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Telephone-based Frontal Assessment Battery (t-FAB): standardization for the Italian population and clinical usability in neurological diseases

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Abstract

Background Despite the relevance of telephone-based cognitive screening tests in clinical practice and research, no specific test assessing executive functioning is available. The present study aimed at standardizing and providing evidence of clinical usability for the Italian telephone-based Frontal Assessment Battery (t-FAB).

Methods The t-FAB (ranging 0–12), comprising two subtests, has two versions: one requiring motor responses (t-FAB-M) and the other verbal responses (t-FAB-V). Three hundred and forty-six Italian healthy adults (HPs; 143 males; age range = 18–96 years; education range = 4–23 years) and 40 participants with neurological diseases were recruited. To HPs, the t-FAB was administered along with a set of telephone-based tests: MMSE, verbal fluency (VF), backward digit span (BDS). The in-person version of the FAB was administered to both HPs and clinical groups. Factorial structure, construct validity, inter-rater and test–retest reliability, t-FAB-M vs. t-FAB-V equivalence and diagnostic accuracy were assessed. Norms were derived via Equivalent Scores.

Results In HPs, t-FAB measures yielded high inter-rater/test-retest reliability (ICC = .78–.94), were internally related ($p \le .005$) and underpinned by a single component, converging with the telephone-based MMSE, VF, BDS ($p \le .0013$). The two t-FAB versions were statistically equivalent in clinical groups (ps of both equivalence bounds < .001). Education predicted all t-FAB scores (p < .001), whereas age only the t-FAB-M score ($p \le .004$). t-FAB scores converge with the inperson FAB in HPs and clinical groups ($r_s = .43-.78$). Both t-FAB versions were accurate in discriminating HPs from the clinical cohort (AUC = .73-.76).

Discussion The t-FAB is a normed, valid, reliable and clinically usable telephone-based cognitive screening test to adopt in both clinical and research practice.

Keywords Telephone-based \cdot Cognitive screening \cdot Frontal assessment battery \cdot Teleneurology \cdot Executive functioning \cdot Stroke \cdot Neurological disease

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Introduction

Telephone-based cognitive screening (TBCS) is relevant to clinical and experimental telemedicine, as allowing firstlevel neuropsychological evaluations when in-person access to clinics is not possible due to logistical [1, 2], geographical [3], economical [4] and safety reasons [5]. TBCS also facilitates the implementation of epidemiological/population-based studies [6], decentralized clinical trials [7] and prevention campaigns [8]. Moreover, at variance with other remote assessment media (e.g., videoconference), the telephone proves to be well accepted by receivers of different socio-demographic backgrounds as requiring minimal digital and health literacy [9, 10], being also judged by users as adequate to meet clinical/research questions [9]. It has to be then noted that, as other telehealth practices, TBCS has the potential to reduce the psychosocial burden related to in-person healthcare, weighting not only on patients, but also on their caregivers and professionals carers, which has significantly increased since the onset of the COVID-19 pandemic [11, 12].

Although several TBCS tools for the assessment of global cognitive status have been developed in recent years [6], no standardized test selectively screening executive functions is available, especially in Italy [13, 14]. Indeed, fully standardized Italian TBCS tests are currently limited to multi-domain screening tests for global cognition [2, 15].

Nevertheless, executive deficits feature a variety of neurological diseases affecting cortical and subcortical frontal circuitries [16] and convey relevant information towards differential diagnosis and prognosis [17]. Moreover, subclinical or mild dysexecutive features are highly prevalent in healthy elderlies due to the anatomo-functional changes of frontal networks resulting from physiological aging [18, 19], which were shown to negatively impact on daily living functional outcomes [17]. Screening for executive dysfunctions is thus crucial in both neurology and geriatrics, and the availability of standardized TBCS tests for frontalexecutive dysfunctions should be part of telemedicine [14], especially when dealing with elderly clinical populations. Indeed, aging individuals often come with a range of frailties that would prevent or delay their access to outpatient in-person clinics, due to both logistical (e.g., motor disabilities) and health safety reasons (e.g., an increase exposure to SARS-CoV-2 infection) [3, 8, 14]. Such instruments would be also useful to be adopted as outcome measures/endpoints within large-scale studies or decentralized clinical trials in neurological and geriatric populations with frontal-executive impairments [20].

Among frontal-executive screeners, the in-person version of the Frontal Assessment Battery (FAB) [21] represent one of the most psychometrically and diagnostically sound tests worldwide [22]. In Italy, the FAB has been shown to come with optimal psychometrics, diagnostics and clinical usability evidence [18, 19, 23, 24].

Therefore, this study aimed at standardizing, in the Italian population, a telephone-based version of the FAB (t-FAB), also exploring its clinical usability in different neurological diseases.

Methods

Participants

The normative sample comprised 346 Italian healthy participants (HPs) from different regions of Italy. Inclusion criteria were: (1) negative anamnesis for neurological/psychiatric disorders, not being (2) under active psychotropic medications or (3) in uncompensated/severe metabolic/internal conditions, (4) not having system/organ failures, (5) presenting with uncorrected hearing deficits. Medical history for all participants was collected through a semi-structured interview. HPs were recruited via the authors' personal acquaintances and advertising at the University of Milano-Bicocca and the University of Padova.

A total of 40 participants affected by neurological diseases were consecutively recruited at two neuropsychology services in Northern Italy. Inclusion criteria for clinical groups were a neurologist-posed clinical diagnosis of a given target disease based on current diagnostic criteria and supported by neurological, neuroradiological and neuropsychological examinations. Ten participants with ischemic/hemorrhagic stroke presenting with unilateral, cortical/subcortical hemispheric lesion (5 right and 5 left brain-damaged) were recruited at the neuropsychology service of IRCCS Istituto Auxologico Italiano, Milano. Five participants affected with hypokinetic extra-pyramidal disorders (three with Parkinson's disease [25], and three with atypical parkinsonisms [26]), 20 with small vessel disease (SVD) [27] and 4 with a mixed, atrophic-vascular dementia (MD) [28] were recruited at the neuropsychology service of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano. The full selection process of participants with neurological conditions is shown as follows ("Results", paragraph "Standardization").

