Tampere University

Aleksi Siro

REMOTE COMPUTER-BASED TESTING OF EXECUTIVE FUNCTIONS IN ASSESMENT OF BRAIN WELLBEING

Master's thesis
Faculty of Information Technology and Communication Sciences
Examiners: Kaisa Hartikainen
Jari Peräkylä
Jari Viik
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ABSTRACT

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The impact of prolonged stress on brain structure and function has gained increased interest as burnout has become one of the major concerns in modern life. Prolonged stress has been linked with decreased grey matter volumes in the prefrontal cortex, responsible for higher cognitive control functions like executive functions (EF). EF is an umbrella term for multiple cognitive control processes that are needed in various everyday life situations. There are three core EF: working memory, inhibitory control and cognitive flexibility.

Modern work environment exposes people to multiple stressors and challenges cognitive abilities in an unprecedented way. That’s why it would be beneficial that there would be easily accessible neuropsychological tests that are accurate, reliable, repeatable, and sensitive to even subtle cognitive impairments. One possible tool for such evaluation could be a computer-based Executive reaction time (ERT) test (Hartikainen et al., 2010). ERT test simultaneously assess all core EF and emotion-attention interaction. To assess feasibility of remote testing of EF, a novel remote version of the ERT test was developed and tested. Users only had to install a third-party software to complete the ERT test. Often the changes in the EF are detected if the test is challenging enough. To meet this criterion, new trial type was included in the test. The new trial type was designed to challenge inhibitory control and cognitive flexibility. In the new trail type, subjects are required to give the answer in reversed pattern. In the thesis the feasibility of remote assessment of EF, the effects of burnout on EF and effectiveness of new trial type were evaluated.

In total 26 subjects participated in the project. All subjects filled a consent form, Beck’s depression inventory (BDI), Bergen burnout inventory (BBI-15), Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A) and a novel COVID-19 brain health questionnaire developed in the Behavioral Neurology Research Unit, Tampere University Hospital as part of Sustainable Brain Health -Project. Based on the BBI-15 results the subjects were divided into two study groups, subject with (n = 6) and without burnout (n = 20).

No statistical differences in reaction times (RT) or error rates were detected between the study groups. Reversed trial type significantly prolonged the reaction times and increased the total error rates Incorrect responses of subjects with burnout were significantly increased in reversed trial with the negative emotional distractor but not with the neutral emotional distractor. For assessing the impact of negative emotional distractor on reaction times (RT) and error rates, mean RT in context of negative distractor was subtracted from mean RT in context of neutral distractor within subjects. Same was done for error rates. Absolute value of the subtraction score (absΔERT). reflecting the extent but not direction of emotional impact on RTs in reversed trial type correlated with the BRIEF-A’s initiate, working memory and metacognition indicis absΔERT in regular trial types correlated with each BBI-15 index. The BBI-15 results correlated with 83 % of BRIEF-A indicis.

While no significant decrement in objective measures of EF due to burnout was detected probably due to small sample size an index reflecting the extent of emotional modulation of executive functions did correlate with symptoms of burnout. The ERT test can be efficiently conducted remotely. Subjects were able to install and conduct the ERT test with the provided instructions. New trial type challenged subjects’ EF as intended as it significantly increased reaction times and certain error types. Therefore, remotely executed ERT test has the potential to be used as an efficient assessment tool of EF, burnout and more generally brain wellbeing.

Keywords: executive functions, stress, burnout, cognitive assessment, remote assessment

The originality of this thesis has been checked using the Turnitin OriginalityCheck service.

TIIVISTELMÄ

Aleksi Siro: Tietokonepohjainen etätesti toiminnanohjauksen ja aivoterveyden arvioinnissa
Diplomityö
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Kroonistuneen stressin vaikutuksia aivojen rakenteisiin ja toimintoihin tutkitaan yhä enemmissä määrin, sillä työuupumus on nykyään yksi suurimmista huolenaiheista työelämässä. Pitkittynyt stressi on liitetty harmaan aineen tilavuuden pienemiseen etuotsalohkojen aivokuoressa. Etuotsalohkopiirit mahdollistavat korkeamman asteen kognitiiviset kontrollitoiminnot kuten toiminnanohjauksen. Toiminnanohjaus on yläkäsite monille kognitiivisille toiminnoille, joita tarvitaan arkielämässä. Toiminnanohjaus voidaan jakaa kolmeen pääluokkaan: työmuistiin, vasteenestoon ja joustavuuteen.

Nykyajan työelämä altistaa ihmiset useille stressilähteille ja haastaa kognitiivisia toimintoja ennennäkemättömällä tavalla. Siksi olisi hyödyllistä, että olisi olemassa helposti saatavilla olevia neuropsykologisia testejä, jotka ovat tarkkoja, luotettavia, toistettavia ja herkkiä vähäisillekin kognitiivisille häiriöille. Yksi mahdollinen työkalu tällaiseen arviointiin voisi olla tietokonepohjainen Executive reaction time (ERT) -testi (Hartikainen et al., 2010). ERT-testillä voidaan arvioida samanaikaisesti kaikkia kolmea toiminnanohjauksen pääluokkaa sekä lisäksi tunteiden ja tarkkaavaisuuden vuorovaikutusta. Etätestauksen toimivuuden arvioimiseksi ERT-testistä kehitettiin uusi etäversio. Käyttäjien täytyi asentaa kolmannen osapuolen ohjelmisto testin suorittamiseksi. Toiminnanohjauksen muutokset havaitaan herkemmin testeillä, jotka ovat riittävän haastavia. Tämän vuoksi ERT-testiin lisättiin uusi käänteinen tilanne. Uusi tilanne haastaa vasteenestoa sekä joustavuutta. Opinnäytetyössä arvioidaan toiminnanohjauksen etätestaamisen toimivuutta, työuupumuksen vaikutuksia toiminnanohjaukseen sekä uuden käänteisen tilanteen tehokkuutta.

Kaiken kaikkiaan 26 henkilöä osallistui testiin. Koehenkilöt täyttivät esitietolomakkeen, masennuskyselyn (BDI), työuupumuskyselyn (BBI-15), toiminnanohjauskyselyn (BRIEF-A) sekä COVID-19 aivoterveys kyselyn, jonka Käyttäytymisneurologian tutkimusyksikkö on kehittänyt osana Kestävä Aivoterveys -hanketta. Työuupumuskyselyn perusteella koehenkilöt jaettiin kahteen ryhmään: uupuneisiin (n = 6) ja terveisiin (n = 20).

Uusi käänteinen tilanne merkittävästi pidensi koehenkilöiden reaktioaikoja ja lisäsi kokonaisvirheiden ja väärien vastauksien lukumäärää. Tilastollista eroa terveiden ja uupuneiden reaktioaikojen sekä virhemäärien välillä ei löytynyt. Käänteisessä tilanteessa uupuneiden koehenkilöiden väärien vastauksien lukumäärä kasvoi merkittävästi negatiivisella tunneärsykkeellä. Negatiivisen tunneärsykkeen vaikutusta reaktioaikoihin ja virheisiin arvioitiin vähentämällä reaktioaika negatiivisen ärsykkeen aikana neutraalin ärsykkeen aikaisesta reaktioajasta koehenkilökohtaisesti. Sama tehtiin eri virhetyypeille. Itseisarvo käänteisen tilanteen vähennyslaskun tuloksesta, mikä heijastaa tunneärsykkeen vaikutuksen määrää, muttei suuntaa, korreloi BRIEF-A:n Initiate, working memory ja metakognitio indeksien kanssa. Vastaava tunneärsykkeen vaikutuksen määrää heijastava indeksi ei-käänteisessä, normaali, tilanteessa korreloi kaikkien BBI-15 indeksien kanssa. BBI-15 kyselyn tulokset korreloivat 83 % BRIEF-A indeksien kanssa.

Vaikka toiminnanohjaus ei objektiivisten mittarien valossa eronnut merkittävästi uupuneiden ja terveiden välillä mahdollisesti pienestä otoskoosta johtuen, tunteen vaikutuksen määrä toiminnanohjaukseen korreloi uupumusoireiden kanssa. ERT-testi pystyttiin toteuttamaan etänä. Koehenkilöillä ei ollut ongelmia asentaa ja toteuttaa testiä annettujen ohjeiden pohjalta. Uusi tilanne haastoi koehenkilöiden toiminnanohjausta oletetusti, sillä se kasvatti merkittävästi reaktioaikoja ja tiettyjen virheiden lukumäärää. Etänä toteutettua ERT-testiä voitaisiin mahdollisesti käyttää toiminnanohjauksen, työuupumuksen ja yleisemminkin aivohyvinvoinnin arvioinnissa.

Avainsanat: toiminnanohjaus, stressi, burnout, etätestaus, kognition arviointi

Tämän julkaisun alkuperäisyys on tarkastettu Turnitin OriginalityCheck –ohjelmalla.

PREFACE

I would like to thank my mentors Kaisa Hartikainen and Jari Peräkylä who were helping and guiding me throughout the thesis. I would also like to thank Mia Pihlaja. She was a great help in recruiting subjects. Without her input, I would not have been able to collect enough data for this thesis.

Tampere, 5 May 2022

Aleksi Siro

CONTENTS

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LIST OF SYMBOLS AND ABBREVIATIONS

absΔERT Regular	Absolute value of subtraction between negative and neutral distractor's reaction times in regular trial type.
absΔERT Reversed	Absolute value of subtraction between negative and neutral distractor's reaction times in reversed trial type.
ACTH	Adrenocorticotropic hormone
ANOVA	Analysis of variance
BRI	Behavioral regulation index
CI	Confidence interval
CRF	Corticotropin-releasing factor
ΔERT Regular	Subtraction between negative and neutral distractor's reaction times in regular trial type.
ΔERT Reversed	Subtraction between negative and neutral distractor's reaction times in reversed trial type.
EF	Executive functions
ERT test	Executive reaction time test
GEC	Global executive composite
HPA axis	Hypothalamic-pituitary-adrenal axis
MI	Metacognition index
NBS	Neurobehavioral Systems
OR	Odds ratio
PFC	Prefrontal cortex
RT	Reaction time
SAM axis	Sympathetic-adreno-medullar axis
α	Significance level
Δ	delta

1. INTRODUCTION

Work well-being and burnout are commonly addressed topics in the news all around the world nowadays. This topic has gained more attention as researchers have gotten a better understanding of the adverse effects of burnout. Several studies suggest that burnout might cause changes in the brain's signaling pathways and even reduce its volume in various regions (Arnsten, 2009; Blix et al., 2013; McEwen and Morrison, 2013; Godoy et al., 2018). The prefrontal cortex (PFC) is the most recently evolved brain region and it enables higher cognitive abilities, like executive functions. Unfortunately, the PFC is highly sensitive to stress. Even mild exposure to stress can compromise cognitive abilities. (Arnsten, 2009) Not to mention what can happen to cognitive abilities when stress becomes chronic. For example, in the worst case scenario burnout or other stress related exhaustion can cause changes that are visible in cognitive testing even after three years (Jonsdottir et al., 2017).

