Cognitive Deficits in the THINC-Integrated Tool (THINC-it) Are Associated With Psychosocial Dysfunction in Patients With Major Depressive Disorder

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ABSTRACT

Objective: To evaluate the extent to which cognitive measures in the recently developed THINC-integrated tool (THINC-it) are associated with global and domain specific psychosocial disability in patients with current and remitted major depressive disorder (MDD).

Methods: Cross-sectional data (N = 127) were obtained from participants with current (n = 105) or remitted (n = 22) MDD who completed the THINC-it between July 2014 and June 2018. Major depressive disorder was diagnostically assessed with *DSM-IV* and *DSM-5* criteria. The THINC-it includes 4 objective cognitive tests: the Spotter (ie, Choice Reaction Time), Symbol Check (ie, *n*-back), CodeBreaker (ie, Digit Symbol Substitution), and Trails (ie, Trail Making Test part B), as well as a measure of self-perceived cognitive deficits, the Perceived Deficits Questionnaire for Depression-5-item (PDQ-5-D). Psychosocial dysfunction was assessed with the Functioning Assessment Short Test.

Results: The whole group analysis (ie, lifetime MDD) indicated that poor objective cognitive performance on the CodeBreaker (β = 0.346, *P* = .002) and Trails tasks (β = 0.232, *P* = .017) and greater self-reported cognitive deficits on the PDQ-5-D (β = 0.596, *P* < .001) were associated with more severe global psychosocial disability. In addition, performance on the CodeBreaker and Trails tasks showed dissociable relationships with specific psychosocial deficits (eg, occupational functioning, daily autonomy). The relationship between cognitive and psychosocial deficits was stronger in participants with current compared to remitted MDD.

Conclusions: Cognitive deficits identified by the THINC-it are associated with global and specific psychosocial deficits, highlighting the clinical value and utility of the THINC-it as a cognitive screening instrument in patients with MDD.

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Major depressive disorder (MDD) is a major health problem globally, places a major burden on clinicians, and frequently results in many years lived with functional disability.[1–3] Cognitive dysfunction is observed in MDD, which includes deficits in memory, executive function, and attention and slower reaction time.[4] Furthermore, the cognitive dysfunction observed in MDD often persists, even after other symptoms of depression have remitted.[5–7] Importantly, this cognitive dysfunction is also associated with functional deficits in a number of psychosocial domains including occupational functioning, interpersonal relationships, daily autonomy, and self-perceived quality of life.[7–9]

The association between cognitive dysfunction and impaired psychosocial functioning is observed not only in individuals during a major depressive episode,[7,10,11] but also in individuals with remitted MDD.[7,9] Both poorer global cognitive scores and deficits in specific domains of cognitive function have been associated with impaired psychosocial functioning. For example, impairment in instrumental activities of daily living has been associated with lower global cognitive scores and executive dysfunction in patients with MDD.[11–14]

The broad relationship between cognition and psychosocial dysfunction highlights the clinical importance of detecting and treating cognitive deficits, which may play a core role in the pathology and maintenance of functional deficits in MDD.[15,16] Recent studies also suggest that cognitive deficits are associated with greater symptom severity, unemployment, and illness relapse.[8,17–19] Existing treatments (eg, cognitive-behavioral therapy and antidepressants) primarily target mood symptoms, resulting in cognitive deficits remaining untreated in the majority of MDD patients.[20,21] Lack of detection and treatment of cognitive deficits in MDD may therefore be a key barrier to functional recovery and long-term mental health.

