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FRONTAL ASSESSMENT BATTERY IN EARLY COGNITIVE IMPAIRMENT: PSYCHOMETRIC PROPERTY AND FACTOR STRUCTURE

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Abstract: *Background:* The Frontal Assessment Battery (FAB) is a reliable and valid bedside tool for testing executive function in dementia. Given the increasing interest in utility of FAB as a screening tool in early cognitive impairment (ECI), there is a surprising lack of studies evaluating its psychometric property and factor structure, nor the influence of factors such as age, education and gender, in ECI. *Objectives:* This study aims to investigate the psychometric properties and factor structure of FAB in older adults with ECI, as well as the influence of age, gender and education. *Design, Setting and Participants:* This is a retrospective, observational cross-sectional study with 300 community dwelling, predominantly Chinese older adults (14 normal, 130 mild cognitive impairment (MCI), and 156 mild dementia) who presented to Memory Clinic from January 2011 to December 2013. *Measurements and Analysis:* We collected data on demographic, cognitive, functional and behavioral evaluation. To examine the psychometric properties of FAB, we examined the concurrent, convergent, and discriminant validity; internal consistency by Cronbach's alpha; and factor structure by exploratory factor analysis. The influence of age, education and gender was examined using unadjusted and adjusted correlational analyses with CDR-SOB. We performed analysis for the whole group and for MCI subgroup. *Results:* FAB total score decreases significantly from normal to dementia group attesting to concurrent validity. It correlated significantly with digit span backwards and Chinese Mini Mental State Examination (r=0.38 and 0.47 respectively, p<0.01) and poorly with Neuropsychiatric Inventory-Questionnaire and depression (r=0.004 and -0.02 respectively), supporting its convergent and discriminant validity. Factor analysis yielded a single-factor solution for FAB with fair Internal consistency (alpha=0.610). FAB is relatively unaffected by age, gender and education level. These good psychometric properties extend to MCI, albeit with greater influence by education level. FAB items of conceptualization and mental flexibility have good discriminatory ability between MCI and normal subjects. *Conclusion:* FAB has good concurrent, convergent and discriminant validity with fair internal consistency in ECI that is premised on a one-factor structure. It is relatively unaffected by age, gender or education. Taken together, FAB is a useful bedside screening tool for executive function in ECI.

Key word: Mild cognitive impairment, dementia, frontal assessment battery, psychometric property, factor analysis.

Introduction

The Frontal Assessment Battery (FAB) was developed by Dubois in 2010 for testing executive function at bedside (1). It is a short bedside screening instrument that evaluates six domains of frontal lobe function, namely conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control and environmental autonomy (1). The FAB has been pathologically correlated to specific areas of cerebral degeneration in different disease profiles, namely the medial and dorsolateral frontal cortex in frontotemporal dementia (2) and Alzheimer's disease (AD) (3); the whole brain in frontotemporal dementia (4) and AD (5); and the parieto-temporal lobe in Parkinson's disease (6). In clinical settings, FAB has demonstrated utility in differentiating between various neurodegenerative conditions such as frontotemporal dementia and AD (7, 8); progressive supranuclear gaze palsy, multisystem atrophy and Parkinson's disease (9); AD and vascular dementia (10); as well as AD and dementia of Lewy body (11). A systematic review on FAB (12) and a critical review of four existing executive function screening tools (13) recently concluded that FAB may be helpful to differentiate neurodegenerative disorders which are commonly confused in diagnosis and that it was a clinically reliable and valid tool.

Besides etiologic differentiation, there is increasing interest in the utility of FAB as a bedside screening tool for executive function in early cognitive impairment to complement more memory-biased instruments such as the Mini Mental State Examination (MMSE) (14, 15). FAB had been investigated as a tool to differentiate mild cognitive impairment (MCI) between AD and vascular etiology (16). The total FAB and subtest scores had also been compared between AD subjects with MCI and dementia (17). Current concepts suggest that MCI individuals may have deficits in executive functioning in addition to the memory domain (18). Despite the clinical interest and widespread use of FAB in clinical settings, there is a surprising lack of studies that evaluate its psychometric properties in the older population with MCI and dementia. Specifically, there is a conspicuous gap in terms of

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psychometric studies of FAB in MCI, and it remains to be established if the observed reliability and validity of FAB in dementia can be translated to the pre-dementia population of MCI.

