REVIEW ARTICLE

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Assessment of cognitive fluctuation in dementia: a systematic review of the literature

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Objective: Cognitive fluctuations (CF) are defined as spontaneous alterations in cognition, attention and arousal. They are a recognised feature of the dementias, especially dementia with Lewy bodies (DLB) and Parkinson's disease dementia. However, the accurate identification and assessment of CF presents a major clinical difficulty, with the operationalisation of the term 'cognitive fluctuation' remaining elusive, despite several attempts to identify, quantify and assess the phenomenon. No published reviews of CF in dementia exist despite this being an important clinical phenomenon and a core diagnostic feature of DLB.

Methods: We systematically explored the literature and measures available for the definition, assessment and quantification of CF in the dementias.

Results: We identified only three psychometric measures, which have been developed for the identification and assessment of CF, and these have not been adequately tested as yet for reliability and validity.

Discussion and Conclusions: We conclude that further research is warranted into the assessment of CF, and this is timely given the increasing recognition of the clinical importance of CF as a dementia symptom, particularly in the Lewy body dementias. Copyright © 2012 John Wiley & Sons, Ltd.

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Introduction

Cognitive fluctuations (CF) are defined as spontaneous alterations in cognition, attention and arousal. They occur in all the major causes of dementia, but their prevalence is dependent upon the dementia subtype: CF occur in approximately 20% of people with Alzheimer dementia (AD) (Kolbeinsson and Jonsson, 1993, Robertson *et al.*, 1998, Escandon *et al.*, 2010), in around 35–50% of people with vascular dementia (VaD) (Hachinski *et al.*, 1975, Roman *et al.*, 1993), and in people diagnosed with dementia with Lewy bodies (DLB), the proportion experiencing CF increases to around 90% (Byrne *et al.*, 1989, McKeith *et al.*, 2005). CF is also a common feature in Parkinson's disease with dementia (PDD) where around 29% of patients have been reported to demonstrate CF (Ballard *et al.*, 2002).

The prominence of CF in the Lewy body dementias of DLB and PDD is likely to relate to the strong and possibly aetiological association between CF in these conditions and the presence of Lewy body related neuropathology (McKeith *et al.*, 2005).

In addition to the diagnostic importance of CF in DLB and PDD, there is significant clinical importance in that CF has a functional impact on patients in terms of a high prevalence of visual hallucinations (O'Brien *et al.*, 2005). Furthermore, CF has been shown to have a significant independent effect on activities of daily living (ADLs) in these patients and an increased care burden for carers (Ballard *et al.*, 2001b).

Clearly CF are of significant diagnostic importance. However, their accurate identification and assessment presents a major clinical challenge (Mega *et al.*, 1996, Galasko, 1999, Cummings, 2004, McKeith *et al.*, 2005, Palmqvist *et al.*, 2009), with the operationalisation of

the term 'cognitive fluctuation' remaining elusive, despite several attempts to identify, quantify and assess the phenomenon (McKeith *et al.*, 1992a, Walker *et al.*, 2000a & Walker *et al.*, 2000b, Bradshaw *et al.*, 2004, Ferman *et al.*, 2004). There is considerable difficulty in characterising and assessing the core features of CF in dementia, as Mega *et al.* (1996) reported that: '*. . .the variability (of tests) is at least partly attributable to mixed agreement regarding what constitutes fluctuations and difficulty differentiating between DLB and AD late in the disease course.*' This represents a major clinical issue as the inaccurate diagnosis of people with DLB often leads to the inappropriate prescription of antipsychotic medications for these patients, where around 40% of patients with DLB show increased sensitivity to these agents, often with serious or even fatal consequences (McKeith *et al.*, 1992b, Walker *et al.*, 1999). There is also evidence that people with DLB respond better to cholinesterase inhibitors compared with patients with AD, and these two groups appear to have different disease trajectories (McKeith *et al.*, 2000, Serrano and Garcia-Borreguero, 2004).

This review systematically examines and critiques the available literature and psychometric measures available for the clinical assessment and diagnosis of CF in the dementias. We consider the strengths and weaknesses of the currently available measures and how future work may build upon them to provide more comprehensive means of assessing CF in dementia.

Methods

A systematic search strategy was employed to identify all the available literature on and psychometric tests for CF in the major dementias of old age. This search strategy followed guidelines published by the Centre for Reviews and Dissemination (Centre for Reviews and Dissemination (CRD), 2005).

