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ARTICLE

Web-based cognitive screening in bipolar disorder: validation of the Internet-based Cognitive Assessment Tool in remote administration settings

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ABSTRACT

Background: Cognitive impairments are prevalent during remission in bipolar disorder (BD), but existing cognitive screening tools are time- and resource-intensive. Digital, web-based options can facilitate detection and monitoring of these impairments across clinical and research settings.

Methods: This cross-sectional study investigated psychometric properties of the Internet-based Cognitive Assessment Tool (ICAT) when self-administered in home-based settings. Newly diagnosed, remitted outpatients with BD and healthy controls (HC) underwent cognitive testing with the standard paper-pencil tool Screen for Cognitive Impairment in Psychiatry (SCIP) in-clinic and ICAT at-home as part of baseline assessments for an intervention trial (ClinicalTrials ID: 2021-000862-14).

Results: Data were analyzed for 31 BD patients and 29 HC. We demonstrated a strong positive correlation between at-home ICAT and in-clinic SCIP total scores within patients with BD ($r(29) = 0.66$, $p < .001$), which survived subsyndromal mood symptoms adjustment (partial $r(25) = 0.67$, $p < .001$), indicating adequate concurrent validity. There was a moderate positive correlation between ICAT and SCIP total scores across the entire sample ($r(54) = 0.56$, $p < .001$) and between subtest scores ($r = 0.29$–0.61, $ps \leq .03$), except the executive functions tasks ($p = .1$). BD patients exhibited no impaired performance compared to HC on ICAT or SCIP ($ps \geq .08$).

Conclusions: ICAT is a valid and feasible online tool for remote cognitive screening in remitted patients with BD. Web-based screening constitutes an accessible and efficient approach for implementing systematic cognitive screening in BD.

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1. Introduction

Accumulating evidence shows that cognitive deficits across attention, memory, and executive functions persist during fully or partially remitted phases in 50–70% of patients with bipolar disorder (BD) [1–3]. These deficits increase functional disability and the risk of psychiatric hospitalization [4–7], underscoring that achieving symptomatic remission alone is an inadequate treatment endpoint [8]. Consequently, the International Society for Bipolar Disorders (ISBD) Targeting Cognition Task Force [9,10] stresses the urgent need for systematic screening for cognitive impairment in the clinical management of BD. Implementing cognitive screening enhances the identification of patients with detectable cognitive deficits, providing a foundation for targeted educational and intervention strategies [10]. This screening is crucial for clarifying patients' cognitive status and recognizing those with and without cognitive deficits [10]. Given the often weak or poor association between patients' subjective cognitive complaints and objective performance on neuropsychological tests [11–13], the task force recommends assessing both subjective and objective cognition, which provides somewhat different, albeit complementary insights into patients' cognitive status [9,10]. For objective cognition assessment, the recommendation is to use a short, feasible screening tool such as the paper-pencil-based Screen for Cognitive Impairment in Psychiatry (SCIP) [14] based on its high sensitivity and validity in detecting cognitive impairments in affective disorders [15,16]. However, despite the ISBD Targeting Cognition Task Force recommendations [9,10] and positive initial clinical experiences at our specialized

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outpatient clinic in Copenhagen [17], cognitive screening is not yet systematically implemented in the clinical care of patients with affective disorders. An impediment to the widespread implementation of existing paper-pencil instruments is that they require in-person administration by healthcare staff, which is both time and resource consuming [18].

Digital (computer-based) options offer innovative, flexible, and cost-effective solutions, addressing the need for more accessible, scalable, and efficient methods to screen for cognitive impairment. Indeed, they overcome barriers related to financial, geographical, and physical limitations, allowing for broad access to cognitive testing on a large scale. Given this, we recently developed the Internet-based Cognitive Assessment Tool (ICAT), which is a self-administered, online screening platform adapted from SCIP [19]. The ICAT is an easy-to-administer, user-friendly tool with 20 min administration time which has shown good concurrent validity and sensitivity to cognitive impairments in BD [20]. The next important step is, therefore, to investigate whether ICAT exerts corresponding psychometric properties when self-administered in *remote, home-based* settings. Thus far, the potential of remote, self-administered digital cognitive assessment in affective disorders has been explored with diverse screening tools, including Cambridge Neuropsychological Test Automated Battery (CANTAB®) Connect [21,22] and the THINC-Integrated (THINC-it®) tool [23]. While CANTAB Connect is well-validated and assesses multiple domains, it is time-consuming and does not assess verbal learning and memory. Similarly, although the recently designed THINC-it tool has short administration time, it was originally developed specifically for patients with depression and also lacks assessment of verbal memory [23]. However, verbal learning and memory assessment should be integrated in web-based screening tools for BD, as deficits within this domain are prevalent and negatively impact functioning in this patient group [4]. This supports the relevance of continued development of self-assessment instruments for remote cognitive screening in BD, such as ICAT. Indeed, implementing relevant web-based screening tools in routine clinical practice would enable systematic, time- and resource-efficient screening, flexibly allowing clinicians to monitor patients' cognitive status and adjust treatment plans following these outcomes.

