

Translation and Psychometric Validation of the Persian Version of Amyotrophic Lateral Sclerosis Cognitive Behavioral Screen (ALS-CBS) and Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R)

Running Title: Validation of the Persian Version of ALS-CBS and ALSFRS-R

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۵۹ Abstract

۶۰ **Background:** The Amyotrophic Lateral Sclerosis (ALS) Cognitive Behavioral Screen (ALS-
۶۱ CBS) and the Revised ALS Functional Rating Scale (ALSFRS-R) are widely recognized tools for
۶۲ evaluating cognitive, behavioral, and functional changes in ALS patients. Given the increasing
۶۳ number of ALS cases in Persian-speaking communities, there is a critical need for culturally and
۶۴ linguistically adapted versions of these instruments. The objective of this study was to translate
۶۵ the ALS-CBS and ALSFRS-R into Persian and evaluate their validity and reliability to ensure their
۶۶ applicability in clinical practice and research.

۶۷ **Methods:** The Persian versions of the ALS-CBS and ALSFRS-R questionnaires were developed
۶۸ using the translation–back translation method. The translated questionnaires were administered to
۶۹ 36 individuals diagnosed with ALS. To assess content validity, neuromuscular specialists
۷۰ evaluated each item based on relevance, clarity, simplicity, necessity, and comprehensiveness,
۷۱ using content validity ratio (CVR) and content validity index (CVI) measures. Internal consistency
۷۲ reliability was assessed using Cronbach's alpha coefficient. Test–retest reliability was evaluated
۷۳ using the intra-class correlation coefficient (ICC). Statistical analysis was conducted using SPSS
۷۴ version 23.

۷۵ **Results:** All questionnaire items demonstrated satisfactory face validity after expert-guided
۷۶ revisions. The minimum acceptable values for CVI (≥ 0.78) and CVR (≥ 0.62) were achieved by
۷۷ correcting items that initially scored below the threshold. Reliability analysis revealed ICC values
۷۸ of 0.969 and 0.816 for the cognitive and behavioral sections of the ALS-CBS, and 0.909 for the
۷۹ ALSFRS-R. Cronbach's alpha coefficients were 0.791 for the ALS-CBS behavioral section and
۸۰ 0.825 for the ALSFRS-R, indicating acceptable internal consistency.

^1 **Conclusion:** The Persian versions of the ALS-CBS and ALSFRS-R have been shown to be both
^2 valid and reliable. These adapted tools provide valuable resources for assessing the cognitive,
^3 behavioral, and functional status of ALS patients in Persian-speaking populations, ultimately
^4 supporting more accurate diagnosis, monitoring, and disease management.

^5 **Keywords:** Reliability; Validity; Cognitive; Behavioral; Functional; Amyotrophic lateral
^6 sclerosis; ALS-CBS; ALSFRS-R

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۱.۴ Introduction

۱.۴.۰ Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by
۱.۴.۱ the degeneration of both upper and lower motor neurons. Patients with ALS experience severe and
۱.۴.۲ progressive weakness in the limb, bulbar, and respiratory muscles, typically leading to death within
۱.۴.۳ 2 to 5 years of symptom onset (1, 2). According to a 2019 systematic review, the global prevalence
۱.۴.۴ of ALS is 4.42 per 100,000, whereas a 2010 study from Iran reported a crude prevalence of 1.57
۱.۴.۵ per 100,000 (3-6).

۱.۴.۶ The non-motor symptoms of ALS have gained increasing attention in recent years, with cognitive
۱.۴.۷ and behavioral disturbances—often following a frontotemporal pattern—emerging as key clinical
۱.۴.۸ features (1, 2). Executive function, language, and fluency are the most commonly affected
۱.۴.۹ cognitive domains (7), while apathy appears to be the most frequent behavioral symptom.
۱.۴.۱۰ Unfortunately, no studies to date have examined the spectrum of cognitive and behavioral
۱.۴.۱۱ symptoms in Iranian ALS patients. While the motor manifestations of ALS are well documented,
۱.۴.۱۲ these non-motor impairments have only recently been recognized for their clinical significance.
۱.۴.۱۳ Such symptoms may negatively impact treatment adherence and are often associated with specific
۱.۴.۱۴ genetic mutations and a more aggressive disease course (8, 9). As such, early detection and
۱.۴.۱۵ accurate measurement of cognitive and behavioral impairment in ALS patients is critical.

