Validation study of a French version of the modified Telephone Interview for Cognitive Status (F-TICS-m) in elderly women

Running Title: Validation of TICS-m in French

Keywords: TICS-m; telephone screening; cognitive impairment; dementia; MMSE; validation; elderly

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Key points

1. Characterization of cognitive status in large-scale epidemiologic studies is challenging.

2. Cognitive assessment by telephone represents an interesting cost-effective method.

3. In a sample of 120 community-dwelling French women, the Telephone Interview for Cognitive Status (F-TICS-m) showed satisfactory concurrent validity against the gold-standard classification from a neuropsychological examination.

4. Our results are consistent with previous evaluation studies in other languages and settings to support the validity of TICS-m to appraise global cognitive functioning.

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ABSTRACT

Objective: To evaluate the performance of a French version of the modified Telephone Interview for Cognitive Status (F-TICS-m) in identifying cognitive decline among elderly women.

Methods: All women aged 72-86 participating in the "Etude Epidémiologique auprès de Femmes de l'Education Nationale" (E3N) cohort and living in or near Paris constituted the target population of the validation study. Volunteer women (n=120) underwent both a 20-min telephone interview and a face-to-face neuropsychological examination at an interval of few days (median interval: 10 days). The telephone interview included F-TICS-m, as well as a recall of key elements of a short story, arithmetic/verbal problems and two verbal fluency tests. Neuropsychological examination consisted of a standardized battery of cognitive tests (including the Mini-Mental State Examination (MMSE), the Free and Cued Selective Reminding Test-FCSRT, Trailmaking tests A and B, the similarities subtest of the Wechsler Adult Intelligence Scale-III…) and the Instrumental Activities of Daily Living questionnaire and the Geriatric Depression Scale. Neuropsychological examination led to classification of each subject as cognitively normal (n=92) or impaired/demented (n=28).

Results: F-TICS-m showed satisfactory internal consistency (Cronbach's alpha=0.69). It correlated linearly with MMSE (Pearson's r=0.72). Concurrent validity against the gold-standard classification was satisfactory, with an area under the ROC curve (AUC) of 0.83. The combination of F-TICS-m and the other telephone tests had no additional effect on discrimination power in our sample (AUC=0.81).

Conclusion: F-TICS-m is a valid instrument for assessing the overall cognitive status of French elderly women. Its validity in men and its reproducibility warrant further studies.

INTRODUCTION

Dementia is an important public health concern, with a prevalence that is rapidly increasing with population ageing (Kalaria *et al.,* 2008). In the absence of curative treatments, prevention has become a crucial challenge, and epidemiologic studies on risk factors in cognitive decline are warranted. However, progress in the field has been hampered by difficulties in evaluating cognitive status in large populations. Health care data are unable to exhaustively identify dementia cases due to underdiagnosis (Kurz *et al.,* 2001; Tyas *et al.,* 2006; Falagas *et al.,* 2007). Consequently, epidemiologic studies on cognitive decline/dementia must develop active strategies for characterizing cognitive status. Conventional in-person neuropsychological assessment techniques are the gold-standard for identifying the cognitively impaired, but this approach is costly, especially in geographically dispersed studied populations. Telephone interviews provide an interesting alternative, since they are inexpensive and well accepted by elderly subjects. Thus, several telephone-administered cognitive tests have been developed during the last two decades (Ball and McLaren, 1997). In particular, the Telephone Interview for Cognitive Status (TICS) (Brandt *et al.,* 1988) has been broadly modelled on the Mini-Mental State examination (MMSE) (Folstein *et al.,* 1975), currently the most widely used screening instrument for cognitive impairment (Shulman *et al.,* 2006), though initially designed for face-to-face administration. The modified TICS-m (Brandt *et al.,* 1993; Welsh *et al.,* 1993) is a further refinement of the TICS instrument: a delayed recall task was added in order to broaden cognitive scope and accuracy.

The English version of TICS-m has demonstrated its value as a screening instrument in various populations (Welsh *et al.,* 1993; Plassman *et al.,* 1994; Gallo and Breitner, 1995; de Jager *et al.,* 2003; Lines *et al.,* 2003) and has been used in several Anglo-Saxon

epidemiologic studies (Grodstein *et al.,* 2003; Barber and Stott, 2004; Crooks *et al.,* 2005). Furthermore, TICS and/or TICS-m have been translated into many languages and evaluated: Spanish (Gude *et al.,* 1994), Finnish (Jarvenpaa *et al.,* 2002), Hebrew (Beeri *et al.,* 2003), Italian (Ferrucci *et al.,* 1998; Dal Forno *et al.,* 2006), Japanese (Konagaya *et al.,* 2007) and German (Loerbroks *et al.,* 2008), but not yet French.

