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Development of a diagnostic checklist to identify functional cognitive disorder versus other neurocognitive disorders

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ABSTRACT

Background Functional cognitive disorder (FCD) poses a diagnostic challenge due to its resemblance to other neurocognitive disorders and limited biomarker accuracy. We aimed to develop a new diagnostic checklist to identify FCD versus other neurocognitive disorders.

Methods The clinical checklist was developed through mixed methods: (1) a literature review, (2) a three-round Delphi study with 45 clinicians from 12 countries and (3) a pilot discriminative accuracy study in consecutive patients attending seven memory services across the UK. Items gathering consensus were incorporated into a pilot checklist. Item redundancy was evaluated with phi coefficients. A briefer checklist was produced by removing items with >10% missing data. Internal validity was tested using Cronbach's alpha. Optimal cut-off scores were determined using receiver operating characteristic curve analysis.

Results A full 11-item checklist and a 7-item briefer checklist were produced. Overall, 239 patients (143 FCD, 96 non-FCD diagnoses) were included. The checklist scores were significantly different across subgroups (FCD and other neurocognitive disorders) ($F(2, 236)=313.3$, $p<0.001$). The area under the curve was excellent for both the full checklist (0.97, 95% CI 0.95 to 0.99) and its brief version (0.96, 95% CI 0.93 to 0.98). Optimal cut-off scores corresponded to a specificity of 97% and positive predictive value of 91% for identifying FCD. Both versions showed good internal validity (>0.80).

Conclusions This pilot study shows that a brief clinical checklist may serve as a quick complementary tool to differentiate patients with neurodegeneration from those with FCD. Prospective blind large-scale validation in diverse populations is warranted.Cite Now

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Functional cognitive disorder diagnosis is based on positive diagnostic features suggesting internal inconsistency. However, the diagnosis lacks standardisation and an operationalised clinical approach is needed.

WHAT THIS STUDY ADDS

⇒ We developed a clinical checklist based on literature evidence and clinical expert consensus, with excellent discriminative power to distinguish between functional cognitive disorder and other neurocognitive disorder subgroups in this pilot evaluation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The diagnostic checklist may serve as an accessible way to improve identification of functional cognitive disorder versus other neurocognitive disorders in clinical and research grounds. Future prospective blind studies will clarify whether it supports the stratification of diagnostic workflow and reduces the need for costly and harmful investigations and therapies. The checklist also influences inclusion/exclusion criteria for future trials in cognitive disorders and supports history-taking.

INTRODUCTION

Functional cognitive disorder (FCD) is the cognitive subtype of functional neurological disorder (FND) and accounts for around one-third of patients seen in specialised

memory services.[1] Diagnosis is challenging as FCD can superficially resemble a neurodegenerative illness.[1] A recent consensus panel defined FCD as cognitive symptoms with clinical evidence of internal inconsistency (ie, ability to perform a task at certain times with impairment at other times, particularly if the task is the focus of attention), but the application of current diagnostic criteria to distinguish FCD from neurodegeneration has not been evaluated.[2]

FCD is likely underdiagnosed in clinical practice and often grouped together with subjective cognitive impairment or mild cognitive impairment (MCI), diagnostic labels that encompass a variety of underlying conditions.[1 3] There is also a real chance of misdiagnosis with early-stage neurodegeneration, triggering life-changing decisions and exposure to potentially harmful medications including anticholinesterase inhibitors, particularly in less specialised settings.[4] Anecdotal evidence from clinical practice also shows that patients with a neurodegenerative condition can be wrongly diagnosed with FCD. In both circumstances, patients are deprived of appropriate care for their needs, postdiagnostic support and accurate prognosis information, further impacting on individual, healthcare and wider societal costs, with reduced productivity, unemployment and quality-of-life impairment.[5]

Over the last decade, our understanding of the biological basis of neurocognitive disorders, in particular Alzheimer's disease (AD), led to the emergence of novel fluid and brain imaging biomarkers. However, currently available investigations have significant limitations in accurately distinguishing between FCD and other neurocognitive disorders, are not widely available, and there is no agreement on consensus approach.[6] Patients with amyloid positive/tau negative cerebrospinal fluid (CSF) biomarkers and positron emission tomography (PET) scans have an increased risk of false positive AD diagnosis at autopsy[7 8] and may never progress to MCI and dementia in comparison with controls.[9 10] More recently, blood-based biomarkers did not demonstrate superiority over clinical reference models in predicting underlying AD,[11] suggesting they are not suitable for indiscriminate testing. Additionally, structural neuroimaging findings[1 12] and psychometric profiles of FCD[1 13–16] may be indistinguishable from those with early neurodegeneration, especially in individuals with a higher cognitive reserve.[17] Hence, a demonstration of normal or borderline test results is insufficient and inappropriate to make a correct diagnosis, particularly in patients who continue to experience debilitating cognitive symptoms.

