Graduate thesis

NTNU
Norwegian University of Science and Technology
Faculty of Social and Educational Sciences
Department of Psychology

Elise Ødegård Gjestad

The Relationship Between Executive Impairment and Emotional Disturbances in Stroke Patients

Graduate thesis in Clinical Programme in Psychology
Supervisor: Ramune Grambaite
December 2018

NTNU
Norwegian University of
Science and Technology

Elise Ødegård Gjestad

The Relationship Between Executive Impairment and Emotional Disturbances in Stroke Patients

Graduate thesis in Clinical Programme in Psychology
Supervisor: Ramune Grambaite
December 2018

Norwegian University of Science and Technology
Faculty of Social and Educational Sciences
Department of Psychology

NTNU
Norwegian University of
Science and Technology

Contents

Preface

This paper is based on a large longitudinal data set collected by a team of researchers at Akershus University Hospital. All the neuropsychological data used in this paper was collected by Ramune Grambaite. I am very grateful to have been able to use this data to develop my own research goals and analyses for this final thesis.

I also wish to express my deepest gratitude to Ramune Grambaite for being my supervisor on this thesis, and for all her patience, knowledge, interesting discussions and for helping me be more ambitious. It has been an inspiring journey, where I even got the opportunity to take some of the results from this study to a conference on the other side of the world.

I want to thank Jurate Saltyte-Benth for looking over my statistical analyses and providing with essential feedback on how to improve them.

My family has always supported me, and I owe them eternal thanks for always having an open door whenever I wanted to return home, in good times or bad. The same goes for my dear friends. I especially want to thank Robert Mahy, for taking the time to proofread this paper.

Finally, I want to thank my partner and love, Rune Brørs Petterson. You have taken care of me when I've needed it, always given me motivation, and waking up next to you every morning is the greatest gift.

Trondheim, December 2018

Elise Ødegård Gjestad

Abstract

Executive impairment and emotional symptoms are commonly seen post-stroke. These symptoms may impact several aspects of daily life, such as employability and ability to maintain reasonable self-care. In this study, we examine the association between executive impairment and emotional symptoms in post-stroke patients. Increased knowledge about these relationships can help provide better care for stroke patients.

The aim of this study was to examine the associations between executive impairment and emotional symptoms in stroke patients. The study is based on a group of 86 patients (MMSE>23) with ischemic infarctions (37 with cortical infarctions and 49 with lacunar supratentorial infarctions), recruited from a stroke unit at Akershus University Hospital. The average age at recruitment was 64.4 years, and 68% were male. Neuropsychological examination was performed one week and three months post-stroke.

The patients were divided into two groups based on their performance on executive tests. When comparing the patients with executive impairment (defined as 1.5 SD below the mean for the normative sample on at least one executive test) to the remaining patients, the impairment group had significantly higher levels of depressive symptoms on the depression subscale of HADS ($p<.05$) at both one week and three months post-stroke. Multiple regression models showed that the depression subscale of HADS significantly influenced the outcome on 7 executive measures, while the anxiety subscale significantly influenced 2.

The results of this study indicate that some stroke patients might have an increased need for follow-up, due to the relationship between depressive symptoms and executive impairment, and the consequences this may have for treatment.

Introduction

Acute stroke is defined by the World Health Organization (WHO) as "a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin" (Hatano, 1976). This occurs due to brain cell death by deprivation of oxygen, by the blood flow to the brain being disturbed. This may happen either by occlusions of the blood supply (ischaemic stroke) or by ruptured blood vessels (haemorrhagic stroke) (National Collaborating Centre for Chronic Conditions, 2008). The majority of the strokes are ischaemic, and the majority of the ischaemic strokes are lacunar, i.e. located to the deep structures of the brain (Prins, van Dijk, & den Heijer, 2005). Stroke may have a varied presentation, depending on which areas of the brain that have been deprived of oxygen, but is often characterised by one-sided limb weakness, speech disturbance, or disturbance of vision or balance (National Collaborating Centre for Chronic Conditions, 2008). Quick treatment is essential in order to save the cells that are still viable, but will die if the oxygen deprivation continues (the penumbra) (Lezak, Howieson, & Loring, 2004).

In Norway in 2016, 13 161 patients with acute stroke were registered, of which 10 915 had not been diagnosed with stroke during the four previous years. The age adjusted incidence rate was at 245 per 100 000. Of the patients with a first-time stroke, 5 055 were women and 5 860 were men. For both men and women, the largest amount of first-time stroke was found in those within the age group 70-89 years (Kvåle et al., 2018), and the likelihood of experiencing a stroke increases with age (National Collaborating Centre for Chronic Conditions, 2008). The majority of strokes are found in the group over 75 years of age, with an average age of first time stroke in women 77.7 years, and in men 75.3 years (Ellekjær & Selmer, 2007).

Between 2012 and 2016, the mortality rate of stroke in Norway decreased from a total number of 2 426 to 1 927. Possible contributors to this development may be an increased use of thrombolysis within 40 minutes of the stroke occurring, as well as specialised treatment in a stroke ward (Kvåle et al., 2018). The decrease in the mortality rate combined with an ageing population being at risk for strokes means the group of people living with sequelae post-stroke may grow. Strokes are one of the main causes for cognitive impairment, increasing the risk of disability, reduced quality of life, and mortality (Tang et al., 2018). Increased knowledge of how these sequelae are expressed; which consequences they have for the individual; and what

may be done to alleviate them, is therefore of interest, both for the scientific community and society as a whole.

Cognitive impairment post-stroke

Stroke can lead to an array of different cognitive impairments, depending both on the location and the size of the stroke (Engstad, Viitanen, & Almkvist, 2007). Damage to different parts of the brain can result in similar symptoms due to the disruption of neurological pathways (Wyller & Sveen, 2002). Additionally, early in the course of the stroke, secondary diffuse (e.g. swelling) effects may cause issues that are unrelated to the location of the stroke (Lezak et al., 2004). The changes in cognition may vary from barely noticeable to the patient to completely life-changing. Often affected domains include executive functions, psychomotor speed and attention (Engstad et al., 2007). Regardless of the size and location of the brain damage, disturbances to cognitive, emotional and executive systems are usually found (Lezak et al., 2004).

In the acute phase, cognitive impairment occurs in 70% of the patients, with spontaneous improvement in the period after the stroke (Riepe, Riss, & Bittner, 2004). One in four patients gets lasting impairments (Wyller & Sveen, 2002). The improvement seen in the majority of the patients is largest immediately after the incident and usually plateaus two years post-stroke (del Ser, Barba, & Morin, 2005). Most of the spontaneous improvement happens in the first three months (Lezak et al., 2004).

89% of the brain infarctions found in the Rotterdam Scan Study were lacunar infarctions located to the basal ganglia and subcortical areas (Prins et al., 2005). These deep frontal changes in brain matter were associated with weakened executive functions and psychomotor speed, in all likelihood due to disruptions in pathways between frontal areas and other deep structures (Sachdev, Brodaty, & Valenzuela, 2004). This pattern of impairment is often found as a consequence of occlusions of the frontal circulatory system with the carotid arteries (Engstad et al., 2007).

While changes to executive functions are common after stroke, extensive frontal lobe damage may have little impact on abilities measures by traditional neuropsychological tests (Lezak et al., 2004). These tasks are often clear-cut and given with detailed instruction and may thus not reflect the patient's performance on the more diffuse tasks of daily life. In turn, this may cause the impairment to be discovered late, if at all, which may have an adverse effect on

the prognosis (Engstad et al., 2007), and be detrimental for both mental and physical health (Diamond, 2013). While damage to some parts of the brain, e.g. the language areas, is easily spotted, impairments in executive functions tend to show up globally and affect all aspects of behaviour (Lezak et al., 2004). It is therefore essential to have an understanding of what these functions actually entail.

Executive functions

Executive functions, also known as cognitive control functions, is an umbrella term that refers to a group of top-down mental processes that control and organise other mental processes (Gilbert & Burgess, 2008). They enable the ability to coordinate thoughts and actions, in order to prioritise goals and plan complex behaviours (Miller & Wallis, 2009). These high-level cognitive processes provide the individual with the ability to behave in a flexible way, and adapt to new and changing situations (Gilbert & Burgess, 2008). Using executive functions is effortful and requires the individual to have enough mental energy. Acting according to habits and being impulsive is easier than to change the course of action (Diamond, 2013). Executive functions may therefore be influenced by post-stroke fatigue, which is a common complaint after stroke, and occurring in 39 to 72% of patients (Colle, Bonan, Gellez Leman, Bradai, & Yelnik, 2006).

One of the first models that highlighted the role of these functions is Baddeley's (1992) theory of working memory. In addition to the two subsystems dubbed the visuospatial sketchpad and the phonological loop, which manage visual images and speech-based information respectively, he also postulated the existence of a central executive: a system that controls the attention and thus the use of other cognitive abilities.

While it is often referred to as one construct, the executive function is comprised of several factors. General consensus is that there are several core functions that make up this larger entity (Diamond, 2013). This division is supported both by correlation analyses (where the studies typically found a correlation coefficient between different domains of executive functions <.4), factor analyses and functional magnetic resonance imaging (fMRI) studies of the brain, combined with the observation that a patient may struggle with some, but not all, aspects of their executive functions (Gilbert & Burgess, 2008; Miyake et al., 2000). It has therefore been said that the executive functions are both unified and diverse (Miyake & Friedman, 2012), as they are connected both in use and in location, yet still are clearly separable.

Miyake et al. (2000) suggests that there are three core functions, those three being inhibition, working memory and cognitive flexibility. They note that while there may be aspects of executive functioning that are not covered by this model (Friedman & Miyake, 2017), and the core constructs may be divided further into groups (Smith & Jonides, 1997), the main purposes of the executive functions are covered by the model.

