

Does your loved one with cognitive symptoms need to see a doctor? Check it on-line

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Submitted to Journal:
Frontiers in Computational Neuroscience

Article type:
Brief Research Report Article

Manuscript ID:
840200

Received on:
29 Dec 2021

Revised on:
19 Jun 2022

Journal website link:
www.frontiersin.org

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

Author contribution statement

All the authors contributed to the conceptualization, methodology design, and review of the analysis of the study data. García Ribas G drafted the manuscript, all other authors contributed to the final form and approved the manuscript.

Keywords

cognitive decline, cognitive symptoms, memory problems, Dementia, Online questionnaire, Alzheimer's disease, IQCODE, AD8

Abstract

Word count: 212

Widespread access to emerging information and communication technologies (ICT) allows its use for screening of diseases in the general population. At the initiative of the Spanish Confederation of Associations of Families of People with Alzheimer's disease and other dementias (CEAFA), a website (<http://www.problemasmemoria.com>) has been created that provides information about Alzheimer's disease and include questionnaires to be completed by family or friends concerned about memory problems of a relative. A cross-sectional, randomized, multicenter study was performed to evaluate feasibility, validity, and user satisfaction with an electronic method of completion versus the current method of paper-based questionnaires for clinically dementia screening completed by the informants: the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) and the Alzheimer's disease-8 screening test (AD8). A total of 111 pairs were recruited by seven memory clinics. Informants completed IQCODE and AD8 questionnaires both in their paper and electronic versions. The correlation between paper and electronic versions was significantly positive for IQCODE ($r = 0.98$; $p < 0.001$) and AD8 ($r = 0.96$; $p < 0.001$). The execution time did not differ significantly, and participants considered their use equally easy. This study shows that an electronic version of the IQCODE and AD8 questionnaires are suitable for its on-line use via internet and achieve the same results as the traditional paper versions.

Contribution to the field

This is the first study to compare an informant-based method of cognitive impairment screening on paper with its online version. The electronic versions of the IQCODE and AD8 questionnaires presented on the website www.problemasmemoria.com constitute a valid and reliable method, comparable to the paper versions for dementia and cognitive impairment detection, with high rates of acceptability by informants evaluating the subjects, who perform this activity in a reasonably short time. These results warrant further studies to validate the diagnostic performance of the electronic versions administered on-line and their contribution to reduce the time to diagnosis and improve early detection of AD and other dementias.

Funding statement

CEAFA Spanish Confederation of Associations of Families of People with Alzheimer's disease and other dementias sponsored the study.

Ethics statements

Studies involving animal subjects

Generated Statement: No animal studies are presented in this manuscript.

Studies involving human subjects

Generated Statement: The studies involving human participants were reviewed and approved by Hospital Regional Universitario Carlos Haya. The patients/participants provided their written informed consent to participate in this study.

Inclusion of identifiable human data

Generated Statement: No potentially identifiable human images or data is presented in this study.

Data availability statement

Generated Statement: The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

In review

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21 **Keywords:** Cognitive decline¹, cognitive symptoms², memory problems³, dementia⁴, online
22 questionnaires, Alzheimer⁶, IQCODE⁷, AD8⁸

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24 **Number of words:** 2739

25 **Number of figures:**0

26 **Number of tables:** 2

27 Abstract

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29 screening of diseases in the general population. At the initiative of the Spanish Confederation of
30 Associations of Families of People with Alzheimer's disease and other dementias (CEAFA), a
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42 version of the IQCODE and AD8 questionnaires are suitable for its on-line use via internet and
43 achieve the same results as the traditional paper versions.

44 1 Introduction

45 Dealing with the negative consequences of population aging is one of the most important endeavors
46 that health and care-giving systems face, globally. Dementia, particularly Alzheimer's disease (AD),
47 constitutes a fundamental part of this challenge [1]. Among the problems posed by these diseases,
48 procrastinated diagnosis stands out, in particular, leading to delayed management. The existence of
49 effective secondary prevention measures [2] and palliative care [3] makes the delay in diagnosis even
50 more excruciating. It is estimated that even in developed countries, only 20%-50% of patients are
51 correctly diagnosed [4].