The objective of the present study was to evaluate the performance of a French version of TICS-m (F-TICS-m) as compared with conclusions from a complete neuropsychological examination. The validation study was conducted in the framework of the "Etude Epidémiologique de Femmes de l'Education Nationale" (E3N) study (Vercambre *et al.,* 2009).

METHODS

Subjects and procedure

The target population for the present study included all E3N cohort participants born between 1925 and 1930, alive at the beginning of the validation study and living in or near Paris. All eligible women were contacted by mail or telephone and informed of the purpose of the research and procedure. Volunteers able to speak/understand French and who had no hearing impairment underwent a telephone interview and were invited to undergo a standard neuropsychological examination at Paul Brousse Hospital (Villejuif, France) within two weeks. Those who participated in this second step were included in the validation study. At the end of the examination, results were communicated to the participant and a report was sent to her physician.

Telephone interviews and face-to-face examinations were conducted between September 2007 and September 2008. All study subjects signed an informed consent form in compliance with the rules of the French National Commission for Computed Data and Individual Freedom (Commission Nationale Informatique et Libertés) from which we obtained approval.

The F-TICS-m instrument

The French version of TICS-m (available on www.idf.inserm.fr/site/eri20/page.asp?page=785) compiles all translated items from the English version of either the TICS or TICS-m questionnaires. Minor modifications of culture-dependent questions were made (e.g. the question concerning the present American vice-president was changed to a question about the last French president). Moreover, we chose to follow the BEC96 method (Signoret, 1989) for the 10-word list memory task: 10 words from the Alzheimer's Disease Assessment Scale (Mohs, 1996) were given three times (each followed by a free recall); then, following other questions, there was a delayed recall without

prior presentation. In the total, only scores from the first and last recalls were taken into account.

Ultimately, the F-TICS-m instrument included consecutive questions evaluating temporal and spatial orientation (scored on 5 and 3 points, respectively); the immediate recall task of the10-word list (scored on 10 points); the attention and calculation tasks of the MMSE (serial 7s and spell backwards) (scored on 6 points); six questions evaluating semantic memory (scored on 6 points); a delayed recall of the 10-word list (scored on 10 points); and two tasks involving language (repetition of two complex sentences and comprehension of a simple command) (scored on 3 points). Thus, F-TICS-m had a maximum score of 43.

Telephone interview

Each telephone interview was carried out by one of the two neuropsychologists involved in the project (HC and LL). Before beginning cognitive assessment, the neuropsychologist asked the respondent if she was alone in a quiet room with no pen or pencil and no temporal information within easy reach (newspaper, calendar, agenda). F-TICS-m administration was followed by four other cognitive tests (feasible by telephone) that were added to increase sensitivity to non-Alzheimer dementia. These additional tests were proposed in the following order: a recall of key elements of a short story (subtest of Wechsler's clinical memory scale, third edition (Wechsler, 2001)); arithmetic /verbal problems; and two verbal fluency tests (name as many words starting with "s" as possible within one minute; name as many fruits as possible within one minute). The latter three tests were chosen from the BEC96 battery (Signoret, 1989). At the end of the telephone interview, self-rated morale was appraised through a simple question ("How was your mood over the last two weeks: good, average, or poor?"). The telephone interview lasted no more than 20 minutes (10 minutes for F-TICS-m and 10 minutes for other tests).

Neuropsychological examination

Within two weeks after the telephone interview (median delay: 10 days), each participant underwent a complete standardized examination by a neuropsychologist (HC or LL). This included anamnesis, a cognitive test battery and other questionnaires, as cited below. The cognitive domains evaluated were, by order: (1) global cognitive functioning: French version of MMSE (Derouesne *et al.,* 1999); (2) memory: 16 words of the Free and Cued Selective Reminding test or FCSRT (Van der Linden *et al.,* 2004); (3) executive function: Trail Making tests A and B (Tombaugh, 2004); (4) visual-constructive capacities: Clock Drawing test (Shulman, 2000); (5) autonomy: four Instrumental Activities of Daily Living (Barberger-Gateau *et al.,* 1999); (6) depression: Geriatric Depression Scale-15 items (Sheikh and Yesavage, 1986); (7) language: a French picture-naming test (DO80) (Deloche and Hannequin, 1997) and lexical evocations (Cardebat *et al.,* 1990); and (8) reasoning: similarities subtest of the Wechsler Adult Intelligence Scale-III (Wechsler, 2000).

