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Norms for standard neuropsychological tests from the French CONSTANCES cohort

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Abstract

Background: Neuropsychological testing plays a key role in various clinical contexts. Even though a substantial number of adults suffer neurological disorders such as early-onset dementia, stroke, traumatic brain injury or multiple sclerosis, most of normative data do not include persons below 65. The aim of this study was to produce updated norms for the Mini-Mental State Examination, the Free and Cued Selective Reminding Test, the Trail Making Test, verbal fluency tasks and the Digit Symbol Substitution Test for middle-aged and older adults.

Methods: The sample consisted of 51,879 participants aged 45–70 years from the CONSTANCES study. Norms are presented in percentiles stratified on age, education and gender.

Results: The results illustrated the effect of age in all tests considered. For tests involving speed processing, the impact of age was observed including in tight age ranges categories (5 years). The results also showed the well-known effect of education and an effect of gender in tests involving verbal memory and speed processing.

Conclusions: The norms provided allow apprehending the variability of the cognitive performances of middle-aged to older population, with a high precision in age categories. The tests considered are broadly used in neuropsychological practice and should be helpful in a variety of clinical contexts.

Introduction

Neuropsychological assessment plays a key role in a variety of clinical contexts. Indeed, neuropsychological examination is essential in the diagnosis of dementia as well as in most neurological disorders such as stroke, traumatic brain injury or multiple sclerosis. Identification of low performances relies on the use of appropriate normative scores which allow clinicians determining whether a score is in the expected range. Such norms are available for a wide panel of tests for different age ranges. Nevertheless, the middle-aged group is rarely represented. Yet, dementia does not exclusively affect people over the age of 65. Early-onset dementia refers to people diagnosed with dementia under 65. A review relying on 11 studies estimated that between 6.9% to 45.3% of all patients diagnosed with dementia had early-onset dementia [1]. In particular, frontotemporal dementia is diagnosed in 10% of cases before 45 years of age, and in 60% of cases between 45 and 64 [2]. Furthermore, such normative data are very important to document cognitive decline that may be present long before dementia onset [3]. Beyond dementia, other neurological disorders may be experienced by middle aged adults. For instance, persistent cognitive deficits have been reported to affect over 20% of adults one year post-brain injury [4] and from 11% to 30% of adults one year poststroke [5]. Despite this matter of fact, most studies having computed norms for neuropsychological tests did not include persons below 65 [6].

Two other major issues limit the relevance of numerous published norms. First, several studies rely on a relatively small number of participants [7,8], which is a substantial limitation for a study aiming at addressing the inter-individual variability of cognitive performances in general population. The need of accounting for this huge variability is particularly outstanding in elderly population [9] or patients with neurological disorders [10] for whom cognitive performances variability is greater than for any other group population.

Second, for a reliable clinical interpretation, the use of updated norms is essential. Indeed, cognitive abilities improve from one generation to the next [11]. Such improvement is known as the "Flynn effect" and is explained by the general improvement of education and environmental conditions.

The lack of norms designed for the middle-aged population, the lack of up-to-date norms as well as norms gathered from small-sized samples lead clinicians to use inadequate norms and increase the risk of diagnosis misclassification.

The aim of this study was to compute updated and reliable norms for five tests – the Mini-Mental State Examination (MMSE) assessing global cognitive functioning, the Free and Cued Selective Reminding Test (FCSRT) assessing verbal episodic memory, the Trail Making Test (TMT) assessing executive functions, semantic and phonological fluency tasks assessing language and the Digit Symbol Substitution Test (DSST) assessing psychomotor speed – in a population aged 45 to 70, from the large-sized CONSTANCES study.

Methods

Study design

The methodology of the national CONSTANCES cohort has been detailed elsewhere [12]. Since January 2012, 176,000 volunteers aged 18 and over had been randomly selected among French adults covered by the National health insurance. We considered only the participants aged 45 and over who received a standardized neuropsychological testing. CONSTANCES obtained the authorization of the National Data Protection Authority and was approved by the Institutional Review Board of the National Institute for Medical Research. All participants gave informed consent.

