global cognition

The meta-analysis on effects of cognitive training on global cognition at the end of the intervention period included six studies (Alloni 2018; Cerasa 2014; Folkerts 2018; Lawrence 2018; París 2011; Petrelli 2014) with 178 participants (Analysis 1.1). We found no clear evidence of a difference between cognitive training and control interventions. The result favoured cognitive training, but did not reach statistical significance (standardised mean difference (SMD) 0.28, 95% confidence interval (CI) −0.03 to 0.59; I^2 = 0%; low-certainty evidence; Figure 4).

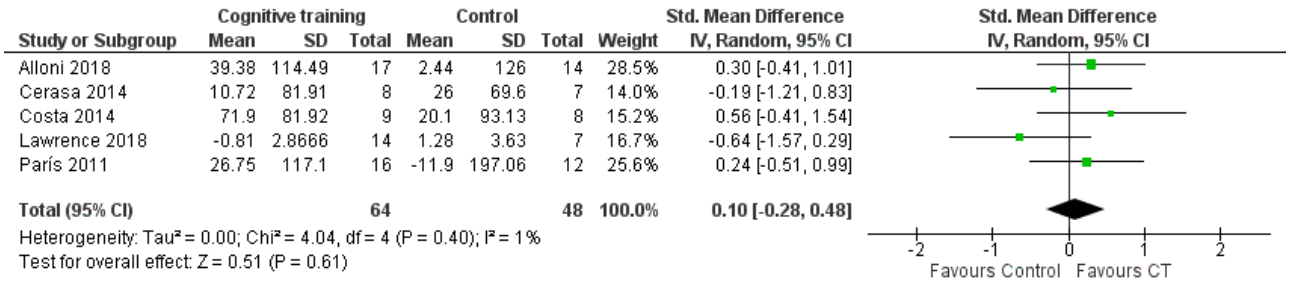
Figure 4. Forest plot of comparison: 1 Cognitive training versus control group, outcome: 1.1 Global cognition post-treatment.



Executive function

We pooled five studies (Alloni 2018; Cerasa 2014; Costa 2014; Lawrence 2018; París 2011) to examine the effects of cognitive training on executive function measured immediately after the end of the intervention (Analysis 1.2). We found no evidence of a difference between cognitive training and control interventions (SMD 0.10, 95% CI −0.28 to 0.48; I^2 = 1%; 112 participants; low-certainty evidence; Figure 5).

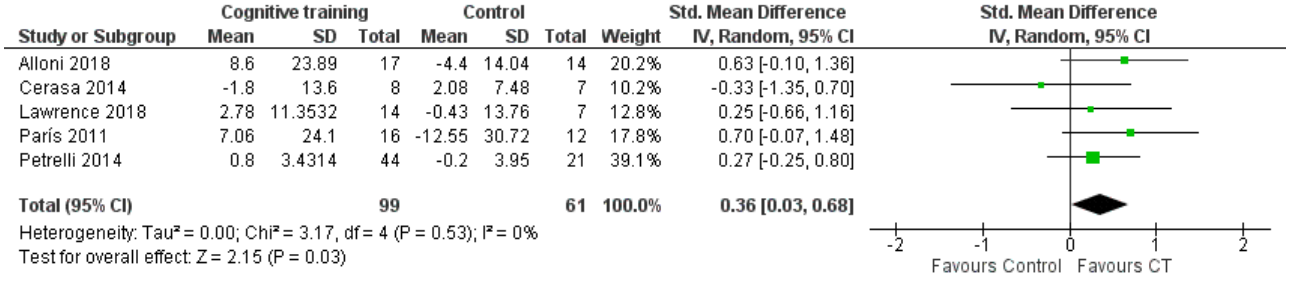
Figure 5. Forest plot of comparison: 1 Cognitive training versus control group, outcome: 1.2 Executive function post-treatment.



Attention

Pooling data from five studies (Alloni 2018; Cerasa 2014; Lawrence 2018; París 2011; Petrelli 2014) showed that cognitive training was superior to control in effects on attention at the end of treatment, although the result was imprecise and compatible with a large or with very little effect (SMD 0.36, 95% CI 0.03 to 0.68; I^2 = 0%; 160 participants; low-certainty evidence; Analysis 1.3; Figure 6). Imprecision was increased in a sensitivity analysis excluding Petrelli 2014, where fewer than 50% of participants had PD-MCI, and the result was no longer statistically significant (SMD 0.41, 95% CI −0.01 to 0.83; I^2 = 0%; 4 studies; 95 participants; low-certainty evidence; Analysis 2.1).

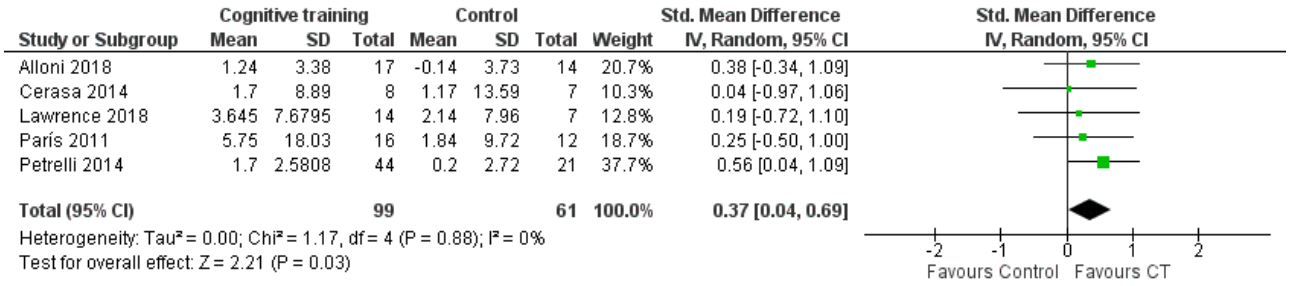
Figure 6. Forest plot of comparison: 1 Cognitive training versus control group, outcome: 1.3 Attention post-treatment.



Verbal memory

Our analysis of effects on verbal memory showed that cognitive training was superior to control at the end of treatment, although this result was also imprecise and compatible with large or very small effects (SMD 0.37, 95% CI 0.04 to 0.69; I^2 = 0%; five studies (Alloni 2018; Cerasa 2014; Lawrence 2018; París 2011; Petrelli 2014); 160 participants; low-certainty evidence; Analysis 1.4; Figure 7). In the sensitivity analysis excluding Petrelli 2014, there was no clear evidence of any effect (estimate smaller and more imprecise) (SMD 0.25, 95% CI −0.16 to 0.66; I^2 = 0%; 4 studies; 95 participants; low-certainty evidence; Analysis 2.2).

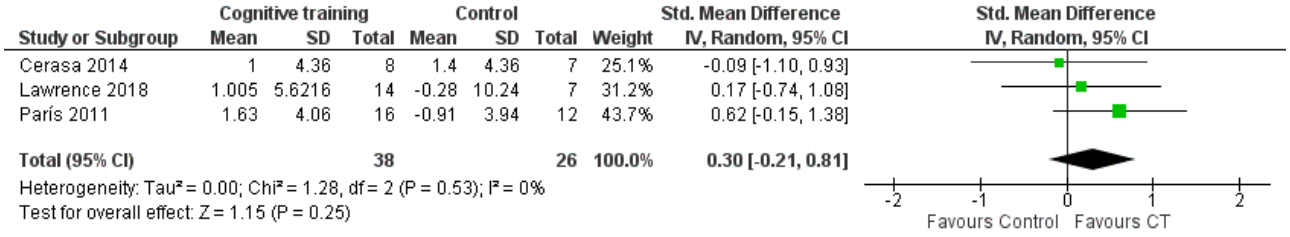
Figure 7. Forest plot of comparison: 1 Cognitive training versus control group, outcome: 1.4 Verbal memory post-treatment.



Visual processing

We found no evidence of an effect of cognitive training on visual processing ability at end of treatment (SMD 0.30, 95% CI −0.21 to 0.81; I^2 = 0%; three studies (Cerasa 2014; Lawrence 2018; París 2011); 64 participants; low-certainty evidence; Analysis 1.5; Figure 8).

Figure 8. Forest plot of comparison: 1 Cognitive training versus control group, outcome: 1.5 Visual processing post-treatment.

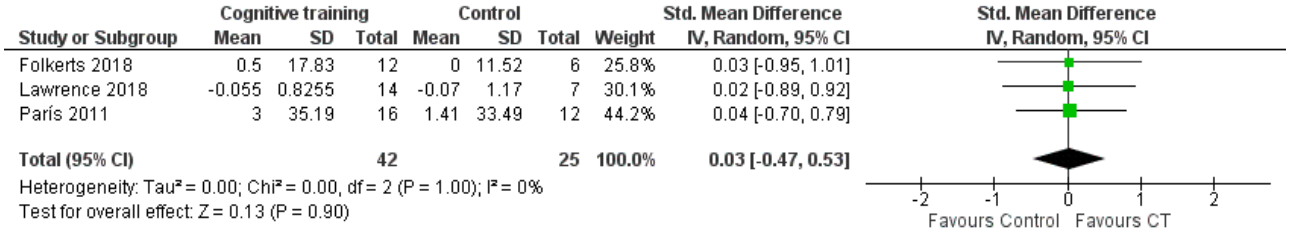


Secondary outcomes

Activities of daily living

We found no evidence of an effect of cognitive training on ADLs at the end of the intervention period (SMD 0.03, 95% CI −0.47 to 0.53; I^2 = 0%; three studies (Folkerts 2018; Lawrence 2018; París 2011); 67 participants; low-certainty evidence; Analysis 1.6; Figure 9).

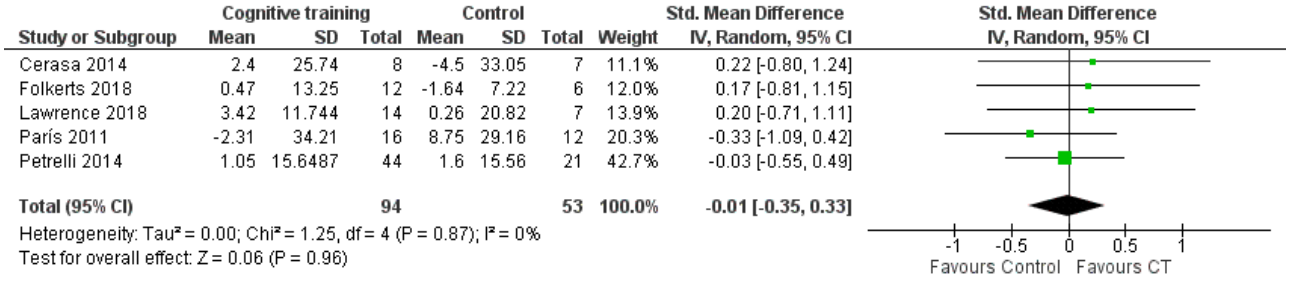
Figure 9. Forest plot of comparison: 1 Cognitive training versus control group, outcome: 1.6 Activities of daily living post-treatment.



