Chapter 13
The IQCODE: Using Informant Reports to Assess Cognitive Change in the Clinic and in Older Individuals Living in the Community

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Contents

Abstract The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) uses the report of an informant to assess an individual's change in cognition in the last 10 years. Unlike cognitive screening tests administered at one point in time, it is unaffected by pre-morbid cognitive ability or by level of education. When used as a screening test for dementia, the IQCODE performs as well as the Mini-Mental State Examination (MMSE), which is the most widely used cognitive screening instrument. Other evidence of validity comes from correlations with

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change in cognitive test scores, and associations with neuropathological and neuroimaging changes. The main limitation of the IQCODE is that it can be affected by the informant's emotional state. The IQCODE is suitable for use as a screening test in clinical settings, for retrospective cognitive assessment where direct data are not available, and for assessment in large scale epidemiological studies. Versions are available in many languages.

Keywords Dementia • Alzheimer's disease • Mild cognitive impairment • Cognitive decline • Screening • Informant • Validity • MMSE • Diagnosis • Stroke • Pre-morbid

13.1 Introduction

The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is a brief screening instrument designed to assess cognitive change in older populations based on informant reports [1]. To date its main applications have been in screening individuals for cognitive decline and dementia in large clinical or epidemiological studies, assessing pre-morbid cognitive status in clinical settings, or estimating cognitive change post stroke, trauma, or surgery. However, available evidence suggests that the IQCODE can be useful in many other situations where retrospective assessment of cognitive change is needed and an informant is available.

13.2 IQCODE History and Development

The IQCODE is based on a parent interview which required informants to respond to 39 questions assessing the magnitude of change over the previous 10 years in two cognitive domains: memory function (acquisition and retrieval) and intelligence (verbal and performance). Following an initial psychometric evaluation, the size of the questionnaire was reduced to 26 questions which were easy to rate and whose responses correlated well together. The new instrument was named IQCODE and was formatted for easy self-completion by informants. Questions take the form "Compared to 10 years ago, how is this person at . . ." (e.g. remembering things about family and friends such as occupations, birthdays, addresses, etc.). Informants are asked to respond to each question using a Likert scale ranging from 1, "much improved" to 5, "much worse" [2].

The size of the IQCODE has subsequently been further reduced to 16 items [2]. This short version is typically preferred and recommended since it has been found to be highly correlated with the full version (0.98) and to have equivalent validity against clinical diagnosis. The full questionnaire of the Short-IQCODE is presented in Table 13.1.

Table 13.1 Short (16-item) form of the IQCODE

Compared with 10 years ago how is this person at:					
	1	2	3	4	5
1. Remembering things about family and friends e.g. occupations, birthdays, addresses	Much improved	A bit improved	Not much change	A bit worse	Much worse
2. Remembering things that have happened recently	Much improved	A bit improved	Not much change	A bit worse	Much worse
3. Recalling conversations a few days later	Much improved	A bit improved	Not much change	A bit worse	Much worse
4. Remembering his/her address and telephone number	Much improved	A bit improved	Not much change	A bit worse	Much worse
5. Remembering what day and month it is	Much improved	A bit improved	Not much change	A bit worse	Much worse
6. Remembering where things are usually kept	Much improved	A bit improved	Not much change	A bit worse	Much worse
7. Remembering where to find things which have been put in a different place from usual	Much improved	A bit improved	Not much change	A bit worse	Much worse
8. Knowing how to work familiar machines around the house	Much improved	A bit improved	Not much change	A bit worse	Much worse
9. Learning to use a new gadget or machine around the house	Much improved	A bit improved	Not much change	A bit worse	Much worse
10. Learning new things in general	Much improved	A bit improved	Not much change	A bit worse	Much worse
11. Following a story in a book or on TV	Much improved	A bit improved	Not much change	A bit worse	Much worse
12. Making decisions on everyday matters	Much improved	A bit improved	Not much change	A bit worse	Much worse
13. Handling money for shopping	Much improved	A bit improved	Not much change	A bit worse	Much worse
14. Handling financial matters e.g. the pension, dealing with the bank	Much improved	A bit improved	Not much change	A bit worse	Much worse

(continued)

Table 13.1 (continued)

15. Handling other everyday arithmetic problems e.g. knowing how much food to buy, knowing how long between visits from family or friends	Much improved	A bit improved	Not much change	A bit worse	Much worse
16. Using his/her intelligence to understand what's going on and to reason things through	Much improved	A bit improved	Not much change	A bit worse	Much worse

