The Frontal Assessment Battery (FAB): normative data from an Italian sample and performances of patients with Alzheimer's disease and frontotemporal dementia

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Summary

The Frontal Assessment Battery (FAB) is a short neuropsychological tool aiming to assess executive functions at the bedside. Two-hundred and thirty-six normal controls were administered the FAB and three other tasks assessing attentional and executive functions. The FAB was also administered to 28 patients suffering from mild Alzheimer's disease (AD, n. 15 subjects) or frontotemporal dementia (FTD, n. 13 subjects).
The FAB showed good concurrent and discriminant validity and high internal consistency. Test-retest and inter-rater reliability were fairly good. A multiple regression analysis showed a significant positive effect of education and a negative effect of age. Cut-off values of non-parametric distribution were computed.
A difference on FAB scores within dementia patients was observed, with subjects with FTD performing worse than patients suffering from AD.

KEY WORDS: Alzheimer's disease, executive functions, frontal lobes, frontotemporal dementia, neuropsychology.

Introduction

In recent years a great deal of attention has been devoted to devising new tests for the rapid assessment of cognitive functions in the elderly. Many reasons underlie this development of short neuropsychological tools. The growth of the aged population is accompanied by an increase in the number of individuals who may require testing for cognitive impairment. Furthermore, advances in the neurobiology of dementia have allowed the identification and differentiation of several degenerative forms of dementia whose diagnostic criteria include patterns of neuropsychological deficit. For instance, assessing frontal lobe functions and identifying dysexecutive syndrome may be crucial in discriminating between Alzheimer's disease (AD) and frontotemporal dementia (FTD) (1). This has important implications as regards the reaching of correct diagnoses and treatment decisions, since some drugs are available that have been shown to be effective in some types of dementia, like AD, but not in others, namely FTD. Therefore, differential diagnosis has to be made, by means of reliable testing, in the early stages of the disease, i.e., the time-span of best response to these drugs.

Clinical assessment of frontal lobe functions, however, is difficult and no single test reliably identifies dysexecutive syndrome (2). Thus, extensive and time-consuming neuropsychological batteries are needed which may be not well tolerated by patients suffering from dementia. These patients, indeed, often show impaired concentration, increased fatigue, and reduced tolerance of frustration, all of which may prevent extensive neuropsychological examination.

In view of these issues, Dubois et al. (3) devised the Frontal Assessment Battery (FAB), which is a short neuropsychological tool aimed at assessing executive functions at the bedside. The FAB consists of six subtests, each exploring functions related to the frontal lobes: conceptualization (by means of a similarities task), mental flexibility (by means of a phonological fluency task), motor programming (by means of Luria's motor series), sensitivity to interference (by means of a conflicting instructions task), inhibitory control (by means of a go-no-go task), and environmental autonomy (by means of evaluation of prehension behavior).

The FAB was shown to have good psychometric properties, and good concurrent and discriminant validity. Sensitivity to focal frontal lobe damage has also been found (4), as has good inter-rater reliability (3). However, the study of Dubois et al. (3) presents several shortcomings. First, in their study, the number of normal controls who were administered the FAB was quite small (n. 42) and was insufficient to provide normative data. Second, test-retest reliability was not assessed. Finally, before the FAB can be definitively considered a measure of frontal lobe dysfunction, it would be necessary to demonstrate that patients with non-frontal lobe dysfunction perform at a higher level than patients with frontal lobe damage (3).

The present study thus aimed to evaluate in depth the psychometric properties of the FAB by assessing test-retest reliability, collecting normative data in a sample of Italian subjects, and evaluating FAB performances of patients suffering from mild forms of primary degenerative dementia, i.e., AD and FTD.

Methods

Subjects

The study involved 236 normal subjects (111 men and 125 women) and 28 patients suffering from primary degenerative dementia. None of the normal controls (NCs) had a history of significant neurological and/or psychiatric disorders and, according to a corrected Mini Mental State Examination (MMSE) score (5), all were free from cognitive impairment. Furthermore, all NCs aged over 60 years had a score of 0 on the Clinical Dementia Rating (CDR) (6). Table I shows the demographic characteristics of the NCs.

The 28 patients with dementia had diagnoses of AD (DSM IV-TR criteria) (7) or FTD (Lund and Manchester group criteria) (8). Fifteen were affected by AD, 3 men and 12 women, mean age 73.46 years (SD 7.2) and mean education 7.1 years (SD 4.9), and thirteen were suffering from FTD, 3 men and 10 women, mean age 63.15 years (SD 10.6) and mean education 9.7 years (SD 4.0). Two women among the 13 FTD patients met the diagnostic criteria for subtypes of FTD, in one case primary progressive non-fluent aphasia and in the other semantic dementia (9), and these patients are considered separately. The remaining 11 FTD patients presented with symptoms of frontal variant FTD (fv-FTD).

All the patients had mild dementia (MMSE score equal to or greater than 18 and CDR score of 1). The FTD patients had a slightly higher mean corrected MMSE score (21.0, SD 2.9) than the AD patients (19.5, SD 2.1). The difference, however, was not significant (Mann-Whitney U=42.0, p ns).

