How we can THINC-it Better: A new Digital Screening Tool in Depression Assessment

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Abstract

In the past decades, cognition as one of the key factors in depression has been highlighted. It has been found that cognitive impairment (CI) might both precede the onset of depression and persist during remission. This factor is influencing education, work performance and social life, even after euthymia is reached. Even with the growing number of research, there is no universal agreement in how to assess CI in depression. This makes it challenging to consider the CI symptom and make it a part of the treatment plan of depression. This studies aim is to investigate the sensitivity of a newly developed cognitive screening tool, THINC-it, in a non-patient group, for identifying CI related to symptoms of depression. The THINC-it was measured together with existing tools for cognition (BRIEF-A) and depression (MADRS), assessing both objective and subjective measures of cognition. Our results show that the global scores of THINC-it correlate significantly with the scores on both BRIEF-A and MADRS-S. The objective scores did not significantly correlate with the scores on BRIEF-A and MADRS-S. However, the subjective scores of THINC-it correlates with BRIEF-A and MADRS-S. When dividing in levels of depression, participants showing either low or moderate symptoms of depression, scored significantly higher on THINC-it compared to participants without depressive symptoms. THINC-it seems to be an adequate screening-tool clinicians' can implement as part of their screening and treatment of depression, used in all the stages of the illness in order to assess cognitive functioning.

Key words: *Cognitive impairment, depression, cognitive screening tool, THINC-it, BRIEF-A, MADRS-S*

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Sammendrag

De siste årene har kognisjon som en av nøkkelfaktorene i depresjon blitt fremhevet. Kognitiv svekkelse kan være tilstede både før depresjon, og henge igjen etter de depressive symptomene et lettet. Dette påvirker både utdanning, arbeid og sosialt liv. Selv med den voksende litteraturen, er det ingen universell måte å evaluere kognitiv svekkelse på hos pasienten. Dette gjør det vanskelig teste og å implementere i en behandlingsplan. Målet for denne studien er å undersøke sensitiviteten til ett nytt kognitivt screeningverktøy, THINC-it, i normalbefolkningen for å identifisere kognitiv svekkelse i relasjon med depresjonssymptomer. THINC-it ble måle med eksisterende verktøy for kognisjon (BRIEF-A) og depresjon (MADRS), som vurderer både objektive og subjektive mål av kognisjon. Resultatene viser at de globale scorene av THINC-it korrelerer signifikant med resultatene på både BRIEF-A og MADRS-S. De objektive scorene var ikke signifikant korrelert med scorene på BRIEF-A og MADRS-S. Imidlertid korrelerer de subjektive scorene i THINC-it med BRIEF-A og MADRS-S. Forskjellige depresjonsnivåer, lave eller moderate symptomer, viste en signifikant forskjell i THINC-its subjektive score sammenliknet med deltakerne uten depresjonssymptomer. THINC-it ser ut til å være et dekkende screening-verktøy klinikere kan implementere som en del av deres vurdering og behandling av depresjon, og brukes i alle stadier av lidelsen for å vurdere kognitiv fungering.

Nøkkelord: Kognitiv svekkelse, depresion, kognitivt screeningverktøy, THINC-it, BRIEF-A, MADRS-S.

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List of Abbreviations

BRIEF-A – Behavior Inventory of Executive Function – adult

CI – Cognitive impairment

DE – Depressive episode

EF – Executive functioning

DSM-5 – The Diagnostic and Statistical Manual of Mental Disorders, version 5

ICD-10 – The international classification of diseases and related health problems, 10th edition

MADRS-S – Montgomery Åsberg Depression Rating Scale – Self-report

MDD – Major depressive disorder

PDQ-5 – Perceived Deficits Questionnaire for Depression, 5 item version

THINC-it – THINC integrated tool

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How we can THINC-it Better: A New Digital Screening Tool in Depression Assessment

Worldwide over 300 million people are calculated to suffer from depression, ~4.4% of the world population, including all age ranges. Depression is the most common mental disorder, and between 2005-2015 number of people living with depression increased 18.4%. The disease is estimated, by 2020, to be the second leading cause of global burden of disease (World Health Organization, 2017). Over 50% of people experiencing their first episode of depression will experience a relapse within a two-year period (Burcusa, & Iacono, 2007, 2014; Hammar, 2018), and over 10% is estimated to develop chronic depression (Norsk Helseinformatikk, 2018).

Depressive symptoms become more severe as multiple episodes occur, and a lot of people have a hard time resuming normal life (school, social and work) even when euthymia is achieved (Clark, DiBenedetti, & Perez, 2016; Lee, Hermens, Porter & Redoblado-Hodge, 2012; Snyder, 2013). About 1/3 of all disability pension is due to mental illness, and depression is the second most frequent contributor. A 10 year follow up study in Norway found that people receiving disability pension has a higher lifetime prevalence of depression (Lassemo, Sandanger, Nygård, & Sørgaard, 2016).

In the past decades, a focus on cognitive impairment (CI) in depression has grown, and it is now considered an important aspect of the illness. Even in first-episode patients, signs of impairment can be recognized and CI could be a major triggering factor in depression. New research is also focusing on the remission phase of depression. After the symptoms of depression had receded, patients still had a hard time going back to work and resume their normal life (Carvalho et al., 2014; McClintock et al., 2011; Svendsen, Kvessig, Munkholm, Vinberg, & Miskowiak, 2012).

Due to a lack of standardized cognitive screening assessment, clinicians might not have a consistent treatment tool which incorporates cognitive deficit screening throughout the depression treatment (Greer, Kurian, & Trivedi, 2010). Despite the existence of multiple cognitive tests, many of them are time consuming and/or based on self-report questionnaires and thus do not measure objective cognitive decline. Another problem is that a lot of tests only measures one aspect of a cognitive domain (i.e. executive functions), meaning that different tests must be conducted in order to get a full picture (Bakkour et al., 2014). A shift in treatment and follow-ups, incorporating cognitive aspects, could be worth investigating to help patients get symptom free and back to functional recovery (Clark et al., 2016; Greer et al., 2010).

The purpose of this study is to test the sensitivity of a new digital cognitive screening tool which is short and easy to administer and can be incorporated into a treatment plan. THINC-integrated tool (THINC-it) can be used before, during and after treatment to monitor cognitive symptoms in people with depression. Improving both symptomatic *and* functional recovery are the core of every treatment. The tool can help with the efficiency of treatment and highlight residual symptoms that seem to linger during remission. The research question is: could the THINC-it be sensitive enough to pick up signs of cognitive impairment in a non-patient group if symptoms of depression, measured by MADRS-S, are present. The cognitive screening tool BRIEF-A is used in this study to validate the cognitive sensibility of THINC-it.

1.0 Depression

Depression is a heavy burden for anyone affected with the illness. Difficulty staying in school or at work, and maintaining a social life is a big part of the disease together with negative mood and feelings, which reduces a person's quality of life (Lépine & Briley, 2011). Between 10% and 20% of people experiencing recurrent depressive episodes (DE) will develop a chronic, therapy resistant, condition (Jaeger, Berns, Uzelac, & Davis-Conway, 2006; Lund, u.d.).

A treatment-gap exists where an estimate of around 50% of people with depression do not get the right treatment, or even seek treatment (Patel et al., 2010; Smith, Alves, & Knapstad, 2016). Torvik and colleagues (2018) found, during structured interviews, how even in people meeting diagnostic criteria for depression, only 36% and 15% were recorded in the Norwegian national health registries in the primary or specialist care respectively. This despite people identifying with having the disorder and reported their symptoms to their primary care provider.

CI is one of the new fields of interest in depression, as impairment is present in many patients throughout onset, during and in the remitted state of depression. An early diagnosis and mapping out all the symptoms associated with depression is important for treatment and relapse risk (Greer et al, 2010; Hammar et al., 2010; Lépine & Briley, 2011).

In sum, depression as a condition is still under investigation, and there are constantly new findings in the field. It is at present time an underdiagnosed illness in the population, due to a variety of reasons.

1.1 Diagnostic Criteria for Major Depressive Disorder

The international classification of diseases and related health problems, 10th edition (ICD-10) is the classification system used in Norway to diagnose depression. The criteria for depression in ICD-10 (WHO-CIDI 3.0) includes: (1) depressed mood, (2) loss of interest, (3) change in weight/appetite, (4) problems with sleep, (5) psychomotor agitation/retardation, (6) loss of energy/fatigability, (7) worthlessness, (8) difficulty concentrating, (9) suicidal tendencies, (10) loss of confidence, and (11) self-reproach. The ICD-10 requires >8 symptoms for a major depressive disorder (MDD), >5 for a moderate depressive disorder, and >3 for a minor depressive disorder (Saito et al., 2010).

1.2 Prevalence of MDD

An estimate by WHO is that 50% of people who suffer from depression in high-income countries do not get adequate treatment, or treatment at all. The numbers are estimated to be as high as up to 90% in low-income countries (Entis, 2017). Women are more prone to the disease (5.1%) than men (3.6%) (World Health Organization, 2017). Already at the level of mild depression, people will experience some difficulties with work and socialization. When the depression is severe, work, social life and domestic activities all become very limited (World Health Organization, 2017).

1.2.1 Cost of depression. A report by the Norwegian Institute of Public Health (Folkehelseinstituttet) from 2008 estimated the cost for depression treatment to 1.5 billion NOK each year (Dalgard, & Bøen, 2008). By 2016 the cost was estimated to 185 billion annually for mental illness in Norway, where depression and anxiety is over half of the

disease burden (Holte, 2017). Of people receiving disability benefits, 63% have a mental illness. Within mental illness, neurosis and behavioral disorders ranked highest (28.7%). More men receive disability benefits for mental illness (40%) compared to women (32%). From 2000-2015, the number of people receiving disability benefits has increased with 5.2% and young people, 18-35 years of age, seem to be the biggest recipients (Lindbol, & Ellingsen, 2018).

2.0 Cognition

2.1 Cognitive Domains

The Diagnostic and Statistical Manual of Mental Disorders, version 5 (DSM-5), operates with six key domains of neurocognitive domains: 1) social cognition (theory of mind), 2) executive functioning, 3) learning and memory, 4) attention, 5) language and 6) perceptual-motor function (Sachdev et al., 2014).

Cognitive dysfunction refers to one or more deficits in the domains mentioned above and may be a key mediator of functional impairment in MDD. *Executive functioning (EF)*, *memory*, *attention*, and *processing speed* are cognitive domains weakened in patients with MDD compared to healthy controls. Severity of depression, duration and comorbidity are factors negatively correlated with cognitive functioning (Douglas et al., 2018; Hammar & Årdal, 2009; Lam, Kennedy, McIntyre, & Khullar, 2014; Shilyansky et al., 2017).

2.1.1 Executive functioning. EF consist of a large umbrella of other cognitive domains and is considered the brains chief executive captain. The definition of EF has no real consensus (Hammar, & Årdal, 2009). In the DSM-5, under EF the following subdomains are

mentioned: planning, decision making, working memory, response to feedback, inhibition and flexibility (American Psychiatry Association, 2013). It is associated with functions in the prefrontal cortex, but also in context with other brain regions (Hughes, 2013; Mackie, & Fan, 2017; Takeuchi et al., 2012). Deficits in EF can interfere with self-inhibition, self-monitoring, and every-day functioning, including social, academic and work functioning (Diamond, 2013).

2.1.2 Memory. "Memory is the means by which we draw on our past experiences in order to use this information in the present" (Sternberg, Sternberg, & Mio, 2012, p. 534). Especially working memory is a domain seemingly impaired in depression. Working memory is describes as "a limited-capacity system that provides temporary access to a select set of representations in the service of current cognitive processes" (Joormann, & Gotlib, 2008, p. 182) Studies show people suffering from depression often have impaired memory (Shelton, & Kirwan, 2013), and ruminative thoughts and a focus on negative material in memory is a common trait in the illness. A study by Becker and colleagues (2009) hypothesize that stress preceding depression, affects the hippocampus in the brain, and memory deficits could by this indication therefore be present already early in first-episode depression.

