

Correlation and adaptation among functional and cognitive instruments for staging and monitoring Alzheimer's disease in advanced stages

Adaptação e correlação entre instrumentos cognitivos e funcionais para o estadiamento e acompanhamento da doença de Alzheimer em fases avançadas

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Abstract

Background: Although Alzheimer's disease (AD) is the most prevalent form of dementia, little is known about cognitive and functional aspects in its advanced stages. **Objective:** This study aimed the adaptation and correlation among specific instruments for AD in advanced stages with regard to cognition objectively weighted, besides the comparison between static and ecological aspects of functional capacity. **Methods:** 95 moderate, moderately severe and severe AD patients (33 men and 62 women) underwent the scales CDR (Clinical for Dementia Rating), FAST (Functional Assessment Scale), MMSE (Mini-Mental State Exam), MMSEsev (Severe Mini-Mental State Examination), SIB-8 (Severe Impairment Battery) and TSI (Test for Severe Impairment), for the comparison with a golden-standard ecological scale the PADL (Performance Activities of Daily Living). **Results:** The evidence suggests an increasing and statistically significant linear correlation between the ecological functional scale and cognitive tests according to the stratification of AD stages once weighted by static functional scale. **Discussion:** The results indicate that for patients in advanced stages of AD, appropriate cognitive tests and performance-based functional scales are useful in more accurate assessment of disease staging and monitoring its progression.

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Keywords: Alzheimer's disease, dementia, cognition, functional capacity.

Resumo

Contexto: Apesar de a doença de Alzheimer (DA) ser a forma de demência mais prevalente, pouco se sabe sobre aspectos cognitivos e funcionais em suas fases avançadas. **Objetivo:** Foi objetivo deste trabalho a adaptação e correlação entre instrumentos específicos para a DA em fases avançadas no que diz respeito à sua cognição objetivamente ponderada, além da comparação entre aspectos da capacidade funcional estática e ecológica. **Métodos:** Noventa e cinco pacientes (33 homens e 62 mulheres) com DA moderada, moderadamente grave e grave foram submetidos às escalas CDR (*Clinical for Dementia Rating*), FAST (*Functional Assessment Scale*), MEEM (*Mini-Mental State Examination*), MMSEsev (*Severe Mini-Mental State Examination*), SIB-8 (*Severe Impairment Battery*) e TSI (*Test for Severe Impairment*) para comparação com uma escala ecológica padrão-ouro, a PADL (*Performance Activities of Daily Living*). **Resultados:** As evidências encontradas sugerem uma correlação linear crescente e estatisticamente significativa entre a escala funcional ecológica e os testes cognitivos conforme a estratificação das fases da DA uma vez ponderadas pela escala funcional estática. **Conclusão:** Os resultados indicam que, para pacientes em fases avançadas da DA, testes cognitivos apropriados e escalas funcionais baseadas no desempenho são úteis na avaliação mais acurada do estadiamento da doença e acompanhamento de sua progressão.

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Palavras-chave: Doença de Alzheimer, demência, cognição, capacidade funcional.

Introduction

Cognitive deficits severe enough to interfere with instrumental and basic activities of daily living are a main clinical finding in Alzheimer disease (AD), and once detected at the patient evaluation it might be an indication not only of the possibility of dementia, but also of its severity¹, though with disease progression tools to evaluate cognition and functionality have limited positive and negative values².

Aside well-known aspects of cognition, in 1980 World Health Organization, trying to find a classification for functioning, included different aspects of functionality: 1) physiological and cognitive capacities; 2) capacity to undertake activities and 3) capacity to keep social roles³. This was an important step for the definition, but did not solved the conceptual terminological issue, more so with regard to the effect of disease on the subjects functional behaviour, since the concepts of lesion, incapacity and handicap were left out.

This said, the concept of functionality may be redefined as the quality of participation of an individual in occupations meaningful at the personal and cultural level, for which the understanding of the interaction between this individual and the environment is essential. In summary, functionality considered as a result requires an evaluation that takes in consideration not only dominions. This is possible if functionality is conceived with the incorporation of meaning, temporality, and the coexistence of function with dysfunction, considering previous education level⁴ in different contexts, beyond the mere metrical identification of cognitive incapacities⁵.