Moreover, prior studies in Western and Asian studies which evaluated the psychometric properties of FAB focused mainly on reliability (test-retest, Inter-rater and internal consistency) and aspects of validity but there is a paucity of studies which specifically examined the factor structure of FAB. In the only study till date (19) which examined the factor structure of FAB in healthy participants, exploratory factor analysis yielded a two-factor structure. The first factor was labelled as cognitive control and included conceptualization, mental flexibility and inhibitory control. The second factor was labelled as behavioral control and included motor programming, sensitivity to interference and environmental autonomy. The two-factor structure was thought to be consistent with the theoretical construct of the original FAB proposed by Dubois (1). In addition, the authors also explored if FAB can be analyzed as a three-factor structure comprising cognitive control, automatic behavioral control and monitored behavioral control, which was thought to be compatible with the theoretical concept of executive function proposed by Normal and Shallice (20). This uncertainty about the optimal factor structure of FAB even amongst healthy participants underscores the need for similar studies in well-characterized populations of early cognitive impairment.

Previous validation studies of cognitive tools such as the MMSE have shown that factors such as age and education can influence the test scores, necessitating the need for adjusted cutoffs. Similarly, a study that examined the diagnostic performance of FAB in early cognitive impairment reported that higher cutoff scores of 13/14 are required for those with higher education (14). In light of reports that executive function can be affected by age and education level, it would be salient to establish the comparative influence of factors such as age, gender and education level on FAB compared with other instruments such as MMSE. This is a salient consideration in many developing countries where a significant proportion of older adults have comparatively lower levels of education attainment.

These considerations provide the impetus for the current study, in which we aim to investigate the psychometric properties of FAB in a predominantly Chinese population of older adults with MCI and dementia. We examined its concurrent, convergent and discriminant validity; factor structure and internal consistency. We also compared the influence of age, gender and education on correlation with Clinical Dementia Rating (CDR) staging between FAB and MMSE. Lastly, we performed subgroup analysis in MCI population to ascertain if the psychometric properties of FAB are applicable in the earliest stages of cognitive impairment. The results of our study would provide insights into utility of FAB as a bedside screening tool for executive function in early cognitive impairment in older adults.

Patients and Methods

Setting and Participants

We studied retrospectively 300 community dwelling older adults who presented to the Cognition and Memory Disorder Service of the Tan Tock Seng Hospital, Singapore, from January 2011 to December 2013. Inclusion criteria for data analysis includes age 50 years or older, diagnosis of MCI or CDR 0.5 -2 dementia, and completion of standardized clinical, neuropsychological and FAB assessment. As per the workflow in our clinic, we administered FAB only to subjects with Abbreviated Mental Test score of more than 7 (14). We further excluded subjects who were diagnosed with dementia other than Alzheimer's disease, vascular dementia or mixed dementia; CDR global score greater than 2; and who were unable to complete FAB and/or neuropsychological assessment. This study was approved by the National Healthcare Group Domain Specific Review Board.

Clinical Assessment

All participants underwent standardized assessment by a geriatrician and nurse clinician, blood investigations, and neuroimaging. A consensus meeting was conducted to determine the diagnosis, etiology, and staging of cognitive impairment based upon multi-disciplinary inputs from the physician, nurse clinicians, and psychologist. Dementia was diagnosed based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria, and etiology classified using published international criteria for dementia, as previously described (21). MCI was diagnosed using the revised Petersen criteria (22). The severity of cognitive impairment was rated using the locally validated clinical dementia rating scale (CDR) (23), in which global cognitive performance was rated, independent of dysfunction caused by non-cognitive factors, in six functional categories. CDR 0 indicates no cognitive impairment; CDR 0.5 designates either MCI or very mild dementia; and CDRs 1, 2, and 3 indicate mild, moderate, and severe dementia, respectively. To provide a more quantitative measure of dementia severity, the rating in each of the six categories was summed to yield the Sum of Boxes (24).

