

TeLPI Performance in Subjects With Mild Cognitive Impairment and Alzheimer Disease

A Validation Study

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Abstract: APA guidelines for the evaluation of age-related cognitive decline and dementia emphasize the need for baseline (premorbid) data against which current performance can be compared. As this information rarely exists, clinicians must rely on instruments especially designed for estimation of premorbid abilities. No such instrument was available in Portugal until the development of the TeLPI, an irregular words oral reading test. This study aims to examine TeLPI's validity as a measure of premorbid ability in the spectrum of aging cognitive decline, from mild cognitive impairment (MCI) to moderate Alzheimer disease (AD), by the analysis of its stability in normal versus impaired samples. A total of 104 patients, classified into 2 clinical groups, MCI (n = 53) and probable mild to moderate AD (n = 51), were compared with a group of cognitively healthy controls (C_MCI: n = 53; C_AD: n = 51) and matched for sex, age, education, and residence. As expected, the Mini-Mental State Examination and Montreal Cognitive Assessment results were significantly different between the groups (AD < MCI < controls), reflecting the severity of cognitive impairment. TeLPI median scores of controls, MCI, and probable AD patients were comparable after correcting for years of education, revealing no significant effect of cognitive impairment on TeLPI performance, and suggesting its validity for estimating premorbid intelligence in subjects with cognitive decline and dementia.

Key Words: TeLPI, neuropsychological test, premorbid intelligence, mild cognitive impairment, Alzheimer disease

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APA (1998) guidelines for the evaluation of dementia and age-related cognitive decline emphasize the need for baseline test data from previous years (premorbid) against which current performance can be compared. The very concept of cognitive decline assumes the existence of some previous normal level of functioning, against which patient outcomes can be compared and measured in a reliable and valid way.^{1–3} Unfortunately, this information rarely exists

and clinicians have to estimate premorbid abilities relying on instruments specifically designed for this purpose.^{1,4}

Both qualitative and quantitative methods have been proposed for estimating premorbid abilities. However, given the fact that qualitative methods (such as predictions based on educational and/or occupational achievement) have raised issues of accuracy,⁵ different quantitative methods have been developed to assess premorbid intelligence worldwide. The irregular words reading test paradigm is one such method, and it was developed on the basis of the observation that the phonological component of language involved in reading aloud is better preserved in patients with cognitive decline compared with the semantic component, as phonology seems to be less dependent on the integrity of higher cognitive process compared with semantics.⁶ As such, patients continue to be able to read aloud previously known words, even when the meanings of these words can no longer be accessed.⁷ In these tests, each word presents at least 1 case of nonbiunivocal and thus irregular grapheme-phoneme correspondence. As correct pronunciation of words presenting irregular letter-sound pairings cannot be accomplished by applying grapheme-to-phoneme conversion rules and through guesswork, it has been argued that performance on irregular words reading tests is most likely to depend on previous knowledge than on current cognitive capacity.⁸

This paradigm has gained great acceptance in neuropsychological assessment; however, contemporary methodologies prefer the combination of different existing methods: reading irregular words, regression equations, and demographic variables.⁶ Reports indicating the increased accuracy of estimation through the combination of various methods⁶ led to the development worldwide of different instruments for estimating premorbid intelligence quotient (IQ) that associate with > 1 method. The National Adult Reading Test (NART⁸), the North American Adult Reading Test (NAART⁶), the American Adult Reading Test (AMNART⁹), the French NART (FNART³), the Word Accentuation Test (WAT⁴) in Spain, the Wechsler Test of Adult Reading (WTAR¹⁰), the Japanese NART (JART¹¹), the Swedish NART (NART-SWE¹²), the Hopkins Adult Reading Test (HART¹³), the Test of Premorbid Functioning (TOPF¹⁴), and TOPF-UK¹⁵ are some of these of instruments. No such instrument was available in Portugal until the recent development of TeLPI,^{16–17} a Portuguese irregular words oral reading test.

Similar in concept to the National Adult Reading Test-Revised (NART-R¹⁸), the TeLPI is a reading test containing 46 Portuguese words of decreasing familiarity. Each word presents at least 1 case of nonbiunivocal and thus irregular grapheme-phoneme correspondence. The

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TeLPI is correlated with the Full Scale Intelligence Quotient (FSIQ) of the Portuguese version of the Wechsler Adult Intelligence Scale—third edition (WAIS-III¹⁹) and incorporates demographic variables in regression formulas that explain 63% of FSIQ variance in accordance with other international reading tests.^{12,13} Furthermore, the TeLPI exhibits very good psychometric properties, namely excellent internal consistency and test-retest reliability,¹⁷ in line with other reading tests.^{10,13}

The TeLPI fills an important gap in the neuropsychological assessment of Portuguese patients, and various validation studies are being carried out with this instrument in order to support its potential use in clinical and research settings.