Sample

68,285 participants aged 45 and over have been recruited. Participants aged over 70, those who did not provide information on education or did not complete the tests were excluded (see **fig. S1**, online only). Five age groups ([45–50[; [50–55[; [55–60[; [60–65[; [65–70]) and three educational levels: no diploma (<5 years of education); primary, vocational or high school degree (5–13 years of education); college degree (≥ 14 years of education) were considered.

Neuropsychological testing

The following tests were administered:

1. MMSE [13] assessing general cognitive functioning (maximum score=30).
2. FCSRT [14] assessing verbal episodic memory. After the learning phase consisting in memorizing 16 words belonging to 16 semantic categories, the volunteer is invited to recall as many words as possible in two minutes. The category for each word that has not been recalled is provided. This procedure is repeated three times. The delayed recall takes place after a 20-minute delay. Four scores were considered: the three free recall trials (maximum score=48); the

three free and cued recalls (maximum score=48); the delayed free recall (maximum score=16); and the delayed free and cued recall (maximum score=16) were considered.

3. TMT [15] assessing executive functions. This test consists of 25 circles displayed on a sheet of paper. In part A – assessing attention and psychomotor speed – the circles are numbered from 1 to 25 and have to be connected in ascending order by drawing a line. In part B – assessing planning abilities and mental flexibility – the circles contain numbers or letters to be connected in ascending order by alternating numbers and letters. In case of error, correction is provided. The score was the time (in seconds) to complete the task.

4. Fluency tasks assess language skills in particular, lexico-semantic access, and word search strategy. The tasks consisted in naming in one minute as many words as possible belonging to animals (semantic fluency) or starting by letter R (phonological fluency). The score was the number of generated words.

5. DSST [16] assessing psychomotor speed. On the top of the page, a coding matrix contains the digits 1 to 9, each of them paired with a symbol. Underneath, a series of digits with a blank space for sketching the symbol is presented. The participant has to assign as many symbols as possible to the respective digits in 90 seconds. The score was the number of correct symbols.

In addition to cognitive testing, depressive symptomatology was assessed by the Center for Epidemiologic Studies Depression Scale [17].

Statistical analysis

We first described sociodemographic and health characteristics of participants. Age, gender, and education effect was assessed with univariate and multiple linear regression analysis to determine the stratification variables. The 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles

stratified on age, gender, and education were reported. Statistical analyses were performed with R statistical software.

Results

The mean age of the whole study sample was 57.7 (SD=7.1). Of the 51,879 participants, 52% were women, 3.4% had low education (<5 years), 49.2% had medium educational level (5–13 years) and 47.4% had higher education (≥ 14 years). The CESD mean score was 10.5 (SD=9) (missing data=4790).

The results from the full multiple linear regression models revealed that age and education were associated with MMSE (full model: $F(7, 51783)=924.2$; $p<.001$) and semantic fluency (full model: $F(7, 51353)=586.6$; $p<.001$). Gender, age and education were associated with the free recall of the FCSRT (full model: $F(7, 50558)=1486$; $p<.001$), the total FCSRT recall (full model: $F(7, 50518)=611.7$; $p<.001$), the delayed FCSRT free recall (full model: $F(7, 50457)=1058$; $p<.001$), the total FCSRT delayed recall (full model: $F(7, 50451)=244.7$; $p<.001$), the TMT-A (full model: $F(7, 51589)=800.2$; $p<.001$) and TMT-B (full model: $F(7, 51259)=1188$; $p<.001$), phonological fluency (full model: $F(7, 51187)=957.7$; $p<.001$) and DSST (full model: $F(7, 51478)=2161$; $p<.001$).

Norms are presented in Tables 1 to 6. The 10th percentile corresponds to the threshold under which 10% of participants get the worst performances. The 75th percentile corresponds to the threshold above which 25% of participants get the best performances except for TMT (the lower score, the better performance).

MMSE was available for 51,791 participants (mean score=28.1, SD=1.9) (Table 1). As may be seen, scores vary little with age and gender and more substantially with education.