Adapted versions of the IQCODE have also been produced to allow assessment in other languages (Arabic, Chinese, Dutch, Finnish, French, Canadian French, German, Italian, Japanese, Korean, Norwegian, Persian, Polish, Portuguese, Spanish, Thai and Turkish) or based on shorter [3–5] or more flexible [6] time frames than 10 years. Short forms of the IQCODE are also available in Spanish [7], Chinese [8], Portuguese [9] and in other languages (which to our knowledge have not been validated). In addition, in a recent review of the literature on dementia screening instruments suitable for self- or informant-assessment, particularly in a format that could be applicable for digital administration (e.g. computer-based or on the internet), the IQCODE was found to be one of three most promising instruments which warranted further validation for delivery on digital platforms [10].

13.3 Administration and Scoring

The IQCODE takes 10–25 min to complete depending on the form chosen (long/short) and whether it is administered in pen and paper form or electronically. It is generally perceived as easy to answer and can be mailed to informants or administered by telephone or by computer (although we are not aware of any validation data with non-pen-and-paper administration media).

Scoring the IQCODE requires adding up all ratings and dividing by the number of items, thus yielding a measure ranging from 1 to 5. An alternative scoring strategy used by some investigators involves using the sum of all responses as a summary measure. Norms have been developed by Jorm and Jacomb for 5-year age groups from 70 to 85+ years [11]. However, the use of an absolute cut-off, ranging from 3.3 to 3.6 in community samples to 3.4–4.0 in patient samples, is typically preferred and easier to communicate. A practical way of selecting a valid and effective cut-off is to identify studies (see Table 13.2) with characteristics most similar to the target population in the planned study and apply their cut-offs. Alternatively a weighted average computed from Table 13.2, of 3.3 for community samples and of 3.5 in patient samples, is also defensible (also note below, see Sect. 13.6, findings from systematic reviews which are consistent with the approach suggested above).

Table 13.2 Performance of the MMSE, and the long and short versions of the IQCODE as screening tests for dementia

Study	Sample	Diagnostic criteria	Cutoff	N	Mean age/ age range	Sens.	Spec.	ROC curve
MMSE								
Bustamante et al. (2003) [12]	Hospital out-patients and controls (Brazil)	1, 4	25/26	76	71	0.80	0.91	–
Callahan et al. (2002) [13]	Epidemiological study (USA)	1	23/24	344	74	0.95	0.87	0.96
Ferrucci et al. (1998) [14]	Geriatric clinic patients (Italy)	2	23/24	104	75	0.97	0.55	–
Flicker et al. (1997) [15]	Memory clinic patients (young, Australia)	1, 5	21/22	299	73	0.91	0.82	–
Flicker et al. (1997) [15]	Memory clinic patients (old, Australia)	1, 5	21/22	78	80	0.75	0.71	–
Forcano Garcia et al. (2002) [16]	Geriatric clinic patients (Spain)	1, 5	23/24	103	78	0.81	0.85	0.86
Gonçalves et al. (2011) [17]	Memory clinic patients (Australia)	2, 5	24/25	204	77	0.83	0.73	0.82
Isella et al. (2006) [18]	Cognitively normal volunteers and 45 MCI patients (Italy)	6	27/28	100	71	0.82	0.73	–
Jorm et al. (1996) [19]	Ex-servicemen (half former prisoners of war) (Australia)		23/24	144	73	0.45	0.99	0.81
Knafelc et al. (2003) [20]	Memory clinic patients (Australia)	1	23/24	323	75	0.84	0.73	0.86
Li et al. (2012) [21]	Neurology clinic patients with MCI (China)	6	26/27	928	70	0.89	0.76	0.85
Li et al. (2012) [21]	Neurology clinic patients with mild AD (China)	5, 8	24/25	554	70	0.81	0.84	0.91
MacKinnon et al. (1998) [22]	Memory clinic patients (Switzerland)	2, 5	23/24	106	80	0.76	0.90	–
Morales et al. (1997) [23]	Urban epidemiological study (Spain)	1	21/22	97	75	0.73	0.78	–

(continued)

Table 13.2 (continued)