The study was approved by the Ethical Committees of the University of Milano-Bicocca, Milano (ID: RM-2021–382, 19/02/2021), the University of Padova, Padova (ID: 4107, 19/02/2021) and IRCCS Istituto Auxologico Italiano, Milano (ID: 25C122, 18/05/2021). Participants provided their informed consent. Data collection for HPs started in March 2021 and ended in January 2022, whereas that for clinical populations started in July 2021 and ended in January 2022.

Materials

The t-FAB was adapted from Aiello et al.'s [24] version of the FAB. The in-person FAB total score ranges from 0 to 18 and it comprises 3 subtests (each ranging from 0 to 6), each including two tasks: Conceptualization, Mental flexibility (language-mediated executive functions, FAB-1), Motor programming and Sensitivity to interference (motor-mediated executive functions, FAB-2) and Inhibitory control and Environmental autonomy (inhibition; FAB-3) [24]. In the t-FAB, Conceptualization and Mental flexibility tasks were the same of the in-person version, whereas *Programming* and Environmental autonomy tasks were removed. Sensitivity to interference and Inhibitory control tasks were modified to adapt to the telephonic administration (i.e., for participants' responses to be audible by the examiner through the telephone). Two versions of both Sensitivity to interference and Inhibitory control tasks, different as to their response modality, were developed: the first requiring the examinee to provide a motor response (t-FAB-M; e.g., "tap once on the table when I tap twice"), the second to provide a verbal one (t-FAB-V; e.g., "say «one» when I say «two»"). In case of lateralized sensorimotor deficits, participants with neurological diseases were asked to use their unaffected hand. Both t-FAB-M and t-FAB-V versions of Sensitivity to interference and Inhibitory control tasks were administered to all participants (order: FAB-M first). In addition, each t-FAB is divided into two subtests: t-FAB-1 (Conceptualization plus Mental flexibility) and t-FAB-2-M/-V (Sensitivity to interference plus Inhibitory control). The total t-FAB score of both versions ranged 0-12.

The full t-FAB protocol is provided in Supplementary Material 1. All the above adaptations were jointly conceptualized and operationalized by an author board that comprised a neurologist (IA), three neuropsychologists (SZ, SM, NB), three neuroscientists (ENA, VP, LD) and two physiatrists expert in psychometrics (LT, SS), all with extensive expertise in the field of cognitive test standardization. No disagreement emerged in this first phase, and the protocol was subsequently approved without reservation by the remaining authors [30, 31].

For assessing construct validity, the following tests were remotely administered to the following HP subsamples:

- phonemic, semantic and alternate verbal fluency tests (PVF; SVF; AVF) (HP subsample of N=330: 138 males, 192 females; age: 48.39±18.81 years, 18–96; education: 13.46±3.75 years, 4–23), along with the derived Cognitive Shifting Index (CSI), a measure of cognitive flexibility [29];
- the Italian telephone-based Mini-Mental State Examination (Itel-MMSE; HP subsample of N=253: 99 males,

154 females; age: 47.11 ± 18.67 years, 18–96; education: 13.7 ± 3.65 years, 4–22) [30; 31];

a backward digit span (BDS) task [32] (HP subsample of N = 270: 110 males, 160 females; age: 47.24 ± 18.33 years, 18–96; education: 13.67 ± 3.63 years, 4–22), comprising two scores: the longer recalled digit sequence (a measure of working memory capacity; BDS-WM) and the total number of recalled sequences (a measure of sustained attention during task execution; BDS-T) [33].

To assess invariance between the t-FAB and its in-person version, 50 HPs (19 males, 31 females; age: 46.22 ± 16.83 years, 20-86; education: 13.82 ± 3.53 years, 5-23) underwent the paper-and-pencil FAB 48 hours before (*N*=25) or after (*N*=25) the remote assessment to rule out carry-over effects. A different subgroup of 20 HPs (11 males, 9 females; age: 42.6 ± 17.9 years, 19-80; education: 12.1 ± 3.46 years, 5-16) were administered the FAB either 14 days before (*N*=10) or after (*N*=10) the t-FAB.

For test-retest reliability, the t-FAB was administered two times, at a 30-day distance, to 27 HPs (12 males, 15 females; age: 47.56 ± 21.14 years, 23–85; education: 14.74 ± 4.42 years, 5–21), whereas, for inter-rater reliability, 25 protocols (8 males, 17 females; age: 45.2 ± 17.67 years, 21-74; education: 14.4 ± 3.19 years, 8–20) were simultaneously scored by two independent raters blinded to each other's decisions.

All the above HP subsamples were randomly selected through random number tables from the whole normative sample.

Participants with neurological diseases also underwent the in-person FAB, delivered 7–14 days before t-FAB administration.

Before telephone-based testing, all participants underwent a detailed sound-check to ensure a good quality of the call [15].

All tests were administered to both HPs and individuals with neurological diseases by licensed psychologists with thorough expertise in neuropsychological assessment and/or trainees neuropsychologists (ANP, ADL, GS, and TD). Testers underwent a thorough administration training performed by the corresponding author (ENA). Statistical analyses were performed by four neuroscientists with thorough expertise in cognitive data analyses (ENA, VP, LD, and ANP) and approved by the whole author panel.

Statistical analyses

Analyses were run via SPSS 27 (IBM Corp., 2020), R 4.1.0 (https://cran.r-project.org/) and jamovi 1.6.23 (https://www.jamovi.org/). The 2-tailed significance level was set

at $\alpha = 0.05$ and Bonferroni correction applied to multiple comparisons whenever necessary.