Free recall of the FCSRT was available for 50,566 participants (mean score=32.4, SD=5.6) (Table 2). Scores slightly decrease with age and increase with level of education. Scores are slightly higher in women.

Total FCSRT recall score was available for 50,526 participants (mean score=46.3, SD=2.3) (Table S1, online only). There is a ceiling effect with a median score of 47 or 48 for the majority of groups.

Delayed FCSRT free recall was available for 50,465 participants (mean score=12.7, SD=2.3) (Table S2, online only) and show the same trends as those observed for the free recall.

Total FCSRT delayed recall was available for 50,459 participants (mean score=15.7, SD=1.1) (Table S3, online only). There is a slight effect of education for all categories and an effect of gender for the less-educated category. Both effects are probably minimized by a ceiling effect.

TMT-A was available for 51,597 participants (mean score=34.4, SD=12.3) (Table S4, online only) and TMT-B for 51,267 participants (mean score=69.0, SD=31.7) (Table 3). There is an overall effect of education. Scores substantially decrease with age, in particular for TMT-B. We also observe a gender effect, more pronounced for the TMT-B.

Semantic fluency was available for 51,361 participants (mean score=23.4, SD=6.0) (Table 4). Scores appear to vary little with age and gender, and more substantially with education.

Phonological fluency was available for 51,195 participants (mean score=15.1, SD=4.8) (Table 5). We observe the same trends as on semantic fluency, with a stronger effect of gender.

DSST was available for 51,486 participants (mean score=65.4, SD=14.8) (Table 6). Scores decrease with age and increase with education and female gender.

Discussion

This study provides updated and reliable norms for five neuropsychological tests broadly used in clinical practice for adults aged 45–70.

First, the results illustrate the effect of age in almost all tests, and more particularly in tests involving speed processing, such as TMT and DSST, illustrating age-related speed processing decline considered as one the cardinal markers of normal cognitive aging [18]. The impact of age can be observed including in tight age ranges categories (5 years) as may be seen for the DSST: median scores are of 52 and 57, respectively for men and women aged [50–55[, and of 48 and 53, respectively for men and women aged [55–60[. Therefore, it seems important to rely on narrow age categories, especially for time-based tests for which we observe scores differences for a 5-year interval.

The results also illustrate the well-known effect of education on neuropsychological performances [19–21]. The link between cognition and education is one of the founding arguments of the concept of cognitive reserve [22] postulating that a high educational level confers to individuals greater compensatory capacities in dealing with age-related cognitive decline. Therefore providing education-stratified normative data is fundamental to properly assess individuals' performances.

The results also show an effect of gender, in particular for FCRST, phonological fluency and DSST. This finding is consistent with previous studies that have shown that women perform better on tests involving verbal material such as verbal fluency tasks [20] or FCRST [14,23] and in tests involving processing speed [24] such as DSST.

The main goal of this study was to take advantage of the large-sized CONSTANCES cohort to derive norms for the middle-aged population, providing precise age categories of five years,

allowing apprehending the heterogeneity of cognitive performances [1]. Adequate normative data are needed not only for older adults but also for middle-aged people who can experience various neurological disorders including early-onset dementia, multiple sclerosis, stroke or brain injury. Even though numerous normative data for people aged 45 and over have been published, most of them presented a small number of participants in that age category [25,26]. Moreover, some studies lacked of stratification on age and education [25] or relied on very large age categories (i.e., 20 years) [26]. Such studies may have too methodological limitations to properly address the inter-individual variability of cognitive performances in elderly but also middle-aged population. As an example, the present study showed that men aged 45 with a medium level of education (5–13 years of education) had a median free recall FCSRT score of 32 versus 28 for individuals aged 65 with the same education, that is, four words less.

This study has limitations. The norms provided in our study concern only five tests. Nevertheless, these tests cover different cognitive functions and are commonly used in diagnostic process [27–29]. Another limitation is the number of participants enrolled in the lowest category of education (i.e., 143 to 199 participants). However, this limitation can be mitigated in the context of the overall increase in educational attainment which explains the low number of people with less than five years of education.