Search terms included:

- 'cognitive' and 'fluctuati*'

and

- 'attention' or 'dementia' or 'neurodegen* disease*' or 'Alzheimer*' or 'vascular' or 'stroke' or 'Parkinson*' or 'Lewy bod*'

Wildcard (*) forms were used to identify variations in the required search terms; e.g. 'Lewy bod*' was used to retrieve 'Lewy body' and 'Lewy bodies';. 'fluctuati*' was used to retrieve 'fluctuation', 'fluctuations' and 'fluctuating'.

The following databases were searched using these terms: the Web of Knowledge, Medline, Embase, PsychInfo, CSA Illumina and the Cochrane Database of Systematic Reviews. Search terms were systematically applied across these five databases. The number of relevant hits from these databases are summarised in Table 1. The retrieved articles were referenced in EndNote (Version 10.0) (2006) and duplicates removed. Searches were conducted between 11 and 14 February 2011.

Inclusion criteria

All the retrieved article titles and abstracts were initially screened for potential inclusion into the review. Inclusion criteria included:

- Specific mention of, or focus on CF
- Specific mention of, or focus on, dementia, including DLB, AD, VaD and PD.
- A specific focus on the clinical assessment and/or the diagnosis of CF in dementia.

Exclusion criteria

- Articles entirely reporting on electroencephalography (EEG) or neuroimaging data, as this review is concerned with clinical assessment and neuropsychological performance rather than neurophysiological function or neural architecture *per se*. However, studies reporting both neurophysiological and clinical assessment/neuropsychological findings in CF were included although we comment only on the latter.
- Conference proceedings where full details of the study were not described.
- Qualitative research as quantitative assessment and measurement of CF in the dementias is the primary remit of this review.

Table 1 Number of articles retrieved from various databases using the terms 'cognitive' and 'fluctuati*' and 'attention' or 'dementia' or 'neurodegen* disease*' or 'Alzheimer*' or 'vascular' or 'stroke' or 'Parkinson*' or 'Lewy bod*'

Database (including date range)	Number of articles
Web of Knowledge (1982 – 2011)	92
Medline (1979 – 2011)	70
Embase (1980 – 2011)	112
PsychInfo (1967 – 2011)	73
CSA Illumina (1967 – 2011	67
Cochrane Database of Systematic Reviews (1993 – 2011)	1
Total number of articles (minus duplicates)	176

- Articles examining movement fluctuations in people with Parkinson's disease.
- Articles examining CF in delirium, schizophrenia, multiple sclerosis or children.

The 176 articles initially retrieved from the preceding detailed searches were screened by their titles and abstracts, and articles not meeting the inclusion and/or meeting the exclusion criteria described earlier were removed. This left a total of 34 articles that were potentially eligible for review. Screening of articles for inclusion in this review was conducted by DL and repeated by J-P T and/or AT to confirm that criteria were met for includable articles. The 34 potentially eligible articles were retrieved through Internet downloading and inter-library loans and read in full by DL and JPT and/or AT; all articles were read by at least two of the authors, and a third reading was conducted where necessary for clarification of any disagreement. After another application of the inclusion and exclusion criteria, these 34 articles were further reduced to a final list of 12 articles that were eligible for inclusion; these are presented in Appendix A (with * denoting the final includable articles). The reference lists of the includable articles were hand-searched in order to ensure that no key articles were missed through the database search strategy. No further articles were identified through this method indicating that the electronic searches were both sensitive and specific in identifying relevant articles for inclusion in this review.

Details of the excluded studies from this review are presented in Appendix B.

The quality of the includable studies was assessed using the Scottish Intercollegiate Guidelines Network (SIGN) quality assessment criteria for studies of diagnostic accuracy (Methodology checklist 5) Whiting *et al.* (2004). Quality assessments of includable studies are presented in Table 2. The application of such quality criteria is recommended by the Centre for Reviews and Dissemination guidelines on conducting systematic reviews (Centre for Reviews and Dissemination (CRD), 2005).