In Miyake et al. (2000)'s model, inhibition is the ability override initial drive and replace these impulsive actions with ones that are more appropriate or needed (Diamond, 2013). This may be expressed in many different aspects of life: inhibitory control of attention, which enables selective attention; cognitive inhibition, which involves suppressing mental representations; and self-control. Self-control includes both suppression of initial wants, delayed gratification, and being able to delay reactions. This core executive function is often tested with tools such as continuous performance tests (Epstein et al., 2003) and interference tests (Delis, Kaplan, & Kramer, 2001). Self-control ability increases from childhood into adulthood, and is found to be a predictor for later well-being (Moffitt et al., 2011), while it decreases in normal ageing (Gazzaley, Cooney, Rissman, & D'Esposito, 2005).

Working memory entails mentally working with information that is no longer perceptually present (Smith & Jonides, 1997). It is critical for reasoning and any kind of mental reordering of items (Diamond, 2013). Diamond (2013) points out that there is a point of discussion among researchers on whether or not inhibition is a separate construct from working memory, or if they are parts of the same ability. Working memory may be tested using measures such as Letter-Number Sequencing (Wechsler, 2003), which requires not only memory, but also reordering of the items remembered. Working memory naturally declines as the individual ages (Fiore, Borella, Mammarella, & De Beni, 2012).

The third and final core function in this model is cognitive flexibility. It involves changing of mindsets, perspectives and concepts, and being able to adjust to changing circumstances (Diamond, 2013). The ability may be tested using fluency tasks and task-switching (Delis et al., 2001; Reitan & Wolfson, 1985).

In contrast to this model, Lezak et al. (2004) presents a different conceptualisation of the executive functions. In this model, there are four components: volition; planning and decision making; purposive action; and effective performance.

Lezak et al. (2004) describes volition as the individual's capacity for intentional behaviour. This requires motivation and awareness of one's self. A weakening in volition may result in passivity, which can be hard to test for in a neuropsychological setting.

The ability to plan and make decisions is a complex one, and requires intent, impulse control, sustained attention and ability to view the surroundings and oneself relatively objectively. Examples of tests that may be used to assess this ability are complex figure tasks and the Tower Task (Delis et al., 2001), though observation of everyday activities may be the best at picking this up. Decision making and problem solving are abilities where differences can be observed between patients with anterior lesions and patients with posterior lesions (Channon & Crawford, 1999). The third aspect, purposive action, is the ability to put this plan into action in a purposive way. This requires the ability to initiate, maintain, switch and stop sequences of behaviour (Lezak et al., 2004). Finally, in order to have an effective performance, one must be able to monitor, correct and regulate one's behaviour once it has started.

As demonstrated above, executive functions include many different aspects, and even experts on the subject do not completely agree on how the division between these should be, though they agree that a division is present (Miyake & Friedman, 2012; D. T. Stuss & Alexander, 2000). There are clear similarities between the models, however: They all describe executive functions as the most complex of human behaviours (Lezak et al., 2004), and also the ones most vulnerable in adverse situations (Diamond, 2013). They are the functions that enable the use of other cognitive, emotional and social skills, and are necessary to be able to adapt and act in daily life, and can be described as the control functions of the brain (D. T. Stuss & Alexander, 2000). The fact that these abilities are so diverse, and that it is possible to struggle with some aspects, but not all, underlines the importance of using several neuropsychological tests to examine executive functions.

Frontal circuits

Frontal lobe damage is often implicated in executive dysfunction (Lezak et al., 2004). Within the frontal lobe, five circuits linking the cortical and subcortical structures are found. Emotional disturbances and disorders of executive function are among the possible

consequences of front-subcortical circuit dysfunction (Cummings, 1993). The five frontal cortical-subcortical circuits are the motor circuit, the oculomotor circuit, the dorsolateral prefrontal circuit, the lateral orbitofrontal circuit and the anterior cingulate circuit (Tekin & Cummings, 2002).

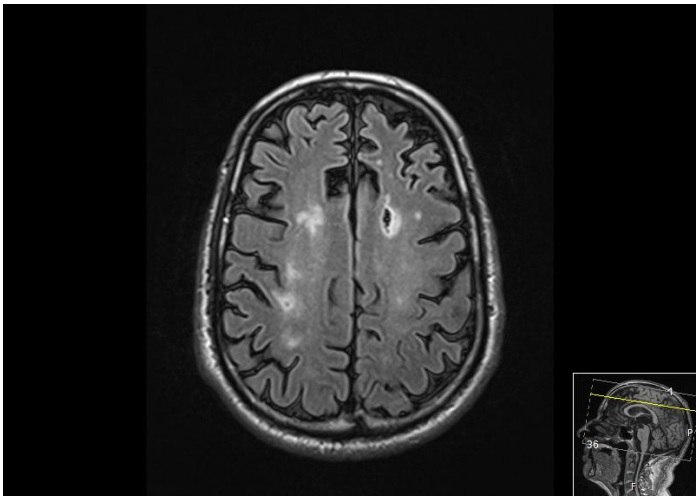


Figure 1 shows one of the MR images taken from one of the patients in the study with ischaemic stroke in frontal white matter regions. A total of 61% of the study participants had ischaemic changes in frontal parts of the brain.

Figure 1 Patient with frontal stroke.

All five circuits involve the same main anatomical structures. They are originating in the prefrontal cortex, projecting to the striatum, connecting to the globus pallidus and substantia nigra, and from there to the thalamus (Tekin & Cummings, 2002). The circuits remain segregated from each other throughout (Cummings, 1993), but they also have open connections to anatomically distant, yet functionally related brain structures (Tekin & Cummings, 2002).

Each of these circuits has a certain behavioural syndrome associated with it. Executive function deficits are associated with lesions in the dorsolateral prefrontal circuit. Damage to this part of the brain is associated with significant impairment on the Stroop task compared to patients with posterior lesions, as well as generally slower response times (D.T. Stuss, Floden, Alexander, Levine, & Katz, 2001). Patients with orbitofrontal lesions have been found to have results on this test comparable to healthy controls (Vendrell et al., 1995).

However, that is not to say that damage to this part of the brain is the only context in which executive dysfunction occurs. Executive function disturbances may arise as a result of damage to a large array of brain regions (Lezak et al., 2004), though the connection between

executive functions and the frontal lobes is the one that is most established in the literature (Godefroy, 2003), and thus it warrants examination.

The dorsolateral prefrontal circuit is described by Tekin and Cummings (2002) as "originating in Broadmann's area 9 and 10 on the lateral surface of the anterior frontal lobe and projects to the dorsolateral head of the caudate nucleus." From there, the pathway continues to the lateral part of the mediodorsal globus pallidus interna and the rostrolateral substantia nigra. From the basal ganglia, the circuit goes to the ventral anterior and mediodorsal thalamus, and from the mediodorsal thalamus back to the dorsolateral frontal cortex. Damage to any of the parts of the circuit may result in marked motoric and executive impairments, including impairments in fluency, set shifting, learning and problem solving (Cummings, 1993).

There is an association between depression and lesions in the dorsolateral prefrontal cortex and the caudate nucleus (Tekin & Cummings, 2002). Depression in degenerative diseases is correlated with reduced activity in the orbitofrontal and dorsolateral cortices as well as the caudate nucleus (Mayberg, 1994).

Neuropsychological associations of anxiety and depression

Anxiety disorders and mood disorders are common ailments in the general population, with a lifetime prevalence rate of 28.8 and 20.8% respectively (Kessler et al., 2005). It may occur on its own, or comorbid to other somatic or cognitive disorders (Stordal, Solhaug, Bosnes, & Følstad, 2012).

Even in individuals without any kind of brain damage, depression may influence a broad range of cognitive domains (Fossati, Ergis, & Allilaire, 2002), and contribute to slower mental processing and attentional deficits (Lezak et al., 2004). The link between depressive symptoms and a reduction in psychomotor speed is often referred to in clinical practice, and often, clinicians will report that patients with depression move and act slower than other patients. Psychomotor retardation is one of the symptoms of depression listed in the ICD-10 (World Health Organization, 1992). Memory impairment has been found in individuals with depression (Taconnat et al., 2010), related to both learning and recall (Lezak et al., 2004). Fatigue is also often a problem for patients with depression (Fava, 2003), which in turn may influence other cognitive domains. Landrø, Stiles, and Sletvold (2001) found that individuals with major

depressive disorder displayed a general deficit on neuropsychological tests, and in particular struggled with working memory and selective attention.

Executive dysfunction has been pointed out as one of the most prominent affected cognitive domains in depression (Fava, 2003; Fossati et al., 2002). It is possible that the memory impairment often found in neuropsychological studies of depression is exacerbated by deficits in executive functions. Taconnat et al. (2010) found that compared to healthy adults, individuals with depression performed worse on memory tasks, but that this difference disappeared when external organising aid was provided. This implies that the observed memory problems in fact was a problem of strategies. Executive dysfunction may also be impaired by the fatigue and reduced quality of life found in depression (Diamond, 2013), as well as rumination (Watkins & Brown, 2002), and is associated with a poorer outcome (Fossati et al., 2002).

While not being described in the literature to the same degree as depression, anxiety disorders have also been found to be associated to cognitive deficits (Airaksinen, Larsson, & Forsell, 2005). The heterogeneity of anxiety disorders complicates the picture, as does the high comorbidity between anxiety and depression (Nitschke & Heller, 2003). In their review, Nitschke and Heller found that attentional biases were present in all anxiety disorders examined, while memory biases were found in panic disorder, post-traumatic stress disorder, social phobia and generalised anxiety disorder. Airaksinen et al. (2005)'s findings were comparable; the patients with anxiety disorders showed significant impairments in episodic memory and executive functioning.

Anxiety and depression in stroke patients

Major depression commonly occurs post-stroke (Pohjasvaara, Vataja, Leppävuori, Kaste, & Erkinjuntti, 2001; Whyte & Mulsant, 2002), and most studies report a prevalence between 20 and 50% (Barker-Collo, 2007). In their review study, Whyte and Mulsant (2002) found that prevalence varies across studies, with numbers ranking from 9 to 37% of the patients. Post-stroke depression is associated with increased mortality and disability (Barker-Collo, 2007), as well as quality of life (Townend et al., 2007).