In a recent systematic review, we found several bedside clinical signs discriminating between FCD and neurodegeneration.[16] We then conducted a Delphi study with expert clinicians, using fictional cognitive vignettes of FCD and neurodegeneration and observed high inter-rater agreement on the separation of FCD from neurodegeneration but lower consensus regarding the conceptualisation and management in FCD versus other neurodegenerative conditions, emphasising the need for diagnostic operationalisation and the importance of careful clinical characterisation.[6]

We hypothesised that a brief bedside checklist could constitute a practical clinical tool to differentiate FCD from neurodegeneration, in patients with cognitive symptoms. The checklist was developed based on key clinical features identified in the literature and consensus expert opinion. We then conducted a pilot diagnostic accuracy study in a retrospective sample of patients attending outpatient memory services across seven centres in the UK.

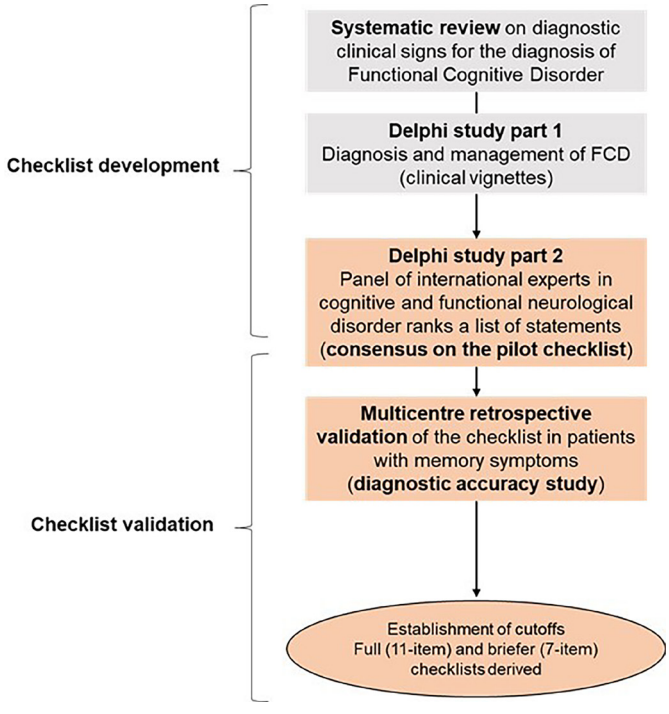


Figure 1 Schematic representation of checklist development. In light grey, published studies from our group that informed the checklist development stage.[6 16] In orange, studies covered in this article. FCD, functional cognitive disorder.

METHODS

The checklist was developed iteratively using a mixed-methods approach in three related studies (figure 1).

Development of the checklist prototype: Delphi study

A modified Delphi methodology was followed. Experts in cognitive disorders and FND were invited to participate, as we previously described.[6]

A systematic literature review[16] informed a survey with clinical characteristics that were found to be typical of FCD.[1] Experts were asked to rank each statement according to how much they thought the items favour a diagnosis of FCD, using a Likert scale ranging from 'extremely unimportant (1)' to 'extremely important (7)', through three consecutive rounds.[18] The survey was opened in March 2022, and the third round was

Table 1 Consensus criteria for inclusion or exclusion of the statements in the checklist

Level of consensus	Scoring
Strong	>80% of scores ≤2 or ≥6
Moderate	66%–80% of scores ≤2 or ≥6
Low	50%–65% of scores ≤2 or ≥6
No consensus	<50% of scores ≤2 or ≥6

concluded by August 2022, when the prototype of the future diagnostic checklist was achieved.

Statistical analysis

The overall rating assigned to each statement was quantified using median and interquartile range (IQR). Strong or moderate consensus to include or exclude a statement was achieved when a statement was rated in the top or bottom 2 scores of the 7-point Likert scale by at least 80% and 66% of the participants, respectively (table 1).[19]

Diagnostic accuracy study

Data collection and patient population

The checklist was retrospectively piloted in a sample of consecutive patients with cognitive symptoms (memory, attention and concentration difficulties, and/or problems with thinking) attending seven independent specialist memory services across the UK (National Health Service (NHS) Lothian, NHS Fife, NHS Forth Valley, North Bristol NHS Trust, Ashford and St. Peter's Hospitals, St George's University Hospitals and Oxford University Hospitals. All patients had been evaluated by eleven consultant-level clinicians (nine consultant neurologists and two consultant neuropsychiatrists). 'Reference' expert diagnoses (FCD and other neurocognitive disorders) were made independently of the checklist items according to local pragmatic practices based on clinical assessment, multidisciplinary discussion, neuropsychological testing, brain imaging and fluid diagnostic tests when deemed appropriate (eg, AD was diagnosed based on multi-domain cognitive decline, abnormal CSF/genetics and/or neuroimaging). A multifactorial dementia label was used for patients with more than one cause accounting for their cognitive impairment. Patients with an uncertain diagnosis, no aetiology for their cognitive symptoms, advanced dementia (ie, significant cognitive and/or physical disability and reliance on others for their own care), any toxic, metabolic or systemic disease, a major psychiatric disorder or psychoactive medication likely to account for the cognitive difficulties were excluded. Comorbidities, including mild mood disorders, were allowed in all disease groups if they did not account for the whole symptomatology. Three of the clinicians contributing with patient data had not been involved in the development of the checklist during the initial Delphi study. None of the 11 clinicians were involved in the statistical analyses. All were familiar with the proposed criteria for FCD[2] and identified FCD cases based on the presence of internal inconsistency (eg, variability in task performance, significant discrepancy between the self-reported symptoms and everyday functioning or cognitive test performance), in the absence of another medical or psychiatric condition better explaining the symptoms.[2]