2.1.3 Attention. "Attention is the active cognitive processing of a limited amount of information from the vast amount of information available through the senses, in memory, and through cognitive processes; focus on a small subset of available stimuli" (Sternberg et al., 2012, p. 530). The DSM-5 mentions the following subdomains: sustained attention, divided attention, selective attention and processing speed (American Psychiatry Association, 2013). Attention is a limited and selective resource. Attention is found to be diminished in

depressed patients in comparison to healthy controls (Williams et al., 2000) and the ability to concentrate is a main symptom of the illness (Saito et al., 2010). In depression, it is postulated that attention is driven towards negative thought processing and stimuli, towards life events and self-rated information (Lu et al., 2017; Peckham, McHugh, & Otto, 2010; Schlosser et al., 2011).

2.1.4 Psychomotor ability. "Psychomotor ability refers to a wide range of actions involving physical movement related to conscious cognitive processing. Psychomotor ability may be measured by accuracy or speed (reaction time)" (NauRA, 2017, para. 1). Retardation in psychomotor abilities is a common finding in clinical depression studies and is one of the main symptoms of depression today (American Psychiatry Association, 2013). Psychomotor functions impaired in depression include speech, gross motor activity, fine motor activity, drawing tasks, eye movement, and facial movements. Psychomotor speed is in many studies found to be a cognitive domain strongly affected (Mogn & Rund, 2016).

3.0 Cognitive Functioning in Depression

Two thirds of depressed patients are estimated to suffer from CI (Rock, Roiser, Riedal, & Blackwell, 2014). Over the past decades, a large body of research have been conducted on the topic. As mentioned above, cognitive domains mainly reported with deficits in depression include *EF, memory*, *attention* (Andersson, Lövdahl, & Malt, 2010; Bortolato, Carvalho, & McIntyre, 2014; Cambridge, Knight, Mills, & Baune, 2018; McIntyre et al., 2013; Mondal, Sharma, Das, Goswami, & Gandhi, 2007; Rock et al., 2014; Shilyansky et al., 2016) together with *processing speed* (Clark et al., 2016; Hammar, & Årdal, 2009; Lee et al, 2012; Svendsen

et al., 2012). Douglas and colleagues (2018) found 87.4% of inpatients with depression suffered from at least one impaired cognitive domain, 55.2% on impairment on at least two domains and 7.1% suffered impairment in all four cognitive domains. In outpatients with depression, 52.9% suffered impairment in one domain, 17.6% suffered in two domains and 2.9% suffered in four domains. In the inpatient group, the highest percentage of CI was found in verbal learning and memory, EF/attention, visual spatial learning and memory, and psychomotor speed respectively. In the outpatient group it was verbal learning and memory, visual spatial learning and memory, psychomotor speed, and EF/attention respectively.

Another study, measuring 7 different domains (processing speed, attention, working memory, verbal and visual learning, problem solving, and social cognition), found 1/5 of patients suffered from deficits in all domains, and more than half impaired in processing speed/problem solving (Mohn, & Rund, 2016). Despite of the large growing body of literature on the topic, there seem to be a lack of consensus regarding impairment. Sub-groups of depression show different CI, early vs late-onset depression, first episode vs multiple episodes, acute vs remitted phase. Different studies show conflicting results, and the reason might be due to a lack of standardized cognitive assessment tools, and/or population and sample size tested, among other things (Hammar, & Årdal, 2009; Hasselbalch et al., 2011; Rock et al., 2014).

Inability to suppress unwanted mental representation, uncontrollable feelings and a tendency to give up faster, are all due to CI (Diamond, 2013). In tasks involving effortful attention, mental flexibility and memory, studies show depressed patients in the acute phase score significantly lower than healthy individuals (Hammar, & Årdal, 2009; Hasselbalch et al., 2011). CI can cause deterioration in interpersonal relationships and a contribution at home can be minuscule. At work, errors in tasks and displaced workload onto colleagues can be a consequence (Ebert et al., 2017). One study shows that peoples subjective experience of CI

has a greater impact on workplace performance, than depressive symptom severity (McIntyre et al., 2015).

A review by Foland-Ross and Gotlib (2012) found that the cognitive characteristics of depression, such as the interpretation of ambiguous information as negative, deficits in cognitive processing and difficulties disengaging from negative information, are often accompanied by the diagnosis of depression.

In sum, CI can affect people in all stages of depression, and it also affects patients differently. While some people might experience low cognitive impairment in some domains, they can experience high impairment in other, and no patient are the same. The self-reported CI seem to have an immense impact on peoples' life.

3.1 Objective and Subjective Cognitive Functioning in Depression

It seems to be a discrepancy between objective measures (neuropsychological tests) and subjective measures (self-report) in depression, thus self-perceived CI and objective CI does not seem to correlate (Srisurapanont, Suttajit, Eurviriyanukul, & Varnado, 2017). Subjective reports of cognition appear to be linked to mood and does not correlate with objective performance on tests (Farrin, Hull, Unwin, Wykes, & David, 2003). Severity of depression symptoms lead patients to report higher subjective cognitive deficits, than what objective measures display. It would be easy to conclude that a lifting of depressive symptoms would ameliorate subjective cognitive reports, however – objective CI is still present relative to healthy controls (Svendsen et al., 2012). Lahr and colleagues (2007) found participants reporting complaints about the cognitive domains of memory and attention, in addition to symptoms of depression in their study. They further showed the discrepancy between neuropsychological objective cognitive scores and patients' subjective complaints.

Two objective tests, the Trail-Making-Test-B and Five Point Test, measuring EF did however differ, and patients performed lower than controls. Meaning that EF might be sensitive to CI in depression. One study did however find objective test scores to be related to depression severity, compared to subjective complaints (Mohn, & Rund, 2016).

People with depression show a tendency towards pessimism and self-depreciation. The discrepancy could be due to a lack of ecological validity where perceived cognition in every-day life is not equivalent to test batteries (Mohn, & Rund, 2016).

In sum, even if objective and subjective measures of cognition do not always seem to match, they are both equally important considering treatment and remission outcome. A standardized tool, taking into consideration both objective and subjective cognitive measurements, would be favorable in assessment of CI in patients.

3.2 Cognition in First Episode Depression

Most studies on cognition in depression has been focused on severe MDD with multiple episodes. Fewer studies have focused on first-episode patients, this despite the indication that cognitive dysfunction could be found even before full onset of the first DE (Lee et al., 2012).

A handful of longitudinal studies has focused on whether CI precedes the onset of depression. Airaksinen and colleagues (2007) found low episodic memory performance to be a premorbid marker of depression, where low scores were prominent already 3 years before an individual was diagnosed with depression. Another study by Vinberg and colleagues (2013), found attention and especially EF to be impaired and precede the onset of depression.

It is therefore difficult to say whether cognitive deficits are independent of MDD or a consequence of the disorder.

In first-episode patients, the most common cognitive deficits are within EF, memory and attention. The cognitive deficits in first-episode depression is less severe than in recurrent MDD, but it is important to start early intervention as cognitive deficits seem to degrade with multiple DE and increase the risk for recurrent episodes (Talarowska, Zajączkowska, & Gałecki, 2015). A review by Lee and colleagues (2012) on first-episode depression reported performances in different cognitive domains where patients performed significantly worse than healthy controls. Worse performance was reported in psychomotor speed tasks, attention, visual learning and memory, attentional switching, verbal fluency and cognitive flexibility with small to medium effect sizes. Attention and EF are traits which persist after remission of depressive symptoms and seem to be important trait markers for first-episode MDD. Schmidt and Hammar (2013) found impaired inhibition and semantic fluency to be present in first-episode depression.

Related to illness severity, thus state, is poorer EF, working memory, psychomotor speed, verbal and visual learning and memory performance (Lee et al., 2012; Talarowska et al., 2015). The severity of illness should therefore be considered when implementing a treatment plan for cognitive deficits in MDD.

3.3 Cognition in Early Onset Depression

A U.S. survey by the National Institute of Mental Health, young adults, age 18 to 25, displayed the highest prevalence of depression (10.5%). It was also reported that 12.8% of adolescents, age 12-17, are suffering from a major DE (Center for Behavioral Health

Statistics and Quality, 2017). Park and colleagues (2014) found that over 50% of first major DE patients were age 30 years and younger, with the highest prevalence of first-episode were age 18-20 years (~39%), with the youngest people registered being 9 to 11 years old (~3-4%) at onset of first DE.

When searching for CI in depression on google scholar (Google's scholarly literature search engine) several of the studies includes Alzheimer's and dementia patients, and an older population in general. Even though depression can be linked to an increased risk of both Alzheimer's disease and dementia (Talarowska et al., 2015), first-episode depression occurs in very young adolescents and adults, and CI is present at early stages. In younger adults with MDD, cognitive deficits have not been studied to the same extents as in grownups.

When studying undergraduates, Robinson and Alloy (2003) fount that they more often than not make negative inferences towards life events and tend to negatively reminisce. This group had a higher tendency towards developing depression, and experiencing depression of a longer duration.

The cognitive deficits most prominent in younger adults with MDD seems to be EF, attention, cognitive flexibility and working memory, needed in complex tasks. Visuospatial skills and ability for planning seems to be unimpaired in young adults with MDD (Baune, Czira, Smith, Mitchell, & Sinnamon, 2012). CI in early onset depression, might be crucial to how the disease develop through life. Early onset depression has been proven to lead to more frequent episodes of depression, and being more severe and long term, compared to later onset depression. (Baune, Fuhr, Air, & Hering, 2014; Russo, Mahon, & Burdick, 2015). One study found subjective cognitive complaints in younger patients with major depression were more severe than what extensive neuropsychological tests indicated. In the

neuropsychological tests, the patients did not differ markedly from the healthy controls. This could indicate a bias in the self-perception of depressed patients (Lahr et al., 2007).

It is estimated that around 50% of people experiencing depressive symptoms could develop a first-onset major depression (Horwath, Johnson, & Klerman, 1992), and CI has been found in first-episode depression (Hammar, & Årdal, 2009). Hence, it could be important for general practitioners to assess cognitive function in people experiencing symptoms of depression without qualifying for a diagnosis.

3.4 Cognitive Functioning in MDD Remission

Over 50% of people experiencing a first-episode depression will experience a relapse at one point in their life. With each episode the chance of a relapse increases, and just at the second episode there is reported a relapse risk of up to 80%. People will usually experience between 5 to 9 episodes in a lifetime (Burcusa, & Iacono, 2007; Lassemo et al., 2016; McClintock, Husain, Greer & Cullum, 2010). A two-year follow-up study showed that 26.8% of patients in the primary health care, and 33.5% of patients in the specialized health care experienced a relapse in depression, with recurrence highest within the first months of recovery (Hardeveld et al., 2013).

CI is often reported by patients themselves, both during and after a DE. A study showed that up to 50% of patients reported cognitive symptoms after remission (Fava et al., 2006). Conradi and colleagues (2011) did a 3-year follow up study of residual symptoms in depressed patients (n = 267) and found that cognitive problems were present 94% of the time during a major DE, and 44% during a non-major DE. Other studies have found up to 60% of patients still had significantly functional disabilities in multiple cognitive domains after 6

months remission from depression. Neurocognitive deficits persist in the absence of depression symptoms, suggesting they are independent of each other (Baune et al., 2010; Bortolato et al., 2014; Jaeger et al., 2006; McIntyre et al., 2015; Miller et al., 1998).

The impairment of psychosocial functioning in remission may be explained by a lingering in deficits in EF, memory, processing speed and attention (Lam et al., 2014). Multiple studies have shown CI during partial remitted, or fully remitted patients with depression (Chamberlain, & Sahakian, 2006; McClintock et al., 2011; Rock et al., 2014; Svendsen et al., 2012). In a study by McClintock and colleagues (2011), 69.6% of patients reported mild decreased concentration/decision making, and 67.3% reported mild psychomotor disturbance.

