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# Clinical Application of the Bulgarian Version of the SCCAN: Pilot Data from Patients with Alzheimer's Disease and Ischemic Stroke

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Research article

#### **Abstract**

Aim: This study evaluated the clinical utility of the Scales of Cognitive and Communicative Ability for Neurorehabilitation (SCCAN) upon assessing Bulgarian in-patients who present with either ischemic stroke or Alzheimer's disease (AD). The aim was to determine whether this tool could detect cognitive-communicative problems that may be missed by customary screening tools.

Methods: We conducted two independent pilot studies: one with 14 AD patients, and a second with 19 stroke patients and 31 healthy controls. All participants completed the Bulgarian SCCAN, which assesses eight domains including oral expression, orientation, memory, auditory and reading comprehension, writing, attention, and problem-solving. Stroke and control participants also underwent the Mini-Mental State Examination (MMSE). Descriptive statistics were used so group performance and correlations could be examined. Tests that are nonparametric were also used.

Results: SCCAN revealed domain-specific deficits in clinical cohorts. In the AD group, memory and orientation were the most impaired domains. Stroke patients, on the other hand, showed significant impairments, particularly in memory, oral expression, and auditory comprehension, while orientation and attention were relatively preserved. Overall, stroke patients performed significantly better on the SCCAN than the AD group. These findings reveal distinct cognitive-communicative profiles in AD versus stroke populations.

Conclusion: SCCAN's Bulgarian version identified cognitive-communicative deficits with clinical sensitivity in patients with AD as well as with those with ischemic stroke. The tool may guide individualised neurorehabilitation and complement standard screening methods. Additional verification is advised.

cognitive-communicative disorders, Alzheimer's SCCAN, disease, ischemic stroke, neurorehabilitation, screening

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#### 1. Introduction

Cognitive-communicative disorders frequently result from neurological events including ischemic stroke and Alzheimer's disease (AD). Memory, attention, executive control, and daily communication can all be impacted by these diagnoses (Togher et al., 2014). Regretfully, conventional screening methods usually fall short in detecting these deficiencies early on, which delays prompt intervention (Bayles et al., 2020).

The Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE) are frequently used in clinical settings (Tombaugh & McIntyre, 1992; Nasreddine et al., 2005). Orientation, short-term memory, and simple verbal activities are evaluated by these tools. Although tasks such as verbal fluency and sentence recall on the MoCA provide some information about expressive language, these tools do not comprehensively assess expressive language, literacy, or higher-order reasoning. As a mild or subclinical communication impairments may go undetected, particularly in early AD or among stroke survivors with preserved global cognition.

To address this limitation, Milman and Holland (2012) developed the clinician-administered Scales of Cognitive and Communicative Ability for Neurorehabilitation (SCCAN) that evaluates all relevant cognitive and communicative domains. By producing detailed profiles of each patient's strengths and weaknesses, SCCAN supports tailored neurorehabilitation planning.

The Bulgarian version underwent a standardised adaptation process, including expert review, forward and backward translation, and pilot testing to ensure linguistic and cultural validity (Beaton et al., 2000).

The current study provides initial data on individuals with AD and stroke in two groups, while also assessing the ability to identify cognitive-communication deficits in these two specific populations.

### 2. Material and methods

### 2.1 Participants

This study included three groups: AD, patients with mild to moderate ischemic stroke, and neurologically healthy controls. All participants were recruited from the Neurology Department of UMHAT "St. George" in Plovdiv, Bulgaria. Detailed inclusion and exclusion criteria for each group are described in Section 2.2. In brief, AD and stroke diagnoses were confirmed clinically according to established criteria, and controls were matched on age and education with no history of neurological or psychiatric conditions. All participants had adequate vision, hearing, and comprehension to complete the assessments.

Education was documented and converted to years of schooling (primary = 8, secondary = 12, tertiary = 16). Mean years of education were: stroke group – 11.8 (SD = 2.5), control group – 13.4 (SD = 2.2), and AD group – 12.6 (SD = 2.1). A Kruskal–Wallis test showed a marginally non-significant difference in education between groups (H(2) = 5.50, p = .064). Occupation was not recorded. This difference was considered when interpreting the findings.

Information on bilingualism, multilingualism or handedness was not collected. All participants were assumed to be monolingual Bulgarian speakers based on self-reported language use and the requirement for fluent Bulgarian to complete the assessments. This limitation is acknowledged.

