



Assessing and measuring cognitive function in major depressive disorder

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ABSTRACT

Cognitive dysfunction is a major component of major depressive disorder (MDD). No 'gold-standard' tool exists for the assessment of cognitive dysfunction for adults with MDD. The use of measurement-based care to improve treatment outcomes invites the need for a systematic screening, evaluation and measurement tool. The aim herein was to provide a succinct summary of literature documenting clinical implication of cognitive dysfunction in MDD, and a review of available screening, diagnostic and measurement tools for cognitive dysfunction in MDD is provided. We also take the opportunity to introduce a screening tool (ie, the THINC-it tool) targeted at addressing the unmet needs. We found that there are limitations to the current measurement scales; for example, many are not targeted for MDD and not all digitally available tests are free of charge. Furthermore, the spectrum of cognitive dysfunction in MDD is poorly represented by the existing tests and as such, there is a lack of sensitivity in the ability to screen a patient with MDD for a cognitive dysfunction. Recognising and addressing the limitations in the current screening techniques for cognitive dysfunction as well as being presented with the current tools available provides the ability to perform an educated cognitive screening for a patient with MDD.

INTRODUCTION

Major depressive disorder (MDD) is a highly prevalent disorder with high rates of recurrence and treatment resistance, which is associated with significant morbidity and has been identified as the leading cause of disability among adults globally.^{1,2} The human capital costs associated with MDD are principally mediated by workplace disability (ie, inability to return to or perform adequately at work) caused by deficits across multiple domains of cognitive functions (eg, attention, executive function, psychomotor speed and memory).³⁻⁷ Moreover, cognitive dysfunction often persists after affective symptoms have resolved, leading to prolonged disability after remission has been achieved.⁸ Cognitive dysfunction has also been identified as a key factor in other areas of psychiatry as it transdiagnostically affects participants with MDD, bipolar disorders and psychotic disorders. As such, cognition has been identified by the National Institute of Mental Health (NIMH) as a research priority as evidenced by the biobehavioural matrix: the Research Domain Criteria (RDoC). Domains and subdomains of RDoC define and operationalise overlapping and discrete aspects of cognition, including positive/negative emotionally valenced cognitive function, social cognition and general cognition.

Measurement-based care (MBC) improves treatment outcomes in chronic medical disorders and provides opportunities to increase precision, consistency and appropriateness of care.⁹ As such, given the impact of MBC, the appropriateness and suitability of the tools used is important. The prevalence of cognitive dysfunction in MDD and the effects on human capital costs invite the need for systematic screening, evaluation and measurement tools.¹⁰ Hitherto no single 'gold-standard' tool for the assessment or measurement of cognitive function exists. The main aim of this article was to provide a succinct summary of available literature documenting the extent of and clinical implication of cognitive dysfunction in MDD as well as a rationale for MBC. We also review available screening, diagnostic and measurement tools for cognitive dysfunction in MDD, and introduce an accessible screening tool for cognitive dysfunction among adults with MDD (ie, the THINC-it tool).

METHODS

Online databases, PubMed and Google Scholar, were searched from inception through February 2016 for published clinical trials, reviews

and meta-analyses exploring the reliability of and/or limitations regarding cognitive screening tools in MDD. The following keywords were used for the search: *major depressive disorder, cognition, cognitive deficit, cognitive dysfunction, screening tools, measurement tools and test battery*. References from relevant reviews and the reference lists from included articles were screened manually. Articles selected for inclusion in this review were those which discussed the overarching topic herein.