Executive functions (EF) refer to a group of mental processes which are involved in our everyday life activities. In everyday life we have to keep multiple things in our mind at the same time, make decisions, resist temptations, solve problems and perhaps adapt to the changes. People with good EF can handle these kinds of everyday life situations well. In other words, EF helps us to maintain our actions and thoughts so that a certain goal is achieved. These goals can be anything from sticking to a diet to finishing a project. Therefore, EF are essential in everyday life as well as in the working environment. Depending on the source, EF can be divided into multiple categories. According to Diamond A. three generally agreed core EF are inhibitory control, working memory and cognitive flexibility. (Diamond, 2013) The modern working environment challenges our cognitive abilities, especially EF. Due to that, many would benefit from continuous assessment of EF in their working places. However, it is alarming that the effects of EF are often ignored when the ability to work is evaluated. (Hartikainen et al., 2021)

Due to the hecticness of modern working life, many employees find the burnout as a major risk in their jobs. In Finland 2018 employees aged 15-64, 40 % were feeling tired, 40 % reported sleeping disorders and 11 % said that everything is overwhelming. These numbers have steadily increased for 41 years. Also, 58 % felt that serious burnout is a serious risk in their jobs, whereas in previous years the number has been close to 50 %.

(Sutela et al., 2019) Another Finnish study focused on how COVID-19 has affected work well-being. The study reveals that pandemic has negatively affected especially the well-being of employees under 36 years. Similar effects weren't as clear with employees over 36 years. However, in general cynical thoughts and detachment from job have been increasing during the COVID-19 pandemic. (Kaltiainen and Hakanen, 2021) In several studies burnout has been linked with the EF impairment (Linden et al., 2005; Sandström et al., 2005; Beck et al., 2013; Diestel et al., 2013; Feuerhahn et al., 2013; Krabbe et al., 2017). Yet, there are several studies where such correlation has not been found. (Österberg et al., 2009; McInerney et al., 2012; Oosterholt et al., 2014). Thus, more research on correlation between burnout and EF impairments has to be done. Burnout is not only affecting the EF, but people who are suffering from burnout have an increased risk of developing other diseases as well, like depression and sleeping disorders (Maslach et al., 2001; Maslach and Leiter, 2016; Salvagioni et al., 2017), which can lead to a situation where EF are compromised even more. In order to understand burnout, how it may affect the EF and how possible effects to the EF could be measured, one must also understand stress. How the brain handles stress, what are the general signaling pathways, how stress affects the body, etc. Also, it is important to understand how some of the individual properties affect stress.

EF have been found to correlate in various aspects in life. It has been found to correlate with mental health, school and job success and general quality of life (Chan et al., 2008; Diamond, 2013). This makes EF a great parameter when brain health and well-being is assessed. However, often only those whose cognitive abilities are already significantly decreased are tested with the neuropsychological tests due to the lack of resources. Because of that many who would benefit from such tests are left out. This is concerning because even subtle changes in the EF can cause notable challenges in one's well-being (Hartikainen et al., 2021). Therefore, there is a great demand for easily accessible, fast, reliable and accurate tests to evaluate the EFs.

One way to test EFs and therefore, brain health and general well-being, is to use computer-based objective Executive reaction time (ERT) test. Kaisa Hartikainen and her research group developed first version of their ERT test already in 2010. The test was shown to be capable of detecting detect mild EF alterations. (KaisaM. Hartikainen et al., 2010) The test was developed to be a sensitive measure of EF and emotion-executive function interaction in different clinical populations and in response to different clinical interventions such as cardiac surgery (Liimatainen et al., 2016) and neuromodulation (Pihlaja et al., 2020; Peräkylä et al., 2021) ERT test simultaneously tests all three core EF dimensions and emotion-attention interaction. The ERT test consists of 512 individual trials where the subject has to give the response to the visual stimuli based on certain rules. The functionality of the ERT test is explained in detail in section 4.2. Previously the ERT test has shown good reliability and correlation to the Behavior Rating Inventory of Executive Function–Adult Version (BRIEF-A) questionnaire, which is a clinically approved broad questionnaire for EF evaluation (Erkkilä et al., 2018). Even though this ERT test has gained good results, there is still room for improvement. For example, in the test conducted by Diestel et. al., the defects in EF due to burnout were seen when the test required demanding usage of EF (Diestel et al., 2013). This finding could partly explain the inconsistency in research findings on the effect of burnout on EF. Therefore, one of the objectives of this thesis is to further develop ERT test to be more sensitive to mild deficits in EF by making the test even more demanding on EF.

The ERT test was developed further by adding a new trial type that challenges inhibitory control and cognitive flexibility. Another task on developing the test is to make the ERT test remotely usable. By making the test remotely executed, the test can be easily distributed throughout Finland and subjects can do the test whenever it is suitable for them. This provides easy access for the test for several people despite where they live. So, it makes it possible to evaluate the general brain health in a large population. Previously ERT test has shown good test-retest reliability (Erkkilä et al., 2018) so the ERT test could be used weekly e.g. in working places to track well-being of the employees. Employees could do the test during the workday and based on results the employers could do possible improvements to the working environment. Based on previous chapters following research questions can be conducted:

1. Is remote testing of EF reliable and feasible? 2. Does the ERT test detect differences in EFs and emotion EF interaction in subjects with burnout and those without? 3. Is the new reversed trial type more challenging to the subjects? 4. How well do subjective BRIEF-A and Bergen burnout inventory (BBI-15) results correlate with the newer version of the ERT test results?

This thesis was conducted in collaboration with Sustainable Brain Health -project. Sustainable brain health project is a multidisciplinary project coordinated by Tampere University of Applied Science. The aim of this project is to find out occupational stressors impacting brain health in teachers, nurses and IT personnel and tools to support wellbeing at work. With the gathered information the aim is to improve existing methods and find novel methods that could be used to improve brain health and wellbeing in both individual and organizational levels. This thesis relates to the part of the project conducted in the Behavioral Neurology Research Unit, Tampere University Hospital.

2. THEORETICAL BACKGROUND

In this chapter important concepts considering this thesis are covered. The first section will cover stress as a phenomenon, which structures are involved in stress response and how it affects our body. In the second section, burnout is discussed. The third section will cover each core EF. Finally testing of EF and problems in EF assessment is discussed.

2.1 Stress

Stress can be defined as a condition where the body's homeostasis is disturbed (Schneiderman et al., 2005; Chu et al., 2021). Those signals that cause disturbances in the body's homeostasis are called stressors. Stressors can be psychological for example, negative emotions or physical for example, infections. (Godoy et al., 2018)

Stress response, often called as fight-or-flight response results in alteration of homeostasis. It causes multiple physiological and behavioral changes in our body simultaneously. For example, heart rate increases as well as blood pressure and glucose production. (Herman et al., 2016; Tsigos et al., 2020) At the same time, we become more sensitive to our surroundings through our senses e.g. visual and auditory. While certain functions are enhanced during the stress response other functions that are not essential at the moment like digestion are suppressed temporally (Tsigos et al., 2020).

These changes in our body were helpful for example, in situations where our ancestors faced dangerous wild animals. Nowadays it is rare to find yourself in a face-to-face situation with a bear or other dangerous wild animal, but it seems that our body can nowadays feel even greater stress than our ancestors. In a modern hectic world, there are more everyday situations where the stress response can be activated. It is quite common that the stress response is activated by just thinking about e.g. money problems, upcoming public speech or even upcoming deadlines. Without proper stress handling methods, the stress can prolong easily. Normally when the cause of stress response has been overcome and after an appropriate recovery time, the body will return to its normal state.

It is often said that stress should be avoided. However, stress is not always a bad thing. Sometimes it can help us gain extra energy and focus to complete certain tasks or survive in nature. But when the stress is prolonged and without appropriate recovery time, negative effects start to build up and it can cause serious consequences to our body both physiological and mental. (Chu et al., 2021)

2.1.1 Stress response

The stress response is a complex phenomenon where multiple parts of our body are involved. There are four key components in the stress response, prefrontal cortex (PFC), amygdala, hypothalamic-pituitary-adrenal (HPA) axis and sympathetic-adreno-medullar (SAM) axis. Whenever a physical or psychological stimulus triggers the fight-or-flight response, first SAM axis is activated and quickly after the HPA axis is activated as well. Activation of the SAM axis causes short-term effects to the body. The goal of the SAM axis is to secrete epinephrine and norepinephrine into the body's blood circulation and cause rapid changes to the body. (Godoy et al., 2018; Thau et al., 2021) Activation of HPA-axis causes both short-term and long-term effects. (Godoy et al., 2018) General signaling pathways of the stress response and its effects to the body's functions are explained in Figure 1.