As part of the clinical assessment, we also collected information on functional status using the Barthel index for basic activities of daily living (bADL) (25) and the Lawton and Brody's scale for instrumental activities of daily living (iADL) scale (26). Cognitive performance was assessed using the locally validated Chinese Mini Mental State Examination (CMMSE), which was modified to suit the cultural context of Singapore and has a total possible score of 28 instead of 30 (27). We assessed mood using the DSM-IV criteria for major depression [28], and neuropsychiatric symptoms using the Neuropsychiatric Inventory-Questionnaire (NPI-Q) (29).

Table 1
Baseline characteristics across cognitive subgroups

	Overall (n = 300)	Normal (n = 14)	MCI (n = 130)	Dementia (n = 156)	p value
Demographics					
Age, years	73.60 ± 5.24	67.57 ± 5.87	72.55 ± 6.68[a]	75.01 ± 7.41[ab]	<0.001
Years of education	7.88 ± 4.63	10.36 ± 4.34	8.21 ± 4.76	7.39 ± 4.49	0.04
Male (%)	43	35.7	37.7	47.4	0.22
Chinese Ethnicity (%)	92	100	88.5	94.2	0.11
Function testing					
bADL (range 0-100)	97.3 ± 10.3	98.93 ± 2.13	98.15 ± 8.17	96.4 ± 12.1	0.28
iADL (range 0-23)	17.56 ± 4.21	20.93 ± 2.92	19.57 ± 2.76	15.58 ± 4.32[ab]	<0.001
CDR-Global score	0.623 ± 0.308	0	0.50a	0.782 ± 0.332[ab]	<0.001
CDR-SOB	2.28 ± 1.85	0.035 ± 0.134	1.212 ± 0.647[a]	3.38 ± 1.91[ab]	<0.001
Cognitive and psychological testing					
CMMSE (range 0-28)	22.50 ± 3.27	25.79 ± 1.58	23.55 ± 2.80	21.33 ± 3.26[ab]	<0.001
Digit-Span backwards	8.37 ± 2.71	10.43 ± 4.40	8.68 ± 2.72	7.92 ± 2.39[ab]	0.001
Depression (%)	14	0	13.1	16	0.23
NPI-Q (range 0-30)	3.43 ± 3.77	1.00 ± 1.41	2.79 ± 2.75	4.07 ± 4.36[ab]	0.003

Values denote means ± SD unless specified otherwise; a. p<0.05 compared with normal by post hoc test, b. p<0.05 compared with MCI by post hoc test; bADL: basic activities of daily living, CDR-Global score: clinical dementia rating global score, CDR-SOB: clinical dementia rating sum of boxes, CMMSE: Chinese mini mental state examination, iADL: instrumental activities of daily living, MCI: mild cognitive impairment, NPI-Q: neuropsychiatric inventory questionnaire.

Demographic data such as age, gender, years of education and race were also collected.

Neuropsychological testing was performed for patients with milder degrees of cognitive impairment (generally global CDR ≤ 1) or with an atypical clinical presentation. Our neuropsychological assessment battery, which was modelled after the Consortium to Establish a Registry for Alzheimer's Disease psychometric instruments, assessed the domains of verbal memory, language, visuospatial abilities, and executive functioning, and had been locally validated (30). Items in the battery which evaluate executive function include category fluency (animal naming) and digit span backwards. For the purpose of this study, category fluency was not used for further analysis as it duplicates the item for mental flexibility in FAB.

FAB

The FAB was administered in English or Mandarin to subjects during the initial visit by a single blinded rater before diagnosis was established. The FAB comprised 6 subtests: (1) conceptualization (making links between 2 objects from the same category, e.g. an orange and a banana), (2) mental flexibility (animal naming in a 1-min trial), (3) motor programming (Luria's 'fist-edge-palm' motor series), (4) sensitivity to interference (conflicting instructions in which subjects must provide an opposite response to the examiner's alternating signal, e.g. tapping once when the examiner taps twice), (5) inhibitory control (go/no-go paradigm where the subject must inhibit a response that was previously given to the same stimulus, e.g. not tapping when the examiner taps twice), and (6) environmental autonomy (placing your hands out and instructing the subject not to touch them, looking out for abnormal behavior such as imitation, utilization and prehension behavior). Each subtest is scored from 0–3, yielding a total score of 18. The FAB has been locally validated , with an optimal cutoff score was 12/13 (sensitivity 92%, specificity 78.7%) to distinguish early cognitive impairment from cognitively normal controls (14).