Clinicians were invited to fill in the diagnostic checklist using information from the clinical letters and medical charts from at least 10 consecutive FCD patients attending their clinics and 10 others with other neurocognitive diagnoses to create 2 groups of a balanced number of patients with FCD and non-FCD diagnoses. Extraction was done between September 2023 and February 2024. Besides the checklist items, coded as present or absent, attending clinicians also extracted: sex, age of symptom onset, age at diagnosis and final diagnosis at last follow-up. Patients were followed longitudinally for at least 12 months. During the extraction, items not available in the records were left blank, to reduce any potential bias and diagnostic imprecision. Missing data were registered for analysis. For the full-checklist analysis, it was assumed that if certain features were not mentioned in the medical records, they were likely not present because clinicians are less likely to mention absent findings even if they were asked as part of the interview, as in previous studies.[20 21]

Statistical analyses

Statistical analysis on deidentified data was performed by VC. The study follows the Standards for Reporting of Diagnostic Accuracy (STARD) guidelines.[22]

Checklist reduction

The per cent of positive responses for each item in the FCD and non-FCD diagnostic groups was compared with verify if all items were more frequent in the FCD group. Phi coefficients were calculated for each pair of questions to assess for redundant items (ie, correlation higher than 0.9). As all items were more frequent in the FCD group, and there were no near-perfect correlations, no item was eliminated based on the two previous steps. A briefer checklist was produced by removing items with more than 10% missing values.[23] The internal validity of the checklist was tested with Cronbach's alpha: 0.8–0.9 good, >0.9 excellent.[24]

Checklist performance

Scores on the total and brief diagnostic checklist were obtained for all patients, with higher scores suggesting FCD. The normal distribution was confirmed using the Shapiro-Wilk and the Kolmogorov-Smirnov tests. Independent t-tests were calculated for continuous variables and χ^2 analyses for categorical variables. One-way analyses of variance were performed to compare mean total scores across diagnostic groups (FCD and other neurocognitive disorders including AD). Statistical significance was established at two-sided $p \leq 0.05$.

Optimal cut-off scores for discrimination between FCD and other neurocognitive disorders were determined using receiver operating characteristic (ROC) curve analysis. The associated area under the curve (AUC) statistic indicates the discriminative accuracy and was classified as follows: ≤0.7 poor, 0.7–0.8 fair, 0.8–0.9 good and≥0.9 excellent.[25] Sensitivity, specificity, positive predictive value (+PV) and negative predictive value (–PV) were calculated for each cut-off value. Given that the objective of this checklist is to identify FCD versus other neurocognitive disorders rather than screening all at-risk patients when determining the optimal checklist score cut-off point, a threshold with higher specificity was selected. Youden indices (optimal cut-off points) were also calculated.[26] All statistical analyses were performed using R V.3.3 and MedCalc[27] for ROC curves.

The protocol was registered in OSF (https://osf.io/rpqc6). The current study is part of the innovative training network (Encompassing Training in fUnctional Disorders across Europe; https://etude-itn.eu/).[28]

RESULTS

Delphi study

45 experts participated in the first round, and 39 (87%) in subsequent rounds. Most of the experts worked in cognitive clinics in tertiary hospitals.[6] 29 pilot items were initially generated based on an initial review.[16] In round 1, strong (≥80%) or moderate (≥66%) consensus was obtained for three items: 'discrepancies between self-reported and observed cognitive functioning', 'patients giving a detailed history of their memory complaints with specific examples' and 'ability to detail their list of prescribed drugs and/or recall previous interactions with other doctors'. Two items were merged due to redundancy after discussion: 'symptoms of longer duration without progression' and 'stability or improvement over time'. Participants were anonymously sent their own rating and received feedback regarding the level of group consensus achieved for each statement. Five additional items were suggested, which were reviewed in round 2 together with those for which no consensus had been achieved in the previous round, and moderate to strong consensus (≥66%) was obtained for 'marked variability of the symptoms in different situations' and 'comorbid non-cognitive functional disorder'. Items with low/borderline low (≥50%) consensus were discussed openly by the group in the final round, which culminated in the inclusion of six additional items(online supplemental file 1).