Study	Sample	Diagnostic criteria	Cutoff	N	Mean age/ age range	Sens.	Spec.	ROC curve
Morales et al. (1997) [23]	Rural epidemiological study (Spain)	1	21/22	160	74	0.83	0.74	–
Nasreddine et al. (2005) [24]	Memory clinic patients (Canada)	2	25/26	183	75	0.78	1.00	–
Perroco et al. (2008) [9]	Old Age Clinic Patients with low education (Brazil)	1, 4	25/26	91	71	0.94	0.78	0.94
Swearer et al. (2002) [25]	Primary care clinic outpatients and independent retirement community residents (USA)	2	23/24	46	80	0.13	1.00	–
IQCODE (Long Version)								
Bustamante et al. (2003) [12]	Hospital out-patients and controls (Brazil)	1, 4	3.41+	76	71	0.83	0.97	–
De Jonghe et al. (1997) [26]	Psychiatric patients (49 with dementia) (Netherlands)	1	3.90+	82	78	0.88	0.79	–
Del-Ser et al. (1997) [27]	Neurology clinic outpatients (Spain)	1	3.62+	53	69	0.84	0.73	0.81
Flicker et al. (1997) [15]	Memory clinic patients (young, Australia)	1, 5	3.90+	299	73	0.74	0.71	–
Flicker et al. (1997) [15]	Memory clinic patients (old, Australia)	1, 5	3.90+	78	80	0.79	0.78	–
Fuh et al. (1995) [8]	Non-demented community resident and dementia patients (Taiwan)	1	3.40+	399	69	0.89	0.88	0.91
Hancock and Larner (2009) [28]	Memory clinic patients	2, 5	3.60+	144	67	0.86	0.39	0.71
Isella et al. (2006) [18]	Cognitively normal volunteers and 45 MCI neuropsychology out-patients (Italy)	6	3.45	100	71	0.84	0.75	–
Jorm et al. (1991) [29]	Patients seen by a geriatrician (Australia)	3, 4	3.60+	69	80	0.80	0.82	0.87
Jorm et al. (1994) [2]	Epidemiological study (Australia)	1	3.60+	684	70	0.69	0.80	0.77

Study	Sample	Diagnostic criteria	Cutoff	N	Mean age/ age range	Sens.	Spec.	ROC curve
Jorm et al. (1996) [19]	Ex-servicemen (half former prisoners of war) (Australia)	3	3.30+	144	73	0.79	0.65	0.77
Law and Wolfson (1995) [30]	Epidemiological study (Canada)	1	3.30+	237	81	0.76	0.96	–
Lim et al. (2003) [31]	Cognitively normal volunteers and 53 dementia patients (Singapore)	2	3.40+	153	–	0.94	0.94	–
Morales et al. (1997) [23]	Urban epidemiological study (Spain)	1	3.27+	97	75	0.82	0.90	0.89
Morales et al. (1997) [23]	Rural epidemiological study (Spain)	1	3.31+	160	74	0.83	0.83	0.83
Mulligan et al. (1996) [32]	Geriatric patients (Switzerland)	1	3.60+	76	82	0.76	0.70	0.86
Perroco et al. (2008) [9]	Old Age Clinic Patients with low education (Brazil)	1, 4	3.53+	91	71	0.85	1.00	0.94
Siri et al. (2006) [33]	Geriatric clinic patients (Thailand)	2, 5	3.42+	100	73	0.90	0.95	0.98
Stratford et al. (2003) [34]	Memory clinic patients (Australia)	4	4.00+	577	73	–	–	0.82
Tang et al. (2003) [35]	Stroke patients (China)	2	3.40+	189	68	0.88	0.75	0.88
Tokuhara et al. (2006) [36]	Japanese American primary care patients	5	3.40+	230	–	1.0	0.87	–
IQCODE (Short version)								
Ayalon (2011) [5]	Epidemiological study (USA)	1, 2	3.30+	462	80	0.77	0.93	0.89
Ayalon (2011) [5]	Epidemiological study (USA)	7	3.30+	441	79	0.55	0.93	0.89
Del-Ser et al. (1997) [27]	Neurology clinic outpatients (Spain)	1	3.88	53	69	0.79	0.73	0.77
Forcano Garcia et al. (2002) [16]	Geriatric clinic patients (Spain)	1, 5	3.62+	103	78	0.82	0.81	0.91
Gonçalves et al. (2011) [17]	Memory clinic patients (Australia)	2, 5	4.20+	204	77	0.72	0.67	0.77
Harwood et al. (1997) [37]	Medical inpatients (England)	1	3.44	177	65+	1.00	0.86	–
Jorm et al. (1994) [2]	Epidemiological study (Australia)	1	3.38	684	70+	0.79	0.82	0.85
Jorm et al. (1996) [19]	Ex-servicemen (half former prisoners of war) (Australia)	3	3.38+	144	73	0.75	0.68	0.77

(continued)

Table 13.2 (continued)