Building on our previous in-clinic ICAT validation study [20], the aim of the current study was to investigate the psychometric properties of ICAT when self-administered by fully or partially remitted outpatients with BD or healthy controls (HC) in *remote, home-based* settings. We focused on establishing (i) the concurrent validity of ICAT when completed in at-home settings, as reflected by its correlation with in-clinic SCIP performance within patients and across both patients and controls and (ii) its sensitivity to cognitive impairments in patients with BD compared to HC. We hypothesized that (i) ICAT test scores would correlate with SCIP test scores in patients with BD, also when adjusting for mood symptoms, and across the entire sample, and (ii) patients would display poorer cognitive performance in both ICAT and SCIP compared to HC.

2. Materials and methods

2.1. Participants

We collected available baseline data for this study from patients with BD recruited from Copenhagen Affective Disorder Clinic as part of their participation in our ongoing clinical study, the 'Effects of low-dose aspirin in bipolar disorder' (A-bipolar) randomised controlled trial (RCT) [24] and from HC recruited from the Blood Bank at Frederiksberg Hospital [25]. Patients were recruited between January 2022 and May 2024, while HC were recruited from March to September 2023.

Patient group inclusion criteria were 18–65 years of age, newly diagnosed BD (subtype I or II) within two years according to ICD-10 criteria, with diagnosis confirmed using the diagnostic semi-structured interview Schedules for Clinical Assessment in Neuropsychiatry (SCAN) [26], full or partial remission (as reflected by total scores ≤14 or ≤7 on the Hamilton Depression Rating Scale 17-items (HRDS-17 [27]) and the Young Mania Rating Scale (YMRS [28]), respectively) and fluent in Danish. Diagnostic verification assessments with SCAN [26] were carried out by trained researchers (JZ, CFB, HBK). Patients were excluded if they had serious somatic illness, including chronic kidney disease, severe cardiac insufficiency, gastric ulcer, gastro-intestinal bleeding, or other pathological bleeding tendency, received non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulants or selective serotonin reuptake inhibitors (SSRIs), were pregnant or breastfeeding, or had current alcohol/substance use disorders at the time of enrolment. Eligible HC were 18–55 years of age and fluent in Danish. Healthy controls were excluded if they presented with a personal or first-degree family history of psychiatric illness, dyslexia, neurological illness, previous severe head trauma, or current alcohol or substance use disorder.

Written informed consent following oral and written study information was collected from all participants before inclusion. Studies were performed in accordance with the principles stated in the Declaration of Helsinki. The A-bipolar and HC normative group studies have been approved by the Danish Research Ethics Committee for the Capital Region of Denmark (A-bipolar: H-21014515; HC normative group: F-22065023), the Danish Medicines Agency (A-bipolar: EudraCT no. 2021-000862-14; HC normative group: not applicable), and the Danish Data Protection Agency Capital Region of Denmark (Privacy) (A-bipolar: P-2021-576).

2.2. Procedures

The experimental design was cross-sectional, as we analyzed available baseline data from study participants, from which data were pooled [24,25]. Patients attended the Copenhagen Affective Disorder Research Center (CADIC), Psychiatric Centre Copenhagen, and HC attended the Neurocognition and Emotion in Affective Disorders (NEAD) Centre, Department of Psychology, and were instructed to avoid caffeine intake before their assessment. Here, they were assessed in-person for objective cognitive functioning with the paper-and-pencil-based SCIP and rated for depressive and (hypo)manic

symptoms with the HDRS-17 [27] and YMRS [28] scales, respectively, as well as functioning with the observer-rated Functioning Assessment Short Test (FAST) scale [29]. Immediately after their in-clinic visit, we sent each participant a unique webpage link to the ICAT platform via the national secure Digital Post mail system, used in Denmark by ~95% of the adult population for the distribution and storage of personal information and official documents [30]. As the last part of the assessment, we informed participants to access the ICAT platform via a link sent to their Digital Post mail system, allowing them to complete the remote ICAT unsupervised using their own PC devices and internet browsers. We requested participants to complete the remote ICAT assessment ideally *on the same day* as their in-person SCIP assessment visit if practically possible, but otherwise within a few days. Participants were informed to complete the test in quiet, undisturbed surroundings and to avoid consuming caffeine two hours before taking the test. For the present study, ICAT was designed only to be compatible for and administered on PC/laptop devices.

2.3. Remote cognitive screening: the Internet-based Cognitive Assessment Tool

The ICAT is a digital, online cognitive test battery designed to mirror the cognitive subtests of SCIP [20] (Table 4). The SCIP exists in three parallel versions, which were administered in a counterbalanced manner within the HC group. This approach was implemented to minimize overlap with other neuropsychological test measures, as HC subjects participated in multiple cognition studies in addition to the present study. In contrast, only SCIP version 3 was administered in the BD patient group.