52 To improve the early detection of AD several strategies have been proposed, with varying degrees of
53 clinical applicability and cost-effectiveness. These include routine screening of the general
54 population, patients seen in primary care or nursing home residents [5, 6]. It should be noted that
55 biomarkers with good properties of sensitivity and specificity and readily applicable to asymptomatic
56 or early symptomatic populations at risk are not yet available [7, 8]. This leads to an initial disease
57 suspicion still based on cognitive and/or functional complaints that are noticed by patients and/or
58 relatives and considered abnormal enough to seek a consultation [9]. Most screening techniques are
59 based on the assessment of the affected subject, raising the issue of lack of awareness of illness, often
60 already present in the initial stages of it [10, 11], and strongly affecting the initiative or willingness to
61 be evaluated. In addition, the practical difficulties of conducting a direct assessment of many
62 potential patients have led to considering distance interviews, either by telephone [12], or the internet
63 [13, 14].

64 Furthermore, although the role of relatives and/or proxies in the support and care of the patient with
65 AD is fundamental and well established [15], their role in the early detection of symptoms as the first
66 step leading to the correct diagnosis is often limited and unrecognized [16]. The delay in a correct
67 assessment of the importance of initial symptoms is usually due to incorrect attribution of these
68 symptoms to aging or other clinical entities, such as depression [17]. Patients and proxies may
69 usually have doubts as to whether a particular symptom should lead to seek consultation or not.

70 Taking all the evidence so far, it seems that a good way to enhance the detection of AD in its early
71 stages would be to make available internet-based screening tests for proxies of potential patients with
72 cognitive impairment.

73

74 This is the main motivation for carrying out the AIPAD-online study described below. Its aim is to
75 demonstrate the validity of the online application of a screening test for cognitive impairment, based
76 on the evaluation of an informant with good knowledge of the patient, versus its traditional paper
77 form.

78 **2 Methods**

79 A randomized, multicenter, cross-sectional study was designed to analyze the feasibility, validity and
80 user satisfaction with the electronic completion method as compared to the usual paper-based
81 standard method.

82 After approval by the Ethics Committee of the Hospital Regional Universitario Carlos Haya, the
83 study was conducted in the Departments of Neurology, Geriatrics or Psychiatry of seven centers
84 distributed across the Spanish territory. A convenience sample of 100 to 120 caregivers was
85 estimated, allowing half of the participants starting with electronic completion method and the other
86 half starting with paper-based method of questionnaire completion.

87 Inclusion criteria comprised subjects older than 50 years who attend as caregivers of outpatients in a
88 specialized memory clinic. The caregiver (informants) must have sufficient knowledge of the
89 patient, usually a first-degree relative or partner living in the same patient's home, as required by the
90 screening paper versions of the test, and willing to sign an informed consent. Informants having any
91 physical or mental problem were excluded.

92 The primary objective of the AIPAD-online study was the evaluation of the feasibility of the
93 electronic version of two questionnaires for dementia screening, namely IQCODE (Informant
94 Questionnaire on Cognitive Decline in the Elderly) short version [18], and AD8 (Alzheimer's
95 Disease) [19] and their correlation with the traditional paper version previously translated and
96 validated into Spanish [20-23]. Both questionnaires were completed by the same informant.

97 Informants completed both the electronic and paper versions of the questionnaires one at the
98 beginning of the visit and the other at the end. The version order was randomly assigned. A website
99 was developed [www.problemasmemoria.com] and sponsored by the Spanish Confederation of
100 Associations of Families of People with Alzheimer's disease and other Dementias (CEAFA) for the
101 electronic version of the questionnaires, and previously validated paper version were used [20-23].
102 The sentence formulation of the items was identical in both versions.

103 The IQCODE questionnaire is a tool for detection of cognitive impairment and dementia in older
104 people that is completed by a caregiver or family member with a relationship with the patient for at
105 least five previous years. The short version of the IQCODE can be completed in 10-15 minutes with
106 almost no influence of education [18]. The questions refer to the situation of the elderly person
107 compared to the one they presented five or ten years ago. Each question is answered with a five-point
108 Likert-type scale with scores ranging from 1 (to 5: Much improvement = 1 point; Little improved = 2
109 points; It has hardly changed = 3 points; It has gotten a little worse = 4 points; It has gotten very bad
110 = 5 points. The total score is calculated by the sum of the scores divided by 17, so the final score

111 range is 1 to 5 points. A higher score means greater cognitive decline. Cronbach's alpha coefficient
 112 has been calculated in seven studies, with a range of 0.93-0.97. The total score can also be calculated
 113 with the sum of the scores for each question, with a range of 17 to 85 points [18].