Demographic characteristics are presented in Table 1.

Table 1. Demographic Characteristics of the Study Groups

	N	Age Range (years)	Mean Age (SD)	Sex (F/M)
AD	14	63–82	73.1 (6.6)	7 / 7
Stroke	19	36–93	69.0 (13.4)	6 / 13
<b>Controls</b>	31	57–78	66.8 (5.7)	23 / 8

Note. SD = standard deviation; F = female; M = male

A Kruskal–Wallis test revealed a significant age difference among the three groups (H(2) = 7.18, p = .028), with the AD group being significantly older than the control group (Mann–Whitney U = 107.5, p = .007).

No significant age differences were observed between the stroke and control (p = .144) or stroke and AD (p = .401) groups.

This was considered when interpreting the findings

# 2.2 Inclusion and Exclusion Criteria

AD Group. We enrolled patients aged 60 or older with a probable diagnosis of Alzheimer's disease, confirmed by a neurologist according to the Bulgarian National Consensus for Early Diagnosis and Treatment of Dementia (Bulgarian Dementia Society, 2015). This consensus endorses the NIA-AA (2011) and IWG (2014) harmonised criteria and the DSM-5 criteria for major neurocognitive disorders. Diagnosis was based on detailed anamnesis (patient and caregiver), neuropsychological testing showing at least 2 SD below age norms in ≥1 domain, evidence of impairment in daily functioning, and neuroimaging (CT/MRI) to exclude other causes.

All participants were native Bulgarian speakers, gave written consent, and were not receiving intensive cognitive rehabilitation at the time of testing. Exclusion criteria included other neurological or psychiatric conditions, major sensory impairments, and severe somatic illness that could affect

participation. Stroke Group. Adult patients (≥ 18 years) with a mild to moderate ischemic stroke (National Institutes of Health Stroke Scale, NIHSS 1–8) and a Glasgow–Liège Coma Scale score of 19 or higher were included. Testing took place 3–5 days after the stroke. People with prior strokes, severe aphasia, or major neurological or psychiatric comorbidities were excluded from the study.

Control Group. Volunteers were adults (≥ 18 years), with no history of neurological or psychiatric illness, no cognitive complaints, and lived independently with normal communication skills. Participants were selected to match the clinical groups in age and education.

Time since onset and therapy status. For the AD group, all participants had a history of progressive cognitive decline of at least one year at the time of testing, consistent with mild to moderate stages of the disease.

For the stroke group, testing was conducted between the third and fifth day after the ischemic event. None of the participants in either group were receiving speech-language or psychological therapy at the time of testing, nor had they undergone structured cognitive rehabilitation before assessment.

#### 2.3 Measures

In both pilot investigations, the primary evaluation tool was the SCCAN in its Bulgarian adaptation. All SCCAN and MMSE results presented in this study are raw scores. Normative data for the Bulgarian adaptation of the SCCAN are not yet available; therefore, no standardised or index scores were computed.

In accordance with international standards, the Bulgarian version was created via forward and backward translation and cultural adaptation (Beaton et al., 2000).

Proper names, colloquial language, and culturally relevant information were all modified (e.g., 911 was changed to 112, the United States of America map was changed to a map of Bulgaria, and American prescription drugs and language exercises were changed to their Bulgarian equivalents).

The participants in the ischemic stroke group also completed the MMSE to evaluate their overall cognitive status. The control group underwent the same process. As a standard screening instrument, the Bulgarian version of the MMSE—validated by Raycheva et al. (2013)—was employed.

Since evaluating SCCAN performance in this population was the main goal, MMSE values were not gathered for the AD group. The SCCAN consists of eight subtests that comprehensively assess key aspects of cognitive-communicative functioning: Oral Expression (naming and verbal formulation), Orientation (temporal and spatial awareness), Memory (recall and recognition), Auditory Comprehension (understanding spoken language), Reading Comprehension (understanding written language), Writing (writing to dictation and

spontaneous writing), Attention (focused and sustained attention), and Problem Solving (reasoning and executive functions). Each subtest yields a raw score, and the sum provides the SCCAN Total Score, reflecting overall cognitive-communicative ability.

#### 2.4 Procedure

The study was carried out over two years, from 2023 to 2025, at the Neurology Department of St. George University Hospital in Plovdiv, Bulgaria. Approval was given by the ethics committee at the Medical University-Plovdiv. Each participant was told, both in writing and in person, what the study involved. They were encouraged to ask anything they weren't sure about, and only after that did they sign the consent form. The study followed the ethical principles outlined in the Declaration of Helsinki (World Medical Association, 2013).

