

Fluctuating cognition in dementia with Lewy bodies and Alzheimer's disease is qualitatively distinct

J Bradshaw, M Saling, M Hopwood, V Anderson, A Brodtmann

J Neural Neurosurg Psychiatry 2004;**75**:382–387. doi: 10.1136/jnnp.2002.002576

See end of article for authors' affiliations

Correspondence to: Michael M Saling, Department of Psychology, The University of Melbourne, Parkville, Victoria, 3010, Australia; Email: m.saling@psych.unimelb.edu.au

Received 28 August 2002
In final revised form 30 July 2003
Accepted 4 August 2003

Objectives: To document and illustrate qualitative features of fluctuating cognition as described by care givers of patients with probable dementia with Lewy bodies (DLB) and Alzheimer's disease (AD). To determine whether the quality of the fluctuations differs between DLB and AD. To examine the clinical utility of two recently developed rating scales.

Methods: Care givers of 13 patients with early probable DLB and 12 patients with early probable AD were interviewed using the Clinician Assessment of Fluctuation and the One Day Fluctuation Assessment Scale, both developed recently. Descriptions of fluctuating cognition were recorded verbatim, analysed, and rated.

Results: Descriptions of fluctuating cognition in DLB had a spontaneous, periodic, transient quality, which appeared to reflect an interruption in the ongoing flow of awareness or attention that impacted on functional abilities. Descriptions of fluctuations in AD frequently highlighted episodes of memory failure, or a more enduring state shift in the form of "good" and "bad" days, typically occurring in response to the cognitive demands of the immediate environment. These qualitative differences could be detected reliably by independent raters, but were not always captured in standard severity scores.

Conclusion: Fluctuations occurring in DLB have particular characteristics that are distinguishable from fluctuations occurring in AD. Interpretation and application of the fluctuation criterion continues to limit the diagnostic sensitivity of the consensus criteria for DLB. Findings suggest that explicit documentation and a wider appreciation of these distinctions could improve the reliability with which less experienced clinicians identify this core diagnostic feature in the clinical setting.

Dementia with Lewy bodies (DLB) is a neurodegenerative condition characterised by fluctuating cognition with pronounced variations in attention and alertness, persistent well formed visual hallucinations, and spontaneous motor features of parkinsonism.¹ It was recently concluded that, "fluctuating cognition (FC) appears to be a more frequent and specific diagnostic feature than either visual hallucinations or parkinsonism"² (p 1056). This emphasises the core diagnostic significance of FC and raises the following questions: first, how readily can FC be detected in the clinical setting? and second, are the fluctuations that occur in DLB distinguishable from fluctuations in other dementias?

When the first set of operational criteria for the diagnosis of senile dementia of the Lewy body type (SDLT) was proposed in 1992,³ "fluctuating cognitive impairment" was considered mandatory for diagnosis and of central importance in differentiating SDLT from Alzheimer's disease (AD). The interpretation and application of the FC criterion was, however, problematic. In an evaluation of the predictive validity and interrater reliability of the clinical diagnostic criteria for SDLT, McKeith and colleagues found that the SDLT criteria did not provide "clear guidance to less experienced clinicians about the particular characteristics of the fluctuating pattern and course of illness that distinguish SDLT patients from other dementia sufferers"⁴ (p 876). Differing interpretations of the operational criteria led to variation between raters (kappa values of 0.50 to 0.88), and appeared to be influenced largely by clinician experience. An international consortium on DLB subsequently revised these criteria and published new diagnostic guidelines in 1996.¹ Despite its importance as a core clinical feature, "substantial difficulties" in defining and quantifying FC¹ (p 1115) led to the decision that FC was no longer mandatory for the

diagnosis of DLB. This has motivated research endeavours to clarify the concept.

In current usage, FC is a broadly defined phenomenon.^{1–8} As such, it is not specific to DLB, and has been reported in patients with a variety of dementing syndromes.^{4–9–12} Whether or not the fluctuations that occur in DLB can be differentiated from those occurring in other dementias has become a contentious issue. It has been argued that "well defined operationalised criteria for distinguishing an abnormal fluctuation—different from the day-to-day variations of the "typical AD" patient—are still lacking"¹³ (p 1407). Under-detection of DLB has been attributed to the poor definition of the criterion of cognitive fluctuation.¹⁴ Lopez and colleagues¹⁵ found that reliably differentiating episodes of mild fluctuation in consciousness from diurnal hypersomnia, frequently observed in other dementia subgroups, was difficult for raters to reach agreement upon. It is generally agreed that further work is necessary to improve the identification and characterisation of differences between the pattern of fluctuation and disturbed consciousness in DLB and AD.¹⁶