Given the diversity of cultural contexts and the heterogeneity of educational levels that are characteristic of the Portuguese population (particularly relevant when considering the elderly), the development of a reliable instrument for providing a valid measure of premorbid IQ against which actual or normative IQ can be compared is of particular importance. Consequently, and as cognitive impairment and dementia represent major health issues among elders in Portugal, Alzheimer disease (AD) and mild cognitive impairment (MCI) were the natural target groups selected for the first clinical validation of the TeLPI.

Both AD (as the most common neurodegenerative disorder with a prevalence of 4.4% in elders above 65 years old²⁰) and MCI (as a transitional stage between normal and impaired cognition or dementia²¹) have serious impact on health systems worldwide.²² As longitudinal studies show that MCI patients progress to dementia at a rate of 10% to 15% per year, the differentiation from age-related decline and cognitive impairment in both MCI and AD is, thus, extremely important. No such analysis can be made unless a comparison between actual and premorbid IQ is established.¹

Hence, the aim of the present study is to validate the TeLPI¹⁷ for premorbid intelligence estimation in MCI and AD patients by analyzing the stability of TeLPI's scores in subjects with cognitive impairment when compared with healthy controls.

METHODS

Design

In the current study, 3 groups of participants were considered: (I) an MCI group, (II) an AD group, and (III) a control group. Patients (MCI and AD) were recruited at the Dementia Clinic, Neurology Department of Coimbra University Hospital (Coimbra University Hospital, Coimbra, Portugal). Control subjects (cognitively healthy adults) were selected from the community and matched with patients for sex, age, educational level, and area of residence.

Participants

The total study sample is composed of 208 participants distributed between 3 groups: (I) the MCI group with 53 patients, (II) the AD group with 51 patients diagnosed with mild to moderate dementia, and (III) the control group with 104 cognitively healthy adults. The demographic data of the participants is provided in Table 1.

To implement and confirm standard clinical criteria, all patients were submitted to a comprehensive neurological and neuropsychological evaluation. The neurological evaluation was performed by a neurologist and included: a detailed history from the patient and from reliable source, neurological examination, and psychiatric evaluation. Mainly to exclude other causes of cognitive deterioration or relevant medical conditions, patients were investigated with the routine laboratory analysis considered in the evaluation of dementia, imaging studies [structural (computed tomography and/or magnetic resonance imaging) and functional (single-photon emission computed tomography)], and apolipoprotein E (APOE) genotyping. Positron emission tomography and cerebrospinal fluid analysis were carried out more restrictively but always considered in younger patients (below 60 y of age). Neuropsychological assessment was performed by a trained neuropsychologist and included a comprehensive neuropsychological assessment battery with the following instruments: the Mini-Mental State Examinations (MMSE^{23,24}), Montreal Cognitive Assessment (MoCA^{25,26}), Alzheimer's

TABLE 1. Descriptive Statistics for the Sample Subgroups

	MCI		AD		Clinical	Control	Total
	Clinical	Control	Clinical	Control			
n	53	53	51	51	104	104	208
Age	73.49 ± 8.19	71.64 ± 7.16	74 ± 8.53	73.04 ± 8.02	73.23 ± 8.36	72.33 ± 7.59	72.78 ± 7.98
Education	8.38 ± 5.34	8.19 ± 5.42	6.20 ± 3.53	5.76 ± 3.72	7.31 ± 4.65	7 ± 4.80	7.15 ± 4.72
Sex	32 (60.4%)	32 (60.4%)	32 (62.7)	32 (62.7)	64 (61.5%)	64 (61.5%)	128 (61.5%)
PR							
CLPMA	46 (86.8%)	46 (86.8%)	33 (64.7%)	33 (64.7%)	79 (75.9%)	79 (75.9%)	158 (75.9%)
CLPMU	6 (11.3%)	6 (11.3%)	15 (29.4%)	15 (29.4%)	21 (20.2%)	21 (20.2%)	42 (20.2%)
CLPRA	1 (1.9%)	1 (1.9%)	3 (5.9%)	3 (5.9%)	4 (3.9%)	4 (3.9%)	8 (3.9%)
MMSE	27.38 ± 2.04	28.55 ± 1.32	21.18 ± 3.52	28.24 ± 1.35	24.64 ± 4.38	28.39 ± 1.34	26.53 ± 3.72
MoCA	19.91 ± 3.80	24.11 ± 3.28	11.27 ± 3.66	23.41 ± 3.45	15.75 ± 5.71	23.77 ± 3.37	19.80 ± 6.15
TeLPI							
NE	10.79 ± 8.27	11.53 ± 8.77	16.04 ± 9.92	15.45 ± 10.13	13.37 ± 9.45	13.45 ± 9.62	13.41 ± 9.51
FSIQ E	102.4 ± 16.33	101.32 ± 16.97	92.46 ± 13.30	93.07 ± 16.47	97.85 ± 16.64	97.27 ± 17.15	97.56 ± 16.86