Quality of life

We found no evidence of an effect of cognitive training on quality of life immediately after the end of sessions (SMD −0.01, 95% CI −0.35 to 0.33; I^2 = 0%; five studies (Cerasa 2014; Folkerts 2018; Lawrence 2018; París 2011; Petrelli 2014) 147 participants; low-certainty evidence; Analysis 1.7; Figure 10).

Figure 10. Forest plot of comparison: 1 Cognitive training versus control group, outcome: 1.7 Quality of life post-treatment.



Adverse events

Folkerts 2018 reported no adverse events. The remaining studies did not provide any information about adverse events (Alloni 2018; Cerasa 2014; Costa 2014; Lawrence 2018; París 2011; Petrelli 2014).

Analyses on effects of cognitive training at longer-term follow-up (12 to 24 weeks)

Global cognition

The meta-analysis on effects of cognitive training on global cognition at longer-term follow-up (12 to 24 weeks) included two studies (Alloni 2018; 24 weeks; Lawrence 2018; 12 weeks) with 41 participants. We found no evidence of a difference between groups (mean difference 0.28, 95% CI −1.73 to 2.28; I^2 = 0%; low-certainty evidence; Analysis 1.8).

Executive function

We found no evidence of an effect of cognitive training on executive function at longer-term follow-up (SMD −0.22, 95% CI −0.85 to 0.41; I^2 = 0%; two studies (Alloni 2018; 24 weeks; Lawrence 2018; 12 weeks); 41 participants; low-certainty evidence; Analysis 1.9).

Attention

We found no evidence of an effect of cognitive training on attention at longer-term follow-up (SMD 0.21, 95% CI −0.59 to 1.01; I^2 = 36%; two studies (Alloni 2018; 24 weeks; Lawrence 2018; 12 weeks) 41 participants; low-certainty evidence; Analysis 1.10).

Verbal memory

We found no evidence of an effect of cognitive training on verbal memory at longer-term follow-up (SMD 0.15, 95% CI −0.47 to 0.78; I^2 = 0%; two studies (Alloni 2018; 24 weeks; Lawrence 2018; 12 weeks); 41 participants; low-certainty evidence; Analysis 1.11).

DISCUSSION

Summary of main results

The aim of this review was to evaluate the effectiveness of cognitive training interventions for people with PDD and PD-MCI and to report on the quality of the evidence. Our results do not support a beneficial effect of cognitive training on general cognition shortly after the intervention has ended. Although cognitive training was associated with better scores on attention and verbal memory, the differences between the intervention and control groups were not robust to the exclusion of a study where only 20% of the

sample had PD-MCI. We found no evidence of benefit in other specific cognitive domains (executive function, visual processing ability) and no differences between cognitive training and control interventions in relation to ADLs and quality of life. Because most studies were in people with PD-MCI who, by definition, have no significant functional impairment at baseline, effects on ADLs were unlikely to be detected. We considered the evidence to be of low certainty overall due to imprecision and study limitations (see Quality of the evidence).

Overall completeness and applicability of evidence

Only seven studies with a total of 225 participants met our inclusion criteria, therefore the evidence base remains very small. Only one study (and no identified ongoing studies) included people with PDD, reflecting an important gap in the evidence. Most of the included studies involved people with PD and mild cognitive impairment living in community settings. Uncertainty about the degree and nature of cognitive impairment in the study populations is an important limitation of our review. In one included study (Cerasa 2014), participants had significant cognitive impairment on a standard neuropsychological test, but their status against MCI criteria was unclear. We also included two studies in which the sample was a mixed population of people with and without MCI (París 2011; Petrelli 2014), as we were unable to access separate data. Given that diagnostic criteria for PD-MCI have only recently been defined, and the variability in diagnosis (Marras 2013), we considered it important to be inclusive in our approach and to consider studies with mixed samples of people with and without clinically significant cognitive decline (as verified by performance on a standardised test) as eligible. As our sensitivity analyses showed that results were influenced by the inclusion of a study in which only a small proportion of the sample had cognitive impairment, it will be important that data on participants with and without cognitive impairment can be separated in future versions of this review or in other evidence syntheses.

Cognitive training across studies targeted either one or many cognitive domains. Single-domain cognitive training focused on executive function in Alloni 2018, memory in Costa 2014 (prospective memory via training of shifting ability), and attention in Cerasa 2014. The remaining four studies evaluated cognitive training that targeted multiple domains of cognitive function (Folkerts 2018, executive function and visuo-spatial ability; Lawrence 2018 and París 2011, attention, working memory, psychomotor speed, executive function, and visuo-spatial ability; Petrelli 2014, attention, memory, and executive function, with additional psychoeducational elements). In all included studies cognitive training was computerised; in some studies this was augmented with paper and pencil homework assignments. To date we are unable to comment on whether multidomain or single-domain cognitive training may differentially affect cognition in people with PD-MCI and PDD.

Most of the included studies measured both general cognition and specific areas of cognitive function. Although outcomes were similar, studies used different measures, and in most studies primary outcome measures were not specified. It will be important that future research incorporates key core outcomes so that results across studies can be compared. We found only two studies reporting on long-term effectiveness of cognitive training, measuring outcomes at 12 and 24 weeks. We found no evidence that cognitive training benefits global or specific areas of cognitive function in the longer term. However, studies were small, and risk of bias identified in several areas limits any conclusions about whether these interventions could benefit people with PDD and PD-MCI at long-term follow-up. Overall, the current evidence therefore provides limited information in terms of potential long-term benefit. Given the small number of studies and small sample sizes, our analyses may have had limited power to detect differences in cognition and in the secondary outcomes of ADLs and quality of life.

There was limited information on adverse events, with only one study reporting that the intervention was not associated with any adverse outcomes. This is in line with systematic reviews of cognitive training in older people and people with mild to moderate Alzheimer's disease and vascular dementia (Bahar-Fuchs 2019), which found few studies mentioning adverse effects.

Although retrospectively it appears that we excluded many studies, we considered it important to include only studies where participants with PD also had clinical cognitive impairment to ensure that our review did not replicate previous reviews of effectiveness of cognitive training in PD without cognitive impairment (Leung 2015).

We were not able to conduct any subgroup analyses due to the small number of studies identified. An important aim for future versions of this review will be to assess whether the nature of the comparator intervention influences efficacy, as was found in a review of cognitive training in mild to moderate dementia (Bahar-Fuchs 2019).

Quality of the evidence

All of the included studies were at unclear or high risk of bias in two or more domains. Many of the studies did not report details of random sequence generation, allocation concealment, or blinding. In some studies participants were excluded from analyses, indicating that intention-to-treat principles were not applied. For example, in two studies participants who did not receive more than 75% of the treatment were excluded from analyses.

According to the GRADE criteria, we considered the overall certainty of the evidence to be low for all outcomes due to risk of bias and imprecision. The numbers of studies and participants were small, and the confidence intervals around all effect estimates were wide. This GRADE rating means that new evidence may substantially change the effect estimates. Despite clinical heterogeneity across studies, such as inclusion of people with varying degrees of cognitive impairment, there was no or limited statistical heterogeneity across all of our analyses.

Potential biases in the review process

Although we searched systematically several sources, including the Cochrane Central Register of Controlled Trials (CENTRAL), conference proceedings, and review articles, the possibility remains that we may have missed some studies. We found several RCTs that reported excluding people with moderate to severe dementia; although these studies did not meet our inclusion criteria, it is possible that they included people with PD-MCI and mild PDD.

Agreements and disagreements with other studies or reviews

Leung 2015 conducted a systematic review on the effectiveness of cognitive training for people with PD but no cognitive impairment. Although in some of our analyses cognitive training was favoured, which was in line with this review, our results did not reach statistical significance after sensitivity analyses were conducted. Given the small number of studies to date and risk of bias identified in several areas, our confidence in the conclusions of our review is limited.

AUTHORS' CONCLUSIONS

Implications for practice

Given that many people with Parkinson's disease (PD) experience cognitive difficulties, the potential benefit of use of cognitive training interventions is large. It will be important that large-scale trials of effectiveness are conducted, especially in people with PD dementia (PDD). Evidence from this review suggests that cognitive training interventions are generally associated with high levels of adherence. Given the small evidence base, risk of bias, and overall low certainty of the evidence, implications for clinical practice cannot be identified without further research.

Implications for research

Interventions that aim to improve cognition for people with PDD and PD-related mild cognitive impairment (PD-MCI) are becoming increasingly important as pharmacological treatment for cognitive symptoms is limited. Our review highlights the paucity of research in the area and that further research is necessary in order to establish whether cognitive training interventions in people with PDD and PD-MCI may be beneficial. It is important that these trials follow the CONSORT statement. We await evidence from several ongoing trials evaluating the effectiveness of cognitive training in people with PD-MCI.

Despite some progress in definitions of cognition-based interventions, there is still confusion with regard to how these interventions are defined and described. Our review suggests overall that although most studies provide enough information to be able to separate interventions, treatment protocols are not provided, and often different approaches are grouped under the same definition. It will be important for future research to concentrate on large-scale trials of clinical effectiveness versus a control comparison intervention, as many studies had to be excluded because the comparison group was another intervention. Updates of this review could additionally examine effectiveness of cognitive training against other active interventions.

Future studies should define cognitive impairment and specify type of diagnosis. Most studies to date exclude 'people with severe cognitive impairment', so it is likely that in some studies people with mild dementia or MCI were included. It will be important for future research to address this limitation and describe samples in greater detail reporting diagnostic criteria. Future studies should also try to address variation in training period, tasks used (i.e. cognitive only, cognitive and motor tasks), and sensitivity to change of outcome measures.

It will be important to examine whether any effects observed are generalised to everyday function and tasks of daily living. In the current review we are unable to draw any conclusions as to whether cognitive training is associated with improvements in daily life due to the small number of included studies. Future studies should test whether type of intervention evaluated influences efficacy, and comparisons between multicomponent cognitive training interventions, incorporating additional elements such as transfer training and physical training, versus cognitive training alone.