The main strength of this study obviously relies on the very large sample allowing accessing a wide population variability in terms of age, sex and education.

To conclude, cognitive deficits are frequent in numerous neurological disorders which can affect not only older adults but also middle-aged ones. In order to track changes in cognitive functioning, tailor personalised rehabilitation strategies taking into account individual's cognitive resources and weaknesses, neuropsychological testing is an essential tool which has to be interpreted in the light of reliable and updated norms. In this perspective, the normative

scores provided in this study should help physicians and psychologists in their daily clinical practice.

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Disclosure of conflict of interest

None.

Study approval

All confidentiality, safety and security procedures were approved by the French legal authorities. The CONSTANCES project has obtained the authorization of the National Data Protection Authority (CNIL no. 910486). It was approved by the National Council for Statistical Information, National Medical Council, Institutional Review Board of the National Institute for Medical Research-INSERM (n° 01-011) and local Committee for Persons Protection.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Flowchart: Study sample for the norms of the different tests (MMSE, FCSRT, TMT, Verbal fluency, DSST) in the CONSTANCES cohort.

Table S1. Normative data stratified by age, gender and education for the three free and cued recalls of the FCSRT (number of words retrieved), CONSTANCES cohort ($n = 50,526$).

Table S2. Normative data stratified by age, gender and education for the delayed free recall of the FCSRT (number of words retrieved), CONSTANCES cohort ($n = 50,465$).

Table S3. Normative data stratified by age, gender and education for the delayed free and cued recall of the FCSRT (number of words retrieved), CONSTANCES cohort ($n = 50,459$).

Table S4. Normative data stratified by age, gender and education, for the TMT-A (time in seconds), CONSTANCES cohort ($n = 51,597$).

Table and figure captions

Figure S1

MMSE, Mini-Mental State Examination; FCSRT, Free and Cued Selective Reminding Test; TMT, Trait Making Test; DSST, Digit Symbol Substitution Test.

Table 1 Normative data stratified by age, gender and education for the MMSE, CONSTANCES cohort ($n = 51,791$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	187	140	1750	1790	2359	2967
5%	21	21	24	24	26	26
10%	22	22	25	25	27	27
25%	24	24	27	27	28	28
50%	27	26	28	28	29	29
75%	28	28	29	29	30	30
90%	29	29	30	30	30	30
95%	30	29	30	30	30	30
[50–55[
<i>N</i>	194	225	2216	2301	2168	2827
5%	21	22	24	24	26	26
10%	23	22	25	25	27	27
25%	25	24	27	27	28	28
50%	27	26	28	28	29	29
75%	29	28	29	29	30	30
90%	29	29	30	30	30	30
95%	30	30	30	30	30	30
[55–60[
<i>N</i>	199	195	2847	2756	2191	2766
5%	21	20	24	24	26	26
10%	22	21	25	25	27	27
25%	24	24	27	27	28	28
50%	27	26	28	28	29	29
75%	28	28	29	29	30	30
90%	29	29	30	30	30	30
95%	30	30	30	30	30	30
[60–65[
<i>N</i>	172	142	3010	3051	2269	2423
5%	21	20	24	24	26	26
10%	21	21	25	25	27	27
25%	24	23	27	27	28	28
50%	25	25	28	28	29	29
75%	27	28	29	29	30	30
90%	29	29	30	30	30	30
95%	29	29	30	30	30	30
[65–70]						
<i>N</i>	168	155	2782	2969	2393	2179
5%	20	21	24	24	26	26
10%	21	22	25	25	27	27
25%	24	24	27	27	28	28
50%	26	26	28	28	29	29
75%	28	28	29	29	30	30
90%	29	29	30	30	30	30
95%	30	29	30	30	30	30