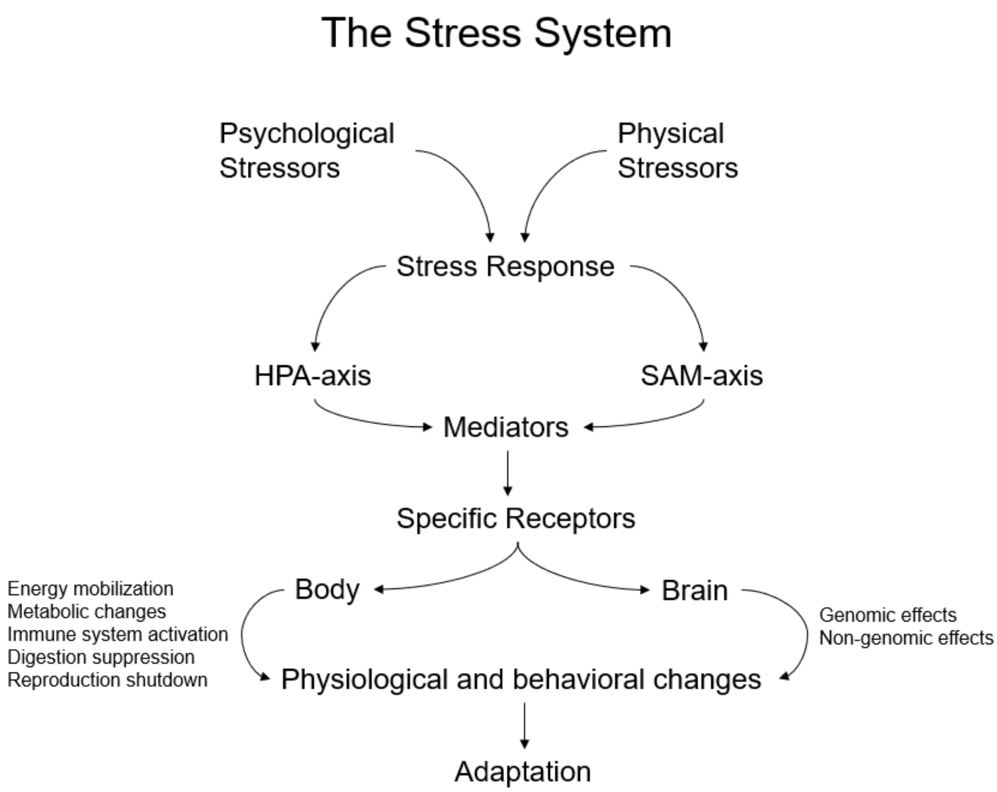

Figure 1. *Schematic presentation of stress signaling pathway. Either psychological or physical stressor activates HPA- and SAM-axis. Activation of these signaling pathways causes several physiological and behavioral changes. (Godoy et al., 2018).*

The phenomena start when the amygdala triggers the hypothalamus to secrete a hormone called corticotropin-releasing factor (CRF). CRF then activates the pituitary gland to secrete another hormone called adrenocorticotropic hormone (ACTH). Finally, ACTH activates the secretion of cortisol and other glucocorticoids in the adrenal gland. (Godoy et al., 2018) Cortisol, epinephrine and norepinephrine together cause the physiological and behavioral changes mentioned earlier. After the threat has been overcome, the concentrations of cortisol, epinephrine and norepinephrine start to decrease in the bloodstream so that the body can move to the recovery phase and regain its homeostasis.

Due to cortisol's chemical structure, it can cross the blood-brain-barrier and bind to specific glucocorticoid receptors. High numbers of glucocorticoid receptors are especially found in frontal lobes, amygdala and hippocampus. (Lupien et al., 2007) Sapolsky and McEwen proposed an idea that chronic exposure to cortisol could have neurotoxic effects on the hippocampus that can lead to neuron atrophy in hippocampal structures (Sapolsky et al., 1986). Finding of Echouffo-Tcheugui et. al. supports this theory as they found out that the higher cortisol levels were linked with the lower grey matter volumes in the brain regions that are involved in the EF and impaired memory (Echouffo-Tcheugui et al., 2018).

2.1.2 Burnout

Nowadays it is quite common to feel at least some amount of exhaustion in the work as many struggle to balance between free time and work. When one cannot recover from work related stress it can lead to a vicious cycle and eventually to burnout. When an employee is starting to feel exhaustion, cynicism, detachment, lack of accomplishment or ineffectiveness towards a job, there is a high probability that the employee has burnout (WHO, 2019).

The World Health Organization defines burnout as an occupational phenomenon due to chronic workplace stress (WHO, 2019). Usually, burnout is not caused by a single stressor but rather by the sum of multiple stressors over time. There is a general agreement among researchers that the stressors that permit burnout are large workload, lack of control, lack of acknowledgment, problems with other employees and mismatched values (Maslach et al., 2001; Maslach and Leiter, 2016). Kalimo et al. remind that there are also individual risk factors that may increase the probability of developing burnout (Kalimo et al., 2003). For example, low self-esteem, inappropriate stress handling methods or previous neurological defects could be added to the list of individual risk factors.

Burnout has gained more interest over the past few years as the researchers have gained a better understanding of how prolonged stress affects the individual's health and general well-being. Several studies suggest that those who have burnout have a higher risk of developing adverse medical conditions like depression, sleeping problems, cardiovascular diseases. (Maslach et al., 2001; Maslach and Leiter, 2016; Salvagioni et al., 2017)

2.2 Executive functions

EFs is a hypernym for multiple higher cognitive control processes involved in our everyday life. The three core categories of EF are working memory, inhibitory control and cognitive flexibility. Each of the core EF are explained more in the coming sections. All dimensions of the EFs are needed in our everyday life, e.g. working memory aid to remember information that is no longer present, inhibitory controls helps to maintain the focus and cognitive flexibility allows us to see things from new a perspective. Therefore, it can be said that the main purpose of EFs is to regulate our behavior and actions towards desired goals. (Diamond, 2013) Any defect, large or small to any of those dimensions, can cause changes into the one's cognitive abilities and mental health that may cause lower quality of life in the long run (Echouffo-Tcheugui et al., 2018). The interconnections between the dimensions are presented in Figure 2.

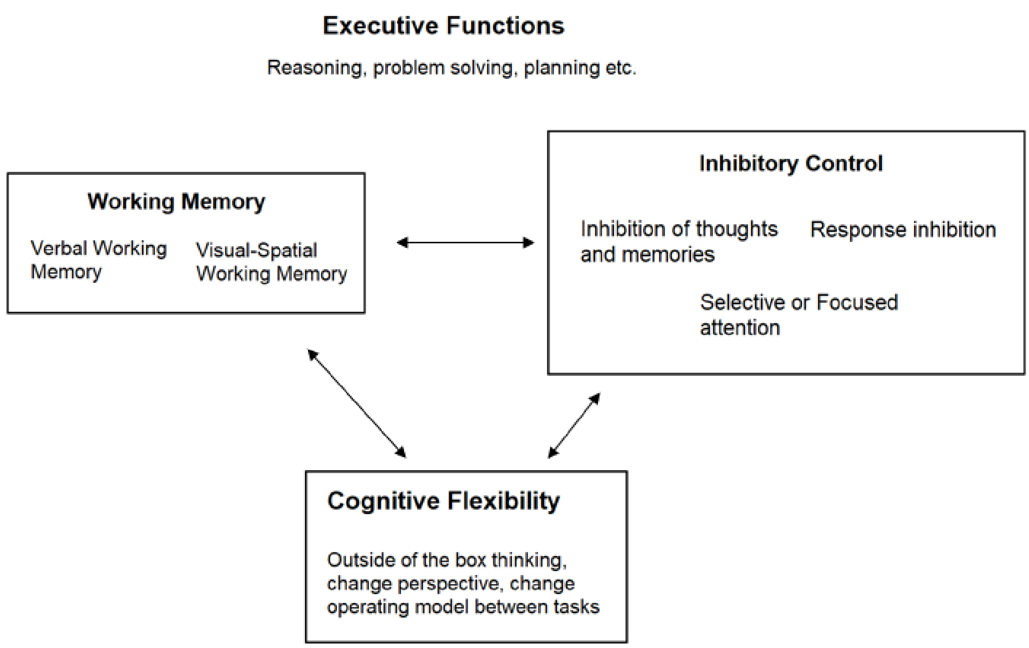

Figure 2. *Core EFs and their interconnections. All core EFs are linked and working with each other. (Diamond, 2013).*

There are several brain structures that are involved in the normal functioning of the EF, but one of the most important one is the prefrontal cortex (PFC). The PFC has several crucial tasks as it regulates our actions, emotions, thoughts (Arnsten, 2009), thinking, planning and reasoning (Funahashi, 2017). Another important structure is medio-dorsal nucleus of thalamus that is part of fronto-thalamic-circuit. Medio-dorsal nucleus has been found to be important structure in EF and particularly in working memory (Peräkylä et al., 2017).

All the dimensions of EF are working together and if one dimension is malfunctioning due to any reason, it does affect the other dimensions as well. Constant exposure to the stress can cause malfunctioning of the EF. Chronic stress can cause neurotoxic events, change the brain's signaling pathways (Golkar et al., 2014) and reduce the brain's gray matter volume especially in the PFC (Arnsten et al., 2015; Blix et al., 2013; Savic, 2015). Therefore, often those who have burnout have impaired EFs. (Linden et al., 2005; Sandström et al., 2005; Beck et al., 2013; Diestel et al., 2013; Feuerhahn et al., 2013; Krabbe et al., 2017).

2.2.1 Working memory

In general, working memory helps us maintain task-relevant information in mind when there is no longer sensory information present. Throughout the day a lot of information is processed in the brain. Depending on the task some sensory information is relevant, and some is irrelevant. Because working memory has a limited capacity of holding on to task-relevant information, it is important to concentrate thoughts only on relevant information. (Diamond, 2013)

Besides being a storage place for information, working memory allows for manipulating information (Diamond, 2013; Chai et al., 2018). The information that is manipulated can be just received sensory information or it is also possible to retrieve older information from the long-term memory and combine new information with that. For example, during mental arithmetic tasks working memory is needed. One must remember numbers and arithmetic calculation rules in order to successfully complete the calculation. The possibility of processing the information separates working memory from short-term memory, which is just information storage. Working memory can be divided into verbal and visual-spatial working memory. Verbal working memory is needed to make sense of verbal information and visual-spatial working memory is used when the stimuli include shapes, colors or movement. Working memory contributes to making more appropriate decisions and actions with the co-operation of inhibitory control. With good inhibitory control individuals can prevent filling the working memory with irrelevant information by guiding the focus on important stimuli. (Diamond, 2013) In terms of the ERT test, a set of rules are told to the subject and they have to remember those throughout the ERT test. In the ERT test, a series of visual stimuli are represented to the subject and based on the stimuli, the subject must react in an appropriate way according to the response-rule.

2.2.2 Inhibitory control

Inhibitory control is one of the core EF. Good inhibitory skills are needed in various activities in everyday life. Good inhibitory skills make it possible that one can control their emotions, attention, thoughts, actions in such a way that they are task relevant and do not interfere the task completion (Diamond, 2013) For example, in the hectic working environment one must focus only on the stimuli that are relevant for the certain task (Dillon and Pizzagalli, 2007; Diamond, 2013).

