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Predicting risk of 2-year incident dementia using the CAMCOG total and subscale scores

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Abstract

Background: being able to identify individuals at high risk of dementia is important for diagnostics and intervention. Currently, there is no standard approach to assessing cognitive function in older aged individuals to best predict incident dementia.

Objective: to identify cognitive changes associated with an increased risk of 2-year incident dementia using the Cambridge Cognitive Examination (CAMCOG).

Design: longitudinal population representative sample aged 65+ years.

Methods: individuals were from the Medical Research Council Cognitive Function and Ageing Study. Classification and Regression Tree analysis was used to detect the optimal cut-off value for the CAMCOG total, subscales and composite memory and non-memory scores, for predicting dementia. Sensitivity and specificity of each cut-off score were assessed.

Results: from the 2,053 individuals without dementia at the first assessment, 137 developed dementia at the 2-year follow-up. The results indicate similar discriminative accuracy for incident dementia based on the CAMCOG total, memory subscale and composite scores. However, sensitivity and specificity of cut-off values were generally moderate. Scores on the non-memory subscales generally had high sensitivity but low specificity. Compared with the CAMCOG total score they had significantly lower discriminative accuracy.

Conclusion: in a population setting, cut-off scores from the CAMCOG memory subscales predicted dementia with reasonable accuracy. Scores on the non-memory scales have lower accuracy and are not recommend for predicting high-risk cases unless all non-memory subdomain scores are combined. The added value of cognition when assessed using the CAMCOG to other risk factors (e.g. health and genetics) should be tested within a risk prediction framework.

Keywords: cognition, dementia risk prediction, Cambridge Cognitive Examination (CAMCOG), classification and regression tree (CART) analysis, predictive accuracy, older people

Introduction

Identification of individuals at high risk of dementia may be important for better targeting of services, improved care and risk factor reduction. Numerous methods for identifying high-risk cases exist including risk algorithms [1] or specific criteria for pre-clinical states such as Mild Cognitive Impairment (MCI) [2]. Despite differences, both methods typically include cognitive criteria such as impairments in global functioning or specific domains. However, there is currently no agreed method for assessing cognition in order to maximise dementia risk prediction. As a result large variation exists in the test selected, cut-off values for impairment [e.g. 1, 1.5 or 2 standard deviations (SDs) below the mean] and in adjustments made in the normative values (e.g. age and education) [2]. This heterogeneity makes cross-study comparison difficult [3]. Exploration of how to operationalise criteria for cognitive impairment in order to accurately predict dementia risk, determined by assessing the psychometric properties of neuropsychological assessments therefore warrants attention.

The CAMCOG is a brief neuropsychological battery that has been used to detect cognitive impairments in older aged adults and for dementia screening [4, 5]. Both total and subscale scores are able to differentiate individuals with and without dementia [6, 7], and MCI cases from control or dementia groups [8–10]. These results are, however, based on cross-sectional associations in clinical samples and do not inform about the utility of the CAMCOG for predicting dementia risk.

The aim of this study is to determine cut-off values for the CAMCOG total and subscale scores that are predictive of 2-year incident dementia using a population-based framework. We also compare the diagnostic accuracy of single subscale scores with that of the overall CAMCOG score for discriminating individuals who do and do not progress to dementia at 2 years to identify whether individual subscales can be useful for predicting incident dementia.

Methods

Study design and population

Data are from the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS) (<http://www.cfes.ac.uk>). Full details have been described previously [11]. Individuals aged 65 years and older were randomly selected from the Family Health Service Authority lists in England and Wales. In total, 13,004 participants were enrolled at baseline. Information on socio-demographics, health status, cognitive function [including the Mini-Mental State Examination (MMSE)] [12] and selected items from the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) [13] were collected. In a second phase, a subsample (20%, $n = 2,640$), was randomly selected according to age, centre and cognitive ability to complete a more detailed diagnostic assessment which included

the CAMCOG [13]. Individuals have been re-interviewed every 2 years. Data from the baseline, first assessment and 2-year follow-up interviews were used in the analyses.

CAMCOG

The maximum possible CAMCOG score in this study was 103 (after exclusion of the three items related to the tactile recognition of coins) [14]. Questions that may have been missed due to sensory/motor impairment were re-coded to 0 rather than treated as missing. Subscale scores were derived for: orientation, language comprehension and expression, perception, memory (learning, recent and remote), praxis, abstraction and attention and calculation. Summing scores only from the memory or non-memory subscales created composite scores. Participants could contribute to the analyses of subscales without having a complete CAMCOG total score.

Dementia

Dementia was derived using the full-AGECAT diagnostic algorithm [13] and defined as an AGECAT organicity rating case level of 3 or above. This is equivalent to diagnosis based on the Diagnostic and Statistical Manual of Mental Disorders III-R [15]. Dementia diagnosis was made independently of CAMCOG scores.