۱.۴.۱۶ ALS is a profoundly debilitating condition, not only for patients but also for their caregivers,
۱.۴.۱۷ imposing a substantial emotional and physical burden (10, 11). Addressing the needs of this
۱.۴.۱۸ population requires locally relevant research, beginning with the adaptation of reliable tools to
۱.۴.۱۹ assess disease severity. The Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised
۱.۴.۲۰ (ALSFRS-R) and the Amyotrophic Lateral Sclerosis Cognitive Behavioral Screen (ALS-CBS) are
۱.۴.۲۱ two widely used instruments for evaluating motor and cognitive-behavioral impairments in ALS.

Both are brief, easy to administer, and suitable for clinical and research settings (8, 9, 12-14). These tools have been translated into multiple languages (15-18), yet validated Persian-language versions are still lacking. This represents a significant gap in clinical assessment and research for Persian-speaking ALS populations.

The absence of validated Persian versions of the ALSFRS-R and ALS-CBS hinders accurate diagnosis, monitoring, and treatment planning. Culturally and linguistically adapted tools are essential to ensure appropriate evaluation across diverse populations. Psychometric validation of such tools is typically guided by Classical Test Theory (CTT), which emphasizes the assessment of internal consistency, reliability, and content validity (19). CTT provides a practical and well-established framework for developing robust, culturally sensitive measurement instruments.

Given the lack of validated ALS assessment tools in Persian and the growing need for culturally adapted clinical instruments, this study aimed to address these gaps by: (1) translating the ALSFRS-R and ALS-CBS into Persian, (2) assessing their content validity through expert evaluation using CVR and CVI indices, (3) evaluating their reliability using internal consistency and test-retest methods, and (4) confirming their feasibility and applicability for use in Persian-speaking clinical contexts. The resulting tools are intended to enhance the quality of ALS assessment and care in Persian-speaking populations.

Methods and Materials

Study Design and Participants

This cross-sectional study was conducted on 36 patients diagnosed with ALS by neuromuscular specialists between 2020 and 2023. Participants provided written informed consent prior to enrollment. Illiterate individuals, those diagnosed with dementia, or those unable to provide

۱۴۹ informed consent were excluded from the study. The study protocol was approved by the Ethics
۱۵۰ Committee of Mashhad University of Medical Sciences (IR.MUMS.MEDICAL.REC.1399.412
۱۵۱ and IR.MUMS.MEDICAL.REC.1399.408).

۱۵۲ *Questionnaires*

۱۵۳ The ALS-CBS consists of two main components: (a) a cognitive screen section and (b) a
۱۵۴ behavioral screen section. It requires approximately five minutes to complete and is applicable in
۱۵۵ patients with limb or bulbar weakness. The cognitive section is administered by the physician,
۱۵۶ while the behavioral section is completed by the caregiver. The cognitive section assesses
۱۵۷ attention, concentration, mental tracking and monitoring, and word initiation and retrieval. The
۱۵۸ behavioral section includes 15 items evaluating domains such as apathy, inhibition, empathy,
۱۵۹ emotional control, frustration tolerance, cognitive flexibility, insight, judgment, food preferences,
۱۶۰ decision making, and language. Additionally, four items assess mood-related symptoms, including
۱۶۱ depression, anxiety, fatigue, and emotional lability (8, 20).

۱۶۲ The ALSFRS-R evaluates functional abilities across four domains: bulbar, fine motor, gross motor,
۱۶۳ and respiratory. It comprises 12 items rated by the physician through a patient interview,
۱۶۴ addressing speech, salivation, swallowing, handwriting, cutting food and handling utensils (with
۱۶۵ or without gastrostomy), dressing and hygiene, turning in bed and adjusting bedclothes, walking,
۱۶۶ climbing stairs, dyspnea, orthopnea, and respiratory insufficiency (13). Each item is scored from
۱۶۷ 0 to 4, with a maximum total score of 48 indicating normal function and 0 indicating severe
۱۶۸ disability.

۱۶۹ *Persian Versions of ALS-CBS and ALSFRS-R*

۱۷۰ After receiving permission from the original developers, the ALS-CBS and ALSFRS-R were
۱۷۱ translated into Persian using a standard translation–back translation approach. Initially, three

۱۷۲ native Persian-speaking neurologists fluent in English independently translated the questionnaires.
 ۱۷۳ These versions were synthesized into a single consensus version (Tr1). Back translation into
 ۱۷۴ English was performed by three independent translators with expertise in neurology and
 ۱۷۵ psychometrics, all semi-native in English and unaware of the original versions. The back-
 ۱۷۶ translated versions were reviewed by three Persian-speaking neurologists fluent in English to
 ۱۷۷ refine and improve the Persian translation. The second version (Tr2) was finalized and assessed
 ۱۷۸ for validity and reliability.