114 The AD8 questionnaire is a very brief informant questionnaire containing just 8 yes/no questions. Its
 115 diagnostic accuracy for both cognitive decline, dementia and AD has been subjected to rigorous
 116 validation. The total score of the AD8 is equal to the number of affirmative answers [19].

117 Demographic variables of the patients and informants, questionnaire results in both versions, the time
 118 for completion of the questionnaires in both systems, and a questionnaire for satisfaction and
 119 usability of both versions were collected in an ease-of-use Likert type scale ranging from 1 (not easy
 120 at all) to 5 (very easy). To obtain a description of the sample, in subsequent visits, clinical diagnostic
 121 impression was collected, based on the NINCDS-ADRDA criteria for probable AD as patients with
 122 Alzheimer disease was the only diagnosis observed [24], or Petersen criteria for mild cognitive
 123 impairment [25]. No other dementia severity assessment was recorded for the study.

124 Statistical analysis included descriptive quantitative and qualitative variables of the sample and the
 125 Spearman's correlation between the IQCODE and AD8 questionnaires in their paper versus electronic
 126 versions. The SPSS 14.0 statistical analysis program (Chicago, IL.) for the study of the data was
 127 used.

128 **3 Results**

129 A sample of 118 cases in electronic format and 113 cases in paper format was obtained. Seven
 130 questionnaires/patients did not meet the inclusion criteria and consequently the final sample consisted
 131 of 111 cases for which information was available both electronically and in paper format. A total of
 132 73 patients (65.8%) and 75 of informants (65,6%) were women. Mean age was 77.8 years-old (range,
 133 60-97) for patients and 57.4 years-old (range, 32-92) for informants.

134 The most frequent educational levels of patients were basic education (ISCED levels 1-2.
 135 REFERENCIA (International Standard Classification of Education, ISCED 2011, UNESCO)in 66
 136 patients (59.5%), Upper secondary education (ISCED level 3) in 13 patients (11.7%), and university
 137 education (ISCED levels 4-8) in 21 patients (18.9%). Eleven patients (9.9%) did not have education
 138 level. For the informants, the percentages were 29 (26.1%) with basic education, 39 (35.1%) with
 139 upper secondary education and 42 (37.8%) with university education, with only one informant
 140 (0.9%) without education level. The type of relationship of patients with the informants was most
 141 commonly a sibling in 57 (51.8%) and partner in 30 (27.3%). Most informants, 79 (71.2%), saw the
 142 patient daily, 19 (17.1%) saw the patient every 2-3 days, and 12 (10.8%) saw the patient once-a-
 143 week. In one case (0.9%) the patient was visited once a month. Reasons for the consultation were
 144 memory loss in 66 patients (60%), behavioral disorder in 10 patients (9.1%) and cognitive
 145 impairment not otherwise specified in 14 patients (12.7%). Combined consultation reason was
 146 observed in 21 patients (21%). Data was not detailed in one patient.

147 A total of 57 patients (51.3%) included met the NINCDS-ADRDA criteria for probable AD and 42
 148 (39.3%) of them met the criteria for mild cognitive impairment (MCI). Four patients were not
 149 classified for either MCI or probable AD.

150 Total scores of the IQCODE and AD8 questionnaires are displayed in Table 1. In the case of the total
 151 scores calculated as a sum of the responses, the scores were converted to a percentage scale to make

152 them more readily interpretable. No significant statistical differences were observed in the mean
153 scores between electronic and paper questionnaires versions.

154 User satisfaction was very similar for electronic and paper versions (Table 1). Spearman's correlation
155 coefficient was calculated to analyze the degree of association between easiness of completion of the
156 electronic and paper versions of the IQCODE ($r = 0.84$) and AD8 ($r = 0.88$) questionnaires.
157 Correlations were high, positive, and statistically significant ($p < 0.01$). Consistent with this high
158 degree of association between the electronic and paper versions, there were not statistically
159 differences between the ease of completion of the two versions of the IQCODE and AD8
160 questionnaires. Completion times of the scales were similar, although slightly higher in the case of
161 electronic versions (Table 1). Also, internal consistency and reliability analysis was high for both test
162 in paper and electronic versions (Table 1).

