Psychometric Properties of the 37-item Functional
Assessment of Cancer Therapy-Cognitive Function
(FACT-Cog) scale in Cancer Patients.

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Abstract

Background: The Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog) scale is a self-assessment scale validated in routine clinical practice to assess cognitive function in cancer patients. This study aimed to validate the 37-item version of FACT-Cog exploring particularly the psychometric properties of four items related to multitasking that were not previously included in the scoring algorithm and assess its correlates in Lebanese cancer patients.

Methods: A cross-sectional study was carried out including 261 patients with breast, colorectal and lung cancers undergoing chemotherapy (Ethics: CEHDF1016). Validity was confirmed using a factor analyses using the principal component analysis technique with a varimax rotation. Analyses of internal consistency, “test-retest” reliability, and convergent validity were also performed. Finally, a multiple linear regression was conducted, using the total cognition scale as a dependent variable.

Results: The scale had an appropriate construct validity, and items loaded on subscales with adequate sample adequacy to factor analyses outcomes. The test-retest reliability was appropriate for the total cognition score/all sub-scores except for the FACT-Cog QOL. Moreover, a weak but significant and inverse correlation between the FACT-Cog scores and patient’s pain, fatigue, anxiety and depression. Finally, better cognition functioning was noted with age and in working patients, whereas lower functioning was observed in previous smokers and in patients with ovary/brain metastasis.

Conclusions: The 37-item tool is valid and reliable. Questions related to multitasking could be included in the scoring system.

Background

Cancer-related cognitive changes and impairment have long been documented but frequently misdiagnosed despite their negative impact on patient’s daily functioning and quality of life [1, 2]. Cancer induced cognitive impairment is defined as dysfunction in memory, learning, concentration, perception, executive function, visual-spatial abilities, and information processing, during or after the discontinuation of chemotherapy [3, 4]. These changes could lead to daily challenges, impaired familial and community functioning, worse outcomes on decision-making, and poor adherence to treatment, leading to reduced quality of life and increased burden on caregivers. Cognitive assessment is not yet performed as part of the routine evaluation and management of cancer patients. Hence, studies are needed to develop and validate tools to systematically include cognitive screening into clinical oncology practice [1]. These tools would adequately assess cognitive function and the different factors affecting it as part of a comprehensive care plan. Several instruments, including objective and subjective measures, were primarily designed to evaluate cognitive impairment in cancer patients, including neuropsychological tests, considered as the golden standard for objective measures. However, self-evaluation of cognitive function based on the patients’ description of their symptoms could help clinicians better understand the
impact of cancer and its treatment on patients’ quality of life. This hypothesis was supported by neuroimaging studies that confirmed the correlation between the self-reported cognitive decline and alteration in the central nervous system. Also, self-reported measures were more sensitive in assessing the association between anxiety and depression than neuropsychological tests.

The FACT-Cog scale is a self-assessment scale validated in routine clinical practice to assess cognitive function and quality of life in various cancer populations [5]. It is of particular interest since it focuses on the noticeability and functional interference of multiple specific domains associated with perceived cognitive functioning [6]. The initial scale consisted of 33 questions evaluating four different components of the perceived cognitive function, i.e., impairments, abilities, comments from others, and the impact on quality of life. In 2016, FACT-Cog scoring directions were updated to include four items related to multitasking (MT), not previously included in the scoring algorithm: “I have trouble keeping track of what I am doing if I am interrupted”; “I have trouble shifting back and forth between different activities that require thinking”; “I am able to shift back and forth between two activities that require thinking”; and “I am able to keep track of what I am doing, even if I am interrupted”. However, the internal consistency and correlation coefficients between individual items and the total score were not calculated. Moreover, studies have shown that ethnicity and cultural preferences can affect patients’ perception of their cognitive function [7, 8]. In the absence of a validated version in Lebanon, it was deemed essential to validate the French version of FACT-Cog, in a country whose second mother language is French, to use it in future epidemiological and clinical studies.

Therefore, this study aimed to validate the 37-item French version of FACT-Cog and assess its correlates in Lebanese cancer patients.

Methods

Study Design

A prospective clinical study was conducted between November 2017 until December 2019 at Hôtel-Dieu de France (HDF) Hospital, including 261 cancer patients. Patients had to be over 18 with a primary diagnosis of breast, colorectal, or lung cancer (all stages for all three types) and be treated with chemotherapy to be eligible. Patients were recruited during their outpatient chemotherapy at the daycare hospital.

Non-inclusion criteria consisted of patients with relapse/other types of cancer, who have had neurosurgeries or suffer from disorders of the central nervous system (dementia, multiple sclerosis, epilepsy, Parkinson’s disease, and mental retardation) that may affect cognitive evaluation. Patients who received adjuvant hormone therapy (especially for breast cancer patients) were also excluded.

The final sample was divided into three groups: patients receiving their first chemotherapy ever, those who have already had several sessions, and those undergoing palliative chemotherapy (for patients
requiring more than 10 sessions of chemotherapy). None of the participants received any financial incentive.