ICAT assesses domains of verbal learning, working memory, executive function, delayed verbal memory, and psychomotor speed. Specifically, it consists of the following five subtests: List Learning (LL), Consonant Repetition (CR), adapted Letter-Number Sequencing task (LNS), Delayed List Learning (DLL), and Visuomotor Tracking (VMT). The adapted LNS subtest was based on the Wechsler Adult Intelligence Scale 3rd Edition (WAIS-III) Letter-Number Sequencing [31] and hence replaced the SCIP Verbal Fluency subtest since a digital format of verbal fluency could not be adequately implemented owing to technical limitations. Thus, four of the five neurocognitive subtests in the ICAT were developed based on the SCIP subtests (Table S1 for overview).

ICAT has two versions and is designed with written and audio-recorded instructions to be self-administered without needing in-person assistance. Each ICAT version is designed similarly, only differing in the word and letter stimuli presented in the subtests. In the version applied in this study, a pre-recorded guidance video was integrated to provide instructions resembling those provided by a human test administrator. Participants completed the ICAT application through receiving a webpage link in their DigitalPost inbox where they were required to fill out an electronic informed consent form that complies with the General Data Protection Regulation (GDPR). As a first step, the platform implements Automatic Speech Recognition (ASR) techniques to record and recognize participants' oral responses during the completion of verbal learning and memory subtests. Accordingly, a technical setup page ensured that the microphone and a sound check for speaker interfaces for each participant's device were configured correctly prior to the initiation of the assessment. Since ASR technology is still in its early-stages [32], we ensured the accuracy and validity of the ASR component by manually double-checking the accordance between extracted ASR-generated oral response word outputs and the automatically generated scores for the verbal learning and memory subtests. The comprehensive design process and system descriptions are outlined in detail in Hafiz et al. [19]. The version of ICAT used in this study required approximately 20–25 min to complete, including microphone set-up, viewing of an introductory video before initiating the assessment, as well as listening to pre-recorded auditory and reading written instructions before each subtest. As a result, the ICAT version applied in this study was slightly longer than the SCIP assessment, which on average takes approximately 15–20 min to complete.

2.4. In-clinic cognitive screening: the Screen for Cognitive Impairment in Psychiatry

The Danish version of the SCIP [14,15] was utilized to assess participants' objective cognitive functioning in-clinic at CADIC, Psychiatric Centre Copenhagen or NEAD Centre, Department of Psychology, University of Copenhagen, administered by trained researchers. SCIP is a paper-and-pencil cognitive screening tool that spans five domains: verbal learning, working memory, executive functioning, delayed verbal memory recall, and psychomotor speed. Specifically, it contains the following subtests: Verbal Learning Task – Immediate (VLT-I), Working Memory Task (WMT), Verbal Fluency Task (VFT), Verbal Learning Task – Delayed (VLT-D), and Psychomotor Speed Task (PST) [14].

2.5. Functioning

The FAST scale [29] was used to evaluate current level of functioning. This observer-based interview assesses functioning in daily life situations over the past 15 days, covering the domains of autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, and leisure. The FAST scale consists of 24 items rated on a four-point Likert scale: 0 = no difficulty, 1 = mild difficulty, 2 = moderate difficulty, and 3 = severe difficulty. A total score (range: 0–72) is calculated by summing all items scores. A higher score reflects poorer functioning.

2.6. Statistical analyses

We performed statistical analyses employing IBM Statistical Packages for the Social Sciences (SPSS) v28.0 (Armonk, NY) with α-level = $p < .05$ (two-tailed). Data normality was determined using Shapiro–Wilk's test [33] (estimated with normally distributed data: $p \geq .05$, nonparametric data: $p < .05$) supplied with visual inspection of histograms and Q–Q plots for

each variable-of-interest included in the statistical analyses. Independent samples *t*-test (*t*) or Mann–Whitney's *U*-test (*U*) were used for group comparisons (depending on data normality distribution) on demographic and clinical factors, functioning, as well as objective cognitive test performance scores (ICAT and SCIP, respectively). Pearson's Chi-square test (χ^2) was conducted to assess between-group differences on dichotomous data variables.

The sensitivity of ICAT and SCIP for assessment of cognitive impairment was evaluated for each subtest and total scores. Cohen's *d* or *r* was calculated as effect size measures to supply the independent sample *t*-test or the Mann–Whitney *U*-test results if significant between-group differences were identified. To investigate the concurrent validity of ICAT compared to SCIP, correlational analyses were performed using Pearson's correlation (*r*) for normally distributed data, and Spearman's rho (σ) for non-normally distributed data. Correlations were examined between total scores of ICAT and SCIP, as well as exploratory for performances on each corresponding subtest.

3. Results

3.1. Group comparisons of demographic and clinical characteristics

Table 1 displays the demographic and clinical characteristics of the patient and HC groups. Data were collected from *n* = 60 participants (patients with BD, *n* = 31; HC, *n* = 29). Patients were comparable to HC on age and sex distribution (*ps* ≥ .3) but had fewer educational years and more subsyndromal depressive and (hypo)manic symptoms than HC (*ps* ≤ .007; Table 1). Within patients, 58% were diagnosed with BD type I, had an illness onset of median (Mdn) = 18 years (interquartile range (IQR): 17–21) and duration of untreated or treated illness of Mdn = 10 years (IQR = 6–16). With regards to psychotropic medication, 65% received antipsychotics, 55% lithium, 39% anticonvulsants, and 7% antidepressants at the time of assessment. Specifically, for those receiving antipsychotic medication, all were prescribed quetiapine with the majority 45% (*n* = 14) receiving sedating doses of <100 mg daily while 19% (*n* = 6) received ≥100 mg daily. Finally, patients reported substantially poorer functioning than HC (FAST total score; *U* = 807.50, *p* < .001, *r* = 0.81; Table 1).