Either Pearson's or Spearman's technique was adopted to test for construct validity in HPs based on data distributing normally or not, respectively (i.e., skewness and kurtosis values <|1| and |3|, respectively) [34]. Test–retest and interrater reliability in HPs were assessed through intra-class correlations. Factorial structure in HPs was explored through a principal component analysis (PCA) by entering each task separately for the t-FAB-M and t-FAB-V.

According to the recommendations by Hobart et al. [35], which relate to health measurement studies for clinical neurology, the minimum sample size for all the aforementioned reliability and validity analyses in HPs were set at N=20 and N=80, respectively, except for the PCA, for which a N=100 was deemed as sufficient according to guidelines delivered by Kyriazos [36].

Equivalence between the t-FAB-M and t-FAB-V was assessed in HPs through a two one-sided test procedure (TOST) for dependent samples [36]. Accordingly, a between-mean effect size is regarded as equivalent to 0 if falling within the upper and lower equivalence bounds. In such a case, both equivalence bounds will yield a p < 0.05. Sample size estimation for this procedure, performed via the R package *TOSTER* (https://cran.r-project.org/web/packa ges/TOSTER/TOSTER.pdf) [37], yielded a minimum of N = 52 observations for detecting equivalence with a 95% power, $\alpha = 0.05$ and upper and lower equivalence bounds of -0.5 and 0.5, respectively.

Convergence between the t-FAB-M/-V and its in-person version was tested in both HPs and clinical groups via correlational techniques. Sample size estimation for such analyses, as performed via the R package *pwr* (https://CRAN.R-project.org/package=pwr), yielded a minimum *N* of 20 by addressing a one-tailed hypothesis testing (i.e., positive correlation) at α =0.05, an expected medium-to-large effect size ρ =0.5 and an 80% power.

Norms were derived through the Equivalent Score (ES) method [38, 39]; outer and inner tolerance limits (TLs), as well as ES thresholds, were computed on ranked scores adjusted for significant anagraphic–demographic confounders via a stepwise regression procedure. The

quasi-continuous ES scale allows for clinical judgments as follows: ES = 0 (adjusted scores lower than the outer TL) indexing an "impaired" performance; ES = 1, which indicates a "borderline" score; ES = 2–3-4 indicate a "normal" score. To derive norms, consistently with previous studies [2] and by adopting the R package *pwr* (https://CRAN.Rproject.org/package=pwr), a minimum sample size of 287 participants was deemed as adequate, by addressing a smallto-medium effect size ($f^2 = 0.05$), with a 95% power and $\alpha = 0.05$, within a multiple regression model ($df_{numerator} = 3$).

Diagnostic accuracy was tested via receiver-operating characteristics (ROC) analyses by addressing t-FAB scores of the whole clinical group (stroke, EPD, SVD, MD) against the whole normative sample. For this single-test ROC analysis, the minimum sample sizes for the normative and clinical groups were estimated, according to Obuchowski [40], by means of *easyROC* (http://www.biosoft.hacettepe.edu.tr/ easyROC/), at N=190 and N=19, respectively, a case-control allocation ratio of 10 and to detect an AUC=0.7 with a power of 90% and α =0.05.

Diagnostic accuracy was further explored for descriptive purposes (due to the small sample sizes addressed) by comparing (1) each clinical subgroups against the normative sample and (2), within the whole clinical cohort, t-FAB scores of participants performing defectively (i.e., ES = 0/1) on the in-person FAB against those performing within the normal range (i.e., $ES \ge 2$). As to ROC analyses addressing the SVD group, due to the high heterogeneity in cognitive status as assessed by the MMSE, participants were subdivided into those obtaining an MMSE $ES \le 1$ (impaired/borderline performance; N=6) and those obtaining an MMSE ES > 1 (normal performance; N=14) [41].

Results

Standardization

Normative sample stratification is shown in Table 1. HPs' background and cognitive profiles are summarized in Table 2. Ceiling effects at the t-FAB (i.e., a score of 12/12)

Table 1	Sample stratification
for age,	education, and sex

Male/female	Age						
Education	30≤	31-45	46-60	61–70	71-80	≥81	Total
5≤	0/0	0/0	0/0	1/2	1/2	1/8	3/12
5–8	5/0	2/2	8/13	4/2	3/4	2/3	24/24
9–12	1/1	0/1	2/12	4/5	3/2	1/1	11/22
13–16	33/29	9/11	21/43	5/13	1/3	0/1	69/100
≥17	13/20	4/5	9/11	7/7	2/0	1/2	36/45
Fotal	52/50	15/19	40/79	21/29	10/11	5/15	143/203

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N	346
Age (years)	$48.57 \pm 18.92 (18-96)$
Sex (M/F)	143/203
Education (years)	$13.42 \pm 3.76 (4-23)$
N for Italian regions	
North Italy	81.8%
Center Italy	4.9%
South Italy	13.3%
N for occupation	
Predominantly manual	24.2%
Manual/clerical	24.2%
Predominantly clerical	51.6%
Itel-MMSE ($N = 253$)	$21.58 \pm .82$ (17–22)
PVF (<i>N</i> =330)	42.58 ± 13.45 (13–85)
SVF (<i>N</i> =330)	55.54±13.17 (3–84)
AVF (<i>N</i> =330)	42.19 ± 13.67 (4–74)
CSI (N=330)	$.86 \pm .22$ (.1–2.22)
BDS-WM (<i>N</i> =277)	4.76±1.25(0-6)
BDS-T (<i>N</i> =277)	4.94±2.01 (0-8)
t-FAB	
t-FAB-M	10.84 ± 1.46 (2–12)
t-FAB-V	10.98 ± 1.24 (4–12)
t-FAB-1	5.22±.86 (2-6)
t-FAB-2-M	5.62±.97 (0-6)
t-FAB-2-V	$5.77 \pm .73 (0-6)$

N number of participants, *M* male, *F* female, *Itel-MMSE* Italian telephone-based Mini-Mental State Examination, *PVF* phonemic verbal fluency, *SVF* semantic verbal fluency, *AVF* alternate verbal fluency, *CSI* Cognitive Shifting Index, *BDS-WM* backward digit span—working memory, *BDS-T* backward digit span—total, *t-FAB* telephone-based Frontal Assessment Battery, *t-FAB-M* motor-mediated t-FAB, *t-FAB-V* verbal-mediated t-FAB, *t-FAB-I* tasks *Conceptualization+Mental flexibility*, *t-FAB-2-M/V* tasks *Sensitivity to interference+Inhibitory control*

were detected in 35.8% (t-FAB-M) and 39.3% (t-FAB-V) of HPs. Acceptability rate was of 100%.