In light of the significant cognitive dysfunction in individuals with current and remitted MDD, it is important to be able to screen for cognitive deficits using a valid and sensitive tool that also detects psychosocial dysfunction. This is particularly important for individuals with impairment in areas such as occupational functioning that have been associated with cognitive dysfunction.[10] Existing cognitive screening tools are time-consuming and costly and place significant administrative burden on the psychiatrist or interviewer. For example, the widely used Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) requires a trained clinician to administer the scale individually to the participant, typically takes 30 minutes to complete, and requires that subsequent data entry be managed by

Clinical Points

- The THINC-integrated tool (THINC-it) provides valid, brief, and easily administered measurement of cognitive function. The results of this study demonstrate that objective cognition in the THINC-it is associated with functional disability in major depressive disorder patients.
- This research highlights the value and clinical utility of the THINC-it in screening for cognitive and functional deficits in depressed individuals.

the clinician or their staff. In contrast, the Montreal Cognitive Assessment is brief (approximately 10 minutes) but requires administration and manual scoring by a trained assessor. These administrative and technical barriers highlight the need to develop valid and brief screening tools for cognitive impairment in MDD. Importantly, these tools should be self-administered and automatically scored to reduce burden on health care providers.

The THINC-integrated tool (THINC-it) was developed in response to the need for valid, brief, and self-administered screening tools for cognitive impairment in MDD.[22] While cognitive performance measured by the THINC-it has been shown to differentiate between depressed patients and healthy controls[22] and demonstrate a relationship with self-reported functional deficits,[23] the relationship between THINC-it measures and clinically evaluated psychosocial functioning is yet to be examined. Accordingly, the current study evaluated the extent to which cognitive outcomes in the THINC-it are associated with clinically assessed psychosocial dysfunction in patients with current and remitted MDD. We evaluated whether performance in objective THINC-it measures (ie, Spotter, Symbol Check, CodeBreaker, and Trails) or self-perceived cognition (ie, Perceived Deficits Questionnaire for Depression-5-Item; PDQ-5-D) was associated with overall psychosocial functioning as measured by the Functioning Assessment Short Test (FAST).[24] Domain specific relationships were also examined between THINC-it measures and specific psychosocial outcomes (ie, autonomy, occupational functioning, subjective cognitive dysfunction, financial issues, interpersonal relationships, leisure time). Given previous associations identified between cognitive and psychosocial dysfunction in MDD,[25] we hypothesized that objective cognitive performance in individual THINC-it tasks and self-reported cognition in the PDQ-5-D would be associated with FAST total score. Exploratory analyses evaluated domain specific relationships between THINC-it tasks and specific psychosocial deficits in the FAST (eg, occupational function).

METHODS

Cross-sectional data were collated and analyzed from 3 studies employing the THINC-it: (1) the Cognitive Function and Mood study (CoFaM-S),[26] (2) the Cognitive and Emotional Recovery Training Program for Depression (CERT-D),[27] and (3) the Anti-inflammatory treatment of inflammation associated depression (PREDDICT)[28] study. The CoFaM-S, CERT-D, and PREDDICT studies were reviewed by the human research ethics committee of the Royal Adelaide Hospital and the University of Adelaide (CoFaM-S approval number: 111230, CERT-D approval number: R20170611, PREDDICT approval number: R20170320) and were conducted in accordance with the Declaration of Helsinki. Detailed study information was provided to participants, and written informed consent to participate was obtained. All participants were at least 18 years of age, and age limits of 75 and 80 years were imposed for the PREDDICT and CERT-D studies, respectively. No upper age limit was imposed for the CoFaM-S study. Participants were recruited from clinical referral within the Central Adelaide Local Health network and by online and paper advertisements in the general population.

Inclusion criteria included diagnosis of MDD according to the *DSM-IV* criteria[29] for the CoFaM-S study and according to the *DSM-5* criteria[30] for the CERT-D and PREDDICT studies. Individuals were classified as currently depressed (n = 105) if primary symptoms of MDD (ie, pervasive negative mood, lassitude) were experienced over the past 2 weeks as reported by the Mini-International Neuropsychiatric Interview (MINI).[31] Individuals were defined as remitted (n = 22) if they had a reported previous history of MDD while being free of MDD symptoms in the past 2 weeks according to MINI criteria. Remitted participants also demonstrated Hamilton Depression Rating Scale (17 items) scores < 7, indicating "normal" mood.[31,32] The lifetime depression group (N = 127) was composed of individuals who were either currently depressed or remitted from MDD. Exclusion criteria included a primary diagnosis of any psychiatric disorder other than MDD, neurodegenerative or neurologic disorders, or a reading, learning, or language impairment. In addition, the use of concomitant medications that may affect cognitive function (eg, corticosteroids) was also considered as an exclusion criterion. The widely used adult version of the MINI (MINI 600) was used to confirm previous and/or current diagnosis of MDD and to screen participants for comorbid psychiatric disorders.[33]

