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Short communication

Utility of Frontal Assessment Battery in detection of neuropsychological dysfunction in Richardson variant of progressive supranuclear palsy

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ARTICLE INFO

Article history:
Received 14 September 2014
Accepted 1 December 2014
Available online 9 December 2014

Keywords:
Progressive supranuclear palsy
Executive dysfunction
Cognitive impairment
Subcortical dementia

ABSTRACT

Progressive supranuclear palsy is characterized by motor, cognitive and behavioral features. In Richardson's syndrome of PSP (PSP-RS) executive dysfunction is quite prominent. Frontal Assessment Battery (FAB) is one of the most popular screening tests in the differential diagnosis of bradykinetic rigid syndromes. The study aimed at analyzing FAB subscores in relation to neuropsychological assessment results. Twenty patients with PSP-RS (12 with probable and eight with possible diagnosis) participated in the study. Sixteen PSP-RS patients scored below 15 on FAB. Among four patients having scored above cut-off (12 points) on FAB, two demonstrated both executive and language deficits, while the other two presented with only selective executive deficits on comprehensive neuropsychological evaluation. FAB is a useful screening measure in PSP, but it may not detect subtle executive deficits. Moreover, language performance seems to contribute significantly to FAB scores. Thus, FAB should be treated as "frontal" rather than "executive" screening task, in line with its name.

1. Introduction

Progressive supranuclear palsy (PSP) is a cluster of progressive clinical syndromes characterized by motor and – to various extent – also by cognitive, language and behavioral symptoms: Richardson's syndrome (PSP-RS), PSP-parkinsonism (PSP-P), pure akinesia with gait freezing (PSP-PAGF), with progressive apraxia of speech evolving into progressive non-fluent aphasia (PSP-PNFA) and mixed corticobasal syndrome with PSP clinical features and/or pathology (PSP-CBS). Since 1974 PSP has been regarded within the spectrum of atypical Parkinsonian syndromes, Parkinson's plus syndromes [1] and was a prototypical subcortical dementia syndrome [2]. Currently, together with CBS, PSP is more and more often seen within the spectrum of frontotemporal lobar degeneration (FTLD)/Pick Complex due to overlapping pathology and clinical behavioral features [3].

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http://dx.doi.org/10.1016/j.pjnns.2014.12.002

Patients with PSP-RS present with predominantly vertical gaze palsy, postural instability and falls, axial rigidity, bilateral and symmetric bradykinesia and unresponsiveness to levodopa treatment [1]. Neuropsychological profile of PSP is supposed to be dominated by executive dysfunction: difficulties with initiation, planning multi-stage activities, impulsivity and perseveration [4]. However, a subset of PSP patients develop speech and language deficits that may be as severe as corresponding to non-fluent progressive aphasia and/or progressive apraxia of speech (PSP-PNFA), which is in line with PSP as a part of Pick Complex spectrum [3], but may also be only an additional feature.

Cognitive decline in PSP is usually insidious and underrecognized. It may be masked by apathy and depression, which contributes delayed diagnosis of dementia. Three cognitive screening tests have been demonstrated to differentiate between patients with PSP and individuals with other neurodegenerative diseases, including atypical parkinsonian syndromes: Dementia Rating Scale (DRS) [5,6], Addenbrooke's Cognitive Examination (ACE) [6] and Frontal Assessment Battery at bedside (FAB) [5,7,8]. FAB with a cut-off of 12 points correctly differentiates between patients with Alzheimer's disease and frontotemporal dementia (FTD), in individuals with MMSE score ≥24 [9]. However, a cut-off of 15 was shown to differentiate patients with PSP from individuals with Parkinson's disease or multiple system atrophy [7].

FAB consists of six clinical tasks addressing verbal conceptualization, letter fluency, motor sequencing and inhibition [5]. Thus, performance on this test relies mainly on the integration of language and executive functions. FAB is much shorter than DRS or ACE so only its global score is usually reported [5,7,8,10]. What is more, to our knowledge only one study reported the detailed results of FAB in reference to complex neuropsychological examination results in a PSP cohort [7].