It has been argued that cognitive training may activate mechanisms of cerebral plasticity and slow PD-associated cognitive decline (Boller 2004). Future studies should investigate the potential mechanisms through which cognitive training may mediate effects on cognition using structural and functional imaging methods, and the extent to which these interventions may slow the progression of cognitive decline (Boller 2004). Research in the area should also address heterogeneity in outcomes, which may hinder future meta-analyses. In conclusion, our review suggests that there is an urgent need for further large-scale studies of cognitive training for people with PDD and PD-MCI.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Alloni 2018

Methods	Randomised Controlled Trial (RCT)
Participants	Diagnosis of idiopathic Parkinson's disease (PD) according to UK Parkinson's Disease Society Brain Bank (UKPDBB) diagnostic criteria, Hoehn and Yahr scale ≤ 4, and presence of single-domain (executive) or multiple-domain mild cognitive impairment (MCI) with executive involvement. Number randomised n = 31.
Interventions	Computerised exercises of the CoRe tool tailored to individuals' performance aimed at training executive function (logical analogies and sequences, find the elements and functional planning); over 4 weeks; 12 sessions lasting 45 minutes each. Control group received an intervention incorporating motor rehabilitation combined with recreational activity.
Outcomes	• Global cognitive function 1. Mini-Mental State Examination (MMSE) 2. Montreal Overall Cognitive Assessment (MoCA) • Memory - Verbal and spatial memory 1. Verbal and digit span 2. Corsi's block-tapping test 3. Logical Memory test with immediate and delayed recall 4. Rey's 15-words test with immediate and delayed recall 5. Rey's Complex Figure Test (ROCF) Delayed Recall • Executive function: Logical-executive functions 1. Raven's Progressive Matrices 2. Weigl's Sorting test 3. Frontal Assessment Battery 4. Semantic fluency and phonological fluency (F-A-S Tests) • Attention 1. Attentive Matrices 2. Trail Making Test Part A – (TMTa) – and Trail Making Test Part B (TMTb) – 3. Stroop test • Visuo-spatial abilities 1. ROCF Copy
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Mentions participants were randomly allocated. No further details.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Authors communicated that participants were not blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	No further details.

Alloni 2018 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers of completers provided but no reasons for attrition.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None identified.

Cerasa 2014

Methods	RCT of intensive computerised attention-training vs control group
Participants	People with a diagnosis of PD (n = 20), with no dementia (Diagnostic and Statistical Manual of Mental Disorders 4th edition) but predominant deficits in either attention or information processing speed, working memory, or executive function (but no deficit in other domains such as language, verbal and spatial long-term memory). Number randomised: n = 20.
Interventions	Computerised 12 one-hour sessions over 6 weeks performing several attention ability and information processing tasks tailored to attention deficits. Control group received simple visuo-motor co-ordination exercises.
Outcomes	Primary outcomes: • Global cognition 1. MMSE • Spatial and verbal memory 1. ROCFT Immediate and Delayed Recall 2. Selective Reminding Test • Visual-spatial processing 1. Judgment of Line Orientation (JLO) • Executive function/verbal fluency 1. Controlled Oral Word Association Test (COWAT) • Sustained attention 1. Symbol Digit Modalities Test (SDMT) • Information processing speed 1. Paced Auditory Serial Addition Test 2. Digit span forward/backward 3. Stroop test 4. TMTa, TMTb, and Trail Making Test B-A (TMTB-A) • Depression 1. Beck Depression Inventory-II (BDI-II) • Anxiety 1. State-Trait Anxiety Inventory • Quality of life 1. Parkinson's Disease Questionnaire (PDQ-39)
Notes	

Cerasa 2014 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Mentions random assignment only.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were blind to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blind.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition and reasons reported.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None identified.

Costa 2014

Methods	RCT with 2 arms and a healthy control group
Participants	People with PD (n = 17) defined according to UKPDBB criteria (Hughes 1992), and presence of MCI according to Litvan and colleagues criteria (Litvan 2012). Participants performed 1.5 Standard Deviations (SDs) below the normative population in 2 tests of a neuropsychological screening battery, 1 of which investigated executive function. All treated with levodopa or dopamine agonists, or both. Excluded participants with psychiatric disorder, significant apathy and depression, or neurological conditions other than PD. Number randomised (n = 17).
Interventions	Computerised cognitive training aimed at improving shifting ability on prospective memory tasks • 45-minute paper and pencil exercises involving different stimuli (e.g. letters, numbers, and shapes), modelled on existing paradigms sensitive to frontal-striatal activity requiring participants to alternately select between stimuli belonging to different semantic categories or different features that increased in difficulty (Macdonald 2011). • 12 sessions in total over 4 weeks Control group: performed language and respiratory exercises of similar frequency and duration to the cognitive training exercises, which included dictation and reordering of sentence sequences.
Outcomes	• Verbal fluency 1. Phonemic word fluency (verbal fluency alternate task) 2. semantic fluency

Costa 2014 *(Continued)*

	3. alternating phonemic/semantic fluency • Attention 1. TMTa and TMTb
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Mentions only random assignment to the 2 treatment arms.
Allocation concealment (selection bias)	Unclear risk	No details are provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were blind to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Researcher conducting post-assessments was blind.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition in the study.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None identified.

Folkerts 2018

Methods	RCT (cross-over RCT)
Participants	People with Parkinson's disease dementia (PDD) living in long-term care; diagnosed according to the Movement Disorders Society (MDS) task force Level I guidelines and PDD diagnosed with the MMSE (10 to 25 points). Number randomised (n = 12).
Interventions	Although intervention is described as cognitive stimulation therapy, it was a structured standardised Cognitive Training (CT) programme (NEUROvitalis) adapted to the cognitive and psychomotor profile of participants; performed over 8 weeks, twice weekly for 60 minutes. Control group received usual care (arts, sports, music).
Outcomes	Cognition 1. Consortium to Establish a Registry for Alzheimer's Disease test battery - "CERAD Plus" (plus a word fluency test and the TMT; total score as an index for global cognition (maximum 111 points) Neuropsychiatric symptoms 1. Neuropsychiatric Inventory

Folkerts 2018 *(Continued)*

	Depression 1. Geriatric Depression Scale-Short form (GDS-15) 2. Cornell Scale for Depression in Dementia Activities of daily living 1. Barthel Index Quality of life 1. EQ-5D-5L 2. QUALIDEM
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants were randomised by picking a note with the participant's identification code, comprised of 2 random letters and random numbers.
Allocation concealment (selection bias)	Low risk	Mentions that randomisation was done by a member of the staff not involved in the study.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not all assessors were blind.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition and reasons for each group are reported.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None identified.

Lawrence 2018

Methods	RCT of standard CT vs tailored CT vs transcranial direct current stimulation vs standard CT + transcranial direct current stimulation vs tailored CT + transcranial direct current stimulation vs control group.
Participants	People diagnosed with idiopathic PD in accordance with the UKPDBB criteria, with MCI in accordance with the MDS Parkinson's Disease–Mild Cognitive Impairment (PD-MCI) Level II diagnostic criteria. Number randomised (n = 42).
Interventions	Standard cognitive training known as Smartbrain Pro targeting specific cognitive domains, for 45 minutes, 3 times a week for 4 weeks. Tailored cognitive training of the same format and duration where cognitive activities were individualised to participant's baseline neuropsychological test results. Both treatment arms were included in the meta-analyses.

Lawrence 2018 *(Continued)*

	Control group received no intervention.
Outcomes	• Executive function 1. Stockings of Cambridge (of the Cambridge Neuropsychological Tests Automated Battery) 2. COWAT • Attention 1. Letter-Number Sequencing 2. Stroop (Colour-Word Interference) test • Memory 1. Hopkins Verbal Learning Test-Revised Immediate Recall subtest 2. Paragraph Recall Test • Visuo-spatial abilities 1. JLO 2. Hooper Visual Organization Test • Language 1. Boston Naming Test-Short Form 2. Similarities Test • Global cognition 1. Parkinson's Disease-Cognitive Rating Scale 2. MMSE • Premorbid intelligence 1. National Adult Reading Test • Activities of daily living 1. Unified Parkinson's Disease Rating Scale (Section II) • Quality of life 1. PDQ-39
Notes	We included both the standard and the tailored cognitive training treatment groups in the analyses.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence generated by computer following CONSORT guidelines.
Allocation concealment (selection bias)	Low risk	Participants were randomised to treatment (5 intervention and 1 control) by a computer-generated list using block randomisation at a ratio of 1:1. Probably done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No further details provided.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Authors mention that it was not possible to blind researchers.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition reported. No details of reasons are provided.
Selective reporting (reporting bias)	Low risk	All outcomes reported.

Lawrence 2018 *(Continued)*

Other bias	Low risk	No other bias detected.

París 2011

Methods	RCT of cognitive training vs control group
Participants	People who met UKPDBB diagnosis criteria for Parkinson's disease, with I–III Hoehn and Yahr, without dementia (MMSE ≥ 23), including those who had MCI (50% met Petersen and colleagues 2005 criteria for MCI). Number randomised (n = 33).
Interventions	Cognitive training 3 times a week over 4 weeks with each session lasting 45 minutes. Control group received speech group therapy.
Outcomes	• Cognition 1. MMSE 2. Addenbrooke's Cognitive Examination • Premorbid intelligence 1. Wechsler Adult Intelligence Scale III Vocabulary subtest • Attention and working memory 1. WAIS III–Digit Span Forward and Backward 2. California Verbal Learning Test II–List A1 • Information processing speed 1. SDMT 2. TMTa and TMTb 3. Stroop test • Verbal memory 1. CVLT-II–Short-Delay Free Recall and Long-Delay Free Recall 2. Wechsler Memory Scale-III–Logical Memory test • Learning 1. CVLT-II–List A Total • Visual memory 1. ROCFT Immediate and Delayed Recall • Visuo-spatial abilities 1. JLO • Verbal fluency 1. Phonemic–F-A-S Test 2. Semantic–Animals F-A-S Test • Executive function 1. Tower of London-Total Moves, Total Correct, and Total–Rules Violations 2. TMT-B 3. Stroop test (Interference) • Quality of life 1. PDQ-39 • Depression 1. GDS-15 • Cognitive difficulties in activities of daily living 1. Cognitive Difficulties Scale

París 2011 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only mentions random allocation. No further details provided.
Allocation concealment (selection bias)	Low risk	Mentions blind allocation. Probably done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blind to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Mentions attrition and reasons, but also describes excluding participants completing less 75% of sessions.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None identified.