Participants (N = 127) with a lifetime diagnosis of MDD were included in the current study on the basis of completing the THINC-it and the Functioning Assessment Short Test (FAST) between July 2014 and June 2018. The mean age of participants was 42.35 years (SD = 15.68 years), 75 (59%) participants were female, and mean years of education was 14.26 (SD = 2.48). Among the participants included in the study, 105 (83%) had a current diagnosis of MDD, while the remaining 22 (17%) were remitted of MDD according to the MINI 600. Notably, a greater number of currently depressed participants were recruited relative to remitted participants, as CERT-D and PREDDICT are clinical trials evaluating treatments for acute MDD. Demographic statistics stratified by MDD status (current or remitted) are presented in Supplementary Table 1.

Cognitive Assessment

The THINC-it is a newly developed digital screening instrument for cognitive dysfunction in MDD patients.[22,34]

Four objective cognitive tests are included: the Spotter (ie, Choice Reaction Time), Symbol Check (ie, *n*-back), CodeBreaker (ie, Digit Symbol Substitution), and Trails (ie, Trail Making Test part B), as well as 1 self-reported scale of cognitive dysfunction (Perceived Deficits Questionnaire–Depression, 5-item [PDQ-5-D]). Mean performance for each THINC-it test by participants in the current analysis is presented in Table 1, and conventional cognitive test equivalents are presented in Table 2.

Psychosocial Assessment

Psychosocial dysfunction was assessed using the FAST, a semistructured, clinician-administered interview gauging patient dysfunction over the previous 15 days.[24] Dysfunction is rated on a scale from 0 (no difficulty) to 3 (severe difficulty) across 6 functional subdomains: autonomy, occupational dysfunction, subjective cognition, financial issues, interpersonal relationships, and leisure time. Global psychosocial dysfunction (ie, FAST total score) is calculated as the sum of all FAST subdomains (see Table 1).

Table 1. Performance on Individual THINC-it Tests and Psychosocial Dysfunction in the FAST (N = 127)[a]

THINC-it test	Mean (SD) Value
Trails, total time, s	29.80 (14.91)
Spotter	
Response time, ms	629.44 (216.96)
Number correct	37.95 (2.70)
Symbol Check	
Response time, ms	1,268.52 (271.26)
Number correct	23.22 (11.20)
CodeBreaker	
Completion time per symbol, ms	2,676.14 (1,613.91)
Number correct	50.10 (16.97)
PDQ-5-D total score	10.17 (4.97)
FAST score	
Total	20.47 (12.00)
Autonomy	2.94 (2.47)
Occupational functioning	4.34 (4.41)
Cognitive functioning	5.85 (3.55)
Leisure time	2.86 (1.95)
Financial issues	1.27 (1.68)
Interpersonal relationships	5.91 (4.22)

Abbreviations: FAST = Functioning Assessment Short Test, PDQ-5-D = Perceived Deficits Questionnaire for Depression-5-item, THINC-it = THINC-integrated tool.

Statistical Analyses

Normality tests indicated that performance in the Spotter, CodeBreaker, and Trails tasks was skewed (*P* values < .05); therefore, scores were $\log_{10}$ transformed prior to statistical analysis (see Table 2). All THINC-it outcomes were subsequently converted into *z* scores, following the procedure of an earlier validation study.[22] FAST total score was normally distributed (*P* = .09).