Cognitive dysfunction in major depressive disorder

Cognitive dysfunction as a core domain of MDD affects multiple domains and is noted to be progressive.¹¹ Cognitive dysfunction is defined as deficits in one or more facets of interrelated functions (eg, short-term memory, long-term memory, perception and problem solving). Cognition can be categorised into two functionally related categories, namely 'hot' and 'cold' cognition. Deficits in cold cognition include general cognitive deficits in one or more non-emotionally valenced domain. Deficits in hot cognition causes processing bias—focusing attention on negative stimuli and/or askew information processing.¹² The clinical implication of MDD is underscored by replicated evidence indicating that cognitive dysfunctions in MDD are the principal mediator of workplace disability and psychosocial dysfunction.¹³⁻¹⁵ The changing workplace ecosystem towards the 'human capital economy' where opportunities are predominantly available for those individuals with the highest education and skillsets underscores the relevance of cognitive dysfunction in young adults (age 18–65 years) with mood disorders.⁹

The process of evaluating cognition in MDD can be disaggregated into screening, measurement and diagnostic, each with its own independent objective.¹⁶ Screening tests aim to identify 'caseness' (ie, cognitive dysfunction) in individuals with an existing deficit and to identify non-deficit in those without cognitive impairment (ie, true positives and negatives). Screening tests are used to determine the presence of cognitive impairment by comparing the patient's score on a standardised test to predetermined norms. Measurement tools aim to quantify the extent of an identified deficit. Measurement tools may be employed cross-sectionally and/or as a repeat measure to evaluate deficit change

over time with or without treatment. Measurement tools are used to track progress or decline of the cognitive impairment by again comparing patient's scores to the predetermined norms. A diagnostic tool provides information relevant to the underlying disease/disorder/syndrome. For example, a mild cognitive impairment is a specific diagnosis which has been defined as a cognitive impairment more profound than expected by a patient's age, however, not a large enough impairment to notably interfere with daily lifestyle.¹⁷ Furthermore, screening tests in specific are important from a clinical and a research standpoint. For clinical purposes, a screening test can quickly determine the presence of cognitive dysfunction and alert the physician to administer more tests to diagnose cognitive impairment. Similarly in a research setting, a screening test can be used for multiple purposes ultimately identifying the presence or absence of a specific trait in a population and whether it is useful in a specific clinical setting.

Limitations of existing depression scales: measuring cognition

As there is a lack of standardised tool for screening, measuring and diagnosing cognitive dysfunction in MDD, there are many limitations, which have arisen in regards to homogeneity and reliability between tests. In addition, tools currently available for screening present many complications such as not being designed for use in MDD, exclusively available using pen and paper, and being costly.¹⁸ Given the heterogeneity of the psychiatric population, there is a difficulty in discerning the subgroups which experience cognitive dysfunction.^{19 20}

Existing cognitive screening tools for cognitive function

The series of tests that are often used as best practice for measuring cognitive function in MDD were not developed for use in the MDD population. Instead, these tests were designed for use in other illnesses, such as dementia and schizophrenia.^{16 21 22} While there are a variety of tests specified for use with other disorders, they are not interchangeable between illnesses—such that a cognitive test for those with schizophrenia will not prove to be as sensitive or specific for the specific domains of cognitive dysfunction more commonly affected in those with MDD.²¹ Widely used screening tools in dementia, the Mini Mental State Examination and the Montreal Cognitive Assessment (MoCA), are insufficient in MDD due to ceiling effect—a limitation in score at the top of a scale.¹⁹ With the scoring limits on these tests proving not be sensitive enough for detecting the spectrum of cognitive impairment seen in MDD, this results in false negatives in screening procedures.^{18 20}

Depressive symptom screening

Screening tools for symptomatology in MDD contain items that assess subjective reporting of cognitive impairment (ie, Montgomery-Åsberg Depression Rating Scale (MADRS) question 6 and Patient Health Questionnaire 9 (PHQ-9) question 7).^{23 24} However, common screening tools (ie, Center for Epidemiological Studies—Depression Scale (CES-D), Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire 2 and 9 (PHQ-2 and PHQ-9) and Zung Depression Scale) for depression are limited with respect to their ability to provide sufficient information as it relates to cognition as there are relatively few items assessing cognition on each of the scales (table 1).^{23–25} The items on the existing scales do not capture the complexity and circumstances (eg, ecological validity, subjective measure) which are known to be dissociated from the projective measures of cognitive function.²⁶ Moreover, there is no existing instrument that has been validated in adults with MDD that is scalable, digitalised, brief, easy to administer and available at no cost.