AD group indicates Alzheimer disease patients (clinical) and subgroup of controls matched with mild cognitive impairment (MCI) patients (control); clinical group, all patients with MCI and AD; CLPMA, resident in the center of the country, inland, and in predominantly urban area; CLPMU, resident in the center of the country, inland, and in moderately urban area; CLPRA, resident in the center of the country, inland, and in predominantly rural area; control group, all controls; FSIQ E, TeLPI Full Scale Intelligence Quotient estimation; MCI group, mild cognitive impairment patients (clinical) and subgroup of controls matched with MCI patients (control); MMSE, Mini-Mental State Examination (maximum score = 30); MoCA, Montreal Cognitive Assessment (maximum score = 30); NE, number of errors given on TeLPI (maximum score = 46); PR, place of residence.

It is to be noted that, sex is characterized by female patient's n and representative percentage (%). Data of other variables are presented as mean ± SD.

Disease Assessment Scale (ADAS^{27,28}), Clinical Dementia Rating (CDR^{29,30}), Subjective Memory Complaints scale (SMC^{31,32}), and the Geriatric Depression Scale (GDS-30^{33,34}). The diagnosis was established by a multidisciplinary team consensus, considering the results of the assessment and based on the Petersen workgroup²¹ criteria for MCI and APA,³⁵ as well as on McKhann³⁶ international criteria for possible AD. The MCI group included patients classified as “amnesic MCI” (single or multidomain³⁷) and a CDR classification of 0.5. In contrast, the AD group only included patients with mild to moderate severity (classified with CDR \leq 2 and an MMSE ranging from 13 to 29). In addition, patients were excluded from the study if any of the following criteria were met: birthplace or completion of formal education outside Portugal; inability to read or understand written Portuguese; acute/unstable somatic disease; recent psychiatric comorbidities or therapeutic changes (6 mo before the current neuropsychological evaluation); and significant motor, visual, or auditory deficits that could influence the neuropsychological assessment results.

Control group participants were recruited in the community and selected for this study according to the age, sex, educational level, and area of residence of the clinical samples, resulting in an almost perfect match between the MCI or AD group and the associated controls. Inclusion criteria for controls were: birthplace and completion of formal education in Portugal; ability to read and understand written Portuguese; absence or correction of motor, speech, audition, or vision disorders; no past history of head injury with loss of consciousness, major psychiatric, or neurological disorders that could affect cognitive ability and of chronic unstable systemic disorders with impact in cognition; no symptoms of cognitive impairment including diminished autonomy in daily activities; no history of alcoholism or substance abuse; and absence of significant depressive complaints and of medication with possible impact in cognition (eg, psychotropic or psychoactive drugs).

Procedures

All participants were recruited between June 2009 and January 2012, and each participant was assessed in a single session by an expert in neuropsychology. Only patients with a well-established diagnosis, fulfilling the inclusion criteria, with a stable clinical condition, and who completed the entire clinical evaluation were considered to be eligible for this study. The condition of participants in the control group was also confirmed by a neuropsychologist in an interview after a standard questionnaire that included a complete sociodemographic survey, an inventory of current clinical health status, past habits, and a medical history. This information was also checked with general practitioners and/or an informant (usually an individual that lived with the participant or a close relative). All instruments were applied strictly following manual instructions.

The present research complied with the Declaration of Helsinki ethical guidelines for human experimentation and was approved by the Ethics board of Coimbra University Hospital, by the “Fundação para a Ciência e Tecnologia” [Portuguese Foundation for Science and Technology], and by the Faculty of Psychology and Educational Sciences Scientific Committee. All subjects gave their informed consent after the aim of the study was explained to them. For the AD patients who were incapable of providing consent, a legal representative provided it on their behalf.

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS, version 19.0; IBM SPSS, Chicago, IL). Descriptive statistics and the χ^2 test were used for sample characterization, and the 2-sample *t* test, along with the analysis of covariance (ANCOVA), allowed for group comparisons.