**Ethical aspect**

The study was approved by Hôtel-Dieu de France Hospital ethical committee (HDF, CEHDF1016, July 2017) and Medical Direction (Protocol N.DAM-2017/288, November 2017). All patients gave their written informed consent before enrollment.

**Sample Size Calculation**

Comrey and Lee suggested that a minimum of 10 observations per variable is necessary to perform an exploratory factor analysis [9]. Since the FACT-Cog (PCI subscale) is a 20-item questionnaire, a minimum of 200 patients was required for this study. Other subscales have fewer items, and thus necessitate smaller samples.

**Sociodemographic information**

Clinical and demographic data were collected, including age, gender, weight and height (to calculate the body mass index, BMI), Body Surface Area (BSA, calculated using the Mosteller formula) [10], ethnicity/nationality, marital status, education level, and the use of alcohol, tobacco, and medications.

Cancer-related clinical features were also recorded from patients' medical records. It included information on the type and stage of cancer, metastases, and the number of chemotherapy cycles.

**FACT-Cog validation**

David Cella, PhD, who holds the copyright of the scale, approved the use of the French and English versions of the Functional Assessment of Cancer Therapy - Cognitive Function (FACT-Cog, version 3) to evaluate cognitive function (Licensing agreement granted on November 2, 2017). The FACT-Cog scale was reliable and valid in assessing the cognitive function before, during, and after chemotherapy, in different cancer populations, including breast, colorectal, and lung cancer (The Functional Assessment of Chronic Illness Therapy system of Quality of Life questionnaires and all related subscales, translations, and adaptations (“FACIT System’’)).

The questionnaire was administered twice (noted Test and Retest) in 108 patients three weeks apart, corresponding to the time between two sessions of chemotherapy. A trained research assistant performed data collection and made sure that all questions were answered.

**FACT-Cog scale scoring**

This instrument assesses patients’ memory, attention, concentration, language, and thinking skills and the impact of cognition disturbances on their quality of life. It consists of 37 questions exploring four different subscales of the cognitive function: perceived cognitive impairments (CogPCI: 20 items); perceived cognitive abilities (CogPCA: 9 items); comments from others (CogOth: 4 items); and the impact of perceived cognitive impairments on quality of life (CogQOL: 4 items). The patient must answer the
questions by referring to the last seven days, expressing how many times a given situation has occurred during this period.

The total FACT-Cog score is the sum of the four subscales and ranges from 0-148. The higher the total score, the better the cognitive function, and the lower the impact on patients' quality of life. The detailed FACIT's recommended scoring method is presented in Supplementary file 1.

Other assessment measures
Pain was assessed using the visual analogue scale (VAS) ranging from 0 (no pain) to 10 (maximum pain). The self-report Hospital Anxiety and Depression Scale was used to evaluate anxiety and depression (HADS-A and HADS-D, respectively). Symptoms of the previous week were reported on a scale from 0 (not at all) to 3 (most of the time). Finally, the level of fatigue was measured following the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ C30 scale).

Statistical analysis
Statistical analyses were performed using SPSS software version 25.0. Descriptive statistics were calculated for all the variables. The Kolmogorov-Smirnov test verified the normality of the variables within each group: all the variables were not normally distributed, except for the total scale at the first cycle. Thus, the Spearman's correlation test was used to examine the association between scales and subscales. A $p \leq 0.05$ was considered statistically significant.

The validity of the subscales’ construct in this sample was confirmed, by launching four factor analyses for the items of the subscales. Using the principal component analysis technique, a varimax rotation was applied when extracted factors were not significantly correlated, and a promax rotation was applied when factors were correlated.

The Kaiser-Meyer-Olkin (KMO) measurement and the Bartlett sphericity test were performed to ensure the adequacy of the sampling. The number of factors retained corresponded to Eigenvalues greater than one.

Cronbach's alpha was recorded for reliability analysis of the total scale and subscales: $\alpha \geq 0.7$ and $\geq 0.8$ were considered as acceptable and excellent internal consistency values, respectively [11]. The “test-retest” reliability was evaluated by the intra-class correlation coefficient (ICC, mean measurement) for the scores of the scales. Values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 were indicative of poor, moderate, good, and excellent reliability, respectively [12].

Finally, studies have shown that self-reported questionnaires, such as FACT-Cog tend not to be associated with neuropsychological performance but rather depression and anxiety [5, 6, 13]. We therefore performed a convergent validity analysis to explore this hypothesis using Spearman correlations; this measure allowed examining to what extent the FACT-Cog scale/subscales correlated not only with depression and anxiety but also with pain and fatigue. An absolute correlation coefficient value (IRI) of 0.70 and above
indicates a strong correlation, a moderate correlation between 0.40 and 0.70, and a weak correlation for values below 0.4 [14].

Multiple linear regression was conducted to answer the secondary objective, using the total cognition scale as a dependent variable; a backward LR method was applied to choose the most parsimonious model and decrease confounding. Assumptions of the model adequacy, linearity, normality, and homoscedasticity were assessed before adopting the final presented model. Bootstrapping was conducted to improve the stability of coefficients’ confidence intervals.