Often people subconsciously react to a certain stimulus in some way before even realizing it. This can be seen for example, when someone touches something hot and immediately, they pull the hand away from the hot object. The same principle occurs when a notification from a social media platform, noisy environment or smell of food distracts us from doing what is more appropriate. People with decreased inhibitory skills easily get on the sidetrack and are often more likely to be more inefficient compared to the ones with better inhibitory skills. Therefore, inhibitory control offers a choice to change the behavior, prevents us from acting impulsively and an opportunity to adapt to the environment. (Diamond, 2013) These subconscious reactions also affect how people react to possible threats and other negative stimuli. As human cognitive abilities are limited, not all incoming stimuli can be processed at the same time. Because of this all the stimuli compete for attention and the most important ones have to be prioritized. Prioritization helps to focus on certain stimuli while ignoring others. (Desimone and Duncan, 1995) It seems that the brain prioritizes threat related stimuli over the others. (Vuilleumier, 2005; Hartikainen, 2021) This can be seen for example, when a sudden loud noise is heard, people start to look for the source of that loud noise or when something suddenly comes to sight. Signals that have emotional value are prioritized and they automatically capture the attentional resources (Hartikainen et al., 2000, 2007), especially threat related stimuli like wild animals, spiders or angry faces (Vuilleumier, 2005; K. M. Hartikainen et al., 2010; Hartikainen et al., 2012; Hartikainen, 2021).

Hartikainen et al. found that task-irrelevant emotional stimuli automatically capture attention and temporarily compromise task performance. In the test, Hartikainen et al. used a similar approach like in the ERT test. The subjects were presented neutral, happy and threatening images prior to targets, and it was tested how this affects the reaction times to subsequent targets. When an emotional image, either pleasant or threatening was presented in either visual field, it significantly increased the reaction times to targets presented in the left visual field i.e. to the right hemisphere. The effect was greater with the unpleasant images. However, the emotional images did not affect the reaction times to targets presented in the right visual field, i.e.to the left hemisphere. This indicates that the emotionally unpleasant stimuli are competing for attentional resources especially in the right hemisphere. (Hartikainen et al., 2000, 2007)

Normal emotion-attention interaction may impair due to brain disorder or damage. It has been found that those people who are suffering from anxiety will more likely focus their attention to the threat-related stimuli. (Bar-Haim et al., 2006). It appears that subjects with previous mild head injury allocate more attentional resources to threat related stimuli than control subjects (Mäki-Marttunen et al 2014). Also, subjects with depression have difficulties in disengaging attention away from negative emotional stimuli (Joorman 2004). Therefore, assessing interaction between emotion attention and EF and how it changes over time provides insight into alterations in brain's affective circuits in different clinical populations.

In order to study emotion-attention and emotion-EF interactions and its alterations emotional threat-related stimuli, an image resembling a spider and an emotionally neutral control image resembling a flower have been included into the ERT test. Neutral and threat related distractors can be seen in Figure 4. By doing so it is possible to assess whether threat-related stimuli hijack the attention of the subject and cause alterations to the reaction times. Another way to test inhibitory control is to change rules during the test. In the ERT test, subjects learn to give their answer based on certain rules. When the rules are changed during the test subjects have to learn a new operating model and inhibit older ones. This is hoped to increase the error rates of the subjects.

2.2.3 Cognitive flexibility

As mentioned in the previous chapter, humans often react to certain stimuli in certain ways without even thinking about it. Thinking and processing of information consumes more energy and therefore, it is more efficient to work on autopilot. However, during our daily tasks, it is highly beneficial that one can change their perspective, both spatial and personal, adapt to the changing environment, find new ways to solve certain problems or change their actions to be more appropriate. (Diamond, 2013) These mentioned skills are valuable especially in those working environments where a high level of mental processes is needed.

Over the years, researchers have created multiple tests that can estimate people's cognitive flexibility. One simple experiment made by Zelazo et al. illustrates with the Wisconsin card sorting test how young children, with immature frontal circuits and undeveloped EF, have difficulties changing their way of overcoming the problem. In the experiment Zelazo and her team told a group of 3 years old that they have to sort cards with different shapes based on the color. Young children had no problems in sorting the cards based on color. When the researchers changed the sorting rule from color to shape, children were no longer able to sort the cards correctly. Even though the children seemingly understood that they had to change the sorting criteria, the majority of them kept sorting the cards based on the color. (Zelazo et al., 1996)

As our cognitive abilities evolve while aging, this kind of sorting experiment would be easy to perform flawlessly at an older age. Despite that one could perform cognitive flexibility tests without any errors, the reaction time is usually increased when the subject has to switch from one task to another one inside one test (Meiran, 1996). Similarly, like in Zelazo's study, the response rule is changed in the ERT test. Green color is often associated as a go-signal or correct while red color is associated with NoGo or something wrong. These color signals are usually over learned and it is hard to inhibit actions if their meanings are reversed. Thus, in the ERT test response color or Go-signal is changed from green to red back and forth. Based on Meiran's study (1996), the reaction times should slightly increase in the first trials when Go-signal is changed. The subject must as well change their response based on the visual stimuli.

2.3 Effects of burnout to brain structures and executive functions

The human brain is constantly evolving throughout our whole life. Our experiences, actions, and emotions shape the brain's neuron connectivity constantly. Stress is not an exception. As researchers have become more and more interested in stress, it has been noticed that during prolonged stress, the brain might undergo physiological changes. (Arnsten, 2009; Blix et al., 2013; McEwen and Morrison, 2013; Godoy et al., 2018) Because of the prolonged stress, neurons in the brain might start to connect differently. In some regions neuronal connectivity can decrease while in other regions it can make neuronal connectivity stronger. These changes in the neuron connectivity can cause minor or even major changes in one's cognitive abilities and therefore to one's well-being.

The PFC, which is responsible for higher cognitive functioning including EF, can be impaired when exposed to the stressors constantly. It has been noticed that chronic stress can significantly decrease the gray and white matter volume in all regions of the PFC

(Blix et al., 2013; Savic, 2015; Arnsten et al., 2015) while the dendritic growth in the amygdala is induced (Arnsten et al., 2015). Because of the neural connection between the PFC and the amygdala, PFC is capable of inhibiting the amygdala and HPA axis activation in normal situations. However, due to the impairment of this connection due to prolonged stress, there is a chance of more probable activation of the amygdala in situations that a person would normally feel comfortable (Golkar et al., 2014). Because chronic stress may cause several changes mentioned above to the brain regions that are involved in EF and stress response, cognition may be compromised in the long run. As time has passed, researchers have found more evidence that burnout might impair the EF. For example, Jonsdottir et al. found out that those with the burnout were not performing as well as the control group in the tests that required the usage of all dimensions of the EF (Jonsdottir et al., 2013). After that and even before many research groups have got similar results on the relationship between burnout and executive dysfunction (Linden et al., 2005; Sandström et al., 2005; Beck et al., 2013; Diestel et al., 2013; Feuerhahn et al., 2013; Krabbe et al., 2017). A deeper understanding of the relationship between executive dysfunction and burnout is needed so that in the future the interventions could be done quicker. Effects of burnout on the EF and general well-being shouldn't be underestimated as burnout can cause changes that can last for years (Koutsimani et al., 2021). Fortunately, the changes can be reversed (Beck et al., 2013). Although it can take a long time.

Inhibitory control seems to be also impaired due to the burnout. In the meta-analysis made by Bar-Haim et al., they found out that anxious people are more likely to focus their attention to threat-related stimuli (Bar-Haim et al., 2006) which supports the same suggestion made by Mathews et al. (Matthews and Mackintosh, 1998). Joormann et al. suggests that depressed people have difficulties in shifting their attention away from the negative stimuli (Joormann, 2004). Because the symptoms of burnout are similar to depression and anxiety there is a chance that burnout is affecting the same neural pathways as in depression and anxiety therefore, those who have the burnout are also more likely to hold on to the negative events and lack of emotional inhibitory control. Burnout can cause significant impairment to the working memory. Jonsdottir et al. made a follow up study where the patient's working memory were tested with Digit Span and Digit Symbol Wechsler's Adult Intelligence Scale Revised (WAIS-R) test before and after the follow up. They found out that stress-related exhaustion negatively affected working memory even after three years. (Jonsdottir et al., 2017)

The effects of burnout to the EF are not that univocal because there are also studies where cognitive defects haven't been reported (Österberg et al., 2009; McInerney et al., 2012; Oosterholt et al., 2014). Even though not all researchers have found correlation between burnout and impairment of EF, the subjects often reports feelings of tiredness (Krabbe et al., 2017), reduced cognitive abilities and the subjects reported that they felt that the tests were more demanding compared to healthy subjects (Oosterholt et al., 2014). The tiredness could be explained by the research made by de Andrende et al. where they found out that subjects with burnout were using more brain resources in the cognitive tasks compared to the healthy subjects. (de Andrade et al., 2016).

3. ASSESSMENT OF EXECUTIVE FUNCTIONS

Assessment of EF can help individuals in various ways. Fully functioning EF are needed for successful everyday life. In a clinical setting, assessment of EF allows early interventions and with the results treatment plans can be adjusted. Subjects can be asked to take tests multiple times to see if the treatment has been useful for the patient or the tests can be used for the diagnosis. In non-clinical setting the assessment of EF can be utilized e.g. in the working environment to see how the workload, working environment, etc. are affecting the employee's EF. Because properly functioning EF can be considered as a measure of brain health (Erkkilä et al., 2018) and an overall factor impacting the quality of life (Diamond, 2013), it is highly important that the used tests are as accurate as possible.

During the COVID-19 pandemic, remotely done activities have gained more popularity. This along with aims to overcome resource limitations in neuropsychological testing due to the limited number of neuropsychologists and uneven access to their services raises the question whether reliable cognitive assessment could be done remotely. Yet there are not many studies where remote cognitive assessment have been evaluated, but in those studies where they have, the results have been promising. (Segura and Pompéia, 2021; Myers et al., 2022) Despite the fact that there is still a lot of work to do there are a few platforms like BrainCheck, Savonix and Neurotrack that has the option of evaluating cognitive skills including EF in online. Yet, they are focusing on how medical conditions like dementia and Alzheimer's disease are affecting cognitive abilities. While EF assessment with ERT test could be used in more creative ways e.g. in guiding depression treatment (Peräkylä et al., 2021) ,or how occupational stressors can affect the EF and to the ERT test results as evaluated in this thesis.