For subjects in advanced stages of dementia almost all the tools now available do not access adequately the performance and are not enough to serve as a follow up measure of disease evolution⁶. The main objective of this investigation is the adaptation and study of the correlation among tools specific for the evaluation of AD with regard to cognition objectively evaluated and functional capacity evaluated by static scales *versus* ecological performance.

Methods

Participants

For this transversal investigation 95 subjects with AD of both genders in moderate to severe stage along their caregivers were included. All participants were followed at the Severe Dementia Outpatients Clinic (Behavioural Neurology Section) and Brain Aging Group (Nudec) – Federal University of São Paulo (Unifesp), and, at the time of inclusion all fulfilled criteria for probable AD according to DSM-IV⁷.

For this investigation were considered as exclusion criteria: lack of a caregiver with a minimum conviviality of four days per week; illiterates; visual, auditory or motor limitation severe enough to hamper the performance; evidence of vascular brain insult in the last 12 months; chronic treatment for any neurological or psychiatric condition superimposed to AD; Mini-mental State Examination (MMSE) under or above 5-15; CDR 1.

For the participation in this investigation all caregivers or a legal representative signed a Free and Informed Consent on details about the study methods and the objectives to be attained, the right to study results, and results confidentiality. The investigation was approved by Unifesp Institutional Review Board (register 1373/09).

Instruments

As tools for screening and staging for this study were used Clinical Dementia Rating – CDR⁸, standard MMSE⁹, Functional Assessment Staging Test – FAST¹⁰ in its subdivisions of stages 5 (moderate), 6 (moderately severe) and 7 (severe). With regard to cognitive evaluation the protocol include the Severe Mini-mental State Examination – MMSEsev¹¹; the Severe Impairment Battery – SIB-8¹², modified for 8 items and the Test for Severe Impairment – TSI¹³.

For comparison of the cognitive evaluation with ecological functional performance it was used as a gold standard the Performance Test of Activities of Daily Living – PADL¹⁴, that was initially developed in partnership of researchers from London and New York for the evaluation of self-care in psychiatric settings. Actually this scale tries to evaluate 16 activities of daily life by the observation of real performance in a clinical setting, and takes about 20 minutes to be completed. This scale requires items like a glass, tissue paper, comb or hair brush, nail file, spoon, wall clock, telephone, paper and pencil among others and the performance is classified as 0) not correctly performed, 1) correctly performed or 9) unable.

After translation from English to Brazilian Portuguese, back translation, comparison and adaptation of the scales (JRW e PHFB), evaluation and joint decision among bilingual judges, natives or proficient and specialists in this area a scales pilot protocol was applied to evaluate the sensibility and cultural adequacy. In the field work each participant was interviewed just once with sessions duration ranging from 60 to 90 minutes. According to necessity there could be short breakings between tests, and, if necessary a session could be completed at another day.

Statistical analysis

Initially the statistical analysis of the data collected at this research was descriptive. For quantitative variables mean, median, standard deviation was calculated and bidimensional dispersion diagram graphics and box plots were done. Qualitative variables were analysed by absolute and relative frequency.

Inferential analyses were undertaken to accept or reject evidences shown by the descriptive analysis by point to point and interval estimative of Pearson linear correlation coefficient to quantify the linear correlation between tests and scales. Data were stored using the Windows Excel 2010. For statistical analysis the SPSS Pack, version 19.0 was used. Significance was set at 5% ($p \leq 0,05$).

Results

This sample was composed by 33 (34,7%) males and 62 (65,3%) females with advanced AD⁷. Mean age was 74,7 years, ranging from 60 to 89, with a standard deviation of 1.5 years. Mean disease duration was 7.3 years, ranging from 3 to 8, with a standard deviation of 1.7 years.

The descriptive analysis of the sample according to screening tools, cognitive, and functional scales is shown in table 1 with raw values, mean, median, range, and standard deviation.

The estimates of Pearson linear correlation coefficients indicate that there is an increasing and statistically significant linear correlation between PADL and the other scales: for MMSEsev ($p = 0,001$), SIB-8 ($p < 0,001$) and TSI ($p < 0,001$). It should be pointed out that while the numerical value is higher for PADL and SIB-8, the strength of the correlation between PADL and MMSEsev in the three intervals with 95% confidence is the statistically the same, though the “weaker” correlation, because there is an intersection among the respective intervals, as shown in table 2 and figure 1.