Results

3.1. Demographic and clinical data of patients

Our study included 261 cancer patients (70.9% women). The mean age of patients was 59.32 ± 12.1 years with an average BMI of 25.55 ± 4.23 Kg/m². Patients were receiving chemotherapy for breast cancer (51%), colorectal cancer (25.2%), and lung cancer (25.8%). The median number of chemotherapy cycles was 2 [1–7].

3.2. Validation of the FACT-Cog scale

3.2.1. FACT-Cog PCI Test results (Table 2):
Table 1  
– Sociodemographic and other characteristics of the patients (N = 261)*.

| Characteristic           | Frequency (%) |
|--------------------------|---------------|
| **Gender**               |               |
| Female                   | 185 (70.9%)   |
| Male                     | 76 (29.1%)    |
| **Nationality**          |               |
| Lebanese                 | 249 (95.4%)   |
| Syrian                   | 8 (3.1%)      |
| Other                    | 4 (1.5%)      |
| **Marital status**       |               |
| Single                   | 36 (13.8%)    |
| Married                  | 211 (80.8%)   |
| Widowed                  | 9 (3.4%)      |
| Divorced                 | 5 (1.9%)      |
| **Level of education***  |               |
| Primary                  | 47 (18.2%)    |
| Secondary                | 125 (48.45%)  |
| University               | 86 (33.33%)   |
| **Profession/Work**      |               |
| No                       | 126 (48.5%)   |
| Yes                      | 134 (51.5%)   |
| **Socioeconomic status** |               |
| Low                      | 18 (6.9%)     |
| Middle                   | 222 (85.1%)   |
| High                     | 21 (8%)       |
| **Alcohol consumption**  |               |
| No                       | 222 (85.1%)   |
| Yes                      | 39 (14.9%)    |
| **Smoking**              |               |
| No                       | 156 (59.8%)   |
| Yes                      | 79 (30.2%)    |
| Previous smoker          | 26 (10%)      |
| **Allergy**              |               |
| No                       | 249 (95.4%)   |

* Some variables did not sum up to 261 due to missing data.

† Some patients have several metastases localizations; therefore, the number exceeds the number of patients with metastases.

‡ The variables distribution being not normal, we used the median and interquartile range.
|                         | Frequency (%) |
|-------------------------|---------------|
| **Hypertension**        |               |
| Yes                     | 12 (4.6%)     |
| No                      | 173 (66.3%)   |
| Yes                     | 88 (33.7%)    |
| **Diabetes**            |               |
| No                      | 216 (82.8%)   |
| Yes                     | 45 (17.2%)    |
| **Dyslipidemia**        |               |
| No                      | 189 (72.4%)   |
| Yes                     | 72 (27.6%)    |
| **Type of cancer**      |               |
| Breast                  | 133 (51%)     |
| Colorectal              | 66 (25.2%)    |
| Lung                    | 62 (23.8%)    |
| **Presence of metastases** |         |
| No                      | 217 (83.1%)   |
| Yes                     | 44 (16.9%)    |
| **Type of metastases †**|               |
| Bone                    | 14 (29.2%)    |
| Lung                    | 12 (25%)      |
| Hepatic                 | 16 (33.3%)    |
| Ovarian                 | 5 (10.4%)     |
| Brain                   | 1 (2.2%)      |
| **Type of chemotherapy**|               |
| Adjuvant                | 127 (48.7%)   |
| Neoadjuvant             | 63 (24.1%)    |
| Palliative              | 71 (27.2%)    |
| **Mean ± Standard Deviation (SD)** | **Median [25–75 Percentiles] ‡** |
| Age (years)             | 59.32 ± 12.1  | 60 [52–67] |
| Body Mass Index (BMI; Kg/m²) | 25.55 ± 4.23  | 25.39 [22.92–27.98] |
| Body Surface Area (BSA; m²) | 1.78 ± 0.19    | 1.78 [1.66–1.91] |

* Some variables did not sum up to 261 due to missing data.

† Some patients have several metastases localizations; therefore, the number exceeds the number of patients with metastases.

‡ The variables distribution being not normal, we used the median and interquartile range.
| Variable                        | Frequency (%) |
|--------------------------------|---------------|
| CogPCI score                   | 58.51 ± 13.26 | 61 [48-69.87] |
| CogPCA score                   | 23.35 ± 5.53  | 23 [20-26.75] |
| CogOth score                   | 13.45 ± 3.17  | 12 [14–16]   |
| CogQOL score                   | 10.88 ± 4.68  | 12 [8–15]    |
| Total FACT-Cog score           | 106.48 ± 21.52| 111 [95.5–120]|
| Pain VAS score                 | 2.02 ± 2.87   | 0 [0–3]      |
| Number of chemotherapy cycles  | 7.11 ± 12.57  | 2 [1–7]      |

* Some variables did not sum up to 261 due to missing data.

† Some patients have several metastases localizations; therefore, the number exceeds the number of patients with metastases.