It has been suggested that the frequency and severity of occurrence are the main aspects of FC that differentiate DLB from AD and other dementias. McKeith identified "the marked amplitude between best and worst performance" as a

Abbreviations: AD, Alzheimer's disease; BPRS, Brief Psychiatric Rating Scale; CDR, Clinical Dementia Rating Scale; DLB, dementia with Lewy bodies; FC, fluctuating cognition; FSIQ, Full Scale IQ; HADS, Hospital Anxiety and Depression Scale; MMSE, Mini Mental State Examination; NART, National Adult Reading Test; PIQ, Performance IQ; SDLT, senile dementia of Lewy body type; UPDRS, Unified Parkinson's Disease Rating Scale; VaD, vascular dementia; VIQ, Verbal IQ; WASI, Wechsler Abbreviated Scale of Intelligence

distinguishing feature of the fluctuations in cognition and consciousness in DLB, contrasting this with "minor day-to-day variations" that can occur in dementia of any cause¹⁴ (p 144). Identification of these *quantitative* differences in frequency and severity has not significantly improved the clinician's ability to detect FC in the clinical setting. Lopez and colleagues¹⁷ recently evaluated the merits of the consensus guidelines for DLB. Consistent with previous reports, their prospective analysis revealed low sensitivity of the diagnostic criteria. They argued that clarification and standardisation of the assessment of some of the most difficult signs and symptoms, such as FC, is important, especially if they differ qualitatively between dementing disorders. This raises an important question: do the fluctuations that occur in DLB have particular *qualitative* characteristics specific to DLB that can be distinguished from fluctuations occurring in other dementing conditions?

The broad aim of this study was a descriptive one, namely, to document and illustrate qualitative features of FC as described by care givers of patients with probable DLB and those with probable AD. On the basis of our clinical experience, we expected that FC would differ qualitatively between DLB and AD groups. To date, differences of this type have not been systematically described. A secondary aim was to examine the clinical utility of two recently developed FC rating scales. It was predicted that the Clinician Assessment of Fluctuation would prove to be a more useful assessment method compared to the One Day Fluctuation Scale, because it provides greater scope for eliciting a descriptive and qualitative account.

METHODS

Patients

The sample comprised two groups of subjects, patients with clinical features of early probable DLB ($n = 13$) and a group with clinical features of early probable AD ($n = 12$). Clinical diagnoses were made using the NINCDS-ADRDA criteria for AD¹⁸ and the consensus criteria for DLB.¹ Patient selection was restricted to subjects in a mild-to-moderate stage of illness, since there are fewer clinically distinguishable features between dementia subgroups in the more advanced stages of disease.

To improve diagnostic discrimination of primary DLB patients from those with dementia associated with idiopathic Parkinson's disease, all patients diagnosed with DLB had not had parkinsonian signs for longer than two years prior to the onset of dementia. A 12 month cutoff period is more commonly applied on the basis of the consensus criteria but this time frame was only ever intended as a guide to clinical practice and was selected "arbitrarily".^{1,2} The cut-off period was therefore extended by a further 12 months, as it was considered unnecessarily restrictive to exclude patients who only marginally exceeded the 12 month cutoff (McKeith, personal communication, April 1999). This provided some protection against the high false negative rate that characterises screening for DLB cases.¹⁹

Patients were recruited over a two year period (February 2001–February 2003) principally from neurology, psychiatry, and movement disorder outpatient clinics and aged care inpatient units of a large metropolitan tertiary hospital in Melbourne. Regional memory clinics and consultant neurologists and psychiatrists in private practice were other key referral sources. This ensured a broad referral base and aimed to minimise the influence of ascertainment bias on the nature of presenting clinical symptoms. All patients were examined and the diagnosis confirmed in a neuropsychiatry clinic at the hospital. DLB patient selection was strictly consecutive and included all patients referred into the study who met the consensus criteria and agreed to participate.

There was no explicit pairwise matching of patients who met clinical diagnostic criteria for AD, but the AD cases were matched as a group on a range of demographic and dementia severity variables to ensure comparability. Groups were matched on age, education, and severity of illness, as determined by the Clinical Dementia Rating scale (CDR²⁰) and Mini Mental Status Examination (MMSE²¹) (table 1).

Informed consent was obtained according to hospital ethics committee guidelines. Routine clinical investigations were conducted to exclude reversible causes of dementia. Patients were also excluded if formal neurological or psychiatric examination revealed evidence of any other brain disorder, physical, or mental illness sufficient to contribute significantly to the clinical picture, or if they showed signs of significant cerebrovascular disease evident as focal neurological signs or on brain imaging.