The time range between the in-person cognitive screening with SCIP and remote cognitive screening with ICAT was 1–12 days (68% of patients completed these assessments 0–2 days apart). Among included patients, 60% and 40% completed ICAT version 1 and 2, respectively, while this distribution was 45% and 55% among HC. There was no significant difference between performance scores on ICAT in HC between the two versions (*p* = .6), supporting no difference in the degree of difficulty between versions. Healthy controls underwent baseline assessment with in-clinic, in-person SCIP cognitive screening and remote, at-home ICAT cognitive screening completing the baseline assessment visit and the ICAT home-based screening 0–1 days apart (86% on the same day).

Table 1. Demographic and clinical characteristics comparison of patients with BD and HC.

	BD (*n* = 31)	HC (*n* = 29)	*p* Value
Demographics			
Age in years, Mdn (IQR), range	28 (24.50–37.50), [20–51]	31 (25.50–42.50), [22–54]	.4
Sex, female/male (%)	13 (42%)/18 (58%)	17 (59%)/12 (41%)	.3
Years of education, *M* (SD)	15 (2)	17 (2)	**.007****
Clinical characteristics			
BD type I/II, %	18 (58%)/13 (42%)	–	–
Illness onset (years), Mdn (IQR)	18 (17–21)	–	–
Illness duration (years), M (SD)	12 (9)	–	–
HDRS-17 total score, Mdn (IQR)	9 (4–10)	0 (0–1.50)	**<.001*****
YMRS total score, Mdn (IQR)	3 (2–7)	0 (0–1)	**<.001*****
Psychotropic medication, *n* (%)			
Antidepressants	2 (7%)	–	–
Antipsychotics[a]	20 (65%)	–	–
Anticonvulsants	12 (39%)	–	–
Lithium	17 (55%)	–	–
Functioning			
FAST total score, Mdn (IQR)	16 (10–21)	1 (0–2)	**<.001*****

BD: bipolar disorder; HC: healthy controls; *M*: mean; SD: standard deviation; Mdn: median; IQR: interquartile range; HC: healthy controls; HDRS-17: Hamilton Depression Rating Scale 17-items. *Statistics*: *U*: Mann–Whitney *U*-test for non-parametric data (median (IQR)), χ^2: Chi-square for categorical variables.
**$p < .01$, ***$p < .001$ (two-tailed).
[a]Quetiapine ≥ 100 mg/day: *n* = 6 (19%).

3.2. Discriminative ability assessment

We decided a priori not to calculate ICAT total score for participants with missing data in any of the ICAT subtests. This decision was made to prevent data distortion and ensure the validity of between-group comparisons. Missing subtest data were mainly due to a transient technical issue with the ICAT ASR component in registering participants' oral responses during the study period, resulting in missing or inaccurate verbal response registration. Consequently, data were missing on the following ICAT subtests: *List Learning:* BD, *n* = 2, HC, *n* = 3; *Delayed List Learning*: HC, *n* = 3.

3.3. Assessment of hypothesis 1: concurrent validity

Consistent with hypothesis 1, there was a strong positive correlation between ICAT and SCIP total scores within our sample of patients with BD ($r(29) = 0.66$, $p < .001$; Figure 1(B)), which prevailed following adjustment for residual mood symptoms (HDRS-17 and YMRS total scores) (partial $r = 0.67$, $p < .001$).

Further, across the entire sample, there was a moderate positive correlation between performance total scores of ICAT and SCIP ($r(54) = 0.56$, $p < .001$; Table 2; Figure 1(C)). Correlation analyses also showed weak to moderate correlations between performance scores on the individual domain-specific ICAT and SCIP subtests (*r* = 0.29–0.61, *ps* ≤ .03; Table 2), except between subtests 3 (executive functioning) (*p* = .1).