‡ The variables distribution being not normal, we used the median and interquartile range.
Table 2
– Factor analysis with VARIMAX rotation for FACT-CogPCI subscale.

| Item*   | Questions                                                   | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 | Total Subscale† |
|---------|-------------------------------------------------------------|----------|----------|----------|----------|----------|----------------|
| CogA3¹  | My thinking has been slow                                  | 0.813    |          |          |          |          | 0.529         |
| CogA1¹  | I have had trouble forming thoughts                       | 0.777    |          |          |          |          | 0.548         |
| CogC32¹ | My thinking has been slower than usual                     | 0.759    |          |          |          |          | 0.574         |
| CogF25⁵ | My reactions in everyday situations have been slow        | 0.751    |          |          |          |          | 0.513         |
| CogC7²  | I have had trouble concentrating                           | 0.648    |          |          |          |          | 0.640         |
| CogC31² | I have had to work harder than usual to keep track of what I was doing | 0.647 | | | | | 0.534 |
| CogV15⁴ | I have had trouble finding the right word(s) to express myself |          | 0.784    |          |          |          | 0.665         |
| CogV13⁴ | I have had trouble recalling the name of an object while talking to someone |          | 0.766    |          |          |          | 0.561         |
| CogV16⁴ | I have used the wrong word when I referred to an object   |          |          | 0.761    |          |          | 0.602         |
| CogV17b⁴ | I have had trouble saying what I mean in conversations with others |          |          | 0.658    |          |          | 0.644         |
| CogF24⁵ | I have forgotten names of people soon after being introduced |          |          |          | 0.738    |          | 0.515         |

* The classification of items taking into account the cognitive domains allows the identification of six reclassified domains of interest¹,²: 1- Mental acuity; 2- Attention & Concentration; 3- Memory; 4- Verbal fluency/ability; 5- Functional interference; and 6- Multitasking ability.

† p < 0.001 for all correlation for items with total subscale and for Cronbach’s alpha.

‡ Items in bold (CogMT1 and CogMT2) are the new items included in the algorithm scoring.
| Item*          | Questions                                                                 | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 | Total Subscale† |
|---------------|---------------------------------------------------------------------------|----------|----------|----------|----------|----------|-----------------|
| CogM12³       | I have had trouble remembering new information, like phone numbers or simple instructions | 0.734    |          |          |          |          | 0.575           |
| CogMT1⁶‡      | I have trouble keeping track of what I am doing if I am interrupted       | 0.525    |          |          |          |          | 0.522           |
| CogF23⁵       | I have had to work really hard to pay attention or I would make a mistake | 0.508    |          |          |          |          | 0.633           |
| CogF19⁵       | I have walked into a room and forgotten what I meant to get or do there   | 0.496    |          |          |          |          | 0.541           |
| CogC33c³      | I have had to use written lists more often than usual so I would not forget things |          | 0.834    |          |          |          | 0.272           |
| CogC33a⁴      | I have had to work harder than usual to express myself clearly             |          | 0.786    |          |          |          | 0.453           |
| CogMT2⁶‡      | I have trouble shifting back and forth between different activities that require thinking |          | 0.5       |          |          |          | 0.420           |
| CogM9³        | I have had trouble finding my way to a familiar place                     |          |          | 0.728    |          |          | 0.444           |
| CogM10³       | I have had trouble remembering where I put things, like my keys or my wallet |          |          | 0.544    |          |          | 0.598           |
| **Cronbach alpha for factors and total scale** |                                                                       |         |         |          |          |          | **0.887**       |

* The classification of items taking into account the cognitive domains allows the identification of six reclassified domains of interest ¹,²: 1- Mental acuity; 2- Attention & Concentration; 3- Memory; 4- Verbal fluency/ability; 5- Functional interference; and 6- Multitasking ability.

† p < 0.001 for all correlation for items with total subscale and for Cronbach's alpha.

‡ Items in bold (CogMT1 and CogMT2) are the new items included in the algorithm scoring.
A factor analysis was carried out over the whole sample, using the Varimax rotation since the factors were not highly correlated. A KMO measure of sampling adequacy of 0.870 was found, with a significant Bartlett’s test of sphericity (p < 0.001). The sample was adequate, and communalities were all higher than 0.3. None of the FACT-CogPCI subscale items were removed; items converged over a solution of five factors that had an Eigenvalue > 1, explaining a total of 64.39% of the variance (Table 2). Items loaded on five factors: mental acuity, memory and attention, verbal fluency, functional interference, and spatial orientation. Table 2 shows the mapping with the objective cognitive domains of the neuropsychological tests. The Quartimax rotation gave similar results, with slight variation in the loading of one item, the CogM9 that is related to the “memory” domain (See Supplementary file 2).

As for the reliability analysis, results were in the acceptable range according to the number of included items. The only item that showed a low correlation coefficient of 0.272 was the item CogC33c “I have had to use written lists more often than usual so I would not forget things”. The Cronbach alpha values of the two newly evaluated items CogMT1 and CogMT2, were 0.522 and 0.420, respectively.