Statistical Analysis

Data analysis was performed on IBM SPSS for Windows Version 22.0 (SPSS Inc., Chicago, Illinois). All tests were 2-sided with the level of significance set at 0.05. Inferential statistics were applied to compare differences in demographic data, functional status, cognitive and neuropsychological testing scores between normal, MCI and dementia groups. We used one-way analysis of variance with Bonferroni correction for post-hoc comparison of continuous variables, and Chi-square test for categorical variables.

We next evaluated the psychometric property of FAB. Analysis was performed for the entire study population (N=300) and in the subgroup with MCI (N=130). For concurrent validity, we examined the differences in FAB total and item scores across cognitive subgroups. We performed Pearson's correlation analysis between FAB with digit span

Table 2
FAB item scores across cognitive subgroups

	Overall (n = 300)	Normal (n = 14)	MCI (n = 130)	Dementia (n = 156)	p value
Conceptualization	1.36 ± 1.16	2.360 ± 0.929	1.56 ± 1.19[a]	1.11 ± 1.09[ab]	<0.001
Mental flexibility	2.04 ± 0.700	2.710 ± 0.469	2.230 ± 0.629[a]	1.810 ± 0.689[ab]	<0.001
Motor programming	2.130 ± 0.977	2.710 ± 0.825	2.380 ± 0.874	1.87 ± 1.00[ab]	<0.001
Sensitivity to interference	2.27 ± 1.03	2.790 ± 0.426	2.550 ± 0.798	1.99 ± 1.15[ab]	<0.001
Inhibitory control	1.72 ± 1.08	2.00 ± 1.04	1.94 ± 1.06	1.52 ± 1.07[b]	0.003
Environmental autonomy	2.920 ± 0.342	2.930 ± 0.267	2.940 ± 0.241	2.900 ± 0.412	0.60
FAB total score	12.40 ± 3.08	15.50 ± 2.44	13.58 ± 2.73	11.15 ± 3.15[ab]	<0.001

Values denote means ± SD unless specified otherwise; a. p<0.05 compared with Normal by post hoc test, b. p<0.05 compared with MCI by post hoc test.

Table 3
Correlation between FAB with cognitive tests, depression and NPI-Q for all subjects (N=300) and MCI subjects (N=130)

	FAB	Digit-Span backwards	CMMSE	Depression	NPI-Q
All subjects (N=300)					
FAB	1				
Digit-Span backward	0.38[a]	1			
CMMSE	0.47[a]	0.34[a]	1		
Depression	-0.02	-0.01	0.02	1	
NPI-Q	0.004	0.08	0.14[b]	0.35[a]	1
MCI subjects (N=130)					
FAB	1				
Digit-Span backward	0.43[a]	1			
CMMSE	0.43[a]	0.31[a]	1		
Depression	0.09	-0.04	0.01	1	
NPI-Q	0.12	0.02	0.07	0.45[a]	1

a. Correlation is significant at the 0.01 level (2-tailed); b. Correlation is significant at the 0.05 level (2-tailed); CMMSE: Chinese mini mental state examination; NPI-Q: neuropsychiatric inventory questionnaire

backwards and CMMSE for convergent validity, and with depression and NPI-Q for discriminant validity. Construct validity was examined by exploratory factor analysis to ascertain the underlying factor structure, and internal consistency was determined via Cronbach's alpha. Lastly, we performed unadjusted and adjusted correlational analyses with CDR sum of boxes using Pearson's correlation to determine the influence of age, education, and gender on FAB and CMMSE scores.

Results

Baseline Characteristics (Table 1)

Out of the 300 subjects, 14 were cognitively intact, 130 had MCI and 156 had dementia. Our study subjects were predominantly Chinese and female with relatively intact bADL. Compared with cognitively intact subjects and MCI, persons with dementia were older, more impaired in iADL, and endorsed higher CDR global and sum of boxes scores (all p<0.05). Persons with dementia also had lower CMMSE, lower digit span backward and higher NPI-Q scores.