Petrelli 2014

Methods	RCT of structured cognitive training targeting specific cognitive functions plus psychoeducation elements vs unstructured cognitive training of randomly assembled cognitive tasks vs waiting-list control
Participants	Idiopathic PD according to UKPDBB criteria, including people who had MCI according to MDS task force Level I guidelines (Litvan 2011). 23% (15 of the 50) met Litvan and colleagues 2011 criteria for MCI. Number randomised (n = 70).
Interventions	"NEUROvitalis", a structured cognitive training intervention targeting several cognitive domains (attention, memory, executive function). Unstructured training called "Mentally fit" targeting attention, memory, and less specific functions such as language and creative thinking, 12 group sessions, 90 minutes each over 6 weeks. Control group was waiting list.
Outcomes	• General cognitive function 1. MMSE 2. DemTect • Attention 1. Brief Test of Attention • Memory 1. Verbal short- and long-term memory DemTect 2. Visual long-term memory DemTect

Petrelli 2014 *(Continued)*

- Executive functions
1. Working memory DemTect digit span reverse
2. Verbal phonemic and semantic fluency DemTect
- Visuo-construction
1. Rey's Complex Figure Test
- Depression
1. BDI-II
- Quality of life
1. PDQ-3

Notes	We included both the structured ("NEUROvitalis") and the unstructured ("Mentally fit") cognitive training treatment groups in the analyses.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Mentions random allocation using a computer program.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Only participants in the 2 treatment groups were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blind.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition and reasons were reported, but also describes excluding participants completing less than 75% of sessions.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None identified.

PD: Parkinson's disease
UKPDBB: UK Parkinson's Disease Society Brain Bank diagnostic criteria
MCI: mild cognitive impairment
MMSE: Mini-Mental State Examination
MoCA: Montreal Overall Cognitive Assessment
ROCF: Rey's Complex Figure Test
F-A-S Tests: Semantic fluency and phonological fluency
TMTa: Trail Making Test Part A
TMTb: Trail Making Test Part B
JLO: Judgment of Line Orientation
COWAT: Controlled Oral Word Association Test
SDMT: Symbol Digit Modalities Test
TMTB-A: Trail Making Test B-A
BDI-II: Beck Depression Inventory-II
PDQ-39: Parkinson's Disease Questionnaire
SDs: Standard Deviations

PDD: Parkinson's disease dementia
CT: Cognitive Training
GDS-15: Geriatric Depression Scale-Short form
PD-MCI: Parkinson's Disease–Mild Cognitive Impairment

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
ACTRN12617000634370	Ongoing RCT of a cognitive-plus-exercise-enrichment intervention vs standard care for people with PD and no cognitive impairment.
Adamski 2016	Non-Randomised Controlled Trial (RCT), feasibility study of computerised cognitive training (BrainStim) in people with Parkinson's disease (PD) where only healthy controls were randomised. No control group, and people with PD had no cognitive impairment.
Atias 2015	Non-RCT feasibility pre-and-post study of cognitive training (AttenGo) designed to improve executive function in participants with PD with no cognitive impairment; (Mini-Mental State Examination (MMSE) > 25). No control group.
Biundo 2015	RCT of the effects of computer-based cognitive training alone or combined with non-invasive brain stimulation in people with Parkinson's Disease–Mild Cognitive Impairment (PD-MCI). No control group.
Canning 2008	Non-RCT feasibility study of multiple-task walking training incorporating cognitive activities (counting backwards, memory recall, generating category lists, and simple arithmetic tasks) in participants with PD with no cognitive impairment (MMSE ≥ 24).
Disbrow 2012	Pre-and-post experimental study of a computer-based cognitive and motor training programme designed to improve motor-related executive function in participants with PD. Participants were screened for dementia.
Díez-Cirarda 2017	Pre-and-post study of a group-based cognitive intervention for people with PD; no control group; people with dementia were excluded.
Edwards 2013	RCT of a self-administered cognitive speed-of-processing training (SOPT, InSight) designed to improve information processing speed in realistic visual contexts vs no-contact control condition in participants with PD (MMSE ≥ 24). Participants with dementia were excluded. Primary outcome was field of view performance.
Farzana 2015	Non-RCT pre-and-post study of individual home-based cognitive stimulation in people with PD and mild to moderate cognitive impairment (MMSE > 24); information on diagnosis of dementia/mild cognitive impairment (MCI) not reported.
Fearon 2017	Pre-and-post evaluation of a virtual reality-based intervention combining motor and cognitive training for people with PD and no cognitive impairment.
Fellman 2018	RCT of cognitive training of working memory vs quiz training in people with PD and no cognitive impairment; people with dementia were excluded.
Fernandez-del-Olmo 2018	RCT of cognitive training vs cognitive training with concurrent physical exercise in people with PD without cognitive impairment.
Goedeken 2018	RCT of an Implementations Intentions (encoding strategy training) intervention vs verbal rehearsal (control group) for people with PD. People with dementia were excluded.
Hindle 2016	RCT of cognitive rehabilitation in people with Parkinson's disease dementia (PDD) vs relaxation therapy vs treatment as usual.

Study	Reason for exclusion
Kim 2016	Pre and post study of cognitive training (PD-CoRE) in people with PD and executive dysfunction; no control group.
Maggio 2018	RCT of virtual reality cognitive rehabilitation versus standard cognitive training in people with PD and mild to moderate cognitive impairment (MMSE from 11 to 26); no control group.
Mahmoud 2018	RCT of a motor imagery training intervention vs cognitive remediation therapy for people with PD and cognitive dysfunction diagnosed by a cognitive assessment on RehaCom. No control group. All outcome measures were RehaCom tasks rather than standardised instruments.
McCormick 2018	RCT (ongoing) assessing the feasibility and acceptability of individual cognitive stimulation therapy for people with PD-related dementias (PD-MCI; PDD or Dementia with Lewy bodies) vs treatment as usual.
Mirelman 2011	Feasibility non-RCT of virtual reality training with cognitive components (attention, response selection, and processing visual stimuli) in participants with PD. People with dementia were excluded. No control group.
Mohlman 2011	Non-RCT feasibility study of a cognitive remediation programme to train attentional ability in people with PD. People with dementia were excluded. No control group.
Monticone 2015	RCT of a multidisciplinary intervention of task-oriented exercises, Cognitive Behavioral Therapy, and occupational therapy in people with PD. People with dementia or MMSE < 24 were excluded.
Motlagh 2017	RCT of cognitive training for freezing of gait in people with PD and no cognitive impairment vs control.
Naismith 2013	Non-RCT (controlled study) of computer-based cognitive training (based on the Neuropsychological Educational Approach to Remediation (NEAR)) with psychoeducation vs a waiting-list control group in people with PD, of whom some had MCI. People with dementia were excluded.
NCT01156714	RCT of exercise training vs computerised memory training vs combined exercise and motor training vs control in people with PD and no cognitive impairment.
NCT01469741	RCT of prospective memory training for participants with PD treated with levodopa/carbidopa. People with dementia are excluded (ongoing trial).
NCT02826785	Pre and post feasibility study of a cognitive training strategy intervention for people with PD who experience at least 1 problem with their daily cognitive performance; people with dementia were excluded.
NCT02922530	RCT (ongoing) of a novel mobile cognitive tracking and training tool in people with PD with no cognitive impairment targeting depression and quality of life. Control group is a commercially available cognitive training intervention.
NCT03335150	Ongoing RCT of cognitive rehabilitation (Cognitive Symptom Management and Rehabilitation Therapy for Parkinson's disease: CogSMART-PD) for people with PD-MCI vs a support group intervention.
NCT03680170	RCT of web-based working memory updating training vs low-dose short-term memory training in people with PD without cognitive impairment.
NCT03836963	3-arm RCT of cognitive and memory strategy training in veterans with PD-MCI. Active comparators are cognitive and memory training as stand-alone interventions.

Study	Reason for exclusion
NCT04048122	RCT of cognitive rehabilitation known as MC4PD strategy training versus standard care for people with PD and subjective cognitive decline. People with dementia will be excluded (Montreal Overall Cognitive Assessment < 21). Primary outcome is goal attainment.
Nombela 2011	Non-RCT, feasibility pre-and-post study of cognitive training incorporating Sudoku exercises (working memory using numerical items, whilst requiring no mathematical calculation) in participants with PD, with their performance matched to controls. No control group. Does not mention level of cognitive impairment (baseline MMSE = 25).
Peters 2012	Ongoing RCT of a multidisciplinary intervention (exercise rehabilitation, cognitive and speech activities) vs standard exercise rehabilitation in participants with PD. People with cognitive impairment that could affect their ability to participate in the intervention are excluded.
Peña 2014	RCT of integrative structured cognitive training programme (REHACOP; attention, memory, processing speed, language and executive function tasks) vs occupational group activities in participants with PD. People with dementia were excluded.
Piemonte 2016	RCT of declarative memory training targeting gait and activities of daily living in people with PD with no cognitive impairment.
Pompeu 2012	RCT of Nintendo Wii-based motor and cognitive training vs balance exercise therapy in participants with PD without MCI or dementia (MMSE ≥ 23). The cognitive component of the training included attention and use of working memory to solve motor tasks, and performance management.
Pompeu 2016	RCT testing the efficacy of a European physiotherapy guideline vs Microsoft Kinect games training on postural control, cognition, and quality of life. People with PD had no cognitive impairment.
Quayhagen 2000	RCT of cognitive stimulation provided by carers (memory, problem-solving, and conversational fluency activities) vs dyadic counselling vs supportive seminars vs day care for people with Alzheimer's disease, cardiovascular, or PDD. No separate data are provided, and no formal criteria to diagnose dementia in PD were used.
Reuter 2012	RCT of cognitive training (attention, executive function, memory training) vs cognitive and transfer training vs cognitive, transfer, and psychomotor training in participants with Parkinson's disease and MCI. No control group.
Sammer 2006	RCT of cognitive training (working memory tasks targeting executive function) vs control in participants with PD without cognitive impairment (average MMSE = 27). Cognitive stage not defined.
Sinforiani 2004	Non-RCT, feasibility pre-post study of cognitive training (attention, abstract reasoning, visuo-spatial abilities) incorporating motor training in participants with PD presenting with mild cognitive deficits. No control group. People with severe cognitive impairment or dementia, or both were excluded.
Stiver 2015	Not an RCT. Testing the feasibility of brain mobile gaming (reducing cognitive interference) in people with vascular MCI and PD-MCI and age-matched controls.
Strouwen 2017	Ongoing RCT of integrated gait and cognitive training (performing cognitive exercises, and functional training simultaneously) on activities of daily living vs consecutive gait and cognitive training (taking place separately) in participants with PD without cognitive impairment (MMSE ≥ 24), aimed primarily at increasing gait performance (primary outcome).
Valdés 2017	RCT of speed of information processing vs delayed control group in people with PD with an MMSE score ≥ 24.
Vlagsma 2020	RCT of cognitive rehabilitation vs computerised cognitive training for attention (CogniPlus) in people with PD and executive dysfunction.