In recurrent brief depression, cognitive impairment is found in the domains of various aspects of EF, working memory, processing speed and verbal and visual memory. Between severity of depression and impairment, no significance was found, nor between earlier major DEs, duration between episodes or duration of episodes. Psychomotor retardation might help to explain several areas of impairment (Andersson et al, 2010)

Patients subjective view of one's own remission is reported to be positive in only one-quarter of patients, even when they have not reached the remitted phase. On the other hand, multiple patients report a lower-quality of life and more functional impairment, and do not consider themselves to be remitted, even when clinical remission is achieved (Zimmerman et al., 2012). One study focused on patients experience of warning signs before the onset of a DE (already had one or more episodes). The majority of people did not interpret the warning signs as an onset of a new DE, but instead attributed them to external factors. It often started with fatigue and developed to an alteration in cognition and disturbed sleep cycles among

others, including a disability to sustain attention and concentrate in working situations (Hagerty, Williams, & Liken, 1997).

Reviews regarding the remitted phase of depression show CI in the domains of attention, EF and memory (Bora et al., 2013; Hasselbalch et al., 2011), with severity of impairment in remission dependent on severity of depression (Paeleck-Habermann, Pohl, & Leplow, 2005). Other studies find that number of DE is associated with CI severity, or no findings in the remitted phase at all (Hammar, & Årdal, 2009). On the other side, some studies have found improvement in specific domains of cognitive functioning i.e. memory and attention (Huang, 2009)

4.0 Treatment and Assessments

Regardless of the research in the past decades showing the importance of CI in depression, physician's guidelines (Norways health directory and American Psychiatry Association) for diagnosing and treating depression do not include the assessment of CI. Nor do they include course of treatment, or follow up of CI in patients (American Psychiatry Association, 2010; Helsedirektoratet, 2009). Individual assessment of CI could seem to be up to the therapist's discretion.

4.1 Therapeutic Interventions

Cognitive behavioral therapy (CBT) is a widely studied, and clinically used, treatment for depression. However, this therapy mainly focuses on mood symptoms (Cuijpers et al., 2013). Additional methods might be necessary for treating the objective symptoms of CI.

Literature referring to cognitive improvement in depression therapy has been scares, but a couple of methods are being focused on to directly target CI in depression in a therapeutic setting.

Cognitive remediation is a technique designed to enhance attention, memory, and different EFs, focusing on restoring these mental processes using cognitive exercises. The technique is mainly used in patients with brain injuries, dementia and Alzheimer's disease. However, Priyamvada and colleagues (2015) found, over a 3 month follow up, that memory and attention were improved with the use of cognitive remediation in depressed patients. This approach in depression is at present not much studied, however, the findings are promising – yet inconclusive (Baune, & Renger, 2014). Cognitive domains most often improved in these trials are attention, information processing, psychomotor speed and/or verbal memory (Porter, Bowie, Jordan, & Malhi, 2013).

Mindfulness-based cognitive therapy is another approach, designed for relapse prevention in depression. If focuses on alleviating rumination and negative cognitive patterns. It is not yet clear what the effects are on specific cognitive domains with this treatment, but it has proven effective in relapse of depression (Chiesa, Mandelli, & Serretti, 2012), and could help shift attention towards more positive stimuli (Verhoeven, Vrijsen, van Oostrom, Speckens, & Rinck 2014).

Regarding antidepressants, it is evident that their main focus is not on targeting cognitive symptoms, but on mood symptoms in depression (Bortolato et al., 2014). Different antidepressants might alleviate certain symptoms. However, reviews show conflicting results throughout different studies regarding the use of antidepressants as a target for CI (Bennabi, Vandel, Papaxanthis, Pozzo, & Haffen, 2013; Salagre et al., 2017).

4.3 Cognitive Assessment Tools

Belgaied and colleagues (2014) distributed a survey to psychiatrist in the US, France, Germany, Spain, Australia and Hong Kong to assess their methods of cognitive assessment in their clinical practice. For MDD, 62% of psychiatrist relied on patient history interviews alone, and "believed cognitive assessment was irrelevant to the disease" (p. 137). For the psychiatrist using cognitive tests, most were not relying on normative data, and based on the MATRICS criteria, only 3% used appropriate instruments. Another study by McAllister-Williams and colleagues (2017) focusing on clinicians in the UK, uncovered that clinicians might not be fully aware of the CI present in depression. They also found a lack of recognition in the persistence of CI in remission. There was a consensus regarding uncertainty of which cognitive assessment to use, and the lack of appropriate and easily accessible objective tools available in the clinic.

A lack of consensus towards which tools to use to assess objective cognition in MDD treatment is prominent, despite cognition and cognitive deficits being increasingly recognized within MDD (Bortolato et al., 2014; Ragguette et al., 2016; Svendsen et al., 2012). Bakkour and colleagues' (2014) review of assessment tools found 9 instruments used in MDD trials, with California Verbal Learning Test (CVLT), Train Making Test A (TMT-A) and Cambridge Neuropsychological Test Automated Battery (CAN-Tab) being the most frequent. In their study, multiple tests for assessing CI were included, however most were developed to test cognitive decline in schizophrenia. Cognitive tests are developed to target certain illnesses and is not meant to be used across illnesses. Different patient groups have different baselines of cognition and limitation at the top of the scale in assessments, which would provide biased measures in different illnesses than what an instrument is created for (Bakkour et al., 2014; Ragguett et al., 2016).

Different cognitive assessment tools that exist, like NeuroCognitive Performance Test (NCPT by Lumosity), CAN-Tab, and CNS Vital Signs (CVS) are available online, but their primary use is not with MDD patients (Ragguett et al., 2016).

The MATRICS Consensus Cognitive Battery (MCCB) is a battery developed mainly for schizophrenia, but other related disorder such as MDD and bipolar disorder can also benefit from it. It includes seven tests of cognition. It ranges in its use from an outcome measure in cognitive trials, measure of cognitive change in testing applications and a reference point for non-intervention studies (Nuechterlein, & Green, n.d.). The battery seems effective in measuring CI in depression (Mohn, & Rund, 2016). There is however need of a 60-90 minute session with a clinician to perform the test and it is primarily for patients age 20 to 59 years old (Nuechterlein, & Green, n.d.).

Patients with MDD might attribute their cognitive symptoms to innate selves, workplace stress, relational problems or related to other illnesses. They do not attribute their forgetting the keys in the car, not wanting to cook dinner for their families, not wanting to socialize or problems prioritizing daily tasks to symptoms of MDD. Because of this biased attribution, subjective self-assessment tools could leave out critical information needed to help the patient (Ebert et al., 2017).

There are numerous challenges in the assessment of cognition for the clinical practice. From patients unwilling to report their cognitive functioning, to an assumption that cognitive problems mainly occur in elderly in early symptoms of dementia. There is also the question as to how, and by whom, cognitive functioning should be assessed (Baune et al., 2018). The research on cognitive functioning in depression has been instrumental in finding the appropriate assessments for CI in depression (Harrison et al., 2018), and highlights the need for a brief, sensitive and valid assessment tool.

4.3.1 THINC-it. McIntyre and colleagues (2017), the THINC Task Force, developed the THINC-integrated tool (THINC-it), in order to create a cognitive measure to meet the conditions of a brief, sensitive and valid assessment tool. THINC-it is a digital screening tool, which assess both objective and subjective cognitive measures. The goal of the task force was to increase focus on cognitive decline in depressed patients and make it easier and more time efficient to measure cognition. THINC-it use documented objective cognitive assessments (choice reaction time/spotter, one-back test/symbol check, digital symbol substitution test/code breaker and trail making test/trails) together with the subjective self-reported Perceived Deficits Questionnaire for Depression (PDQ-5). As extensive studies show, the cognitive domains of EF, working memory, attention and processing speed being frequently impaired in depressed patients through different stages of the illness (Andersson et al., 2010; Bortolato et al., 2014; Cambridge et al., 2018; Clark et al., 2016; Hammar, & Årdal, 2009; McIntyre et al., 2013; Mondal et al., 2007; Rock et al., 2014; Shilyansky et al., 2016; Svendsen et al., 2012), and these domains are of focus in the THINC-it (McIntyre et al., 2017). The THINC-it was evaluated in 2016 and the sensitivity of the tool in its entirety was found to match more extensive and time-consuming cognitive tests. A validation of the tool in a non-patient group was also found (Harrison et al., 2018). Especially the PDQ-5 and Codebreaker showed strong concurrent validity with its pen and paper counterparts. The composite scores of the tool show an expectable level of concurrent validity as a measure of detecting cognitive decline amongst patients with MDD (McIntyre et al., 2017). The scores on PDQ-5, as a single standing test, has also shown to be associated with the odds of relapse in depression (Saragoussi et al., 2017).

The results of the THINC-it is easy to interpret. The results are color coded, presented on a chart. Green indicates cognitive performance within .5 standard deviation (SD), amber indicates performance within .5-1 SD below healthy controls, and red indicates cognitive performance of >1 SD below healthy controls. See figure 1 for illustration.

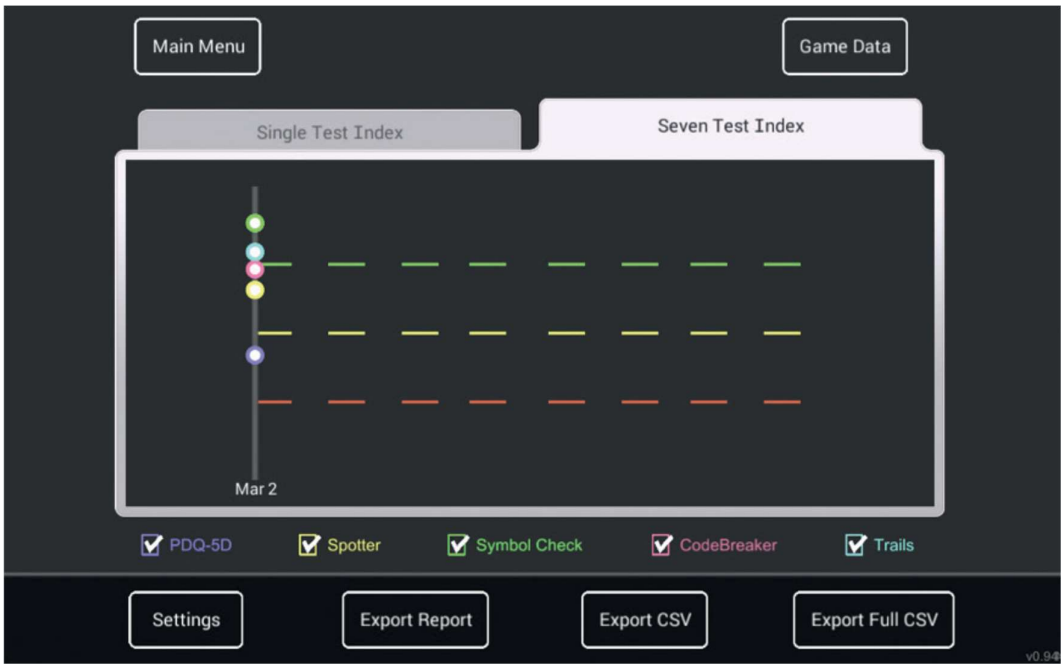

Figure 1. Example of results from the THINC-it physicians guide (THINC-it, 2017).

Early intervention and identification of risk factors is important in any disease. In early onset and first episode depression, identifying cognitive deficits could contribute to reducing the chance of relapse, and reducing further cognitive decline. It is therefore important to implement neuropsychological assessment in clinical practice to evaluate the quality and quantity of cognitive deficits for a tailored treatment of the specific challenges the patient might face.

The THINC-it is still a novel tool, which show promise in identifying important functional problems in depression.