Procedure

An Italian version of the FAB was administered to all the subjects. The NCs were also administered the Italian version of three tests assessing attentional and executive functions, namely an attentional matrices test (AM) (10), the Trail Making Test, Part B (TMT-B) (11), and the Digit-Symbol Substitution subtest of the WAIS-R (DSS) (12).

Statistical analysis

The statistical analysis used various methods: partial correlation matrix, principal component analysis (PCA), analysis of covariance (ANCOVA), simultaneous multiple regression, and separate Mann-Whitney U and chi-square tests.

Results

Table II reports the mean values and standard deviations of the FAB total raw score and the scores of the six FAB subtests recorded in the three groups of sub-

Table I - Demographic characteristics of normal controls.

	Age (years)							
	20-29	30-39	40-49	50-59	60-69	70-79	>80	Total
Education (years)								
3-5	–	–	3	6	5	17	7	38
6-8	3	2	6	8	8	11	1	39
9-13	11	8	21	20	3	4	–	67
> 13	70	8	9	4	–	–	1	92
Total	84	18	39	38	16	32	9	236

Table II - FAB scores (total and on single subtests) of the three groups of subjects.

	NCs (n. 236)	AD (n. 15)	fv-FTD (n.11)
Similarities	1.75 (1.05)	1.20 (.67)	.54 (.82)
Phonological fluency	2.52 (.74)	1.73 (.70)	1.09 (.83)
Motor series	2.63 (.69)	1.13 (1.0)	1.18 (.87)
Conflicting instructions	2.80 (.47)	1.20 (1.01)	.64 (1.21)
Go-No-Go	2.50 (.72)	1.40 (1.24)	.63 (.81)
Prehension behavior	3.00 (0)	2.93 (.26)	2.18 (1.25)
FAB total	15.29 (2.77)	9.60 (3.07)	6.27 (2.90)

Abbreviations: NCs=normal controls; AD=patients with Alzheimer's disease; fv-FTD=patients with frontal variant of frontotemporal dementia. Standard deviations in parentheses.

jects (NCs, AD, fv-FTD). The FAB total scores of the NCs were almost twice as high as those of the subjects with dementia. Furthermore, it is noteworthy that all the NCs performed at ceiling on the subtest “prehension behavior”.

Concurrent validity was evaluated in the NCs by a partial correlation between FAB and AM, TMT-B and DSS scores. Significant correlation was observed between the FAB and the AM (r=.294, p<.0001), the DSS (r=.650, p<.0001) and the TMT-B (r=-.618, p<.0001). In the last case the negative correlation indicates that higher scores on the FAB correlate with shorter times to complete the TMT-B. No significant correlation was shown between FAB and MMSE scores, either in the NCs (r=.144, p ns) or in the subjects with dementia evaluated in the study (r=.191, p ns).

Inter-rater and test-retest reliability were evaluated respectively on 26 and 31 randomly selected NCs, and good inter-rater (k=.79, p<.0001) and test-retest (k=.81, p<.0001) reliability levels were shown. Cronbach’s alpha coefficient between the FAB subtests of the NCs was .78, suggesting good internal consistency.

Using PCA, we then attempted to characterize factors involved in performance of the FAB. The scores on 5 FAB subtests were entered in a PCA with varimax rotation (method of extraction: roots > 1). The subtest “prehension behavior” was not included since it had zero variance. The analysis generated one factor with an eigenvalue magnitude of 2.934, which explained about 59% of the variance. The reference structure matrix after rotation revealed that all subtests loaded on this factor (Table III). This was consistent with a hypothesis of FAB structure homogeneity.

The FAB raw score was found to discriminate between NCs and patients with dementia (AD and fv-FTD) after adjustment for age and education as covariates (ANCOVA, F(1, 254)=10.013, p<.002, power .90).

The effect of demographic variables on the FAB was checked in the NCs by means of a simultaneous multiple regression, taking FAB total scores as the dependent variable and age, sex and education (years of schooling) as the independent ones. This procedure allowed us to evaluate the effect of each variable within the complete model by partially removing the effect they had in common.

The regression analysis showed R^2=.542 with a strong positive effect of education (coefficient=.203, t=5.202, p<.0001) and a negative effect of age (coefficient =-.062, t=-6.537, p<.0001). Gender was not significant. Therefore, younger subjects with a longer education gave better performances on the FAB. According to these results, the best simultaneous linear regression model was constructed to correct the original score by adding or subtracting the effect of the concomitant variables. The corrected scores were ranked and the non-parametric tolerance limits for the lowest 5% of the values were calculated with a 95% confidence interval, according to procedures described by Ackermann (13) and Capitani and Laiacona (14). The cut-off value of the FAB was fixed at 12.03, corresponding to the inner tolerance limit on the 5th centile. This means that 95% of NCs have an adjusted FAB score equal to or greater than 12.03 with a 95% probability of being true (Table IV).