3.1 Traditional neuropsychological tests

Over the years several tests have been developed to evaluate a patient's executive dysfunction. Traditional objective tests can include sorting of cards like in Wisconsin card sorting test, remembering number or letter sequences, inhibition of stimulus like in Stroop test, or they can be traditional subjective questionnaires. All often used objective tests like the Stroop test, Wisconsin card sorting test, trail making test, etc. are still effective when it comes to detecting major changes in the EFs. The problem occurs when the changes in EFs are mild. The traditional neuropsychological tests are not that sensitive for mild changes, causing some people’s impairment in EFs to be undetected and appropriate help might not be offered (Hartikainen et al., 2021). Thus, it is important that in the future, tests are sensitive enough so that early interventions can be made. Depending on the test, the tested EF dimensions vary. In some tests only one EF dimension is tested while in other tests more EF dimensions are studied at the same time. Despite the fact that some tests can evaluate multiple EF dimensions at the same time, it often requires multiple tests before the efficiency of EFs can be evaluated with desired precision and this can be a really time consuming process. (Barr, 2001; Faria et al., 2015) Also, another factor that creates time issues is that the results have to always be evaluated by experts due to the fact that there are multiple factors affecting the results. There can be resource issues as well. Not all who wish to be tested can be tested or the waiting time can be long. If the problems related to the time consumption and lack of resources could be tackled, it would open the possibility for millions of people to be tested.

3.2 Sources of bias

Neuropsychological measurements where testing of EF is included, can suffer from many different biases. For example, in subjective questionnaires some may argue that there are not any cognitive issues even though issues would be visible in objective measurements and vice versa, people might answer slightly differently depending on day or mood, also cultural, age, gender and socio-economic status differences may affect the results. One problem may arise already in the beginning of the tests. Since the used tests are already quite old the subjects might already be familiar with the upcoming test due e.g. internet. The subject might therefore know the functionality of the test and subjects may know what to expect and the results may not be fully reliable. This can lead to biased results. Another problem for both subjective and objective neurophysiological tests is that some tests are validated with small sample sizes. Therefore regional, cultural or socio ecological effects (Howieson, 2019) and personal effects to the outcome can be missed. If the neuropsychological tests would take these parameters into account as well, better personalized guidance and more accurate results could be obtained.

Usually, the tests are time demanding and the motivation of the subjects can decrease and fatigue increases towards the end of testing. Fatigue may lead to less reliable responses and thus erroneous outcomes. On the other hand, those who have burnout, anxiety, depression etc. may get tired faster and the differences can be more visible towards the end when the results are compared to the healthy subjects. Another problem in the testing of EF is that studies do not have uniform results as mentioned in the previous chapter. There have been many studies where the researchers have not found any significant reduction in the EF due to burnout (Österberg et al., 2009; McInerney et al., 2012; Oosterholt et al., 2014). Even though the subjects have reported reduction in their cognitive abilities (Oosterholt et al., 2015). On the other hand, many studies have reported reduction of EF due to burnout (Linden et al., 2005; Sandström et al., 2005; Beck et al., 2013; Diestel et al., 2013; Feuerhahn et al., 2013; Krabbe et al., 2017).

Test sensitivity problems could be overcome by making the used tests challenging enough. Diestel et al. found out that the impairment of EF can be detected when the tests require demanding usage of EF (Diestel et al., 2013). Anyway, even then it is not sure that the neuropsychological tests are able to detect mild cognitive changes. According to Erkkilä et al. (2018) this is exactly the problem with the current neuropsychological tests. Tests are not sensitive enough to detect the mild changes in the EF. Erkkilä et al. (2018) continues that the normally used tests also have shown poor repeatability and they often fail to detect subjective challenges that patients are reporting. (Erkkilä et al., 2018) Defects are most likely detected with patients whose EF performance is already significantly reduced (Hartikainen et al., 2021). Therefore, it is highly important that the tests would be able to separate mild executive dysfunction from healthy peers. If not, the cognitive defects can get worse which eventually will lower the quality of life.

Another factor that has to be addressed in order to get reliable test results from the different EF tests is the learning effect. The test-retest correlations of the neuropsychological tests are usually relatively low because with the novel tasks the EF impairments can be detected most efficiently (Lowe and Rabbitt, 1998; Rabbitt, 2004). This makes it challenging to assess EF with repeated subjective or objective tests. For example, in the reaction time tests, a few first trials are novel to the subject. After that the subject starts to see patterns and guess how to react to the certain stimulus correctly and efficiently. The learning effect can be considered by e.g. by giving the subjects opportunity to practice test beforehand so that in the actual reaction time test the performance would remain as stable as possible. Erkkilä et al. noticed that in the previous version of the ERT test performance stabilization occurred during the first blocks of the first test time. When these blocks were removed, the results were more comparable. In the second test time no similar learning effect was detected. Despite the issues introduced by Rabbit and Lowe, the ERT test showed to be reliable in repeated testing. (Erkkilä et al., 2018) Learning effect can be also controlled by selecting parameters that are not that sensitive for repeated measurements. For example, Lemey, Lowe and Rabbit noticed in separate studies that the test-retest reliability was greater when the assessment was based on reaction times rather than accuracy measurements (Lowe and Rabbitt, 1998; Lemay et al., 2004).

Usually, the laboratory environment and neuropsychological tests are designed in a way that they are neutral or even supportive. This might affect the performance of the subjects in a positive way. Often the emotion attention interaction have not been considered in the tests. Therefore, traditional neuropsychological tests might not reveal how the subjects might function in the everyday environment. This can be another reason why all studies have not reported impairment of the EF (Österberg et al., 2009; McInerney et al., 2012; Oosterholt et al., 2014).

3.3 Executive reaction time test in assessment of executive functions

The advantage of the ERT test (Hartikainen et al 2010) compared to the other tests, is that it will simultaneously measure every main aspect of EF and it includes emotion attention interaction. ERT test is therefore capable of giving better insight of the general brain health and wellbeing of the subject. Also, in the previous study by Erkkilä et. al. ERT test has showed good reliability, repeatability and correlation to BRIEF-A questionnaire results which is used for subjective evaluation of EF (Erkkilä et al., 2018). As the test is done remotely, this gives great freedom for the subjects to complete the test when it is suitable for them and wherever they have access to the computer and internet. Remote testing also makes the distribution of the test easier and as the test environment might not be neutral, the environmental factors may also help to detect subtle EF impairments better.

When assessment of EF is done remotely and unsupervised, it creates several problems that have to be overcome. One problem with the remote testing is how to ensure that the subject is doing as instructed. Even though clear and detailed instructions are provided, there is always a chance that someone might still not understand the instructions. This can lead to contaminated data. One may also face some computer related problems like, the computer doesn't meet the system requirements, computer performance issues or in the worst-case scenario the computer might even break during the test. Also, all do not have good computer usage skills.

4. MATERIALS AND METHODS

In this chapter first the summary of the subjects is presented. Next the functionality of ERT test is explained in detail and the method how data is gathered remotely. Lastly relevant statistical methods that are used for analyzing the data are explained.

4.1 Subjects

Overall 26 volunteers (7 male, 19 female) participated for this test from various working places. Volunteers did not have psychiatric or neurological disorders and they were actively working. Candidates also had access to the computer with Windows operating system and internet connection. Before conducting the ERT test, candidates filled a consent form, Beck's depression inventory (BDI), Bergen burnout inventory (BBI-15), BRIEF-A questionnaires and a COVID-19 brain health questionnaire developed in the Behavioral Neurology Research Unit, Tampere University Hospital. Based on BBI-15 questionnaire results, subjects are divided into two groups, healthy and burnout. The summary of both groups is presented in Table 1.

Table 1. Demographics of the subjects. From both study groups number of participants, gender, age, maximum and minimum age are presented. In the age column the age is presented as mean age and inside the brackets standard deviation of age can be found.

		N	*Age*	*Maximum age*	*Minimum age*
Healthy	Male	8	38,9 (12.7)	55	24
	Female	12	42.6 (13.8)	61	25
Burnout	Male	-	-	-	-
	Female	6	36.7 (10.3)	48	23

The study was approved by the Regional Ethical Committee of Tampere University Hospital, Tampere, Finland.

4.2 Executive reaction time test

The ERT test is a computer-based Go/NoGo test where subject's EFs can be broadly studied. The test simultaneously tests subject's working memory, inhibitory control, emotional control, attention, and cognitive flexibility. Since the subject has to use all dimensions of EF during the test, the test can give better understanding of subject's brain health compared to the other methods. Parameters used to measure EF are reaction time (RT) and different error types. The error types measured are incorrect responses (incorrect), missing responses (miss), incorrect response in reversed trial (incorrectR), missing response in reversed trial (missR) and commission errors, where R stands for reversed cases. Commission error indicates the number of times that subject has reacted in NoGo trial. The reversed case is explained later in this section. The ERT test is divided into eight blocks, four Green-go and four Red-go blocks. Each block consists of 64 trials (32 Go, 16 GoR, 16 NoGo) so in total the test consists of 512 individual trials. In the beginning of each block Go-color, either green or red traffic light is presented for the user. In every second block the green represents Go-signal and vice versa.

Every trial has four phases, first subjects are going to see a picture of a triangle that is presented for 150 milliseconds. The triangle is either pointing downwards or upwards. Subject must remember the orientation of the triangle after it disappears from the screen. Secondly a fixation cross will be visible for another 150 milliseconds. Third, subjects are going to see a picture of the traffic lights for 150 milliseconds. Traffic lights are presented in Figure 3. After that fixation cross is visible again for 1150 milliseconds. Depending on Go-signal, subject is asked to react to the visual stimulus by pressing the arrow keys in the keyboard either up or down (Go-signal) or by not pressing any button (NoGo-signal). After the traffic light has disappeared from the screen subjects have 1550 milliseconds to give their answer before next trial begins. All the subjects were instructed to use index and middle finger of their right hands for answering. Schematic of a single trial is presented in Figure 4.