۱۷۹ *Statistical analysis*

۱۸۰ Content validity of the Tr2 versions was evaluated by 10 neuromuscular specialists who
 ۱۸۱ independently rated each item based on five criteria: relevance, clarity, simplicity, importance, and
 ۱۸۲ comprehensiveness. Experts were asked to select from the following options for each criterion: “It
 ۱۸۳ is necessary,” “It is useful but not necessary,” or “It is unnecessary.” The Content Validity Ratio
 ۱۸۴ (CVR) and Content Validity Index (CVI) were calculated using the following formulas:

$$۱۸۵ \quad \text{CVR} = \frac{[Ne - N/\gamma]}{N/\gamma} \quad (1)$$

$$۱۸۶ \quad \text{CVI} = \frac{\text{Raters with } \gamma \text{ or } \epsilon \text{ score}}{\text{All of the raters}} \quad (2)$$

۱۸۷ Where Ne is the number of experts selecting "It is necessary" and N is the total number of raters.
 ۱۸۸ Based on Lawshe's table for 10 experts, the minimum acceptable values were set at 0.62 for CVR
 ۱۸۹ and 0.78 for CVI (21). Items falling below these thresholds were revised, and the final version
 ۱۹۰ (Tr3) was developed for administration.

۱۹۱ Reliability was assessed using Cronbach's alpha to evaluate internal consistency, with values
 ۱۹۲ ≥ 0.70 considered acceptable (16). In addition, test-retest reliability was examined using the intra-
 ۱۹۳ class correlation coefficient (ICC). To avoid recall bias and ensure reliability of the responses, the
 ۱۹۴ retest was conducted two weeks after the initial administration, a time interval recommended by

۱۹۵ consulting neurologists for cognitive and behavioral questionnaires. ICC values closer to 1.0
۱۹۶ indicated stronger reliability.
۱۹۷ All statistical analyses were performed using SPSS software version 23, and a significance level
۱۹۸ of 0.05 was considered for all tests.

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۲۰۰ Results

۲۰۱ A total of 36 patients were included in the study, of whom 14 (38.9%) were female and 22 (61.1%)
۲۰۲ were male. The mean age of participants was 54.64 ± 11.69 years. Educationally, 50% of the
۲۰۳ participants had a high school diploma or lower, while the remaining 50% had attained university-
۲۰۴ level education. All participants were native Persian speakers.

۲۰۵ Regarding the site of initial symptom onset, 8.3% of patients presented with bulbar symptoms,
۲۰۶ 50% with upper limb involvement, and 41.7% with lower limb onset. The mean disease duration
۲۰۷ was 22.33 ± 25.53 months, ranging from 2 to 120 months.

۲۰۸ Validity Analysis

۲۰۹ As previously described, the Tr2 versions of both questionnaires underwent sequential revisions
۲۱۰ until all items met the minimum acceptable values for content validity ratio ($CVR \geq 0.62$) and
۲۱۱ content validity index ($CVI \geq 0.78$). No items were removed from either questionnaire during this
۲۱۲ process. The CVR and CVI scores for the Tr2 versions are presented in Supplementary Tables 1
۲۱۳ and 2. The final Tr3 versions were developed following all necessary revisions.

۲۱۴ Reliability Analysis

۲۱۵ Test–retest analysis demonstrated a significant correlation between the initial and follow-up
۲۱۶ administrations of both questionnaires, confirming the reliability of the final Tr3 versions (Table

۲۱۷1). Cronbach's alpha was 0.791 for the ALS-CBS behavioral section and 0.825 for the ALSFRS-
۲۱۸R, indicating acceptable internal consistency for both translated scales.

۲۱۹**Table 1.** Intra-class correlation coefficient (ICC) values for cognitive and behavioral subscales of the
۲۲۰ Persian versions of the ALS-CBS and ALSFRS-R questionnaires.

Scale	ICC	95% Confidence Interval	Significance Level
ALS-CBS			
Attention	0.776	0.561-0.886	< 0.001
Concentration	0.838	0.682-0.917	< 0.001
Tracking/Monitoring	0.922	0.847-0.960	< 0.001
Initiation and Retrieval	0.833	0.673-0.915	< 0.001
Cognitive screen	0.969	0.639-0.984	< 0.001
Behavioral screen	0.816	0.640-0.906	< 0.001
ALSFRS-R	0.909	0.834-0.951	< 0.001