The preliminary 11-item version of the 'FCD diagnostic checklist' is presented in table 2, with further guidance

Table 2 FCD versus other neurocognitive disorders diagnostic checklist

Clinical items	Score (0no/not tested; 1-yes)
1. Is there a discrepancy between the level of symptoms reported and everyday functioning?*	
2. Is the patient able to detail specific examples of memory complaints?	
3. Are the cognitive symptoms distractible and/or fluctuating (eg, variable in different situations)?	(Only full checklist)
4. Is the patient able to detail the list of prescribed drugs and/or recall previous interactions with other doctors (eg, prior diagnoses and investigations)?	(Only full checklist)
5. Is there a history of a non-cognitive functional neurological disorder and/or functional somatic disorders (pain, fatigue…)?	
6. Is the patient more aware of the cognitive changes than others (consider if the patient was self-referred and/or attended alone)?†	
7. Is the cognitive performance normal or does it show an inconsistent pattern (eg, worse on immediate recall than delayed recall, stronger performance repeating digits backward compared with digits forward, approximate answers)?†	(Only full checklist)
8. Are the memory symptoms stable or improved over time?†	
9. Is the patient able to date the symptom onset with precision?	
10. Is there an obvious psychological stressor?	
11. Is the patient able to answer compound/double-barrelled questions?	(Only full checklist)
Total score	

Green: strong consensus (≥80% 6–7 point Likert scale); Blue: moderate consensus (≥66%); Orange: low/borderline consensus (≥50% 6–7 point Likert scale), included after group discussion during round 3.
The evaluating clinician assesses yes/no questions, ideally at the time of the initial presentation (although it can be done retrospectively). The pilot checklist has a maximum score of 11 points.
*For details, consult box 1.
†Answering 'Yes' to either one or both options means one point in the score.
FCD, functional cognitive disorder.

Box 1 Item explanation/scoring instructions

Discrepancy between objective/subjective reporting
Subjectively reported marked cognitive difficulties and/or low standardised cognitive test scores, directly in contrast with, for example: ability to keep a cognitively demanding job without any difficulties, conversational abilities observed during interview, ability to perform certain activities such as reading a book, managing finances and driving without difficulties.

Ability to detail memory complaints
During the interview, the patient provides specific examples of memory failures, with detailed and beyond solicited information. In contrast with patients with neurodegeneration, patients with functional cognitive disorder (FCD) might be able to speak for longer periods, if not interrupted.

Distractibility/fluctuation of symptoms
Difficulties only occurring in particular situations, for example, patients who report detailed episodes of memory loss and are able to sustain attention during the interview but show disproportional impairment of the same functions in other situations (eg, during cognitive testing and when the attention is diverted to the symptoms). This is distinct from simple fluctuation over time, which can be observed in many other processes (such as delirium and Lewy body dementia).

Ability to recall a list of drugs and/or previous interactions with other doctors
Ability to recall previous interactions with other doctors, including particular aspects of prior diagnoses and investigations. Similarly, an ability to detail a list of drugs from memory, and their indications, is often a sign of well-functioning memory, which is incongruent with the symptoms reported.

History of a non-cognitive functional neurological disorder and/or functional somatic disorders
The presence of other symptoms, such as pain, fatigue, dissociation and other functional diagnoses, might be a helpful (although not necessary) lead pointing to FCD.

Patient more aware of the cognitive changes than others
In FCD, collateral history often suggests that the patient's concern is significantly higher than in the accompanying person/relatives (a sign of increased introspection and awareness of memory difficulties). Supportive demonstrations are attending the clinic alone and/or being self-referred (patient taking the initiative to see a doctor due to his/her/their concerns).

Normal and/or incongruent cognitive performance
Patients with FCD might show a normal cognitive performance, overperform in relation to neurodegenerative conditions or underperform. More important than a normal cognitive performance is the demonstration of inconsistent patterns of performance, especially in the same cognitive domain (eg, worse on immediate recall than delayed recall, stronger performance repeating digits backward compared with digits forward, approximate answers). This indicates cognitive processes performing better when accessed automatically, rather than explicitly. Some patients may show poor persistence across tasks or give vague responses that improve with encouragement. Other mitigating factors that intervene (eg, fluctuations in consciousness, psychiatric state or a significant headache) should be taken into consideration, as this can explain attention deficits.

Symptoms stable or improving over time

Continued

Box 1 Continued

Patients might present abruptly with symptoms that start severely and remain stable over time. Other times, patients will have a long history of symptoms that did not progress and/or improve over time. Care should be taken in patients with vascular cognitive impairment or post-traumatic brain injury (TBI) who show stability of symptoms or improvement over time with management of comorbidities.

Ability to detail symptom onset with precision/abrupt onset
Some patients will be able to describe symptom onset with precision, sometimes establishing a connection with a previous injury or specific event like a migraine attack, an episode of dissociation or a mild head injury.

Psychological stressor
Psychological stressors can act as predisposing, precipitant or perpetuating factors in FCD. For a subset of patients, the pathophysiology of FCD is linked with depressive symptoms and anxiety, and other stressor life events. For some patients, memory symptoms might be linked to significant life events like a recent bereavement or a physical illness, although this may also occur in neurodegeneration and should never be interpreted in isolation.

Ability to answer compound/double-barrelled questions
Ability to address parts of a compound question was more frequently reported in FCD versus neurodegeneration. Generally, although patients with mild cognitive impairment (MCI) due to neurodegeneration might be able to address these questions (especially if highly educated), in FCD, this will be incongruent with severe symptoms, while in MCI due to neurodegeneration it may just be in keeping with low level of impairment in early stages.

presented in box 1. The score (maximum 11) is obtained by adding positive answers.