Construct validity data with the other telephone-based measures are displayed in Table 3. Each t-FAB score converged with the vast majority of the other telephone-based test scores, the highest associations being found with PVF, SVF and AVF scores. t-FAB total and subtests scores were all internally related at $\alpha_{adjusted} = 0.017$ (t-FAB-M: $0.19 \le r_s(346) \le 0.9$, p < 0.001; t-FAB-V: $0.15 \le r_s(346) \le 0.84$, $p \le 0.005$).

Inter-rater and test-retest reliability were high for both t-FAB-M (test-retest: ICC = 0.88; and ICC = 0.84) and t-FAB-V (test-retest: ICC = 0.94; inter-rater: ICC = 0.78). A clear mono-component factor (reflecting "frontal-executive global efficiency") underpinned both the t-FAB-M (39.5% of variance explained; loading *range* = 0.54-0.67) and t-FAB-V (34.2% of variance explained; loading *range* = 0.43-0.66).

Despite t-FAB-M scores (M = 10.8; SD = 1.46) being lower than t-FAB-V (11 ± 1.23 ; $t_{345} = -3.3$; p = 0.001), the two versions showed statistical equivalence at the TOST procedure (both upper and lower equivalence bound yielding a p < 0.001).

The in-person FAB converged, at $\alpha_{adjusted} = 0.0013$, with both the t-FAB-M ($r_s(20) = 0.78$; p < 0.001) and t-FAB-V ($r_s(20) = 0.75$; p < 0.001) when administered at the 14-day follow-up, as well as at the 48-h follow-up (t-FAB-M: $r_s(50) = 0.44$; p = 0.001; t-FAB-V: $r_s(50) = 0.46$; p = 0.001).

Education predicted all t-FAB scores (p < 0.001), whereas age only t-FAB-M and t-FAB-2-M scores ($p \le 0.004$). Selected correction factors, TLs and ES thresholds are shown in Table 4. An automated correction sheet is provided in the Supplementary Material 2.

Clinical usability

Out of 67 individuals with neurological conditions consecutively screened for eligibility at the neuropsychology clinics, 10 refused to participate without further

	t-FAB-M	t-FAB-V	t-FAB-1	t-FAB-2-M	t-FAB-2-V
BDS-T	$r_s(277) = .22*$	$r_s(277) = .21*$	$r_s(277) = .2^*$	$r_s(277) = .17^{\dagger}$	$r_s(277) = .14^{\dagger}$
BDS-WM	$r_s(277) = .21*$	$r_s(277) = .21*$	$r_s(277) = .19^{\dagger}$	$r_s(277) = .16^{\dagger}$	$r_s(277) = .16^{\dagger}$
PVF	$r_s(330) = .3^*$	$r_s(330) = .28*$	$r_s(330) = .28*$	$r_s(330) = .23^*$	$r_s(330) = .14$ †
SVF	$r_s(330) = .32^*$	$r_s(330) = .25*$	$r_s(330) = .24*$	$r_s(330) = .3^*$	$r_s(330) = .15^{\dagger}$
AVF	$r_s(330) = .39^*$	$r_s(330) = .32^*$	$r_s(330) = .29*$	$r_s(330) = .33^*$	$r_s(330) = .22*$
CSI	$r_s(330) = .2^*$	$r_s(330) = .18*$	$r_s(330) = .14$ †	$r_s(330) = .19^*$	$r_s(330) = .19^*$
Itel-MMSE	$r_s(253) = .22^*$	$r_s(253) = .19^{\dagger}$	$r_s(253) = .14^{\dagger}$	$r_s(253) = .24*$	$r_s(253) = .23*$

†Significant at $\alpha = .05$; *significant at $\alpha_{adjusted} = .0013$, *t-FAB* telephone-based Frontal Assessment Battery, *t-FAB-M* motor-mediated t-FAB, *t-FAB-V* verbal-mediated t-FAB, *FAB-1* tasks *Conceptualization+Mental flexibility*, *t-FAB-2-M/V* tasks *Sensitivity to interference+Inhibitory control*, *BDS-WM* backward digit span—working memory, *BDS-T* backward digit span—total, *PVF* phonemic verbal fluency, *SVF* semantic verbal fluency, *AVF* alternate verbal fluency, *CSI* cognitive shifting index, *Itel-MMSE* Italian telephonebased Mini-Mental State Examination

Table 3 Spearman's correlation coefficients between t-FAB scores and construct validity measures