Concurrent validity (Table 2)

There was a significant decrease in FAB total scores from normal through to MCI and dementia groups, attesting to the concurrent validity of FAB. Similarly, there was a significant trend in all item scores (with the exception of environmental autonomy) across the cognitive subgroups (all p<0.01). Two important trends deserve highlight. Firstly, only two items were able to discriminate between MCI and normal groups, namely, conceptualization (1.56 ± 1.19 vs 2.360 ± 0.929, post hoc p<0.05) and mental flexibility (2.230 ± 0.629 vs 2.710 ± 0.469, post-hoc p<0.05). Secondly, the high mean scores for

environmental autonomy across all cognitive subgroups suggest a ceiling effect for this item in in our study population of early cognitive impairment.

Convergent and Divergent Validity (Tables 3)

FAB was significantly correlated with digit span backwards and CMMSE (r = 0.38 and 0.47 respectively, p<0.01), supporting its convergent validity. Conversely, FAB correlates poorly with NPI-Q (r = 0.004) and DSM IV for major depression (r = -0.02), corroborating its divergent validity. This relationship was maintained in subgroup analysis for MCI patients.

Construct Validity and Internal Consistency (Tables 4)

Factor analysis was appropriate as the Kaiser-Meyer-Olkin measure of sampling adequacy was 0.742, and the Barlett's test of sphericity was 151.44 (p<0.001). Factor analysis for all subjects (N=300) yielded a single-factor solution for FAB, as per the optimal number recommended by parallel analysis [30], Kaiser's criterion (components that have an eigenvalue greater than 1), and visual inspection of the Scree-plot. This single factor accounted for 34.8% of total variance and corresponded to "executive function". Notably, the item of 'environmental autonomy' loaded poorly and when removed, resulted in improvement in internal consistency of FAB (Cronbach's alpha=0.610, vs baseline value of 0.592). We further performed factor analysis for MCI patients (N=130), which was appropriate as the Kaiser-Meyer-Olkin measure of sampling adequacy was 0.691 and Barlett's test of sphericity was 45.61 (p<0.001). However, there was disagreement in the number of factors to retain, with parallel analysis and the Scree-plot suggestive of a single factor and Kaiser's criterion suggestive of two factors. Because of the tendency for Kaiser's criterion to over-estimate the number of factors (32), we opted for the one-factor solution for FAB in the MCI subgroup.

Table 4

FAB item loadings and internal consistency for all subjects (N=300)

	FAB	α if item deleted
Conceptualization	0.626	0.530
Mental flexibility	0.580	0.556
Motor programming	0.629	0.530
Sensitivity to interference	0.758	0.463
Inhibitory control	0.550	0.559
Environmental Autonomy	<0.001	0.610*
Percentage variance	34.8	

*Indicates that Cronbach α if item deleted is increased compared with original 6-item scale (α = 0.592).

Correlation with CDR-SOB (Table 5)

In unadjusted analysis, FAB had higher correlation with CDR-SOB compared with CMMSE (r: -0.46 vs -0.39). When adjusted for gender and education, FAB showed minimal change in correlation compared with CMMSE (0% vs 2.6-5%). Both FAB and CMMSE showed change in correlation when adjusted for age. In subgroup analysis of MCI patients, unadjusted correlation was similarly higher for FAB with CDR-SOB compared with CMMSE (r: -0.26 vs -0.17). Education-adjusted change was greater compared to overall group but lower for FAB compared to CMMSE.

Discussion

Our study contributes to the body of evidence by investigating the psychometric properties of FAB in 300 predominantly Chinese subjects with MCI and dementia. We found that FAB has good concurrent, convergent and discriminant validity with fair internal consistency in early cognitive impairment. The items of conceptualization and mental flexibility were able to discriminate between the normal, MCI and dementia group. Furthermore, FAB correlated better with CDR-SOB compared to CMMSE and this association is relatively unaffected by age, gender and education level. Taken together, our results support the use of FAB as a bedside screening tool for executive function in early cognitive impairment.

There are several findings that merit further discussion. Firstly, factor analysis corroborates the one-factor structure of FAB corresponding to executive function in early cognitive impairment. Subgroup analysis in the MCI subgroup yielded a similar finding. Our findings contrasted with an earlier study (19) in younger (mean age 44.6) cognitively intact subjects, which concluded that FAB has a 2-factor structure comprising cognitive control and behavioral control. While the exact mechanism for the observed differences in factor structures is unclear, these results suggest that executive dysfunction may exist across a continuum, such that different domains of executive functions which are discriminatory in non-diseased states converge downstream into a common factor with the onset of cognitive impairment in older persons.