Study	Reason for exclusion
Walton 2016	RCT of computerised cognitive training targeting executive function, processing speed, and attention in people with PD with no cognitive impairment (MMSE ≥ 24). The primary outcome was freezing of gait.
Zimmermann 2014	RCT of cognition-specific computer-based cognitive training (CogniPlus) vs a non-cognition-specific computer sports game (Nintendo Wii) in participants with PD without cognitive impairment (average MMSE = 29). People with moderate or severe dementia were excluded.

RCT: Randomised Controlled Trial
PD: Parkinson's disease
MMSE: Mini-Mental State Examination
PD-MCI: Parkinson's Disease–Mild Cognitive Impairment
MCI: mild cognitive impairment
PDD: Parkinson's disease dementia

Characteristics of studies awaiting assessment *[ordered by study ID]*

NCT01646333

Methods	RCT (ongoing) of memory and problem-solving training vs non-directive supportive therapy
Participants	• Clinical diagnosis of Parkinson's disease (PD) • Clinical diagnosis of MCI Exclusion criteria: clinical diagnosis of dementia or other PD-associated comorbid conditions (e.g. severe anxiety, depression, excessive daytime sleepiness, or psychosis) that can influence cognitive testing.
Interventions	Memory and problem-solving training consisting of a day calendar manual and note-taking system and problem-solving techniques focusing on memory compensation and problem-solving strategies. Control group: supportive therapy (offering participants and carers the opportunity to discuss and reflect upon both PD and non-PD related problems).
Outcomes	Primary outcome: verbal learning measured by the California Verbal Learning Test-II Long Delay Free Recall Scaled Score Secondary outcomes: well-being measured by the Linear Analog Scale Assessment Overall Well Being scale Outcomes measured at 2 and 6 months.
Notes	Unclear whether this study is cognitive training or cognitive rehabilitation; contact with author has not been possible. Trial appears to be ongoing.

NCT01647698

Methods	Randomised Controlled Trial (RCT) (ongoing) of the effectiveness of adaptive vs non-adaptive working memory training (increasing in number of items required to be remembered) vs no training; ongoing trial, 3 arms
Participants	People with PD who self-report concerns about working memory or show deficits as identified by a clinical examination (excludes people with dementia).

NCT01647698 *(Continued)*

Interventions	Computerised adaptive working memory training testing working memory capacity and non-adaptive working memory training.
Outcomes	Primary outcomes: working memory (measured by 3 separate tasks): operation span task, symmetry span task, Stenberg memory scanning task Secondary outcomes: fluid intelligence (Cattell's Culture Fair Intelligence Test and Rave's Progressive Matrices), executive function: Dysexecutive Questionnaire Outcomes measured at 5-, 10-, and 22-week follow-up.
Notes	Unclear whether this sample has Parkinson's Disease–Mild Cognitive Impairment (PD-MCI). Trial is ongoing (control group receives no training); unable to contact author.

NCT02920632

Methods	RCT (ongoing) of online cognitive training (COGTIPS - COGnitive Training In Parkinson Study) vs online cognitive training of games that incorporate cognitive activities
Participants	• Subjective cognitive complaints, measured by the Parkinson's Disease Cognitive Functional Rating Scale score > 3 (PD-CFRS); a score above 3 indicates significant cognitive complaints that are milder than complaints associated with Parkinson's disease dementia. Questionnaire is filled in by the participant. • Participants' Hoehn and Yahr stage is lower than 4 • Access to a computer or tablet and willing to sign informed consent Exclusion criteria: indications for a dementia syndrome, measured by the self-administered Gerocognitive Examination (score < 14) or the Montreal Cognitive Assessment (score < 22).
Interventions	8-week training (COGTIPS) - training contains several games that are designed to train cognitive functions; 3 times a week for 45 minutes Control group receives online gaming cognitive activities.
Outcomes	Primary outcome: executive function measured by the Tower of London Secondary outcomes: subjective cognitive complaints measured by the PD-CFRS; executive function measured by the Stroop colour-word task, the Letter fluency task, and the Tower of London; risk reduction of PD-MCI/Parkinson's disease dementia (PDD) development at follow-up Outcomes measured at 6 months, 1 year, and 2 years.
Notes	Although risk reduction of PD-MCI/PDD development at follow-up is an outcome for the study, participants may meet PD-MCI criteria at baseline. Trial is ongoing.

RCT: Randomised Controlled Trial
PD: Parkinson's disease
PD-MCI: Parkinson's Disease–Mild Cognitive Impairment
PDD: Parkinson's disease dementia

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12618000999235

Trial name or title	A randomised controlled trial of cognitive training and non-invasive brain stimulation in PD: the impact on cognition and quality of life

ACTRN12618000999235 *(Continued)*

Methods	4-arm RCT of transcranial direct current stimulation and cognitive training vs sham transcranial direct current stimulation and cognitive training vs transcranial direct current stimulation and placebo cognitive training vs sham transcranial direct current stimulation and placebo cognitive training (n = 52).
Participants	1. Diagnosed with idiopathic PD by neurologist/geriatrician using UK Parkinson's Disease Society Brain Bank (UKPDBB) diagnostic criteria 2. Self-reported problems with cognition that do not significantly impact on functional independence 3. Presence of MCI in accordance with the Movement Disorder Society Task Force criteria for PD-MCI Level II diagnostic criteria, using an Standard Deviation (SD) level of 1.5 4. Stable response to antiparkinsonian medication for a minimum period of 2 months.
Interventions	Cognitive training Control group receives sham cognitive training.
Outcomes	• Primary outcomes: 1. Attention and working memory: Letter-Number Sequencing subtest from the Wechsler Adult Intelligence Scale-IV (WAIS-IV) 2. Attention: Stroop (Colour-Word) Test 3. Executive function: Stockings of Cambridge (of the Cambridge Neuropsychological Tests Automated Battery) 4. Executive function: Controlled Oral Word Association Task 5. Language: Boston Naming Test 6. Language: Similarities subtest of the WAIS-IV 7. Memory: Hopkins Verbal Learning Test-Revised 8. Memory: Location Learning Test 9. Visuo-spatial processing: Judgement of Line Orientation test 10.Visuo-spatial processing: Hooper Visual Organization Test • Secondary outcomes: 1. Quality of life: Parkinson's Disease Questionnaire (PDQ-39) Outcomes measured at 1 week and 12 weeks.
Starting date	August 2018
Contact information	n.gasson@curtin.edu.au
Notes	

NCT02225314

Trial name or title	Computer-based cognitive training for individuals with PD-MCI
Methods	3-arm RCT of computerised auditory and accuracy training vs visual processing and working memory training vs active control (n = 25).
Participants	People speaking English with a confirmed medical diagnosis of Parkinson's disease and meeting established criteria for MCI in PD (Litvan 2012), defined as individuals with performances of approximately 1 to −2 SDs below the mean on at least 2 tests within 5 cognitive domains assessed in clinical neuropsychological evaluations People with dementia are excluded.

NCT02225314 *(Continued)*

Interventions	Treatment arm 1: computer-based cognitive training known as Brain Fitness, which consists of 6 types of exercises that train auditory processing speed and accuracy Treatment arm 2: computer-based cognitive training known as InSight, a computer-based cognitive training programme that consists of 5 types of exercises that train visual processing and working memory 60 minutes per day, 5 days a week Active-control training programme: computerised learning programme consisting of 5 programmes (i.e. Wright Brothers, History of Britain, Sister Wendy's American Collection, In Search of Shakespeare, and View the Cosmos) designed to improve knowledge about literature, art, and history.
Outcomes	Primary outcome: per cent accuracy on cognitive training quizzes (Brain Fitness; auditory processing and accuracy tasks; InSight: visual processing and working memory tasks) Secondary outcomes: PDQ-39, California Verbal Learning Test-II Long Delay Free Recall Scaled Score Change Outcomes measured at 3 months.
Starting date	19 August 2014
Contact information	sklageman@vcu.edu
Notes	

NCT02525367

Trial name or title	Online cognitive training in PD, multiple sclerosis, and depressed patients treated with electroconvulsive therapy
Methods	RCT vs active control condition (double-blind) (n = 28).
Participants	• Diagnosed with Parkinson's disease UKPDBB diagnostic criteria • Problems in cognition with deficits in executive function lying between 1 and 2 SDs below the mean of the healthy Dutch population • Stable medication
Interventions	Online computerised cognitive training (targeting executive functions, attention, working memory, and processing speed) over 8 weeks, 3 times a week for 45 to 60 minutes. Control group: active control condition of cognitive activities based on crystallised intelligence.
Outcomes	Primary outcomes: feasibility over 8 weeks as reported by participants on a 4-point Likert-type scale. Secondary outcomes: 1. Cognitive functioning: Trail Making Task 2. Subjective cognitive complaints: Cognitive Failures Questionnaire 3. Executive functions: Stroop (Colour Word) Test 4. Letter fluency, episodic memory: Rey Auditory Verbal Learning and Location Learning tests Measured at 8 and 12 weeks

NCT02525367 *(Continued)*

Starting date	August 2015
Contact information	oa.vandenheuvel@vumc.nl
Notes	

NCT03285347

Trial name or title	Effect of computer-based cognitive training on attention and executive functions in patients with Parkinson's disease
Methods	RCT (2 treatment arms) (n = 30).
Participants	• Diagnosed with Parkinson's disease and executive dysfunction • Scoring between 22 and 28 on Montreal Cognitive Assessment
Interventions	Computer-based cognitive training (either Brain + Evolution or Scientific Brain Training PRO) over 8 weeks. Control group: receives no intervention (follow-up visits incorporating a computerised card game).
Outcomes	• Primary outcomes: 1. Processing speed: Symbol Digit Modalities Test 2. Quality of life: PDQ-39 • Secondary outcomes: 1. Depression: Hospital Anxiety and Depression Scale (HADS) 2. Working memory: digit span from the WAIS-IV 3. Verbal fluency: s-words; animal names; A/F-words 4. Stroop colour/word test: Stroop; response inhibition 5. Trail Making Test A and B: cognitive flexibility
Starting date	October 2017
Contact information	annemette.loekkegaard@regionh.dk
Notes	

NCT03582670

Trial name or title	Prospective memory training in Parkinson's disease
Methods	Randomised Controlled Trial (RCT) (n = 90).
Participants	1. Males and females over 50 years of age 2. Meet criteria for typical idiopathic Parkinson's disease (PD) 3. Hoehn and Yahr stage I-III 4. Have Parkinson's Disease–Mild Cognitive Impairment (PD-MCI) according to Movement Disorder Society Level II diagnostic criteria