3.2.2. FACT-CogPCA Test results (Table 3)
Table 3 – Factor analysis for FACT-CogPCA.

| Item* | Questions                                                                 | Memory/Mental acuity | Multitasking/verbal ability/concentration | Total subscale correlation | P-value          |
|-------|---------------------------------------------------------------------------|----------------------|------------------------------------------|----------------------------|-----------------|
| CogPM1³ | I have been able to remember things, like where I left my keys or wallet                      | 0.826               | 0.529                                    |                             | P < 0.001       |
| CogPCH1¹ | My mind is as sharp as it has always been                                            | 0.691               | 0.56                                     |                             | P < 0.001       |
| CogPCH2³ | My memory is as good as it has always been                                          | 0.686               | 0.743                                    |                             | P < 0.001       |
| CogPM2³ | I have been able to remember to do things, like take medicine or buy something I needed | 0.658               | 0.560                                    |                             | P < 0.001       |
| CogPMT2⁶† | I am able to keep track of what I am doing, even if I am interrupted              | 0.894               | 0.650                                    |                             | P < 0.001       |
| CogPMT1⁶† | I am able to shift back and forth between two activities that require thinking      | 0.88                | 0.533                                    |                             | P < 0.001       |
| CogPV1⁴  | I have been able to bring to mind words that I wanted to use while talking to someone | 0.519               | 0.533                                    |                             | P < 0.001       |
| CogPC1²  | I have been able to concentrate                                                   | 0.45                | 0.627                                    |                             | P < 0.001       |
| CogPF1²  | I am able to pay attention and keep track of what I am doing without extra effort     | 0.428               | 0.659                                    |                             | P < 0.001       |

Cronbach alpha 0.813  P < 0.001

* The classification of items taking into account the cognitive domains allows the identification of six reclassified domains of interest ¹,²: 1- Mental acuity; 2- Attention & Concentration; 3- Memory; 4- Verbal fluency/ability; 5- Functional interference; and 6- Multitasking ability.

† Items in bold (CogPMT1 and CogPMT2) are the new items included in the algorithm scoring.

A factor analysis, using the principal component analysis, was carried out. A KMO measure of sampling adequacy of 0.805 was found, with a significant Bartlett’s test of sphericity (p < 0.001). The sample was adequate and communalities were all higher than 0.3. None of the FACT-CogPCA subscales items were removed; items converged over a solution of two factors that had an Eigenvalue > 1, explaining a total of 53.55% of the variance. A Promax rotation was used since factors were correlated (Table 3). As for the
reliability analysis, results were in the acceptable range according to the number of included items. The correlation coefficient values of the two newly evaluated items CogPMT1 and CogPMT2, were 0.650 and 0.533, respectively. Table 3 presents the comparison with the objective cognitive domains of the neuropsychological tests: items related to the same domain loaded into the same factor.

3.2.3. FACT-CogOTH Test results (Table 4)

| Item  | Questions                                      | Factor loading | Total subscale correlation | p-Value  |
|-------|------------------------------------------------|----------------|----------------------------|----------|
| CogO3 | Other people have told me I seemed to have trouble thinking clearly | 0.902          | 0.814                      | P < 0.001|
| CogO2 | Other people have told me I seemed to have trouble speaking clearly | 0.866          | 0.72                       | P < 0.001|
| CogO4 | Other people have told me I seemed confused     | 0.816          | 0.779                      | P < 0.001|
| CogO1 | Other people have told me I seemed to have trouble remembering information | 0.762          | 0.814                      | P < 0.001|
| Cronbach alpha |                                  | 0.847          |                            | P < 0.001|

A factor analysis, using the principal component analysis, was carried out; no rotation was necessary since all items loaded on the same factor. A KMO measure of sampling adequacy of 0.780 was found, with a significant Bartlett’s test of sphericity (p < 0.001). The sample was adequate, and communalities were all higher than 0.3. Items loaded on one factor. None of the FACT-Cog OTH subscale items were removed; items converged over a solution of one factor that had an Eigenvalue > 1, explaining a total of 70.28% of the variance (Table 4). As for the reliability analysis, results were in the acceptable range according to the number of included items.

3.2.4. FACT-CogQOL Test results (Table 5)
Table 5
- Factor analysis for FACT-CogQOL

| Item   | Questions                                      | Factor loading | Total subscale correlation | P-Value |
|--------|------------------------------------------------|----------------|---------------------------|---------|
| CogQ41 | These problems have interfered with the quality of my life | 0.96           | 0.954                     | < 0.001 |
| CogQ35 | I have been upset about these problems         | 0.94           | 0.941                     | < 0.001 |
| CogQ37 | These problems have interfered with my ability to work | 0.927          | 0.921                     | < 0.001 |
| CogQ38 | These problems have interfered with my ability to do things I enjoy | 0.922          | 0.914                     | < 0.001 |
| Cronbach alpha            |                                      | 0.954          |                           | < 0.001 |

A factor analysis, using the principal component analysis, was carried out; no rotation was necessary since all items loaded on the same factor. A KMO measure of sampling adequacy of 0.868 was found, with a significant Bartlett’s test of sphericity (p < 0.001). The sample was adequate, and communalities were all higher than 0.3. None of the FACT-CogQOL subscale items were removed; items converged over a solution of one factor that had an Eigenvalue > 1, explaining a total of 87.87% of the variance (Table 5).