Procedure

Earliest symptoms, their onset and course, and the presenting cognitive complaint were carefully documented using a semistructured interview with both the subject and a reliable care giver. Well recognised clinical rating scales, namely the Unified Parkinson's Disease Rating Scale (UPDRS²²)—motor examination, Brief Psychiatric Rating Scale (BPRS²³), and Hospital Anxiety and Depression Scale (HADS²⁴) were used to document the presence or absence of key psychiatric and neurological features. The level of general cognitive ability was assessed using the Wechsler Abbreviated Scale of Intelligence (WASI²⁵). Premorbid level of function was estimated by the National Adult Reading Test (NART²⁶). Clinical ratings are summarised in table 2.

Two recently published semistructured and standardised clinical assessment methods²⁷ were used to assist in the identification and quantification of FC, the Clinician Assessment of Fluctuation and the One Day Fluctuation Assessment Scale. For each subject, a clinical neuropsychologist (JB) interviewed a reliable care giver and administered the two scales to evaluate the presence and nature of FC.

Quantitative scoring of the Clinician Assessment of Fluctuation was based upon the clinician's interpretation of care giver responses to the two key items that make up the scale. The scale has been designed for use by experienced clinicians and focuses on fluctuating confusion and impaired consciousness during the month prior to the assessment. In keeping with the authors' recommendation, detailed discussions working through previously assessed cases took place among investigators to achieve consistency in scoring²⁷ (p 254). If present, the frequency and severity of each of the features of FC was assessed to produce a severity score between 0 and 12, with 12 representing severe fluctuating confusion. The One Day Fluctuation Assessment Scale is a structured protocol consisting of seven items and focuses upon FC over the day prior to the assessment. Each item

Table 1 Demographic characteristics of the DLB and AD groups

| | Probable DLB (n = 13) | | Probable AD (n = 12) | |
|----------------------------|--------------------------|--------|-------------------------|--------|
| Sex (M:F) | 9:4 | | 4:8 | |
| Age at assessment (years)* | 76.1 | (4.9) | 80.4 | (4.0) |
| CDR | 1.3 | (0.5) | 1.0 | (0.4) |
| Education (years) | 11.1 | (4.4) | 9.9 | (2.8) |
| NART | 112.5 | (14.8) | 107.0 | (10.6) |
| MMSE | 23.1 | (4.0) | 24.4 | (2.0) |

Data are given as mean (SD). * $p < .05$.
CDR, Clinical Dementia Rating Scale; NART, National Adult Reading Test; MMSE: Mini Mental State Examination.

Table 2 Neurological, psychiatric, and intellectual function in the DLB and AD groups

| | Probable DLB | Probable AD | Effect Size |
|--------------------|--------------|-------------|-------------|
| UPDRS-Motor scale* | 15.0 (7.6) | 3.8 (2.6) | 1.40 |
| HADS-Anxiety | 5.7 (2.0) | 4.0 (2.9) | 0.66 |
| HADS-Depression* | 5.5 (3.6) | 2.3 (1.4) | 1.03 |
| BPRS* | 13.8 (5.8) | 7.4 (4.4) | 1.07 |
| FSIQ* | 79.3 (9.3) | 93.8 (12.6) | 1.11 |
| VIQ | 88.1 (15.7) | 93.7 (11.9) | 0.40 |
| PIQ* | 75.3 (5.7) | 95.1 (11.2) | 1.49 |

Data are given as mean (SD). * $p < .01$
 UPDRS, Unified Parkinson's Disease Rating Scale (range 0–56); HADS, Hospital Anxiety and Depression Scale (range 0–21); BPRS, Brief Psychiatric Rating Scale (range 0–114); FSIQ, Full Scale IQ; VIQ, Verbal IQ; PIQ, Performance IQ.

was scored as present or absent and graded in terms of severity to provide a summed severity score ranging from 0 to 21.

In addition to the standard assessment of the presence, frequency and severity of FC on each of the scales, care giver descriptions of FC were also recorded verbatim to document qualitative characteristics of FC in each patient group. These descriptions were derived from responses to both items of the Clinician Assessment of Fluctuation, and question two of the One Day Fluctuation Assessment Scale, the only question on this scale that makes provision for an open ended response.

Two independent raters, clinical neuropsychologists with experience in aged care settings, were provided with the care giver responses generated by each of the three questions that elicited qualitative descriptions of FC (p 255).²⁷

- “Does the patient ever have spontaneous impaired alertness and concentration,—that is appear drowsy but awake, look dazed, not be aware of what is going on around?”
- “Has the level of confusion experienced by the patient tended to vary a lot recently from day to day or week to week?”
- “Has the patient had a period (or periods) today when he or she seemed to be confused and muddled and then a period (or periods) when he or she seemed to be improved and functioning better? Give examples of the worst and best period of function.”