Diagnostic accuracy study

Patient population

A total of 239 patients (143 FCD and 96 neurocognitive disorders), including 129 female and 110 male, were included (table 3). Compared with other neurocognitive disorders, FCD patients had a younger onset of symptoms (mean age 50 years vs 65 years) and younger age at diagnosis ($p<0.001$). The mean duration of symptom prior to diagnosis (3 years) and sex did not differ between groups.

Checklist reduction and internal validity

All items on the checklist were significantly more frequent in patients in the FCD group (table 3). As expected, many items were correlated, but no pair had a perfect correlation (online supplemental figure 2). Four items had more than 10% missing data (3, 4, 7 and 11) and a briefer checklist without these four items was produced. The full checklist had a good internal validity (Cronbach's alpha=0.85), and so did the brief version (Cronbach's alpha=0.80).

Checklist performance

There was a significant difference in the full and brief checklist scores between FCD and other neurocognitive disorders (figure 2A,B). Across diagnostic subgroups, the

Table 3 Patient demographics and per cent of positive responses on single items of the checklist

	FCD (n=143)	Non-FCD (n=96)	P value	Missing replaced by absent	Total (n=239)
Sex=male (no., %)	59 (41)	51 (53)	0.095	–	110 (46)
Age at symptom onset, mean (SD)	49.8 (12)	64.5 (12)	<0.001	–	55.7 (14)
Age at diagnosis, mean (SD)	53.1 (11)	67.1 (11)	<0.001	–	58.7 (13)
Full checklist score, mean (SD)	7.9 (2)	2.09 (2)	<0.001	–	5.6 (3)
Brief checklist score, mean (SD)	5.2 (1)	1.4 (1)	<0.001	–	3.7 (2)
Years until diagnosis, mean (SD)	3.4 (5)	3.2 (3)	0.710	–	3.3 (4)
Checklist items (no., %)					
Internal inconsistency (item 1)	128 (90)	18 (19)	<0.001	0	146 (61)
Detailed account of symptoms (item 2)	136 (95)	41 (43)	<0.001	4 (2)	177 (74)
Distractibility/fluctuation (item 3)	102 (71)	17 (1)	<0.001	29 (12)	119 (50)
Recalling list of drugs/previous interactions (item 4)	92 (64)	20 (21)	<0.001	74 (31)	112 (47)
FND/functional somatic symptoms (item 5)	77 (54)	7 (7)	<0.001	3 (1)	84 (35)
More concerned than others (item 6)	109 (76)	3 (3)	<0.001	7 (3)	112 (47)
Cognitive performance (item 7)	107 (75)	15 (16)	<0.001	28 (12)	122 (51)
Symptoms stable or improving (item 8)	135 (94)	21 (22)	<0.001	2 (1)	156 (65)
Abrupt symptom onset (item 9)	66 (46)	7 (7.3)	<0.001	7 (3)	73 (31)
Psychological stressor (item 10)	98 (69)	33 (3)	<0.001	1 (<1)	131 (55)
Compound questions (item 11)	83 (58)	19 (20)	<0.001	109 (46)	102 (43)

FCD, functional cognitive disorder; FND, functional neurological disorder.