NCT03582670 *(Continued)*

Interventions	Strategy training (specific memory strategy training with training games, as well as feedback on accuracy and performance) vs process training (event- and time-based prospective memory tasks but no strategy training or feedback) vs control intervention (does not attend any sessions).
Outcomes	Primary outcome measures: 1. Virtual Week [Time Frame: 4 to 6 weeks]. A computerised board game that simulates daily life and real-world prospective memory challenges. Main outcome variable is the proportion of correct prospective memory responses for each task type (12 event based, 12 time based). Change of performance on the Virtual Week from the pre- and post-session will also be measured. 2. Prospective and Retrospective Memory Questionnaire [Time Frame: through completion of the study, up to 16 weeks]. Change in scores on this questionnaire will be measured.
Starting date	July 2018
Contact information	erfoster@wustl.edu
Notes	

van de Weijer 2016

Trial name or title	Effect of health games on cognitive function in Parkinson's disease - The Parkin'play study
Methods	Multicentre RCT (n = 222).
Participants	• Diagnosis of idiopathic PD according to UKPDBB diagnostic criteria • Cognitive impairment at baseline in line with the Level 1 criteria for MCI and a cutoff of 1.5 SD below the normative mean (diagnosis based on Litvan 2012) • Aged 40 to 75 years • Not receiving any other cognitive therapy/intense physical activity • Stable dopaminergic medication (for the last 3 months) Excludes people with advanced problems in cognitive functioning.
Interventions	Web-based computerised cognitive training 'health game' targeting multiple cognitive domains over 12 weeks (via MyCognition AquaSnap). Control group: waiting list.
Outcomes	• Primary outcome: cognition as measured by standard neuropsychological assessment 1. Executive function: Stroop Colour Word Test; category and letter fluency 2. Memory: Rey Auditory Verbal Learning 3. Visual perception: Judgement of Line Orientation 4. Visuoconstruction: Rey-Osterrieth Complex Figure 5. Language: Boston Naming Test - Short Form; and compound score of overall (global) cognition and online assessment (MyCQ; MyCognition Quotient; 5 domains: attention, psychomotor speed, working memory, episodic memory, executive function) • Secondary outcomes: 1. Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) to measure motor function 2. Depression: HADS 3. Self-report evaluation of perception 4. Memory and motor-function in daily life: Cognitive Failures Questionnaire

van de Weijer 2016 *(Continued)*	5. Functional abnormalities associated to cognitive impairment: Parkinson's Disease Cognitive Functional Rating Scale 6. Functional disability: re-Rasch-built Overall Disability Scale 7. Quality of life: PDF-39 8. Impulsive behaviour: Barratt Impulsiveness Scale 11 Biological outcomes: change in activity of the resting-state network associated with executive functions measured by functional magnetic resonance imaging Outcomes measured at 12 and 24 weeks.
Starting date	7 January 2016
Contact information	mark.kuijf@mumc.nl
Notes	

RCT: Randomised Controlled Trial
PD: Parkinson's disease
PD-MCI: Parkinson's Disease–Mild Cognitive Impairment
UKPDBB: UK Parkinson's Disease Society Brain Bank diagnostic criteria
SD: Standard Deviation
WAIS-IV: Wechsler Adult Intelligence Scale-IV
PDQ-39: Parkinson's Disease Questionnaire
HADS: Hospital Anxiety and Depression Scale

DATA AND ANALYSES

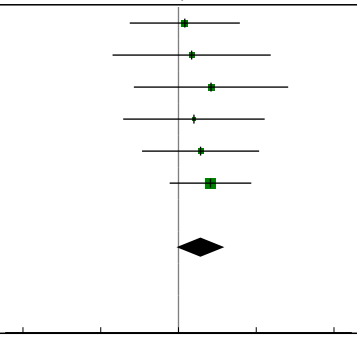
Comparison 1. Cognitive training versus control group

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global cognition post-treatment	6	178	Std. Mean Difference (IV, Random, 95% CI)	0.28 [-0.03, 0.59]
2 Executive function post-treatment	5	112	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.28, 0.48]
3 Attention post-treatment	5	160	Std. Mean Difference (IV, Random, 95% CI)	0.36 [0.03, 0.68]
4 Verbal memory post-treatment	5	160	Std. Mean Difference (IV, Random, 95% CI)	0.37 [0.04, 0.69]
5 Visual processing post-treatment	3	64	Std. Mean Difference (IV, Random, 95% CI)	0.30 [-0.21, 0.81]
6 Activities of daily living post-treatment	3	67	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.47, 0.53]
7 Quality of life post-treatment	5	147	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.35, 0.33]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
8 Global cognition long term	2	41	Mean Difference (IV, Random, 95% CI)	0.28 [-1.73, 2.28]
9 Executive function long term	2	41	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.85, 0.41]
10 Attention long term	2	41	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.59, 1.01]
11 Verbal memory long term	2	41	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.47, 0.78]

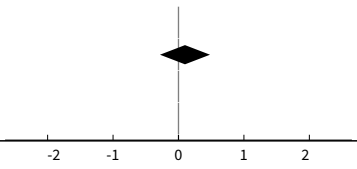
Analysis 1.1. Comparison 1 Cognitive training versus control group, Outcome 1 Global cognition post-treatment.

Study or subgroup	Cognitive training N	Cognitive training Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Alloni 2018	17	0.2 (3)	14	-0.1 (3.7)		18.87%	0.08[-0.63,0.79]
Cerasa 2014	8	0.5 (1.9)	7	0.2 (0.7)		9.14%	0.17[-0.85,1.19]
Folkerts 2018	12	8 (47.9)	6	-12 (39.8)		9.6%	0.42[-0.57,1.41]
Lawrence 2018	14	0.6 (3.1)	7	0 (3)		11.42%	0.2[-0.71,1.11]
París 2011	16	0.4 (1.7)	12	-0.2 (2.4)		16.68%	0.28[-0.47,1.04]
Petrelli 2014	44	0.8 (2.4)	21	-0.3 (2.8)		34.29%	0.41[-0.11,0.94]
Total ***	**111**		**67**			**100%**	**0.28[-0.03,0.59]**
Heterogeneity: Tau²=0; Chi²=0.7, df=5(P=0.98); I²=0%							
Test for overall effect: Z=1.8(P=0.07)							



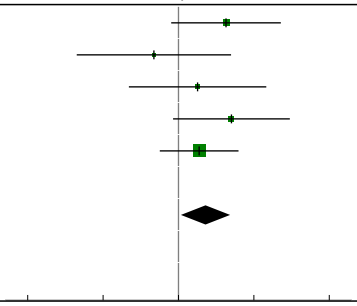
Analysis 1.2. Comparison 1 Cognitive training versus control group, Outcome 2 Executive function post-treatment.

Study or subgroup	Cognitive training N	Cognitive training Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Alloni 2018	17	39.4 (114.5)	14	2.4 (126)		28.47%	0.3[-0.41,1.01]
Cerasa 2014	8	10.7 (81.9)	7	26 (69.6)		14.04%	-0.19[-1.21,0.83]
Costa 2014	9	71.9 (81.9)	8	20.1 (93.1)		15.23%	0.56[-0.41,1.54]
Lawrence 2018	14	-0.8 (2.9)	7	1.3 (3.6)		16.69%	-0.64[-1.57,0.29]
París 2011	16	26.8 (117.1)	12	-11.9 (197.1)		25.58%	0.24[-0.51,0.99]
Total ***	**64**		**48**			**100%**	**0.1[-0.28,0.48]**
Heterogeneity: Tau²=0; Chi²=4.04, df=4(P=0.4); I²=0.96%							
Test for overall effect: Z=0.51(P=0.61)							



Analysis 1.3. Comparison 1 Cognitive training versus control group, Outcome 3 Attention post-treatment.

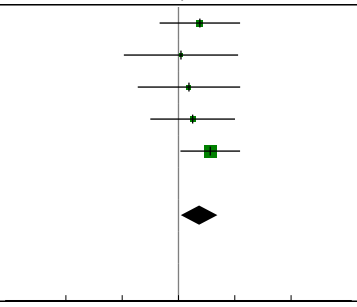
Study or subgroup	Cognitive training N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Alloni 2018	17	8.6 (23.9)	14	-4.4 (14)		20.15%	0.63[-0.1,1.36]
Cerasa 2014	8	-1.8 (13.6)	7	2.1 (7.5)		10.17%	-0.33[-1.35,0.7]
Lawrence 2018	14	2.8 (11.4)	7	-0.4 (13.8)		12.83%	0.25[-0.66,1.16]
París 2011	16	7.1 (24.1)	12	-12.5 (30.7)		17.77%	0.7[-0.07,1.48]
Petrelli 2014	44	0.8 (3.4)	21	-0.2 (4)		39.08%	0.27[-0.25,0.8]
Total ***	**99**		**61**			**100%**	**0.36[0.03,0.68]**
Heterogeneity: Tau^2=0; Chi^2=3.17, df=4(P=0.53); I^2=0%							
Test for overall effect: Z=2.15(P=0.03)							



Favours Control — Favours CT

Analysis 1.4. Comparison 1 Cognitive training versus control group, Outcome 4 Verbal memory post-treatment.

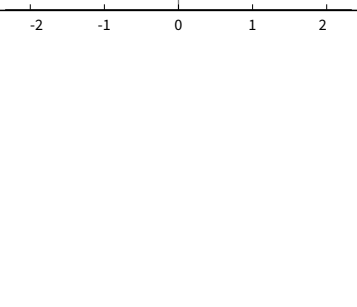
Study or subgroup	Cognitive training N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Alloni 2018	17	1.2 (3.4)	14	-0.1 (3.7)		20.67%	0.38[-0.34,1.09]
Cerasa 2014	8	1.7 (8.9)	7	1.2 (13.6)		10.25%	0.04[-0.97,1.06]
Lawrence 2018	14	3.6 (7.7)	7	2.1 (8)		12.76%	0.19[-0.72,1.1]
París 2011	16	5.8 (18)	12	1.8 (9.7)		18.67%	0.25[-0.5,1]
Petrelli 2014	44	1.7 (2.6)	21	0.2 (2.7)		37.65%	0.56[0.04,1.09]
Total ***	**99**		**61**			**100%**	**0.37[0.04,0.69]**
Heterogeneity: Tau^2=0; Chi^2=1.17, df=4(P=0.88); I^2=0%							
Test for overall effect: Z=2.21(P=0.03)							



Favours Control — Favours CT

Analysis 1.5. Comparison 1 Cognitive training versus control group, Outcome 5 Visual processing post-treatment.