For consistency and comfortability, each person was tested in a quiet room with steady lighting. The assessments included the Bulgarian version of the SCCAN and the MMSE. In cases of uncertainty, clinical data were examined to verify diagnostic information. All assessments were conducted by the first author, a neurologist and licensed medical speech-language pathologist with specific training in cognitive and communicative assessment.

Sessions usually lasted anywhere from 35 to 60 minutes, depending on the participants' level of alertness and fatigue. Older adults or those with health issues were given breaks whenever needed. After testing, all identifying information was removed. The data were then coded and stored securely, according to current privacy rules.

## 2.5 Statistical Analysis

Data were organised and analysed using IBM SPSS Statistics, version 22. Descriptive statistics, including means and standard deviations, were calculated for all variables. Due to the small sample sizes and the presence of non-normally distributed variables, non-parametric statistical methods were applied throughout the analyses. Normality of distributions was assessed using the Shapiro–Wilk test.

The results indicated that several variables were not normally distributed, supporting the use of non-parametric statistical methods throughout the analyses.

Since all comparisons were pairwise between two groups at a time (e.g., AD vs. Stroke, Stroke vs. Controls), the Mann–Whitney U test was appropriate, and the Kruskal–Wallis test was not applicable.

Effect sizes (r) were calculated for all between-group comparisons. Spearman's rank correlation coefficient was used to examine associations between SCCAN total scores and MMSE performance, as well as internal correlations among SCCAN subtests.

The AD group was analysed descriptively due to the small sample size (n=14), and findings were interpreted with caution. Statistical significance was set at p < .05 (two-tailed).

#### 3. Results

## 3.1 Participant Characteristics

The final sample included 14 people with probable AD, 19 people with ischemic stroke, and 31 neurologically healthy controls across three cohorts of 64 people. Table 1 presents thorough demographic

statistics including age and sex apportionment.

# 3.2 Group-Level SCCAN and MMSE Performance

A comprehensive comparison of mean  $(\pm SD)$  SCCAN subtest, total, and MMSE scores across the three groups is presented in Table 2.

**Table 2.** SCCAN and MMSE Scores (Mean  $\pm$  SD) in AD, Stroke, and Control Groups

Subtest (Max)	AD (n=14)	Stroke (n=19)	Controls (n=31)
Oral Expression (19)	$10.1 \pm 3.9$	$16.1 \pm 4.2$	$18.2 \pm 2.4$
Orientation (12)	$7.1 \pm 3.4$	$11.4 \pm 1.2$	$12.0 \pm 0.0$
Memory (19)	$3.6 \pm 1.2$	$10.6 \pm 4.2$	$15.9 \pm 3.2$
Auditory Comprehension (13)	$7.1 \pm 2.6$	$10.6 \pm 2.1$	$11.9 \pm 1.5$
Reading Comprehension (12)	$7.8 \pm 2.2$	$10.5 \pm 2.3$	$11.1 \pm 1.3$
Writing (7)	$5.7 \pm 1.8$	$6.4 \pm 1.6$	$6.9 \pm 0.2$
Attention (16)	$6.9 \pm 3.2$	$11.9 \pm 3.8$	$13.5 \pm 2.8$
Problem Solving (23)	$11.2 \pm 4.8$	$17.9 \pm 5.6$	$20.1 \pm 3.9$
SCCAN Total (94)	$48.9 \pm 13.9$	$74.5 \pm 17.5$	$85.6 \pm 8.6$
MMSE Total (30)	_	$26.0 \pm 4.5$	$29.2 \pm 1.1$

Note. All scores are raw values. "Max" in the first column indicates the maximum possible score for each subtest or test.

The results differed between the AD and stroke groups.

People with AD performed more poorly on the SCCAN (M = 48.9, SD = 13.9) compared to the stroke group (M = 74.5, SD = 17.5).

This difference was statistically significant (Mann–Whitney U=26.00, p<.001), and the effect size (r=.68) was strong, reflecting a notably large effect. In terms of MMSE performance, the stroke group achieved a mean score of 26.0 (SD = 4.5), suggesting mild global cognitive decline.

By contrast, individuals in the control group obtained a mean SCCAN score of 85.6 (SD = 8.6), with an average MMSE score of 29.2 (SD = 1.1), which is consistent with preserved cognitive functioning.