Table 2 Summary information from retrieved psychometric measurements of cognitive fluctuation in the dementias

Title/Authors/Journal	Details of measurement	Psychometric properties	Assessment of quality/utility
The Mayo Fluctuations Composite Scale (MFCS) Ferman *et al*. (2004) *Neurology* 62, 181 – 187.	A 19 item informant-rated questionnaire, mostly with dichotomous answer frame ($n = 16$ items) but also with three four-option questions exploring attention, somnolence, daytime sleep and communication	Acceptable test–retest reliability; Positive predictive value of 83% in differentiating DLB from AD. This provided a calculated sensitivity of 63% and specificity of 88% in distinguishing DLB from AD using a cut-off score ≥ 3.	Moderate to high quality of predictive value of four items** out of the 19-item questionnaire. Although the study did not compare DLB with VaD groups (6.0 citations per year)*
The Clinician Assessment of Fluctuation (CAF) Walker *et al*. (2000b). *Br J Psychiatry*, 177, 252 – 256.	A brief two-item, clinician-administered, informant-rated scale with questions regarding frequency and duration of CF. Qualitative in nature exploring two domains: frequency and duration of fluctuations.	Good sensitivity (81%) and specificity (92%) at distinguishing DLB versus AD. Sensitivity (81%) and specificity (82%) DLB versus VaD. Sensitivity (64%) and specificity (77%) VaD versuss AD. ROC curve cut-off score of ≥ 5 for reliably distinguishing DLB from AD and controls. Based on sensitivity and specificity data reported above. A 90% agreement rate with the ODFAS was also reported.	Moderate quality, although clinically difficult to use as responses are highly subjective in nature and no clearly defined scoring frame on which to base clinical diagnoses. Good sensitivities and specificities, but needs to be administered by an experienced clinician (8.9 citations per year)*
The One Day Fluctuation Assessment Scale (ODFAS) Walker *et al*. (2000b). *Br J Psychiatry*, 177, 252 – 256.	A brief seven-item clinician rated scale of fluctuating cognition based on the previous day, exploring: fluctuation, drowsiness, falls, attention, communication, disorganised thinking, and levels of consciousness.	Reasonable internal consistency (Cronbach's $\alpha = 0.78$). ROC curve cut-off score of ≥ 6 for reliably distinguishing DLB from AD and controls based on good sensitivity (93%) and specificity (87%) at distinguishing DLB from AD and controls. A 90% agreement rate with the CAF was also reported.	Moderate to high quality, although scoring the questionnaire is difficult owing to variations in scoring across domains and little information provided as to which domains may be more or less specific in assessing CF. (8.9 citations per year)*

Quality of studies estimated using the Scottish Intercollegiate Guidelines Network (SIGN) quality assessment criteria (Whiting *et al*., 2004).
DLB = Dementia with Lewy Bodies; AD = Alzheimer's disease; VaD = Vascular dementia; CF = cognitive fluctuation; ROC = receiving operating characteristics.
*Average citations per-year since publication (from the Web of Knowledge, February 2011);
**elaborated further in discussion.

Results

Of the 12 includable articles retrieved from web searches and interlibrary loans, two reported the development and validation of three psychometric instruments for identifying and rating CF (Walker *et al.*, 2000b, Ferman *et al.*, 2004). Three (Imamura and Hirono, 1999, Walker *et al.*, 1999, Walker *et al.*, 2000a), which are the earliest studies reviewed in the present study and published before these instruments were reported, used identification of CF by experienced clinicians. The other nine studies used one or more of the validated instruments for CF for distinguishing differences in the frequency of CF between different groups of patients with dementia (Walker *et al.*, 2000a & Walker *et al.*, 2000b, Ballard *et al.*, 2001a, Bradshaw *et al.*, 2004, Ferman *et al.*, 2004, Serrano and Garcia-Borreguero, 2004, Varanese *et al.*, 2010, Escandon *et al.*, 2010; and Rongve *et al.*, 2010).

We summarise the key findings from these literature searches in two tables. First, a summary of the three psychometric instruments reported for clinically assessing CF in two papers (Walker *et al.*, 2000b, Ferman *et al.*, 2004) (Table 2). Second, the findings from the 10 clinical (Walker *et al.*, 1999 & Walker *et al.*, 2000a, Ballard *et al.*, 2001a, 2001b, 2002, Escandon *et al.*, 2010;) and validation (Imamura and Hirono, 1999, Bradshaw *et al.*, 2004, Rongve *et al.*, 2010, Varanese *et al.*, 2010) studies focussing on the clinical assessment and diagnosis of CF are summarised in Table 3.

Discussion

Perhaps the major finding from our systematic review is the paucity of literature to guide clinicians in the accurate identification of CF. Although reviews and consensus criteria have long highlighted the importance of CF in the diagnosis and differential diagnosis of dementia, only two papers (Walker *et al.*, 2000b, Ferman *et al.*, 2004) have reported on the clinical utility of three different scales (One Day Fluctuation Assessment Scale (ODFAS), the Clinician Assessment of Fluctuation (CAF), and the Mayo Composite Fluctuations Scale (MCFS)).