Gold-standard classification

After all examinations had been carried out, two neuropsychologists blinded to telephone scores (HC and IHL) classified participants according to results from the neuropsychological examination. Criteria were approved by an experienced geriatrician (CT). Four groups were observed: (1) normal cognitive status (cognitive scores within age- and education-adjusted norms), (2) mild cognitive impairment (according to Ravaglia et al. (Ravaglia *et al.,* 2008): deficit in one cognitive domain, but no evidence of functional dependency), (3) possible dementia (poor scores in many cognitive domains, but not so pathological and/or possibly related to depression), and (4) probable dementia (abnormal scores in many cognitive

domains with impact on autonomy). To evaluate discriminative ability of F-TICS-m, we contrasted scores of cognitively healthy women (1) with cognitively impaired women (2+3+4).

Statistical analysis

In order to assess the performance of the French version of TICS-m, we consecutively evaluated its internal consistency, construct validity and concurrent validity (i.e. discriminative ability) (Gifford and Cummings, 1999), but first, we evaluated selection biases in our study, in comparing women included in the analysis sample with the rest of the female target population and with women who participated only in the telephone interview. We described then distribution and covariates of F-TICS-m. Cronbach's alpha was calculated to evaluate the performance of the set of F-TICS-m items at measuring a single unidimensional latent construct (internal consistency); Pearson's correlation was used to quantify the linear relationship between F-TICS-m and MMSE scores (construct validity). To assess concurrent validity, we compared F-TICS-m distribution according to the gold-standard cognitive status as defined through the neuropsychological examination. We also carried out receiver operating curve (ROC) analysis (Swets, 1979), which summarizes the discriminative ability of the instrument as a whole. We computed the area under the curve (AUC statistics) for different cognitive tests and compared them with each other: F-TICS-m, F-TICS (F-TICS-m from which the delayed recall score had been post-hoc subtracted) and face-to-face MMSE. In addition, in order to determine whether F-TICS-m performance could be improved by adding other telephone tests, we compared discrimination statistics obtained with F-TICS-m alone to those obtained with the overall telephone score, constructed as the average of the five Z-scores to the different cognitive tests comprising the telephone interview.

Since sensitivity and specificity do not indicate whether the test will provide the correct screening result, we also calculated F-TICS-m positive and negative predictive values for different cut-off points.

All statistical analyses were performed using SAS software, version 9.1 (SAS Institute, Inc., Cary, NC). All results were considered significant at the 5 % level. All statistical tests were two-sided.

RESULTS

Selection and subject characteristics

Among 726 eligible E3N participants, 310 responded to our mailing/telephone contact. Among them, 121 women refused to participate and 4 no longer fulfilled the inclusion criteria (e.g. they had moved out of the Paris area). Among the 185 women who took part in the telephone interview, 65 did not undergo the neuropsychological examination, mainly due to motor impairment. Finally, the validation sample included 120 women. Among them, face-to-face neuropsychological examination identified 28 who were cognitively impaired (6 probable dementia, 4 possible dementia and 18 mild cognitive impairment). The remaining 92 women were considered to have no cognitive impairment.

Compared to non-included women, those who had participated in both the telephone interview and face-to-face examination were somewhat younger (mean age: 78.8 vs. 79.2 years old, p-value in the Wilcoxon-Mann-Whitney test =0.01) and more likely to have responded to all E3N questionnaires (73.3% vs. 49.5%, p-value in Chi^2 test <0.001). No significant difference was found in education level (p-value to the Chi^2 test = 0.53). Compared to included women, those who were interviewed only by telephone did not differ significantly in terms of F-TICS-m score, age, education level or self-reported morale, but they were less likely to have responded to all E3N questionnaires than those who underwent neuropsychological examination (58.5% vs. 73.3%, p-value to the Chi^2 test = 0.04).

Distribution and covariates of F-TICS-m

In the 120-woman validation sample, observed F-TICS-m scores ranged between 16 and 40, with a mean (SD) of 32.6 (4.2). Cut-off points for first, second and third quartiles were, respectively, 31, 33 and 35.