The raters assigned each response to either the DLB or AD category, on the basis of their knowledge of the two conditions.

Statistical analysis

A χ^2 analysis was used to analyse the distribution of sex across the DLB and AD groups. Group means on the demographic and clinical variables were compared with t tests for independent samples. Mann Whitney U tests for two independent groups were performed on the same data as a non-parametric check. Effect sizes were also computed. Verbatim care giver responses were subjected to content analysis and interpretation. The percentage of responses correctly classified by the two independent raters was recorded and κ co-efficients were calculated to determine interrater reliability.

RESULTS

Subject data

There were proportionately more men in the DLB than in the AD group (69% v 33%), although the difference did not reach

statistical significance. The effect of sex on the quantitative scores of the Clinician Assessment of Fluctuation and One Day Fluctuation Assessment Scale was also examined. To optimise the power of the sex comparison, the AD and DLB groups were combined with sex as the independent variable. This comparison was also not significant. The DLB group did not differ significantly from the AD group in dementia severity, years of education, or premorbid level of function (table 1). The mean age of the AD group was, however, significantly older than that of the DLB group by four years, $t(23) = 2.43$, $p < 0.05$.

The DLB group had greater extrapyramidal motor impairment, albeit at the mild end of the severity range as measured by the UPDRS, $t(23) = 4.99$, $p < 0.01$ (table 2). Patients with DLB also received higher ratings on the BPRS, indicating a greater degree of psychopathology, $t(23) = 3.11$, $p < 0.01$. The DLB patients obtained significantly higher scores than AD patients on the HADS depression scale, $t(23) = 2.97$, $p < 0.01$, but these fell in the mild (8–10) or non-clinical (0–7) ranges. In contrast, there were no group differences on the HADS anxiety scale. Performance IQ (PIQ) in the DLB group fell significantly below that of the AD group, $t(22) = 5.47$, $p < 0.01$, and contributed to a significant group difference in Full Scale IQ (FSIQ), $t(22) = 3.22$, $p < 0.01$.

Dementia was the most common presenting feature in the DLB group. For patients in whom parkinsonism preceded the onset of dementia (38%), an average of 14 months had elapsed prior to detectable features of cognitive decline (mean, 14.4 months; standard deviation, 3.29 months). Dementia was the presenting feature in 100% of the AD cases.

Quantitative assessment of FC in DLB and AD Clinician Assessment of Fluctuation Scale

Using this scale, clinically significant FC (score ≥ 5) was identified in 77% of patients with DLB and in none of the patients with AD; the group difference in terms of standard quantitative scores was significant, $t(23) = 5.04$, $p < 0.01$ (table 3).

One Day Fluctuation Assessment Scale

The quantitative score on the One Day Fluctuation Assessment Scale also revealed a significant difference between the DLB and AD groups (table 3), $t(23) = 2.09$, $p < 0.05$. This finding, however, was largely attributable to high scores in only two patients in the DLB group, and a Mann Whitney U test performed on the same data was not significant. The One Day Fluctuation Assessment Scale identified clinically significant FC (score ≥ 6) in only 46% of patients with DLB, and in 33% of those with AD. Careful inspection of the clinical picture in one DLB patient with an elevated score on the One Day Fluctuation Assessment Scale raised the possibility that fluctuations were physical

Table 3 Mean score (and standard deviation) on the Clinician Assessment of Fluctuation & One Day Fluctuation Assessment Scale

| | Probable DLB | Probable AD | Effect Size |
|--|--------------|-------------|-------------|
| Clinician Assessment of Fluctuation* | 5.8 (3.7) | 0.3 (1.2) | 1.40 |
| One Day Fluctuation Assessment Scale*† | 6.2 (2.8) | 4.0 (2.5) | 0.78 |

* t statistic, $p < 0.01$

† U statistic, not significant.

manifestations of parkinsonism related to timing of levodopa administration.

Qualitative characterisation of FC in DLB and AD Clinician Assessment of Fluctuation Scale

Qualitative care giver descriptions of FC differed between the two dementia groups. In response to items on the Clinician Assessment of Fluctuation, DLB care givers frequently provided descriptions that suggested a lapse in the stream of awareness or attention (“he detaches, he’s off with the pixies”; “she has temporary lapses and can’t focus properly”). Descriptions of blank staring during which the patient appeared to disengage from the ongoing flow of activity or conversation were common in the DLB group, whereas AD care givers did not describe this phenomenon. Rather, AD care givers described periods of “confusion” characterised, for example, by repetitiveness in conversation or forgetfulness in relation to a recent event or a plan of action. In general, descriptions of FC in the AD group often related to task or situational demands (“he moves the cattle then forgets which paddock he moved them to and gets confused”; “he gets confused when he is under pressure, like when he lost his bank book and got really muddled”). FC in the DLB group appeared to be unrelated to demands on memory function, and occurred spontaneously in the absence of a situational explanation.