The CAF has been used in three reported studies (Bradshaw *et al.* (2004), Rongve *et al.* (2010), Varanese *et al.* (2010)), but it has been found difficult to use because of the descriptive and open-ended nature of several questions, and because it is heavily dependent on expert clinician skills to administer. Consequently, it is unlikely to find favour or utility beyond use in research studies.

The ODFAS has domains, which overlap and some of which do not appear to assess CF at all. Bradshaw *et al.* (2004) also noted that the ODFAS only detected fluctuations in a minority of patients with DLB (46%), and, indeed, a high score in one patient on this scale appeared to be driven by fluctuations arising secondary to Parkinsonism-related fluctuations. In addition, whereas both the ODFAS and CAF allow for informant qualitative descriptions of CF, which appear to differ between patients with AD and DLB, the quantitative domains of these assessment scales tend to occlude these important discriminative qualitative differences (Bradshaw *et al.*, 2004).

The four items identified in the MCFS by Ferman *et al.* (2004) namely (1) Drowsiness or lethargy all the time or several times a day; (2) daytime sleep of 2 or more h (before 7 pm); (3) staring into space for long periods; and (4) times when the patient's flow of ideas seems disorganised, unclear or not logical), which reliably distinguished DLB from AD show great promise, but it is not clear whether these items would also be able to separate CF in DLB from CF occurring in VaD because no VaD group was included in the original derivation of this scale. The MCFS has been further investigated in two studies (Escandon *et al.*, 2010; and Rongve *et al.*, 2010) but neither attempted to replicate the original paper and demonstrate its utility in identifying CF and its practical application in distinguishing DLB from other subtypes of dementia. Escandon *et al.* (2010) reported similar frequencies of positive responses to the four items in a mild AD group to those in the AD group in Ferman *et al.* (2004), whereas Rongve *et al.* (2010) combined data from the MCFS and CAF, making it impossible to examine the utility of separate items from either instrument. Furthermore, despite the clear identification of CF in DLB, the psychometric properties of the three scales described in Table 2 remain questionable. Although sensitivities and specificities range from moderate to good levels, the operationalisation of the term CF and its subsequent identification is obscured by several different constructs being probed by them, for example daytime somnolence (MCFS) and falls (ODFAS). Thus, operationalised criteria for CF include items, which are diverse and may have a different aetiological basis to CF, for example reduced levels of arousal versus communication difficulties versus staring blankly versus falls. For example, does daytime somnolence reflect nighttime sleep disturbance or is it related to an underlying REM sleep behaviour disorder (although current evidence does not

Table 3 Summaries of studies reporting experimental or validation findings on the clinical assessment and diagnosis of CF in the dementias