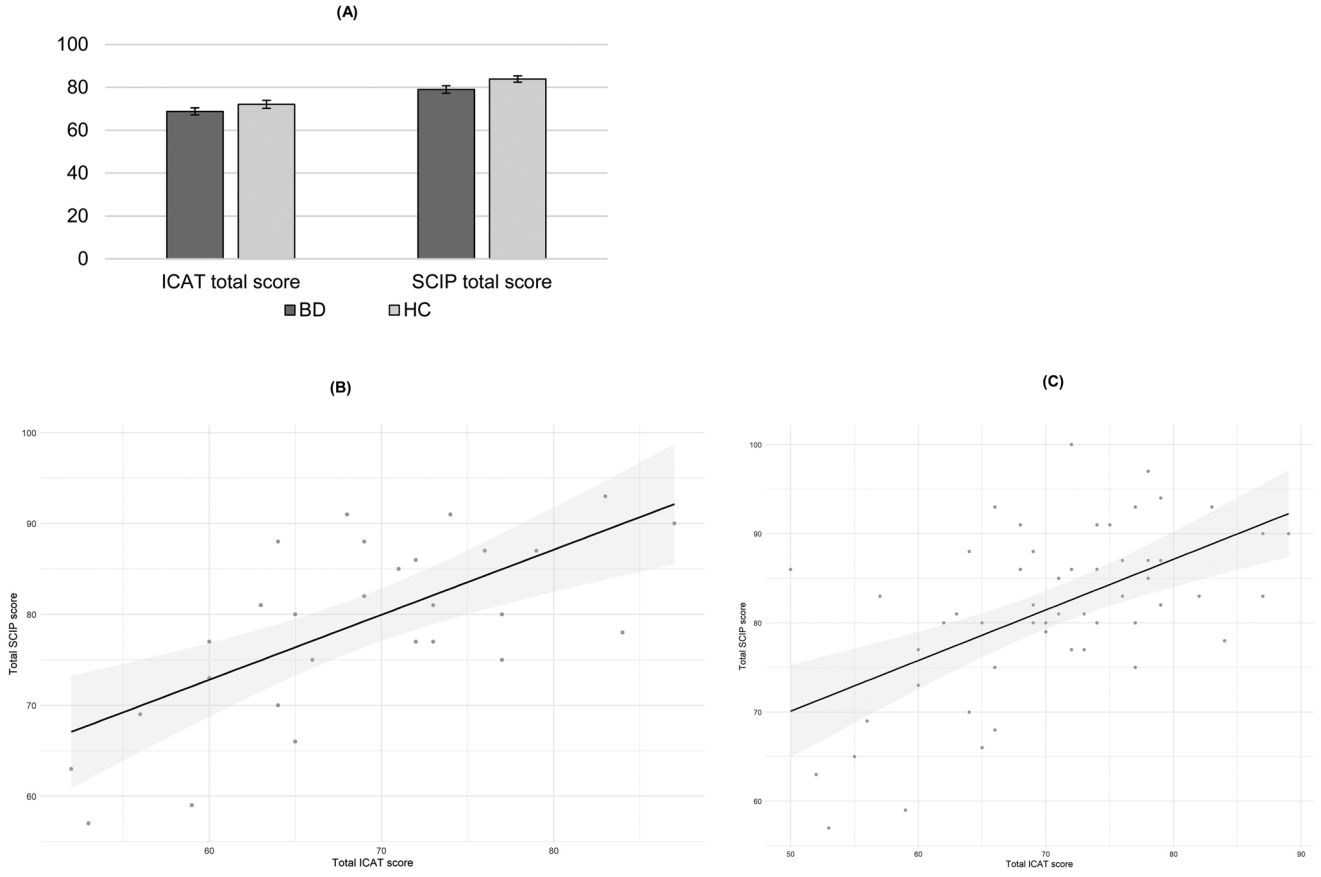

Figure 1. (A) ICAT and SCIP total scores in the BD patients and HC groups. Error bars represent standard error of the mean (SEM) values. (B) Scatterplot depicting the strong correlation between SCIP and ICAT total scores within fully or partially remitted patients with BD (n = 29) (r = 0.66, p < .001). (C) Scatterplot depicting the moderate correlation between SCIP and ICAT total scores across the entire sample (r = 0.56, p < .001).

Table 2. Correlation matrix between SCIP and ICAT subtest tasks across entire sample.

		SCIP subtests					
ICAT subtests		1. VLT-I	2. WMT	3. VFT	4. VLT-D	5. PST	SCIP total score
1. LL (ASR)	r_s	**0.61*****					
	p-level	**<.001**					
	N	55					
2. CR	r_s		**0.29****				
	p-level		**.028**				
	N		60				
3. WAIS LNS	r_s			0.20			
	p-level			.1			
	N			58			
4. DLL (ASR)	r_s				**0.52*****		
	p-level				**<.001**		
	N				57		
5. VMT	r_s					**0.32***	
	p-level					**.013**	
	N					60	
ICAT total score	*r*						**0.56*****
	p-level						**<.001**
	N						54

r: Pearson's correlation; r_s: Spearman's rho; SCIP: Screen for Cognitive Impairment in Psychiatry; ICAT: Internet-based Cognition Assessment Tool; LL: List Learning; CR: Consonant Repetition; WAIS-IV LNS: Wechsler Adult Intelligence Scale III: Letter-Number Sequencing; DLL: Delayed List Learning; VMT: Visuomotor Tracking; ASR: Automatic Speech Recognition; VLT-I: Verbal Learning Task – Immediate; WMT: Working Memory Task; VFT: Verbal Fluency Task; VLT-D: Verbal Learning Task – Delayed; PST: Psychomotor Speed Task. The significance of the bolded values in Table 2 are to highlight the correlations that were statistically significant. This is indicated directly within the table using exact p-level values supplied with asterisks and clarified in the accompanying notes/abbreviations:
*p < .05 (two-tailed).
**p < .01 (two-tailed).
***p < .001 (two-tailed).