F-TICS-m statistics among the 92 cognitively normal women are presented in Table 1 by age group, level of education, E3N compliance status and self-reported morale. On average, women in the younger age group had higher F-TICS-m score (p<0.05). More educated women tended also to score higher (p=0.06). The F-TICS-m score in intellectually intact women was associated neither with E3N compliance nor with self-reported morale.

Internal consistency and construct validity

In our data, Cronbach's alpha of F-TICS-m equalled 0.69. F-TICS-m correlated linearly with face-to-face MMSE score, with a Pearson's correlation coefficient of 0.72.

Discriminative ability

Compared to women in the normal group, both groups of women with mild cognitive impairment and possible or probable dementia had a significantly lower mean F-TICS-m score (p-values in Wilcoxon-Mann-Whitney test ≤ 0.001) (Table 2).

AUC statistics for F-TICS-m, F-TICS, face-to-face MMSE and overall telephone score equalled, respectively, 0.83, 0.78, 0.72 and 0.81 (Figure 1). F-TICS-m outperformed both F-TICS and MMSE, with sensitivity and specificity values higher for the majority of score cut-offs. As compared with overall telephone score, F-TICS-m alone did not present less satisfactory overall discriminative capacity.

Discrimination statistics for cognitive impairment are presented in Table 3 for selected cut-points of the F-TICS-m score. For instance, specificity, sensitivity and positive and negative predictive values were 0.89, 0.68, 0.66, and 0.90, respectively, for a cut-off of 30, and 0.60, 0.86, 0.39, and 0.93, respectively, for a cut-off of 33.

DISCUSSION

In our sample of elderly French women participating in the E3N cohort, F-TICS-m proved to be efficient at identifying cognitive impairment. In addition, combining F-TICS-m with four other cognitive telephone tests did not appreciably improve its discriminative ability, thus supporting the validity of F-TICS-m alone to appraise global cognitive functioning. Our results are consistent with previous evaluation studies of TICS (Dal Forno *et al.,* 2006; Konagaya *et al.,* 2007) and TICS-m (Welsh *et al.,* 1993; de Jager *et al.,* 2003) in other languages, which demonstrated the widespread usefulness of this instrument. More specifically, the 10-word delayed recall of the TICS-m provides valuable information on cognitive assessment, since use of this task appears to improve discriminative accuracy in our sample of highly functioning women.

Some limitations of the present study have to be discussed. First, the rather low response and completion rates may have resulted in biases when non-responders differed substantially from responders in terms of the studied characteristics. Besides, the number of cognitively-impaired women was small compared with the number of non-impaired women, as expected in a population setting. Although statistics are less robust than with larger numbers, our sample size is consistent with previously published validation studies of cognitive tests by telephone (de Jager et al., 2003; Jarvenpaa et al., 2002; Konagaya et al., 2007). On the whole, women participating in the validation study showed largely intact cognitive ability (only 7 scored below 25 points on MMSE in face-to-face examination). Thus, the prevalence of impairment in our study may well have been lower than that of the general population and positive predictive value may have been underestimated. Second, the study sample comprised only women, precluding extending our findings to male populations; moreover, participants were mainly former teachers and thus highly educated. Nevertheless, the English version of TICS-m had previously shown no difference between men and women, nor between low and

high education groups (de Jager *et al.,* 2003), suggesting that the F-TICS-m may be used at the population level. Third, we cannot rule out the possibility that subtle variations in ratings may have occurred among the raters, although the telephone interview and neuropsychological examination were highly standardized. Our data did not enable calculation of test-retest and inter-rater reliability. However, studies involving other language versions have suggested good reproducibility (Dal Forno *et al.,* 2006; Loerbroks *et al.,* 2008). Indeed, in a sample of 35 educated, highly functioning older women which was similar to our sample, a test-retest study of two TICS assessments at 31-day intervals showed a correlation of 0.7 (Kang *et al.,* 2007).

Our study has several strengths. It is the first to evaluate a French version of TICS-m. In addition, all participants underwent the same type of confirmatory assessment (regardless of telephone screening results), thus excluding verification bias (Donald and Van Til, 2001). Another strong feature of our study was that it involved a sample from the general population (i.e. a population with a relevant basal rate of impairment) rather than using a case-control design (that would artificially exclude subjects with intermediate cognitive decline or specific dementia etiology). Although performance statistics are generally lower in the former context (because of a more heterogeneous range of cognitive abilities), it provides more reliable cut-off points for screening purposes (Ritchie and Fuhrer, 1996) and is essential for demonstrating accuracy at detecting any type of impairment, rather than just one specific type (Cullen *et al.,* 2007).