Title/Authors/Journal	Key findings	Limitations	Conclusions
Clinical diagnosis of dementia with Lewy bodies in a Japanese dementia registry. Imamura *et al*. (1999). *Dementia and Geriatric Cognitive Disorders*, 10(3): 210 – 216.	CF was positive in 87% of DLB patients. Two sub-types of episodic cognitive deterioration were suggested: (1) pronounced disturbances of attention and alertness (inattention type); and (2) disturbances of orientation in time and space, and misidentification of familiar people (disorientation type).	Small sample of DLB patients. The study did not implement any standardised tests for CF. Testing was only conducted on one occasion using the Neuropsychiatric Inventory and only one clinician diagnosed the presence of CF in the sample.	Patients with DLB have a dementia syndrome that is distinct from AD even in the mild to moderate stages of cognitive impairment.
A psychophysiological investigation of fluctuating consciousness in neurodegenerative dementias. Walker *et al*. (1999). *Human Psychopharmacology*, 14, 483 – 489.	Used computerised reaction time tests in AD and DLB patients and showed increased levels of CF compared to controls. More variable and slower reaction time tests distinguished DLB from AD. CF was identified by clinicians.	No standardised test for CF used. No VaD or PDD groups included. The possibility that praxis difficulties of DLB group could have impacted on reaction time performance was not considered.	CF is associated with impaired performance on attentional tasks. Greater variability in reaction times in DLB group which was considered to concord with the severity of CF.
Quantifying fluctuation in dementia with Lewy bodies, Alzheimer's disease and vascular dementia. Walker *et al*. (2000a). *Neurology*, 54, 1616 – 1625.	Patients with DLB had a greater prevalence and severity of CF than patients with AD or VaD rated using clinical and attentional measures. Findings indicated that CF occurs on a second-to-second basis in patients with DLB. CF was identified by clinicians.	No examination of the validity of tests for CF was conducted within the framework of consensus clinical criteria. No standardised test for CF used. Possible that PDD patients were included in the DLB group, given the 12 month diagnostic rule for diagnosing DLB versus PDD (McKeith *et al*., 2005) was no specifically applied.	CF is significantly more common and severe in DLB than in the other dementias. The periodicity in CF is more frequent ('second-to second basis') in DLB and VaD than in those with AD.
Attention and fluctuating attention in patients with dementia with Lewy bodies and Alzheimer's disease. Ballard *et al*. (2001a) *Archives of Neurology*, 58, 977 – 982.	Based on tests of reaction times DLB patients significantly more impaired than AD patients on all measures of attention and fluctuating cognition measured using the CAF (for all comparisons $t > 2.5$; $p < 0.001$).	No VaD group included. Possible that PDD patients were included in the DLB group, given the 12 month diagnostic rule for diagnosing DLB versus PDD (McKeith *et al*., 2005) was no specifically applied. The possibility that praxis difficulties of DLB group could have impacted on reaction time performance was not considered.	Although fluctuating cognition is common in AD, CF is significantly more frequent and intense in DLB, especially in people with less severe AD or DLB, implying that CF is more a feature of moderate than severe dementia.
The characterisation and impact of 'fluctuating' cognition in dementia with Lewy bodies and Alzheimer's disease. Ballard *et al*. (2001b). *International Journal of Geriatric Psychiatry* 16: 494 – 498.	Based on tests of reaction times, cognitive fluctuations (using the CAF) and ADLs there was a strong correlation ($r = 0.87$; $p < 0.0001$) between CF (measured using the CAF) and ADLs particularly on attentional measures.	Small sample sizes recruited into the study. No VaD group included. Possible that PDD patients were included in the DLB group, given the 12-month diagnostic rule for diagnosing DLB versus PDD (McKeith *et al*., 2005) was no specifically applied. The possibility that praxis difficulties of DLB group could have impacted on reaction time performance was not considered.	Fluctuating attention was the cognitive domain most affected in dementia. CF has significant independent impact on ADLs.
Fluctuations in attention: PD dementia vs DLB with parkinsonism. Ballard *et al*. (2002). *Neurology*, 59, 1714 – 1720.	Using tests of reaction times in patients with DLB and PDD had similar levels of attentional deficits. These were more marked compared with	No VaD group included. Ages and cognitive abilities of groups not well matched. Possibility that praxis difficulties of DLB and PD	People with PDD and DLB with high levels of clinician rated CF tended to have slower reaction times, impaired vigilance and reduced MMSE scores

(*Continues*)

Table 3. (Continued)