3.4. Assessment of hypothesis 2: sensitivity to cognitive impairment

In contrast with hypothesis 2, the BD patients showed no impaired performance on ICAT (Mdn = 69, IQR = 64–75 vs. Mdn = 74, IQR = 67–78) or SCIP (Mdn = 80, IQR = 73–88 vs. Mdn = 83, IQR = 80–89) (*p*s ≥ .08; Table 3, Figure 1(A)). Moreover, BD patients versus HC displayed no significantly impaired cognitive performance across any of the subtests on ICAT (*p*s ≥ .2) or SCIP (*p*s ≥ .07), except for SCIP subtest 2 (working memory) (p = .006) (Table 3).

3.5. Exploratory correlational analyses between cognitive performance, functioning, and age

Correlational analyses revealed no associations between functioning (FAST total score) and objective global cognitive performance when assessed remotely (ICAT total score) or in-person (SCIP total score), neither across the entire sample (*p*s ≥ .2) nor within patients only (*p*s ≥ .5). However, a negative relation was observed between worse in-clinic working memory performance (lower SCIP subtest 2 scores) and poorer functioning (larger FAST total score) across the entire sample ($r_s(60) = -0.29$, $p = .024$). However, for the remaining domain-specific subtest performance scores on ICAT or SCIP, we detected no significant correlations with FAST total score, neither across the entire sample (*p*s ≥ .2) nor within patients alone (*p*s ≥ .2). Finally, we observed no association between age and overall performance on the ICAT (ICAT total score) across the entire sample ($p = .9$) nor within patients alone ($p = .6$)Table 4.

Table 3. Performance score comparisons on the Internet-based Cognition Assessment Tool (ICAT) and the Screen for Cognitive Impairment in Psychiatry (SCIP).

	BD (*n* = 31)	HC (*n* = 29)	*p* Value
ICAT subtests + total score			
1. List Learning, Mdn (IQR)	21 (17–26)	23 (20–26)	.2
2. Consonant Repetition, Mdn (IQR)	22 (20–23)	23 (21–23)	.3
3. WAIS LNS, Mdn (IQR)	10 (10–12)	11 (10–12)	.3
4. Delayed List Learning, Mdn (IQR)	7 (4–9)	7 (5–10)	.6
5. Visuomotor Tracking, Mdn (IQR)	9 (7–11)	8 (7–10)	.4
Total score, Mdn (IQR)	69 (64–75)	74 (67–78)	.1
SCIP subtests + total score			
1. Verbal Learning Task – Immediate, Mdn (IQR)	25 (23–27)	25 (23–27)	.9
2. Working Memory Task, Mdn (IQR)	20 (18–21)	22 (20–23)	**.006****
3. Verbal Fluency Task, Mdn (IQR)	16 (14–18)	18 (15–20)	.3
4. Verbal Learning Task – Delayed, Mdn (IQR)	8 (7–9)	9 (7–10)	.07
5. Psychomotor Speed Task, Mdn (IQR)	12 (10–14)	12 (11–14)	.8
Total score, Mdn (IQR)	80 (73–88)	83 (80–89)	.08

BD: bipolar disorder; HC: healthy controls; Mdn: median; IQR: interquartile range; HDRS-17: Hamilton Depression Rating Scale 17-items.
Missing data: *ICAT List Learning*: BD, *n* = 2, HC, *n* = 3; *ICAT Delayed List Learning*: HC, *n* = 3; *ICAT total score*: BD, *n* = 2, HC, *n* = 4.
**$p < .01$ (two-tailed).

4. Discussion

This is the first study investigating the concurrent validity and sensitivity of *remote* cognitive screening with ICAT in patients with BD. Consistent with our first hypothesis, ICAT scores showed a strong correlation with in-clinic SCIP scores within the BD sample ($r = 0.66$), even after adjusting for subsyndromal mood symptoms. This indicates that ICAT is a valid tool for home-based cognitive screening in remitted patients with BD. Additionally, across the entire sample, including BD and HC participants, the correlation between ICAT and SCIP scores was moderate ($r = 0.56$). Further, we demonstrated significant weak to moderately positive correlations across the entire sample between all but the executive function ICAT and equivalent SCIP subtests. Contrary to our second hypothesis, patients with BD did not show cognitive impairments compared to the HC group on either the ICAT or SCIP assessments. This lack of impairment limited our ability to evaluate the sensitivity of ICAT in detecting cognitive deficits within the current BD sample.

The observed strong correlation between performance on the home-based, self-administered ICAT and in-clinic, in-person-administered SCIP aligns with our earlier reported levels ($r = 0.72$) of adequate concurrent validity of ICAT when administered in in-clinic settings [20]. Compatibly, the correlations between domain-specific ICAT subtest performance patterns with their respective SCIP counterparts corroborate these in-clinic results [20] and align with correlation coefficient ranges reported in other web-based cognitive test validation studies [21, 34]. The exception was the executive function subtests, where we observed no association between ICAT and SCIP performances. Yet, this was not surprising since the two subtests differed in content and demands. Together, the current findings contribute to the development of digital cognitive screening in psychiatry, supporting the suitability of self-administered, remote testing with ICAT in BD patients [35].