Table 4 Adjustment grids and Equivalent Scores (ES) for t-FAB scores

	Education								
		5	8	11	13	16	18		
	Age			·					
t-FAB-M	35	1.17	0.46	-0.02	-0.27	-0.59	-0.77		
	40	1.21	0.50	0.02	-0.23	-0.55	-0.72		
	45	1.27	0.56	0.08	-0.18	-0.49	-0.67		
	50	1.34	0.63	0.14	-0.11	-0.42	-0.60		
	55	1.42	0.71	0.23	-0.03	-0.34	-0.52		
	60	1.52	0.81	0.33	0.07	-0.24	-0.42		
	65	1.64	0.92	0.44	0.19	-0.12	-0.30		
	70	1.77	1.06	0.58	0.33	0.01	-0.17		
	75	1.93	1.22	0.74	0.48	0.17	-0.01		
	80	2.11	1.40	0.92	0.66	0.35	0.17		
	85	2.32	1.60	1.12	0.87	0.55	0.38		
	90	2.54	1.83	1.35	1.10	0.78	0.61		
t-FAB-V		1.83	0.65	0.12	-0.10	-0.32	-0.43		
t-FAB-1		0.96	0.48	0.15	-0.02	-0.23	-0.35		
t-FAB-2-M	35	0.47	0.17	- 0.03	- 0.13	- 0.27	-0.34		
	40	0.49	0.19	-0.01	-0.11	-0.25	-0.32		
	45	0.52	0.22	0.02	-0.09	-0.22	-0.29		
	50	0.55	0.26	0.05	-0.05	-0.18	-0.26		
	55	0.60	0.30	0.09	-0.01	-0.14	-0.22		
	60	0.65	0.35	0.14	0.04	-0.09	-0.17		
	65	0.70	0.41	0.20	0.10	-0.03	-0.11		
	70	0.77	0.47	0.27	0.17	0.03	-0.04		
	75	0.85	0.55	0.35	0.24	0.11	0.04		
	80	0.94	0.64	0.44	0.33	0.20	0.13		
	85	1.04	0.74	0.54	0.44	0.30	0.23		
	90	1.16	0.86	0.66	0.55	0.42	0.34		
t-FAB-2-V		0.69	0.25	0.05	-0.04	-0.12	-0.16		
	Equivalent Scores								
	oTL	iTL	0	1	2	3	4		
t-FAB-M	8.07	8.77	≤8.07	8.08–9.45	9.46–10.5	10.51-11.03	≥11.04		
t-FAB-V	8.48	9	≤8.48	8.49-9.83	9.84-10.68	10.69-10.93	≥10.94		
t-FAB-1	3.54	4.07	≤3.54	3.55-4.49	4.50-4.84	4.85-5.45	≥5.46		
t-FAB-2-M	3.16	4	≤3.16	3.17-4.90	4.91-5.66	5.67-5.84	≥5.85		
t-FAB-2-V	3	5	≤3	3.01-5.77	5.78-5.86	5.87-5.99	≥6		

t-FAB = telephone-based Frontal Assessment Battery, t-FAB-M = motor-mediated t-FAB, t-FAB-V = verbal-mediated t-FAB, FAB-1 = tasks Conceptualization + Mental flexibility, t-FAB-2-M/V = tasks Sensitivity to interference + Inhibitory control, AS adjusted score, iTL inner tolerance limit, σTL outer tolerance limit, RS raw score

t-FAB-M: AS = RS + 0.000002*[(age^3)-167,162.855491]-3.484874 *[log10(education)-1.106787]

t-FAB-V: $AS = RS + 15.62586^{(1)}(1) + 15.62586^{(1)}(1)$

t-FAB-1: AS = RS -1.020062*[ln(education)-2.548471]

t-FAB-2-M: $AS = RS + 0.000001*[(age^3) - 167, 162.855491] - 1.462853*[log10(education) - 1.106787)$

t-FAB-2-V: AS = RS + 5.921931*(1/education-0.083175)

Adjustment factors have been extracted from the above adjustment equations and do not always reflect empirical co-occurrences. Supplementary Material 1 provides a sheet for the automated computation of ASs

	Total	EPD	SVD		Stroke		MD
			MMSE ES > 1	MMSE ES ≤ 1	Left	Right	
N	40	6	14	6	5	5	4
Sex (M/F)	17/23	4/2	5/9	2/4	3/2	2/3	1/3
Age (years)	73.1±11.5 (38–91)	76±5.06 (70–82)	76.07±8.87 (56–87)	81.33 ± 7.97 (68–91)	54.6±12.42 (38–67)	68.8 ± 9.73 (54–78)	74.5 ± 9.98 (60-82)
Education (years)	13.3 ± 4.39 (5–18)	14±5.18 (5–18)	12±4.37 (5–18)	14.5 ± 3.94 (8-18)	14±4.18 (8–18)	13.8 ± 5.31 (8–18)	13.5±4.8 (8–18)
MMSE (N=38)							
Raw scores	27.26 ± 2.84 (20-30)	29 ± 1.27 (27-30)	28.71 ± 1.27 (26–30)	23.33 ± 1.75 (21–26)	30 ± 0 (30)	26 ± 1.87 (23–28)	25±4.08 (20–30)
$ES \le 1$		1	-	_	-	2	3
FAB $(N=33)$							
Raw scores	14.45 ± 3.09 (5–18)	15 ± 1.68 (13-17)	15.77±1.79 (13–18)	12.8 ± 5.17 (5-17)	13±0(13)	12.25 ± 3.3 (8–16)	14±4.2 (9–18)
$ES \le 1$		-	-	2	1	3	2
t-FAB-M	8.63 ± 2.66 (4-12)	9±3.23 (4–12)	9.43 ± 1.99 (6-12)	7.5 ± 3.89 (4-12)	10±2.35 (6–12)	7.4 ± 1.67 (6–10)	6.75±2.22 (4–9)
t-FAB-V	9.3 ± 2.17 (4-12)	9.5±3.02 (4–12)	10±1.71 (7–12)	8.67±2.25 (7–12)	9.8±1.79 (8–12)	9.4±1.67 (8–12)	6.75±2.22 (4–9)

Table 5 Demographic, clinical, and cognitive data of participants with neurological diseases