The relationship between individual THINC-it *z* scores and FAST total score was tested with regression analyses, each of which employed an individual THINC-it outcome as the independent variable and FAST total score as the dependent variable. A standard α level of 0.05 was employed. Age, sex, and years of education were included as covariates, as these factors can influence the relationship between cognitive and psychosocial dysfunction.[8,35] Initial analyses with the entire participant sample (ie, lifetime MDD) also included data source (ie, CERT-D, PREDDICT, CoFaMS) as a covariate, to examine whether features distinct to each study affected the relationship between cognition and psychosocial function. THINC-it outcomes significantly associated with FAST total score were subsequently employed as independent variables in domain specific regression analyses. Domain specific models included FAST subdomains as dependent variables. This exploratory approach was followed first in the whole sample (ie, lifetime MDD) and then separately for those with current and remitted MDD.

Multicollinearity of THINC-it outcomes was low, as indicated by variance inflation factors < 2. Post hoc power analyses were conducted with the G*power software.[36] Given the number of THINC-it independent variables and the effect sizes identified (β = 0.205–0.590), our analyses achieved 80% power to detect a relationship between cognitive performance in the THINC-it and psychosocial functioning in the FAST.

Table 2. Domain-Specific Relationships Between THINC-it *z* Scores and FAST Total Score (N = 127), Expressed by Standardized β Coefficients[a]

Conventional Test Equivalent	THINC-it Tests	β for Relationship With FAST Total Score
CogState Identification Task	Spotter	
	Mean response time ($\log_{10}$)	0.110 (.366)
	Number correct ($\log_{10}$)	−0.013 (.891)
CogState One-Back test	Symbol Check	
	Mean response time	0.110 (.312)
	Number correct	0.033 (.751)
Digit Symbol Substitution Test	CodeBreaker	
	Mean completion time ($\log_{10}$)	0.346 (.002)*
	Number correct	−0.345 (.002)*
Trail Making Test part B	Trails	
	Time to complete ($\log_{10}$)	0.232 (.017)*
Perceived Deficits Questionnaire for Depression-20-Item	PDQ-5-D	0.596 (< .001)**

[a]*P* values are in parentheses. Linear regression models adjusted for age, gender, and years of education.
*Significant at *P* < .05.
**Significant at *P* < .001.
Abbreviations: FAST = Functioning Assessment Short Test, PDQ-5-D = Perceived Deficits Questionnaire for Depression-5-item, THINC-it = THINC-integrated tool.

RESULTS

Lifetime MDD

Initial regression analyses using the entire sample (ie, lifetime MDD) indicated that poor performance in the CodeBreaker task in measures of "number correct" (β = −0.345, *P* = .002) and response time (β = 0.346, *P* = .002) was associated with increased global psychosocial dysfunction (ie, FAST total score). Likewise, slower performance in the Trails task was significantly related to greater psychosocial dysfunction overall (β = 0.232, *P* = .017). Finally,

Table 3. Domain-Specific Relationships Between THINC-it *z* Scores and FAST Subdomains in the Whole Sample (ie, Lifetime MDD, N = 127), Expressed by Standardized β Coefficients[a]

	FAST Subdomains					
THINC-it Tests	Autonomy	Occupational Functioning	Subjective Cognition	Leisure Time	Financial Issues	Interpersonal Relationships
CodeBreaker						
Mean completion time	0.205 (.062)~	0.272 (.013)*	0.337 (.001)*	0.143 (.203)	0.013 (.912)	0.248 (.027)*
Number correct	−0.255 (.021)*	−0.271 (.014)*	−0.367 (.001)*	−0.202 (.075)	−0.023 (.846)	−0.214 (.059)~
Trails						
Time to complete	0.197 (.040)*	0.114 (.133)	0.253 (.010)*	0.115 (.240)	−0.091 (.363)	0.191 (.052)~
PDQ-5-D	0.413 (<.001)**	0.391 (<.001)**	0.590 (<.001)**	0.472 (<.001)**	0.219 (.015)*	0.418 (<.001)**

[a]*P* values are in parentheses. Linear regression models adjusted for age, gender, and years of education.
*Significant at $P < .05$.
**Significant at $P < .001$.
~Marginal significance.
Abbreviations: FAST = Functioning Assessment Short Test, PDQ-5-D = Perceived Deficits Questionnaire for Depression-5-item, THINC-it = THINC-integrated tool.