Care giver descriptions of fluctuation in the DLB group suggested that patients lost the ability to engage in meaningful cognitive or physical activity (“he kind of drifts off and doesn’t concentrate or respond”; “he seems vague, he looks around and doesn’t know what he is doing”). In the AD group it was more often the case that actions or thoughts were deflected onto another task or question as a result of memory failure (“she forgets what she was going to do, then starts something else”). When episodes of “confusion” occurred in AD, care givers provided typical examples of forgetting (“he will ask the same question 10 times in an hour”). By contrast, the episodic confusion in DLB often took on a confabulatory or fleeting delusional quality (“one day she is telling me she has been to New York, the next day she is lucid”; “some days she thinks there are extra people staying for dinner”).

Relatively short lived alterations in cognitive and functional abilities were also used to describe FC by the DLB care givers (“he’s spasmodic”, “most days he’s in and out”, “she has temporary lapses”), whilst the descriptions from the AD care givers suggested a more persisting, enduring quality to the ‘fluctuations’, often in the form of “good days” and “bad days”. Daytime somnolence was reported by care givers of both groups, but was perhaps more frequent in the DLB group.

One Day Fluctuation Assessment Scale

This scale provided less opportunity for eliciting qualitative information. Most of the items required only a simple “yes” or “no” response and did not seek examples or other descriptive information. As mentioned earlier, question two does provide for an open ended response. (“Has the patient had a period (or periods) today when he or she seemed to be confused and muddled and then a period (or periods) when he or she seemed to be improved and functioning better? Give examples of the worst and best period of function.”) Just over three quarters (77%) of DLB and 67% of AD care givers responded “yes” to this item. Examples given echoed the qualitative differences described above. (table 4). The qualitative examples provided by AD care givers again highlighted specific episodes of memory failure in contrast to the more transient periods of confusion described in the DLB group.

Qualitative features of FC in DLB and AD— identification by independent raters

Clinician Assessment of Fluctuation Scale

This scale generated qualitative descriptions of FC in response to each of the two items on this scale. Differences in the quality of care giver responses to item one (“Does the patient ever have spontaneous impaired alertness and concentration,—that is appear drowsy but awake, look dazed, not be aware of what is going on around?”) were not readily detected by the raters. This item taps FC on the basis of periods of impaired alertness and concentration. Each rater accurately assigned only 55% and 64% of responses, respectively, to the DLB category. Care givers from both patient groups commonly described daytime somnolence, increased drowsiness, and dazed or glazed appearances, in response to this question, indicating that this qualitative feature of FC is not specific to DLB. Interestingly, the raters considered this to be a feature more common in AD, with an average of 79% of responses correctly assigned to the AD category (rater 1, 86%; rater 2, 71%). A κ co-efficient of 0.78 indicated an acceptable level of agreement between the raters for item one.

By contrast, an average of 90% of DLB care giver responses generated by item two (“Has the level of confusion experienced by the patient tended to vary a lot recently from day to day or week to week?”) were correctly assigned to the DLB category (rater 1, 80%; rater 2, 100%), while 100% of AD care giver responses were correctly assigned to the AD category by the raters. This indicated that there were detectable group differences in the quality of care giver responses to this item. Interrater reliability was also acceptable with a κ co-efficient of 0.79.

One Day Fluctuation Assessment Scale

On the basis of responses generated by item two, the only open ended item on this scale, (“Has the patient had a period (or periods) today when he or she seemed to be confused and muddled and then a period (or periods) when he or she seemed to be improved and functioning better? Give examples of the worst and best period of function.”) the raters correctly assigned 78% and 100% of DLB care giver responses to the DLB category, respectively, while an average of 94% of AD care giver responses were correctly assigned to the AD category (rater 1, 100%; rater 2, 88%). This further supported the existence of discernable differences in the quality of fluctuations between the two patient groups. Interrater agreement yielded a κ co-efficient of 0.66 for this item.

DISCUSSION

Our findings show that FC in AD and DLB is qualitatively distinct. Even on the basis of this relatively small sample, clear qualitative differences in the nature of FC emerged. Qualitative analysis of care giver responses to two recently developed clinical rating scales, the Clinician Assessment of Fluctuation and the One Day Fluctuation Assessment Scale, revealed that while most care givers responded positively to the presence of fluctuations, verbatim descriptions of FC in DLB had particular qualitative characteristics that differed from those obtained in an AD group.