4.4 Aim of the Study

Depression is an illness which affects many people's life, and CI has proven to be a factor for many patients suffering from the illness. CI is not only affecting people during an episode of depression, but also in the remitted state of the illness. As a result of the research presented above, we argue that a standardized cognitive screening tool which can be used in assessment of cognitive deficits in depression is needed. The tool tested in this present study, THINC-it, might provide health care professionals with an easy, more effective way to include treatment specific options for patients. This will be of clinical relevance as a possible improvement or alleviation of a physician's screening process in depression diagnosing and which interventions necessary to choose in treatment. The aim of this study is to investigate a newly developed cognitive screening tool in a non-patient group, to explore the sensitivity of the tool in relation to objective and subjective measures of CI compared to symptoms of depression. We predict that:

Hypothesis 1: THINC-it composite scores will correlate with the scores of BRIEF-A.

Hypothesis 2: THINC-it measures will correlate with the scores on the MADRS-S. Cognitive deficits will correlate with higher symptoms of depression.

Hypothesis 3: BRIEF-A and MADRS-S will correlate, showing higher self-reported measures in CI is associated with higher levels of depressive symptoms.

Hypothesis 4: There will be a significant difference in performance in digital and self-reported measures of cognitive functioning related to group affiliation regarding level of depressive symptoms.

5.0 Methods

The purpose of this study was to evaluate the sensitivity of a new self-administered digital screening tool, testing for cognitive dysfunction. A cross-sectional design was utilized with a between-participant approach, as the measurements were taken at a single point in time to examine the relationship between different clinical tools. This design used with a quantitative research method, gives access to a larger body of participants.

The cognitive screening tool (Thinc integrated tool [THINC-IT]), was measure towards an existing cognitive measurement test (Behaviour rating inventory of executive function, adult version [BRIEF-A]) and a depression rating scale (Montgomery and Aasberg depression rating scale self-rating [MADRS-S]) to see if there were any relationships between the scales. This study aimed to find correlation between variables, not causality. Since it is a novel tool being tested, the sensitivity and accuracy of the tool is that of interest.

5.1 Participants

The participants in the study were students at the University of Bergen. Convenience sampling was used for the reason of time sensitivity. Students are also a population seen to display various degrees of depression symptoms. A review found a prevalence of depression in university students to range from 10% to 85% (Ibrahim, Kelly, Adams, & Glazebrook, 2013). The requirements to participate in the study was: being a student, speak both English and Norwegian as the surveys included different parts in different languages, be able to give consent to participate, and not currently be diagnosed with depression.

The participants were recruited via social media, and through The Citizen Lab's (Medborgerlabens) mailing list. The Citizen Lab is a research lab connected the University of

Bergen, where many fields of study can conduct their experiments, and it has a wide range of participants in its register. This study was carried out at the Citizen Lab's locations. A total of 74 participants were recruited, 32.4% males (n = 24) and 67.6% females (n = 50), age 19-40 years old (M = 23.5, SD = 4.2). Two participants were excluded for parts of the survey, as they did not finish the BRIEF-A questionnaire. However, their scores on MADRS-S and THINC-IT were valid to use.

5.2 Data Collection

The survey was administered both on paper and via computer. The THINC-IT was conducted on a computer with English instructions, and the MADRS-S and BRIEF-A plus demographics were administered on paper, in Norwegian. The whole test put together took approximately 30 minutes to finish. The survey, consisting of 4 parts, was presented in the same order to all participants.

5.2.1 Measures. The survey was presented in the following order.

For demographic variables the students were asked to report gender, age, field of study and their degree. They were also asked to report whether they had been diagnosed with depression earlier, and if so, what treatment they received, and if they have any immediate family with the diagnosis.

Next was the THINC-it digital program. THINC-it is an online screening tool integrating different aspects of cognitive functioning via four specific neuropsychological tests and one self-report questionnaire (McIntyre et al., 2017). The program is opened, and the patient fill out age, education, location, handedness and gender before they continue to the

test. The four tests, and one questionnaire can then be opened separately, or taken together as one continuous test. The "THINC-it physicians guide" (2017) describes it various tests as follows:

Number one: Self-report questionnaire. This is a five-question subjective measure, PDQ-5, evaluating attention\concentration and planning\organization. The questions are: "During the last 7 days, how often did you" 1) Have trouble getting things organized? 2) Have trouble concentrating on what you were reading? 3) Forget the date unless you looked it up? 4) Forget what you talked about after a telephone conversation? And 5) Feel like your mind went totally blank? Answers were: "never in the past 7 days", "rarely (once or twice)", "sometimes (3-5 times)", "often (about once a day)" and "very often (more than once a day)". The total score is dependent variable.

Number two: Spotter. A choice-reaction time task assessing attention, psychomotor speed and EF. Arrows facing either to the left or right appears on the screen, and the participant selects the right arrow as fast as possible. Response-time and accuracy are dependent variables.

Number three: Symbol check. Inspired by the N-back test, it assesses working memory, EF and attention. Symbols are moving in a laterally sequence, and one symbol disappears. You should then remember which symbol is gone. Response-time and accuracy are dependent variables.

Number four: Code breaker. Inspired by the digit symbol substitution test, assesses EF, attention and processing speed. Symbol and numbers should be correctly matched in this task. Response-time and accuracy are dependent variables.

Number five: Trails. Inspired by the trail making test part B. This test assesses EF. Here you should connect numbers and letters in an ascending order (A-1-B-2-C-3 etc.). Response-time and accuracy are dependent variables.

THINC-it aims to cover the dimensions of EF, learning and memory, attention and processing speed. It is a self-administered test who takes approximately 10-15 minutes to administer through an app one can download to one's own device (computer or tablet) for free (THINC-it, 2017).

According to McIntyre and Page (personal communication, April 25, 2018), the midpoint for all tests is 2000 out of 4000. "Poor" and "good" performance thresholds are set 1000 (red) and 3000 (green) index scores respectively as a rough guide. The midpoints (average performance) are set according to the normal data supplied from the study control groups. A score of 1000 or below falls significantly outside (below) the expected range for a normal individual's performance. In terms relative to "average" performance, a score of 3000 in one test should be broadly comparable to 3000 in another test. As one gets towards the extremes (0 or 4000) the comparability between scores across tests drops somewhat inevitably simply due to the nature of the tests themselves.

The next part of the survey was completed on paper. BRIEF-A is a subjective self-rapport form for adults used to measure EF in mental illness and development. The form consists of 9 scales describing different aspects of EF. It takes approximately 10-15 minutes to administer and consists of 75 items, scored on a Likert-scale (Roth, Isquith, & Gioia, 2014).

MADRS-S is a self-administered questionnaire, measuring the severity of depression symptoms. It was developed in 1979 and has since been considered a well-established tool to measure the most common symptoms in depression. It has a satisfactory construct validity,

but compared to the physicians MADRS, it is seen as complimentary rather than redundant. The MADRS-S also show a satisfactory reliability. The questionnaire consists of 9 items. It assesses the mood, sleep, ability to concentrate, emotional involvement, feelings of unease, appetite, pessimism, initiative, zest for life and emotional involvement in patients. The answers, ranging from 0-3, is summarized and higher scores (ranging from 0-27) indicates increased severity. 0-12 points: no or very light depression. 13-19 points: Mild depression. 20-34 points: moderate depression. >35 points: Severe depression (Fantino & Moore, 2009).

5.3 Research ethics

The participants were informed of the anonymity of the survey, voluntary participation and confidentiality. Because of the sensitive subject in the survey, a way to contact the participants was necessary in case they would show signs of depression. This would give us the opportunity to reach out and give the necessary information about what their options were. They were also given the opportunity to contact us if they had any questions or needed further information about health services they could contact, or about any questions regarding the study. A few (< 4%) participants scored over the cutoff point (5 points) on the depression rating scale, sub-question of suicidality. The PI (special psychologist) of this study directly contacted these participants in order to ensure their safety.

5.3.1. Ethical approval. The study was approved by Regional Committees for Medical and Health Research Ethics (REK), no. of approval: 2017/1755 (See appendix part A).

5.4 Data management

The data from computers were saved to a secure desktop through the universities own "safe desktop" program, immediately after the participant was finished. The paper was stored in a locked safe in the counselor's office. The identifiable information about the participants and the survey was kept separately, only linked by an identification number on the papers. All the information will be deleted by the end of the study.

6.0 Results

6.1 Statistical analysis

The statistical analyzes were performed and analyzed using the computer program Statistical Package for the Social Sciences (SPSS), version 25. The data was screened for missing data and outliers. An <0.05 alpha level was used for all statistical tests. The statistical analyses undertaken for this study were: 1. Correlation to examine the relationship between the different tests, and within the THINC-it measuring tool. 2. ANOVA to check the relationship between groups of high depression symptom scores vs low depression symptom scores with objective and subjective measures of cognition. Some additional analyses were also run.

6.2 Correlations

When testing the sensitivity of a new assessment tool, it is positive to have existing validated tests for comparison. Our first, second and third hypothesis was that there would be a correlation between the different measuring tools (THINC-it, BRIEF-A and MADRS-S) on cognition and depression. We expected, therefore, that composite scores of THINC-it would correlate with self-perceived cognitive measures, and with symptoms of depression. We also

expected that the already existing tests, BRIEF-A and MARDS-S would positively correlate. Using a co-relations test, correlation, is a good way of testing the association between scores on different cognitive tests (Coolican, 2014). Using Pearson product-moment correlation coefficient, the relationship between the composite scores of the different surveys was investigated.

6.2.1 Composite scores. *Hypothesis 1:* THINC-it and BRIEF-A showed a medium negative correlation, r = -.32, n = 72, p < .05, with low scores of cognition associated with high levels of perceived cognitive deficits (Coefficient of determination: 10,24% shared variance). There is a moderate effect size. Effect size range from .1 = small, .3 = moderate and .5 = large, according to Cohen (1988, as cited in Coolican, 2014).

Between the subjective subpart of the THINC-it, PDQ-5, and the GEC raw-score scores of BRIEF-A a strong negative correlation was found, $r = -.73$, $n = 72$, $p < .01$. There is a large effect size ($R^2 = 53.29\%$ shared variance). Between the four objective subparts of the THINC-it and GEC raw-score of BRIEF-A, a non-significant negative correlation was found, $r = -.12$, $n = 72$, $p = .32$.

Hypothesis 2: THINC-it and MADRS-S showed a small negative correlation, r = -.29, n = 74, p < .05, with low scores on cognition associated with higher levels of depression symptoms ($R^2 = 8{,}41\%$ shared variance).

Hypothesis 3: The MADRS-S and BRIEF-A are already established questionnaires within the physician's offices (Fantino, & Moore, 2009; Roth et al., 2005). They showed a high positive correlation, r = .73, n = 72, p < .001, with high levels of depression symptoms associated with high levels of perceived cognitive deficits ($R^2 = 53{,}29\%$ shared variance).

6.2.1.1 Outliers. The scatterplot shows one outlier, scoring high on both THINC-it (showing no signs of cognitive deficits) and MADRS (showing high signs of depression). Removing the outlier from the correlations gives a medium negative correlation between THINC-it and BRIEF (r = -.36, n = 71, p < .01). It also shows a medium negative correlation between THINC-it and MADRS-S (r = -.35, n = 73, p < .01) and a high positive correlation between MARDS-S and BRIEF (r = .72, n = 71, p < .01) (Cohen, 1988). On further analysis, the outlier did not seem to have much effect on the outcome, therefor the outlier was not removed from additional analyses.

6.3 ANOVA

In our last hypothesis, *hypothesis 4*, we also expected there to be a discrepancy between the different levels of depressive symptoms with measures of cognition. ANOVA is used when there are more than two variables, and it investigates whether the scores are from different populations (Coolican, 2014).

6.3.1 Depression symptoms and subjective measures of cognition. A one-way between group analysis of variance was performed to explore the impact of degree of depression symptoms as measured by the MADRS-S questionnaire with subjective cognitive decline as measured by BRIEF-A. Participants were divided into 3 groups according to their scores: 1) No depressive symptoms (N = 55). 2) Mild depressive symptoms (N = 11). 3) Moderate depressive symptoms (N = 6). No participants scored in the “severe depressive symptoms” group.