Table 1. CDR, FAST, MMSE, MMSEsev, SIB-8, TSI and PADL distribution between sample subjects

CDR	Moderate	22	23.2%
	Severe	73	76.8%
FAST	Moderate (5)	16	16.8%
	Severely moderate (6)	52	54.7%
	Severe (7)	27	28.4%
FAST	5	16	16.8%
	6A	21	22.1%
	6B	15	15.8%
	6C	16	16.8%
	7A	15	15.8%
	7B	12	12.6%
MMSE	Average	9.6	
	Median	10.0	
	Minimum-maximum	5.0-15.0	
	Standard deviation	3.0	
MMSEsev	Average	20.7	
	Median	21.0	
	Minimum-maximum	12.0-30.0	
	Standard deviation	4.2	
SIB-8	Average	13.8	
	Median	14.0	
	Minimum-maximum	4.0-24.0	
	Standard deviation	5.3	
TSI	Average	14,8	
	Median	15.0	
	Minimum-maximum	5.0-23.0	
	Standard deviation	5.8	
PADL	Average	9.6	
	Median	9.0	
	Minimum-maximum	5.0-16.0	
	Standard deviation	3.2	

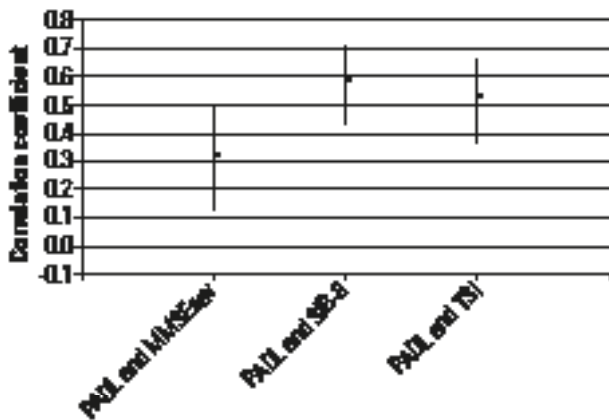
CDR: Clinical Dementia Rating; FAST: Functional Assessment Staging Test; MMSE: Mini-Mental State Examination; MMSEsev: Severe Mini-mental State Examination; SIB-8: Severe Impairment Battery; TSI: Test for Severe Impairment; PADL: Performance Activities of Daily Living.

Table 2. Point and interval estimates of Pearson's linear correlation coefficient between PADL and MMSEsev, SIB-8 and TSI

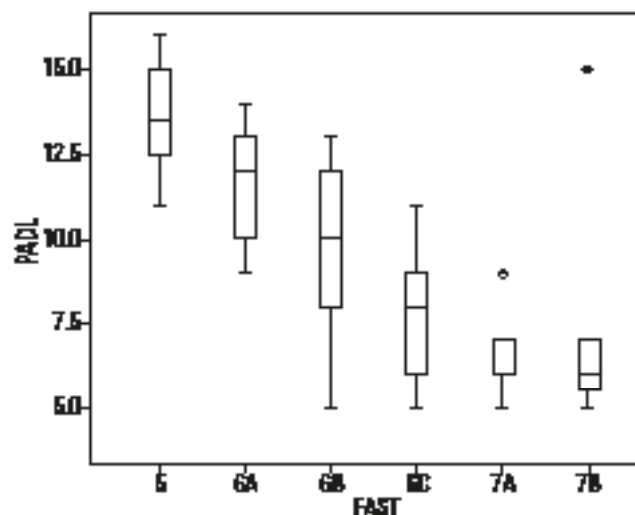
	n	Coefficient ^a	Interval ^b	p
PADL and MMSEsev	95	0.323	[0.130; 0.492]	0.001
PADL and SIB-8	95	0.588	[0.438; 0.706]	< 0.001
PADL and TSI	95	0.531	[0.369; 0.662]	< 0.001

^aPearson's linear correlation coefficient; ^b95% confidence interval for Pearson's linear correlation coefficient.

PADL: Performance Activities of Daily Living; MMSEsev: Severe Mini-Mental State Examination; SIB-8: Severe Impairment Battery; TSI: Test for Severe Impairment.

**Figure 1.** Point and interval estimates of Pearson's linear correlation coefficient between PADL and MMSEsev, SIB-8 and TSI.

PADL: Performance Activities of Daily Living; MMSEsev: Severe Mini-Mental State Examination; SIB-8: Severe Impairment Battery; TSI: Test for Severe Impairment.