While not as studied as post-stroke depression, post-stroke anxiety is also common (Whyte & Mulsant, 2002), with reports of anxiety after stroke ranging from 4 to 28%, and remaining consistent over time (Barker-Collo, 2007).

Both depression (Townend et al., 2007) and anxiety (Barker-Collo, 2007) remain high months after the initial stroke. In a study by Bergersen, Frøslie, Stibrant Sunnerhagen, and Schanke (2010), it was found that 2 to 5 years after discharge from the hospital, 36% experienced a possible anxiety disorder, and 28% experienced possible depression. Compared to the healthy adult population, the stroke group experienced a significantly higher degree of mental distress, though it did not differ greatly from other chronically ill populations.

It has been suggested that the increase in anxiety and depression among stroke patients is heavily influenced by the drastic life changes as the patient has to get used to living with sequelae (Lezak et al., 2004). Several of the risk factors for post-stroke depression are the same as the risk factors for depression without stroke, which may indicate influence by psychosocial mechanisms (Whyte & Mulsant, 2002). However, while this probably plays a role, it is unlikely to be the only one. A higher amount of emotional symptoms have been observed in stroke survivors than in patients with orthopaedic issues giving similar challenges, and anosognosia does not alleviate the depression (Loubinoux et al., 2012).

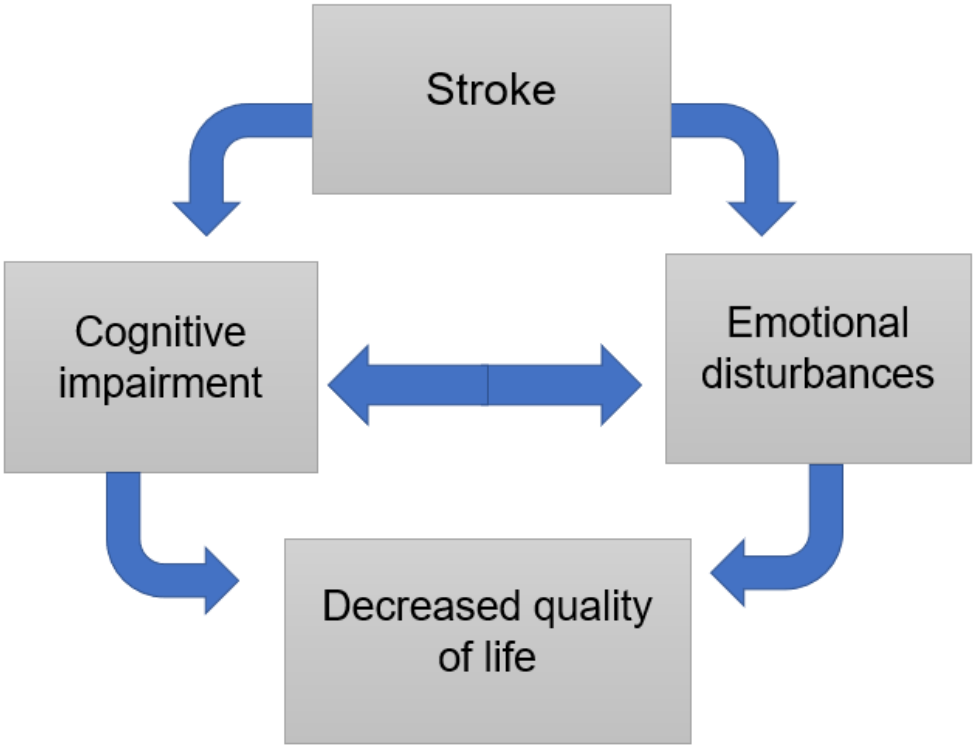


Figure 2 Ecosystem of post-stroke cognitive impairment and emotional disturbances.

Overall, the literature points to a complex relationship between, stroke, cognitive impairment, and emotional disturbances, as illustrated in Figure 2.

Studies have found a link between post-stroke depression and cognitive impairment, in particular memory, orientation, language and attention (Kauhanen et al., 1999). In a study by Pohjasvaara et al. (2002), a higher score on the BDI self-rated depression scale (Beck, Steer, & Brown, 1996) was correlated with executive dysfunction, while no correlation was found between executive dysfunction and clinical evaluation of depression. In another study, an association was found between behavioural regulation, psychomotor speed, and non-verbal problem solving and major depression (Kauhanen et al., 1999).

Several studies have explored the possibility of using antidepressant medication to improve outcome in post-stroke depression. Selective serotonin reuptake inhibitors (SSRIs) have been found to improve depressive symptoms, and this effect may also help other domains, such as motor recovery (Loubinoux et al., 2012). Narushima, Paradiso, Moser, Jorge, and Robinson (2007) found that treatment with antidepressants improved outcome following stroke, independent of whether or not the patients fulfilled the criteria for major depression. Using a protocol of 12 weeks of antidepressant treatment starting within 6 months of the initial stroke, a positive effect was found 21 months after treatment ended. No effect was found immediately after treatment. The authors theorise that the medications play a role in modulating the frontal cortical-subcortical circuits, as described earlier in this paper.

In their work, Vataja et al. (2005) suggest the existence of a subgroup of stroke patients that is characterised by both executive dysfunction and mood disturbances. This group has a higher likelihood of lesions affecting the frontal-subcortical circuits compared to patients with depression, but without executive dysfunction. This may carry implications for treatment practices for this group of patients, and thus is worth examining further.

Research Goals

With an increase in the amount of stroke survivors, research that may enable a better understanding of the relationship between cognitive and emotional symptoms post-stroke remains highly important, as it may contribute to current treatment and rehabilitation. Frontal functions are areas of special interest, as they influence the use of other cognitive skills and play an important role in the individual's daily life, such as employability and ability to maintain reasonable self-care. Using a varied test battery and a longitudinal data set, a better understanding of vulnerable subgroups of stroke patients may be gained.

This study aims to explore different aspects of executive function and their relationship with emotional symptoms one week and three months post-stroke, with the following hypotheses:

H1: Executive function improves during the first three months post-stroke. The improvement is significantly higher in the group of patients with executive impairment, compared to those without.

H2: There is a relationship between performance on tests of executive functions and self-reported anxiety and depression levels.

H2.1: Executive functions correlate with levels of anxiety and depression.

H2.2: The patients who have persistent executive impairment, that lasts at least three months, experience more emotional disturbances compared to those without executive impairment.

H3: The relationship between executive function and depression levels is stronger than the relationship between executive function and anxiety levels.

Methods

Participants

The participants in the study were recruited from the Stroke Unit, Department of Neurology, at Akershus University Hospital, Lørenskog, Norway. This study is based on data from a larger project run by this unit.

The group includes 37 patients with cortical infarctions, and 49 patients with lacunar supratentorial ischaemic infarctions. Initially, 97 participants were included, and 86 remained in the study until the three-month mark. The data analyses in this project are based on the 86 patients where longitudinal data was available, enabling observation of change over time.

The average age at recruitment was 64.4 years, and 68% of the participants were male. The inclusion criteria for the project were either cortical or lacunar ischemic infarctions, Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) score ≥ 23, age between 40 and 79 years, no symptoms of visual or auditory neglect, and no aphasia. All participants reported to never have experienced a stroke before. Exclusion criteria were prior strokes, or another stroke occurring between the testing phases of the study, as well as a history of other neurologic and/or psychiatric disorders. The sample is described in detail in another study (Selnes et al., 2015).

Design

The study was approved by the Regional Ethics Committee in Norway and was carried out in accordance with the Helsinki Declaration, as well as the Norwegian Health and Research Act. All participants in the study gave informed written consent.

The data was collected at one week and three months after the initial stroke, while the participants were being monitored and/or received follow-up at the Department of Neurology. All the tests were performed by the same neuropsychologist, and the testing was performed in Norwegian. A variety of different neuropsychological tests were used, as well as comprehensive psychological and medical screenings. Results from some tests included in the larger project were not included in this particular study, as they were deemed non-relevant.

Measures

To examine the participants' general cognitive ability, the Vocabulary and Matrixes subtests from the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) were used. In addition, several tests were included as measures of executive function. The tests chosen are not purely measures of executive function, as several of them also measure other abilities, such as attention and processing speed (Delis et al., 2001; Wechsler, 2003). However, the term executive function is still used as a descriptor for the tests, as they all measure functions related to the anterior part of the brain and can be said to be part of the larger executive function construct. These tests are: the Trail Making Test A and B (TMT-A and TMT-B) (Reitan & Wolfson, 1985); the Digit Symbol-Coding and the Letter-Number Sequencing subtests of the WAIS-III (Wechsler, 2003); the Controlled Oral Word Association Test – Letter Fluency Test (FAS) and Category Fluency Test (Reitan & Wolfson, 1985); and the Colour-Word Interference Test 1-4 (the CWIT or Stroop) of the Delis-Kaplan Executive Function System (D-KEFS) (Delis et al., 2001). Emotional symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) and the Geriatric Depression Scale (GDS-20) (Sheikh & Yesavage, 1986).

Vocabulary (WASI) (Wechsler, 1999). This subtest is considered both a measure of the participant's verbal ability and general cognitive ability. The participant is required to define the words presented by the test administrator, and answers are scored according to abstraction levels as well as correctness.

Matrixes (WASI) (Wechsler, 1999, 2003). A timed pattern completion test, it presents the participants with images increasing in difficulty, where they must choose how to best complete the presented figure. It is a measure of abstract problem solving, as well as language-independent general cognitive ability.

Trail Making Test (TMT) (Reitan & Wolfson, 1985). The test consists of part A and part B. During part A, the participant draws lines to connect circles numbered 1-25 in ascending order. In part B, the participant must alternate between drawing the line between letters and numbers in ascending and alphabetical order. The test is a measure of visual scanning, processing speed, mental flexibility and general executive functions (Lezak et al., 2004). Part B requires more mental flexibility than part A, where speed is a bigger factor. The TMT is timed, with a lower second count representing a better score.