There was a statistically significant difference at the $p < .05$ in BRIEF-A scores for the depression groups, F (2, 69) = 20.4, $p < .001$, $\eta^2 = .37$. Post-hoc comparison using the Tukey HSD test indicate that the mean score for Group 1 (M = 98.91, SD = 16.55) was significantly different from group 2 (M = 124.36, SD = 15.24) and group 3 (M = 137.67, SD = 28.13). Group 2 and 3 did not differ significantly. Self-rating cognitive functioning on BRIEF-A seem to match their score on MADRS-S. See figure 2.

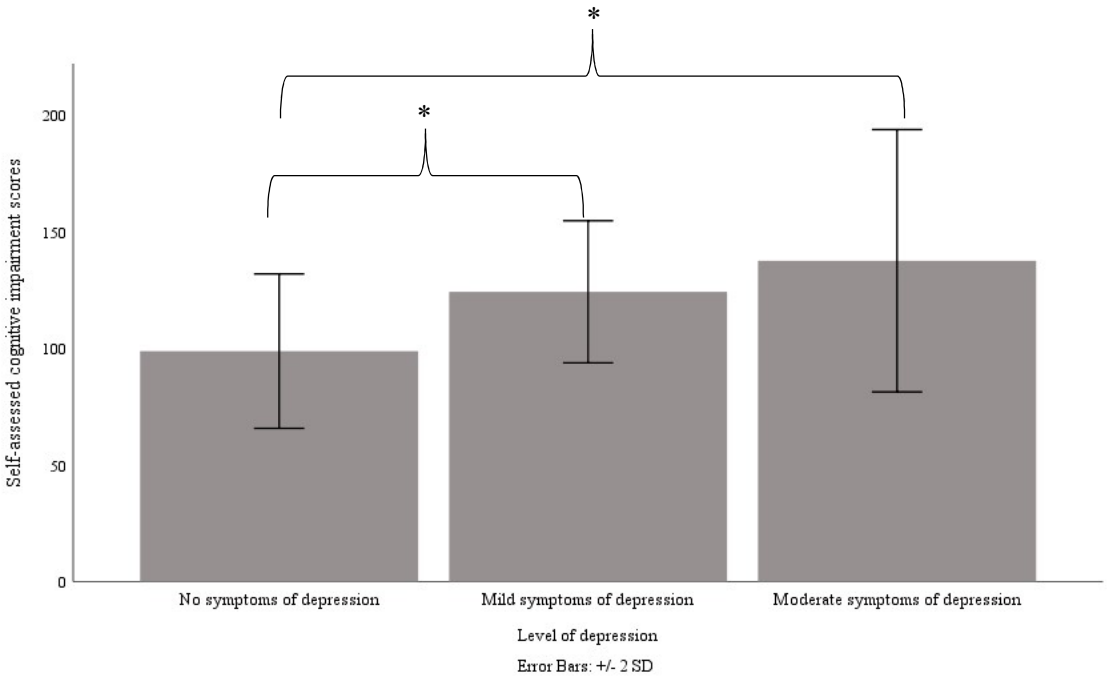

Figure 2: Cognitive scores (BRIEF-A) in levels of depression (MADRS-S)

* $p < .001$

The same analysis was run between the subjective part of THINC-it, the PDQ-5, and MADRS-S scores. The homogeneity of variance assumption is not violated, with a statistical difference at $p < .001$ level for the three depression levels: F (2, 71) = 27.6, $p < .001$, $\eta^2 = .44$. Post-hoc comparison using the Tukey HSD test indicate that the mean score for Group 1 (M = 3071.43, SD = 450.34) was significantly different from group 2 (M = 2200, SD = 713.20) and

group 3 (*M* = 1766.67, *SD* = 612.1), both *p* <.001. Group 2 and 3 did not differ significantly (*p* = .22). See figure 3.

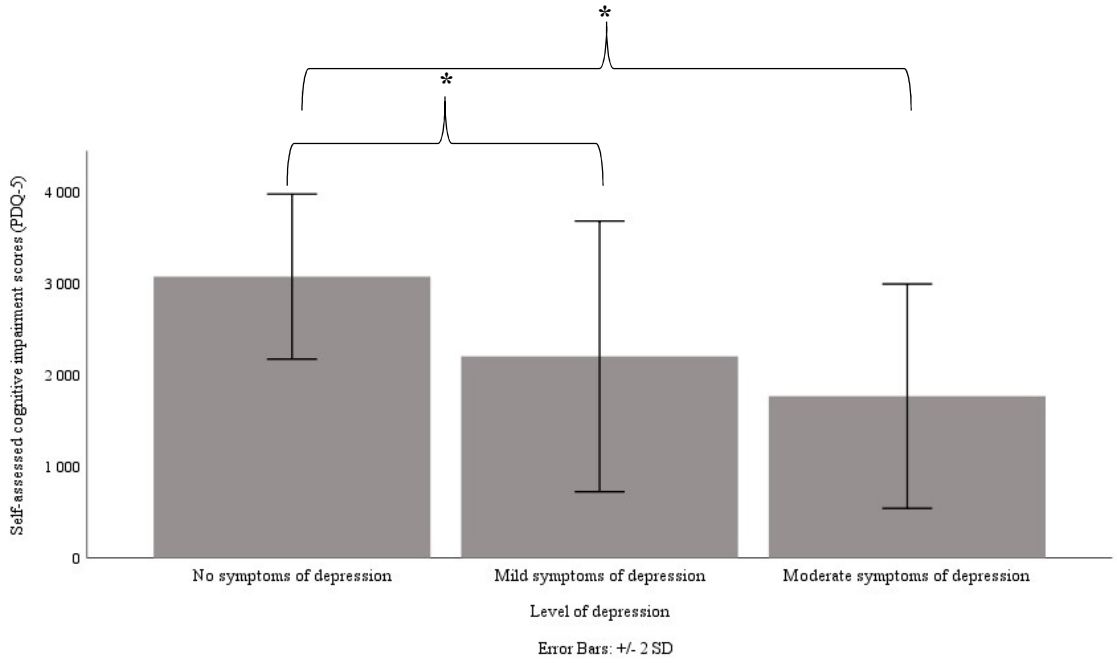

Figure 3: Cognitive scores from the PDQ-5 (THINC-it), in levels of depression (MADRS-S).

* *p* < .01

6.3.2 Depression and objective measures of cognition. Testing the four objective measures in the THINC-it there was no statistically significant difference between either of the depression groups, *F* (2, 71) = .29, *p* = .75. The composite score of the THINC-it did not show a statistically significant differences between either of the depression groups, *F* (2, 71) = 2.81, *p* = .06.

6.4 Additional Analysis

We had the opportunity to run additional analysis in our dataset based on findings from previously mentioned litterature. In our survey we asked the participants weather they had previously diagnosed depression. Results from previous studies indicated that in a remitted state of depression, CI will still be present (Fava et al., 2006). In our study, 9 participants reported they had previously been diagnosed with depression, and 65 participants reported they had not previously been diagnosed with depression. An independent-sample t-test was conducted to compare cognitive measures from the THINC-it, in previously depressed and not previous depressed participants. There was not a significant difference in the scores for previously depressed (M = 10934.4, SD = 1373.6) and not previously depressed (M = 11618.6, SD = 2392.4) participants; t (72) = .836, p = .40.

Another additional analysis was conducted on the five sub-tests on the THINC-it with levels of depression in MADRS-S. THINC-it consists of 5 separate tests, where a score of ~1000 indicates a SD of > 1 SD below healthy controls, ~2000 indicates 0.5 to 1 SD below healthy controls and >3000 indicates scores within 0.5 SD. Figure 3 show participants mean score relative to depression score in the different THINC-it subparts. An ANOVA was run between all the sub-tests of the THINC-it, (PDQ-5, Spotter, N-back, Code breaker and Trail making test-B) and levels of depression in the MADRS-S to investigate which cognitive domains was most affected in our participants. The homogeneity of variance assumption was not violated, however none of the tests showed significant results except the PDQ-5, which is already analyzed as reported previously in section 6.3.1.

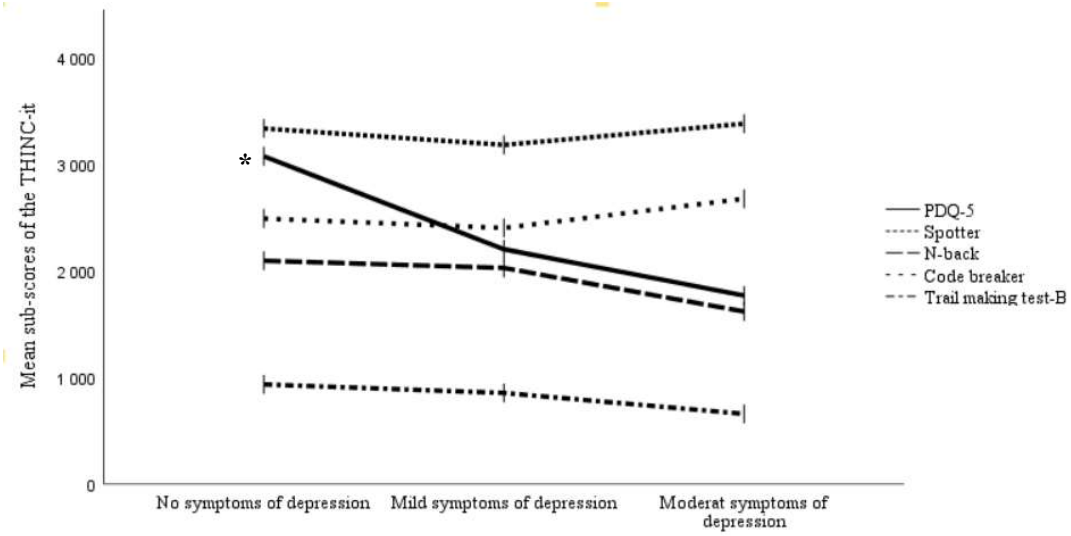

Figure 3. %-Line chart of degree of depression symptoms with scores of the THINC-it sub-scores.

* p <.001

The low scores on Trail making test-B/trails will be discussed in the section "Strengths and Limitation" of this paper.

7.0 Discussion

There has been a vast number of research focusing on cognition in depression the last decades, still, the literature is divergent and inconclusive, as different research point to different findings. There is however a strong trend towards the existence of cognitive impairment, both in the early and mild stages of depression, and in the recurrent more severe cases.

The use of cognitive assessment tools in the field of depression research is non-conclusive. The discrepancy between the use of cognitive assessment tools and the growing evidence regarding CI in depression calls for a standardized tool, which can be implemented

as part of the clinical assessment in order to target CI and consider residual CI as part of the remission profile.

One step in order to achieve this is to investigate a novel screening tool, developed with the purpose to assess cognitive functioning in depression in accessible way, aiming both for research and eventually clinical settings.

The main aim of the present study was to investigate a non-patient group and the relation between self-reported symptoms of depression, self-reported cognitive functioning and objective cognitive functioning measured by the THINC-it. We expected a correlation between the novel screening tool, THINC-it, and the widely used self-report questionnaire BRIEF-A. We predicted that even in a non-patient group, if depressive symptoms were present, we would also reveal signs of CI. Furthermore, we postulated that there would be a difference in self-perceived deficits of cognition and objective measures in people presented with different levels of symptoms of depression from MADRS-S.

7.1 Summary of Findings

Results from the present study confirmed our first hypothesis regarding measures of CI, where poor scores on the THINC-it was associated with higher levels of self-reported CI in BRIEF-A. When dividing the THINC-it into objective and subjective sub-parts, the PDQ-5 seem to be an adequate measure of subjective cognition compared to the more extensive BRIEF-A self-report questionnaire. Meaning that a short self-report questionnaire for CI could be just as good as measurement as a longer, more time-consuming questionnaire. However, the objective subpart of the THINC-it did not correlate with the subjective measures of BRIEF-A, supporting previous studies that objective and subjective measures of

cognition do not correlate (Carvalho et al., 2014). Even if the parts of the THINC-it showed incongruity, the tool as a whole seem to be able to identify CI symptoms in a reliable and useful way.