As for the reliability analysis, results were in the acceptable range according to the number of included items.

3.3. Test-retest analysis of total scale and subscales
High test-retest correlation was found between Cycle 1 and Cycle 2, for the scale and all subscales, except for the QOL subscale that had a relatively lower value (Table 6).

Table 6
- Test-Retest reliability of FACT Cognition subscales and total scale.

|                  | Average ICC | 95% Confidence Interval | p-value |
|------------------|-------------|-------------------------|---------|
| FACT CogPCI      | 0.818       | 0.734; 0.875            | < 0.001 |
| FACT CogOTH      | 0.823       | 0.741; 0.879            | < 0.001 |
| FACT CogPCA      | 0.773       | 0.669; 0.845            | < 0.001 |
| FACT CogQOL      | 0.541       | 0.328; 0.686            | < 0.001 |
| Total Cognition  | 0.866       | 0.805; 0.909            | < 0.001 |

3.4. Scale and subscales reliability and correlations
A borderline internal consistency was found between subscales (p < 0.700). All correlations were significant (p < 0.001) and were moderate to high between the total scale and subscales; however, correlations between subscales were of lower magnitude (Table 7).

| FACT CogPCI | FACT-CogOTH | FACT-CogPCA | FACT-CogQOL | Total Cognition |
|-------------|-------------|-------------|-------------|----------------|
| FACT CogPCI | 1           | 0.566       | 0.627       | 0.307          | 0.898          |
| FACT CogOTH | 0.566       | 1           | 0.489       | 0.312          | 0.659          |
| FACT CogPCA | 0.627       | 0.489       | 1           | 0.386          | 0.783          |
| FACT CogQOL | 0.307       | 0.312       | 0.386       | 1              | 0.605          |

*Cronbach Alpha between subscales = 0.667; †p < 0.001 for all correlations

3.5. Convergent validity with pain, depression, anxiety, fatigue

The convergent validity with pain, fatigue, anxiety, and depression was also evaluated: inverse, weak but significant correlations between the FACT-Cog total score/subscales scores were found (IrI = 0.206–0.351; p-values less than 0.05). For the subscales, PCI correlated with depression, OTH with anxiety, and depression, and PCA with fatigue, anxiety, and depression. A detailed description is presented in Table 8.

| Scale        | Total cognition | PCI subscale | OTH subscale | PCA subscale | QOL subscale |
|--------------|-----------------|--------------|--------------|--------------|--------------|
| EVA          | -0.145 (p = 0.020)* | -0.102 (p = 0.104) | 0.044 (p = 0.486) | -0.096 (p = 0.124) | -0.225 (p < 0.001)* |
| Fatigue score† | -0.209 (p = 0.009)* | -0.028 (p = 0.731) | -0.171 (p = 0.033)* | -0.274 (p = 0.001)* | -0.344 (p < 0.001)* |
| HADS-A score‡ | -0.351 (p < 0.001)* | -0.338 (p < 0.001)* | -0.218 (p < 0.001)* | -0.206 (p < 0.001)* | -0.306 (p < 0.001)* |
| HADS-D score§ | -0.322 (p < 0.001)* | -0.300 (p < 0.001)* | -0.253 (p < 0.001)* | -0.241 (p < 0.001)* | -0.283 (p < 0.001)* |

† Fatigue as evaluated by the EORTC-QLQ C30 scale;
‡ Hospital Anxiety and Depression Scale (anxiety);
§ Hospital Anxiety and Depression Scale (depression);
* Statistically significant results.
3.6. Correlates of total cognition: multivariable analysis

A multivariable analysis, taking the total cognition score as a dependent variable, showed that higher cognition scores were significantly associated with older age (Beta = 0.252) and in those who work compared to those who do not (Beta = 8.415), whereas lower scores were noted in previous smokers versus non-smoker (Beta=-13.484), in patients having ovary metastasis (Beta=-21.285), and brain metastasis (Beta=-8.283) versus those without metastasis (Table 9).

| Correlate                  | Unstandardized Beta | 95% Confidence Level       | p-value |
|----------------------------|---------------------|----------------------------|---------|
| Chemotherapy cycle number  | -0.090              | -0.359; -0.120             | 0.462   |
| Age                        | 0.252               | 0.036; 0.474               | 0.025   |
| Body Mass Index (BMI)      | -0.601              | -1.290; 0.014              | 0.067   |
| Working versus not working | 8.415               | 3.346; 13.642              | 0.002   |
| Previous tobacco smoking versus non-smoking | -13.484 | -25.321; -1.944 | 0.024 |
| Allergy                    | 8.737               | -2.508; 19.613             | 0.110   |
| Ovary Metastasis vs No Metastasis | -21.285 | -36.670; 5.063 | 0.017 |
| Brain Metastasis vs No Metastasis | -8.283 | -13.385; -3.122 | 0.023 |
| Lung Metastasis vs No Metastasis | -6.012 | -17.804; 5.307 | 0.915 |
| Bone Metastasis vs No Metastasis | -5.382 | -20.458; 7.551 | 0.300 |

*Model Summary: $R = 0.333; R^2 = 0.111$ – All variables introduced at baseline: socio-demographics, chronic diseases risk factors, chronic treatments, cancer types and chemotherapy types. Confidence levels were calculated through bootstrapping. Numbers in bold represent significant results.