Controlled Oral Word Association Test – Letter Fluency Test (FAS) and Category Fluency Test (Reitan & Wolfson, 1985). These two tests are measures of letter and category fluency. The first of the tests, the FAS, requires the participant to list as many words as possible in one minute, starting with the letter F, followed by the letters A and S. The Categories test asks the participant to list as many animals as possible in one minute. The score on both tests is based on the total amount of actual words listed by the participant.

Digit Symbol-Coding (Wechsler, 2003). This subtest of the WAIS-III measures processing speed and attention, as well as learning and organisation of information. The participant is shown nine digits with corresponding symbols and is then required to fill in these symbols in the appropriate boxes on a sheet of paper with numbers. They are instructed to do this as fast and correctly as possible. The score is calculated by counting the amount of correctly drawn symbols during a set time of 120 seconds.

Letter-Number Sequencing (Wechsler, 2003). Another WAIS-III subtest, this is a measure of working memory, attention and mental control. During this test, the participant is read several letters and numbers, in a jumbled order. They must then repeat the numbers in ascending order, followed by the letters in alphabetical order. The score consists of the amount of correctly recited series.

Colour-Word Interference Test (Delis et al., 2001). Part of the D-KEFS test battery, these tests consists of four conditions, measuring different aspects of attention and response inhibition. The conditions are 1) Colour naming (where the participant is shown coloured squares and tell the administrator which colour they are), 2) word reading (the participant has to read the words printed in black ink); 3) inhibition (where the participant names the colour of the ink, while the words spell another colour); 4) inhibition/switching (where the additional task of reading the word, not the colour, if words printed in boxes, is added). All tasks are timed and must be performed as quickly as possible. The score is the number of seconds spent on each task.

Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). This is a self-report questionnaire, where the patient is given 14 statements. 7 correspond to symptoms of anxiety, and 7 to symptoms of depression (e.g. “I get sudden feelings of panic”; “I feel cheerful”). They must then indicate how much they agree with the statement during the past week by marking a number between 0 (“not at all”) and 3 (“most of the time”). A total score above 7 (Leiknes, Dalsbø, & Siqveland, 2016) on the entire questionnaire, or above 4 on either

of the subscales, indicates a possible clinical problem, and further diagnostics is recommended. The Norwegian version of the questionnaire was used, which is considered a valid screening tool for psychological distress (Leiknes et al., 2016). HADS is considered to be a good screening tool for depression and anxiety in patients with physical illness (Stern, 2014).

Geriatric Depression Scale (GDS-20) (Sheikh & Yesavage, 1986). This is a screening tool for depressive symptoms in older adults and was used at three months post-stroke. A short version of GDS, GDS-20 was chosen. It is a self-report questionnaire, consisting of 20 questions (e.g. "Do you often get bored?" and "Are you in good spirits most of the time?"). The participant is required to either agree or disagree with the statements. A score above 4 may be a sign of mild depression; one above 8 indicates moderate depression; above 11 indicates severe depression. GDS-20 has been found to be a strong predictor of quality of life (Jönsson, Lindgren, Hallström, Norrving, & Lindgren, 2005), and has proved to be a good screening tool for depression (Gottfries, Noltorp, & Nørgaard, 1997).

To assess hypotheses H1 and H2.2, the data was split into two groups. The executive impairment group comprises the participants who scored at least 1.5 standard deviations (i.e. a T-score of 35 or below) below the mean for their normative group on one or more of the executive tests described above, at both one week and three months post-stroke. The comparison group comprises the remainder of the study participants, not satisfying the criteria for inclusion into the executive impairment group. 1.5 standard deviations was chosen as the cut-off point rather than 1 standard deviation, in order to lessen the risk of classifying intact individuals as impaired (Lezak et al., 2004; Petersen, 2004).

Statistical Analyses

The analyses in this study were performed using the Statistical Package for Social Sciences software, version 25. To compare improvement in executive functions in the groups, differential scores were computed by subtracting the 1-week score from the 3-month score. To compare categorical variables, the χ^2 test was used.

Prior to the analysis, the data was examined for normality using values for skewness and kurtosis, as well as a visual examination using histograms, Q-Q plots and stem-and-leaf plots. The results indicated a non-normal distribution of the emotional measures (HADS and GDS-20) (kurtosis >2, (George & Mallery, 2010)), as well as CWIT 1 and 2. After consultation

with a statistician, it was decided to still utilise the independent measures t-test to examine group differences in continuous variables between the executive impairment group and the comparison group, with bootstrapping performed as described by Field (2013). The t-test was considered the best fit for the data due to the large sample size and the robustness of the test.

For estimation of effect sizes, Cohen's *d* was calculated by using the formula $d = (M_1 - M_2)/\sigma$, where σ is the pooled SD (Lakens, 2013).

Linear regression analysis was used to examine the effects of the emotional variables on the executive measures of the whole group (hypotheses H2.1 and H3). This method was chosen as it provides with a standardised β value that enables comparison across models, as well as showing if each of the independent variables significantly contributes to the changes seen in the dependent variable. First, bivariate linear regression models were estimated for the executive variables (TMT-A and B, Letter-Number Sequencing, FAS, Categories, Digit-Symbol Coding, CWIT 1-4) with HADS Depression subscale, HADS Anxiety subscale and GDS-20 as independent variables. Multiple linear regression models were then estimated to the executive variables found to be significantly associated to one or more of the independent variables. CWIT 1, Categories and FAS were excluded.

Multiple linear regression analysis was then used to examine the effect of both symptoms of anxiety and depression on the selected executive measures. To control for age effect, age was entered as one of the independent variables together with HADS-A and HADS-D. By including both the measures for depression and anxiety into the same model one can assess which of the two factors has the bigger impact on executive function. A separate analysis used GDS-20 and age as the independent variables. Separate models were estimated for executive measures and emotional measures and 1 week and likewise for the measures collected at 3 months.

The assumptions for linear regression analysis were tested by using standard methods. None of the independent variables were a combination of other independent variables. The Tolerance and VIF values were all well within the acceptable limits, showing no issues with multicollinearity (Field, 2013). Linearity, homoscedasticity and normal distribution of the residuals were examined using histograms and scatter plots. No issues related to linearity and homoscedasticity were found. A slight tendency of skewed distribution of residuals was followed by bootstrapping the confidence intervals, as recommended by Field (2013).

Results

A summary of the demographic characteristics of the sample is presented in Tables 2 and 3. Significant group differences were found in the measures marked in the table. All the executive measures were significantly different, as the groups were defined by whether executive impairment was present.

When comparing the emotional measures (Table 1), a significant group difference was found for the depression subscale of the Hospital Anxiety and Depression Scale at both points in time (p=.01 and p=.03, respectively), but not the anxiety subscale. There was no significant difference between the groups in the GDS-20 responses. Cohen's *d* was then calculated, showing medium effect sizes for the depression subscale of HADS, as well as a small to medium effect size for GDS-20 (Field, 2013).

Table 1. *Independent t-test comparing group differences on emotional measures.*

	Groups					
	Impairment	Comparison	t	df	p	*d*
HADS-A 1w (*SD*)	5.5 (3.9)	5.3 (3.8)	0.3	84	.80	.05
HADS-A 3m (*SD*)	4.4 (4.0)	4.3 (3.6)	0.1	84	.89	.03
HADS-D 1w (*SD*)	4.3 (3.6)	2.6 (2.6)	2.6*	84	.01	.54
HADS-D 3m (*SD*)	4.4 (3.6)	2.8 (2.9)	2.3*	79	.02	.49
GDS-20 3m (*SD*)	4.4 (4.5)	3.2 (3.3)	1.4	75	.17	.30

For the whole group, the mean scores on the depression subscale of HADS at one week and three months were 3.4 (SD 3.2) and 3.6 (SD 3.3) respectively. The mean score on the anxiety subscale was 5.4 (SD 3.8) at one week and 4.4 (SD 3.8) at three months. The mean score on GDS-20 was 3.8 (SD 4.0).

Table 2. *Patient characteristics.*

	Whole Group (N=86)	Executive Impairment Group (N=42)	Comparison Group (N=44)
Age 41-79 (*SD*), y	64.6 (9.2)	65.4 (9.9)	63.8 (8.7)
Education 7-17 (*SD*), y	11.0 (2.9)	10.8 (3.1)	11.1 (2.8)
Gender, n male (%)[1] *	59 (68.6%)	35 (83.3%)	24 (54.5%)
Handedness, n right (%)[1]	77 (89.5%)	37 (88.1%)	40 (90.9%)
NIHSS-1 day (*SD*)	2.7 (2.6)	4.0 (4.0)	3.1 (2.5)
NIHSS-3 months (*SD*)*	0.7 (1.6)	1.0 (1.9)	0.4 (1.1)
MMSE (*SD*)	28.4 (1.7)	27.5 (1.8)	29.3 (1.2)
Matrix Reasoning (*SD*)*	13.9 (5.3)	11.8 (4.8)	15.9 (4.9)
Vocabulary (*SD*)*	59.2 (10.1)	55.0 (11.3)	63.1 (6.7)