Study	Sample	Diagnostic criteria	Cutoff	N	Mean age/ age range	Sens.	Spec.	ROC curve
Knafelc et al. (2003) [20]	Memory clinic patients (Australia)	1	3.60+	323	44–93	0.94	0.47	0.82
Li et al. (2012) [21]	Neurology clinic patients with MCI (China)	6	3.19+	928	70	0.98	0.71	0.87
Li et al. (2012) [21]	Neurology clinic patients with mild AD (China)	5, 8	3.31+	554	70	0.89	0.78	0.90
MacKinnon et al. (1998) [22]	Memory clinic patients (Switzerland)	2, 5	3.60+	106	80	0.90	0.65	–
Narasimhalu et al. (2008) [38]	Dementia clinic patients and stroke patients (Singapore)	2	3.38+	576	66	0.78	0.86	0.89
Perroco et al. (2008) [9]	Old Age Clinic Patients with low education (Brazil)	1, 4	3.53+	91	71	0.85	1.00	0.96
Phung et al. (2015) [39]	(Lebanon)	2	3.35+	236	65+	0.92	0.94	
IQCODE-MMSE (3MS) (Combined)								
Bustamante et al. (2003) [12]	Hospital out-patients and controls (Brazil)	1, 4	25/26 or 3.41+	76	71	0.83	0.98	–
Flicker et al. (1997) [15]	Memory clinic patients (young, Australia)	1, 5	21/22 or 4+	299	73	0.86	0.57	–
Flicker et al. (1997) [15]	Memory clinic patients (old, Australia)	1, 5	21/22 or 4+	78	80	0.92	0.61	–
Hancock and Larner (2009) [28]	Memory clinic patients	2, 5	23/24 or 3.60+	144	67	0.95	0.36	–
Khatchaturian et al. (2000)† [40]	Stratified population survey (USA)	5, 8	86/87 or 3.27	839	~81 65–90	0.98	0.68	0.96
Knafelc et al. (2003) [20]	Memory clinic patients (Australia)	1	Weighted sum	323	44–93	0.91	0.63	0.88

[1]DSM-IIIR Dementia, [2]DSM-IV Dementia, [3]ICD-9, [4]ICD-10 Dementia, [5]Clinical diagnosis, [6]Mild Cognitive Impairment (Petersen 1996 criteria), [7]Cognitive Impairment No Dementia (CIND), [8]NINCDS-ADRDA, † using the 3MS

13.4 Psychometric Characteristics

The reliability and validity of the IQCODE have been thoroughly researched. Its internal consistency assessed using Cronbach's alpha can be viewed as excellent and has been found to range between 0.93 and 0.98 across 11 studies [1, 8, 9, 11, 22, 23, 35, 41–44]. Receiver Operating Characteristic (ROC) curve analysis of the predictive value of single Short-IQCODE questions indicates that individual items have areas under the curve of more than 0.80 except for item 7 (0.75), which further confirms the internal consistency of the questionnaire (i.e. all questions are good at predicting dementia) [9]. In addition, test-retest reliability has been shown to be very good over short and long periods, with correlations of 0.96 over 3 days and 0.75 over 1 year [11, 29].

The structure of the IQCODE has been examined through factor analysis in several studies. All found a large main factor thought to represent "cognitive decline" and accounting for 42–73 % of the variance, while other factors were small, explaining at most 10 % of the variance [8, 11, 23, 26, 42, 44].

13.5 Validation Against Clinical Diagnosis

The validity of the IQCODE against clinical diagnosis has been demonstrated in multiple studies. Table 13.2 presents sensitivity and specificity statistics of the long and short forms of the IQCODE and the MMSE against clinical diagnoses [2, 5, 8–10, 12–20, 22–25, 27–32, 34, 35, 37, 38, 40, 41, 45, 46]. The IQCODE characteristics compare well with those of the MMSE, which suggests that it is a valid screen for dementia and that in some circumstances it may be a more sensitive instrument. However, moderate correlations between the IQCODE and the MMSE in 15 studies (4,538 participants) ranging from −0.245 to −0.78 [5, 28, 45, 47] with a sample-size weighted average of −0.49 suggest that these two tests, although largely overlapping, have each some unique variance. As a consequence, a number of studies have investigated whether the concurrent administration and scoring of the IQCODE and the MMSE improves dementia detection. They have generally reported somewhat increased sensitivity and/or specificity of the combined tests, but cost-benefits of this combination varied depending on the methodology or the type of sample used [12, 15, 20, 22, 28, 32, 45].