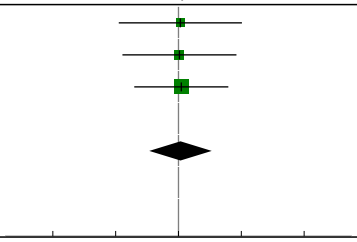
Study or subgroup	Cognitive training N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Cerasa 2014	8	1 (4.4)	7	1.4 (4.4)		25.05%	-0.09[-1.1,0.93]
Lawrence 2018	14	1 (5.6)	7	-0.3 (10.2)		31.23%	0.17[-0.74,1.08]
París 2011	16	1.6 (4.1)	12	-0.9 (3.9)		43.71%	0.62[-0.15,1.38]
Total ***	**38**		**26**			**100%**	**0.3[-0.21,0.81]**
Heterogeneity: Tau^2=0; Chi^2=1.28, df=2(P=0.53); I^2=0%							
Test for overall effect: Z=1.15(P=0.25)							



Favours Control — Favours CT

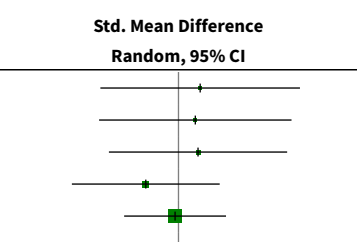
Analysis 1.6. Comparison 1 Cognitive training versus control group, Outcome 6 Activities of daily living post-treatment.

Study or subgroup	Cognitive training		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Folkerts 2018	12	0.5 (17.8)	6	0 (11.5)		25.77%	0.03[-0.95,1.01]
Lawrence 2018	14	-0.1 (0.8)	7	-0.1 (1.2)		30.07%	0.02[-0.89,0.92]
París 2011	16	3 (35.2)	12	1.4 (33.5)		44.17%	0.04[-0.7,0.79]
Total ***	**42**		**25**			**100%**	**0.03[-0.47,0.53]**
Heterogeneity: Tau²=0; Chi²=0, df=2(P=1); I²=0%							
Test for overall effect: Z=0.13(P=0.9)							



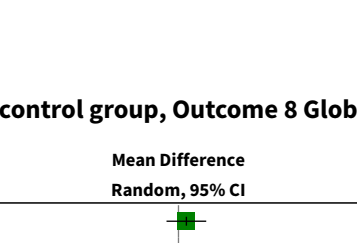
Analysis 1.7. Comparison 1 Cognitive training versus control group, Outcome 7 Quality of life post-treatment.

Study or subgroup	Cognitive training		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Cerasa 2014	8	2.4 (25.7)	7	-4.5 (33.1)		11.12%	0.22[-0.8,1.24]
Folkerts 2018	12	0.5 (13.3)	6	-1.6 (7.2)		11.97%	0.17[-0.81,1.15]
Lawrence 2018	14	3.4 (11.7)	7	0.3 (20.8)		13.94%	0.2[-0.71,1.11]
París 2011	16	-2.3 (34.2)	12	8.8 (29.2)		20.28%	-0.33[-1.09,0.42]
Petrelli 2014	44	1.1 (15.6)	21	1.6 (15.6)		42.69%	-0.03[-0.55,0.49]
Total ***	**94**		**53**			**100%**	**-0.01[-0.35,0.33]**
Heterogeneity: Tau²=0; Chi²=1.25, df=4(P=0.87); I²=0%							
Test for overall effect: Z=0.06(P=0.96)							



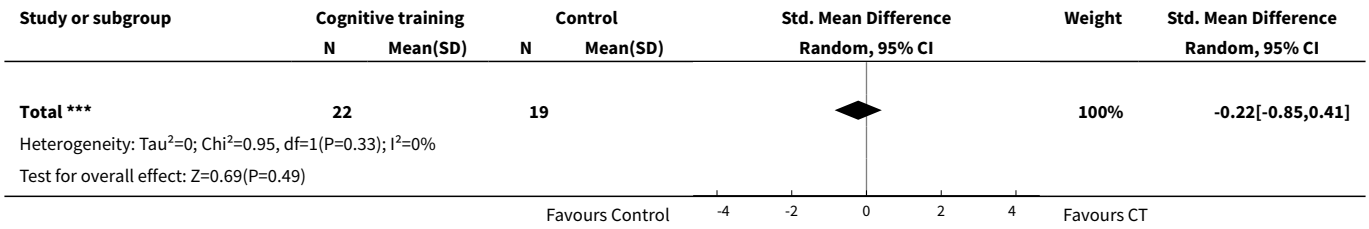
Analysis 1.8. Comparison 1 Cognitive training versus control group, Outcome 8 Global cognition long term.

Study or subgroup	Cognitive training		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Alloni 2018	11	-0.1 (3.1)	13	-1.2 (3.7)		54.46%	1.08[-1.64,3.8]
Lawrence 2018	11	0.8 (2.8)	6	1.4 (3.1)		45.54%	-0.68[-3.65,2.29]
Total ***	**22**		**19**			**100%**	**0.28[-1.73,2.28]**
Heterogeneity: Tau²=0; Chi²=0.73, df=1(P=0.39); I²=0%							
Test for overall effect: Z=0.27(P=0.79)							

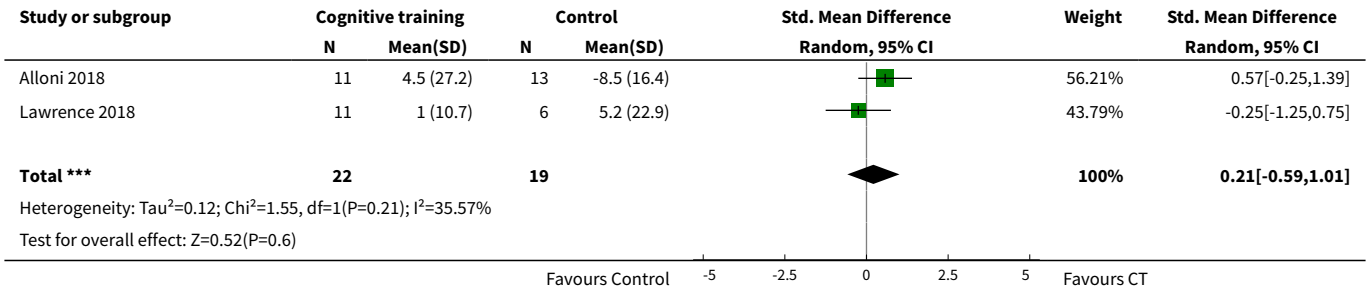


Analysis 1.9. Comparison 1 Cognitive training versus control group, Outcome 9 Executive function long term.

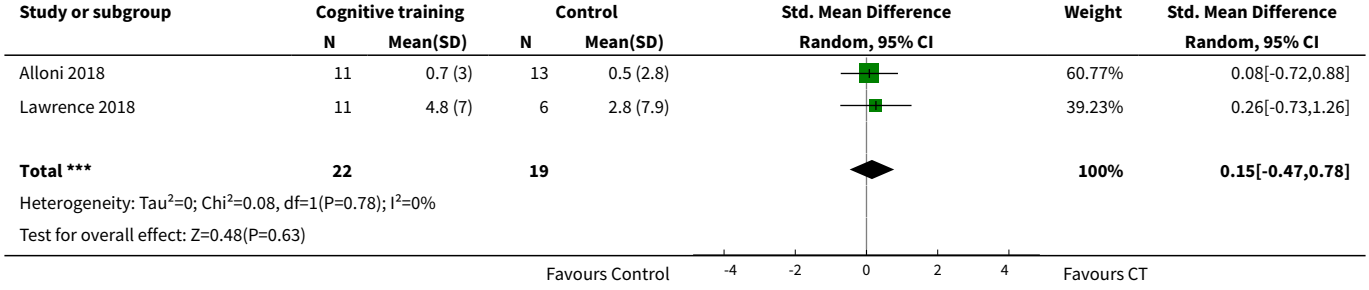
Study or subgroup	Cognitive training		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Alloni 2018	11	4.3 (116.3)	13	1.1 (121.7)		61.87%	0.03[-0.78,0.83]
Lawrence 2018	11	-0.9 (3)	6	1.2 (3.4)		38.13%	-0.62[-1.64,0.4]



Analysis 1.10. Comparison 1 Cognitive training versus control group, Outcome 10 Attention long term.



Analysis 1.11. Comparison 1 Cognitive training versus control group, Outcome 11 Verbal memory long term.

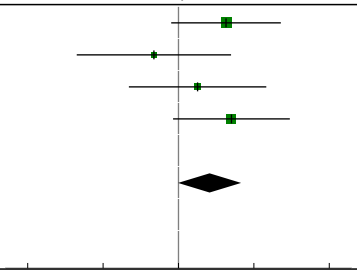


Comparison 2. Sensitivity analyses: cognitive training versus control group

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Attention post-treatment	4	95	Std. Mean Difference (IV, Random, 95% CI)	0.41 [-0.01, 0.83]
2 Verbal memory post-treatment	4	95	Std. Mean Difference (IV, Random, 95% CI)	0.25 [-0.16, 0.66]

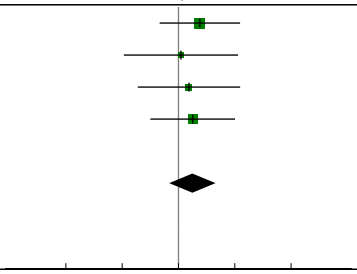
Analysis 2.1. Comparison 2 Sensitivity analyses: cognitive training versus control group, Outcome 1 Attention post-treatment.

Study or subgroup	Cognitive training N	Cognitive training Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Alloni 2018	17	8.6 (23.9)	14	-4.4 (14)		33.08%	0.63[-0.1,1.36]
Cerasa 2014	8	-1.8 (13.6)	7	2.1 (7.5)		16.7%	-0.33[-1.35,0.7]
Lawrence 2018	14	2.8 (11.4)	7	-0.4 (13.8)		21.06%	0.25[-0.66,1.16]
París 2011	16	7.1 (24.1)	12	-12.5 (30.7)		29.16%	0.7[-0.07,1.48]
Total ***	**55**		**40**			**100%**	**0.41[-0.01,0.83]**
Heterogeneity: Tau^2=0; Chi^2=3, df=3(P=0.39); I^2=0.07%							
Test for overall effect: Z=1.93(P=0.05)							



Analysis 2.2. Comparison 2 Sensitivity analyses: cognitive training versus control group, Outcome 2 Verbal memory post-treatment.