Table 3. *Executive measures.*

	Whole Group (N=86)	Executive Impairment Group (N=42)	Comparison Group (N=44)
Digit-Symbol 3m (*SD*)*	44.1 (15.1)	35.3 (10.8)	52.3 (13.9)
TMT-A 1w (*SD*)*	55.5 (30.6)	71.9 (35.3)	39.8 (12.3)
TMT-A 3m (*SD*)*	48.0 (20.0)	58.0 (22.1)	39.5 (11.3)
TMT-B 1w (*SD*)*	136.0 (65.4)	176.4 (66.3)	93.4 (35.6)
TMT-B 3m (*SD*)*	118.8 (53.7)	149.3 (57.1)	89.8 (28.8)
Letter-Number 1w (*SD*)*	7.6 (2.5)	6.7 (2.4)	8.5 (2.4)
Letter-Number 3m (*SD*)*	8.3 (2.4)	7.7 (2.7)	8.9 (2.0)
FAS 1w (*SD*)*	31.4 (12.6)	23.6 (9.3)	38.8 (10.8)
FAS 3m (*SD*)*	35.4 (13.0)	27.9 (9.6)	42.5 (11.8)
Categories 1w (*SD*)*	17.5 (5.7)	14.1 (4.2)	20.7 (4.0)
Categories 3m (*SD*)*	18.3 (4.6)	16.1 (4.3)	20.3 (7.5)
CWIT Colours 1w (*SD*)*	39.1 (13.5)	46.9 (15.1)	31.8 (5.0)
CWIT Colours 3m (*SD*)*	37.5 (10.8)	43.4 (10.3)	32.0 (7.8)
CWIT Reading 1w (*SD*)*	28.7 (10.6)	34.0 (12.7)	23.6 (3.9)
CWIT Reading 3m (*SD*)*	26.7 (6.9)	29.8 (6.1)	23.8 (6.4)
CWIT Inhibition 1w (*SD*)*	85.5 (37.8)	105.8 (41.8)	67.1 (20.9)
CWIT Inhibition 3m (*SD*)*	78.4 (30.6)	92.7 (32.1)	64.8 (21.7)
CWIT Switching 1w (*SD*)*	94.9 (47.6)	119.9 (57.0)	72.2 (18.0)
CWIT Switching 3m (*SD*)*	83.1 (24.5)	97.8 (20.6)	69.4 (19.5)

*Significant group difference, $p<.05$. [1]=χ^2 used. For the remainder an independent samples t-test was used. Executive impairment group = study participants scoring 1.5 standard deviations below the mean on a test measuring an aspect of executive function at both one week and three months. Comparison group = the study participants not satisfying criteria for executive impairment.

Change over time was calculated by subtracting test scores at one week from test scores at three months. Comparison of the change over time in the impairment and comparison groups (Table 4) showed that the impairment group's change values were significantly lower on the measures TMT-A, TMT-B, and CWIT 1-4. As these scores are time spent on the task, a lower score represents a better result, and so they had improved more at three months than the comparison group. The impairment group also had a higher change value on the Category Fluency Test. There was no difference in the remaining measures, including the measures of emotional distress. For the whole group, improvement was found on all measures, except for the anxiety subscale of HADS, which indicated a slight increase in anxiety. The same tendency is observed when the sample is split into groups. On the significant measures, the effect sizes were in the range medium to large. The non-significant measures had low effect sizes.

Table 4. *Comparison of change over time between groups.*

	Groups					
	Impairment	Comparison	t	df	p	*d*
TMT-A (*SD*)	-13.9 (27.6)	-.1.3 (11.4)	-2.7*	54	.01	.60
TMT-B (*SD*)	-29.4 (35.4)	-8.6 (25.3)	-3.1*	72	<.01	.68
Letter-Number (*SD*)	1.0 (2.1)	0.4 (2.0)	1.4	84	.15	.29
FAS (*SD*)	4.2 (7.2)	3.6 (8.3)	0.4	84	.72	.08
Category (*SD*)	2.0 (4.3)	-0.4 (5.6)	2.2*	84	.03	.48
CWIT 1 (*SD*)	-3.5 (9.0)	0.2 (7.5)	-2.1*	84	.04	.45
CWIT 2 (*SD*)	-4.2 (9.7)	0.2 (7.4)	-2.5*	68	.02	.51
CWIT 3 (*SD*)	-16.8 (24.6)	-2.3 (21.1)	-2.9*	82	.01	.63
CWIT 4 (*SD*)	-22.9 (50.1)	-2.7 (13.0)	-2.5*	44	.02	.55
HADS-D (*SD*)	-0.1 (3.7)	-0.2 (2.0)	0.1	63	.90	.03
HADS-A (*SD*)	1.1 (3.3)	1.0 (3.9)	0.1	84	.90	.02

Note: Change over time was calculated by subtracting test scores at one week from test scores at three months.

The bivariate linear regression analysis showed that while most of the executive measures were significantly associated to the emotional measures, Category, FAS and CWIT 2 and 3 were not (Table 5). They were thus excluded from multiple analysis.

Table 5. *Simple Bivariate Regression Models, β values (N=86).*

	1-HADS A	1-HADS D	2-HADS A	2-HADS D	GDS-20
Digit-Symbol			.06	-.26*	-.18
TMT-A	-.13	.26*	-.02	.24*	.13
TMT-B	-.17	.37*	-.05	.26*	.12
Letter-Number	-.22*	-.37*	.09	-.01	.00
FAS	.05	-.15	.10	-.03	.01
Category	.01	-.11	.11	-.17	-.12
CWIT Colours	.01	.22*	.02	.08	.01
CWIT Reading	.01	.10	.10	.11	.14
CWIT Inhibition	-.06	.03	.05	.18	.13
CWIT Switching	.07	.16	.01	.23*	.18

Note: TMT-A, TMT-B, and CWIT1-4 scores have been multiplied with -1, so that a higher score means a better result. Each of the emotional measures was analysed with the executive data collected at the corresponding date. *p < .05.

Each of the emotional measures was analysed with the executive data collected at the corresponding date. The multiple linear regression analysis was performed with one of the executive measures as the dependent variable and age together with HADS-A and HADS-D as the independent variables. The analysis revealed that HADS-D was significantly negatively associated with the following executive measures: TMT-A 1 week (p=<.01), TMT-A 3 months (p=.02), TMT-B 1 week (p=<.01), TMT-B 3 months (p=.02), Letter-Number Sequencing 1 week (p=.05), CWIT Switching (p=.05) and Digit-Symbol Coding 3 months (p=.01). A negative tendency was found for CWIT Colours 1 week (p=.07).

In contrast to HADS-D, HADS-A had a significant positive influence on the outcome on TMT-A 1 week (p=<.01) and TMT-B 1 week (p=<.01). HADS-A had no negative influences on the executive measures.

When the multiple linear regression analysis was performed with one of the executive measures as the dependent variable and age together with GDS-20 as the independent variables, GDS-20 had a significant negative influence on the outcome only on the Digit-Symbol Coding subtest (p=.05), while a tendency was found on CWIT Switching (p=.08).

In summary, HADS-D significantly influenced the outcome on 7 executive measures, while HADS-A significantly influenced 2. GDS-20 significantly influenced one of the executive measures. All the regression models were found to be statistically significant, due to strong age effects. The results of the multiple regressions are presented below in Tables 6-11.

Table 6. *Variables predicting Trail Making Test A (N=86).*

Trail Making Test A 1 week					**Trail Making Test A 3 months**				
	B (SE)	β	p	R^2		B (SE)	β	p	R^2
Age	-.94 (.33)	-.28	<.01	.23	Age	-.67 (.22)	-.31	<.01	.19
HADS-D* 1w	-3.32 (1.10)	-.35	<.01		HADS-D* 3m	-1.78 (.77)	-.30	.02	
HADS-A* 1w	2.58 (.91)	.32	<.01		HADS-A 3m	.83 (.68)	.16	.23	
					Age	-.91 (.22)	-.38	<.01	.16
					GDS-20	-.71 (.50)	-.14	.16	

TMT-A scores have been multiplied with -1, so that a higher score means a better result.

Table 7. *Variables predicting Trail Making Test B (N=86).*

Trail Making Test B 1 week					**Trail Making Test B 3 months**				
	B (SE)	β	p	R^2		B (SE)	β	p	R^2
Age	-2.13 (.63)	-.31	<.01	.39	Age	-2.50 (.56)	-.43	<.01	.30
HADS-D* 1w	-10.44 (2.10)	-.52	<.01		HADS-D* 3m	-4.75 (1.75)	-.30	.02	
HADS-A* 1w	7.65 (1.72)	.45	<.01		HADS-A 3m	2.22 (1.44)	.16	.20	
					Age	-2.87 (.55)	-.50	<.01	.26
					GDS-20	-1.77 (1.27)	-.13	.17	

TMT-B scores have been multiplied with -1, so that a higher score means a better result.

Table 8. *Variables predicting Letter-Number Sequencing (N=86).*

Letter-Number Sequencing 1 week					Letter-Number Sequencing 3 months				
	B (SE)	β	p	R^2		B (SE)	β	p	R^2
Age	-.11 (.03)	-.39	<.01	.28	Age	-.12 (.03)	-.45	<.01	.20
HADS-D* 1w	-.18 (.09)	-.22	.05		HADS-D 3m	-.05 (.09)	.07	.59	
HADS-A 1w	-.06 (.07)	.07	.41		HADS-A 3m	.01 (.08)	-.16	.87	
					Age	-.12 (.03)	-.44	<.01	.19
					GDS-20	-.01 (.06)	-.01	.94	

Table 9. *Variables predicting CWIT Colours (N=86).*

CWIT Colours 1 week					CWIT Colours 3 months				
	B (SE)	β	p	R^2		B (SE)	β	p	R^2
Age	-.25 (.16)	-.17	.12	.09	Age	-.32 (.13)	-.28	.02	-.25 (.16)
HADS-D 1w	-.97 (.53)	-.23	.07		HADS-D 3m	-.04 (.45)	-.01	.93	-.97 (.53)
HADS-A 1w	.42 (.43)	.12	.33		HADS-A 3m	.15 (.39)	-.05	.70	.42 (.43)
					Age	-.31 (.12)	-.27	.01	
					GDS-20	-.05 (.29)	-.02	.86	

CWIT Colours scores have been multiplied with -1, so that a higher score means a better result.

Table 10. *Variables predicting CWIT Switching (N=86).*

CWIT Switching 1 week					CWIT Switching 3 months				
	B (SE)	β	p	R^2		B (SE)	β	p	R^2
Age	-1.07 (.57)	-.21	.06	.07	Age	-.59 (.29)	-.22	.05	.12
HADS-D 1w	-2.80 (2.58)	-.15	.28		HADS-D* 3m	-2.00 (.99)	-.27	.05	
HADS-A 1w	.45 (1.80)	.03	.80		HADS-A 3m	.81 (.88)	.12	.36	
					Age	-.73 (.28)	-.28	.01	.11
					GDS-20	-1.14 (.64)	-.19	.08	

CWIT Switching scores have been multiplied with -1, so that a higher score means a better result.