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table 2 Normative data stratified by age, gender and education for the three free recalls of the FCSRT (number of words retrieved), CONSTANCES cohort ($n = 50,566$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	165	123	1681	1754	2306	2922
5%	20	21	23	26	26	29
10%	22	26	25	28	28	31
25%	26	29	28	31	31	33
50%	30	33	32	34	34	37
75%	34	35	35	37	37	39
90%	37	37	38	40	40	42
95%	38	38	39	41	41	43
[50–55[
<i>N</i>	171	212	2137	2254	2130	2795
5%	18	22	22	25	25	28
10%	20	25	24	28	27	30
25%	25	28	28	31	30	33
50%	30	32	31	34	34	36
75%	33	35	34	37	37	39
90%	37	38	37	39	40	41
95%	38	40	39	41	41	42
[55–60[
<i>N</i>	171	172	2775	2726	2147	2722
5%	19	21	21	24	24	27
10%	21	24	23	27	26	29
25%	24	27	27	30	29	32
50%	28	31	30	33	33	35
75%	31	34	34	37	36	38
90%	35	38	37	39	39	40
95%	37	39	38	41	40	42
[60–65[
<i>N</i>	148	124	2941	2984	2228	2391
5%	16	18	20	24	22	26
10%	19	21	22	25	24	28
25%	22	25	26	29	28	31
50%	27	30	29	32	31	35
75%	30	33	33	36	35	38
90%	34	36	36	38	38	40
95%	35	38	37	40	39	42
[65–70]						
<i>N</i>	143	148	2693	2911	2337	2155
5%	16	20	19	22	21	25
10%	19	22	21	25	23	27
25%	22	25	24	28	27	30
50%	26	29	28	32	31	34
75%	31	32	32	35	34	37
90%	34	36	34	38	37	39
95%	36	38	36	39	39	41

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table 3 Normative data stratified by age, gender and education, for the TMT-B (time in seconds), CONSTANCES cohort ($n = 51,267$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	177	134	1726	1780	2331	2943
5%	40	40	35	36	30	31
10%	44	44	39	40	34	35
25%	55	53	49	46	40	41
50%	76	74	61	57	49	49
75%	100	110	79	72	60	61
90%	146	154	102	94	75	74
95%	178	205	121	114	86	84
[50–55[
<i>N</i>	183	217	2184	2291	2153	2819
5%	45	44	39	37	32	34
10%	51	48	43	41	36	37
25%	61	59	52	49	42	44
50%	85	76	64	60	51	53
75%	115	107	82	76	64	65
90%	146	145	107	101	79	79
95%	169	174	132	124	88	91
[55–60[
<i>N</i>	188	179	2810	2751	2180	2747
5%	47	44	40	39	34	34
10%	53	51	45	43	38	38
25%	66	63	54	51	46	45
50%	86	86	68	63	56	55
75%	122	120	86	80	70	67
90%	168	157	114	104	86	83
95%	223	191	136	124	100	95
[60–65[
<i>N</i>	145	128	2977	3034	2258	2411
5%	52	54	44	42	36	37
10%	60	61	48	46	41	41
25%	76	75	59	55	49	49
50%	109	94	73	68	61	60
75%	149	128	96	87	75	74
90%	187	180	125	116	92	91
95%	217	197	152	145	108	104
[65–70]						
<i>N</i>	150	143	2739	2946	2373	2170
5%	49	50	47	45	39	41
10%	59	60	52	49	44	45
25%	79	73	62	59	52	53
50%	105	98	80	74	65	65
75%	142	135	104	96	80	80
90%	174	180	139	124	97	97
95%	219	209	167	146	114	114