Our study aimed at assessing the clinical utility of FAB through analysis of FAB results in a PSP-RS group on the level of each item in the context of neuropsychological assessment addressing language, working memory and executive function.

2. Materials and methods

2.1. Participants

Twenty PSP patients, among whom 12 patients with probable and eight patients with possible diagnosis of Richardson variant according to Litvan et al. criteria [1] aged 68 ± 11 years, with time since onset ranging from 1 to 5 years and with 14 ± 4 years of education participated in the study (see Table 1). The patients underwent neurological, neuropsychological and neuroradiological assessments (magnetic resonance imaging, MRI or computed tomography, and regional cerebral flow single photon emission computerized tomography, SPECT-in few cases; to exclude other disorders and in patients who underwent MRI to confirm the presence of characteristic midbrain atrophy). All the patients consented to study participation and the study protocol was approved by local bioethics committee.

2.2. Methods

Neurological examination was conducted by a movement disorders specialist (JS), while neuropsychological assessment was performed by a neuropsychologist (EJS). Mini-mental state examination was used as a screening cognitive measure. FAB was used as an indirect measure of frontal dysfunction. FAB is a 6-item scale, with a global score ranging from 0 to 18, assessing: conceptualization, mental flexibility, programming, sensitivity to interference, inhibitory control and prehension behavior, with each item score ranging from 0 to 3 (see Table 2). Lower score corresponds to higher intensity of frontal features [5].

Comprehensive neuropsychological assessment addressed language, visuospatial function, working & episodic memory, as well as executive function. Language testing comprised of spontaneous speech assessment, naming, comprehension of complex phrases and repetition tasks derived from Boston Diagnostic Aphasia Battery and Set of tasks to assess patients with brain damage by Lucki and Maruszewski. Working memory was tested with Digit Span, Trail Making Test and months backwards. Executive function was examined in terms of planning by means of tower tasks (Tower of Toronto or Tower of London), mental flexibility (verbal fluency trials, Weigl blocks sorting task, The Brixton Spatial Anticipation Test, Luria alternate design, perseveration tendencies throughout testing), sequencing (tower tasks, Luria three-step motor sequencing tasks) and inhibition (rule violations in tower tasks, impulsive errors throughout testing, Stroop interference task). Due to differences in disease severity not all measures were administered to all participants. However, each cognitive domain was addressed in the assessment of every participant (see Table 1).

3. Results

FAB score ranged from 2 to 17 in PSP-RS group, while MMSE scores fell between 19 and 30 (see Table 1). Patients with probable RS-PSP scored 10.67 ± 3.75 on FAB, while patients with possible RS-PSP scored 11.38 ± 4.17. The difference was not statistically significant ($t = 0.396$; $p = 0.697$).

Sixteen PSP-RS patients scored below 15 on FAB. Among four patients having scored above cut-off on FAB, two demonstrated both executive and language deficits, while the other two had only selective executive deficits on comprehensive neuropsychological evaluation. Two out of four patients with high FAB scores had particularly high level of education. All four patients with high FAB scores had comparable to the rest of the group disease duration (ranging from 1 to 5 years) and their age ranged from 48 to 87 years (with two individuals being ≥80 years old).

Fourteen PSP-RS patients scored ≥24 on MMSE. Among these 14 cases with MMSE above cut-off, 11 cases scored < 15 on FAB and only six cases scored < 12 on FAB.

Among analyzed neuropsychological deficits, at least one executive deficit was present in each patient (see Table 1). Cognitive control deficits and sequencing impairment were present in 95% of cases. Working memory was affected in 90% of patients, while language deficits were observed in 80% of cases.

Table 1 – Demographic and clinical data in 20 patients with Richardson variant of progressive supranuclear palsy ordered from highest to lowest FAB scores.