Table 11. *Variables predicting Digit-Symbol Coding (N=86).*

Digit-Symbol Coding 3 months				
	B (SE)	β	p	R^2
Age	-.62 (.16)	-.38	<.01	.28
HADS-D* 3m	-1.53 (.55)	-.34	.01	
HADS-A 3m	.82 (.49)	.21	.10	
Age	-.75 (.16)	-.46	<.01	.24
GDS-20*	-.71 (.36)	-.19	.05	

Discussion

The main goal of this paper was to study how executive impairment and emotional disturbances interact. When comparing the group with persistent executive impairment to the group without executive impairment, the group with executive impairment experienced significantly more depressive symptoms, while no group differences were found in anxiety levels. This is consistent with Vataja et al. (2005)'s theory that there is a subgroup of stroke patients that experience both executive impairment and mood disturbances. The fact the group differences for the anxiety measures were not found to be significant strengthens the theory that the executive impairment is not solely due to psychological distress.

It is surprising that the depression subscale of HADS was significantly higher in the executive impairment group, but not GDS-20, considering that they measure the same construct. This may be related to HADS allowing the respondents to give graded responses; i.e., one can agree partially with a statement. In contrast, GDS-20 requires the respondent to fully agree with the statement as presented. Considering that HADS has shown itself to be a good screening tool (Leiknes et al., 2016), the graded responses might be an advantage, especially when looking for subclinical symptoms.

As initially hypothesised, the executive impairment group improved more than the comparison group on a majority of the executive measures. No group differences for changes over time were found on the tests Letter Fluency, Letter-Number Sequencing and both subscales of HADS. No comparison to GDS-20 is possible in this instance, as GDS-20 was only administered at the three-month point. In conjunction with the previous results, the lack of a group difference for changes in the HADS measures over time is interesting. The impairment group had significantly higher scores of psychological distress, and thus a larger potential for improvement. Despite this, no changes were found, which may have implications for therapeutic practice.

An interesting finding in the improvement data, is that the patients improve on all measures but the anxiety subscale of HADS. This is in line with the findings of Morrison, Pollard, Johnston, and MacWalter (2005), who found that anxiety remained stable over a period of three years post-stroke. This in contrast to post-stroke depression, which was reduced over time in Morrison et al.'s study. The finding of a similar pattern of changes in emotional

symptoms over time in the study of Morrison and colleagues and our study may point to the sample of our study being representative.

The results of the multiple regression analysis showed that when controlling for age, the depression subscale of HADS significantly influenced outcome on most of the executive measures, which also supports the idea that there is a subgroup of patients where depression and executive dysfunction co-occur, as suggested by Vajata et al. (2005).

Additionally, it was hypothesised that the depression subscale would have a stronger link to the executive measures than the anxiety subscale. Not only was this found to be true, but on the two measures where the anxiety subscale influenced the outcome, higher anxiety correlated with a better performance. The regression analysis showed that when the anxiety subscale increased by one, the scores on Trail Making Test A and B was improved by 2.58 and 7.65 seconds respectively.

Several stroke patients experience challenges with initiating actions (Cumming, Marshall, & Lazar, 2013). The average anxiety level in the sample was subclinical, and low levels of anxiety may help improve results by making the patient more alert, while higher levels of anxiety is a greater hindrance to mental efficiency (Lezak et al., 2004). This helpful mobilisation of effort and cognitive ability is referred to as facilitating anxiety, as opposed to debilitating anxiety, which is anxiety that hinders performance (Couch, Garber, & Turner, 1983).

Limitations and strengths

There are some ways in which the sample in this study differs from the expected. First, the average age of the patients in this study was 64.4 years. This is approximately 10 years younger than the average first-time stroke patient (Ellekjær & Selmer, 2007). In large part this is due to the inclusion criteria specifying age between 40 and 79 years. In other words, this study has a young sample of patients. It may be that the results are less affected by age-related cognitive decline than it would have been had there been no upper age limit. This can be both a limitation and a strength: Most stroke studies examine populations older than the current population, and as this group is expected to live longer with the consequences of the stroke, more knowledge of how this affects them will be of use at both a therapeutic and societal level.

Men are overrepresented in the sample, and this tendency is increased when the sample is split into groups based on executive impairment, with 68.6% and 83.3% men respectively. This overrepresentation is likely also due to the young age of the sample, as men on average get their first stroke at a younger age than women (Kvåle et al., 2018). A younger sample is therefore likely to contain a larger percentage of men. The same pattern is found in other studies, such as Schneider, Kornejeva, Vibo, and Kõrv (2017)'s study of young stroke patients in Estonia. This shows that the age skew represents a pattern that is also present in the real world but may nevertheless have had impact on the result of the analyses.

Finally, it is a limitation to the study that two patient groups are compared without a healthy control group. The study partially compensates for this by using an impairment group and a comparison group, consisting of patients without executive impairment. An extension of the data material to include healthy controls would be a reasonable next step should more data be collected.

The study has several strengths adding to the validity and reliability of the results. The sample size is large, and the data set is longitudinal. In addition, the same neuropsychologist collected the neuropsychological and emotional data at both points in time, meaning there is no interference from using several test administrators.

Clinical implications

Executive dysfunction has been linked to reduced responsivity to antidepressant medications (Alexopoulos et al., 2005; Dunkin et al., 2000). It may negatively influence the patient's ability to adhere to and benefit from a treatment regime for anxiety and/or depression (Mohlman, 2005). Increased knowledge of the interactions between executive functions and emotional distress is of importance, as these patients may need specialised follow-up.

The research on which interventions are the most useful in this case is somewhat lacking. In a recent Cochrane review, Chung, Pollock, Campbell, Durward, and Hagen (2013) examined 13 different studies to examine the effect of cognitive rehabilitation programmes on acquired brain injuries (strokes and traumatic brain injuries). No evidence was found that these interventions were helpful for patients with executive dysfunction, though the authors note that more research should be done, with special focus on the effect of cognitive rehabilitation on

executive functions. Improving the quality of life for this patient group through training of executive functions therefore needs further investigation.

The higher levels of psychological distress in the executive impairment group may be due to both physiological processes in the brain, as well as life changes and new challenges in the patients' lives. A possible intervention would be to assist this group in a greater degree with daily life and organizational skills, so that the burden of the symptoms is lessened. This could be done in rehabilitation wards in cooperation between neuropsychologists and occupational therapists, as well as helping bring awareness to this group's need for extra attention during follow-up appointments.

While the executive impairment group experienced more symptoms of depression, both groups had a mean score on the depression subscale of HADS that is below the suggested cut-off point for depression (Stern, 2014). Fewer patients in this study satisfied the criteria for depression than one might expect given for instance the work of Gaete and Bogousslavsky (2008). In this review approximately one third of the patients were found to have post-stroke depression, either shortly after the stroke, or developed over time.

It is possible that the lower rate of depression is connected to the fact that the participants in the study are relatively high-functioning. The exclusion criteria combined with having to go through an intensive neuropsychological examination one week after the stroke meant that the patients with more severe symptoms were not healthy enough to be included in the experimental group. It is therefore possible that the results found in this high-functioning group would be more severe in a more affected group of patients. Thus, the results of this study are especially important as they can spread awareness of this constellation of symptoms.

Conclusion

The study shows that after a stroke, executive impairment and emotional disturbances are common, and while the executive impairment improves within 3 months, the same is not seen for the emotional disturbances. The patients with executive impairment have, as a group, more depressive symptoms than the patients without executive impairment, while there are no group differences in anxiety.

There is a negative relationship between the level of depression the patients experience and how well they do on several executive measures. The relationship between executive function and depression levels is stronger that the relationship between executive function and anxiety levels.

While it is not possible to use only the executive measures to identify which patients are at a higher risk for depressive symptoms and reduced quality of life, it certainly has its place as part of a larger diagnostic process.

Future expansion of the data material to include healthy controls would be useful, as would further research to find the best treatment options for the group described in this paper.

While the current literature is not conclusive in which interventions should be used, it is clear that cognition, emotional distress and cerebrovascular disease influence each other, and a pragmatic approach would be to improve the areas of a patient's life that are possible to improve, in order to minimise symptoms in different areas. Even if treatment of, for example, depression does not change the executive impairment, it might still help increase the quality of life for the patient.

References

Airaksinen, E., Larsson, M., & Forsell, Y. (2005). Neuropsychological functions in anxiety disorders in population-based samples: evidence of episodic memory dysfunction. *Journal of Psychiatric Research, 39*(2), 207-214. doi:https://doi.org/10.1016/j.jpsychires.2004.06.001

Alexopoulos, G. S., Kiosses, D. N., Heo, M., Murphy, C. F., Shanmugham, B., & Gunning-Dixon, F. (2005). Executive Dysfunction and the Course of Geriatric Depression. *Biological Psychiatry, 58*(3), 204-210. doi:https://doi.org/10.1016/j.biopsych.2005.04.024

Baddeley, A. (1992). Working memory. *Science, 255*(5044), 556.

Barker-Collo, S. L. (2007). Depression and anxiety 3 months post stroke: Prevalence and correlates *Archives of Clinical Neuropsychology, 2007*(22), 519-531. doi:10.1016/j.acn.2007.03.002

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Beck Depression Inventory-II.* San Antonio, TX: The Psychological Corporation.