The composite score of THINC-it seems to be more useful in reflecting CI compared to the individual objective and subjective sub-parts. Thus, one might conclude that the whole is greater than the sum of its parts. This might reflect that CI has a divergent profile for different individuals and that the composite score is a better measure than the sub-scores alone.

Our hypothesis' further show a tendency towards confirming lower scores on cognitive functioning in the composite scores of THINC-it negatively correlating with higher scores of depressions in MADRS-S. Regarding BRIEF-A and MADRS-S our findings show higher levels of symptoms of depression correlates with participants' self-report of cognitive functioning. These results are similar to previous findings on this topic (Douglas et al., 2018; Hammar & Årdal, 2009). MADRS-S as a tool mainly target the emotional and biological symptoms of depression, and thereby do not focus directly on cognitive functioning, thus it might not reflect the impact CI have in patients' symptoms load.

When narrowing the focus on depression symptom load from MADRS-S by dividing into three sub-groups, and cognitive sub-parts from THINC-it, the results points to a difference in THINC-its subjective and objective cognitive scores and levels of depression from MADRS-S. Regarding subjective scores (PDQ-5), the results indicate that in individuals with no depression symptoms, no levels of cognitive decline was reported. Participants scoring within the range of low to moderate levels of depression reported lower scores on cognitive functioning. However, the level of depression, low or moderate, does not seem to have impact on self-reported subjective scores (PDQ-5). It is plausible that symptoms of

depression, regardless of symptom load, will influence subjective reported cognitive functioning even in non-diagnosed individuals.

When comparing BRIEF-A to symptom load of depression measured in MADRS-S, the scores is compatible with our findings with the subjective PDQ-5 sub-test in THINC-it reported above. Participants showing no signs of depression did not report cognitive impairment, and participants reporting low to moderate levels of symptoms of depression reported the same amount of subjective cognitive impairment.

We did not expect to see objective impairment in our participants since they are not diagnosed with depression. However, looking closer at the four objective sub-tests in the THINC-it, there is a trend towards lower scores on the sub-tests "symbol check/N-back" and "trail-making test" in participants reporting higher symptoms of depression compared to no symptoms of depression. The symbol check test assesses *EF*, *attention* and *working memory*, and the trail-making test assesses *EF*. One could argue the plausibility that the trend towards objective impairment in especially EF is recognizable in the individuals daily functioning and might therefore be traced in subjective self-report. This is similar to the findings of Lahr and colleagues (2007) who reported that the potential cognitive problems associated with depression might be caused by an actual impairment in EF. Vinberg and colleagues (2013) argues that especially *EF*, but also *attention*, might be impaired and even precede the onset of depression, which seems consistent with the trends visible in our research.

The two remaining objective sub-tests in THINC-it, spotter and code breaker, did not give any further information about the contributors of objective CI in depression in our participants.

In our participants, subjective self-report of CI (both in THINC-it and BRIEF-A) is lower than what the objective sub-tests of THINC-it measure. In other words, the individuals

measured objective functioning within EF, memory and attention is not equivalent to subjective experiences in their ever-day life. These findings are similar to the findings of Svendsen and colleagues (2012) who reported that depression symptom load was associated with higher self-report of CI, than what objective tests actually measured. It is also similar to the findings of Lahr and colleagues (2007) who reported high subjective complains especially in the domains of memory and attention in depressed patients, compared to their actual scores on objective neuropsychological test batteries. In contrast, Mohn and Rund (2016), found in their sample that objective test scores related to symptom load of depression, compared to subjective complaints. The divergent research results are interesting, as it points to an area which might not yet be fully explored or understood.

Supplementary findings from our material indicates some interesting results regarding the issue of remission in depression. As pointed out earlier, some of our participants (12.5%) reported having already experienced at least one episode of clinical depression, and based on previous findings one could expect this group of people to show signs of CI compared to our participants who had not experienced an earlier episode. However, in our results previous episode of depression do not show an effect on CI. This contradicts previous findings where cognition is seen to linger in previously diagnosed individuals (McIntyre et al., 2015). However, other studies have pointed out that not all patients with depression experience CI (Conradi et al., 2011), and not all patients with CI in depression experience it in remission (Hammar, & Årdal, 2009). The sample size of previously depressed people in the present study is small. It is also not clarified which degree of depression was previously present in the participants, how many episodes they have previously experienced, nor how long it has been since the last episode. Nevertheless, this finding does not necessarily out-rule the need for cognitive assessment in depression. In contrast, it highlights the importance of adequate

assessment tools which takes into consideration the possibilities of lingering cognitive symptoms in the remitted phase of depression. Moreover, it also highlights the need for a baseline cognitive assessment to be able to monitor cognitive functioning in the illness.

7.2 Clinical Implications of the Present Study

The literature indicates that there is a need in this patient group regarding cognitive functioning which might not be adequately met. This could be due to a lack of comprehensive understanding of cognitive functioning in depression by the practitioner (Belgaied, 2014; McAllister-Williams, 2017). In addition, the practitioners might fail to consider the possibilities of impaired cognitive functioning in patients, nor have the proper tool or assessment at their disposal. McAllister-Williams and colleagues (2017) goes as far as concluding "clinicians should undergo training regarding cognitive dysfunction in depression" (p. 346). Thus, healthcare professionals could benefit from a) a narrower focus on patients' profile of cognitive functioning, b) requiring a higher awareness of which screening tools that assess CI in depression and c) supplementing treatment goals targeting cognitive impairment. Informing patients on symptoms of cognitive deficits is important in order to help patients' come to terms with the symptoms and come up with coping mechanisms and increase awareness of the patients' situation and thought patterns.

CI has been found to be present in individuals experiencing a first-episode of depression, and in early onset of the illness. Furthermore, it has even been found to precede the onset of depression in some studies (Airakinsen et al., 2007; Vinberg et al., 2013). A routine care screening for cognitive functioning early in the assessment process could be useful for the clinicians' daily practice. An assessment tool which is simple, sensitive and accessible to the practitioner would be helpful. Previous studies have indicated that all

domains of cognition might not be impaired in depression (Douglas et al., 2018), and the THINC-its ability to easily distinguish between cognitive domains can be viewed as favorable, and thus make it easier for clinicians to target treatment within specific domains and implement more extensive tests when needed.

The subjective sub-test of THINC-it, the PDQ-5, could be to be an adequate measure of self-reported cognitive deficits in patients, when compared to the more extensive BRIEF-A self-report questionnaire. The PDQ-5 could be less invasive and overwhelming for patients in a vulnerable state. The quality of patient-physician dialogue might become enhanced because the simplicity in the PDQ-5 could be easier to convey. The PDQ-5 will also make it easier for the practitioner to measure the patients subjective cognitive functioning throughout the course of treatment, up to remission. In the light of Fava and colleagues (2006) findings on how up to 50% of patients report cognitive symptoms after remission, a therapeutic practice including follow-ups in patients every-day coping could be favorable. We have already pointed out that the PDQ-5 could be used as a reliable predictor of depression relapse (Saragouisse et al., 2017), which make this subjective sub-test of THINC-it a valuable measure throughout and after treatment, and even in the state of remission. When patients are regarded to be symptom free from depression in remission, several recent studies have indicated that CI is still present (Hammar & Årdal, 2009). However, patients are expected to return to work and studies, and non-identified CI could represent an extra burden on patients, which are expected to function on a post-morbid level. This could lead to a loop of negative self-representation and poor coping mechanisms and thereby represent a vulnerability factor for enhanced relapse risk. Therefore, it is important to assess cognitive residual symptoms, in order to apply interventions such as cognitive remediation to prevent new episodes.

The THINC-its subjective and objective parts are supplementary to each other, and the THINC-it global score give the clinicians a comprehensive picture of the patients cognitive functioning. The THINC-it do not replace the in-depth assessment of cognitive functioning interpreted by trained neuropsychologists. However, the tool can be used as screening in the clinical practice to evaluate the further need for in-depth assessment, as well giving indications for further choice of therapeutic intervention.

7.3 Strengths and Limitations of THINC-it

THINC-it is a screening tool useful in daily practice of clinicians working with depression, since it is less time consuming than other tests on the marked today. It is free to download and easily accessible for any clinicians' and health care professionals who wish to implement a sensitive and valid tool in their screening for CI. Our study has shown a sensitivity towards self-assessment of CI in a non-patient population.

Comments by the participants in the present study included some remarks about difficulty in understanding how to execute different sub-tests in THINC-it. This could be due to language difficulties, as the tutorials for the tests were in English. Even though one of the inclusion criterions was the ability to understand both Norwegian and English, overestimation of one's own ability to comprehend the English language could be a possible explanation. Another plausible explanation could be that tutorials might not be sufficient in explaining the tests. The largest problem could be seen in the "trails" test, where participants reported understanding the test itself, but failing to execute the test correctly. During the tutorial of the test, it is first explained how you should connect the letter with the numbers, a-1-b-2-c-3 etc. It could be possible that participants thought they understood the task from this information and skipped the rest of the tutorial on how to properly execute this test. The scores on this

subtest underline the importance of making sure the individuals understand what they are expected to do.

Participants reported the “N-back/symbol check” as the hardest test to execute, however results on this particular test was no lower than the subsequent tests in results, apart from “trails”. Meaning that participants perceived their performance as lower than what the test scores indicate. Results on the N-back test showed the greatest relationship with levels of depression in our results. This unexpected finding could be interesting to investigate further.

7.4 Limitations and Strengths of the Present Study

A limitation of this study is that we do not control for outside variables like stressful life-events, and this could thus represent confounding factors when interpreting the results. Another limitation is the small number of participants in the present study, only including students, meaning we cannot generalize our findings to a larger population. Since this group consists of only university students, one could argue that another selection criterion would have given different results. This points to the need for further investigation into the relation between cognition and depression.

The direction of our findings does however seem to concur with previous studies, and the aim of this study was to test out the sensitivity of a new cognitive measuring tool. The tool does seem sensitive enough to assess CI related to depressive symptoms and could complement diagnostic screening of depression**.** Literature points to the lack of an adequate screening tool in assessing CI in depression. Our assessment of a novel tool, THINC-it, might help fill this gap.

7.5 Ethical Reflections

The 72 participants in this study were mainly voluntary university students, without a diagnosis of depression at the implementation of the study, which was one of the inclusion criteria. In the general population, the experience of various depressive symptoms at different stages in life, do not always qualify for a diagnosis of depression. About 23% of our participants reported some degree of depressive symptoms. The aim of the present study was *not* to predict which individual might develop depression, only to test the sensitivity of the THINC-it in detection of CI.

7.6 Future Directions

In this study, the objective and subjective scores of the THINC-it was compared to a cognitive self-assessment questionnaire, and future studies should test the equability to other neuropsychological standardized tests.

A longitudinal study would be favorable in testing THINC-it, in order to follow a long-term profile of CI in depression. Further, in future studies the THINC-it could be tested on patients' in the remitted state to further test the sensitivity of the tool to assess CI in patients not currently experiencing a DE. It should also be tested in regard to number of previous episodes, severity of previous episodes and time since last episode of depression. This can help investigate which cognitive domains still lingers in remission and which different types of depression impact cognitive domains which might affect further relapse of episodes.

8.0 Conclusion

Different assessment methods have different strengths. The strength of THINC-it lies in the ability to assess both objective and subjective CI symptoms of patients, together with time efficiency. All of our hypothesis' were confirmed, showing correlations between all of the measured tools (THINC-it, BRIEF-A and MADRS-S). As predicted, the data showed a discrepancy between objective and subjective sub-parts of THINC-it. The present study showed that THINC-it could be considered to be a sensitive tool in order to detect cognitive impairment in a non-patient group when symptoms of depression is present. Moreover, self-reported measures in the study, PDQ-5 and BRIEF-A, was also correlated with depression symptoms. Finally, the study found that the sub-test of THINC-it, PDQ-5, and the screening tool BRIEF-A had a high correlation, indicating that shorter PDQ-5 could be an adequate measure in order to assess self-reported CI in clinical settings.