Neuropsychological Testing and Materials

In the initial clinical interview conducted by a neuropsychologist, the demographic and clinical data were collected through a complete sociodemographic questionnaire, an inventory of current and past clinical health status, habits, and a medical history. The interview was followed by the administration of the following materials (in addition to the previously mentioned instruments included in the standard battery that was used for inclusion criteria only): MMSE,^{23,24} MoCA,^{25,26} and TeLPI,¹⁷ in this fixed order for all subjects.

Both the MMSE and the MoCA are in paper-and-pencil format and are scored out of a possible 30 points, with higher scores indicating better cognitive performance. The MMSE is a screening test grouped into 7 categories: (I) orientation, (II) registration, (III) attention and concentration, (IV) recall, (V) language, (VI) repetition, and (VII) visual construction.^{23,24} The MoCA screens milder forms of cognitive impairment, through the assessment of 6 cognitive domains: (I) executive functions, (II) visuospatial abilities, (III) short-term memory, (IV) language, (V) attention, concentration, and working memory, and (VI) temporal and spatial orientation.²⁵ The MoCA is a 1-page test with an application time of approximately 10 to 15 minutes, which includes a manual where explicit instructions concerning its administration and scoring system are provided. The greater diagnostic accuracy and discriminant validity of the MoCA as a global cognitive assessment instrument in comparison with the MMSE³⁸ justify its use in the present study.

The TeLPI is an instrument specially developed for the Portuguese population^{16,17} that uses valid regression formulas for predicting WAIS-III¹⁹ FSIQ. The TeLPI is easy to apply, short (3 to 5 min to administer), well tolerated, exhibits excellent concurrent validity, and is, overall, valid for pre-morbid intelligence estimation in adult Portuguese speakers aged 25 to 86 years.¹⁷ The TeLPI is composed of a card with 46 printed irregular words, a registering form with the indication of different possibilities for correct pronunciation (according to linguistic variation in Portugal), the regression formulas used for the WAIS-III¹⁹ FSIQ, Verbal Intelligence Quotient (VIQ), and Performance Intelligence Quotient (PIQ), a manual with explicit instructions concerning its administration and scoring system, and a CD recording admissible pronunciations for European Portuguese, as to simplify scoring. Recording of patients' sessions is recommended, allowing for future consideration in the case of doubts regarding scoring (a procedure followed in the present study). The TeLPI raw score is presented in “number of errors” and is inserted in the regression formulas with years of education allowing different IQ measures to be estimated.¹⁷

RESULTS

Sample Characterization

Characteristics of the sample used are provided in Table 1. For this description, the following variables were considered: sample size, age, educational level, sex,

residence, MMSE scores, MoCA scores, and 2 TeLPI-related data (number of errors and FSIQ estimation).

As mentioned earlier, the control participants were selected as to match patients in the clinical groups and are therefore considered to be demographically equivalent. Consequently, no statistically significant differences were found between the control (total) and clinical (total) groups on age ($t_{206} = -0.81$; $P = 0.41$), years of education ($t_{206} = -0.46$; $P = 0.64$), sex ($\chi^2_1 = 0.000$; $P = 1.0$), and area of residence ($\chi^2_2 = 0.000$; $P = 1.0$).

The predictable differences observed between the control and clinical groups on MMSE ($t_{206} = 9.21$; $P < 0.001$) and MoCA ($t_{206} = 12.65$; $P < 0.001$) are statistically significant.

In contrast with the results obtained from the screening instruments for cognitive deterioration, no statistically significant differences were found between the TeLPI scores ($t_{206} = 0.06$; $P = 0.948$) or FSIQ estimation ($t_{206} = -0.244$; $P = 0.808$), confirming that irregular words reading performance is equivalent between the control and clinical groups.

Analyzing in more detail the differences between groups (MCI/AD/control), age ($t_{102} = -0.92$; $P = 0.360$), sex ($\chi^2_1 = 0.000$; $P = 1.0$), and area of residence ($\chi^2_2 = 0.000$; $P = 1.0$), the nonsignificance relation continues to hold but, as educational levels (1 to 4/5 to 9/10 to 12/ > 12) were used in defining the sample, the difference between the groups with respect to the variable years of education was found to be significantly different ($t_{102} = 2.44$; $P = 0.016$). MMSE scores ($t_{102} = 11.52$; $P < 0.001$), MoCA scores ($t_{102} = 11.66$; $P < 0.001$), number of errors on TeLPI ($t_{102} = -2.93$; $P = 0.004$), and FSIQ estimation ($t_{102} = 2.98$; $P = 0.004$) were also found to be significantly different.