Bergersen, H., Frøslie, K. F., Stibrant Sunnerhagen, K., & Schanke, A.-K. (2010). Anxiety, Depression, and Psychological Well-being 2 to 5 years Poststroke. *Journal of Stroke and Cerebrovascular Diseases, 19*(5), 364-369. doi:https://doi.org/10.1016/j.jstrokecerebrovasdis.2009.06.005

Channon, S., & Crawford, S. (1999). Problem-solving in real-life-type situations: the effects of anterior and posterior lesions on performance. *Neuropsychologia, 37*(7), 757-770. doi:https://doi.org/10.1016/S0028-3932(98)00138-9

Chung, C. S. Y., Pollock, A., Campbell, T., Durward, B. R., & Hagen, S. (2013). Cognitive rehabilitation for executive dysfunction in adults with stroke or other adult non-progressive acquired brain damage. *Cochrane Database of Systematic Reviews*(4). doi:10.1002/14651858.CD008391.pub2

Colle, F., Bonan, I., Gellez Leman, M. C., Bradai, N., & Yelnik, A. (2006). Fatigue after stroke. *Annales de Réadaptation et de Médecine Physique, 49*(6), 361-364. doi:https://doi.org/10.1016/j.annrmp.2006.04.010

Couch, J. V., Garber, T. B., & Turner, W. E. (1983). Facilitating and Debilitating Test Anxiety and Academic Achievement. *Psychol Rec, 33*(237). doi: https://doi.org/10.1007/BF03394841

Cumming, T. B., Marshall, R. S., & Lazar, R. M. (2013). Stroke, cognitive deficits, and rehabilitation: still an incomplete picture. *International Journal of Stroke, 8*(1), 38-45. doi:doi:10.1111/j.1747-4949.2012.00972.x

Cummings, J. L. (1993). Frontal-subcortical circuits and human behavior. *Archives of Neurology, 50*(8), 873-880. doi:10.1001/archneur.1993.00540080076020

del Ser, T., Barba, R., & Morin, M. (2005). Evolution of cognitive impairment after stroke and risk factors for delayed progression. . *Stroke, 2005*(36), 2670 – 2675.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis and Kaplan D-KEFS Executive Functions System*. San Antonio, TX: The Psychological Corporation.

Diamond, A. (2013). Executive Functions. *Annual Review of Psychology, 64*(1), 135-168. doi:10.1146/annurev-psych-113011-143750

Dunkin, J. J., Leuchter, A. F., Cook, I. A., Kasl-Godley, J. E., Abrams, M., & Rosenberg-Thompson, S. (2000). Executive dysfunction predicts nonresponse to fluoxetine in major depression. *Journal of Affective Disorders, 60*(1), 13-23. doi:https://doi.org/10.1016/S0165-0327(99)00157-3

Ellekjær, H., & Selmer, R. (2007). Hjerneslag - like mange rammes, men prognosen er bedre *Tidsskriftet for den norske legeforening, 2007*(127), 740-743.

Engstad, T., Viitanen, M., & Almkvist, O. (2007). Kognitiv svikt etter hjerneslag - dianostikk og håndtering. *Tidsskriftet for den norske legeforening, 2007*(127), 1390-1393.

Epstein, J. N., Erkanli, A., Conners, C. K., Klaric, J., Costello, J. E., & Angold, A. (2003). Relations Between Continuous Performance Test Performance Measures and ADHD Behaviors. *Journal of Abnormal Child Psychology, 31*(5), 543-554. doi:10.1023/A:1025405216339

Fava, M. (2003). Symptoms of fatigue and cognitive/executive dysfunction in major depressive disorder before and after antidepressant treatment. *The Journal of Clinical Psychiatry, 64*(14), 30-34.

Field, A. (2013). *Discovering Statistics Using IBM SPSS Statistics* London: Sage.

Fiore, F., Borella, E., Mammarella, I. C., & De Beni, R. (2012). Age differences in verbal and visuo-spatial working memory updating: Evidence from analysis of serial position curves. *Memory, 20*(1), 14-27. doi:10.1080/09658211.2011.628320

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. . *J Psychiatr Res*(12), 189–198.

Fossati, P., Ergis, A. M., & Allilaire, J. F. (2002). Executive functioning in unipolar depression: a review. *L'Encephale, 28*(2), 97-107.

Friedman, N. P., & Miyake, A. (2017). Unity and diversity of executive functions: Individual differences as a window on cognitive structure. *Cortex, 86*, 186-204. doi:https://doi.org/10.1016/j.cortex.2016.04.023

Gaete, J. M., & Bogousslavsky, J. (2008). Post-stroke depression. *Expert Review of Neurotherapeutics, 8*(1), 75-92. doi:10.1586/14737175.8.1.75

Gazzaley, A., Cooney, J. W., Rissman, J., & D'Esposito, M. (2005). Top-down suppression deficit underlies working memory impairment in normal aging. *Nature Neuroscience, 8*, 1298. doi:10.1038/nn1543

https://www.nature.com/articles/nn1543#supplementary-information

George, D., & Mallery, M. (2010). *SPSS for Windows Step by Step: A Simple Guide and Reference, 17.0 update (10a ed.)* Boston: Pearson.

Gilbert, S. J., & Burgess, P. W. (2008). Executive function. *Current Biology, 18*(3), R110-R114. doi:10.1016/j.cub.2007.12.014

Godefroy, O. (2003). Frontal syndrome and disorders of executive functions. *Journal of Neurology, 250*(1), 1-6. doi:10.1007/s00415-003-0918-2

Gottfries, G. G., Noltorp, S., & Nørgaard, N. (1997). Experience with a Swedish version of the Geriatric Depression Scale in primary care centres. *International Journal of Geriatric Psychiatry, 12*(10), 1029-1034. doi:doi:10.1002/(SICI)1099-1166(199710)12:10<1029::AID-GPS683>3.0.CO;2-D

Hatano, S. (1976). Experience from a multicentre stroke register: a preliminary report. . *Bulletin of the World Health Organisation, 54*(5), 541–553.

Jönsson, A.-C., Lindgren, I., Hallström, B., Norrving, B., & Lindgren, A. (2005). Determinants of Quality of Life in Stroke Survivors and Their Informal Caregivers. *Stroke, 36*(4), 803-808. doi:10.1161/01.STR.0000160873.32791.20

Kauhanen, M. L., Korpelainen, J. T., Hiltunen, P., Brusin, E., Mononen, H., Maatta, R., & Myllyla, V. V. (1999). Poststroke depression correlates with cognitive impairment and neurological deficits. . *Stroke, 30*(9), 1875-1880.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of dsm-iv disorders in the national comorbidity survey replication. *Archives of General Psychiatry, 62*(6), 593-602. doi:10.1001/archpsyc.62.6.593

Kvåle, R., Forland, G., Bakken, I., Nguyen Trung, T., Akerkar, R., Dyngeland, J., . . . M., E. (2018). *Hjerte- og karregisteret • Rapport for 2012–2016*. Retrieved from Oslo:

Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Frontiers in psychology, 4*, 863-863. doi:10.3389/fpsyg.2013.00863

Landrø, N. I., Stiles, T. C., & Sletvold, H. (2001). Neuropsychological Function in Nonpsychotic Unipolar Major Depression. *Cognitive and Behavioral Neurology, 14*(4), 233-240.

Leiknes, K. A., Dalsbø, T. K., & Siqveland, J. (2016). *Måleegenskaper ved den norske versjonen av Hospital Anxiety and Depression Scale (HADS). [Psychometric assessment of the Norwegian version of the Hospital Anxiety and Depression Scale (HADS).]* Retrieved from Oslo:

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological Assessment* (4th ed. ed.). New York: Oxford University Press.

Loubinoux, I., Kronenberg, G., Endres, M., Schumann-Bard, P., Freret, T., Filipkowski, R. K., . . . Popa-Wagner, A. (2012). Post-stroke depression: machanisms, translation and therapy. *Journal of Cellular and Molecular Medicine, 16*(9), 1961-1969. doi:10.1111/j.1582-4934.2012.01555.x

Mayberg, H. (1994). Frontal lobe dysfunction in secondary depression. *J Neuropsychiatry Clin Neurosc, 6*, 428-442.

Miller, E. K., & Wallis, J. D. (2009). Executive Function and Higher-Order Cognition: Definition and Neural Substrates. . In L. R. Squire (Ed.), *Encyclopedia of Neuroscience* (Vol. 4, pp. 99-104). Oxford: Academic Press.

Miyake, A., & Friedman, N. P. (2012). The Nature and Organization of Individual Differences in Executive Functions: Four General Conclusions. *Current Directions in Psychological Science, 21*(1), 8-14. doi:10.1177/0963721411429458

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The Unity and Diversity of Executive Functions and Their Contributions to Complex "Frontal Lobe" Tasks: A Latent Variable Analysis. *Cognitive Psychology, 41*(1), 49-100. doi:https://doi.org/10.1006/cogp.1999.0734

Moffitt, T. E., Arseneault, L., Belsky, D., Dickson, N., Hancox, R. J., Harrington, H., . . . Caspi, A. (2011). A gradient of childhood self-control predicts health, wealth, and public safety. *Proceedings of the National Academy of Sciences, 108*(7), 2693.

Mohlman, J. (2005). Does Executive Dysfunction Affect Treatment Outcome in Late-Life Mood and Anxiety Disorders? *Journal of Geriatric Psychiatry and Neurology, 18*(2), 97-108. doi:10.1177/0891988705276061

Morrison, V., Pollard, B., Johnston, M., & MacWalter, R. (2005). Anxiety and depression 3 years following stroke: Demographic, clinical, and psychological predictors. *Journal of Psychosomatic Research, 59*(4), 209-213. doi:https://doi.org/10.1016/j.jpsychores.2005.02.019

Narushima, K., Paradiso, S., Moser, D. J., Jorge, R., & Robinson, R. G. (2007). Effect of antidepressant therapy on executive function after stroke *British Journal of Psychiatry*(190), 260-265. doi:10.1192/bjp.bp.106.025064

National Collaborating Centre for Chronic Conditions. (2008). Stroke: National Clinical Guideline for Diagnosis and Initial Management of Acute Stroke and Transient Ischaemic Attack (TIA). (NICE Clinical Guidelines, No. 68.) 1, Introduction. . Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK53302/

Nitschke, J. B., & Heller, W. (Eds.). (2003). *The Neuropsychology of Anxiety Disorders: Affect, Cognition, and Neural Circuitry*: John Wiley & Sons, Ltd.