THINC-it seems to be an adequate screening-tool clinicians' can implement as part of their screening and treatment of depression, used in all the stages of the illness in order to assess cognitive functioning.

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Appendix

Attachment A. Ethical Approval

Attachment B. Approval of Participation

Attachment C. Instruction Sheet

Attachment D. Questionnaires

A – Ethical Approval

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK vest	Camilla Gjerstad	55978499	14.11.2017	2017/1755/REK vest
			Deres dato: 19.09.2017	

Vår referanse må oppgis ved alle henvendelser

Åsa Hammar
Universitetet i Bergen

2017/1755 Utprøving av digitalt verktøy for kognitiv funksjon

Forskningsansvarlig: Universitetet i Bergen
Prosjektleder: Åsa Hammar

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK vest) i møtet 25.10.2017. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10.

Prosjektomtale
Dette pilotprosjektet vil undersøke fungeringen av et nyutviklet digitalt screeningverktøy for kognitiv funksjon og sammenhengen mellom egenrapportert kognitiv funksjon og relasjonen til grad av depresjonssymptomer. Studien vil teste ut et nytt spørreskjema (THINC-it tool) for å vurdere kognitive egenskaper hos personer med depresjon. Dette vil bli vurdert opp mot kartlegging med MADRS-S (Montgomery and Aasberg depression rating scale - selvutfylling) og BRIEF-A (Behavior Inventory of Executive Function - adult). Deltakerne i studien er 48 friske studenter.

Vurdering

Forskningsprotokoll
Protokollen mangler oversikt over relevant forskningslitteratur. Komiteen viser til krav til forskningsprotokollen som er gitt i forskrift om organisering av medisinsk og helsefaglig forskning § 8. En mer utfyllende protokoll med referanseliste må sendes til REK vest.

Beredskap
Studien har utarbeidet en plan for beredskap dersom enkelte av studentene som deltar har alvorlige symptomer på depresjon. Det vil bli gitt informasjon om hjelpeinstanser som deltakerne kan kontakte. Ved behov vil forskningsleder følge deltaker til legevakt. Forskerne vil ta kontakt med vedkommende dersom undersøkelsen vil gi utslag på alvorlige depressive symptomer eller kognitiv svekkelse, slik at de kan få den informasjon de behøver for å søke hjelp. Komiteen har ingen merknader til beredskapsplanen.

Informasjonsskriv
Informasjonsskrivet må informere om dato for prosjektslutt og sletting av forskningsdata.

Rekruttering
Helseforskningsloven angir at dersom deltakeren kan anses å være i et avhengighetsforhold til den som ber om samtykke, skal samtykket innhentes av en annen, jf. § 13. Studien legger opp til at studenter vil bli

rekruttert til studien bl.a. i forbindelse med forelesning. Ved rekruttering på forelesning er det en fare for at studentene kan oppleve gruppepress og en forventning om å måtte delta. Komiteen ber derfor om at man ikke rekrutterer egne studenter, og at innhenting av samtykke må skje på en slik måte at det blir reelt frivilling.

Datahåndtering og prosjektslutt
Skjemaene vil bli administrert på private nettbrett og i papirform. REK vest setter som vilkår at datahåndtering og lagring gjøres i tråd med forskningsansvarlig (Universitetet i Bergen) sine rutiner. Datamaterialet vil bli anonymisert etter prosjektslutt 31.10.19. REK vest har ingen innvendinger til dette.

Vilkår

- Komiteen ber om at man ikke rekrutterer egne studenter, og at innhenting av samtykke må skje på
  en slik måte at deltakelsen blir reelt frivilling.
- Revidert forskningsprotokoll må sendes til REK vest.
- Datahåndtering/datalagring må gjøres i tråd med forskningsansvarlig (Universitetet i Bergen) sine rutiner.

Vedtak
REK vest godkjenner prosjektet på betingelse av at ovennevnte vilkår tas til følge.

Sluttmelding og søknad om prosjektendring
Prosjektleder skal sende sluttmelding til REK vest på eget skjema senest 30.04.2020, jf. hfl. § 12. Prosjektleder skal sende søknad om prosjektendring til REK vest dersom det skal gjøres vesentlige endringer i forhold til de opplysninger som er gitt i søknaden, jf. hfl. § 11.

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK vest. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK vest, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Med vennlig hilsen

Marit Grønning
dr.med. professor
komiteleder

Camilla Gjerstad
rådgiver

Kopi til: post@uib.no

B – Approval of Participation

FORESPØRSEL OM DELTAKELSE I FORSKNINGSPROSJEKTET

UTPRØVING AV NYTT DIGITAL SCREENINGSVERKTØY FOR KOGNISJON.

Dette er et spørsmål til deg om å delta i et forskningsprosjekt som omhandler å undersøke et nytt screeningverktøy for å undersøke kognitive evner i samsvar med symptomer til depresjon.

Begrunnelsen for utførelsen av denne studien er å teste et nytt screeningverktøy for kognitive ferdigheter, som forhåpentligvis kan bli benyttet i kliniske sammenhenger. Dette verktøyet er mye mindre tidkrevende enn nåværende metoder og kan enkelt utføres av personen selv.

Studien er utført ved Universitetet i Bergen, Det Psykologiske Fakultet.

HVA INNEBÆRER PROSJEKTET?

Deltakelse i denne studien innebærer utfylling av tre forskjellige skjemaer/undersøkelser. To av skjemaene måler kognitive ferdigheter som arbeidsminnet og oppmerksomhet, og det tredje skjemaet måler symptomer på depresjon.

Undersøkelsen vil ta ca 30 minutter og gjennomføre og vil foregå på både PC og på papir.

MULIGE FORDELER OG ULEMPER

Det er ingen risiko ved å delta på dette studiet

Dersom du føler et ubehag ved utfylling av skjemaene kan du kontakte prosjektansvarlig.

FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE SITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke. Dersom du trekker deg fra prosjektet, kan du kreve å få slettet innsamlede opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner. Dersom du senere ønsker å trekke deg eller har spørsmål til prosjektet, kan du kontakte prosjektleder Åsa Hammar på: Aasa.Hammar@uib.no.

HVA SKJER MED INFORMASJONEN OM DEG?

Informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger gjennom en navneliste.

Prosjektleder har ansvar for den daglige driften av forskningsprosjektet og at opplysninger om deg blir behandlet på en sikker måte. Informasjon om deg vil bli anonymisert eller slettet senest fem år etter prosjektslutt.

GODKJENNING

Prosjektet er godkjent av Regional komite for medisinsk og helsefaglig forskningsetikk, (saksnr. hos REK: 2017/1755/REK vest).

C. Instruction Sheet

GJENNOMFØRING AV UNDERSØKELSEN – INFORMASJON

1. Start på PC og fyll inn:
    - Patient code: **Deltaker nr.**
    - Alder
    - Utdanning: **Hvilket løp går du**
    - Sted: **Bergen**
    - Om du er mann eller kvinne
    - Om du bruker venstre eller høyre hånd
    - **TRYKK SÅ SAVE**

2. Trykk videre på **BEGIN TEST** på midten av skjermen.
    - **Les instruksjonen på skjermen nøye**
    - Det vil først komme noen spørsmål du skal svare på, og videre et par tester.
    - Når testene starter, trykk først på **TUTORIAL** for informasjon om hvordan testen gjennomføres. Bruk tastaturet til gjennomføring av testene. Trykk **OK** mellom hver av testene.

3. Når startskjermen kommer opp igjen er du ferdig med PC, og du kan starte på arkene.

D. Questionnaires

Link for downloading the app THINC-intergrated tool: https://progress.im/en/thinc-it-tool

Kvinne ☐ Mann ☐

Oppnådd utdannelse: Årsstudium ☐ Profesjonsstudiet ☐ Bachelor ☐ Master ☐ Phd ☐

Arbeid/skole:_____

SPØRSMÅL:
(sett sirkel rundt gjeldende svar)

Har du tidligere fått diagnosen alvorlig depresjon? JA NEI

Hvis ja, fikk du behandling? JA NEI

Hvilken form for behandling har du mottatt? _____

Er noen i familien din diagnostisert med depresjon? JA NEI

Hvis ja, hvem? _____

DELTAKER NR. _____

DELTAKER NR. _____

Svar på følgende påstander ved å krysse av i den ruten du mener passer best	**Aldri problem N**	**Av og til problem A**	**Ofte problem O**
Jeg har sinne utbrudd	N	A	O
Jeg gjør slurvefeil når jeg er i ferd med å avslutte oppgaver	N	A	O
Jeg er uorganisert	N	A	O
Jeg har vanskelig for å konsentrere meg om oppgaver (f.eks. dagligdagse gjøremål, lesing eller jobb)	N	A	O
Jeg trommer med fingrene eller dirrer med beina	N	A	O
Jeg må bli påminnet om å komme igang med en oppgave, selv om jeg har lyst	N	A	O
Klesskapet mitt er rotete	N	A	O
Jeg har vanskelig for å bytte fra en aktivitet eller oppgave til en annen	N	A	O
Jeg blir overveldet av større oppgaver	N	A	O
Jeg glemmer hva jeg heter	N	A	O
Jeg har problemer med jobber eller oppgaver som består av mer enn ett trinn	N	A	O
Jeg overreagerer følelsesmessig	N	A	O
Jeg merker ikke når jeg får andre til å bli lei seg eller sint, før det er for sent	N	A	O
Jeg har vansker med å komme igang om morgenen	N	A	O
Jeg har vanskelig for å prioritere aktiviteter	N	A	O
Jeg har problemer med å sitte i ro	N	A	O
Jeg glemmer hva jeg holder på med selv om jeg er midt oppi det	N	A	O
Jeg sjekker ikke arbeidet mitt for feil	N	A	O
Jeg reagerer følelsesmessig for den minste ting	N	A	O
Jeg oppholder meg mye hjemme	N	A	O

Jeg setter i gang med oppgaver (f.eks. matlaging, prosjekter) uten å undersøke om de riktige tingene er på plass	N	A	O
Jeg har vanskelig for å akseptere forskjellige måter å løse problemer på når det gjelder jobb, venner eller oppgaver	N	A	O
Jeg snakker på feil tidspunkt	N	A	O
Jeg feilvurderer hvor vanskelig eller lett oppgaver kan være	N	A	O
Jeg har vanskelig for å komme igang på egenhånd	N	A	O
Jeg har vanskelig for å holde meg til saken når jeg snakker	N	A	O
Jeg blir trøtt	N	A	O
Jeg reagerer mer følelsesmessig i situasjoner enn mine venner	N	A	O
Jeg har vansker med å vente på tur	N	A	O
Folk sier at jeg er uorganisert	N	A	O
Jeg mister ting (f.eks. nøkler, penger, lommebok, hjemmelekser osv.)	N	A	O
Jeg har vanskelig for å finne en ny måte å løse et problem på når jeg ikke får ting til	N	A	O
Jeg overreagerer på små problemer	N	A	O
Jeg planlegger ikke for framtidige aktiviteter	N	A	O
Jeg har et kort oppmerksomhetsspenn	N	A	O
Jeg kommer med upassende seksuelle kommentarer	N	A	O
Når folk er sinte på meg, forstår jeg ikke hvorfor	N	A	O
Jeg har vanskelig for å telle til tre	N	A	O
Jeg har urealistiske mål	N	A	O
Jeg går fra et rotete bad	N	A	O
Jeg gjør slurvefeil	N	A	O
Jeg blir lett følelsesmessig opprørt	N	A	O
Jeg tar beslutninger som får meg i trøbbel (juridisk, økonomisk og sosialt)	N	A	O
Jeg plages av å måtte forholde meg til forandringer	N	A	O
Jeg har vanskelig for å bli begeistret	N	A	O
Jeg glemmer lett instruksjoner	N	A	O