In any case, where the MMSE is selected as the main screening instrument, the IQCODE can be used as an alternative screening test when individuals are not able to complete it and in order to minimize missing values. For example, in a survey of 839 community-based older individuals, Khachaturian et al. [40] found 74 subjects who were unable to complete the Modified Mini-Mental State (3MS; see Chap. 4 at Sect. 4.2.2) but for whom the IQCODE could be completed by an informant. Seventy-one of these were subsequently diagnosed with dementia.

In addition to being a screening tool for dementia, the IQCODE has also been investigated as a predictor of Mild Cognitive Impairment (MCI). Isella et al. found that the IQCODE was as sensitive as the MMSE for discriminating between MCI and healthy controls in an Italian neuropsychology out-patient clinic (sensitivity 0.82, specificity 0.71 for a cut-off of 3.19) [18] and Li et al. found that the IQCODE (sensitivity 0.90, specificity 0.82 for a cut-off of 3.19) was somewhat superior to the MMSE (sensitivity 0.87, specificity 0.75 for a cut-off of 26/30) at detecting MCI in a Chinese neurology clinic [21]. In addition, while the IQCODE was a good predictor of conversion from MCI to dementia over a 2-year follow-up period (sensitivity 0.84, specificity 0.75 for a cut-off of 3.45), the MMSE was not a significant predictor. In another study which included 441 participants with an average age of 79 years and using the clinical criterion of Cognitive Impairment No Dementia (CIND), Ayalon et al. reported that the IQCODE (based on ratings of change over the previous 2 years) had moderate sensitivity (0.55) but excellent specificity (0.93) in discriminating between CIND and normal controls (with a cut-off of 3.30) [5].

The validity of the IQCODE has also been assessed using post-mortem dementia diagnosis based on histological analyses. One study using a cut-off of 3.7 and a neuropathological diagnosis of Alzheimer's disease found the IQCODE to have a sensitivity of 73 % and a specificity of 75 % [48]. Another study used a cut-off of 3.42 and a diagnosis of AD, vascular or mixed dementia, and reported a sensitivity of 97 % and a specificity of 33 % [49].

The IQCODE is not generally useful in differential diagnosis of specific neurodegenerative diseases, although one study found that patients with behavioral variant frontotemporal dementia scored higher than those with probable Alzheimer's disease [50].

13.6 Systematic Reviews

Three recent systematic reviews with meta-analyses investigating the IQCODE's performance in different settings were recently conducted by the Cochrane Collaboration. The first systematic review [51] focused on studies investigating community-dwelling populations and summarized effects reported in ten articles meeting the selection criteria, while also considering the impact of different IQCODE thresholds and contrasting the long and the short form of the questionnaire. It found that, in general, sensitivity and specificity of the IQCODE were above 75 % and that using different typical thresholds, between 3.3 and 3.6, made relatively little difference to screening performance (see Table 13.3). Moreover, no difference in test accuracy was detected between the short and the long form or between the English and non-English versions. The authors concluded that, while the IQCODE performance can be considered reasonable, its widespread application as a screening tool in community or population settings would lead to substantial misdiagnosis and therefore may not be appropriate [51].

Table 13.3 Performance of the IQCODE at different thresholds and in different settings (community and secondary care) based on Cochrane reviews [51, 52]

Setting	Community				Secondary care			
Measures / Thresholds	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio	Negative likelihood ratio	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio	Negative likelihood ratio
3.3	0.80 (0.75–0.85)	0.85 (0.78–0.90)	5.27 (3.70–7.50)	0.23 (0.19–0.29)	0.91 (0.86–0.94)	0.66 (0.56–0.75)	2.7 (2.00–3.60)	0.14 (0.09–0.22)
3.4	0.84 (0.70–0.93)	0.80 (0.65–0.90)	4.25 (2.47–7.90)	0.19 (0.10–0.35)	0.94 (0.44–0.98)	0.73 (0.59–0.85)	3.50 (2.10–5.80)	0.01 (0.03–0.20)
3.5	0.82 (0.75–0.87)	0.84 (0.80–0.88)	5.09 (4.08–6.33)	0.22 (0.16–0.29)	0.92[a]	0.63[a]	[a]	[a]
3.6	0.78 (0.68–0.86)	0.87 (0.71–0.95)	6.00 (2.72–13.26)	0.25 (0.18–0.34)	0.89 (0.85–0.92)	0.68 (0.56–0.79)	2.8 (1.90–4.00)	0.02 (0.10–0.20)

Note that while a similar review was conducted in primary care [53], only a single study [36] was identified and therefore robust summary estimates could not be computed

[a]Summary estimates could not be computed as only one study was available at this threshold

A second Cochrane systematic review [53] investigated the IQCODE within a primary care setting. It only identified a single study [36] (N = 230, sensitivity 1.00, specificity 0.87 at 3.4 threshold) meeting the inclusion criteria, whose methodology was rated as having a high risk of bias. This led the authors to conclude that at this stage it is not possible to provide definitive guidance on the IQCODE's performance in this context [53].