Understanding the importance of capturing varying domains/dimensions of cognitive function has a major role in improving MBC as functional outcomes can vary, dependent on impairment and/or improvement of

Table 1 The total number of items on widely used screening tools for depression and their respective amount of items relating to cognitive symptomatology

Scale	Total number of items	Items for emotional symptoms	Items for cognitive symptoms
MADRS	10	7	2
HAM-D	21	8	2
HAM-D	7	5	0
PHQ-9	9	5	1

HAM-D, Hamilton Depression Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; PHQ-9, Patient Health Questionnaire 9.

varying domains/dimensions.⁹ An attribute of a screening/measurement tool for cognition in MDD is its ability to detect deficits across one or more of the domains known to be affected in MDD. Notably, the sum score of many existing cognitive screening tools is not valuable due to the complexity of cognitive domains. The forgoing cognitive domains (ie, executive function, attention, memory, processing speed and psychomotor skills) are affected at varying levels during all phases in MDD (ie, symptomatic phases and remitted phases).^{27–31}

Current limitations and future directions

The current tools available for screening cognition in patients with MDD do not align with the reality of today's clinical ecosystem. These available tools present many limitations in regards to busy office practice, not only in MDD, but existing screening tools in general have been identified as problematic in different valences of psychiatry.³² Common issues include lengthy process for administration time and scoring time (which are usually carried out by hand with pen and paper), high associated costs, lack of access and/or availability to many healthcare providers, lack of sensitivity and lack of reliability.^{18 32}

Emerging tools must be brief, easy to use, digitalised, adaptable to clinical practice, patient self-administered, interpretable, free of charge, standardised and validated. Furthermore, these tools should present actionable information for patients and providers and should capture subjective and objective information with the goal to enhance the quality of life of the patient and the efficiency of office practice.

Cognitive screening

Computerised testing

The nature of cognitive tests is expanding as technology advances, ultimately attempting to solve the aforementioned issues (availability, cost, etc); CogState, Cambridge Neurological Test Automated Battery (CAN-Tab), NeuroCognitive Performance Test (NCPT by Lumosity) and CNS Vital Signs (CVS) all offer available online cognitive tests.^{33–35} While their tests for cognitive deficits are standardised, they are first not specified for MDD. The online tests offer a wide variety of test and can be targeted by domain of cognitive deficits; however, many must be independently combined to form an overall screening battery and the preset batteries available are modifiable, thus not making the battery standardised across studies. These tests are subject to a lengthy administration process and are not free of charge (table 2). In sum, while offering beneficial advancements such as solving the problem of access and availability, these would not prove to be best practice in screening for MDD.

THINC-it

A recent clinical trial by our group (NCT02508493) explores the opportunity for an application, to be available to download on computers and tablets. The THINC-it tool includes subjective and objective measures of cognitive function and may be self-administered by the patient in the waiting room.

Table 2 Summary of available online tests and their administration time, domains tested, if there is an available battery targeted for MDD, whether batteries are customisable and cost

Programme	Administration time (min) (healthy participant)	Domains tested	Preset MDD batteries available	Customisable batteries	Cost (US\$)
CogState	~57*	Attention, emotional recognition, executive function, memory, paired associate learning, psychomotor function, executive function, verbal learning, visual learning working memory	Yes	Yes	Variable/negotiable
CAN-Tab	~34*	Attention, visual recognition memory, spatial working memory, working memory, emotional recognition	Yes	Yes	\$4500 per 12 months. Depression battery only
NCPT	~60	Working memory, visuospatial memory, psychomotor speed, fluid and logical reasoning, response inhibition, numerical calculation, selective/divided attention	No	Yes	Variety of options. \$14.95/month with reduced rates for yearly subscription. \$299.95 for lifetime
CNS Vital Signs	~30	Verbal memory, visual memory, psychomotor speed, information processing speed, sustained attention	No	Yes	\$35 per session. Discount available in bulk
THINC-it tool	~10–15	Executive function, processing speed, attention, subjective measures, memory	Yes	No	Free

*Administration time based on stated sum time of all included tests in MDD battery.