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table 4 Normative data stratified by age, gender and education for the semantic fluency task (number of words provided in one minute), CONSTANCES cohort ($n = 51,361$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	178	131	1722	1780	2345	2946
5%	11	10	14	14	16	16
10%	13	12	16	15	18	18
25%	16	15	18	18	21	21
50%	20	19	22	22	25	25
75%	25	24	26	26	29	29
90%	28	27	30	29	33	33
95%	30	28	32	31	35	35
[50–55[
<i>N</i>	182	222	2190	2287	2153	2811
5%	11	12	14	14	17	16
10%	13	14	15	16	18	18
25%	16	17	19	19	21	21
50%	20	20	23	22	25	25
75%	25	22	27	26	29	29
90%	29	27	30	30	33	33
95%	31	29	32	32	36	36
[55–60[
<i>N</i>	191	186	2826	2751	2180	2748
5%	11	10	14	14	16	16
10%	14	14	16	16	18	18
25%	17	16	19	19	21	21
50%	20	20	22	22	24	25
75%	23	25	26	26	29	29
90%	26	29	30	30	33	33
95%	28	32	32	32	35	36
[60–65[
<i>N</i>	162	137	2981	3027	2260	2412
5%	10	10	14	14	16	16
10%	12	11	15	15	17	18
25%	14	14	18	18	20	21
50%	18	18	22	22	24	25
75%	22	21	26	25	28	29
90%	27	24	30	29	32	32
95%	29	27	32	31	35	35
[65–70]						
<i>N</i>	160	153	2752	2949	2372	2167
5%	9	10	13	13	15	16
10%	12	12	15	15	17	18
25%	15	15	17	18	20	20
50%	18	18	21	21	24	24
75%	22	21	25	25	28	28
90%	25	25	29	29	32	32
95%	27	27	31	31	34	34

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table 5 Normative data stratified by age, gender and education for the phonological fluency task (number of words provided in one minute), CONSTANCES cohort ($n = 51,195$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	174	127	1710	1771	2342	2941
5%	5	5	7	8	9	10
10%	6	6	8	9	11	11
25%	8	9	11	12	13	14
50%	11	12	14	14	16	17
75%	15	15	17	17	19	20
90%	17	18	20	20	22	23
95%	22	19	22	22	24	25
[50–55[
<i>N</i>	177	220	2183	2282	2149	2807
5%	5	5	7	8	9	10
10%	6	6	8	9	11	12
25%	8	9	11	12	13	14
50%	11	11	14	15	16	17
75%	14	15	17	18	19	20
90%	17	17	20	21	22	23
95%	20	20	21	23	24	25
[55–60[
<i>N</i>	188	180	2815	2748	2176	2743
5%	4	5	6	7	9	10
10%	5	6	8	9	11	12
25%	8	9	10	12	13	14
50%	10	12	13	15	16	17
75%	14	15	16	18	19	20
90%	17	19	19	21	23	23
95%	19	20	21	23	24	25
[60–65[
<i>N</i>	153	129	2975	3019	2255	2407
5%	3	4	6	7	9	10
10%	4	5	8	8	10	11
25%	6	7	10	11	13	14
50%	9	9	13	14	16	17
75%	12	13	16	17	19	20
90%	16	16	19	20	22	23
95%	18	17	21	22	24	25
[65–70]						
<i>N</i>	153	149	2742	2948	2368	2164
5%	3	4	6	7	9	10
10%	4	5	7	8	10	11
25%	6	7	10	11	12	14
50%	8	10	13	14	15	16
75%	12	13	16	17	18	19
90%	15	16	19	20	21	22
95%	19	20	20	21	23	24

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table 6 Normative data stratified by age, gender and education for the DSST (number of symbols correctly completed), CONSTANCES cohort ($n = 51,486$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	185	138	1738	1788	2352	2958
5%	28	32	42	46	54	58
10%	34	38	47	53	58	63
25%	42	47	55	62	66	69
50%	54	57	63	71	74	78
75%	65	71	73	80	82	87
90%	73	79	81	88	90	95
95%	78	85	86	94	96	99
[50–55[
<i>N</i>	190	223	2195	2291	2160	2818
5%	30	32	41	45	52	55
10%	37	38	45	51	57	59
25%	43	46	52	60	63	66
50%	52	57	62	69	72	75
75%	61	65	70	78	80	83
90%	70	73	79	85	87	90
95%	74	81	84	90	92	96
[55–60[
<i>N</i>	194	188	2825	2757	2185	2753
5%	27	27	39	45	49	52
10%	32	34	44	49	53	57
25%	39	45	50	58	60	63
50%	48	53	60	67	68	72
75%	58	63	68	76	77	80
90%	65	69	77	83	84	87
95%	71	77	81	88	89	92
[60–65[
<i>N</i>	168	140	2987	3036	2261	2415
5%	25	24	37	41	46	49
10%	27	29	41	46	50	52
25%	35	38	48	55	57	59
50%	42	48	56	63	65	67
75%	52	57	64	72	73	76
90%	62	66	73	80	81	83
95%	66	71	79	84	86	88
[65–70]						
<i>N</i>	161	153	2746	2948	2365	2168
5%	19	20	34	38	43	45
10%	26	27	38	42	47	49
25%	35	36	45	50	54	56
50%	43	44	53	59	61	63
75%	51	56	61	67	69	71
90%	61	64	69	75	77	79
95%	66	70	74	80	81	83