Statistical analysis

Analyses were undertaken using the R (2.10.1) software. Baseline differences in demographic variables between individuals with and without dementia at 2-year follow-up were tested using the Chi-squared test for categorical variables and the *t*-test for continuous measures. To identify cut-off values for the CAMCOG total and subscale scores for discriminating between individuals who do and do not develop dementia at 2 years follow-up, Classification and Regression Trees (CART) analysis was performed. The CART analysis was run with and without the addition of covariates (age, sex and years of education) and weighted for study design (inverse probability weighting was used to adjust for oversampling of older aged and more cognitively impaired individuals to complete the assessment interview). Inverse probability weighting provides a statistical approach to adjust for the selection method, enabling results to be generalisable to the originally screened sample (for further details of the sampling weights see: [16] and the study webpage <http://www.cfes.ac.uk/pages/bdata/index.html#Weights>). As the weighted and un-weighted results were similar, only the un-weighted results are presented. Diagnostic accuracy of each score was assessed using the area under the Receiver Operating Characteristic curve (AUC), sensitivity and specificity estimates. Differences between AUC estimates for the CAMCOG total score compared with the subscale and composite memory and non-memory scores were undertaken using Hanley and McNeil's method [17, 18].

Table 1. Characteristics of the non-demented baseline sample according to dementia status at 2-year follow-up

	Two-year status	
	No dementia (<i>n</i> = 1,210)	Dementia (<i>n</i> = 137)
Demographics		
Mean age at first assessment (SD) ^a	74.7 (6.8)	80.5 (7.8)
Mean years full-time education (SD) ⁺	9.8 (2.2)	9.4 (2.1)
Women (%)	774 (64.0)	92 (67.2)
CAMCOG scores at baseline ^b		
Memory		
Remote ^c	5 (4, 6)	3 (2, 4)
Recent ^c	4 (3, 4)	3 (2, 4)
Learning ^c	13 (12, 15)	10 (6.5, 12.5)
Non-memory		
Orientation ^c	10 (9, 10)	9 (8, 10)
Language comprehension ^c	9 (8, 9)	8 (7, 9)
Language expression ^c	18 (16, 19)	15 (13, 17)
Attention and calculation ^c	6 (4, 8)	4 (2, 6)
Praxis ^c	11 (9, 12)	9 (6, 10)
Abstract thinking ^c	6 (4, 7)	5 (2, 6)
Perception ^c	7 (6, 8)	5 (4, 7)
Composite scores		
CAMCOG total score ^c	87 (79, 92)	70.5 (60, 79)
Memory ^c	22 (20, 24)	17 (12, 19)
Non-memory ^c	65 (59, 69)	54 (47, 61)

^a*P* < 0.05.^bMedian [Quartile 1 (25th percentile), Quartile 3 (75th percentile)].^c*P* < 0.001.

Results

Sample characteristics

Of the 2,640 individuals interviewed at the first assessment, 587 were excluded with prevalent dementia. In total, 1,347 non-demented participants completed the 2-year follow-up interview. Of these, 137 developed dementia. Individuals with dementia were significantly older [$t(1,345) = 9.4$, $P < 0.001$] and had less years of education [$t(1,330) = 2.0$, $P < 0.05$]. Gender did not differ across groups [$\chi^2(1) = 0.5$, $P > 0.05$] (Table 1).

Prediction of 2-year incident dementia

Table 2 shows the CART analysis derived cut-off values for the CAMCOG total, subscale and composite scores. The CAMCOG total cut-off score of 80.5 had moderate sensitivity (72.1%) and specificity (79.6%) for predicting 2-year incident dementia, with an AUC of 0.76. Sensitivity and specificity were also over 70% for cut-off scores derived from the recent memory subscale and the composite memory score. In contrast, cut-off values derived for the non-memory subscale scores generally had low to high sensitivity (range: 64–96%), but low specificity (range: 16–62%). For the non-memory subdomain scores, the AUC estimate was low for all scales (range: 0.63–0.68). The composite non-memory cut-off value of 61.5 had sensitivity and specificity of 65 and 79%, respectively. Of all non-memory scores, the

Table 2. CART results and performance data for predicting 2-year incident dementia for the CAMCOG total, subscale and composite scores