The third Cochrane systematic review focused on the IQCODE's performance within a secondary care setting [52]. Pooled analyses of 13 studies meeting inclusion criteria and representing data from 2,745 individuals, including 1,413 patients with dementia, found that there was no difference in test accuracy between the short and the long form or between the English and non-English versions. However, the test performed somewhat better in non-memory settings (e.g. in- and out-patient hospital wards; sensitivity 0.95, specificity 0.81) compared to memory settings (e.g. memory clinics or geriatric wards; sensitivity 0.90, specificity 0.54). Across all settings, little performance difference was observed when using different thresholds, with a sensitivity at or above 0.89 and a specificity ranging from 0.63 to 0.73 (see Table 13.3). Due to the relatively low specificity but high sensitivity of the IQCODE in this context, the authors concluded that it would be particularly useful in ruling out those without evidence of cognitive decline [52].

13.7 Neuropsychological Correlates

In addition to studies specifically aimed at validating the IQCODE against some other standard, a number of studies have investigated associations between IQCODE ratings and neuropsychological functioning. IQCODE scores were found to be significantly associated with the following cognitive domains in neuropsychological testing: executive function (visual verbal test, Trail Making Test B [47]); language (Boston Naming Test [47]; Verbal Conceptual Thinking [54]); memory (CERAD word list, WMS-R logical memory [47]; Verbal Memory [54]); and attention (Trail Making Test A [47]; Forward Digit Span [54]).

The IQCODE has also been validated against change in cognitive tests over time. In a community sample, scores on the IQCODE were found to correlate with change over 7–8 years in the MMSE, episodic memory and mental speed [55]. In another study which surveyed women living in the community aged 60 years and above, IQCODE scores were found to be associated with change in language, memory, and attention [47].

In another study, Slavin et al. [56] used a modified version of the short IQCODE with a 5 year timeframe to assess associations between subjective memory difficulties reported by participants, informant reports, and objective memory impairment on neuropsychological tests in a cohort including individuals with (n = 493) and without impairment (n = 334). While participants' reports of subjective memory difficulties did not differ between those with and without impairment, informants' reports did, with a mean score of 2.42 in those with no objective memory impairment, 3.51 in those with difficulty in one memory domain, and 3.91 in those with difficulties in multiple memory domains. Higher scores on the IQCODE have also been found to be

positively associated with major, but not minor, depressive symptoms, and with increased difficulties in instrumental activities of daily living (IADLs) [57].

13.8 Neuroimaging Correlates

If the cognitive changes estimated with the IQCODE are due to progressive conditions such as dementia and other neurodegenerative diseases, these changes would be expected to be associated with concurrent or precursor changes in brain health. Indeed a number of studies have reported such associations. For instance, in a community sample of older ex-servicemen, Jorm et al. [19] found significant associations between the IQCODE and the width of the third ventricle ($r = 0.29$), and infarcts in the left ($r = 0.35$) and right ($r = 0.26$) hemispheres. Cordoliani-Mackowiack et al. [58] reported significant correlations between leukoaraiosis ($r = 0.38$) and IQCODE in elderly stroke patients, while another study found that leukoaraiosis accounted for 18 % of variance in IQCODE scores [54]. Henon et al. [59] found significantly higher mean IQCODE scores in individuals with smaller medial temporal lobe measures. In a diffusion tensor imaging study of stroke patients, Viswanathan et al. [60] detected lower diffusion measures in the non-affected hemisphere, which were interpreted as showing decreased cerebral tissue integrity in those whose pre-morbid cognition was above a cut-off of 3.4 on the IQCODE (i.e. indicating that the side of the brain not affected by stroke was structurally impaired in those with a higher score). High scores on the IQCODE have also been associated with greater cerebral atrophy [61, 62]. Moreover, Henon et al. [59] studied 170 consecutive stroke patients who underwent a CT scan at admission and for whom an informant completed the IQCODE. They found that 55.3 % of patients who were rated 104 or above on the long version of the IQCODE had medial temporal lobe atrophy compared to only 5.3 % of those who scored below this cut-off.

13.9 Alternative Applications

Although the IQCODE was developed to assess cognitive decline from a pre-morbid state in older populations, it has also been successfully applied in other contexts.