Secondly, our results support a trend difference in FAB item scores across cognitive subgroups. For instance, 'environmental autonomy' demonstrated a ceiling effect moving from normal through to early dementia subgroups, which may limit its utility in early cognitive impairment. Significantly, the internal consistency of FAB improved from poor to fair when the 'environmental autonomy' item was removed. This observation had been well reported in previous studies (3, 4, 16, 32, 33, 34) in which the mean score of environmental autonomy remained relatively stable until severe stage of AD. In contrast, 'conceptualization' and 'mental flexibility' items were significantly different between MCI and cognitively normal subjects, unlike other FAB items (as well as the CMMSE)

Table 5
Unadjusted and adjusted correlations of FAB with CDR-SOB for all subjects (N=300) and MCI subjects (N=130)

	CDR-SOB						
	Unadjusted	**Age-Adjusted**	**% Change**	**Gender-Adjusted**	**% change**	**Education-Adjusted**	**% Change**
All subjects (N=300)							
FAB	-0.46[a]	-0.43[a]	5.9	-0.46[a]	0	-0.46[a]	0
CMMSE	-0.39[a]	-0.37[a]	4.1	-0.41[a]	5	-0.38[a]	2.6
MCI subjects (N=130)							
FAB	-0.26[a]	-0.24[a]	7.7	-0.26[a]	0	-0.16	38.4
CMMSE	-0.17	-0.16	5.9	-0.17	0	-0.08	52.9

a. p<0.01

which were discriminatory only between early dementia and normal subjects. Similar findings which attested to the discriminatory ability of the said 2 items in detecting cognitive impairment were reported in a study on OSA patients (34) and another study comparing normal cognition to dementia (15). These results corroborate observations that MCI subjects had significant decline in planning and not inhibition as compared to normal subjects (18), and are consistent with a spectrum of executive dysfunction in subjects from normal cognition to dementia, with the ability to plan being affected early and ability to inhibit being affected at later stages of cognitive impairment. Interestingly, inhibitory control items of the FAB were discriminatory between MCI and normal subjects in a small Japanese study (17), suggesting that further studies are needed to ascertain if socio-cultural factors can modulate the discriminatory ability of planning vis-à-vis inhibitory domains in executive function.

Lastly, despite reports that executive function can be affected by education, the influence of education bias appears to be smaller for FAB compared with MMSE in terms of the correlation with CDR-SOB. As opposed to other tests of executive function, the FAB items are relatively easy to understand and are independent of pen-holding, writing and drawing skills (36), which would render them less sensitive to prior levels of educational attainment. This property of being relatively uninfluenced by education is particularly advantageous in many developing countries where most elderly participants have comparatively lower levels of education compared to Western populations.

We would like to highlight some limitations. Firstly, our study subjects were largely Chinese and female which may limit generalizability to other populations. Secondly, due to the study sample being recruited from a cognition clinic, the number of cognitively intact subjects is necessarily small and would represent a subgroup with attendant subjective memory complaints. Thirdly, being a cross-sectional study, temporality of the reported associations and trends would need to be confirmed with well-designed prospective longitudinal studies. Lastly, the assessment of executive function in our neuropsychological battery was limited to category fluency and digit span backwards, and precluded a more rigorous comparison with a "gold standard" test of executive function. Nonetheless, digit span backwards have been shown in earlier studies to correlate with FAB and other executive function tests (11, 31).

Conclusion

In our study involving predominantly Chinese subjects with early cognitive impairment, we found that FAB has good concurrent, convergent and discriminant validity with fair internal consistency that is premised on a one-factor structure. FAB correlated better with CDR-SOB compared to CMMSE and is relatively unaffected by education level. The good psychometric properties of FAB extend to the pre-dementia stage of MCI. FAB items of conceptualization and mental flexibility have good discriminatory ability between MCI and normal subjects. Taken together, these results support the clinical usefulness of FAB as a bedside screening tool for executive function in early cognitive impairment. Further longitudinal studies should be conducted to examine the actual trend of decline in executive function and the utility of conceptualization and mental flexibility items in predicting MCI progression to dementia.

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