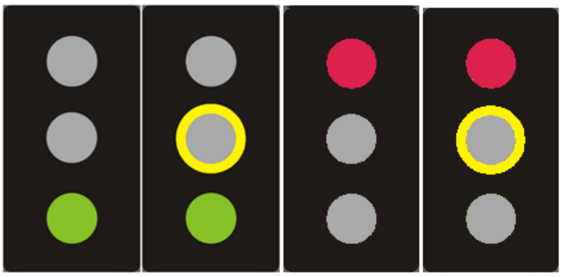

Figure 3. *Traffic lights used in the test to indicate Go- NoGo- and Reverse trial types. Yellow circle in the middle indicates a reversed case. In every second block the green represents Go-signal and vice versa.*

There are two kinds of Go trials in the test, regular and reversed trials. The reversed trials are indicated by a noticeable yellow circle in the middle of the traffic light, while in regular trials there are no such highlights (Figure 3). In regular trial, the subject has to react by pressing the arrow key to the same direction as the triangle were. E.g., if the triangle was pointing downwards, the user has to press the DOWN arrow key and vice versa. In the reversed trial, the arrow keys must be pressed in the opposite direction of the triangle. E.g., if the triangle is pointing downwards, the user has to press the UP arrow key and vice versa.

In the middle of the traffic light an emotional distractor is presented. There are two types of distractors, negative and neutral. For the negative distractor, a drawing that resembles a spider has been used and for the neutral distractor drawing that resembles a flower has been used (Figure 4). The purpose of the emotional distractor is to subconsciously affect to subject’s emotional behavior and see if it has effect on the subjects RT or different errors. Emotional distractors are sharing same line elements so that the effect of negative emotional distractor is controlled.

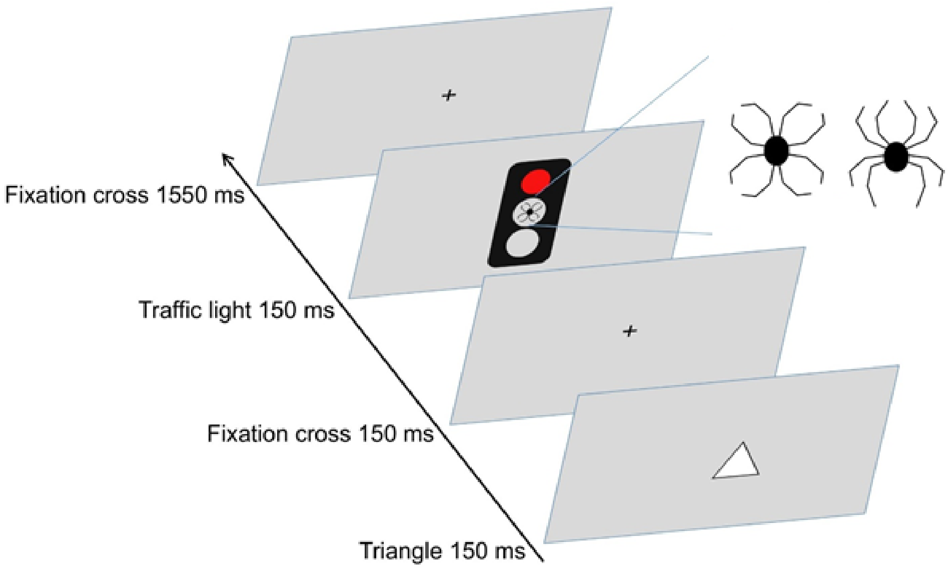

Figure 4. *Schematic presentation of a single trial. Triangle and traffic lights are visible for 150 ms. After the traffic light subject has 1550 ms to give the answer. In the middle of the traffic light emotional distractor can be seen.*

Cognitive flexibility is tested in two ways in this test. By evaluating how well the subjects can adapt to changing reaction colors from green to red and vice versa between the blocks, and how well the subjects can change their response between regular and reversed trials. Working memory is tested by giving specific instructions how and when the subject must react to the visual stimulus. The subject must remember the orientation of the triangle, when to react and when not to, when they have to react in regular manner and when reversed. Inhibitory control can be tested by evaluating how well the subject can resist pressing the button during the NoGo signal and also by evaluating if the emotional distractor will affect the RTs.

4.3 Statistical analysis

Before any statistical analyzes were done, the normality of the RT data was confirmed visually from RT histogram and QQ-plots. If necessary, the RT data was transformed by using Box Cox method. Possible outlier scenarios were detected and removed based on visual inspection of subjects error rates. For the RT analysis, trials with RT over or equal 150 ms, RT and correct responses were included. The RT analyses were conducted with repeated measures analysis of variance (ANOVA). In the ANOVA RTs were analyzed between study groups (healthy and burnout), while emotional distractors (neutral and negative) and go type (regular and reversed trial) were used as within subject factors. The null hypothesis in ANOVA is that no differences in the mean can be seen between the study groups. The alternative hypothesis for ANOVA is that there are differences in the mean RTs between the study groups, the negative emotional distractor affects the RTs and reversed trail type increases the RTs in both groups.

Each error type, total errors, incorrect, miss and commission error were analyzed with the separate generalized binary logistic regression models. In the models subject was used as a random effect predictor and emotion, study group and reversed case as fixed effect predictors. For the regression analyses, trial outcomes had to be dichotomized so that the outcome is binary. For the total errors outcome can be “error” or “correct”, for incorrect and incorrectR “incorrect” or “other”, for miss and missR “miss” or “other”, for commission error “commission error” or “other”. For total error analysis, whole data set was used. When analyzing the incorrect and miss error rates, only regular and reversed go trials were selected. For commission error analysis, only NoGo trials were used. If any interactions were detected, then post hoc analysis was performed for the interacting variables. The null hypothesis in regression analyses is that there are not any differences between the study groups. The alternative hypothesis in regression analyses is that the study group is making more errors, reversed trial type increases the error rate and there are more errors with negative emotional distractor.

The correlation analyses between BRIEF-A, BBI-15 and ERT test results were done by using the Spearman’s rank correlation. Before the analysis, outliers had to be removed from the analyses because outliers have a significant effect on the correlation coefficient and the statistical power is significantly decreased if the used data contains outliers. The outliers for correlation analyses were identified and excluded by using Mahalanobis distance of 5. Due to multiple correlation analyzes were conducted the p-values had to be adjusted. P-values were adjusted with Benjamini and Hochberg method. The null hypothesis in correlation analyses is that there are not any differences between the study groups. The alternative hypothesis in correlation analyses is that the ERT results are correlating with BRIEF-A and BBI-15 results.

For all statistical analyses significance level $\alpha = 0.05$ was used. All the statistical analyses were conducted with the R programming language, version 4.1.0. For logistic regression analyses R package lme4, version 1.1-28 was used and for ANOVA R package ez version 4.4-0 was used.

5. IMPLEMENTATION OF REMOTE EXECUTIVE REACTION TIME TEST

The ERT test was developed by using the Neurobehavioral Systems (NBS) Presentation software. NBS also provides another software called Package Player which provides an opportunity to execute the experiments locally or remotely. For the purpose of the study, a remote option was selected. Subjects just have to install the Package Player software in order to conduct the test. Remote assessment gives a great freedom to the subjects. Subjects can do the test at home or work whenever it is suitable. The cycle of how the experiment is developed and the data is received is presented in Figure 5.

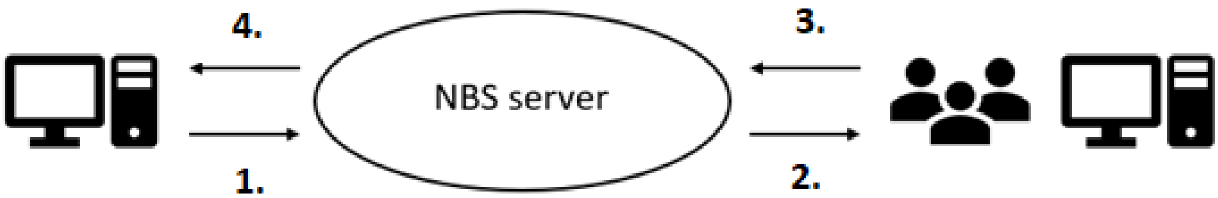

Figure 5. *Schematic presentation of the remote testing of EF protocol 1. Experiment is developed and uploaded to NBS server where subjects can download it. 2. Subjects downloads the experiment and executes it with Package Player software. 3. Once the experiment is done, the results are automatically uploaded to the NBS server. 4. Data is downloaded from the server for analyzing.*

The instructions for the subjects were handled by giving them written instructions. Before subjects were allowed to start the actual ERT test, users had to complete a shorter practice version of the test. The shorter version contained 64 individual trials, 32 green-go and 32 red-go. subjects must have at least 60 % correct answers in total, in order to continue to the actual ERT test. If the subject fails to get enough correct answers, they can decide if they want to recap the instructions or if they want to complete the practice version again immediately. The purpose of the practice test is to familiarize users with the ERT test, control learning bias and to prevent contaminated data. When the subject passes the practice test, subject can continue to the actual test. After the subjects have completed the ERT test, the results will be automatically crypted and uploaded to NBS's server, where the data can be collected for the further use.

6. RESULTS AND DISCUSSION

6.1 Summary of the executive reaction time test results

In total 26 subjects participated to the project. That yielded 11776 trials which were included for further data analysis. High level summary of the healthy subjects' results is presented in Table 2.

Table 2. Summary of ERT test results of subjects without burnout. Mean values and standard deviations (inside the brackets) are presented.

Healthy group

	Mean RT (ms)	*Total errors (%)*	*Incorrect (%)*	*Miss (%)*	*IncorrectR (%)*	*MissR (%)*	*Commission errors (%)*
Neutral	662.1 (168.2)	11.4 (14.3)	7.4 (13.4)	4.3 (12.7)	14.8 (22.2)	3.8 (14.2)	1.9 (3.3)
Negative	662.8 (173.9)	11.6 (14.6)	8.1 (13.6)	4.0 (13.0)	15.4 (22.4)	3.0 (10.1)	2.0 (4.0)

R indicates reversed trial type.

RTs or error rates did not significantly differ between emotional distractors in healthy subjects. High level summary of ERT test results of subjects with burnout is presented in Table 3.

Table 3. Summary of ERT test results of subjects with burnout. Mean values and standard deviations (inside the brackets) are presented.

Burnout group

	Mean RT (ms)	*Total errors (%)*	*Incorrect (%)*	*Miss (%)*	*IncorrectR (%)*	*MissR (%)*	*Commission errors (%)*
Neutral	718.3 (168.7)	8.4 (5.8)	8.7 (8.7)	1.4 (1.4)	9.4 (6.3)	1.0 (1.3)	1.5 (1.2)
Negative	714.0 (157.2)	8.1 (6.3)	6.5 (6.9)	0.7 (0.6)	12.5 (8.2)	1.3 (1.5)	2.1 (2.2)

R indicates reversed trial type.