Petersen, R. (2004). Mild cognitive impairment as a diagnostic entity. *J Intern Med, 256*, 183 – 194.

Pohjasvaara, T., Leskelä, M., Vataja, R., Kalska, H., Ylikoski, R., Hietanen, M., . . . Erkinjuntti, T. (2002). Post-stroke depression, executive dysfunction and functional outcome *European Journal of Neurology, 2002*(9), 269-275.

Pohjasvaara, T., Vataja, R., Leppävuori, A., Kaste, M., & Erkinjuntti, T. (2001). Depression is an independent predictor of poor long-term functional outcome post-stroke *European Journal of Neurology, 2001*(8), 315-319.

Prins, N., van Dijk, E., & den Heijer, T. (2005). Cerebral small-vessel disease and decline in information processing speed, executive function and memory. *Brain, 128*(2034 – 41).

Reitan, R. M., & Wolfson, D. (1985). *The Halstead-Reitan Neuropsychological Test Battery*. Tuscon, AZ: Neuropsychology Press.

Riepe, M., Riss, S., & Bittner, D. (2004). Screening for cognitive impairment in patients with acute stroke. *Dement Geriat Cogn Disord, 17*, 49 – 53.

Sachdev, P., Brodaty, H., & Valenzuela, M. (2004). The neuropsychological profile of vascular cognitive impairment in stroke and TIA patients. *Neurology, 2004*(62), 912 – 919.

Schneider, S., Kornejeva, A., Vibo, R., & Kõrv, J. (2017). Risk Factors and Etiology of Young Ischemic Stroke Patients in Estonia. *Stroke research and treatment, 2017*, 8075697-8075697. doi:10.1155/2017/8075697

Selnes, P., Grambaite, R., Rincon, M., Bjørnerud, A., Gjerstad, L., Hessen, E., . . . Fladby, T. (2015). Hippocampal Complex Atrophy in Poststroke and Mild Cognitive Impairment. *Journal of Cerebral Blood Flow & Metabolism, 35*(11), 1729-1737. doi:10.1038/jcbfm.2015.110

Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. . *Clinical Gerontologist: The Journal of Aging and Mental Health, 5*(1-2), 165-173. doi:http://dx.doi.org/10.1300/J018v05n01_09

Smith, E. E., & Jonides, J. (1997). Working Memory: A View from Neuroimaging. *Cognitive Psychology, 33*(1), 5-42. doi:https://doi.org/10.1006/cogp.1997.0658

Stern, A. F. (2014). The Hospital Anxiety and Depression Scale. *Occupational Medicine, 64*(5), 393-394. doi:10.1093/occmed/kqu024

Stordal, E., Solhaug, H. I., Bosnes, I., & Følstad, A. (2012). Prevalens av depresjon hos eldre: en kort oversikt basert på erfaringer med epidemiologisk forskning fra Helseundersøkelsen i Nord-Trøndelag (HUNT). *Norsk Epidemiologi, 22*(2), 197-201

Stuss, D. T., & Alexander, M. P. (2000). Executive functions and the frontal lobes: a conceptual view. *Psychological Research, 63*(3), 289-298. doi:10.1007/s004269900007

Stuss, D. T., Floden, D., Alexander, M. P., Levine, B., & Katz, D. (2001). Stroop performance in focal lesion patients: dissociation of processes and frontal lobe lesion location. *Neuropsychologia, 2001*(39), 771–786.

Taconnat, L., Baudouin, A., Fay, S., Raz, N., Bouazzaoui, B., El-Hage, W., . . . Ergis, A.-M. (2010). Episodic memory and organizational strategy in free recall in unipolar depression: The role of cognitive support and executive functions. *Journal of Clinical and Experimental Neuropsychology, 32*(7), 719-727. doi:10.1080/13803390903512645

Tang, E. Y. H., Amiesimaka, O., Harrison, S. L. H., Green, E., Price, C., Robinson, L., . . . Stephan, B. C. M. (2018). Longitudinal Effects of Stroke on Cognition: A Systematic Review. *Journal of the American Heart Association, 7*(2). doi:10.1161/JAHA.117.006443.

Tekin, S., & Cummings, J. L. (2002). Frontal–subcortical neuronal circuits and clinical neuropsychiatry: An update. *Journal of Psychosomatic Research, 53*, 647 – 654.

Townend, B. S., Whyte, S., Desborough, T., Crimmins, D., Markus, R., Levi, C., & Sturm, J. W. (2007). Longitudinal prevalence and determinants of early mood disorder post-

stroke. *Journal of Clinical Neuroscience, 14*(5), 429-434. doi:https://doi.org/10.1016/j.jocn.2006.01.025

Vataja, R., Pohjasvaara, T., Mäntylä, R., Ylikoski, R., Leskelä, M., Kalska, H., . . . Erkinjuntti, T. (2005). Depression-Executive Dysfunction Syndrom in Stroke Patients *The American Journal of Geriatric Psychiatry, 13*(2), 99-107.

Vendrell, P., Junqui, C., Pujol, J., Jurado, M. A., Molet, J., & Grafman, J. (1995). The Role of Prefrontal Regions in the Stroop Task. *Neuropsychologia, 33*(3), 341-352.

Watkins, E., & Brown, R. G. (2002). Rumination and executive function in depression: an experimental study *J Neurol Neurosurg Psychiatry, 2002*(72), 400-402. doi:10.1136/jnnp.72.3.400

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI)*. San Antonio, TX: The Psychological Corporation.

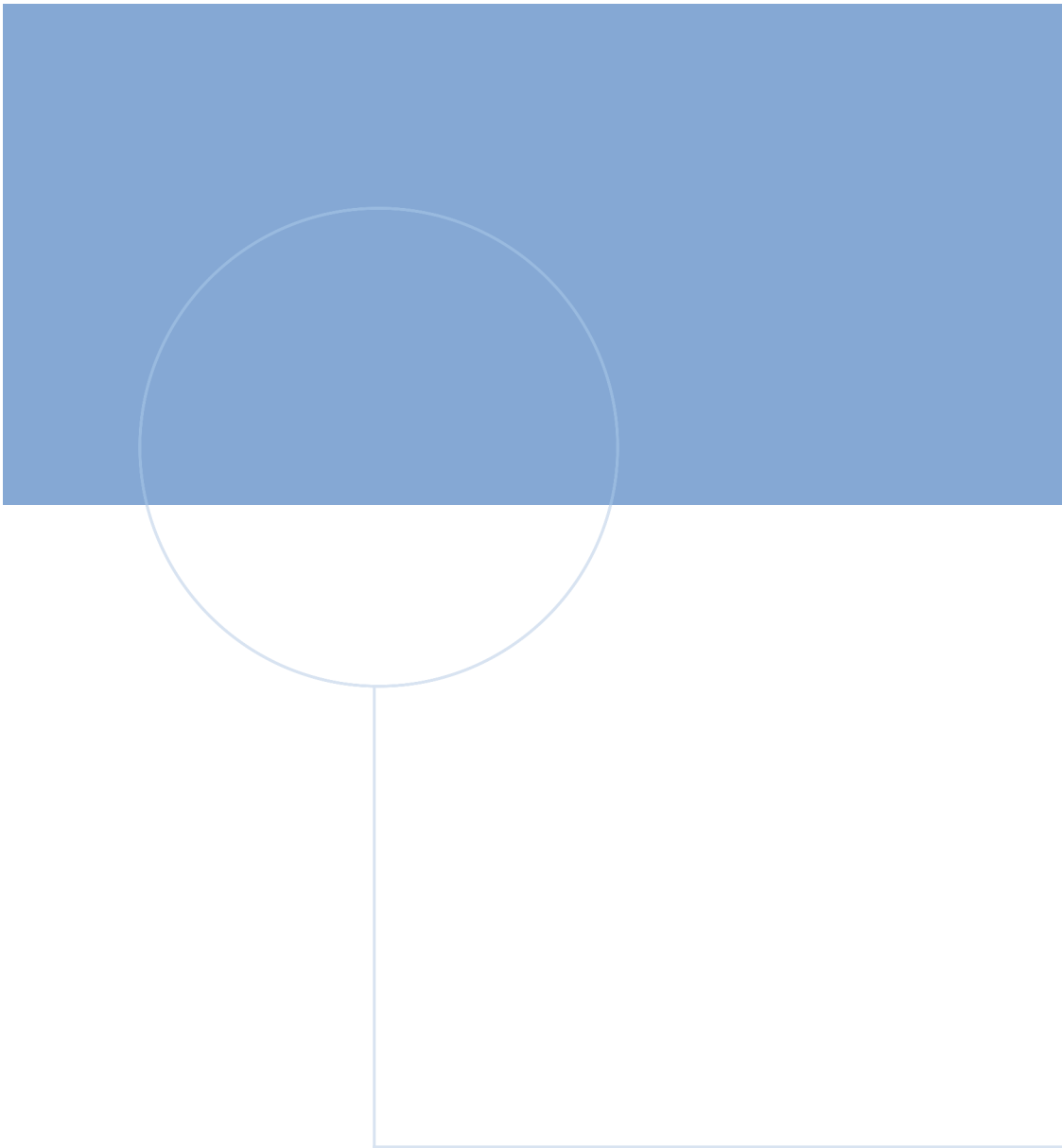
Wechsler, D. (2003). *Wechsler Adult Intelligence Scale - Third Edition: Manual*. San Antonio, TX: The Psychological Corporation.

Whyte, E. M., & Mulsant, B. H. (2002). Post stroke depression: epidemiology, pathophysiology, and biological treatment. *Biological Psychiatry, 52*(3), 253-264. doi:https://doi.org/10.1016/S0006-3223(02)01424-5

World Health Organization. (1992). *The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines.* Geneva: World Health Organization.

Wyller, T., & Sveen, U. (2002). Ikke-språklige kognitive symptomer etter hjerneslag. *Tidsskriftet for den norske legeforening, 2002*(122), 627 – 630.

Zigmond, A., & Snaith, R. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica, 67*(6), 361-370.



NTNU
Norwegian University of
Science and Technology