CAN-Tab, Cambridge Neurological Test Automated Battery; CVS, CNS Vital Signs; MDD, major depressive disorder; NCPT, NeuroCognitive Performance Test.

Measuring cognition in busy clinical practice: bridging the gap

The THINC-it tool is an ongoing research study with the overarching aim to differentiate a clinical population from a healthy control population and establish psychometric testing standards. The THINC-it tool is anticipated to be a free downloadable tool, which can be used on tablets and computers. Furthermore, the THINC-it tool is composed of digital paradigms drawn from the Digit Symbol Substitution Test (DSST), Choice Reaction Time task (CRT), Trail Making Test-B (TMT-B), 1-back memory task (1-BACK) and Perceived Deficits Questionnaire 5 (PDQ-5-D). The battery of objective tests which comprise the THINC-it tool (DSST, 1-BACK, CRT and TMT-B) has been individually validated elsewhere and they have been shown to be sensitive to cognitive deficits in MDD.^{36 37} The DSST is capable of identifying deficit in the domains of executive function, processing speed and attention/concentration. The TMT-B evaluates executive function. The 1-BACK evaluates memory, executive function and attention/concentration. The CRT primarily indexes attentional skills and also contains executive functional elements. Furthermore, the PDQ-5-D is a subjective measure, which broadly evaluates attention/concentration, planning/organisation, as well as retrospective and prospective memory. The combination of the aforementioned tests allows for the THINC-it to have superior conceptual coverage of the cognitive domains affected in MDD. The THINC-it tool is to be self-administered and present subjective and objective data immediately. THINC-it fulfils the need to have a tool targeted towards high-volume clinical practice by reducing administration time to ~20 min in a clinical setting. This is in comparison to a varying time of ~1–3 hours commonly seen in other test batteries. Moreover, the THINC-it tool reduces interpretation time as there is no requirement for the tool to be administered and/or scored by a psychologist/psychologist as patient performance results are immediately available.

While the core principals of the THINC-it tool are resonant of a 'gold-standard' for detecting cognitive dysfunction in MDD, questions arise associated with computer and tablet use in older cohorts and those who are not familiar with computers, as older age has been associated with no computer experience.³⁸ Previous research exploring the use of an online cognition tool—CogState—demonstrates that there are no persistent deficits in administration of the tests correlated with no computer knowledge.³⁸ Furthermore, given the prevalence and advancements in technology, this issue will likely be non-existent in the following decades.

CONCLUSION

Cognitive dysfunction is highly prevalent and persistent in MDD. Effective detection and monitoring of cognitive dysfunction in MDD is of

great importance to improve cognitive outcomes and thus decrease illness-associated disability. The current tools offered for screening cognitive dysfunction in MDD are subpar and as they are unadaptable to the current standard of high-volume clinical practice. The most commonly used tools (ie, MoCA and MINI) for evaluating cognitive dysfunction in other mental health disorders (ie, dementia and schizophrenia) prove to be insufficient to detect mild cognitive dysfunction in MDD due to the ceiling effect. Digitalised cognitive screening tools (ie, CogState, CAN-Tab) have improved on limitations from the original pen-and-paper tools; while addressing the need for digitalised media, the available tools do not address other limitations—cost, administration time, MDD specific, etc. The THINC-it tool can become a validated brief, easy to use and digitalised tool, which is adaptable to clinical practice, patient administered, interpretable and free of charge.

The improvement of MBC through the assurance of appropriate tools for screening cognitive function in MDD would allow for a more efficient way to track patient cognitive enhancement or decline. The development of a 'gold-standard' tool should address the limitations in the current tools used and reflect the large spectrum of cognitive dysfunction present in MDD and, as a result, provide clinicians and researchers alike a validated day-to-day tool. Ultimately, the current tools used are not able to reflect the cognitive spectrum in MDD and require improvement providing the rationale for the development of newer tools (ie, the THINC-it tool) to fill the gap in the market. The THINC-it tool (NCT02508493) appears to address all the non-negotiable requirements for new-age, busy office practice cognitive screening tool. The results of the THINC-it tool validation study, conducted by the Brain and Cognition Discovery Foundation, are expected to be available in late 2016.

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