N number of participants, M male, F female, EPD extra-pyramidal disease, SVD small vessel disease, MD mixed dementia, ES Equivalent Score, MMSE Mini-Mental State Examination, FAB Frontal Assessment Battery, t-FAB telephone-based Frontal Assessment Battery, t-FAB-M motormediated t-FAB, t-FAB-V verbal-mediated t-FAB

explanations, 4 stated not to be available due to working activities, 7 were excluded as being deemed by their respective caregivers as not to be able to participate due to severe behavioral alterations that would have undermined compliance, 3 were unable to execute tasks due to severe hearing deficits and 3 presented with severe medical-general conditions. Background, clinical and cognitive data of the final clinical cohort (N = 40) are reported in Table 5. Within the whole clinical group, FAB scores correlated ($\alpha_{adjusted} = 0.025$) with both t-FAB-M $(r_{c}(33) = 0.62; p < 0.001)$ and t-FAB-V $(r_{c}(33) = 0.43;$ p = 0.012) scores. When discriminating the whole clinical group from the normative sample, moderate-to-high accuracy was detected for both the t-FAB-M (AUC = 0.76; SE = 0.05; 95% CI [0.66, 0.85]) and t-FAB-V (AUC = 0.73; SE = 0.05; 95% CI [0.63, 0.83]).

As to descriptive ROC analyses, AUC values were overall moderate-to-high (AUC = 0.65-0.97) for each clinical group and similar between the t-FAB-M and t-FAB-V (Table 6). Moreover, when descriptively comparing, within the whole clinical group, patients with an ES = 0/1 on the FAB vs. those with an ES \geq 2, moderate-to-high accuracy yielded with respect to both t-FAB-M (AUC = 0.83; *SE* = 0.09; 95% CI [0.66, 0.1]) and t-FAB-V (AUC = 0.7; *SE* = 0.11; 95% CI [0.49, 0.91]).

 Table 6
 ROC analysis for each clinical group against the normative sample

		AUC	SE	CI 95%
Stroke ($N = 10$)	t-FAB-M	.78	.08	[.62, .95]
	t-FAB-V	.74	.01	[.56, .93]
Left $(N=5)$	t-FAB-M	.62	.13	[.37, .88]
	t-FAB-V	.71	.14	[.45, .97]
Right $(N=5)$	t-FAB-M	.94	.03	[.88, 1]
	t-FAB-V	.78	.13	[.51, 1]
EPD $(N=6)$	t-FAB-M	.68	.12	[.44, 92]
	t-FAB-V	.65	.12	[.42,.88]
SVD $(N=20)$	t-FAB-M	.73	.07	[.59, .86]
	t-FAB-V	.7	.07	[.56, .85]
MMSE ES > 1 $(N = 14)$	t-FAB-M	.71	.09	[.55, .88]
	t-FAB-V	.67	.09	[.5, .84]
$MMSE ES \le 1$ $(N=6)$	t-FAB-M	.76	.13	[.51, .1]
	t-FAB-V	.78	.13	[.54, .1]
MD(N=4)	t-FAB-M	.96	.02	[.92, 1]
	t-FAB-V	.97	.02	[.93, 1]

ROC receiver-operating characteristics, *N* number of participants, *AUC* area under the curve, *SE* standard error, *EPD* extra-pyramidal disorder, *SVD* small vessel disease, *MD* mixed dementia, *ES* Equivalent Score, *MMSE* Mini-Mental State Examination, *FAB* Frontal Assessment Battery, *t-FAB* telephone-based Frontal Assessment Battery, *M* motor-mediated t-FAB, *V* verbal-mediated t-FAB

Discussion

The present study provides Italian clinicians and researchers with a statistically sound standardization of a TBCS test for frontal-executive deficits, namely the t-FAB, along with evidence of its clinical usability in neurological populations. This study is unprecedented not only within the Italian literature but also within the international ones, and it enriches the range of standardized TBCS instruments already available in Italy [2, 15].

As far as to its standardization in HPs, the t-FAB comes with regression-based norms, as well as with evidence on convergent validity, internal validity among its scores, a solid underlying factorial structure, high inter-rater and test-retest reliability and invariance as compared to its inperson version. With respect to its clinical usability, the present preliminary evidence suggests that the t-FAB is able to accurately discriminate neurological cases from healthy controls, identifying frontal-executive disturbances in neurological individuals as the in-person FAB does.

The t-FAB comes with two administration versions as to *Sensitivity to interference* and *Inhibitory control* tasks, one requiring motor and the other verbal responses (t-FAB-M and t-FAB-V, respectively). Although HPs reported lower scores on the t-FAB-M version as compared to the t-FAB-V, both versions showed statistical equivalence. Moreover, norms have been provided separately for each version, this allowing a flexible administration of the two versions according to the participant's clinical features. For instance, the t-FAB-M is more appropriate for individuals with motor speech disorders (e.g., dysarthria/anarthria) but spared hand movements, and vice versa with respect to the t-FAB-V. For the same reasons, the two t-FAB versions could be administered as parallel versions when performing follow-ups.

The slight discrepancies in norms between the t-FAB-M and t-FAB-V are likely due to the fact that inhibition of motor responses is more demanding than that of verbal responses [42]. This proposal is supported by the finding that age negatively predicts the t-FAB-M scores only, in accordance with the notion of motor inhibition being more affected than verbal inhibition with advancing age [43]. Notably, the influence of response modalities on inhibitory-related tasks has been proposed to be negligible in clinical populations, where inhibitory process impairment is likely widespread [44]. This further supports the adoption of the t-FAB as a valid screener of frontal-executive functioning in different neurological diseases. In fact, findings herewith reported as to the diagnostic accuracy of the two t-FAB versions show that the t-FAB-M and t-FAB-V are both able to identify frontal-executive dysfunctions in different neurological populations.