Table 4. Domain-Specific Relationships Between THINC-it *z* Scores and FAST Total Score in the Current (n = 105) and Remitted (n = 22) MDD Groups, Expressed by Standardized β Coefficients[a]

	β for Relationship With FAST Total Score	
THINC-it Tests	Current MDD	Remitted MDD
Spotter		
Mean response time (log_{10})	0.252 (.085)	−0.230 (.319)
Number correct (log_{10})	−0.049 (.640)	−0.029 (.874)
Symbol Check		
Mean response time	0.121 (.353)	−0.009 (.962)
Number correct	0.007 (.951)	0.127 (.499)
CodeBreaker		
Mean completion time (log_{10})	0.301 (.013)*	0.283 (.281)
Number correct	−0.285 (.016)*	−0.349 (.181)
Trails		
Time to complete (log_{10})	0.176 (.107)	0.031 (.868)
PDQ-5-D	0.574 (<.001)**	0.356 (.026)*

[a]*P* values are in parentheses. Linear regression models adjusted for age, gender, and years of education.
*Significant at $P < .05$.
**Significant at $P < .001$.
Abbreviations: FAST = Functioning Assessment Short Test, MDD = major depressive disorder, PDQ-5-D = Perceived Deficits Questionnaire for Depression-5-item, THINC-it = THINC-integrated tool.

greater perceived cognitive deficits (ie, PDQ-5-D) were associated with increased psychosocial dysfunction (β = 0.596, $P < .001$). In contrast, performance in the Spotter and Symbol Check tasks was not reliably associated with FAST total score (all *P* values > .312). Standardized β coefficients and associated *P* values for the relationships between THINC-it outcomes and FAST total score are presented in Table 2. The relationships between THINC-it performance and FAST total score were unaffected by the inclusion of data source (ie, CERT-D/PREDDICT/CoFaMS) as a covariate, and hence this variable was removed from subsequent analyses.

Regression analyses of FAST subdomains as dependent variables indicated that lower number correct in the CodeBreaker task was statistically significantly associated with functional deficits in domains of autonomy (β = −0.255, $P = .021$), occupational functioning (β = −0.271, $P = .014$), and subjective cognitive dysfunction (β = −0.367, $P = .001$) and marginally associated with poor interpersonal relationships (β = −0.214, $P = .059$). Poor average completion time was statistically significantly related to deficits in occupational functioning (β = 0.272, $P = .013$), subjective cognition (β = 0.337, $P = .001$), and interpersonal relationships (β = 0.248, $P = .027$) and marginally associated with reduced autonomy (β = 0.205, $P = .062$). CodeBreaker performance was not associated with dysfunction in domains of leisure time or financial issues (all *P* values ≥ .203). Statistics for domain specific relationships between THINC-it outcomes and FAST subdomains are presented in Table 3.

Analysis of the relationship between speed in the Trails task and FAST subdomains indicated that slower performance was statistically significantly related to greater dysfunction in the areas of autonomy (β = 0.197, $P = .040$) and subjective cognitive dysfunction (β = 0.253, $P = .010$). Slower Trails performance was also marginally associated with poor interpersonal relationships (β = 0.191, $P = .052$). Trails performance was not associated with subdomains of occupational functioning, leisure time, or financial issues (all *P* values ≥ .133) (see Table 3).

Greater self-perceived cognitive deficits in the PDQ-5-D were associated with increased psychosocial dysfunction in all FAST subdomains (ie, autonomy [β = 0.413, $P < .001$], occupational functioning [β = 0.391, $P < .001$], subjective cognitive dysfunction [β = 0.590, $P < .001$], leisure time [β = 0.472, $P < .001$], financial issues [β = 0.219, $P = .015$], and interpersonal relationships [β = 0.418, $P < .001$]) (see Table 3).