Qualitative differences could not be accounted for by differences on key demographic and severity variables. The two groups were well matched in terms of dementia severity, education, and premorbid level of intelligence. Patient selection methods also produced a representative sample. The AD patients were older than those in the DLB group and the DLB patients were more likely to be male. These group differences in age and sex distribution are consistent with the known demographic characteristics of the two diseases.^{28–30}

Table 4 Care giver descriptions of FC in response to question two of the One Day Fluctuation Assessment Scale ("Has the patient had a period (or periods) today when he or she seemed to be confused and muddled and then a period (or periods) when he or she seemed to be improved and functioning better? Give examples of the worst and best period of function.")

| Probable DLB | Probable AD |
|--|---|
| <u>Worst:</u> He was hallucinating, his character changed and he got loud, almost aggressive. <u>Best:</u> He was only slightly muddled. | <u>Worst:</u> She repeated the same question over and over 5–8 times in an hour. <u>Best:</u> She didn't repeat herself so much. |
| <u>Worst:</u> She required full direction with ADLs, was lethargic, dribbling and confused to time, place and routine. <u>Best:</u> She was alert, aware of her routine and familiar with the other residents. | <u>Worst:</u> He forgot the time and date and asked me 10 times in an hour. <u>Best:</u> He remembered the day. |
| <u>Worst:</u> He couldn't work out how to charge his electric razor or plug it in. <u>Best:</u> He attended to clerical work and paid the bills. | <u>Worst:</u> She repeated the same question numerous times over a few hours. <u>Best:</u> She recognised people by name. |
| <u>Worst:</u> She was nonsensical, confused, and mumbled incoherently. <u>Best:</u> She was almost as she was. | <u>Worst:</u> She was unsure of where she was going and why. <u>Best:</u> She was fleetingly objective and less repetitive. |
| <u>Worst:</u> She got up at 2:30 am and got dressed for an appointment. <u>Best:</u> Periods where she seems to think quite clearly, made sense and remembered things. | <u>Worst:</u> When he had to sort things out himself and remember what to do. <u>Best:</u> When there was someone to guide and remind him. |
| <u>Worst:</u> He woke in the morning and thought there was a drama somewhere and he had to be there, I couldn't convince him otherwise. <u>Best:</u> He woke up calm, and was more easily convinced not to worry. | <u>Worst:</u> He got snappy, agitated and couldn't think of what he wanted to say. <u>Best:</u> He was talkative and productive, making his own bread. |
| <u>Worst:</u> He kept looking for "the exit", couldn't find the bedroom or the bathroom and had trouble recognising me (wife) <u>Best:</u> He was alert, opened the door, and greeted me after work. He knew me and seemed pleased to see me. | <u>Worst:</u> After an argument she got agitated and couldn't think <u>Best:</u> Normal conversation and presented well to others who don't live with her. |
| <u>Worst:</u> She was seeing people, preparing extra meals, and asking how many people to cook for. <u>Best:</u> Normal conversation, made sense, nothing unusual. | <u>Worst:</u> After a small amount of alcohol she became confused and unsteady <u>Best:</u> When she relaxed and things were highly organised or centred around her. |
| <u>Worst:</u> Illogical discussion, all jumbled, and didn't make sense. <u>Best:</u> Made himself clearly understood. | |

Sex had no effect on the findings. Both groups were characterised as senile onset dementia syndromes.

Consistent with the diagnostic inclusion criteria, the DLB group obtained higher impairment ratings on measures of extrapyramidal motor impairment and psychopathology. These impairment ratings, as well as measures of dementia severity, fell within the mild-to-moderate range suggesting that we had selected a typical early stage group. Poorer performance based intellectual abilities were recorded in the DLB group. This result was anticipated and consistent with the greater impairments in psychomotor speed and visuoconstructional function typically found in patients with DLB.^{31 32}

Verbatim qualitative descriptions of FC in DLB suggested an interruption in the flow of awareness or attention. This was frequently associated with transient episodes of confusion and an inability to engage in meaningful cognitive activity, followed by reversion to a near normal level of function. These episodes occurred spontaneously, in the absence of a situational explanation, suggesting that they were internally driven. By contrast, fluctuations in AD reflected a diminished capacity to cope with the cognitive demands of the immediate environment. In other words, an AD care giver report of "fluctuation" is elicited by situations in which an underlying cognitive impairment manifests itself, typically as repetitiveness in conversation, forgetfulness in relation to a recent task or event, or other behavioural consequences of poor memory. In some cases afternoon sleepiness elicits a report of fluctuation. FC in DLB was often transient, while descriptions of FC by AD care givers suggested a more enduring state shift (good days/bad days, somnolent/alert).