There are some limits of the present study that need to be acknowledged. First, the clinical usability of the t-FAB needs to be further verified in larger neurological samples, in particular focusing on diseases with predominant frontal involvement (e.g., motor neuron disease-frontotemporal degeneration spectrum disorders, acquired focal damages of frontal areas and networks due to traumatic, neoplastic, demyelinating, metabolic or infectious etiologies). Such an issue has to be particularly underlined as to those ROC analyses performed on clinical subsamples (Table 6), which should be treated as purely descriptive and preliminary. Second, further in-depth investigations are needed to assess the diagnostic properties, sensitivity to disease severity, responsiveness and reliable change of the t-FAB in neurological and geriatric cohorts [13]. Finally, with respect to the present stroke cohort, the discrepancies found in diagnostic accuracy between the t-FAB-M and t-FAB-V based on lesion side cannot be properly explored due to the small sample size of individuals presenting with either right- or left-lateralized damaged (N = 5 each).

In conclusion, the present work offers the first telephonebased version of FAB, a normed, valid, reliable and clinically usable TBCS test for screening frontal-executive functioning, encouraging its adoption in both clinical practice and research settings in neurology and geriatrics.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40520-022-02155-3.

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Data availability Data collected and analyzed within the present study are openly accessible at https://osf.io/6v4bu/.

Declarations

Conflict of interest None.

Ethical standard The study was approved by the Ethical Committees of the University of Milano-Bicocca, Milano (ID: RM-2021–382, 19/02/2021), the University of Padova, Padova (ID: 4107, 19/02/2021) and IRCCS Istituto Auxologico Italiano, Milano (ID: 25C122, 18/05/2021).

Statement of human and animal rights All procedures performed in this study that involved human participants were in accordance with the ethical standards of the above mentioned Ethics Committees and with the 1964 Helsinki Delaration and its later amendments or comparable ethical standards.

Informed consent Participants provided their informed consent.

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References

- Christodoulou G, Gennings C, Hupf J et al (2016) Telephone based cognitive-behavioral screening for frontotemporal changes in patients with amyotrophic lateral sclerosis (ALS). Amyotroph Lateral Scler Front Degener 17:482–488. https://doi.org/10.3109/ 21678421.2016.1173703
- Aiello EN, Esposito A, Giannone I et al (2021) ALS cognitive behavioral screen-phone version (ALS-CBSTM-PhV): norms, psychometrics, and diagnostics in an Italian population sample. Neurol Sci. https://doi.org/10.1007/s10072-021-05636-x
- De Cola MC, Triglia G, Camera M et al (2020) Effect of neurological screening on early dementia detection in southern Italy. Int J Med Res 48:0300060520949763
- Caze T, Dorsman KA, Carlew AR et al (2020) Can you hear me now? Telephone-based teleneuropsychology improves utilization rates in underserved populations. Arch Clin Neuropsychol 35:1234–1239. https://doi.org/10.1093/arclin/acaa098
- Soldati AB, Almeida C, Lima M et al (2021) Telephone screening of cognitive status (TICS) in severe COVID-19 patients: Utility in the era of social isolation. eNeurologicalSci. https://doi.org/10. 1016/j.ensci.2021.100322
- Castanho TC, Amorim L, Zihl J et al (2014) Telephone-based screening tools for mild cognitive impairment and dementia in aging studies: a review of validated instruments. Front Aging Neurosci 6:16. https://doi.org/10.3389/fnagi.2014.00016
- Yaari R, Fleisher AS, Gamst AC et al (2006) Utility of the telephone interview for cognitive status for enrollment in clinical trials. Alzheimers Dement 2:104–109. https://doi.org/10.1016/j. jalz.2006.02.004
- Crooks VC, Clark L, Petitti DB et al (2005) Validation of multistage telephone-based identification of cognitive impairment and dementia. BMC Neurol 5:1–8. https://doi.org/10.1186/ 1471-2377-5-8
- Lacritz LH, Carlew AR, Livingstone J et al (2020) Patient satisfaction with telephone neuropsychological assessment. Arch Clin Neuropsychol 35:1240–1248. https://doi.org/10.1093/arclin/acaa097
- Sullivan-Baca E, Babicz MA, Choudhury TK et al (2021) The relationship between health literacy and comfort with teleneuropsychology in a veteran sample. Arch Clin Neuropsychol. https://doi.org/10.1093/arclin/acab079
- de Sire A, Marotta N, Raimo S et al (2021) Psychological distress and work environment perception by physical therapists from Southern Italy during COVID-19 pandemic: The CALABRIA Study. Int J Environ Res Public Health 18:9676. https://doi.org/10.3390/ijerph18189676
- 12. Yuan S, Zhang W, Lü W et al (2021) The psychological impact on patients with memory disorders and their caregivers during

COVID-19. Aging Clin Exp Res 33:2317–2325. https://doi.org/ 10.1007/s40520-021-01911-1