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Discussion
To the best of our knowledge, this is the first study to validate the French version of the 37-item FACT-Cog scale in a population of Lebanese cancer patients, using exploratory factor analysis for the four subscales (FACT-Cog PCI, PCA, OTH, and QOL domains) as per scoring recommendations. Previous validations of the original English, the French, and the Korean version of FACT-Cog were performed on the 33-item scale without the multitasking components nor factor analysis, except for the Korean study [5, 15, 16]. Thus, comparing our results to theirs was not possible.

Only two studies investigated the 37-items scales [6, 17]. The first examined the psychometric properties and measurement equivalence of the English and Chinese FATC-Cog based on the cognitive domains drawing items from the four subscales [6]. The second performed confirmatory structure analysis of the 37-item scale in three populations: 158 cancer patients, community older adults, and undergraduate students using the scoring recommendation in one of the models [17]. Hence, the need to validate the French 37-item Fact-Cog scale on a large sample of cancer patients, and evaluate the internal consistency and the correlation between individual items and the total score, following the scoring recommendation [5]. In our study, none of the items were removed from factor analyses of the four subscales, consistent with research that confirmed the traditional four-factor structure of the 37-item FACT-Cog [17].

When mapping the loading of items to the objective cognitive domains of neuropsychological tests, items related to the same domain loaded to the same factor for FACT-Cog PCA, OTH, and QOL, but not for the FACT-PCI subscale: questions related to mental acuity and concentration loaded together on the same factor, but questions related to memory and multitasking ability loaded over several factors, and items CogF25 and CogC33a did not load with their related questions over the “functional interference” or “verbal acuity” domains, respectively. Our results are similar to those of the original validation article that identified borderline properties for the memory items [5] and to those of the English and Chinese versions of the FACT-Cog, where authors failed at identifying unidimensionality for the memory domain [6]. A possible explanation for such results could be cross-cultural differences and perceptions of these questions.

Furthermore, of all studied items, the only that presented a poor correlation was the CogC33c, related to the memory domain: “I have had to use written lists more often than usual, so I would not forget things”. This is not surprising since this item has been previously revised to capture if the patients noted an increase in the use of such methods to help them remember things, not only implying a simple organizational style [5]. However, even after revision, this item might still capture, to some extent, a personality characteristic rather than a cognitive function. Moreover, as stated in both Chinese [6] and Korean [16] validation studies, this item and the CogM12 “I have had trouble remembering new information, like phone numbers or simple instructions” might not be suitable for today’s context where technological advances reduce our need to recall information or use to-do lists. Therefore, memory items deserve to be revised again [5].
Also, items related to multi-tasking fit their respective subscales (CogMT1 and CogMT2 for FACT-CogPCI; CogPMT1 and CogPMT2 for FACT-CogPCA) with acceptable Cronbach’s alpha values for all items except for the CogMT2 that had a value less than 0.5. Furthermore, there was a high correlation between each item of the subscales and the total cognition score.

The scale had excellent internal consistency values: each of the subscales had excellent Cronbach’s alpha values (over 0.8), supporting the appropriate reliability of this version. The values for the FACT-CogOTH and FACT-CogQOL were even higher than those reported in the first validated French version (0.847 versus 0.7, and 0.954 versus 0.85, respectively) [15], and the Korean validation [16]. The test-retest reliability was also appropriate; the ICC between the test and retest was good for the total cognition score and all sub-scores, except for the FACT-Cog-QOL that had poor reliability, showing that the impact of cognition on QOL may differ across patients between chemotherapy cycles [2].

**Convergent validity with pain, depression, anxiety, fatigue**

Our results demonstrated a weak but significant and inverse correlation between the FACT-Cog scores and patients’ pain, fatigue, anxiety, and depression, similar to previously reported weak to moderate correlations [5, 6] in the 33-item scale, likely due to the multifactorial nature of cognitive decline and the possible interaction between psychological, psychosocial, and demographic factors in the chemo brain [6, 18].

However, regardless of the version used, the language, or the number of items assessed in previous studies, our results are overall consistent with previous research, highlighting sufficient reliability and validity for FACT-Cog. These results further confirm that the English, French, Chinese, and Korean versions of the questionnaire are effective tools to assess cognitive function in cancer patients at any stage of their treatment [5, 6, 15, 16].

**Baseline factors affecting the cognitive function**

The mean total FACT-Cog score in our sample was 106.48 ± 21.52, slightly lower than what was published in the English and Chinese 37-item versions (127 ± 19.6 and 126.6 ± 18, respectively) [19]. The lower cognitive function could be due to the difference in the studied population; our sample included patients with breast, colorectal, and lung cancer (17% having metastatic cancer) versus patients with only breast cancer and 7% metastasis. Better cognitive function was noted with younger patients and those who work compared to those who do not; lower capacity was observed in previous smokers versus non-smokers and patients with ovarian and brain metastasis versus those without metastasis.