Current MDD

In the current MDD group, analysis of FAST total score revealed that poor performance in the CodeBreaker task (ie, number correct [β = −0.285, $P = .016$], mean completion time [β = 0.301, $P = .013$]) was associated with greater global psychosocial dysfunction (see Table 4). In addition, greater score in the PDQ-5-D, indicating greater cognitive dysfunction, was linked with increased psychosocial dysfunction (β = 0.574, $P < .001$).

FAST subdomain analyses showed that slower mean completion time in the CodeBreaker task was associated

Table 5. Domain-Specific Relationships Between THINC-it *z* Scores and FAST Subdomains in the Current MDD Group (n = 105), Expressed by Standardized β Coefficients[a]

	FAST Subdomains					
THINC-it Tests	Autonomy	Occupational Functioning	Subjective Cognition	Leisure Time	Financial Issues	Interpersonal Relationships
CodeBreaker						
Mean completion time	0.152 (.199)	0.213 (.073)~	0.349 (.004)*	0.040 (.743)	−0.015 (.900)	0.221 (.072)~
Number correct	−0.197 (.096)	−0.196 (.100)	−0.337 (.006)*	−0.082 (.503)	0.009 (.943)	−0.172 (.163)
PDQ-5-D	0.353 (<.001)**	0.353 (<.001)**	0.556 (<.001)**	0.420 (<.001)**	0.176 (.080)	0.401 (<.001)**

[a]*P* values are in parentheses. Linear regression models adjusted for age, gender, and years of education.
*Significant at $P < .05$.
**Significant at $P < .001$.
~Marginal significance.
Abbreviations: FAST = Functioning Assessment Short Test, MDD = major depressive disorder, PDQ-5-D = Perceived Deficits Questionnaire for Depression-5-item, THINC-it = THINC-integrated tool.

with greater subjective cognitive dysfunction (β = 0.349, $P = .004$) and marginally associated with reduced occupational functioning (β = 0.213, $P = .073$). Lower number correct in the CodeBreaker task was also associated with poor subjective cognition (β = –0.337, $P = .006$). Greater self-perceived cognitive deficits in the PDQ-5-D were associated with psychosocial dysfunction across all FAST subdomains: autonomy (β = 0.353, $P < .001$), occupational functioning (β = 0.353, $P < .001$), subjective cognition (β = 0.556, $P < .001$), leisure time (β = 0.420, $P < .001$), and interpersonal relationships (β = 0.401, $P < .001$), with the exception of financial issues (β = 0.176, $P = .080$). Statistics for domain specific analyses in the current MDD group are presented in Table 5.

Remitted MDD

Analysis of THINC-it outcomes with FAST total score in the remitted group indicated that self-reported cognitive dysfunction in the PDQ-5-D was significantly associated with overall psychosocial dysfunction (β = 0.356, $P = .026$). In contrast, objectively assessed cognition was not associated with FAST total score (see Table 4). FAST subdomain analyses indicated PDQ-5-D was associated with subjective cognitive dysfunction (β = 0.517, $P = .008$). In contrast, PDQ-5-D score was not significantly related to autonomy (β = 0.192, $P = .369$), occupational functioning (β = 0.257, $P = .105$), leisure time (β = 0.297, $P = .118$), or financial issues (β = 0.001, $P = .995$).

DISCUSSION

The current findings indicate that both objective cognitive outcomes and self-perceived cognitive deficits in the THINC-it are associated with global psychosocial dysfunction. Specifically, poor performance in CodeBreaker and Trails tasks and greater self-reported cognitive deficits in the PDQ-5-D are linked with overall psychosocial dysfunction in patients with lifetime MDD. In addition, the CodeBreaker and Trails tasks were differentially associated with specific functional deficits. In contrast, Spotter and Symbol Check tasks were not related to psychosocial dysfunction.