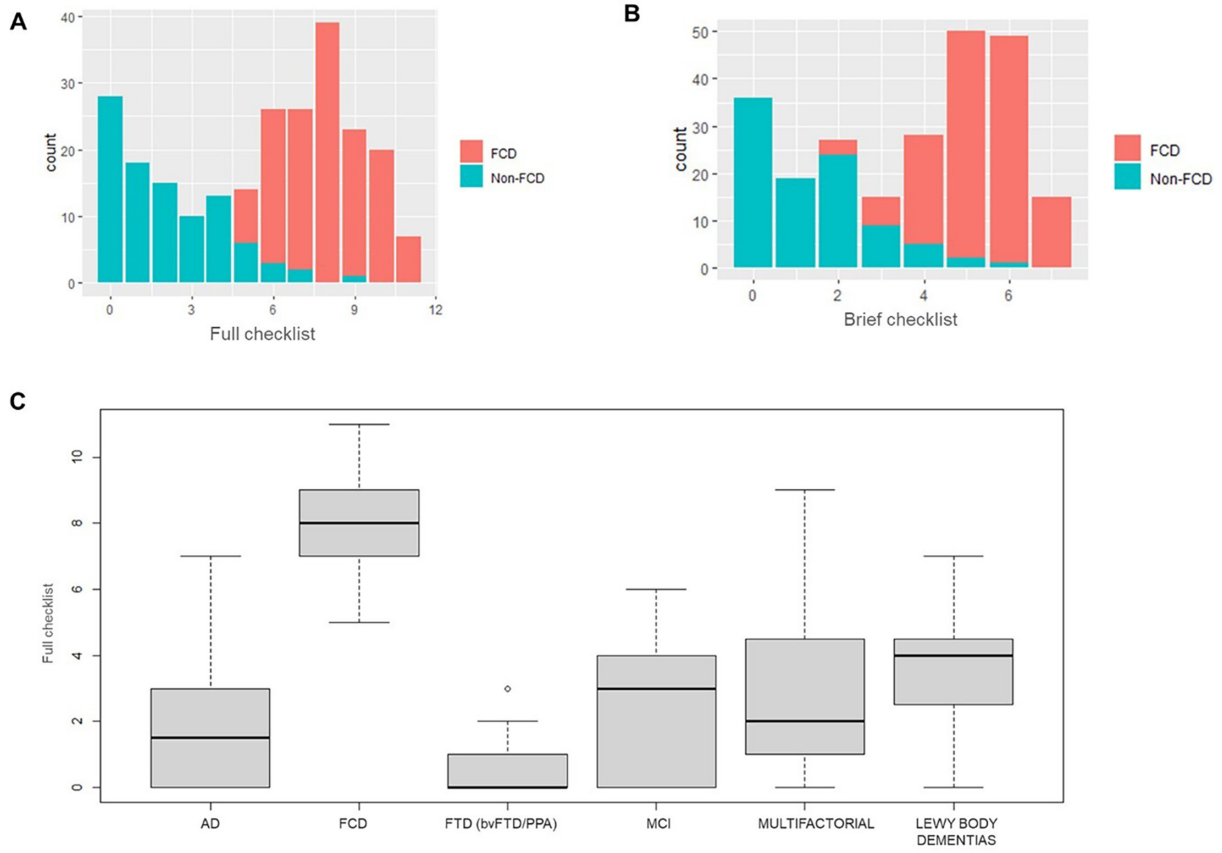


Figure 2 (A, B) Bar plots with distribution of scores across FCD and non-FCD groups, for the full (A) and brief (B) versions of the checklist; (C) distribution of the full checklist scores across diagnostic groups (n≥5 only). AD, Alzheimer's disease; bvFTD, behavioural variant of frontotemporal dementia; FCD, functional cognitive disorder; MCI, mild cognitive impairment; PPA, primary progressive aphasia.

FCD group obtained a mean full checklist score of 7.9, followed by the group with probable AD (mean score 1.9) and then other non-AD cognitive disorders including multifactorial dementia, frontotemporal dementias, Lewy body dementias, MCI, vascular dementia, normal pressure hydrocephalus and autoimmune encephalitis (overall with a mean full checklist score of 2.4) ($F(10, 228)=73.89$, $p<0.001$ for the full checklist and $F(10, 228)=70.4$, $p<0.001$ for the brief version without items 3, 4, 7 and 11) (figure 2C and table 4).

The AUC was excellent both for the full (AUC=0.97, 95% CI 0.95 to 0.99, $p<0.001$) and brief (AUC=0.96, 95% CI 0.93 to 0.98, $p<0.001$) versions of the checklist to discriminate between FCD and other neurocognitive disorders. The best-computed cut-off points for higher diagnostic specificity were 5.5 for the full checklist and 3.5 for the brief checklist. A cut-off score of 6 for the full checklist and 4 for the brief version corresponded to a specificity of 97% and a +PV of 91% (figure 3 with FCD as positive actual state).

DISCUSSION

Cognitive symptoms pose a significant diagnostic challenge to clinicians due to similarities in clinical presentation and diagnostic investigations between FCD and early stages of neurodegeneration, particularly AD. While positive discriminative features have been previously identified,[1 2 16] the usefulness of these features had not been standardised nor examined in a systematic way. This pilot diagnostic checklist represents an initial attempt to group clinical features from the history and examination alone to support an accurate discrimination between FCD and other neurocognitive disorders.[6 16] In this initial retrospective study, this novel tool obtained robust internal validity and excellent accuracy to differentiate between FCD and non-FCD neurocognitive diagnoses. A brief seven-item version showed comparable accuracy and may simplify the assessment in busy or less specialised settings. A score of 6 or above in the full checklist, and 4 or more in the brief checklist, yield a diagnostic specificity of 97% and a +PV of 91% for FCD.

During our multistep Delphi, the panel voting was extended to include discussions regarding the key challenges in identifying FCD among the wider group of neurocognitive disorders. The items for which higher consensus was achieved (at least two-thirds of the panel) were further supported by the existing literature. Specifically, the inclusion of symptom reporting items aimed to capture observed discrepancies between reported symptoms and actual daily functioning, the ability to provide

Table 4 Mean scores on the 'FCD diagnostic checklist' (full and brief versions), across diagnostic subgroups