13.9.1 Retrospective Estimate of Cognitive Change

It would generally be preferable to assess baseline cognition before events that may adversely affect cognition occur. However, there are many occasions when such events cannot be foreseen or where conducting a baseline assessment is either impractical or unlikely to produce reliable results. In such cases the IQCODE can be a useful instrument to estimate cognitive change once acute effects of injury or treatment have waned.

13.9.1.1 Post Surgery

Rooij et al. [63] investigated the cognitive and functional outcomes of planned and unplanned surgical interventions in a population of older (>80 years) individuals after a follow-up of 3.7 years. The IQCODE was used to assess cognitive decline. Of 169 individuals assessed, 17 % were found to have a severe cognitive impairment (IQCODE > 3.9) and 56 % were found to have mild to moderate impairment (3.9 > IQCODE > 3.1). Importantly, those patients who underwent unplanned surgery were found to have a more than twofold increased risk of cognitive impairment at follow-up. It should be noted that this study has significant limitations, as cognitive status prior to surgery was not available and could explain the events leading to unplanned surgery and/or the subsequent assessment of cognitive impairment. Nevertheless, in such clinical contexts the IQCODE can provide useful information on cognitive change potentially relating to clinical factors which otherwise could not have been studied in this cohort.

13.9.1.2 Post Pharmacological Treatment

The IQCODE may be used as a supplementary outcome measure following pharmacological treatments or intervention where neuropsychological measures are also available. For example, in a randomized controlled trial of B-vitamin aimed at lowering homocysteine levels in 266 MCI individuals to optimize cognition, the IQCODE was used as a clinical outcome [64]. B-vitamin treatment was associated with decreased homocysteine levels and improved cognition on executive function (but not the MMSE, episodic or semantic memory, or delayed recall). Treatment was also associated with better IQCODE and CDR scores in those with homocysteine levels in the top quartile. By contrast, the IQCODE was not found to be useful in a study by Aaldriks et al. [65] which used it to estimate cognitive change following different doses of chemotherapy for cancer treatment. Although cognitive decline was detected with other instruments post treatment, the IQCODE was not found to be sensitive to these changes.

13.9.1.3 Post Stroke or Trauma

The IQCODE has been shown to be a predictor of incident dementia in stroke patients [3, 66] and in non-demented hospital in-patients [67] over 2–3 year follow-ups. Moreover, Tang et al. [35] reported that in a population of 3 months post-stroke patients, where the IQCODE was validated against a clinical diagnosis of dementia (DSM-IV), the IQCODE had good psychometric characteristics (sensitivity 88 %, specificity 75 %), albeit not sufficient for use of the IQCODE as a sole dementia screening instrument. These findings have been further confirmed by a recent meta-analysis which showed that the IQCODE was generally effective at detecting post-stroke dementia with a sensitivity of 81 % and a specificity of 83 % [68]. However,

application of the IQCODE to complex clinical populations should be considered carefully, as at least one study found that the IQCODE and the MMSE were poor at detecting dementia in a sample of first-ever stroke patients [69].

Nonetheless, the IQCODE can be used to detect cognitive decline pre-dating stroke or trauma to avoid misattributing cognitive change to a clinical event when impairment was pre-existing. For example, Jackson et al. [70] used the IQCODE with a cut-off of 4 to determine whether cognitive impairment detected post traumatic brain injury was due to this injury or whether it was pre-existing; they found that one patient, representing 3 % of the sample, had pre-existing cognitive impairment. In another study, Klimkowicz et al. [61] were interested in assessing factors associated with pre-stroke dementia. Using the long version of the IQCODE with a cut-off of 104, they estimated that 12 % of 250 stroke patients had likely suffered from pre-stroke dementia and found that old infarcts on CT, cerebrovascular disease, and gamma-globulin levels at admission were the strongest factors associated with pre-stroke dementia. Moreover, based on patients' IQCODE classification, they found that those with post-stroke dementia were more likely to carry a variant of the Alpha-1-antichimotrypsin gene (which contributes to increased amyloid plaque formation) than controls or those classified as suffering from pre-stroke dementia [71].

13.9.2 Prospective Risk Assessment

Priner and colleagues [72] assessed the short form of the IQCODE as a predictor of postoperative delirium following hip or knee surgery. Using a cut-off of 3.1, they found that those with pre-existing impairment at admission had a more than 12-fold increased risk of delirium. In another study, the pre-morbid cognitive status of stroke patients was assessed retrospectively with the IQCODE and those with a score greater than 4 were found to be at higher risk of developing epileptic seizures [73] and of dying [74]. Pasquini et al. also investigated the risk of institutionalization in stroke patients [75] and found that those with an IQCODE score greater than 4 at admission had a higher risk of being institutionalized 3 years later.