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۲۲۲ Discussion

۲۲۳ While several Persian versions of ALS-specific questionnaires, such as the ALS-Specific Quality
۲۲۴ of Life-Revised (ALSSQOL-R) (22), Edinburgh Cognitive and Behavioral Screen (ECAS) (23),
۲۲۵ ALS Assessment Questionnaire 40-item (ALSAQ-40) (24), and Motor Neuron Disease Behavioral
۲۲۶ instrument (MiND-B) (25), have been validated for use in ALS patients, the Persian versions of
۲۲۷ the ALS-CBS and ALSFRS-R have not been validated until now. Thus, the primary aim of this
۲۲۸ study was to evaluate the clinical applicability and psychometric properties of the Persian

۲۲۹ translations of the ALS-CBS and ALSFRS-R scales. Our findings demonstrated that both
۲۳۰ instruments possess acceptable face validity and internal consistency. The demographic profile of
۲۳۱ our participants, including a mean age of 54.64 ± 11.69 years and a gender distribution of 38.9%
۲۳۲ female and 61.1% male, closely aligns with previous epidemiological data reported in ALS
۲۳۳ populations globally (26-28).

۲۳۴ Internal consistency, which assesses the extent to which items within a test measure the same
۲۳۵ construct, was confirmed for both questionnaires. Cronbach's alpha coefficients were 0.791 for
۲۳۶ the behavioral section of ALS-CBS and 0.825 for ALSFRS-R. These values exceed the commonly
۲۳۷ accepted threshold of 0.70, indicating satisfactory reliability (29, 30). Furthermore, test-retest
۲۳۸ reliability assessed via intra-class correlation coefficients (ICC) showed strong agreement, with
۲۳۹ values of 0.969 for the cognitive section and 0.816 for the behavioral section of ALS-CBS, and
۲۴۰ 0.909 for ALSFRS-R. These results reflect a high level of stability and consistency over time.

۲۴۱ Content validation was carried out using CVR and CVI indices, with expert input guiding the
۲۴۲ iterative revision of items in the Tr2 versions of both tools. All items in the final Tr3 versions met
۲۴۳ the minimum acceptable thresholds of CVR (≥ 0.62) and CVI (≥ 0.78), suggesting that the Persian
۲۴۴ versions adequately represent the constructs measured and are culturally appropriate for the Iranian
۲۴۵ context.

۲۴۶ The psychometric properties of our Persian version of ALSFRS-R compare favorably with several
۲۴۷ validated translations. The Arabic version, tested in an Egyptian cohort of 162 ALS patients,
۲۴۸ demonstrated high reliability with test-retest correlation coefficients of $r = 0.99$ and Cronbach's
۲۴۹ alpha values ranging from 0.85 to 0.93 (31). However, that study did not assess content validity
۲۵۰ using CVI or CVR, nor did it report item-level revisions based on expert evaluation. These
۲۵۱ methodological differences likely contributed to the need for revisions in specific domains in our

study, particularly in items related to salivation and respiratory function, which required cultural and linguistic adjustment.

The Russian validation of ALSFRS-R reported an ICC of 0.83, indicating good test-retest reliability (32). Our higher ICC of 0.909 may reflect the additional rigor of our content validation process, which incorporated systematic expert review and item modifications to ensure clarity and conceptual alignment with the original version.

Similarly, the Turkish adaptation of ALSFRS-R demonstrated excellent inter-rater reliability, with ICC values above 0.80 across subscales (33). While both studies affirm the reliability of the translated instruments, our study adds value by including a structured evaluation of content validity, an element not emphasized in the Turkish validation.

The Spanish version of ALSFRS-R, validated in a sample of 73 ALS patients, showed strong internal consistency (Cronbach's $\alpha = 0.77\text{--}0.91$) and test-retest reliability (Spearman's $\rho = 0.80\text{--}0.95$). It also demonstrated convergent validity through correlations with ALSAQ-40 and SRI scales, and explained 73.3% of variance across three factors in factor analysis (34). In contrast, our study did not conduct factor analysis or external validation due to the limited sample size ($n = 36$), but nonetheless confirmed high internal consistency and reliability through expert-based content validation.

The Japanese validation study reported an ICC of 0.97 and item-wise kappa coefficients ranging from 0.48 to 1.00 (35). While these results indicate excellent reliability, differences in study design—such as the inclusion of multiple raters and longitudinal sensitivity analysis—make direct comparison challenging. Our study focused primarily on test-retest reliability and expert-guided content validation, which may explain minor discrepancies in reliability indices. Additionally,

۲۷۴ cultural differences in the interpretation of items related to bulbar and respiratory functions may
۲۷۵ have influenced item-level clarity and consistency.