Title/Authors/Journal	Key findings	Limitations	Conclusions
	patients with AD, PD without dementia and controls. CF was rated by experienced clinicians.	groups could impact on reaction time performance was not considered.	compared with non-fluctuators, AD and controls.
Fluctuating cognition in dementia with Lewy bodies and Alzheimer's disease is qualitatively distinct. Bradshaw *et al*. (2004). *Journal of Neurology Neurosurgery and Psychiatry*, 75(3): 382 – 387.	Interviews with caregivers of dementia patients and clinical assessments of CF indicated distinct profiles of CF in patients with DLB and AD. In DLB CF was more transient and spontaneous than in AD where CF was more related to an inability to cope with the cognitive demands of the immediate environment. With an ODFAS cut off of ≥6 only 46% of DLB patients and 33% of AD patients were correctly identified. With a CAF cut off of ≥5, 77% of DLB patients were correctly identified but none of AD patients.	There was a 14.4 month mean duration from the onset of motor symptoms to the appearance of cognitive deficits in the DLB group. Thus inclusion of PDD patients would be likely given the 12-month diagnostic rule for diagnosing DLB vs. PDD (McKeith *et al*., 2005). Small sample size ($n = 25$), and did not include a group with VaD. AD patients were significantly older than their DLB group potentially skewing the results.	CF in DLB was described as being more frequent and transient, whereas in AD CF was reported as being related to a more enduring state-shift (good days/bad days; somnolent/alert). Reduced sensitivity and specificity for the ODFAS was reported compared to Walker *et al*. (2000b).
Effect of cognitive fluctuation on neuropsychological performance in aging and dementia. Escandon *et al*. (2010). *Neurology*, 74, 210 – 217.	CF examined using MFCS items in normal ageing and AD only. High levels of CF reported in their AD participants.	Did not examine CF across other dementia groups and AD group had only mild impairment. No sensitivity or specificity data for the MFCS was reported. No standardised criteria were used in screening of participants and possible that early DLB or PDD patients were recruited into the sample.	CF present in AD and affects neuropsychological performance. CF was associated with dementia severity.
Core and suggestive Symptoms of Dementia with Lewy Bodies Cluster in Persons with Mild Dementia. Rongve *et al*. (2010). *Dementia and Geriatric Cognitive Disorders*, 29(4): 317 – 324.	Cluster analysis on groups of people diagnosed with mild dementia using standardised tests for CF (the CAF and the MFCS). Four distinct clusters were revealed: a 'Lewy body dementia' (LBD) cluster with high scores for hallucinations, parkinsonism and fluctuation, and a 'non-LBD' cluster with low scores on all DLB symptom scales. Two further clusters with high scores on either RBD or CF scales emerged. Persons in the LBD cluster had lower scores for visiospatial cognitive abilities as compared to the non-LBD group ($p = 0.002$).	Did not report significant findings for CF despite identifying separate clusters for RBD and CF, or examine middle- or later-stage dementia groups. The study combined the CAF and the MFCS to identify CF in their dementia groups, and so is likely to have detected behavioural fluctuations (e.g. wandering/agitation) as CF.	Tentative suggestion that visual hallucinations and motor parkinsonism might be clinically useful at distinguishing DLB from the other dementias, but only in the early stages. No significant findings for CF, or examination of middle or later stage dementia groups.
Fluctuating cognition and different cognitive and behavioural profiles in Parkinson's disease with dementia: comparison of dementia with Lewy bodies and Alzheimer's disease. Varanese *et al*. (2010) *Journal of Neurology*, 257(6): 1004 – 1011.	Using one measure of CF (the CAF) and a behavioural evaluation (using the DRS), patients with PD dementia and CF were similar to patients with DLB in terms of the presence of visual hallucinations and fluctuating attention when compared with PD and AD patients who did not have CF.	No VaD Group and relatively small sample sizes were recruited. More severe dementia in the non-fluctuating PDD group compared to those with PDD and CF potentially confounding the results.	CF is a clinical variable associated with a DLB type impairment in PD dementia, suggesting that patients who experience fluctuations in PD dementia are clinically indistinguishable from patients with DLB.

DLB = dementia with Lewy bodies; AD = Alzheimer's disease; PD = Parkinson's disease; PDD = Parkinson's disease with dementia; VaD = Vascular dementia; CF = cognitive fluctuation; RBD = REM sleep behaviour disorder; ADLs = activities of daily living; MMSE = Mini mental state examination; DRS = Dementia Rating Scale; CAF = Clinician Assessment of Fluctuation; ODFAS = One Day Fluctuation Assessment Scale; MFCS = Mayo Fluctuations Composite Scale.

specifically link it with the latter)? Difficulties in unifying these apparently unrelated constructs may be a function of semantic imprecision in defining them, a lack of clarity in understanding the differing or overlapping substrates, which give rise to them, as well as poor conceptualisation of what CF is in itself. A disorder, which suffers from similar issues is that of delirium, which has been nebulously defined as a disorder of consciousness. However, Bhat and Rockwood (2007) argued that delirium should be more pragmatically operationalised as a disorder of attention, temporal disorientation and altered arousal. The latter dimension is easily measurable (e.g. alert, lethargic, drowsiness, stupor, and unconsciousness) and the application of similar dimensional approaches to CF may aid its conceptualisation and enhance its diagnostic utility.