Jeg har gode ideer, men får dem ikke ned på papiret	N	A	O
Jeg gjør feil	N	A	O
Jeg har problemer med å komme igang med oppgaver	N	A	O
Jeg sier ting uten å tenke	N	A	O
Jeg har et voldsomt temperamentet, men det går fort over	N	A	O
Jeg sliter med å avslutte oppgaver (som f.eks dagligdagse gjøremål, arbeid)	N	A	O
Jeg begynner med ting i siste liten (som f.eks oppdrag, dagligdagse gjøremål, oppgaver)	N	A	O
Jeg har vanskelig for å fullføre en oppgave på egenhånd	N	A	O
Folk sier at jeg blir lett distrahert	N	A	O
Jeg har vanskelig for å huske ting, selv etter noen få minutter (som f.eks anvisning, telefonnr.)	N	A	O
Folk sier at jeg er altfor følsom	N	A	O
Jeg haster igjennom ting	N	A	O
Jeg blir irritert	N	A	O
Jeg forlater rommet eller huset i et eneste rot	N	A	O
Jeg blir forstyrret av uventete forandringer i daglige rutiner	N	A	O
Jeg sliter med å komme på hva jeg kan gjøre i fritiden min	N	A	O
Jeg planlegger ikke oppgavene på forhånd	N	A	O
Folk sier at jeg ikke tenker før jeg handler	N	A	O
Jeg har problemer med å finne ting på rommet, i skapet eller på pulten	N	A	O
Jeg har problemer med å organisere aktiviteter	N	A	O
Etter å ha støtt på et problem kommer jeg ikke lett over det	N	A	O
Jeg har problemer med å gjøre mer enn en ting om gangen	N	A	O
Humøret mitt svinger ofte	N	A	O
Jeg tenker ikke på konsekvenser før jeg gjør noe	N	A	O
Jeg sliter med å organisere arbeidet	N	A	O
Jeg blir fort opprørt over småting	N	A	O

Jeg er impulsiv	N	A	O
Jeg rydder ikke etter meg	N	A	O
Jeg har problemer med å gjøre ferdig jobben min	N	A	O

MADRS
Norsk oversettelse fra svensk v/Ulrik Fr. Malt

Skjema for egenvurdering av depresjon

DELTAKER NR. _____

Hensikten med dette spørreskjemaet er å gi et detaljert bilde av ditt nåværende stemningsleie. Vi vil derfor be om at du på skjemaet under besvarer noen spørsmål omkring stemningsleiet de siste tre døgn.

Skjemaet inneholder en rekke ulike påstander om hvordan man kan ha det. Påstandene uttrykker ulike grader av plager, fra ingen plager til maksimale plager.

Sett et kryss i boksen utenfor den påstanden som du synes stemmer best med hvordan du har hatt det de siste 3 dagene. Er du i tvil hvilken påstand som stemmer best kan du velge å krysse av i en av boksene mellom to påstander.

Tenk ikke for lenge, men forsøk heller å fylle skjemaet ut raskt.

Hvis du har eventuelle spørsmål om skjemaet kan du rette disse til din behandler.

1 Stemningsleie	2 Følelse av indre uro / spenning
Her skal du krysse av for hvordan ditt stemningsleie har vært: Om du har kjent deg trist, tungsindig eller dyster. Tenk etter hvordan du har kjent deg de siste 3 dagene, om humøret har skiftet eller om det har vært det samme hele tiden, og forsøk å huske om du har kjent deg lettere til sinns hvis det har hendt noe positivt.	*Her ber vi deg krysse av for i hvilken grad du har hatt følelser av indre spenning, uro, angst, eller udefinerbar redsel i løpet av de tre siste dagene. Tenk særlig på hvor intense følelsene har vært, og om de har kommet og gått eller vært der nesten hele tiden*.
0. Jeg kan kjenne meg trist eller glad, alt etter omstendighetene.	0. Jeg kjenner meg for det meste rolig.
☐ 1.	☐ 1.
☐ 2. Jeg kjenner meg for det meste nedstemt, men iblant kjennes det lettere.	☐ 2. Iblant har jeg ubehagelig følelser av indre uro.
☐ 3.	☐ 3.
☐ 4. Jeg kjenner meg gjennomgående nedstemt og dyster. Jeg kan ikke glede meg over slikt som vanligvis gjør meg glad.	☐ 4. Jeg har ofte en følelse av indre uro som iblant kan bli meget sterk og som jeg må anstrenge meg for å holde i sjakk.
☐ 5.	☐ 5.
☐ 6. Jeg er så totalt nedstemt og ulykkelig at jeg ikke kan tenke meg at det kan bli verre.	☐ 6. Jeg har fryktelige, langvarige eller uutholdelige følelser av angst.

3 Søvn	4 Matlyst
Her ber vi deg anføre hvor godt du sover. Tenk etter hvor lenge du har sovet og hvor god søvnen har vært de siste tre nettene. Svaret skal gjenspeile hvordan du faktisk har sovet uansett om du har brukt sovemedisin eller ikke. – Hvis du har sovet mer enn du pleier, krysser du av for 0.	*Her ber vi deg anføre hvordan appetitten din er, og tenke etter om den på noen måte er anderledes enn normalt for deg. Husk å vektlegge de tre siste dagene - Om du har bedre appetitt enn normalt, krysser du av i boksen merket 0.*
☐ 0. Jeg sover rolig og godt, og lenge nok til å dekke mitt behov. Jeg har ingen særlige vanskeligheter med innsovning. ☐ 1. ☐ 2. Jeg har visse søvnvanskeligheter. I blant har jeg vanskelig for å sovne eller jeg sover mer urolig eller overfladisk enn jeg pleier. ☐ 3. ☐ 4. Jeg sover minst 2 timer mindre per natt enn normalt. Jeg våkner ofte i løpet av natten selv om jeg ikke forstyrres av noen. ☐ 5. ☐ 6. Jeg sover svært dårlig, ikke mer enn 2-3 timer per natt.	☐ 0. Min appetitt er slik den pleier å være. ☐ 1. ☐ 2. Min appetitt er dårligere enn vanlig. ☐ 3. ☐ 4. Jeg har nesten ikke appetitt. Maten smaker ikke, og jeg må tvinge meg til å spise. ☐ 5. ☐ 6. Jeg orker ikke mat i det hele tatt. Hvis jeg skal få noe i meg må jeg overtales til å spise.
5 Konsentrasjonsevne	**6 Initiativ**
Her ber vi deg vurdere din evne til å holde tankene samlet, og konsentrere deg om ulike aktiviteter. Tenk gjennom hvordan du fungerer i ulike situasjoner som krever ulik grad av konsentrasjonsevne. F.eks. å lese en komplisert tekst, å lese en lett avisartikkel, å se på TV eller å snakke med andre mennesker. Husk: vektlegg de 3 siste dager.	*Her ber vi deg forsøke å vurdere din handlekraft de tre siste dagene. Spørsmålet er om du har lett eller vanskelig for å komme igang med saker du synes du bør gjøre, og i hvilken utstrekning du må overvinne en indre motstand når du skal begynne med noe.*
☐ 0. Jeg har ingen konsentrasjonsvanskeligheter. ☐ 1. ☐ 2. Jeg har for tiden problemer med å holde tankene mine samlet om slikt som normalt burde fange oppmerksomheten. ☐ 3. ☐ 4. Jeg har betydelige problemer med å konsentrere meg om slikt som normalt ikke krever noen anstrengelse fra min side. ☐ 5. ☐ 6. Jeg kan overhodet ikke konsentrere meg om noen ting.	☐ 0. Jeg har ingen vanskeligheter med å påbegynne nye oppgaver. ☐ 1. ☐ 2. Når jeg skal påbegynne noe, byr det meg imot på en måte som ikke er normal for meg. ☐ 3. ☐ 4. Det kreves en stor anstrengelse av meg bare å komme igang med enkle oppgaver som jeg vanligvis utfører mer eller mindre rutinemessig. ☐ 5. ☐ 6. Jeg klarer ikke å pågynne selv de enkleste hverdagssysler.

7 Følelsesmessig engasjement	8 Pessimisme
Her ber vi deg ta stilling til hvordan du opplever din interesse for omverdenen og for andre mennesker, og for slike aktiviteter som pleier å gi deg morro og glede. Husk at du skal vurdere dette ut fra hvordan du har hatt det de tre siste dagene.	*Dette omhandler hvordan du ser på din egen fremtid og hvordan du oppfatter din egen verdi. Tenk etter i hvilken grad du bebreider deg selv, om du plages av skyldfølelse, og om du har vært engstelig oftere enn vanlig for f.eks. din økonomi eller din helse. Husk at du skal vurdere dette ut fra hvordan du har hatt det de tre siste dagene.*
☐ 0. Jeg er interessert i omverdenen og engasjerer meg i den, og det gir meg både morro og glede. ☐ 1. ☐ 2. Jeg føler mindre sterkt for det som pleier å engasjere meg. Jeg har vanskeligere enn vanlig for å bli glad eller vanskeligere for å bli sint når det er nødvendig. ☐ 3. ☐ 4. Jeg har ingen interessse eller følelser for omverdenen, ikke engang for venner og bekjente. ☐ 5. ☐ 6. Jeg har sluttet å oppleve følelser. Jeg føler meg smertefullt likegyldig til og med overfor mine nærmeste.	☐ 0. Jeg ser lyst på fremtiden. Jeg er stort sett ganske fornøyd med meg selv. ☐ 1. ☐ 2. Iblant anklager jeg meg selv og synes jeg er mindre verd enn andre. ☐ 3. ☐ 4. Jeg grubler ofte over mine tabber og føler meg mindreverdig eller verdiløs, selv om andre synes noe annet. ☐ 5. ☐ 6. Jeg ser svart på alt og kan ikke se noe håp. Det føles som jeg er et tvers gjennom verdiløst menneske, og som om jeg aldri skulle kunne få noen tilgivelse for det stygge jeg har gjort.
9 Livslyst	**Ekstra spørsmål**
Spørsmålet gjelder lysten til å leve og om du har opplevd livet som meningsløst. Også om du har tanker om selvmord, og i så fall, i hvilken utstrekning du opplever dette som en reell utvei. Husk: vektlegg kun de siste 3 dagene. ☐ 0. Jeg har normal lyst til å leve. ☐ 1. ☐ 2. Livet føles ikke særlig meningsfylt, men jeg ønsker likevel ikke at jeg var død. ☐ 3. ☐ 4. Jeg synes ofte det ville vært bedre å være død, og selv om jeg egentlig ikke ønsker det kan selvmord av og til oppleves som en mulig løsning. ☐ 5. ☐ 6. Jeg har egentlig innsett at min eneste utvei er å dø, og jeg tenker mye på hvordan jeg skal ta livet av meg.	**X1: Døgnvariasjon i stemningsleiet** ☐ 0. Det er i forbindelse med den aktuelle tilstanden ikke noen klar og forutsigbar sammenheng mellom tid på døgnet og mitt stemningsleie. ☐ 1. Jeg føler meg alltid mer og mer deprimert / fortvilet/engstelig jo lengre ut på dagen en kommer. ☐ 2. Jeg føler meg alltid verst om morgenen, men ut over eftermiddagen og kvelden lysner stemningsleiet eller letter angsten noe. **X2: Overaktiv og deprimert samtidig** ☐ 0. Jeg er utslitt og tung uten forøket aktivitet eller energi. ☐ 1. Jeg er på en merkelig måte både utslitt og tung samtidig som jeg tenker og beveger meg raskere enn det som er vanlig for meg. ☐ 2. Selv om jeg føler meg svært nedtrykt, engstelig og fortvilet, er jeg samtidig mye mer aktiv enn det som er mitt vanlige jeg. Det er som om jeg ikke kan være i ro. Jeg både tenker, snakker, og beveger meg raskere enn det som er vanlig for meg.