	Age at testing	Time since symptom onset (years)	Years of education	MMSE (max. 30)	FAB (max. 18)	Phonemic fluency (K/S)	Semantic fluency (animals)	Working memory impairment	Cognitive control deficit (impulsivity)	Sequencing impairment	Language impairment
1	48	5	10	27	17	4	20	No	Yes	No	Yes
2	87	3	22	26	16	8	9	Yes	Yes	Yes	Yes
3	80	3	15	23	15	13	19	Yes	Yes	Yes	Yes
4	58	1	22	30	15	16	24	No	No	Yes	No
						FAB cut-off					
5	71	3	13	25	14	16	19	Yes	Yes	No	Yes
6	50	3	17	29	13	6	17	Yes	Yes	Yes	No
7	73	3	17	25	13	11	16	Yes	Yes	Yes	Yes
8	60	1	15	28	12	8	10	Yes	Yes	Yes	Yes
9	59	5	15	29	12	5	20	Yes	Yes	Yes	Yes
10	77	3	13	20	12	9	8	Yes	Yes	Yes	Yes
11	63	4	17	25	11	7	5	Yes	Yes	Yes	Yes
12	68	5	16	23	11	6	12	Yes	Yes	Yes	Yes
13	64	3	13	25	10	3	10	Yes	Yes	Yes	No
14	67	2	16	25	9	4	5	Yes	Yes	Yes	Yes
15	84	3	15	27	9	5	12	Yes	Yes	Yes	No
16	71	3	10	22	8	2	4	Yes	Yes	Yes	Yes
17	81	3	9	26	8	6	6	Yes	Yes	Yes	Yes
18	67	3	13	24	8	8	8	Yes	Yes	Yes	Yes
19	62	5	10	19	4	2	6	Yes	Yes	Yes	Yes
20	75	3	9	22	2	3	9	Yes	Yes	Yes	Yes
Percentage of patients demonstrating impairment in a given domain								90%	95%	90%	80%

Table 2 – Distribution of Frontal Assessment Battery Scores in a group of 20 patients with Richardson variant of progressive supranuclear palsy.

	Me (min. ÷ max.)	% of patients who scored < 3
Similarities (conceptualization)	2 (0–3)	80%
Lexical fluency (mental flexibility)	2 (0–3)	80%
Motor series (programming)	1 (0–3)	95%
Conflicting instructions (sensitivity to interference)	2 (0–3)	65%
Go-no go (inhibitory control)	2 (0–3)	55%
Prehension behavior (environmental autonomy)	3 (1–3)	5%

FAB results analysis on the level of single items showed that motor series was the most sensitive item, 80% of the patients demonstrated difficulties in conceptualization and verbal fluency, while conflicting instructions and go no tasks evidenced impairment in 65% and 55% of the patients respectively. Prehension behavior was present only in 5% of the cases.

4. Discussion

Our study analyzed FAB results in terms global scores and single item scores. It showed that most PSP-RS patients demonstrated deficits on motor series and two verbal tasks (fluency & conceptualization). Prehension behavior was very uncommon and deficient performance on two cognitive control tasks (go-no go & conflicting instructions) were less common that problems with motor sequencing or verbal tasks. Our results are in partial agreement with the study of Paviour et al. [7], who demonstrated that lexical fluency and motor series best differentiated between the PSP and MSA groups. Paviour et al. [7] showed also that lexical fluency and motor series subscores from FAB correctly classified 70% of the PSP, MSA and PD patients. In Gerstenecker et al.'s study [4] lexical fluency mean scores were also the lowest subscores obtained by patients with PSP. Language contribution to FAB score and its discriminant validity seems prominent.

Another argument for FAB reliance on language function comes from Paviour et al. [7], who showed better performance on language tasks in patients scoring above FAB cut-off and high correlations between FAB and language (as well as executive) task scores. In our patient series only four individuals scored above the cut-off so statistical analysis is not feasible. Notably, two of them (Patients no. 1 and no. 2) had poor phonemic fluency, while quite good phonemic fluency was observed in one case having scored just one point below FAB cut-off score (Patient no. 5). As letter fluency is one of the most important FAB components, responsible for its good discriminant validity [7], the fact that 80% of our PSP-RS patients presented with language impairment in neuropsychological assessment also indirectly supports the hypothesis that FAB low scores may be partially attributed to language deficits.