The findings presented in Table 3 confirm CF as occurring in all the major forms of dementia (AD, VaD, DLB and PDD), but being more marked in patients with DLB and PDD than in those with AD (Ballard *et al.*, 2001a, Varanese *et al.*, 2010) and in those with PD without dementia (Ballard *et al.*, 2002). Those patients with PD dementia who experience CF appear to be clinically indistinguishable from patients with DLB (Varanese *et al.*, 2010); and CF in DLB has been reported to be more spontaneous and transient than CF seen in people with AD (Bradshaw *et al.*, 2004). Furthermore, the importance of accurately identifying CF has been demonstrated because CF has a significant independent effect on ADLs, having negative implications for ADLs' function for patients and care burden for caregivers (Ballard *et al.*, 2001b). There is equivocal evidence for the link between CF and the severity of dementia with Walker *et al.* (2000a) reporting an association with increasing levels of CF with advancing cognitive decline, whereas Ferman *et al.* (2004) failed to replicate this finding. CF has also been reported to occur more frequently in those with visual hallucinations (Varanese *et al.*, 2010) and the domain most affected in people experiencing CF is attention (Walker *et al.*, 1999, Ballard *et al.*, 2001b, 2002), and as a measure of this Ballard *et al.* (2001a, 2001b & 2002) and Walker *et al.* (2000a & 2000b) have shown increased variability in performance on simple reaction-time tasks in people with DLB and PDD compared with VaD, AD and PD participants. However, the use of reaction-time tests in people with dementia in a clinical setting as a marker of CF is problematic as a result of the lack of available equipment, lack of validation and reliability of this as a surrogate measure, and the requirement for trained staff to administer the tests and interpret results. The assessment of CF in PDD may be important for the assessment of response to treatment, disease severity and become a supportive element in making a diagnosis of PDD from PD.

There also remains a pressing need to further investigate the items in these three instruments (CAF, ODFAS and MCFS) to identify which elements are needed by a clinician to reliably identify CF in dementia and thus to assist in the differential diagnosis of DLB. Thus, further research is required to more fully explore the constructs defined in these scales and to apply these to a more diverse range of dementia diagnoses in order to more fully elucidate, firstly, the prevalence of CF in dementia and, secondly, to clarify the quantitative and qualitative components of CF and so lead clinicians and researchers to a more useable definition and means of assessing the phenomenon in clinical practice.

Conclusions

There remains a lack of a clinically useful instrument for identifying and rating CF in dementia that can be implemented across the spectrum of neurodegenerative and vascular dementias, which can assist in the differential diagnosis of DLB from other causes of dementia. Although the available literature on, and the psychometric assessment of, CF in the dementias is scant, there are clear commonalities using the currently available instruments in DLB compared with AD. People with DLB experience more frequent and intense CF, particularly in the domains of attention. It may therefore be that focussing on the frequency and extent of CF may be a more fruitful line of enquiry for the accurate, early and differential diagnosis of the major forms of dementia. Finally, improvements in the conceptualisation of CF and what constructs adequately describe it are needed and it is likely that any real headway in this direction will only be made with the identification of potential biomarkers and determination of aetiological basis of CF through, for example, the use of investigative modalities (e.g. EEG, MEG, fMRI), which can more directly measure the cortical dynamics that are related to CF.

Conflict of interest

None of the authors have any conflicts of interest to declare.

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Author contributions

Dr Lee researched, prepared and wrote the manuscript.

Dr Thomas commented on drafts, corroborated the inclusion of selected articles for the review and contributed to the writing of the manuscript.

Dr Taylor contributed to the contributed to the writing of the manuscript and repeated the search strategy to corroborate Dr Lee's searching for and retrieval of articles.

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Appendix A. Articles retrieved for this review from electronic searches

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2. *Ballard, C.G., O'Brien, J.T., *et al*. (2001a). Attention and fluctuating attention in patients with dementia with Lewy bodies and Alzheimer disease. *Archives of Neurology*, 58(6): 977–982.

3. *Ballard C.G., Walker, M.P., O'Brien, J.T., *et al*. (2001b). The characterisation and impact of 'fluctuating' cognition in dementia with Lewy bodies and Alzheimer's disease. *International Journal of Geriatric Psychiatry* 16: 494–498.

4. *Ballard C.G. Aarsland D, McKeith I.G. *et al*. (2002). Fluctuations in attention: PD dementia vs DLB with parkinsonism. *Neurology*, 59, 1714–1720.

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18. Lippa, C.F., & McKeith, I.G. (2003). Dementia with Lewy bodies: improving diagnostic criteria. *Neurology*, 60(10): 1571–1572.

19. McKeith, I. (2008). Dementia with Lewy bodies. *Psychiatry*, 7 (1): 20–23.

20. McKeith, I.G., Galasko, D., *et al.* (1996). Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. *Neurology*, 47(5): 1113–1124.

21. McKeith, I.G., Ballard, C.G., Perry, R.H., *et al.* (2000). Prospective validation of the consensus criteria for the diagnosis of dementia with Lewy bodies. *Neurology* 54: 1050–1058.