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table S1 Normative data stratified by age, gender and education for the three free and cued recalls of the FCSRT (number of words retrieved), CONSTANCES cohort ($n = 50,526$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	165	123	1681	1754	2305	2921
5%	39	41	41	43	43	45
10%	40	42	43	45	44	46
25%	43	45	45	46	46	47
50%	46	47	47	47	47	48
75%	47	48	48	48	48	48
90%	48	48	48	48	48	48
95%	48	48	48	48	48	48
[50–55[
<i>N</i>	171	213	2134	2254	2128	2795
5%	34	42	40	43	43	45
10%	38	43	43	45	44	46
25%	44	45	45	46	46	47
50%	46	47	47	47	47	48
75%	47	48	48	48	48	48
90%	48	48	48	48	48	48
95%	48	48	48	48	48	48
[55–60[
<i>N</i>	171	171	2773	2726	2145	2721
5%	36	40	39	43	42	44
10%	39	43	42	44	44	45
25%	43	45	44	46	46	47
50%	45	47	46	47	47	48
75%	47	48	48	48	48	48
90%	48	48	48	48	48	48
95%	48	48	48	48	48	48
[60–65[
<i>N</i>	147	124	2938	2978	2225	2390
5%	35	40	39	43	42	44
10%	37	42	41	44	43	45
25%	41	45	44	46	45	47
50%	45	46	46	47	47	48
75%	47	48	47	48	48	48
90%	48	48	48	48	48	48
95%	48	48	48	48	48	48
[65–70]						
<i>N</i>	143	147	2689	2907	2335	2152
5%	35	40	39	42	41	44
10%	38	41	41	44	43	45
25%	42	44	44	46	45	46
50%	45	46	46	47	47	48
75%	47	47	47	48	48	48
90%	48	48	48	48	48	48
95%	48	48	48	48	48	48

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table S2 Normative data stratified by age, gender and education for the delayed free recall of the FCSRT (number of words retrieved), CONSTANCES cohort ($n = 50,465$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	165	121	1680	1753	2303	2918
5%	8	8	9	10	10	11
10%	8	10	10	11	11	12
25%	10	11	11	12	12	13
50%	12	13	13	14	14	14
75%	13	14	14	15	15	15
90%	14	15	15	16	15	16
95%	15	16	15	16	16	16
[50–55[
<i>N</i>	170	213	2133	2252	2127	2792
5%	6	9	8	10	9	11
10%	7	9	9	11	11	12
25%	10	11	11	12	12	13
50%	12	12	12	14	13	14
75%	13	14	14	15	15	15
90%	14	15	15	15	15	16
95%	15	15	15	16	16	16
[55–60[
<i>N</i>	171	171	2771	2722	2143	2718
5%	6	8	8	9	9	10
10%	7	9	9	10	10	11
25%	9	11	11	12	12	13
50%	11	13	12	13	13	14
75%	13	14	14	14	14	15
90%	14	15	15	15	15	16
95%	15	15	15	16	16	16
[60–65[
<i>N</i>	147	124	2934	2971	2223	2388
5%	6	8	7	9	8	10
10%	7	8	8	10	9	11
25%	9	10	10	11	11	12
50%	10	12	12	13	13	14
75%	13	14	13	14	14	15
90%	14	15	14	15	15	16
95%	15	15	15	16	15	16
[65–70]						
<i>N</i>	143	147	2685	2902	2328	2150
5%	6	7	7	8	8	9
10%	6	9	8	9	9	10
25%	8	10	10	11	11	12
50%	11	12	11	13	12	13
75%	13	13	13	14	14	15
90%	14	14	14	15	15	15
95%	15	15	15	15	15	16