CodeBreaker and Trails tasks are highly reliant on working memory and executive functioning.[37,38] Accordingly, our results are consistent with existing literature which suggests that measures of working memory and executive functioning are associated with global psychosocial dysfunction.[8,9] Poor performance in CodeBreaker and Trails tasks may therefore be a marker for broad psychosocial deficits in patients with MDD, potentially highlighting the need for additional cognitive treatment.[9,27,39] Self-reported cognition in the PDQ-5-D was also associated with global psychosocial dysfunction. However, subjective cognitive deficits are more closely linked to severity of depressive symptoms[40,41] and may therefore reflect the association of impaired mood with psychosocial dysfunction, as opposed to perceived cognitive dysfunction alone.

Correspondence of THINC-it outcomes to specific functional deficits (eg, occupational dysfunction) is also important to consider, as specific deficits may be more easily identified by clinical interviews than global psychosocial disability. Our findings showed that poor daily autonomy and self-perceived cognitive dysfunction (eg, ability to solve problems) were associated with poor cognition in both the CodeBreaker and Trails tasks. It follows that patients presenting with difficulties maintaining daily responsibilities or low perceived cognition should be screened for cognitive deficits, which could play an important pathological role in these domains.[8,9,15] In addition, CodeBreaker performance was linked with deficits in occupational functioning and interpersonal relationships, highlighting the broad application of working memory and attention in decision making, social interactions, and productivity.[42–44] Likewise, Trails performance was also associated with interpersonal deficits, pointing to the role of executive function (ie, cognitive flexibility, set shifting) in social domains.[44–46] Taken together, domain specific results suggest that outcomes in the THINC-it are differentially associated with specific psychosocial deficits and should be employed in screening for cognitive pathology in patients with issues in domains of autonomy, occupational functioning, and interpersonal issues.

In currently depressed patients, poor performance in the CodeBreaker task, but not the Trails task, was associated

with reduced psychosocial functioning. This result may suggest that the CodeBreaker task is particularly sensitive to executive and working memory deficits associated with acute MDD[47] and psychosocial dysfunction.[7,26] The Trails task may rely to a greater extent on cognitive updating,[48] which may not be as strongly linked with acute MDD[43] and hence share a weaker relationship with psychosocial dysfunction.

The relationship between objective THINC-it outcomes and psychosocial dysfunction in the remitted group appeared less reliable than the current MDD group, or when the entire sample was considered together (ie, lifetime MDD). However, this result likely reflects lower statistical power available in the remitted group due to a lower sample size (remitted n = 22) compared to the current MDD group (n = 105). In fact, the magnitude of the relationship observed between CodeBreaker performance and overall psychosocial dysfunction was similar in the current and remitted MDD groups (see Table 4), pointing to a potential relationship. Future research should further examine the psychosocial correlates of THINC-it outcomes in remitted MDD populations.

It is noteworthy that performance in the Spotter and Symbol Check tasks was not associated with overall psychosocial dysfunction. These null relationships may be explained by the primacy of reaction time in these tasks. Specifically, in both the Spotter and Symbol Check tasks, participants are required to respond within 2 seconds; otherwise, their response is considered an error. In contrast, no reaction time restrictions are placed on participants during the CodeBreaker and Trails tasks. In reality, there are rarely such strict time restrictions on the application of cognitive skills in functional tasks. It follows that cognitive skills with greater independence to reaction speed (eg, executive function, working memory) may have stronger application in functional tasks.

Importantly, the CodeBreaker and Trails tasks also incorporate features of processing speed, as performance in both tasks is partially reliant on one's ability to process and respond to visual stimuli. In addition, the CodeBreaker task taps components of working memory, as participants must repeatedly store incoming information and update a mental sequence.[22] It follows that there is significant overlap in the cognitive domains associated with tasks of the THINC-it. However, this overlap does not preclude cognitive domain–specific interpretations of THINC-it task outcomes, as each THINC-it task is *primarily* associated with specific cognitive domains. For example, the cognitive demand of the Trails task is borne out primarily by mentally switching between alphabetic and numeric sequences (ie, set shifting) and partially by the speed at which one can physically respond to this information (ie, processing speed). Like the Trails task, almost all cognitive tests overlap different cognitive domains and are hence not "pure" measures of a single domain; however, the most parsimonious explanation is to consider the primary cognitive domain associated with a particular cognitive test.