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25. McKeith, I.G., Wesnes K.A., *et al.* (2004). Hallucinations predict attentional improvements with rivastigmine in dementia with Lewy bodies. *Dementia and Geriatric Cognitive Disorders*, 18(1): 94–100.

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27. O'Brien, J.T., Firbank, M.J., *et al.* (2005). Change in perfusion, hallucinations and fluctuations in consciousness in dementia with Lewy bodies. *Psychiatry Research-Neuroimaging*, 139(2): 79–88.

28. *Rongve, A,. Bronnick, K., Ballard, C., *et al.* (2010). Core and suggestive symptoms of dementia with Lewy bodies cluster in persons with mild dementia. *Dementia and Geriatric Cognitive Disorders*, 29(4): 317–324.

29. Serrano, C. & Garcia-Borreguero, D. (2004). Fluctuations in cognition and alertness in Parkinson's disease and dementia. *Neurology*, 63 (8 SUPPL. 3): S31–S34.

30. Taylor, R., Gilleard, C.J., *et al.* (1991). Short-term cognitive fluctuation in multi-infarct dementia and dementia of the Alzheimer type. *International Journal of Geriatric Psychiatry*, 6(7): 497–500.

31. *Varanese, S.B., Perfetti B., Monaco D., *et al.* (2010). Fluctuating cognition and different cognitive and behavioural profiles in Parkinson's disease with dementia: comparison of dementia with Lewy bodies and Alzheimer's disease. *Journal of Neurology*, 257(6): 1004–1011.

32. *Walker, M.P., Ayre, G.A., Ashton, C.H. *et al.* (1999). A psychophysiological investigation of fluctuating consciousness in neurodegenerative dementias. *Hum Psychopharm*, 14, 483–489.

33. *Walker, M.P., Ayre G.A., *et al.* (2000a). Quantifying fluctuation in dementia with Lewy bodies, Alzheimer's disease, and vascular dementia. *Neurology*, 54(8): 1616–1624.

34. *Walker, M.P., Ayre, G.A., *et al.* (2000b). The Clinician Assessment of Fluctuation and the One Day Fluctuation Assessment Scale. Two methods to assess fluctuating confusion in dementia. *British Journal of Psychiatry*, 177: 252–256.

*Articles selected for review after application of exclusion and inclusion criteria.

Appendix B. Details of studies excluded from this review

A number of articles (McKeith *et al*., 1995, 1996; 2000 & 2005) have reported the DLB consortium diagnostic criteria for DLB, all of which included reference to the consideration of the positive identification of cognitive fluctuations (CF) in dementia with Lewy bodies (DLB) as a core diagnostic criterion. Similarly, the following articles all described identification of CF in DLB as a core diagnostic feature but they did not, however, discuss how CF might be more accurately assessed or examined: Galasko (1999, 2004 & 2007), Harrison & McKeith (1995), Allardyce & McKeith (1997), McKeith (2002); Lippa & McKeith (2003), Ballard (2003), Frank (2003); Cummings (2004); and McKeith (2008). As such they were excluded from this review.

Two recent reviews investigating the differing neuropsychological profiles of people with Alzheimer dementia (AD) and those with DLB identified 35 separate studies between 1990 and 2005. (Collerton *et al*., 2003; Metzler-Baddley, 2007). These reviews concluded that greater attention and visual perception deficits, and less impaired memory performance are evident in DLB compared with AD. As the present review is focussed on the evaluation of the currently available psychometric tests for CF, these reviews and diagnostic criteria were excluded.

De Machado *et al*., (2006) only studied people with AD, using tests of behaviour and sensory deficits without specific focus on CF, and so this study was excluded. Taylor *et al*., (1991) assessed VaD and AD patients, but they did not identify CF; 'fluctuation' was defined from baseline measures of neuropsychological performance, which were repeated at a 2-year follow-up, as such this study was also excluded from this review. Similarly, Elmstahl *et al*., (1998) reported fluctuating symptoms in people with dementia over a 1-year period and so were not measuring cognitive fluctuation as defined in the present review; thus, this study was excluded from this review. McKeith *et al*., (2004) conducted a study investigating the impact of cholinesterase therapy on memory and attention in people with DLB who experienced visual hallucinations; although the study used standardised tests of CF, the study was a treatment trial and did not focus on the identification of CF in terms of differential diagnosis (as only DLB patients were studied).