	Full checklist	Brief checklist (without items 3, 4, 7, 11)
Diagnostic group (n, %)	**Mean score (SD)**	**Mean score (SD)**
FCD (n=143, 60%)	7.9 (1.6)	5.2 (1.1)
AD (n=58, 24%)	1.9 (1.7)	1.2 (1.1)
Other non-AD cognitive disorders (n=38, 16%)	2.4 (2.3)	1.7 (1.7)
Multifactorial dementia (n=11, 5%)	4.8 (2.7)	2.1 (1.7)
Behavioural variant frontotemporal dementia/PPA (n=10, 4%)	0.6 (1)	0.5 (0.8)
Lewy body dementias (Parkinson's disease dementia and dementia with Lewy bodies) (n=7, 3%)	3.6 (2.2)	2.3 (1.5)
MCI (n=6, 3%)	2.7 (2.1)	1.7 (1.5)
Vascular dementia (n=2, <1%)	4.5 (0.5)	3.5 (0.5)
Normal pressure hydrocephalus (n=1, <1%)	1 (0)	0 (0)
Autoimmune encephalitis (n=1, <1%)	2 (0)	2 (0)
F(2, 236) =	313.3, p<0.001	290.6, p<0.001

AD, Alzheimer's disease; FCD, functional cognitive disorder; MCI, mild cognitive impairment; PPA, primary progressive aphasia.

detailed symptom descriptions, and the presence of cognitive fluctuations or distractibility, all of which support an FCD diagnosis.[2 29 30] Further, increased introspection and awareness of memory problems and a discordance between an informant's rapport and patient's concern were found to be helpful as a screening method,[31] supporting the inclusion of item 6. Comorbidities, such as non-cognitive FNDs, somatic symptoms (pain, fatigue) and psychological stressors, are common in FCD,[15] and potential predisposing and precipitating factors.[5 14] FCD patients often show stability or improvement over time[2 14] and may exhibit a sudden onset,[16 32] in contrast to the progressive and insidious onset seen in neurodegenerative disorders.[1 16] Demographic factors such as younger age, female sex, educational level and family history of dementia did not reach sufficient consensus for inclusion in this checklist, as their added value for individual risk of progression is limited.[33] Similarly, while personality traits may point to increased vulnerability for FCD, these are unlikely to be diagnostically helpful and may emphasise subjective judgments. Performance validity tests did not reach sufficient consensus for inclusion and were found to be abnormal in only a minority of patients;[34] further FCD patients do not necessarily fail these tests more often than other groups.[35] The subsequent retrospective analysis of checklist performance confirmed the relevance of the items included, reinforcing our confidence in the selected set of symptoms and signs to aid in the early identification of FCD versus other neurodegenerative disorders. Yet, it is critical to emphasise that the checklist was designed so that no individual items are taken in isolation, and these findings require further blinded prospective evaluation.

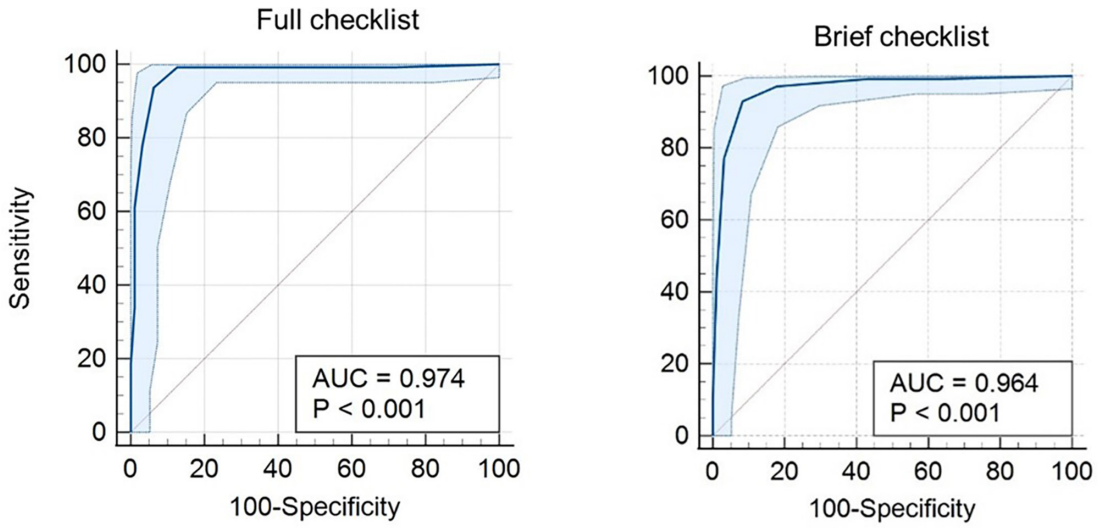
As potential advantages, the diagnostic checklist can be completed in approximately 5 min based on the information obtained from a standard clinical interview and does not rely on subjective severity ratings or invasive diagnostic assays.