# 3.3 Subtest-Level SCCAN Differences (AD vs Stroke)

The stroke cohort outperformed the AD group across all eight SCCAN domains.

Statistically significant differences and considerable effect sizes were observed.

The greatest discrepancy appeared in the Memory subtest (U = 14.5, p < .001, r = .75), while the smallest was found in Oral Expression (U = 38.5, p < .001, r = .60).

A mid-range difference was noted in Orientation (U = 27.0, p < .001, r = .72).

The stroke group also demonstrated markedly higher scores in both Attention and Problem Solving, each associated with large effect sizes ( $r \approx .59-.60$ ).

The cognitive decline in AD appears broader and more pervasive, contrasting with the more focal and variable impairments typically observed following stroke. Table 3 provides a summary of these findings.

Table 3: Comparison of SCCAN Subtest Scores Between the AD and Stroke Groups

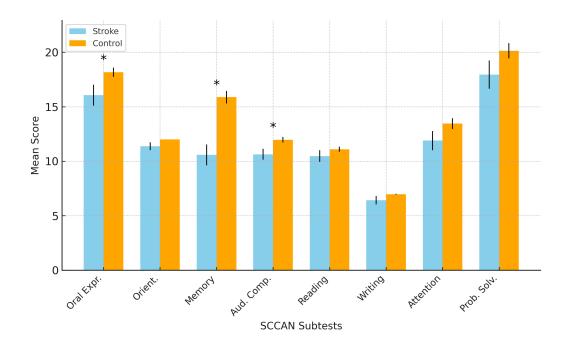
Subtest	$oldsymbol{U}$	p-value	Effect size (r)
Memory	14.5	<.001 ***	0.75
Orientation	27.0	<.001 ***	0.72
Oral Expression	38.5	<.001 ***	0.60
Attention	38.5	<.001 ***	0.60
Auditory Comprehension	40.5	<.001 ***	0.59
Problem Solving	40.5	<.001 ***	0.59
Reading Comprehension	42.5	<.001 ***	0.58
Writing	77.5	.022 *	0.40

Note. \* p < .05; \*\*\* p < .001

## 3.4 Stroke vs Control Comparison

Individuals with stroke scored lower than the control group on both the MMSE (U = 94, p < .001, r = .58) and the SCCAN (U = 135, p = .001, r = .45). The most marked discrepancy was observed in the Memory subtest (U = 498.5, p < .001, r = .58). Additionally, meaningful differences were identified in Oral Expression (U = 413.5, p = .007, r = .38) and Auditory Comprehension (U = 169.0, p = .008, r = .37). In contrast, only minor or negligible differences were found

in Attention, Problem Solving, and Reading Comprehension. This configuration intimates SCCAN's perception regarding remaining cognitive-communicative impairments within stroke, notably within expressive language, receptive language, and memory, though certain redressable or overlearned capabilities could stay comparatively unscathed. All SCCAN and MMSE results reported here are raw scores. Mean SCCAN subtest scores are displayed in Figure 1. These scores relate to the stroke and control groups.



**Fig.1.** Mean raw SCCAN subtest scores in the stroke and control groups. Error bars represent standard errors of the mean. Asterisks (\*) indicate subtests with significant between-group differences (p < .05). Maximum possible scores for each subtest are provided in Table 2.

# 3.5 Correlation Between SCCAN and MMSE

A Spearman rank-order correlation was performed within the stroke group (n = 19) to explore the relationship between SCCAN total scores and MMSE results. A strong, statistically significant positive correlation was identified ( $\rho$  = .719, p < .001). Higher SCCAN performance was associated with better global cognitive functioning. These findings suggest that the Bulgarian version of the SCCAN demonstrates convergent validity, as further supported by the characteristics of the clinical sample.

#### 3.6 Internal Correlations Within SCCAN

SCCAN total scores demonstrated strong internal consistency within the stroke group.

The highest correlations were observed for Oral Expression ( $\rho$  = .910), Memory ( $\rho$  = .861), and Reading Comprehension ( $\rho$  = .824), all statistically significant at p < .05. The SCCAN is designed to assess comprehensive cognitive-communicative functioning.

These associations indicate meaningful contributions from these domains. Table 4 presents the complete correlation matrix.