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table S3 Normative data stratified by age, gender and education for the delayed free and cued recall of the FCSRT (number of words retrieved), CONSTANCES cohort ($n = 50,459$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	165	121	1679	1753	2303	2918
5%	13	14	14	15	15	15
10%	13	15	15	15	15	16
25%	14	16	15	16	16	16
50%	16	16	16	16	16	16
75%	16	16	16	16	16	16
90%	16	16	16	16	16	16
95%	16	16	16	16	16	16
[50–55[
<i>N</i>	170	212	2132	2252	2127	2791
5%	11	14	14	15	15	15
10%	13	15	15	15	15	16
25%	15	16	15	16	16	16
50%	16	16	16	16	16	16
75%	16	16	16	16	16	16
90%	16	16	16	16	16	16
95%	16	16	16	16	16	16
[55–60[
<i>N</i>	171	171	2771	2722	2142	2718
5%	12	14	14	15	14	15
10%	13	14	14	15	15	16
25%	15	16	15	16	16	16
50%	16	16	16	16	16	16
75%	16	16	16	16	16	16
90%	16	16	16	16	16	16
95%	16	16	16	16	16	16
[60–65[
<i>N</i>	147	124	2933	2971	2223	2388
5%	11	13	13	15	14	15
10%	13	14	14	15	15	16
25%	14	15	15	16	16	16
50%	15	16	16	16	16	16
75%	16	16	16	16	16	16
90%	16	16	16	16	16	16
95%	16	16	16	16	16	16
[65–70]						
<i>N</i>	143	147	2685	2902	2328	2150
5%	12	14	13	14	14	15
10%	13	14	14	15	15	15
25%	15	15	15	16	15	16
50%	16	16	16	16	16	16
75%	16	16	16	16	16	16
90%	16	16	16	16	16	16
95%	16	16	16	16	16	16

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

Table S4 Normative data stratified by age, gender and education, for the TMT-A (time in seconds), CONSTANCES cohort ($n = 51,597$).

Age groups	Education					
	No diploma ^a		Primary, vocational or high school degree ^b		College degree ^c	
	Men	Women	Men	Women	Men	Women
[45–50[
<i>N</i>	187	138	1742	1789	2353	2963
5%	19	19	18	18	16	17
10%	22	22	20	20	18	19
25%	26	26	24	23	21	22
50%	33	33	29	29	26	27
75%	45	45	37	36	32	33
90%	58	57	45	45	40	40
95%	73	67	53	52	46	45
[50–55[
<i>N</i>	190	223	2204	2296	2162	2829
5%	20	20	19	19	18	18
10%	24	23	21	21	19	20
25%	28	28	26	25	23	24
50%	36	34	31	31	28	29
75%	46	45	39	38	34	36
90%	59	58	49	47	42	43
95%	67	74	55	54	48	49
[55–60[
<i>N</i>	194	189	2834	2759	2187	2758
5%	22	22	20	20	18	19
10%	26	24	22	22	21	21
25%	31	29	27	27	25	25
50%	38	37	33	32	31	31
75%	49	51	41	40	38	38
90%	66	69	51	49	46	45
95%	74	78	58	55	52	52
[60–65[
<i>N</i>	163	139	2995	3041	2262	2417
5%	26	26	22	22	21	21
10%	28	29	25	23	23	23
25%	34	35	29	28	27	27
50%	44	43	36	34	33	33
75%	54	53	45	42	41	41
90%	68	66	55	52	48	49
95%	79	82	62	60	55	56
[65–70]						
<i>N</i>	164	152	2763	2956	2377	2171
5%	28	23	24	23	23	22
10%	30	27	27	25	25	24
25%	36	35	32	30	29	29
50%	44	43	38	37	36	35
75%	55	56	47	45	44	43
90%	76	68	59	56	54	52
95%	85	84	68	63	61	58

^a <5 years of education.

^b 5–13 years of education.

^c ≥14 years of education.