Even though the mean RT seems longer and error rates smaller in subjects with burnout, burnout did not significantly increase the RTs or error rates when compared to healthy subjects. This is probably due to small sample size with only 6 subjects with burnout.

When looking at Table 3, it can be seen that the subjects who have burnout are faster on average with negative emotional distractor. They also seem to be making less errors in context of negative emotional stimuli. This can be explained by Yerkes–Dodson law. Yerkes-Dodson law describes the relationship between stress and task performance with inverted U-curve. When the task is easy as in regular trial type, the negative emotional distractor increases the attention of the subjects and they will perform better. When the task is harder like in reversed trial type, subjects need to use more resources and their attention decreases which also decreases the performance. The total error rates per scenario is presented in Figure 6.

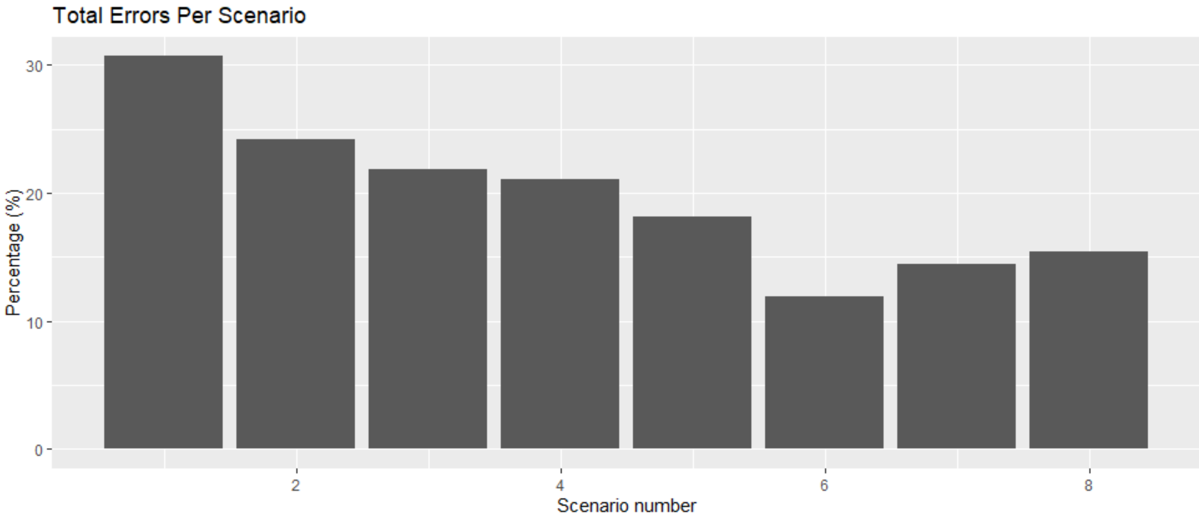

Figure 6. *Percentages of total errors in each scenario. Total error rates are steadily decreasing before the last two blocks. In the final two blocks the total error rates are increasing perhaps due to fatigue.*

From Figure 6, it can be seen that number of the total errors are steadily decreasing throughout the test excluding the last 2 blocks. The decrease in total error rates is most likely due to the learning effect. Even though the ERT test is not that long to complete, it requires a lot of resources to maintain the focus on the test. Due to intensive and exhausting test, subjects are more likely quite tired in the last two blocks and therefore not able to concentrate fully which leads to more errors. In the future when subjects are going to take the ERT test multiple times, the learning effect has to be considered. Erkkilä et al. (2018) noticed that the learning effect occurred during the first blocks of the first test. So, for better control of the learning effect, the number of trials of the practice test could be doubled increased from 64 trials to 128 trials so that the training session corresponds two blocks.

6.2 Outliers

Three subjects were excluded from the analysis due to exceptionally high error rates in one of the error types. Error rates of the outlier subjects are presented in Figure 7. Subject 17 had answered every reversed trial type incorrectly. This indicates that the subject had not understood how to react in reversed trial type and treated reversed trial type similarly to the regular trial type. Otherwise, the error rates of the subject 17 are low. It is unlikely that the instructions before the test were unclear because this was an isolated case. Another reason could have been that the yellow circle in the middle of the traffic light (Figure 3) was not clear enough for the user. Subject 16 was removed from the analysis due to high number of incorrect answers. Subject might have thought that every trial has to be done in reversed order or the subject has potentially guessed the orientation of the triangle. In turn, subject 21 had exceptionally high number of misses in the test. It can be that the user could not register the visual stimuli due to concentration difficulties. After all, the stimulus is only visible for 150 ms. Yet, computer related issue cannot be completely ruled out.

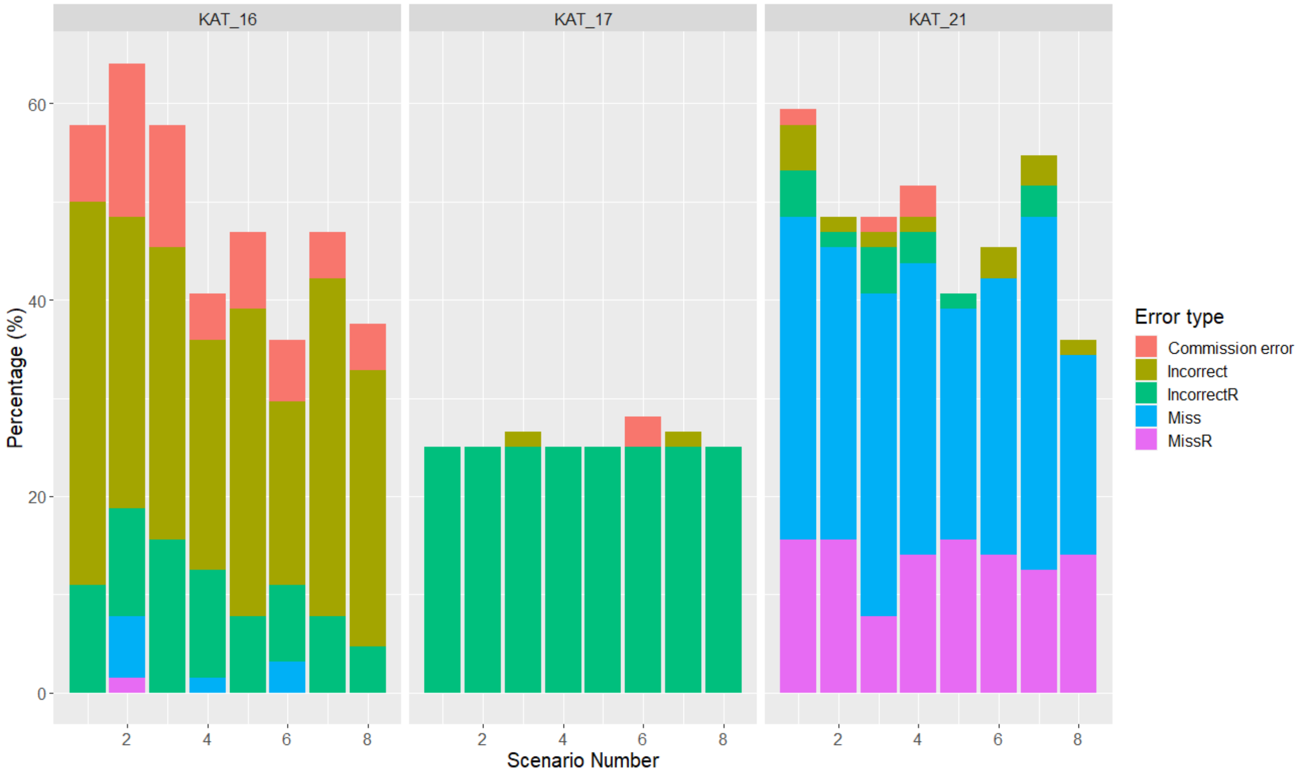

Figure 7. *Error rates of the outlier subjects. Each error type is presented as a percentage and results of each subject presented separately. R indicates reversed trial type.*

During the test development there have been clear oversight. The practice test can be passed even if the subject answers every reversed trial incorrectly. The threshold of 60 % correct answers in both scenario types is clearly too low and this has to be increased for the future tests. With this, it can be ensured that every subject understands the rules of the ERT test. It could be also beneficial to increase the number of trials in the practice test. In the future when the test is potentially used in repeated testing, the learning effect has to be considered. With the increment, the learning effect could be controlled even better.

6.3 Analysis of reaction time

Before any analyses, the normality of the data was confirmed visually from histograms and QQ-plots. Visualizations of histograms and QQ-plots are presented in Figure 8.