Oral Orient. Memory Reading Writing Prob. SCCAN Aud. Attention Expr. Comp. Solv. Total Oral Expr. 1.00 1.00 Orient. 0.63\*0.75\*Memory 0.39 1.00 Aud. 0.57\* 0.42 0.42 1.00 Comp. Reading 0.76\* 0.66\* 0.62\* 0.60\* 1.00 Writing 0.87\* 0.47\*0.73\*0.54\*0.76\*1.00 Attention 0.59\* 0.30 0.55\* 0.34 0.61\* 0.41 1.00 1.00 Prob. 0.61\* 0.59\* 0.33 0.60\* 0.78\* 0.71\* 0.60\* Solv. 0.91\* 0.71\* 0.69\* **SCCAN** 0.61\* 0.86\*0.64\* 0.82\* 0.68\* 1.00

**Table 4**. Correlation matrix (Spearman's rho) among SCCAN subtests and total score in the stroke group (n = 19). Values marked with \* are statistically significant at p < .05

#### 4. Discussion

Total

# 4.1 Summary and Interpretation of Main Findings

These pilot data support the clinical applicability of the Bulgarian SCCAN for detecting cognitive-communicative impairments. In particular, ischemic stroke patients had considerably higher overall and subtest scores than AD patients. The diffuse neurological alterations that impact memory and orientation in early AD are consistent with this pattern (McKhann et al., 2011; Bayles et al., 2020). In the stroke cohort, the pattern of impairment was more variable. Significant deficits emerged particularly in memory, auditory comprehension, and oral expression, while domains such as attention, reading comprehension, and problem solving were comparatively preserved. This profile supports the idea that stroke-related damage may selectively affect language-related and episodic memory processes, while leaving some cognitive functions relatively intact—consistent with earlier studies on localised brain injury (Cumming, Marshall, & Lazar, 2013; Hillis & Heidler, 2002). When compared against neurologically healthy controls, even mild stroke was associated with measurable declines in memory and both expressive and receptive language—deficits that may elude brief global screeners like the MMSE (Milman & Holland, 2012). Convergent validity was further demonstrated by the significant positive correlation that was found between the stroke group's SCCAN and MMSE scores. But compared to the MMSE alone, SCCAN showed higher domain-specific resolution, especially for language, memory, and attention, which increased its therapeutic usefulness (Milman et al., 2008; Tombaugh & McIntyre, 1992).

# **4.2 Internal Consistency and Construct Validity of SCCAN**

Strong correlations between SCCAN total scores and a number of specific subtests—particularly oral expression, memory, and reading comprehensionwere shown by the internal consistency analysis. These results are consistent with the instrument's theoretical framework, which was created to evaluate a wide range of cognitive-communicative skills in several domains related to acquired neurological illnesses (Milman et al., 2008). Psychometric research by Milman et al. (2008) supports this interpretation, showing that all SCCAN subtests in individuals with acquired cognitive-communicative impairments had good test-retest reliability and high internal consistency. Using a customised, domainspecific testing methodology, their investigation validated the instrument's capacity to distinguish between neurologically damaged and healthy individuals. Additional clinical insights from Milman and Missel (2020) further emphasise the tool's flexibility, psychometric robustness, and applicability across inpatient and outpatient settings.

In addition, the observed correlation between SCCAN total scores and MMSE performance in the stroke group ( $\rho=.719$ ) provides further support for the convergent validity of the Bulgarian-adapted SCCAN. While the MMSE captures global cognitive functioning, SCCAN adds value by offering detailed insights into language, attention, and problem-solving abilities—domains often underrepresented in brief cognitive screeners (Tombaugh & McIntyre, 1992; Milman & Holland, 2012).

# 4.3 Clinical Interpretation of Group Differences

The differences in SCCAN scores across the two clinical groups imply different patterns of brain disfunction. The AD group exhibited the greatest declines in memory and orientation. These findings are in line with early damage to regions including the entorhinal cortex, posterior cingulate, and hippocampus that are critical for episodic memory and spatial navigation (Braak & Braak, 1991; Jack et al., 2013). Language problems also appeared early in AD. Verbal fluency and word retrieval also deteriorate in tandem with a decline in oral expression

performance (Taler & Phillips, 2008; Verma & Howard, 2012).