Contrary to our hypothesis and earlier detections [20], patients in the current sample showed no cognitive impairment, as reflected by no statistically different performance on ICAT or SCIP relative to HC. Since this was consistent across both screening tools, this observation does not imply insufficient sensitivity of ICAT to assess cognitive function remotely; rather, this disparity is likely attributable to the limited representativeness of the current sample of newly diagnosed, young ($M \pm SD = 32 \pm 10$ years) patients who agreed to participate in the cognition assessments as part of the baseline assessment in an intervention trial (A-bipolar [24]). This

Table 4. Overview of the Internet-Based Cognitive Assessment Tool subtests and counterpart SCIP subtests.

ICAT subtests and counterpart SCIP subtests					
SCIP	VLT-I	WMT	VFT	VLT-D	PST
ICAT	LL	CR	Adapted WAIS-III LNS	DLL	WMT
Cognitive domain	Verbal learning and memory	Working Memory	Working memory	Verbal learning and memory	Psychomotor speed
ICAT outcome measure	Total number of correctly recalled words across 3 trials	Total number of correctly recalled letters	Total number of correctly recalled sequences	Total number of correctly recalled words	Total number of letters matched to correct codes
ICAT score range	0–30	0–24	0–21	0–10	0–30

SCIP subtasks. VLT-I: Verbal Learning Task – Immediate; WMT: Working Memory Task; VFT: Verbal Fluency Task; VLT-D: Verbal Learning Task – Delayed; PST: Psychomotor Speed Task; *ICAT subtasks*. LL: List Learning; CR: Consonant Repetition; WAIS-III LNS: Wechsler Adult Intelligence Scale Letter-Number Sequencing; DLL: Delayed List Learning; VMT: Visuomotor Tracking.

sample was thus a subgroup of the most well-functioning patients, as also reflected by their relatively short illness duration ($M \pm SD = 12 \pm 9$ years), high education status ($M \pm SD = 15 \pm 2$ educational years), and the general absence of significant functional impairment (70% of patients had FAST total scores <20) [36]. Our sample's absence of cognitive impairment contrasts with most prior literature that documented adequate sensitivity of SCIP and ICAT to detect cognitive impairment in BD [15, 20, 37]. Noteworthy, this is in keeping with the concept of neuroprogression, stating that a longer duration of illness is linked to greater cognitive impairment [38], although this model remains debated [39]. Relatedly, ICAT data could only be gathered for patients with the capacity to participate in the at-home ICAT assessment after having undergone a comprehensive in-clinic enrolment visit (A-bipolar [24]). Held together with the observation that most patients presented with no or only mild functional impairment (Table 1), this may have introduced a selection bias only capturing a subset of relatively well-functioning patients. Accordingly, between-group differences in cognitive performance would possibly have emerged if this study had included a more diverse patient cohort, better representing the cognitive heterogeneity characteristic of BD [40].

The present findings have several implications. Despite international recommendations, systematic, objective cognitive screening is still not implemented in clinical practice due to limited time and resources to screen for cognitive impairment in BD [10]. To address this challenge, ICAT introduces a feasible screening option with real-world relevance, offering potential for widespread implementation of cognitive screening in daily clinical practice. Indeed, the web-based format optimises clinical resources by automatically generating cognitive performance data reports that can be uploaded to patients' electronic medical records. These reports can serve as the basis for feedback during clinical consultations, providing a foundation for addressing factors that independently affect cognitive functioning in BD (e.g. comorbidities, sleep disturbances, lifestyle factors, or certain medications [9, 41–48]). As an extension of the present validation phase, an imperative next step is hence to systematically integrate in-person feedback on patients' cognitive performance patterns in clinical practice, as this will likely lead to high response rates in the implementation phase of ICAT as an at-home screening tool. Further, the systematic implementation of remote testing with ICAT could aid in optimising recruitment processes for research-related pro-cognitive intervention initiatives. While ICAT is deemed equally suitable as existing standard paper-pencil tools for cognitive screening across mood states, we recommend ensuring partial or full remission at the time of screening to exclude potential effects of acute mood symptoms on cognitive performance, aligning with international recommendations [10]. Indeed, the relation between greater depression symptom severity and altered speech patterns, including reduced prosodic emphasis, pitch, and tone [49], could plausibly affect the verbal response ASR-registration on the verbal learning and memory subtests. To overcome this, participants' oral responses are displayed in real-time directly in the platform during completion of the verbal learning and memory subtests, decreasing the risk of systematic errors in speech recognition for those with (subsyndromal) depression-related speech pattern anomalies.

An important strength of the at-home administered ICAT was its close resemblance to a validated in-clinic standard paper-pencil screening tool. Moreover, the possibility of unprecedented large-scale dispersion using ICAT in future register-based studies carries potential to significantly improve generalisability of findings within the field of cognition in affective disorders. In keeping with this, key advantages of ICAT, as compared to existing web-based screening tools, e.g. CANTAB and THINC-it [21–23], are its short administration time and the integration of advanced ASR-based algorithms to assess the domain of verbal learning and memory.