The results for the MMSE and the MoCA represent the predictable deterioration along the spectrum of cognitive impairment, with the AD patients obtaining lower scores compared with the MCI subjects. The robust difference observed between the groups ($P < 0.001$) once again demonstrates the sensitivity of both the MMSE and the MoCA to cognitive deterioration.

As significant differences were found between the MCI group and the probable AD group with respect to variable years of education, test results (that included TeLPI scores) were reevaluated to control for this variable. Using an ANCOVA for the years of education variable, no statistically significant differences were observed on number of errors on the TeLPI between controls, MCI, and probable AD patients ($F_{2,207} = 1.42$, $P = 0.243$, $\eta^2 = 0.014$), suggesting that the diagnosis has a very slight effect on TeLPI results (Cohen criteria³⁹). In contrast, the MMSE ($F_{2,207} = 186.4$, $P < 0.001$, $\eta^2 = 0.649$) and the MoCA ($F_{2,207} = 223.6$, $P < 0.001$, $\eta^2 = 0.689$) maintain the significance.

DISCUSSION

The main objective of this study was to validate the TeLPI as a measure of premorbid intelligence for the MCI and probable AD clinical groups.

We observed that MMSE and MoCA scores were significantly lower in the clinical groups (including the MCI and AD groups) when compared with healthy elders, but, that, in contrast, the TeLPI scores were not statistically different between these groups especially when the variable years of education was controlled. These results confirm that the capacity for reading irregular words in the sample

studied is preserved in the prodromic and initial stages of dementia. Besides, the evidence that TeLPI scores are not substantially influenced by cognitive deterioration in this spectrum of pathologies suggests that this test can be useful for estimating premorbid intelligence. These results are in consonance with previous observations that NART-a-like tests are valid to access premorbid function.^{4,3,12,40,41}

However, and even if rare, there are also studies with different conclusions⁴² reporting that reading of irregular words was compromised in AD patients. A wide range of explanations can be elicited for this discrepancy, such as the clinical and cognitive heterogeneity of AD patients or the well-known fact that reading can be especially impaired in subgroups of younger patients with aphasic forms, who may not have been excluded from samples.

The rigorous methodological criteria used in our study and the selection of well-validated study samples (patients with an ambiguous classification and more advanced dementia cases were excluded) may have contributed to the TeLPI's encouraging results. As demographic equations seem to provide a more accurate estimate for AD groups,⁴³ we believe that the inclusion of demographic variables in the regression formulas is also relevant for the stability of TeLPI scores throughout early stages of dementia.

Other factors may have also contributed to our results: the homogeneity of the clinical groups, a well-characterized cognitively healthy group of adults selected for the control sample, the almost equivalent sizes of the samples (reducing the possible biases of sample sizes in statistical analysis), the almost perfect match between the groups with respect to sociodemographic characteristics, and rigorous application of the TeLPI (including recording of the administration sessions).

Nevertheless, the conclusions of this study need to be understood within certain limits. Although TeLPI results have a high correlation with current ability,¹⁶ this study does not assess participants' current ability as estimated by WAIS-III, and therefore, no direct comparisons can be drawn between the actual and the estimated premorbid ability. It should also be noted that MMSE scores are affected by premorbid intelligence and years of education,^{44,45} and as no Portuguese instrument to assess premorbid ability was available until now, no other instrument (besides TeLPI) was administrated to access premorbid ability in the sample, and therefore, no adjustment to an expected level of performance was made when selecting individuals for our clinical sample. Although there is, in theory, a chance that not only subjects with low premorbid intelligence may have been misleadingly classified as cases of an MCI but also that certain MCI subjects could have been more adequately classified as probable AD, given the possibility of cognitive reserve effects accounting for MMSE and MoCA results, we believe that the rigorous sample selection has minimized such possibilities. The misclassification of low-intelligence subjects or, in contrast, high-intelligence subjects also highlights the importance of an instrument such as the TeLPI in the Portuguese context.

Another methodological limitation is the transversal nature of the present study: although this study has provided useful insights, a logical extension would be a longitudinal study to track performance on the TeLPI as severity of MCI and AD increases.

In conclusion, as one of the aims of neuropsychological assessment in MCI and dementia is to provide a comprehensive state description of the patient on the

basis of current and premorbid ability, important implications for clinical practice can follow from this study. Analyzed data suggest that the TeLPI is a valid instrument for assessing premorbid ability in Portuguese subjects with cognitive impairment.

Developing research involving the use of the TeLPI with other clinical samples will further confirm the validity of the TeLPI's regression formulas in cognitive decline samples. A normative study is also being currently carried out so as to allow for test performance interpretation in comparison with norms with respect to a reference group, which is representative of the Portuguese population.

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