In contrast, the stroke group's communicative profile was more erratic. This variation is consistent with lesion heterogeneity and the localised nature of ischemic episodes. The most obvious deficits were in memory, oral expression, and auditory understanding, but attention, problem solving, orientation, and reading comprehension appeared to be mostly unaffected. Similar findings were reported by Jaya et al. (2017), who found that stroke patients had the greatest deficits on the memory and attention subtests of SCCAN, and that individuals with subcortical lesions had lower overall scores than those with cortical injury. Earlier studies have shown that localised brain lesions outside the perisylvian region may spare well-rehearsed cognitive-linguistic functions (Hillis & Heidler, 2002). Our findings support this, suggesting that overlearned or automatised abilities often remain intact after stroke. These results underline the importance of domain-specific assessment. Mild impairments in expressive or receptive language may impact daily communication but can be missed during brief cognitive screening.

### 4.4 Strengths and Limitations

The inclusion of both clinical and control groups for comparison analysis and the use of a well-structured instrument that identifies domain-specific cognitive-communicative deficits are two of this study's strengths. In order to distinguish between diffuse and focal neurological disorders, a nuanced interpretation of deficiencies was made possible by the use of subtest-level analyses.

Several caveats merit consideration. Notably, the AD cohort was small, thereby undermining statistical power and constraining the generalizability of findings. Importantly, biomarker assessments cerebrospinal fluid analyses and PET imaging—were applied inconsistently; in most cases, diagnoses were established based on clinical criteria and CT scans for stroke. It is becoming more widely acknowledged that these biomarkers are essential for a conclusive diagnosis of AD (Jack et al., 2018). Additionally, lesion heterogeneity among stroke patients adds to the observed diversity in performance patterns and makes it more difficult to map deficits onto particular neuroanatomical substrates (Cumming et al., 2013). We did not analyse potential sex-related effects on SCCAN or MMSE performance. While sex-related differences have been observed in certain cognitive domains, these effects are generally modest and unlikely to have significantly influenced the findings in the present study. Future research with larger and more balanced samples could further explore this aspect. Additionally, bilingualism or multilingualism was not assessed. All participants were assumed to be monolingual Bulgarian speakers, which may limit the generalisability of the findings to multilingual populations. Handedness was not documented, and all

participants were assumed to be right-handed based on observation. Future studies could formally assess handedness and explore its potential influence on cognitive-communicative performance. It should also be noted that the AD group was significantly older than the control group, which may have contributed to some of the observed differences in performance. Although age-related cognitive decline is expected to be modest compared to the effects of AD, future studies should aim to further minimize age differences between groups. Lastly, the cross-sectional design precludes conclusions about the tool's sensitivity to change over time and does not allow assessment of test-retest reliability.

# 4.5 Clinical Implications and Directions for Future Research

As a structured and functionally relevant instrument, the findings support the clinical utility of the Bulgarian-adapted SCCAN in assessing cognitive-communicative impairments across neurological populations. Domain-specific profiles generated by the SCCAN allow for more targeted and individualised intervention and rehabilitation planning, in contrast to brief global screeners such as the MMSE (Milman et al., 2008). Finding deficiencies in areas like expressive language, attention, and problem-solving is crucial in stroke rehabilitation, where cognitive and language impairments may be mild but clinically significant (Hillis & Heidler, 2002; Lezak et al., 2012).

Early and accurate detection of communication impairments is crucial given the rising incidence of AD and stroke-related cognitive impairment worldwide (Livingston et al., 2020). Tools like the SCCAN can be very helpful when neurologists and speech-language pathologists collaborate in interdisciplinary care settings, where they work together during the subacute phase and long-term maintenance.

In order to evaluate the instrument's sensitivity to change over time, future research should use longitudinal designs and use bigger, more varied samples. The Bulgarian SCCAN's diagnostic validity will be further improved by establishing normative data and cut-off scores tailored to the population. These advancements would directly benefit clinical practice. Similar observations have been reported by Milman and Missel (2020), who emphasised the SCCAN's adaptability, robust psychometric properties, and practicality in both inpatient and outpatient neurorehabilitation settings.

#### 5. Conclusion

The clinical usefulness of the Bulgarian-adapted SCCAN in evaluating cognitive-communicative deficits in people with AD and ischemic stroke is suggested by this study.

The test exhibited convergent validity, high internal consistency, and sensitivity to both diffuse and focal

deficits. These results lend credence to the incorporation of SCCAN into Bulgarian clinical neurorehabilitation procedures.

To create normative standards and increase its diagnostic usefulness, further extensive validation research is necessary.

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#### **Conflict of interests**

Authors declare no conflicts of interests.

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