۲۷۶ The Persian version of the ALS-CBS also exhibited robust psychometric characteristics.
۲۷۷ Reliability was high, with ICC values of 0.969 for the cognitive and 0.816 for the behavioral
۲۷۸ sections. The behavioral section showed acceptable internal consistency, with a Cronbach's alpha
۲۷۹ of 0.791. All items met the predefined CVR and CVI thresholds after iterative revisions. These
۲۸۰ findings indicate that the Persian version reliably captures the cognitive and behavioral dimensions
۲۸۱ of ALS.

۲۸۲ When compared to the Italian validation studies, which included large samples (e.g., 293 for the
۲۸۳ cognitive and 265 for the behavioral sections), our sample was smaller but benefited from an
۲۸۴ intensive expert review process. Tremolizzo et al. reported cognitive impairment detection in 12%
۲۸۵ and behavioral symptoms in 55.5% of ALS patients (36). Aiello et al. further demonstrated strong
۲۸۶ correlations between ALS-CBS cognitive scores and ECAS ($r_s = 0.54\text{--}0.71$), and an internal
۲۸۷ consistency (McDonald's ω) of 0.74 for the cognitive and 0.90 for the behavioral sections (36-40).
۲۸۸ Although our study did not assess diagnostic accuracy or convergent validity, it emphasizes
۲۸۹ cultural and linguistic adaptation, offering a complementary validation approach.

۲۹۰ Similarly, the Spanish validation of ALS-CBS by Turon-Sans et al. reported high diagnostic
۲۹۱ performance with AUCs of 84.7% for the cognitive and 83.3% for the behavioral sections, and
۲۹۲ sensitivities of 86.2% and 93.3%, respectively (41). Our study did not include diagnostic
۲۹۳ thresholds or classification accuracy but confirmed content adequacy through expert-driven
۲۹۴ revisions and test-retest reliability, with an ICC of 0.969 for cognitive and 0.816 for behavioral
۲۹۵ domains.

۲۹۶ In the Brazilian validation by Branco et al., the ALS-CBS cognitive section demonstrated strong
۲۹۷ diagnostic performance (AUC = 0.906, sensitivity = 0.900, specificity = 0.872), based on
۲۹۸ comparison with a full neuropsychological battery (42). While we did not assess criterion validity,
۲۹۹ our study focused on enhancing content fidelity through culturally sensitive revisions, particularly
۳۰۰ in domains affected by language structure and caregiver understanding.

۳۰۱ **Strengths and Limitations**

۳۰۲ This study has several key strengths. It is the first to validate Persian translations of the ALSFRS-
۳۰۳ R and ALS-CBS, addressing a critical need for culturally adapted assessment tools for Persian-
۳۰۴ speaking ALS patients. A rigorous translation–back translation process was followed, supported
۳۰۵ by expert panel reviews to ensure linguistic and conceptual accuracy. Content validity was
۳۰۶ thoroughly evaluated using CVR and CVI, with all items revised until they met the minimum
۳۰۷ acceptable thresholds (≥ 0.62 for CVR and ≥ 0.78 for CVI). In addition, both tools showed strong
۳۰۸ internal consistency and test-retest reliability, supporting their psychometric soundness.

۳۰۹ However, several limitations should be noted. The small sample size ($n = 36$) limited statistical
۳۱۰ power and prevented more advanced analyses such as factor analysis and convergent validity
۳۱۱ testing. Furthermore, the back-translation process was conducted by a semi-native neurologist,
۳۱۲ whereas standard practice typically recommends that back-translation be performed by a native
۳۱۳ speaker of the target language ~~who is not specialized in the field~~. This ensures greater linguistic
۳۱۴ and conceptual accuracy. The study also lacked normative data, as no healthy control group was
۳۱۵ included, and external validity was not assessed due to resource limitations. ~~Finally, regional~~
۳۱۶ ~~dialects and subpopulation variations within Iran were not explored, which may affect item~~
۳۱۷ ~~interpretation in broader applications.~~

Future research should involve larger and more diverse samples, include normative comparisons, and assess cross-tool validity to further strengthen the utility of these translated scales.

Conclusion

In conclusion, the successful validation of the Persian versions of the ALS-CBS and ALSFRS-R represents significant progress in the assessment of cognitive, behavioral, and functional changes in Persian-speaking ALS patients. These tools provide clinicians with reliable instruments to monitor ALS progression more effectively, enhancing patient care in Iranian clinical settings. Additionally, researchers can utilize these validated versions to conduct more relevant and culturally appropriate studies in this population. Ultimately, the availability of these tools will contribute to improved outcomes and better understanding of ALS in Persian-speaking communities.

Conflict of Interest

None.

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