Key advantages of the current study were our evaluation of a recently developed cognitive screening instrument that is sensitive to clinical status, is simple to administer, and retains patient confidentiality.[22] Previous research on this topic[23] has relied on the association of THINC-it tasks with self-reported psychosocial function, which may be more closely associated with severity of mood symptoms,[25] highlighting the value of the present results in providing validation of the sensitivity of the THINC-it to psychosocial dysfunction. Our results are clinically valuable by supporting the use of the THINC-it to detect both cognitive and psychosocial impairment and suggest that poor performance may be particularly associated with reduced autonomy, occupational function, and interpersonal relationships. From a patient perspective, the THINC-it is highly endorsed, with subjects reporting an appreciation for its utility, ease of navigation, and legibility of instructions.[22] Routine screening with the THINC-it should therefore be included in screening depressed patients and should be considered together with the results of more broad measures of functional disability (eg, the Sheehan Disability Scale).[49]

A limitation to our findings is the small number of remitted depressed patients (n = 22) included in the sample. Further research is needed to examine the sensitivity of the THINC-it for detecting residual cognitive and psychosocial dysfunction in MDD.[6] It would also be valuable to examine objectively assessed psychosocial function (eg, the Social Skills Performance Assessment)[50,51] to determine whether the relationship of the THINC-it to clinically assessed and self-reported psychosocial dysfunction extends to explicit psychosocial performance.

In summary, the present results suggest that greater magnitude of cognitive impairment in the THINC-it is linked to poor psychosocial functioning. In addition, poor performance in the CodeBreaker and Trails tasks is differentially associated with specific deficits in domains of daily autonomy, subjective cognition, occupational functioning, and interpersonal relationships. These findings underscore the need to screen for cognitive deficits in MDD and highlight the efficacy of the THINC-it for this purpose. Importantly, the THINC-it provides valid and reliable cognitive measures[22] in a freely distributed and self-instructed format that can be completed in 10–15 minutes. Ease of access and brief administration highlight the advantages of the THINC-it in comparison to comparable screening assessments (eg, RBANS, Screen for Cognitive Impairment in Psychiatry[52]) and support the clinical use of the scale in screening for cognitive and associated psychosocial impairment in MDD.

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Author contributions: Prof Baune conceived, designed, coordinated, and supervised the CoFaMS study. Prof Baune conceived, designed, and supervised the PREDDICT and CERT-D studies. Dr Fourrier is the coordinator of the PREDDICT study, and Dr Knight is the coordinator of the CERT-D study. Drs Knight and Mills and Prof Baune mutually developed the hypotheses and conceptual outline of the present manuscript. Dr Knight

analyzed data. Drs Knight, Fourrier, and Mills wrote the manuscript, while Prof Baune edited and provided feedback during its writing. Dr Aboustate, Assoc Prof Hori, and Mss Lyrtzis and Sampson collected data included in the current study and provided feedback during the writing of the manuscript.

Potential conflicts of interest: **Prof Baune** received speaker/consultation fees from AstraZeneca, Lundbeck, Pfizer, Takeda, Servier, Bristol-Myers Squibb, Otsuka, and Janssen-Cilag and was involved in the development of the THINC-it. The remaining authors have no conflicts of interest to declare.

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Supplementary Material

Article Title: Cognitive Deficits in the THINC-Integrated Tool (THINC-it) Are Associated With Psychosocial Dysfunction in Patients With Major Depressive Disorder

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List of Supplementary Material for the article

1. Table 1 Demographic Statistics in the Current and Remitted MDD Groups

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Supplementary Table 1

Demographic statistics in the current and remitted MDD groups.

	Current MDD (n = 107)	Remitted MDD (n = 22)
Age	M = 43.71 (SD = 15.09)	M = 37.32 (SD = 17.844)
Gender		
Female	n = 60 (56%)	n = 17 (77%)
Male	n = 47 (44%)	n = 5 (23%)
Years of Education	M = 14.25 (SD = 2.44)	M = 14.15 (SD = 2.85)