	CART cut-off	<i>n</i> ^a	<i>m</i> ^b	Sensitivity	Specificity	AUC	95% CI	<i>P</i> -value comparing AUCs ^c
Memory								
Remote (range: 0–6)	11.5	1,273	294	0.81	0.66	0.74	(0.70–0.78)	0.0743
Recent (range: 0–4)	3.5	1,288	393	0.73	0.71	0.72	(0.68–0.77)	0.2527
Learning (range: 0–17)	4.5	1,286	522	0.63	0.78	0.71	(0.66–0.75)	0.5058
Non-memory								
Orientation (range: 0–10)	8.5	1,311	162	0.91	0.40	0.65	(0.61–0.70)	0.0004
Language comprehension (range: 0–9)	6.5	1,279	69	0.96	0.16	0.63	(0.59–0.68)	0.0001
Language expression (range: 0–21)	14.5	1,268	199	0.87	0.42	0.65	(0.60–0.69)	0.0003
Attention and calculation (range: 0–8)	4.5	1,279	409	0.71	0.58	0.67	(0.63–0.72)	0.0065
Praxis (range: 0–8)	7.5	1,274	154	0.90	0.34	0.68	(0.63–0.72)	0.0078
Abstraction (range: 0–8)	5.5	1,262	478	0.64	0.62	0.63	(0.58–0.68)	0.0001
Perception (range: 0–8)	5.5	1,272	321	0.78	0.53	0.65	(0.60–0.70)	0.0007
Composite scores								
CAMCOG total score (range: 0–103)	80.5	1,254	406	0.72	0.80	0.76	(0.72–0.80)	–
Memory (range: 0–27)	19.5	1,261	359	0.76	0.77	0.77	(0.73–0.81)	0.7289
Non-memory (range: 0–76)	61.5	1,231	473	0.65	0.79	0.72	(0.68–0.77)	0.2469

^a*n* = Number of individuals having the score (without individuals with missing score).^b*m* = Number of individuals classified as impaired based on a score less than or equal to the cut-off value.^cFour decimal places.

composite score had the highest accuracy for predicting 2-year incident dementia (AUC = 0.72). Cut-off scores derived by age, sex and education groups were roughly similar to those obtained in the whole sample (see Supplementary data available in *Age and Ageing* online, Tables 1 and 2).

Comparing diagnostic accuracy: CAMCOG total versus subdomain and composite scores

Table 2 shows the results of the comparisons of the AUC estimate of the CAMCOG total score with the subscale and composite scores. There were no differences in predictive accuracy between the total score and the individual memory subscale, composite memory and composite non-memory scores. For all other comparisons, the total score was significantly more accurate at identifying individuals who progress to dementia.

Discussion

In this study, we investigated the accuracy of the CAMCOG total and subscale scores for identifying individuals who do and do not progress to dementia over 2-year follow-up in a population representative sample. The results indicated that only some CAMCOG measures are useful for accurately predicting dementia risk.

We were restricted to cognitive assessment based on the CAMCOG. However, the CAMCOG provides both global and domain-specific measures of cognition and does not suffer from floor or ceiling effects [4, 14]. Impairments in cognitive function are typically defined using statistical cut-offs such as 1 or 1.5 SD below the mean. We chose to use CART analysis to determine the cut-off scores as it is a non-parametric classifier and therefore does not require assumptions of normality of the data, in contrast to other methodologies, such as cut-offs based on SDs. As with any study our results need to be replicated.

In this study, we found that a cut-off score derived from the CAMCOG recent memory subscale or the composite memory score could predict future dementia alone with moderate accuracy. The cut-off score derived from the learning memory subscale had high sensitivity with low specificity and the reverse was seen for the remote memory score. In principle, any CAMCOG memory subscale could be used to determine cognitive impairment associated with increased dementia risk.

In contrast, the results suggest that none of the cut-off values derived from any of the individual non-memory subscales were able to accurately identifying individuals at high risk of dementia. Alternative batteries that cover non-memory domains not tested by the CAMCOG such as executive function or information processing speed may better capture non-amnesic deficits, as poor performance on each has been previously associated with worse performance in early dementia [19]. However, the results do suggest that a

composite score based on all CAMCOG non-memory subscales was sufficient for predicting risk. However, combining scores did result in reduced sensitivity in favour of specificity.

Conclusion

If cognitive criteria are to be used to identify individuals at high risk of dementia, or to make an early diagnosis of dementia, their accuracy needs to be assessed. Currently there is no standard approach to measuring the cognitive impairment for predicting incident dementia or for diagnosing MCI. The results here suggest that cut-off scores based on the CAMCOG total or recent memory subdomain scores have reasonable accuracy for identifying high-risk cases and could be used within a dementia risk prediction framework. Further research is needed to determine the best measures for assessing non-memory deficits for predicting dementia risk.

Key points

- In a population setting, CAMCOG total and subscale scores may be used to predict individuals at high risk of incident dementia.
 - CAMCOG memory subscale scores could be used to predict risk of dementia with reasonable accuracy.
 - CAMCOG non-memory subscale scores are not recommended for predicting risk of dementia when only a single domain is impaired.
 - Further research is needed to determine the added value of including the CAMCOG total and subscale scores in dementia risk prediction algorithms that also incorporate other, non-cognitive risk factors (e.g. genetics).
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Conflicts of interest

The funding bodies had no role in the study design, data collection, analysis or decision to publish.

Ethical approval

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Supplementary data

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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