Qualitative differences were reliably detected by independent raters, lending weight to the clinical utility of this type

of information. Accuracy of classification on the basis of qualitative care giver accounts varied, however, between 55% and 100%. Scale items that emphasised marked variation in daily or weekly levels of confusion, and differences between best and worst performance, were most effective in discriminating between the groups. By contrast, items that focused on impaired alertness yielded similar descriptions from DLB and AD care givers, and accuracy of classification dropped as low as 55%.

Consistent with previous research³³, standard severity ratings from both scales showed that FC occurs more frequently and is more prominent in DLB than in AD. The Clinician Assessment of Fluctuation proved to be a more discriminating tool than the One Day Fluctuation Scale because, as the present findings suggest, it elicits more information of a descriptive and qualitative nature.

Quantitative scoring of the Clinician Assessment of Fluctuation is entirely dependent upon the administering clinician's interpretation of qualitative examples provided by care givers. The general wording of the items on this scale casts a rather broad net, capturing a wide variety of episodic or cyclical manifestations. To obtain a quantitative rating on this scale, clinicians must decide whether the care giver responses constitute "clear cut" examples of FC²⁷ (p 252). Implicit in this statement is an assumption that fluctuations in DLB can be differentiated from those occurring in other dementias. AD care givers, however, frequently provided examples of "fluctuating confusion" that were confounded with instances of memory failure. Differing interpretations of what constitutes "clear cut" FC represent a significant source of error which restricts the scale's ability to differentiate DLB and AD at a quantitative level. Explicit identification and documentation of qualitative features of FC is likely to

improve the consistency with which the quantitative data are generated.

This point is well illustrated when the quantitative scores of the AD and DLB groups on the One Day Fluctuation Assessment Scale are considered. We found that the quantitative scoring system of this scale did not yield a clear difference between the two clinical groups. Nevertheless, the only item that makes provision for an open ended response generated qualitative care giver descriptions of FC which did differentiate the groups. The quantitative scoring system does not take this type of information into account. Despite qualitatively distinct descriptions of FC, therefore, the quantitative scoring method has the effect of shielding important differences between the AD and DLB groups.

In conclusion, FC is a clinical feature of core significance in the diagnosis of DLB^{1,2} and accurate identification is crucial for differentiating DLB from AD.^{2,3} In current usage, it remains a broadly defined phenomenon that is not readily detected in the clinical setting.^{14,16,17} The current work shows that FC in DLB differs qualitatively from periodic changes seen in AD. On a practical level, explicit documentation and a wider appreciation of these qualitative distinctions could improve the reliability with which less experienced clinicians identify this core diagnostic feature in the clinical setting. A qualitative classification could form the basis of a manual to accompany clinical rating scales. This would have the advantage, not only of broadening the clinical utility of these scales, but also of helping to ensure consistency in the way the scales are rated. Ultimately, this might improve the reliability with which this core diagnostic feature is identified in the clinical setting.

The differences between the AD and DLB groups that emerged here suggest that FC is a viable and distinctive core feature of DLB. Collecting verbatim care giver descriptions in larger, autopsy confirmed clinical groups might be a useful next step towards a better understanding of fluctuating behaviour and cognition in the major dementing conditions.

Authors' affiliations

J Bradshaw, M Saling, M Hopwood, A Brodtmann, Austin Health, Heidelberg, Australia

J Bradshaw, M Saling, V Anderson, Department of Psychology, The University of Melbourne, Parkville, Australia

M Hopwood, Department of Psychiatry, The University of Melbourne, Parkville, Australia

Funding support: Austin Hospital Medical Research Foundation (AHMRF), Australian Association of Gerontology (AAG)