163 The analysis of the correlation in the two versions of the tests, convergent validity, were very high as
164 shown in Table 2.

165 **4 Discussion**

166 This is the first study to compare an informant-based method of cognitive impairment screening on
167 paper with its online version, showing no significant statistical differences between both
168 administration methods. Methods of screening for AD by traditional methods - usually questionnaires
169 on paper that are self-completed or completed by an informant - have shown good predictive
170 achievement [26]. The performance of similar procedures through a website involves uncertainties
171 related to the ecological environment of the application of the test or questionnaire that raise
172 questions that this study aims to answer. These questions primarily involve the fact of whether there
173 are any differences when answering to the questionnaire through the computer media compared to
174 the traditional method by people with varying degrees of familiarity with the use of computers,
175 especially informants of a certain age.

176 In addition, the design of the website containing the evaluation procedure should have specific
177 characteristics of simplicity, ease of use and minimization of use options to reduce variability. The
178 creation of the website www.problemasmemoria.com containing the assessment questionnaires
179 entailed a series of discussions by experts and reviewing various versions until arriving at the final
180 version, which is the one that was tested and that appears at the website above. Its content includes
181 basic data in relation to both the person being evaluated and the evaluator, and additional information
182 of a clinical nature concerning the individual being evaluated. The fundamental core of the website
183 includes the assessment of the potential patient. This is done through the versions validated in Spain
184 of the two questionnaires that are most widely used for the detection of dementia based on the data
185 given by an informant: the IQCODE and AD8 questionnaires [27-29]. The inclusion of both
186 instruments was designed to compare the performance of both questionnaires and possibly to decide
187 using only one in the case of develop a shortened version for the website.

188 Questionnaires were selected based on the evaluation of the informant to avoid the tendency of
189 patients with cognitive impairment to minimize their deficits and therefore unconsciously distort the
190 results and also because, despite its convenience, these potential patients may not want to cooperate
191 in assessing their own cognitive or functional abilities.

192 The sample taken for the comparative study of the online and paper versions of the two assessment
193 instruments does not differ from the population that regularly came for specialized consultation for
194 memory or cognitive complaints from the socio-demographic point of view and neither in relation to

195 caregivers. It should be noted that the highest proportion of caregivers was made up by children of
196 the person being evaluated, who had a nearly daily relationship with the person.

197 The results of the paper and online versions of the two questionnaires were virtually identical. The
198 reliability and convergent validity were highly significant, with the Cronbach's alpha values in the
199 upper range. In addition, both ease of use and satisfaction of the informants was similar for both the
200 paper as well as the electronic versions, which provides strong support for the electronic application.
201 Both versions were completed in a similar amount of time, though marginally longer in the electronic
202 version, probably related to the lower familiarity with operating a computer versus the use of paper.
203 In both cases, it involved a reasonably short time.

204 This experience of dementia screening supported by a website available online is the first to use the
205 information from an informant. There are other experiences, but they are based on information
206 provided by the subject being evaluated, primarily based on the performance of cognitive tests moved
207 to the internet. Thus, Dougherty et al. [30] used a new battery of multi-domain cognitive tests with a
208 period of application lasting more than 15 minutes. Therefore, this requires a good level of
209 cooperation from the subject being evaluated. Brandt et al. [31] also use for this purpose an episodic
210 memory test that is not yet validated. This involves a time for encoding information so requires the
211 subject to be evaluated as a collaborator. Wesnes et al, [32] have reported positive preliminary data
212 using a new cognitive battery of four tests validated in their paper version, but not online. The results
213 of these experiments are only partially comparable to that presented here, as they involve direct
214 evaluations of the subject rather than information gathered by a reliable informant, although all of
215 them reinforce the idea that this type of screening is feasible and has acceptable predictive
216 capabilities.