The corrected FAB score was able to identify 15/26 (57.7%) patients regardless of the type of dementia (AD and fv-FTD). However, a difference within the dementia patients was observed, the 11 patients with fv-FTD performing significantly worse (mean 7.79, SD 2.81) than the AD patients (mean 12.46, SD 2.52; Mann-Whitney U=20.5, p<.002). Subsequent statistical analysis, however, did not show a significant difference between the two groups on each of the six FAB subtests, with the exception of a trend toward better performances of AD patients on the similarities task (Mann-Whitney U=44.0,

Table III - Factor analysis of the FAB.

Eigenvalues		
Magnitude	Variance	
2.934	.587	
Rotated factor loadings after varimax		
Similarities		.554
Phonological fluency		.784
Motor series		.862
Conflicting instructions		.786
Go-No-Go		.808

Number of variables entered=5. Method of extraction: roots>1; rotation: varimax.

Table IV - Best simultaneous linear regression model of FAB score and grid showing correction values for age and schooling.

FAB corrected score = FAB raw score - [.203(E-12.356)]-[-.062(A-44.589)]
(E=education in years; A=age in years)

	Age (years)						
	20-29	30-39	40-49	50-59	60-69	70-79	>80
Education (years)							
3-5	.70	1.27	1.83	2.40	2.97	3.53	4.09
6-8	-.28	.28	.85	1.41	1.98	2.54	3.11
9-13	-1.26	-.70	-.13	.43	1.00	1.56	2.13
>13	-2.25	-1.67	-1.12	-.55	.01	.58	1.14

Non-parametric tolerance limits of FAB corrected score on the 5th centile with 95% confidence interval: outer=11.53, inner=12.03.

p<.05). Furthermore, 5/15 patients with AD (33.3%) showed pathological performances in contrast to 10/11 (90.9%) patients with fv-FTD (chi-square=8.62, p<.005). It is noteworthy that the two patients with non-fluent progressive aphasia or semantic dementia both had normal corrected FAB scores, 12.97 and 13.00 respectively.

Discussion

In the present study, the FAB was shown to have good factorial validity, internal consistency, and inter-rater reliability. This confirms the psychometric properties of this battery already shown by Dubois et al. (3). Moreover, we also found stable performance on test-retest evaluation. This aspect, which was not checked in the study by Dubois et al. (3), provides further evidence that the FAB is a reliable psychometric tool.
Nevertheless, the subtest "prehension behavior" was found to show zero variance in NCs, indicating that the FAB includes a variable which is, in fact, a constant. We would stress that a subtest showing a ceiling effect in NCs is not suitable for inclusion in a psychometric battery. Furthermore, prehension behavior would be better regarded as a neurological sign of disinhibition ("grasping sign") than as an index of neuropsychological impairment. However, despite this limitation, the FAB score was found to have good concurrent validity, as shown by its highly significant correlation with DSS, TMT-B and AM.
The second goal of the study was to collect normative data for the Italian version of the FAB. The analysis showed that both age and education strongly influenced performance. In the study of Dubois et al. (3), the role of education was not taken into account, whereas age was not found to have significant influence. However, the normal subjects in their study had a limited age range. It is likely that this masked the effect of age on the FAB performances. Conversely, our results indicate that the FAB, despite showing good discriminant validity at group level, cannot be used in clinical practice for identifying dysexecutive syndrome without correction for age and education.
Our last goal was to evaluate FAB performances of patients suffering from primary degenerative dementia (AD and FTD). In view of the crucial role of differential diagnosis in the early stages of the illness (see introduction), we were careful to select only subjects suffering from mild dementia. Furthermore, the two groups were matched for dementia severity on the CDR. The corrected FAB score was found to be well able to discriminate AD patients from FTD subjects, both at group and single-case level. These data do not agree with recent results published by Castiglioni et al. (15) who found that the FAB score did not discriminate between AD and FTD subjects. Their study, however, also included subjects with moderate dementia, as indicated by the range of their MMSE scores (from 12 to 25), and therefore no direct comparison can be made with the present results.
In our study, a considerable proportion (33%) of patients suffering from mild AD gave pathological performances on the FAB. This finding, however, is in accordance with previous data from Italian patients by Binetti et al. (16), who reported executive dysfunction in 28% of patients with mild AD (see also ref. 17). Therefore, it is possible to consider the FAB as a measure of frontal lobe dysfunction also when such a dysfunction is presenting in the context of an Alzheimer's type degenerative dementia. Conversely, three of the 13 patients suffering from FTD gave normal performances on the FAB. The clinical picture in one of them was that of non-fluent progressive aphasia and in another that of semantic dementia (9). We should note that, at least in these two clinical forms, there is no impairment of executive functions in the early stages of the disease (18). This means that only one subject out of the eleven with fv-FTD was not correctly classified by the FAB. Consequently, the FAB may be considered a reliable tool for rapidly distinguishing AD from FTD in clinical practice. When the clinical diagnosis is between early AD and FTD syndrome, pathological performance on the FAB indicates that a patient has an approximately 77% probability of being an FTD case, and a 91% probability of having a "frontal" variant of FTD. Conversely, the same patient has a 66% probability of not being an FTD case.

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