13.9.3 Self-Assessment with the IQCODE

It is unclear whether cognitive decline can be assessed by self-report, as neurodegenerative diseases are also associated with a progressive loss of insight. To investigate this question, a version of the IQCODE adapted for self-report (the IQCODE-SR) has been produced. Jansen et al. [43] investigated whether using the IQCODE as a self-report instrument was feasible. They administered the questionnaire by mail to 2,841 individuals (58.9 % of target population) recruited while visiting their general practitioner. More than 60 % of participants reported completing

the questionnaire without help. While IQCODE-SR scores were not validated against clinical diagnoses, patients suspected of having dementia by their GP scored higher than those who were not (3.7 vs 3.3). Moreover, the authors found that the questionnaire had good internal consistency and concluded that "the IQCODE-SR meets the basic requirements of a good measurement instrument" [43].

Using data from a 3-year longitudinal study, Gavett et al. compared informant- and self-IQCODE ratings at the final assessment with performance and change in performance on a range of neuropsychological tests [47]. They found that while the informants' ratings correlated negatively with the participants' cognitive performance on all tests, associations between self-report and cognitive measures were weak and mixed. More important, however, is that the change in informant ratings over 3 years was significantly associated with change in cognitive performance but also with the subject's report of increased depressive symptomatology and decrease in Instrumental Activities of Daily Living. This suggests that as greater impairment was reported by informants, independently assessed measures of functioning were also declining.

Recently, the validity of the IQCODE-SR was investigated against cognitive decline in a large longitudinal study of ageing, the PATH Through Life project [57]. In a cohort of 1,641 individuals followed-up over 8 years, IQCODE-SR ratings were found to be associated with decline in processing speed, but not with performance in a number of cognitive domains, including verbal fluency, working memory, and immediate and delayed recall. Higher IQCODE-SR scores were also modestly associated with report of IADL problems and with the APOE E4 genotype.

Finally, Ries et al. [76] investigated the cerebral correlates of self-awareness in MCI. They computed a discrepancy score between self-rated and informant-rated IQCODE scores as a measure of awareness and also asked individuals to reflect on whether adjectives presented to them described them accurately while undergoing functional Magnetic Resonance Imaging (fMRI). Analyses showed that in MCI individuals, decreased activation in the medial frontal cortex and posterior cingulate were associated with increased discrepancy scores, suggesting that decreased awareness has an organic origin in cognitive impairment. An implication of this research is that, as disease processes progress, self-assessment on the IQCODE or other instruments is unlikely to be reliable. There is, however, the possibility that in addition to informant reports, discrepancy scores between informant- and self-reports might provide useful additional information.

In aggregate, the findings reviewed suggest that the IQCODE-SR may be somewhat indicative of objective cognitive and functional decline, but is also strongly influenced by depressive symptomatology. This is not surprising in itself, since depression and loss of insight are known risk factors/correlates for AD and other dementias. However, the implication of the available evidence is that the IQCODE-SR is not a robust indicator of cognitive decline by itself, but could be useful as a complement to the IQCODE ratings and should be investigated further.

13.10 Bias and Limitations

A concern for all instruments assessing cognition is they may be influenced by factors unrelated to the construct they have been designed to assess, such as sociodemographic, ethnic, language, gender, clinical, or cultural characteristics of the person being assessed. For example, performance on the most widely used dementia screening test, the MMSE, has been found to be influenced by gender, age, education, socio-economic status, occupation, cultural background, language spoken at home and presence of a mood disorder [77, 78]. The IQCODE has been found to be minimally influenced by education [2, 8, 11, 27, 30, 32, 41, 79, 80] and by proficiency in the language of the country of residence [81]. On the other hand, the IQCODE can be biased by informant characteristics. Informants who are depressed, anxious or stressed tend to report greater cognitive decline than indicated by direct cognitive testing [47, 82], so the emotional state of the informant needs to be considered when interpreting IQCODE scores. Furthermore, two recent studies have found that IQCODE scores from African-American informants are less sensitive to CIND than those of white informants [83, 84]. One of these studies attributed this difference to the lower average level of education in African-Americans [83].

13.11 Conclusion

The IQCODE is a simple, quick, and valid instrument to assess cognitive change. It can be administered in paper form, on the telephone, or in electronic format. It has been mainly validated in older populations, but recent evidence suggests it is a useful tool to investigate change in cognitive status in clinical contexts.

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