217 Our study has limitations such as the number of participants and the selection bias in relation to a
218 sample recruited in the medical setting. Also, the study was limited to patients with cognitive
219 symptoms, so all questionnaires had high values. We did not consider including a control group of
220 volunteers with no cognitive complaints as we expected that the visits to the webpage mainly will be
221 of people worried about initial cognitive symptoms. Although 10.8% of the informants saw the
222 patient every week, and this could derive in lower knowledge about the patient mental status, all the
223 informants fulfilled the requirement of the validated questionnaires, and the way they are usually
224 applied. However, in our opinion, these limitations do not invalidate the primary objective of the
225 study: to evaluate the possible differences between traditionally presented tests versus a test
226 conducted in an online platform. A limitation to transfer these results to the general population is the
227 difficulty to access internet in some socioeconomic levels. There is a cultural constraint for some
228 population groups that has been called digital illiterates. For this reason, our study evaluates tests
229 designed for caregivers and relatives of patients who often have younger age and more access to the
230 internet. However, we believe that limited access to the internet will become less important in the
231 future, even for elderly populations. Although the work was performed long before the COVID-19
232 pandemics, it raises more importance of the availability of web-based questionnaires minimizing in-
233 office consultations. The electronic version of the questionnaire proposed in this work might add a
234 new useful tool for the becoming years as this pandemic, or others to come, will change our
235 interpersonal and patient-doctor relationships.

236 In conclusion, the electronic versions of the IQCODE and AD8 questionnaires presented on the
237 website www.problemasmemoria.com constitute a valid and reliable method, comparable to the
238 paper versions for dementia and cognitive impairment detection, with high rates of acceptability by
239 informants evaluating the subjects, who perform this activity in a reasonably short time. These results

240 warrant further studies to validate the diagnostic performance of the electronic versions administered
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242 other dementias.

243 **Conflict of Interest**

244 The authors declare that the research was conducted in the absence of any commercial or financial
245 relationships that could be construed as a potential conflict of interest.

246 **Author Contributions**

247 All the authors contributed to the conceptualization, methodology design, and review of the analysis
248 of the study data. García Ribas G drafted the manuscript, all other authors contributed to the final
249 form and approved the manuscript.

250 **Funding**

251 CEAFA Spanish Confederation of Associations of Families of People with Alzheimer's disease and
252 other dementias sponsored the study.

253 **Acknowledgments**

254 This research was an initiative of CEAFA Spanish Confederation of Associations of Families of
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256 **Contribution to the Field Statement**

257 This is the first study to compare an informant-based method of cognitive impairment screening on
258 paper with its online version. The electronic versions of the IQCODE and AD8 questionnaires
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264 early detection of AD and other dementias.

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362 **Table 1. Summary statistics of the total scores of the IQCODE and AD8 questionnaires, ease of**
 363 **use, completion times and reliability.**

	Mean (SD)*
Mean score (range of scores, from 1 = he/she has improved much to 5 = he/she has become much worse)	Electronic IQCODE 4.08 (0.65) Paper IQCODE 4.05 (0.64)
Total score IQCODE (maximum 100)	Electronic IQCODE 71.39 (20.39) Paper IQCODE 70.24 (21.56)
Total score AD8 (maximum 8)	Electronic AD8 5.66 (2.36) Paper AD8 5.70 (2.21)
Ease of use (range from 1 = not easy at all to 5 = very easy)	Electronic IQCODE 3.88 (0.92) Paper IQCODE 3.95 (0.84)
	Electronic AD8 4.06 (0.79) Paper AD8 4.07 (0.73)
Completion time for electronic IQCODE	03:32 min (01:38)
Completion time for paper IQCODE	03:08 min (01:08)
Completion time for electronic AD8	01:41 min (00:50)
Completion time for paper AD8	01:44 min (00:56)
Reliability of the electronic and paper versions of the IQCODE and AD8 questionnaires	Cronbach's Alpha
	Electronic IQCODE 0.95
	Paper IQCODE 0.96
	Electronic AD8 0.79
	Paper AD8 0.75

364 *P>0.05 for all the electronic versus paper versions comparisons.

365

366

367 **Table 2. Spearman's correlation between the versions of the IQCODE and AD8 questionnaires.**

	Paper AD8 Total Score	Paper IQCODE Sum Score	Paper IQCODE Total Score
Electronic AD8 Total score	0.96(*)		
Electronic IQCODE Sum Score		0.98(*)	
Electronic IQCODE Total score			0.98(*)

368 * The correlation is significant at two-tailed p-value of 0.01

In review