**Figure 2.** PADL boxplot, according to stratified FAST.

PADL: Performance Activities of Daily Living; FAST: Functional Assessment Staging Test; °: possible outlier; * probable heavy-tailed value.

The stratification of subcategories of the static functional scale FAST, PADL, MMSEsev, SIB-8 and TSI were also analyzed with regard to parametric and nonparametric aspects (distribution and variance). Figure 2 shows the summary of measures in these scales, according to each FAST subcategory. Inferential results showed that subjects in each of the six different FAST subcategories (5, 6A, 6B, 6C, 7A, and 7B) presented a specific and statistically significant performance in

each of these subcategories in the functional ecological PADL ($p < 0,001$) and in the cognitive tests MMSEsev ($p < 0,001$), SIB-8 ($p < 0,001$) and TSI ($p < 0,001$). As such, the comparison and correlation results between FAST subcategories 5 to 7B showed a higher statistical significance ($p < 0,001$) according to the functional ecological scale used as the gold standard for this investigation (PADL) and the cognitive tests (MMSEsev, SIB-8 e TSI).

Discussion

This investigation tried to relate cognitive performance, as evaluated by tools specific for advanced dementia, with functional scales selected according to differences in the psychometric structure. Both CDR and FAST might be considered static or categorical scales, while PADL evaluates more dynamic aspects of functionality, since its method is the observation of the realization or simulation of common activities of daily living that the subject does in his/her ecological environment. The paradigm here is the identification and analysis of possible gaps between patient capacity as referred by the caregiver and the real performance, as evaluated by the examiner.

As it was initially hypothesized, the functional evaluation based in the subject's actual performance had a positive and statistically significant correlation with static functional scales and cognitive tests. Additionally, in the scale based on the caregiver information there was a correlation between the subcategories and the results on the ecological scale, once triangulated with MMSEsev, SIB-8, and TSI and disease stage, in the sense that the worse the performance on these three tests, the higher the disease worsening in the functional scale, thus characterizing a linear relation among the tools used here.

Though advanced dementia is an important issue, there is a lack of investigation on this subject. Investigations on cognition and functionality in advanced AD are scarce. Considering the bulk of investigations to validate tools appropriate for this group of patients¹⁵⁻¹⁷, none was specific for severe dementia. Only one research including AD subjects in varying stages followed in three different centers were evaluated about functional and motor aspects¹⁸, but even so, functional scales were based on caregiver information and there were more subjects with mild than with moderate or severe disease.

On the other hand, important contributions on the relationship between functionality and cognitive impairment are present in the literature. Niegovan *et al.*¹⁹ analyzed a cohort of more than five thousand and eight hundred elderly living in the community during the five years period. This was the first and most representative prospective study linking function and cognition patterns with incidental loss during the aging process. Such estimates currently reflect on family planning and multidisciplinary monitoring of the Canadian national program of public health policies.

Another study, using a refined and elegant prospective design, compared cognitive, behavioral and functional findings in the initial evaluation and after 24 months²⁰. In this case, after compared correlations and linear regressions, authors concluded that during follow-up a positive association between cognitive abilities and instrumental activities tended to decrease, while direct relationship between instrumental impact and neuropsychiatric disorders increases. Unfortunately, the study did not include patients with severe dementia.

AD in advanced stages is an important social responsibility, with implications for prevalence, direct and indirect costs and the suffering to family and caregivers. As pointed before²¹, methods for intervention could improve quality of life for both patient and family, bringing information on cognition and functionality still preserved that are not assessed due to inadequate methods of evaluation.

There are limitations in this study that should be evaluated. Though this was a large sample, this was not a stratified sample from the general population of severe dementia patients, so these results might not be representative of this population as a whole. It should be stressed however that our results are in accordance with the results of comparable studies. Though frequent, were not included in this investigation subjects with neuropsychiatric symptoms, which could be a bias with regard to performance in the scales. In future studies

samples with these conditions and MMSE score under 5 should be included and compared. This being a transversal study, results here described do not reflect the same effects for the same subject in other stages of the disease, something that only a prospective study could address.

In summary, taking an ecological functional scale, the PADL, as gold standard it could be concluded that its correlation with scales here classified as static, because they are based on the informant's opinion (CDR and FAST), and with three cognitive scales (MMSE, SIB-8 and TSI) was appropriate and reliable in the objective evaluation of AD subjects with severe dementia.

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