Study or subgroup	Cognitive training N	Cognitive training Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Alloni 2018	17	1.2 (3.4)	14	-0.1 (3.7)		33.15%	0.38[-0.34,1.09]
Cerasa 2014	8	1.7 (8.9)	7	1.2 (13.6)		16.44%	0.04[-0.97,1.06]
Lawrence 2018	14	3.6 (7.7)	7	2.1 (8)		20.46%	0.19[-0.72,1.1]
París 2011	16	5.8 (18)	12	1.8 (9.7)		29.94%	0.25[-0.5,1]
Total ***	**55**		**40**			**100%**	**0.25[-0.16,0.66]**
Heterogeneity: Tau^2=0; Chi^2=0.3, df=3(P=0.96); I^2=0%							
Test for overall effect: Z=1.17(P=0.24)							



APPENDICES

Appendix 1. Sources searched and search strategies

Source	Search strategy	Hits retrieved
1. ALOIS (www.medicine.ox.ac.uk/alois) [Date of most recent search: 8 August 2019]	Advanced search: (PDD OR PD OR Parkinson OR Parkinsons) AND Non-pharmacological	Jan 2016: 26 Jan 2017: 0 Dec 2017: 0 Sep 2018: 2 Aug 2019: 6
2. MEDLINE In-process and other non-indexed citations and MEDLINE 1950-present (Ovid SP)	1. *Cognitive Therapy/ 2. (cognit* adj2 stimulation).ti,ab. 3. (cognit* adj2 rehabilitation).ti,ab.	Jan 2016: 92 Jan 2017: 15 Dec 2017: 31

(Continued)

[Date of most recent search: 8 August 2019]	4. (cognit* adj2 training).ti,ab. 5. (cognit* adj2 retrain*).ti,ab. 6. "cognitive support".ti,ab. 7. "memory function*".ti,ab. 8. (memory adj2 rehabilitation).ti,ab. 9. (memory adj2 therap*).ti,ab. 10. "memory aid*".ti,ab. 11. "memory group*".ti,ab. 12. "memory training".ti,ab. 13. ("memory retraining" or "memory re-training").ti,ab. 14. "memory support".ti,ab. 15. "memory stimulation".ti,ab. 16. "memory strateg*".ti,ab. 17. "memory management".ti,ab. 18. or/1-17 19. randomized controlled trial.pt. 20. controlled clinical trial.pt. 21. randomized.ab. 22. placebo.ab. 23. randomly.ab. 24. trial.ab. 25. groups.ab. 26. or/19-25 27. (animals not (humans and animals)).sh. 28. 26 not 27 29. parkinson*.ti,ab. 30. exp Parkinson's Disease/ 31. exp Parkinsonism/ 32. PDD.ti,ab. 33. MCI-PD.ti,ab. 34. PD-MCI.ti,ab. 35. or/29-34 36. 28 and 35	Sep 2018: 19 Aug 2019: 21
3. EMBASE	1. (cognit* adj2 stimulation).ti,ab.	Jan 2016: 36

(Continued)

1974-2017 December 10 (Ovid SP) [Date of most recent search: 8 August 2019]	2. (cognit* adj2 rehabilitation).ti,ab. 3. (cognit* adj2 training).ti,ab. 4. (cognit* adj2 retrain*).ti,ab. 5. "cognitive support".ti,ab. 6. (memory adj2 rehabilitation).ti,ab. 7. (memory adj2 therap*).ti,ab. 8. "memory aid*".ti,ab. 9. "memory group*".ti,ab. 10. "memory training".ti,ab. 11. ("memory retraining" or "memory re-training").ti,ab. 12. "memory support".ti,ab. 13. "memory stimulation".ti,ab. 14. "memory strateg*".ti,ab. 15. "memory management".ti,ab. 16. or/1-15 17. randomly.ab. 18. placebo*.ti,ab. 19. "double-blind*".ti,ab. 20. randomized controlled trial/ 21. trial.ti,ab. 22. or/17-21 23. 22 and 16 24. parkinson*.ti,ab. 25. exp Parkinson's Disease/ 26. exp Parkinsonism/ 27. PDD.ti,ab. 28. MCI-PD.ti,ab. 29. PD-MCI.ti,ab. 30. or/24-29 31. 22 and 30	Jan 2017: 13 Dec 2017: 23 Sep 2018: 35 Aug 2019: 36
4. PSYCINFO 1806-December week 1 2017 (Ovid SP) [Date of most recent search: 8 August 2019]	1. (cognit* adj2 stimulation).ti,ab. 2. (cognit* adj2 rehabilitation).ti,ab. 3. (cognit* adj2 training).ti,ab. 4. (cognit* adj2 retrain*).ti,ab.	Jan 2016: 17 Jan 2017: 6 Dec 2017: 9 Sep 2018: 9

(Continued)

	5. "cognitive support".ti,ab.	Aug 2019: 11
	6. (memory adj2 rehabilitation).ti,ab.	
	7. (memory adj2 therap*).ti,ab.	
	8. "memory aid*".ti,ab.	
	9. "memory group*".ti,ab.	
	10. "memory training".ti,ab.	
	11. ("memory retraining" or "memory re-training").ti,ab.	
	12. "memory support".ti,ab.	
	13. "memory stimulation".ti,ab.	
	14. "memory strateg*".ti,ab.	
	15. "memory management".ti,ab.	
	16. or/1-15	
	17. randomly.ab.	
	18. randomi?ed.ab.	
	19. placebo*.ti,ab.	
	20. trial.ti,ab.	
	21. RCT.ti,ab.	
	22. groups.ab.	
	23. or/17-22	
	24. 16 and 23	
	25. parkinson*.ti,ab.	
	26. exp Parkinson's Disease/	
	27. exp Parkinsonism/	
	28. PDD.ti,ab.	
	29. MCI-PD.ti,ab.	
	30. PD-MCI.ti,ab.	
	31. or/25-30	
	32. 24 and 31	
5. CINAHL (EBSCOhost) [Date of most recent search: 8 August 2019]	S1 (MH "Parkinson Disease")	Jan 2016: 461
	S2 TX Parkinson*	Jan 2017: 33
	S3 TX PDD	Dec 2017: 65
	S4 TX MCI-PD	Sep 2018: 83
	S5 TX PD-MCI	Aug 2019: 153
	S6 S1 OR S2 OR S3 OR S4 OR S5	

(Continued)

	S7 TX cognit* S8 (MM "Cognition") S9 TX (brain OR mental) AND (gam* OR exercis* OR puzzle* OR train* OR program*) S10 S7 OR S8 OR S9 S11 S6 AND S10 S12 (MH "Randomized Controlled Trials") S13 TX placebo S14 TX RCT S15 TX "double-blind*" S16 TX "single-blind*" S17 TX randomly S18 S12 OR S13 OR S14 OR S15 OR S16 OR S17 S19 S11 AND S18	
6. Web of Science Core Collection [Date of most recent search: 8 August 2019]	((parkinson* dement*) OR PDD OR "MCI-PD" OR "PD-MCI") *AND* **TOPIC:** ("cognit* train*" OR mental OR (brain* gam*) OR (brain exercis*) OR (memory exercis*) OR puzzle OR sudoku OR crossword*) *AND* **TOPIC:** (randomly OR randomised OR randomized OR placebo OR "double-blind*" OR trial OR RCT OR CCT) **Timespan:** All years. Search language=Auto	Jan 2016: 556 Jan 2017: 19 Dec 2017: 25 Sep 2018: 44 Aug 2019: 36
7. LILACS (BIREME) [Date of most recent search: 8 August 2019]	parkinson OR parkinsons OR PDD [Words] and cognition OR cognitive OR brain OR mental Or memory [Words] and randomly OR randomised OR randomized OR trial OR ensaio clínico OR control OR controlled [Words]	Jan 2016: 71 Jan 2017: 0 Dec 2017: 3 Sep 2018: 6 Aug 2019: 6
8. CENTRAL (the Cochrane Library) (Issue 11, 2019) [Date of most recent search: 8 August 2019]	#1 MeSH descriptor: [Parkinson Disease] explode all trees #2 parkinson* #3 PDD #4 MCI-PD #5 PD-MCI #6 #1 or #2 or #3 or #4 or #5 #7 MeSH descriptor: [Cognition] explode all trees #8 cognit* #9 "brain* train*" #10 "mental exercis*"	Jan 2016: 618 Jan 2017: 132 Dec 2017: 286 Sep 2018: 302 Aug 2019: 421

(Continued)

	#11 sudoku or puzzle* or crossword* or IQ #12 #7 or #8 or #9 or #10 or #11 #13 #6 and #12 in Trials	
9. ClinicalTrials.gov (www.clinicaltrials.gov) [Date of most recent search: 8 August 2019]	[Condition: Parkinson OR parkinsons OR parkinson's OR PD] AND [Intervention: cognitive training OR cognitive exercise OR brain training OR memory training OR memory exercise] limit to Interventional studies	Jan 2016: 0 Jan 2017: 0 Dec 2017: 14 Sep 2018: 11 Aug 2019: 0
10. ICTRP Search Portal (apps.who.int/trialsearch) [includes: Australian New Zealand Clinical Trials Registry; ClinicalTrials.gov; ISRCTN; Chinese Clinical Trial Registry; Clinical Trials Registry – India; Clinical Research Information Service – Republic of Korea; German Clinical Trials Register; Iranian Registry of Clinical Trials; Japan Primary Registries Network; Pan African Clinical Trial Registry; Sri Lanka Clinical Trials Registry; The Netherlands National Trial Register] [Date of most recent search: 8 August 2019]	[Condition: Parkinson OR parkinsons OR parkinson's OR PD] AND [Intervention: cognitive training OR cognitive exercise OR brain training OR memory training OR memory exercise] Recruitment status: all	Jan 2016: 56 Jan 2017: 26 Dec 2017: 2 Sep 2018: 7 Aug 2019: 6
TOTAL before de-duplication and first assessment		3849
TOTAL after de-duplication and first assessment by CDCIG Information Specialists		451

CONTRIBUTIONS OF AUTHORS

VO: correspondence; drafting of review versions; selection of randomised controlled trials; data extraction; data entry; data analysis; interpretation of statistical analyses; editing and revising the review.

KM: selection of randomised controlled trials; data extraction; data entry; data analysis; interpretation of statistical analyses; editing and revising the review.

EP: interpretation of statistical analyses; editing and revising the review

JVH: interpretation of statistical analyses; editing and revising the review.

LC: interpretation of statistical analyses; editing and revising the review.

IL: proposed concept of the review; selection of randomised controlled trials; data extraction; data entry; data analysis; interpretation of statistical analyses; editing and revising the review.

DECLARATIONS OF INTEREST

Vasiliki Orgeta: none known.
Kathryn R McDonald: none known.
Ellen Poliakoff: none known.
John Vincent Hindle: none known.
Linda Clare: none known.
Iracema Leroi: none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We included studies that reported on the effectiveness of cognitive training in mixed populations, where only a proportion of the sample had cognitive impairment as verified by performance on a standardised test.