Surprisingly, higher cognition scores were significantly associated with older age, although aging is a known risk factor for cognitive impairment, especially in older adults with pre-existing cognitive decline [1]. One hypothesis that can explain our results is the exclusion of patients with major cognitive disorders such as dementia or other capacity-limiting disorders preventing patients from completing the questionnaire. Another explanation could be our sample: almost 80% were married, and more than half of
the patients were diagnosed with breast cancer. In these women, particularly, studies have shown that psychological distress is higher than in other groups of cancer [20, 21], which could impact both subjective and objective measures of cognitive impairment [22, 23]. Indeed, patients who had a more altered body image (scarring, hair loss, and weight gain), lower less self-esteem, and lower self-efficacy (mothers with breast cancer, not being able to take care of their families/professional life), had higher levels of anxiety and depression [24–26]. In all cases, the FACT-Cog should be administered to a broader age group to examine the exact effect of age over a lifespan and determine the need for adjusting age scores [15].

To the best of our knowledge, no studies have explored the effect of smoking and working on the cognitive function of cancer patients, as evaluated by the FACT-Cog. However, research established the harmful effect of smoking on cognition, with ever-smokers having a reduced cognitive function compared to never-smokers [27–29], this risk persisting even after smoking cessation [27].

Recent guidelines have emphasized the importance of physical activity and social rehabilitation, both acquired in the workplace, to improve cognition in cancer patients [30–32]. The positive effect could be mediated by several biological mechanisms [33, 34] but also by improved psychological factors such as anxiety and depression [32, 35, 36].

Finally, expectedly, lower FACT-Cog scores were seen in patients with brain metastases since the cognitive decline is among the most reported symptoms [37]. Additionally, cognitive dysfunction in patients presenting ovarian metastases might be consequent to their treatment (adjuvant endocrine therapy for metastatic breast cancer [38–40] or targeted therapy such as bevacizumab for metastatic colorectal cancer [41]).

**Limitations and Strengths**

We acknowledge some limitations related to the study design. In the absence of an Arabic version, we used the French version in a group of French-speaking patients, but some misunderstandings might have happened. Also, we did not include a control group of healthy individuals to explore the normative validation of the scale. Nevertheless, despite all these limitations, and to the best of our knowledge, this study is the largest to validate the FACT-Cog, enrolling a heterogeneous sample of patients with different cancer conditions, treatment statuses, and ages, which allows the generalizability of the results. Moreover, it includes essential components evaluating the desired constructs of the cognitive function [19]. Nevertheless, a study with a larger sample and broader patients’ distribution is suggested to confirm our findings; a confirmatory factor analysis would be interesting to assess the current structure suitability in the French-speaking Lebanese population.

**Conclusions**

Our study validated the 37-item FACT-Cog tool and confirmed its validity and reliability in a population of Lebanese cancer patients. The four new multitasking questions could be easily included in the new
scoring system. In the absence of a validated Arabic version, the French self-reported scale can be easily used in clinical research and practice to optimize the diagnosis and management of cognitive impairment in cancer survivors which could facilitate the pooling of data from multinational studies into a single analytical framework in clinical trials or cognitive research [19].

**Abbreviations**

BMI: Body mass index  
BSA: Body Surface Area  
CogPCA: Perceived cognitive abilities subscale  
CogPCI: Perceived cognitive impairments  
CogOth: Comments from others  
CogQOL: Impact of perceived cognitive impairments on quality of life  
EORTC-QLQ C30 scale: European Organization for Research and Treatment of Cancer  
FACIT: Functional Assessment of Chronic Illness Therapy system of Quality of Life questionnaires  
FACT-Cog: Functional Assessment of Cancer Therapy-Cognitive Function  
HADS-A: Hospital Anxiety and Depression Scale; anxiety subscale  
HADS-D: Hospital Anxiety and Depression Scale; depression subscale  
HDF: Hôtel-Dieu de France  
ICC: Intra-class correlation coefficient  
KMO: Kaiser-Meyer-Olkin  
VAS: Visual analogue scale

**Declarations**

**Ethics Approval and consent to participate:** The study was approved by Hôtel-Dieu de France Hospital ethical committee (HDF, CEHDF1016, July 2017). Participants were fully informed of the purpose and procedures of the study and had the adequate time to ask questions and ponder about their voluntary participation. All patients gave their written informed consent before enrollment.  

**Consent for publication:** Not applicable.
Availability of data and materials: Any data or material required are available upon demand.

Competing interests: The authors have no conflicts of interest to disclose.

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AH and PS designed the study and wrote the protocol. LRK contributed to the design. AH and PS managed the literature search and analyses. RK, RH, GC and JK included the patients and performed the clinical assessment. PS undertook the statistical analysis. AH and PS wrote the first draft of the manuscript. HS critically reviewed and edited the manuscript. LRK and JK supervised the whole process and critically reviewed the article. All authors reviewed and approved the final version of the manuscript.

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