Our data, along with previous studies, plead for the usefulness of a simple test such as TICS-m to efficiently evaluate cognitive function by telephone. Although large batteries of neuropsychological tests are essential in the psychogeriatrics field to make an accurate and reliable diagnosis, TICS-m is particularly suitable for large-scale community screening and/or

epidemiological follow-up: in addition to its low cost, it can be rapidly administered, which ensures better acceptability, especially among the cognitively-impaired and the physically-impaired elderly, who may not be strongly motivated to participate. Despite its advantages, however, TICS-m, like other telephone tests, is not adapted to detecting cognitive difficulties involving praxies and visual-spatial capacities. Moreover, its use is limited to subjects without hearing problems and those with non-reduced social contact.

Interestingly, TICS-m distribution was shown, in previous reports, and in our highly educated population, more symmetric and normal-shaped than MMSE distribution, suggesting that TICS-m is less subject to the ceiling effect that habitually limits MMSE. This statistical characteristic, which is probably due to the difficulty involved in the 10-word memory task (de Jager *et al.,* 2003), makes TICS-m more sensitive for detecting early cognitive impairment than TICS or MMSE alone. This difference between TICS and TICS-m has been reported previously (Welsh *et al.,* 1993), but it appeared more clear-cut in our sample of highly educated women.

In conclusion, our results support the reliability of F-TICS-m for assessing cognitive function in a French female population. Its use in men and its reproducibility warrant further studies, but our results already suggest promising perspectives in the field of geriatric epidemiology.

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Table 1.   F-TICS-m statistics according to selected characteristics of the 92 cognitively

normal women included in the validation study sample

	n	Mean score (SD)	Range	P-value*
Age				
<80 years	63	34.3 (2.8)	22-40	
+80 years	29	33.2 (2.7)	28-38	0.046
Education level				
< 12 years	16	32.4 (4.1)	22-38	
≥ 12 years	76	34.2 (2.4)	28-40	0.064
E3N compliance status				
At least one missing questionnaire	24	33.9 (2.6)	28-38	
No missing questionnaire	68	33.9 (2.9)	22-40	0.89
Self-rated morale				
Good	47	34.1 (2.5)	28-40	
Average	28	34.3 (2.5)	29-38	0.12
Poor	17	32.6 (3.7)	22-37	0.16

F-TICS-m: French version of the modified TICS; SD: standard deviation

* Wilcoxon-Mann-Whitney Test

Table 2. F-TICS-m statistics according to cognitive status as assessed through face-to-face neuropsychological examination

Cognitive status	n	Mean score (SD)	Min	Q1	Median	Q3	Max	P-value*
Normal	92	33.9 (2.8)	22**	32	34	36	40	
Mild cognitive impairment	18	30.9 (3.6)	25	28	30/31	33	37	0.001
Possible or probable dementia	10	23.7 (4.5)	16	23	25	26	30	<0.001

F-TICS-m: French version of the modified TICS; SD: standard deviation; Q1, Q3: first and third quartiles

*Wilcoxon-Mann-Whitney Test

** One woman in the "normal" group, with a 22 F-TICS-m score was highly depressed (the next low score observed in this group was 29). Although she presented slight executive troubles associated with depressive symptoms, she was classified as normal from the dementia point of view, considering her overall test performing

Table 3.   Discrimination statistics for selected cut-off points applied to F-TICS-m score

to identify cognitive impairment.

Cut-off point	Specificity	Sensitivity	Positive predictive value	Negative predictive value
34	0.47	0.86	0.33	0.91
33	0.60	0.86	0.39	0.93
32	0.71	0.75	0.44	0.90
31	0.83	0.71	0.56	0.90
30	0.89	0.68	0.66	0.90
29	0.95	0.54	0.75	0.87
28	0.98	0.50	0.88	0.87
27	0.99	0.46	0.93	0.86

Figure 1.   ROC analysis for cognitive impairment screening*: comparison of F-TICS-m,

F-TICS, face-to-face MMSE and the overall telephone score

F-TICS-m: French version of the modified TICS; F-TICS: F-TICS-m from which the 10-word

delayed recall task was post-hoc removed; MMSE: Mini Mental State Examination; overall

telephone score: score constructed as the average of the five Z-scores on the different

cognitive tests comprising the telephone interview;

ROC: receiver operating curve; AUC: area under the curve

*Gold-standard assessment based on face-to-face neuropsychological examination