Competing interests: none

REFERENCES

- McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. *Neurology* 1996;**47**:1113–24.
- McKeith IG, Ballard CG, Perry RH, et al. Prospective validation of consensus criteria for the diagnosis of dementia with Lewy bodies. *Neurology* 2000;**54**:1050–8.
- McKeith IG, Perry RH, Fairbairn AF, et al. Operational criteria for senile dementia of Lewy body type (SDLT). *Psychol Med* 1992;**22**:911–22.
- McKeith IG, Fairbairn AF, Bothwell RA, et al. An evaluation of the predictive validity and inter-rater reliability of clinical diagnostic criteria for senile dementia of Lewy body type. *Neurology* 1994;**44**:872–7.
- Walker MP, Ayre GA, Perry EK, et al. Quantification and characterisation of fluctuating cognition in dementia with Lewy bodies and Alzheimer's disease. *Dement Geriatr Cogn Disord* 2000;**11**:327–35.
- Ballard C, Walker M, O'Brien J, et al. The characterisation and impact of 'fluctuating' cognition in dementia with Lewy bodies and Alzheimer's disease. *Int J Geriatr Psychiatry* 2001;**16**:494–8.
- Perry RH, Walker M, Perry E. Dementia with Lewy bodies. A new avenue for research into neurobiological mechanisms of consciousness? In: Fisher E, ed. *Progress in Alzheimer's and Parkinson's diseases*. New York: Plenum Press, 1998:Chapter 65.
- Kaufer DI, Catt KE, Lopez OL, et al. Dementia with Lewy bodies: response of delirium-like features to donepezil. *Neurology* 1998;**51**:1512.
- Hachinski VC, Iliff L, Zilhka E, et al. Cerebral blood flow in dementia. *Arch Neurol* 1975;**32**:632–7.
- Roman GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia-diagnostic criteria for research studies: report of the NINDS-AIREN international workshop. *Neurology* 1993;**43**:250–60.
- Kolbeinsson H, Jonsson A. Delirium and dementia in acute medical admissions of elderly patients in Iceland. *Acta Psychiatr Scand* 1993;**87**:123–7.
- Robertson B, Blennow K, Gottfries CG, et al. Delirium in dementia. *Int J Geriatr Psychiatry* 1998;**13**:49–56.
- Mega MS, Masterman DL, Benson DF, et al. Dementia with Lewy bodies: reliability and validity of clinical and pathologic criteria. *Neurology* 1996;**47**:1403–9.
- McKeith IG. Dementia with Lewy bodies. *Br J Psychiatry* 2002;**180**:144–7.
- Lopez OL, Litvan I, Catt KE, et al. Accuracy of four clinical diagnostic criteria for the diagnosis of neurodegenerative dementias. *Neurology* 1999;**53**:1292–1301.
- Ballard CG, O'Brien J, Lowery K, et al. A prospective study of dementia with Lewy bodies. *Age Ageing* 1998;**27**:631–6.
- Lopez OL, Becker JT, Kaufer DI, et al. Research evaluation and prospective diagnosis of dementia with Lewy bodies. *Arch Neurol* 2002;**59**:43–6.
- McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;**34**:939–44.
- McKeith IG, Perry EK, Perry RH, et al. Report of the second dementia with Lewy body international workshop. *Neurology* 1999;**53**:902–5.
- Hughes CP, Berg L, Danziger WL, et al. A new clinical scale for the staging of dementia. *Br J Psychiatry* 1982;**140**:566–72.
- Folstein M, Folstein S, McHugh P. 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;**12**:129–98.
- Lang AE, Fahn S. Assessment of Parkinson's disease. In: Munstaf T, ed. *Quantification of neurologic deficit*. London: Butterworths, 1989:Chapter 21.
- Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep* 1962;**10**:799–812.
- Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;**67**:361–7.
- Wechsler D. *Wechsler Abbreviated Scale of Intelligence*. San Antonio: The Psychological Corporation, Harcourt Brace and Company, 1999.
- Nelson HE. *National Adult Reading Test*. Berkshire: NFER-NELSON, 1982.
- Walker MP, Ayre GA, Cummings JL, et al. The Clinician Assessment of Fluctuation and the One Day Fluctuation Assessment Scale. Two methods to assess fluctuating confusion in dementia. *Br J Psychiatry* 2000;**177**:252–6.
- McKeith IG. Dementia with Lewy bodies: clinical and pathological diagnosis. *Alzheimer's Rep* 1998;**1**:83–7.
- Cercy S, Bylsma F. Lewy bodies and progressive dementia: a critical review and meta-analysis. *J Int Neuropsychol Soc* 1997;**3**:179–94.
- Verghese J, Crystal HA, Dickson DW, et al. Validity of clinical criteria for the diagnosis of dementia with Lewy bodies. *Neurology* 1999;**53**:1974–82.
- Ballard C, O'Brien J, Gray A, et al. Attention and fluctuating attention in patients with dementia with Lewy bodies and Alzheimer's disease. *Arch Neurol* 2001;**58**:977–82.
- Mori E, Shimomura T, Fujimora M, et al. Visuo-perceptual impairment in dementia with Lewy bodies. *Arch Neurol* 2000;**57**:489–93.
- Ballard CG, Aarsland D, McKeith I, et al. Fluctuations in attention. PD dementia vs DLB with parkinsonism. *Neurology* 2002;**59**:1714–20.