- Aiello EN, Rimoldi S, Bolognini N et al (2022) Psychometrics and diagnostics of Italian cognitive screening tests: a systematic review. Neurol Sci 43:821–845. https://doi.org/10.1007/ s10072-021-05683-4
- Zanin E, Aiello EN, Diana L et al (2022) Tele-neuropsychological assessment tools in Italy: a systematic review on psychometric properties and usability. Neurol Sci 43:125–138. https:// doi.org/10.1007/s10072-021-05719-9
- Aiello EN, Esposito A, Giannone I et al (2021) Telephone interview for cognitive status (TICS): Italian adaptation, psychometrics and diagnostics. Neurol Sci. https://doi.org/10.1007/ s10072-021-05729-7
- Elliott R (2003) Executive functions and their disorders: Imaging in clinical neuroscience. Br Med Bull 65:49–59. https://doi. org/10.1093/bmb/65.1.49
- Amanzio M, Palermo S, Zucca M et al (2018) Neuropsychological correlates of instrumental activities of daily living in neurocognitive disorders: a possible role for executive dysfunction and mood changes. Int Psychogeriatr 30:1871–1881. https://doi. org/10.1017/S1041610218000455
- Iavarone A, Lorè E, Falco C et al (2011) Dysexecutive performance of healthy oldest old subjects on the frontal assessment battery. Aging Clin Exp Res 23:351–356
- Aiello EN, Esposito A, Appollonio I et al (2022) Diagnostic properties of the frontal assessment battery (FAB) in Italian healthy adults. Aging Clin Exp Res. https://doi.org/10.1007/ s40520-021-02035-2
- Tsai RM, Boxer AL (2016) Therapy and clinical trials in frontotemporal dementia: past, present, and future. J Neurochem 138:211–221. https://doi.org/10.1111/jnc.13640
- Dubois B, Slachevsky A, Litvan I et al (2000) The FAB: a frontal assessment battery at bedside. Neurology 55:1621–1626. https://doi.org/10.1212/wnl.55.11.1621
- Hurtado-Pomares M, Carmen Terol-Cantero M, Sánchez-Pérez A et al (2018) The frontal assessment battery in clinical practice: a systematic review. Int J Geriatr Psychiatry 33:237–251. https://doi.org/10.1002/gps.4751
- Appollonio I, Leone M, Isella V et al (2005) The frontal assessment battery (FAB): normative values in an Italian population sample. Neurol Sci 26:108–116. https://doi.org/10.1007/s10072-005-0443-4
- Aiello EN, Esposito A, Gramegna C et al (2022) The frontal assessment battery (FAB) and its sub-scales: validation and updated normative data in an Italian population sample. Neurol Sci 43:979–984. https://doi.org/10.1007/s10072-021-05392-y
- Postuma RB, Berg D, Stern M et al (2015) MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord 30:1591– 1601. https://doi.org/10.1002/mds.26424
- Levin J, Kurz A, Arzberger T et al (2016) The differential diagnosis and treatment of atypical parkinsonism. Dtsch Ärztebl Int 113:61. https://doi.org/10.3238/arztebl.2016.0061
- Shi Y, Wardlaw JM (2016) Update on cerebral small vessel disease: a dynamic whole-brain disease. Stroke Vasc Neurol 1:1–10. https://doi.org/10.1136/svn-2016-000035
- Zekry D, Hauw JJ, Gold G (2002) Mixed dementia: epidemiology, diagnosis, and treatment. J Am Geriatr Soc 50:1431–1438. https://doi.org/10.1046/j.1532-5415.2002.50367.x
- Costa A, Bagoj E, Monaco M et al (2014) Standardization and normative data obtained in the Italian population for a new verbal fluency instrument, the phonemic/semantic alternate fluency test. Neurol Sci 35:365–372. https://doi.org/10.1007/ s10072-013-1520-8

- Metitieri T, Geroldi C, Pezzini A et al (2001) The Itel-MMSE: an italian telephone version of the mini-mental state examination. Int J Geriatr Psychiatry 16:166–167. https://doi.org/ 10.1002/1099-1166(200102)16:2%3c166::aid-gps290%3e3.0. co;2-m
- Aiello EN, Esposito A, Pucci V et al (2022) Italian telephonebased mini-mental state examination (Itel-MMSE): item-level psychometric properties. Aging Clin Exp Res 8:1–7. https://doi. org/10.1007/s40520-021-02041-4
- 32. Monaco M, Costa A, Caltagirone C et al (2013) Forward and backward span for verbal and visuo-spatial data: standardization and normative data from an Italian adult population. Neurol Sci 34:749–754. https://doi.org/10.1007/s10072-012-1130-x
- 33. Pasotti F, De Luca G, Aiello EN et al (2022) A multi-component, adaptive working memory assessment battery (WoMAB): validation and norms in an Italian population sample. Neurol Sci 43:958–992. https://doi.org/10.1007/s10072-021-05416-7
- Kim HY (2013) Statistical notes for clinical researchers: assessing normal distribution (2) using skewness and kurtosis. Restor Dent Endod 38:52–54. https://doi.org/10.5395/rde.2013.38.1.52
- Hobart JC, Cano SJ, Warner TT et al (2012) What sample sizes for reliability and validity studies in neurology? J Neurol 259:2681– 2694. https://doi.org/10.1007/s00415-012-6570-y
- 36. Kyriazos TA (2018) Applied psychometrics: sample size and sample power considerations in factor analysis (EFA, CFA) and SEM in general. Psychology 9:2207. https://doi.org/10.4236/psych. 2018.98126
- Lakens D (2017) Equivalence tests: A practical primer for t tests, correlations, and meta-analyses. Soc Psychol Personal Sci 8:355– 362. https://doi.org/10.1177/1948550617697177

- Capitani E, Laiacona M (2017) Outer and inner tolerance limits: their usefulness for the construction of norms and the standardization of neuropsychological tests. Clin Neuropsychol 31:1219– 1230. https://doi.org/10.1080/13854046.2017.1334830
- Aiello EN, Depaoli EG (2022) Norms and standardizations in neuropsychology via equivalent scores: software solutions and practical guides. Neurol Sci 43:961–966. https://doi.org/10.1007/ s10072-021-05374-0
- 40. Obuchowski NA (2005) ROC analysis. AJR Am J Roentgenol 184:364–372. https://doi.org/10.2214/ajr.184.2.01840364
- Carpinelli Mazzi M, Iavarone A, Russo G et al (2020) Minimental state examination: new normative values on subjects in Southern Italy. Aging Clin Exp Res 32:699–702. https://doi.org/ 10.1007/s40520-019-01250-2
- 42. Potter LM, Grealy MA (2008) Aging and inhibition of a prepotent motor response during an ongoing action. Neuropsychol Cogn 15:232–255. https://doi.org/10.1080/13825580701336882
- Tsuchida N, Morikawa S, Yoshida H et al (2013) Motor inhibition in aging: Impacts of response type and auditory stimulus. J Mot Behav 45:343–350. https://doi.org/10.1080/00222895.2013. 806107
- Collette F, Amieva H, Adam S et al (2007) Comparison of inhibitory functioning in mild Alzheimer's disease and frontotemporal dementia. Cortex 43:866–874. https://doi.org/10.1016/s0010-9452(08)70686-5

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