Despite these advantages, the study also contained central limitations. First, the cross-sectional design hindered test–retest reliability assessment. Second, the modest sample size ($n = 60$), exclusively including newly diagnosed patients (n=31), limited the statistical power and sample representativeness. Third, the non-counterbalanced order of in-clinic SCIP followed by at-home ICAT administration could have led to learning effects, although both groups demonstrated poorer numerical performance on ICAT than SCIP, thus minimizing this likelihood. Another caveat was the transient technical issue with ASR-based verbal response registrations, resulting in missing data from three HC subjects and two BD patients on the verbal learning and memory ICAT subtests. In addition, a general obstacle of unsupervised digital screening is that the required technical skills themselves may be demanding for individuals with reduced cognitive capacity or limited technical proficiency. As such, potential impact of varying technology skills – with age as a hypothesized proxy – cannot be excluded. Indeed, the absence of an association between age and ICAT cognitive performance in this study could be explained by the skewed age distribution of the sample, which impeded assessing the sensitivity of ICAT to potential age-related cognitive decline. Simultaneously, home-based screening plausibly resembles real-world challenges closer than paper-pencil tests, administered in structured clinical settings, presumably offering higher ecological validity than traditional in-clinic screening [50]. Finally, as ICAT is designed solely for cognitive screening purposes, which can indicate whether patients may benefit from referral to further cognitive evaluation, it cannot replace a comprehensive clinical neuropsychological assessment.

Guided by these challenges, we have optimised the technical configurations and developed the platform interface to mitigate the risk of sample selection biases in our ongoing and future large-scale, register-based ICAT studies (ICARE, approval no.: p-2024-15990; TRANSCIN, approval no.: p-2023-14744). Importantly, we have integrated evaluation of participants' technology experiences to directly account for the possible impact of tech-savviness on test performance patterns. Additionally, we have upgraded the platform to be compatible for assessment on both PC/laptop as well as tablet devices (e.g., iPads). To control for the potential impact of using different devices (e.g., PC vs. tablet) on test performance patterns, we have also updated the research platform to register the type of device each participant uses when

completing ICAT. The critical next steps include establishing applicability, feasibility, and reliability of ICAT across large-scale cohorts. Specifically, our ongoing register-based studies collect data that will enable (i) establishing demographically adjusted norms, (ii) determining tentative performance cut-off scores to identify cognitive impairment, and (iii) evaluating test–retest reliability to provide change norms. These endeavors will aid the future widespread integration of ICAT to screen for and monitor cognitive function over time in patients with psychiatric disorders across clinical and research settings.

This is the first study to investigate the psychometric properties of the novel web-based cognitive screening instrument, ICAT, when self-administered in a remote, unsupervised home-based setting in remitted patients with BD. The results extended our previous detections, demonstrating that ICAT is a promising, time-efficient screening tool with adequate concurrent validity for remote, self-administered objective cognitive screening in BD. Upcoming large-scale studies will establish the sensitivity and feasibility of remotely administered ICAT in large-scale, representative cognitive profile samples of BD. Our plan of making the ICAT platform available across clinical and research settings can give rise to a paradigm shift in assessment and treatment procedures targeting cognition across psychiatric disorders in the future. As a first step, the ICAT is now being implemented systematically in our cognitive screening initiative in our outpatient clinic, Copenhagen Affective Disorder Clinic, in Denmark. Findings from this study will further inform the feasibility and psychometric properties of ICAT. This can lead to widespread implementation of systematic cognitive screening initiatives independent of time and resource restrictions. In this way, ICAT carries the potential to improve awareness, identification, and intervention of cognitive impairment in clinical management of patients with psychiatric disorders internationally in the future.

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Ethical approval

The present work was conducted in compliance with the Ethical Standards of the Danish Research Ethics Committee for the Capital Region of Denmark as well as in accordance with the principles of the Declaration of Helsinki.

Author contributions

JZ: writing – original draft, writing – review and editing, data curation, formal statistical analyses, visualization, and investigation. CFB: writing – original draft, writing - review and editing, data curation, formal statistical analyses, visualization, and investigation. STC: writing – original draft, writing – review and editing, formal statistical analyses, and investigation. HBK: writing – review and editing, and investigation. OVK: writing – review and editing, and investigation. CLB: writing – review and editing, and investigation. AEJ: writing – review and editing, and investigation. JEB: primary investigator and software architect for the ICAT platform – review and editing. LVK: primary investigator of the A-Bipolar RCT – review and editing. KWM: conceptualization, writing – original draft, Writing – review and editing, data curation, and investigation.

Disclosure statement

JZ has within the last three years received honoraria from Lundbeck Pharma A/S, outside the submitted work. LVK has within the last three years received honoraria from Lundbeck Pharma A/S and Teva, outside the submitted work. KWM has received consultancy fees from Lundbeck, Janssen, Angelini Pharma and Richter Gedeon in the past three years. CFB, STC, HBK, OVK, CLB, and AEJ declare no conflicts of interest.

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Data availability statement

The data are available upon reasonable request.

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