This FAB profile in PSP-RS shows that low FAB scores in PSP may represent a mixture of executive and language deficits, rather than pure executive failure. Verbal fluency may be lowered due to both executive and language impairment. Motor programming deficit may represent both executive or procedural learning deficit.

As shown by our results FAB may not detect selective executive impairment in PSP-RS, such as cognitive control deficits or sequencing impairment alone. It may also fail to reveal executive dysfunction in highly-educated individuals. However, these problems are typical for all screening measures that are usually insensitive to isolated impairments or mild decline in individuals with high premorbid functioning.

FAB, together with DRS and ACE, is one of the most common screening measures used in the differential diagnosis of progressive supranuclear palsy. It may differentiate PSP from MSA and PD [5,7,8]. One of the FAB advantages is that it does not rely on oculomotor function and time pressure is present in only one task (letter fluency) so the results are less biased by these factors than more complex executive tasks, e.g. Trail Making Test. However, FAB is a short scale aimed at assessing so called frontal signs (referring to corresponding neuroanatomical substrate), which are not synonymous with executive dysfunction (on the functional level). Both verbal fluency and motor programming deficits are observed not only in patients with focal frontal lesions but also in cases with striatal or fronto-striatal involvement. FAB consists of short tasks that were proven to be sensitive to prominent focal/diffuse frontal lobe damage, rather than tasks addressing different aspects of executive function, sensitive to mild and/or isolated deficits in the executive domain. As shown by our data and Paviour et al. [7], lower FAB score does not always correspond to longer symptom duration in PSP-RS. However, Litvan et al. [10] has recently shown a yearly decline of about 1 point in a group of 27 patients PSP patients. Thus, it is unclear if FAB may be also used to document progression of deficits in PSP.

Our study has several shortcomings. Firstly, diagnosis of PSP-RS was not confirmed pathologically and both patients with probable and possible diagnosis were included in the study sample. Moreover, not all subjects were able to undergo the extended neuropsychological test battery. It is often the case in PSP and the same problem was frequently reported e.g. by Paviour et al. [7]. Thus, most of the studies reporting cognitive assessment data in PSP patients report only screening test results. However, in our study when the patient was unable to perform a very complex task, his/her performance was rated on the basis of its shorter and less demanding equivalent (e.g. simplified Tower of London instead of Tower of Toronto). Due to small sample size and heterogenous neuropsychological testing methods quantitative analysis of neuropsychological scores was not presented in the manuscript. However, as PSP patients' performance is usually characterized by perseveration and/or impulsivity, executive errors manifest throughout the

testing (e.g. the patients tend to provide the first answer that comes to the their mind impulsively or provide the same answer again and again) and the quantitative profile (test scores alone) does not always reflect the selective executive pattern. Thus, we believe that qualitative analysis of neuropsychological profile is more valid in this case as purely quantitative testing could overestimate non-executive deficits due to executive problems influencing a variety of scores. Lastly, data on frontal behavioral symptoms (e.g. apathy or disinhibition) in our patients were not presented in this paper.

Strong contribution of low letter fluency and motor programming scores in our PSP-RS group as well as the presence of language impairment in 80% of the patients and executive dysfunction in 100% of the patients, emphasizes the fact that in PSP patients executive impairment is usually accompanied by language symptoms. This pattern of deficits is in line with the notion that PSP-RS falls within the spectrum of Pick Complex/FTLD [3] and should not be treated purely as Parkinson-plus or atypical parkinsonism.

5. Conclusions

FAB is a practical, patient- and clinician-friendly measure of frontal symptoms in the differential diagnosis of PSP. However, its score is related to language function and it should not be regarded as a screening executive test. Patients with high FAB scores should undergo full neuropsychological assessment with comprehensive testing of executive functions, as FAB is not sensitive to mild and isolated executive deficits.

Conflict of interest

None declared.

Acknowledgements and financial support

E.J.S. received the scholarship for outstanding young researchers from Polish Ministry of Science and Higher Education during the preparation of the manuscript. We are grateful to all our colleagues who referred PSP patients to us, in particular to: Ewa Narożańska M.D. Ph.D., Witold Sołtan M.D., Piotr Robowski M.D. and Michał Schinwelski M.D.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

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