Our findings add to the literature on diagnostic screening tools for FCD. Previously, a patient-facing tool identified typical symptoms of FCD but was found to overdiagnose FCD in healthy individuals.[36] Other machine learning approaches based on conversational analysis, language and interactional features have shown excellent accuracy but were tested in much smaller sample sizes and require sophisticated equipment and analysis that are not widely available.[29 37]

Implications of the checklist and future research

The application of the checklist by different clinicians across multiple centres supports the diagnosis based on positive signs ('ruling in') instead of exclusionary features (ie, negative investigations).[2] Yet, it is a decision-making aid and is not intended to replace a comprehensive clinical assessment.[38]

Future blinded prospective validations in larger samples and diverse settings, including primary care, low-income countries and in populations with lower education profiles,[4] should be pursued before clinical use is recommended. We plan to explore the checklist's ability to discriminate between FCD and other mimics including atypical presentations of neurodegeneration, psychiatric diagnoses and cognitive effects of medications and sleep disorders,[15] and whether this instrument adds value to existing tools and biomarkers.[38] Future studies may also clarify whether the checklist can contribute to stratifying diagnostic workflow and referral, as well as reducing the need for costly, invasive and potentially harmful diagnostic tests with insufficient specificity. For instance, patients needing an assessment for neurodegeneration, who may be eligible for disease modifying therapies, might take the highest priority for specialised cognitive clinics, while FCD could be better managed in neuropsychiatry services with access to more appropriate therapies like psychotherapy and speech and language therapy.[39] Early identification of FCD also has implications for inclusion/exclusion criteria of disease-modifying therapies for



Positive if greater than or equal to	Sensitivity	Specificity	+PV	-PV
0	99	28	37	99
4	99	87	77	99
5	94	94	86	97
6	78	97	91	91
7	61	99	96	86
8	34	99	93	78
9	19	100	100	74
11	0	100	100	70

Positive if greater than or equal to	Sensitivity	Specificity	+PV	-PV
0	99	37	40	99
1	99	57	50	99
2	97	82	70	99
3	93	92	83	97
4	77	97	91	91
5	44	99	95	80
6	10	100	100	72
7	0	100	100	70

Figure 3 ROC curves for FCD versus other neurocognitive diagnoses (n=239). Full checklist (11 items) on the left, and brief version (7 items) on the right, with FCD as positive state. Coordinates of the ROC curve used to determine cut-off values under the respective curve. A cut-off point maximising specificity and +PV, while keeping a reasonable sensitivity was chosen (grey row). AUC, area under the curve; FCD, functional cognitive disorder; +PV, positive predictive value; –PV, negative predictive value; ROC, receiver operating characteristic.

neurodegenerative disorders and future FCD trials.[39 40] Last but not least, dissemination of the checklist serves an educational purpose by supporting history-taking and increasing the confidence of non-expert clinicians in diagnosing FCD and communicating this diagnosis with higher assurance.

Limitations

This pilot study has important limitations. The checklist was filled retrospectively and clinicians were not blinded, so diagnostic suspicion bias (ie, clinicians eliciting and accurately documenting the features included in the checklist in FCD patients only) cannot be excluded. This approach was chosen to obtain a larger sample size with at least 12 months follow-up to increase confidence in individual diagnoses. While problematic, this is somewhat mitigated by (1) multistep Delphi methodology with multidisciplinary expertise supported by literature; (2) information recorded prior to checklist development and (3) three clinicians involved in the diagnostic accuracy study had not contributed to the development of the checklist. Although the scale could not be filled in real time, this principally affected four items, which motivated the development of a briefer checklist that obtained similar preliminary accuracy. UK-based memory services focus on individuals under 65 years old, potentially limiting the generalisability of these findings, as seen by the modest sample size of other neurodegenerative diagnoses including vascular dementia and Lewy body dementia which predominantly affect older populations. Experienced clinicians may assimilate the information in a different way to those with lower expertise. A further potential criticism relates to the use of a clinical expert diagnosis as 'reference standard'. While from a scientific standpoint pathological support in all cases is desirable, our approach aligns with current pragmatic practices, multidisciplinary assessment and diagnostic criteria of FCD.[2] Yet, we cannot exclude that a small number of FCD patients may be in prodromal stages

of AD, even if 94% of our FCD sample was stable or improving at follow-up. In a previous position statement, this panel argued that conducting invasive tests for every patient would be rather impractical and economically unjustifiable when the diagnosis made by an expert is secure, risks false positive diagnoses and is dependent on local availability.[6] Practically, a small degree of overlap in the scores for the FCD and non-FCD groups is expected, but this made less than 6% and 8% of the patients with non-FCD in our sample, using the full and brief checklist, respectively. Borderline cut-offs should call for further investigations, and follow-up is advised. It is unknown whether the checklist can identify FCD patients with shorter symptom duration for which stability of symptoms or improvement over time may be difficult to judge. Because of these limitations, the checklist including cut-off scores will have to be validated prospectively in larger more diverse cohorts before clinical use is recommended.

CONCLUSIONS

A novel pilot checklist to identify FCD versus other neurodegenerative disorders may be a complementary clinical tool to facilitate an earlier and more accurate FCD diagnosis. Future prospective validation in diverse settings, by clinicians blinded for the diagnosis and with lower expertise, is needed to validate this checklist and assess for potential improvements in consistency and cost-effectiveness of FCD diagnosis and management.

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Competing interests LM receives funding from the Scottish Government Chief Scientist Office. LM provides independent medical testimony in court cases regarding patients with functional disorders, is secretary of the British Neuropsychiatry Association, and receives research funding from the Scottish Government Chief Scientist Office. JSch reports personal fees from UptoDate, outside the submitted work, runs a self-help website for patients with functional neurological symptoms (www. neurosymptoms.org) which is free and has no

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