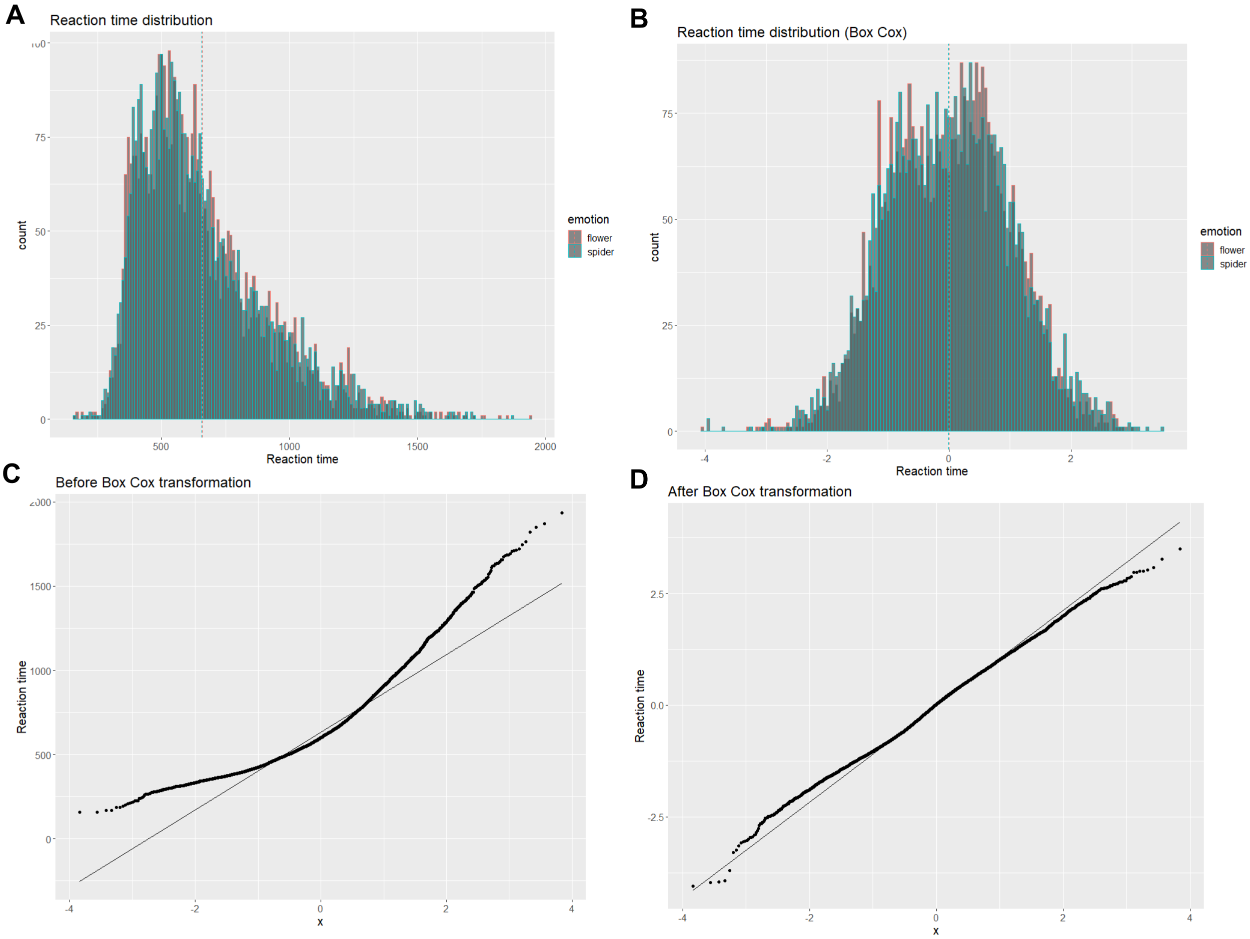

Figure 8. *Reaction time distributions and QQ-plots before and after Box Cox transformation. A: The reaction time distribution before Box Cox transformation. B: Reaction time distribution after Box Cox transformation. C: QQ-plot of reaction time data before transformation. D: QQ-plot of reaction time data after Box Cox transformation.*

As seen in Figure 8, the RT is not normally distributed but rather right skewed. The non-normality of the RT data is visible in the QQ-plot (B). Because one of the assumptions of ANOVA is that the data has to be normally distributed, a Box Cox transformation had to be made so that the assumption of data normality can be met. After the Box Cox transformation, the RT data becomes normally distributed as seen from Figure 8: D.

For ANOVA, only go and GoR trials with correct answers and RT equal or over 150 ms were included. Summary of the used data is in table 4.

Table 4. Summary of RTs between study groups. Standard deviation of the mean reaction times can be found inside the brackets.

		Healthy group		*Burnout group*	
	Go type	*N (trials)*	*Mean RT (ms)*	*N (trials)*	*Mean RT (ms)*
Neutral	Go	2035	573.3 (217.3)	688	663.9 (233.8)
	GoR	981	773.5 (248.4)	344	836.1 (233.0)
Negative	Go	2027	570.9 (218.6)	712	657.2 (236.2)
	GoR	981	770.1 (244.0)	331	847.6 (230.3)

R indicates reversed trial type.

In Table 4 it can be seen that the reversed trial type increased the RT in both study groups. With both distractors, neutral and negative, the difference is around 200 ms between regular and reversed trial types. Also, the impact of emotional stimuli on RTs seem to vary between the burnout status in different conditions. In order to find out if reversed trial type or burnout status has a statistically significant effect on the outcome, ANOVA was performed. The results of ANOVA are presented in Table 5.

*Table 5. Results of the ANOVA. Significant results are marked with a *.*

Effect	*F*	*p-value*	*Ges*
Group	1.12	0.30	0.0051
Emotion	0.04	0.84	0.0002
Go type	387.11*	< 0.001*	0.9324*
Group x Emotion	0.06	0.81	0.0003
Group x Go type	1.61	0.22	0.0544

Emotion x Go type	1.29	0.27	0.0032
Group x Emotion x Go type	2.18	0.15	0.0053

Results from the ANOVA confirm that there is a statical difference between regular and reversed trial type. The reversed trial type slows the subjects regardless the emotional distractor and burnout status (*F = 387.11*, *p-value < 0.001*). The increased RT in the reversed trials indicate that the subjects are using more brain resources in the reversed trial type. This supports Meiran's findings where they concluded that the RTs are usually increased when subjects have to change their response style inside the test (Meiran, 1996)

No differences between study groups were detected. One possible explanation why the differences between the study groups did not become significant in the ANOVA, can be small number of burnout subjects. There were only 6 subjects with burnout compared to 20 subjects without. Small sample size causes ANOVA to be statistically underpowered. Therefore, more data from the subjects who have burnout is required. The age and gender might also affect the ERT results. Now there were only females who had burnout. Therefore, also the effects of age and gender needs to be studied with larger dataset.

6.4 Analysis of error rates

Each error type was analyzed separately and if any significant interactions were found then the post hoc analysis was done to see which parameter causes the significant interaction. For each regression analyses mean percentages were used. Summary of the error data is presented in Table 6.

Table 6. Summary of the error rates between study groups. Different error response rates are presented as a mean value in regular and reversed trials. Standard deviation of the different error responses can be found inside the brackets.

		Healthy group				*Burnout group*			
Distractor		*Total errors (%)*	*Incorrect (%)*	*Miss (%)*	*Commission errors (%)*	*Total errors (%)*	*Incorrect (%)*	*Miss (%)*	*Commission errors (%)*
Neutral	Go	5.2 (5.6)	5.1 (6.4)	1.4 (1.8)	1.3 (1.9)	7.7 (6.2)	8.7 (8.7)	1.4 (1.4)	1.4 (1.2)
	GoR	9.8 (8.0)	9.1 (7.8)	0.7 (1.2)	-	10.4 (5.7)	9.4 (6.3)	1.0 (1.3)	-
Negative	Go	5.3 (5.6)	5.7 (7.1)	1.1 (2.2)	1.1 (1.5)	6.2 (5.9)	6.5 (7.0)	0.7 (0.6)	2.1 (2.2)
	GoR	9.8 (8.5)	9.0 (8.2)	0.8 (2.1)	-	13.8 (8.2)	12.5 (8.2)	1.3 (1.5)	-

Each regression analysis results are presented in a same way. First odds ratio (OR) is presented and after the OR confidence interval (CI) is presented. Odds ratio tells the odds of outcome happening in given conditions. Confidence interval tells the range where the estimated value lies with given confidence level e.g. 95 % like in this thesis. Results of Healthy subjects, negative emotional distracor and reversed trial type has been used as baseline values in the analyses. I.e. the results are always compared to results of these parameters. The results of the regression analyses on total error, incorrect responses, miss responses and commission errors are presnted in Table 7.

*Table 7. Results of the generalized binary logistic regression analysis of total errors, incorrect responses, miss responses and commission errors. Significant results are marked with a *.*

	Total errors	*Incorrect*	*Miss*	*Commission errors*
Group (healthy)	0.52 (0.19 - 1.41)	0.45 (0.16 - 1.25)	0.69 (0.17 - 2.80)	0.80 (0.26 - 2.45)
Emotion (negative)	0.78 (0.56 - 1.08)	0.72 (0.49 - 1.06)	0.45 (0.16 - 1.25)	1.49 (0.69 - 3.21)
Go type (reversed)	1.41 (0.95 - 2.10)	1.09 (0.70 - 1.68)	0.72 (0.24 - 2.20)	-
Group (healthy) x Emotion (negative)	1.31 (0.88 - 1.95)	1.59 (0.99 - 2.56)	1.71 (0.54 - 5.41)	0.57 (0.22 - 1.47)
Group (healthy) x Go type (reversed)	1.49 (0.92 - 2.40)	1.82 (1.08 - 3.06)*	0.70 (0.18 - 2.69)	-
Emotion (negative) x Go type (reversed)	1.80 (1.04 - 3.14)*	1.97 (1.07 - 3.62)*	2.80 (0.54 - 14.38)	-
Group (healthy) x Emotion (negative) x Go type (reversed)	0.54 (0.28 - 1.06)	0.44 (0.21 - 0.91)*	0.53 (0.07 - 3.72)	-

The regression analysis results shows that there is a two-way interaction between emotion and go type in total errors (*OR = 1.80, CI = 1.04 - 3.14*). Two-way interactions can be found also between status and go type (*OR = 1.82, CI = 1.08 - 3.06*) as well as emotion and go type (*OR = 1.97, CI = 1.07 - 3.62*) in incorrect error type. There is also a significant three-way interaction between status, emotion and go type in incorrect error type (*OR = 0.44, CI = 0.21 - 0.91*). With miss responses and commission errors there were no statistically significant differences. First the interaction between emotion and go type in total error was studied by creating another generalized logistic regression models where the data was stratified by go type or emotion. The results are presented in Table 8.

*Table 8. Results of the regression analysis on total errors when the data is stratified by go type and emotion. Significant results are marked with a *.*

	Stratified by emotion		*Stratified by go type*	
	Neutral	*Negative*	*Regular*	*Reversed*
Go type (reversed)	1.85 (1.49 - 2.30)*	2.20 (1.78 - 2.73)*	-	-
Emotion (negative)	-	-	0.94 (0.78 - 1.12)	1.11 (0.87 - 1.41)

When the data is split by go type it can be seen that with both emotional distractors (*flower OR = 1.85, CI = 1.49 - 2.30, spider OR = 2.20 CI = 1.78 - 2.73*) there is significant difference between regular trial total error rates and reversed trial total error rates. I.e. the subject's total errors are e.g. 1.85 times greater with the neutral distractor in reversed trial compared to total errors in regular trial with neutral distractor.

Emotional distractor on the other hand does not have a significant effect on the total error rates in regular and reversed trial types (*Regular OR = 0.94, CI = 0.78 - 1.12, reversed OR = 1.11, CI = 0.87 - 1.41*). In other words, the total errors rates between emotional distractors are statistically the same in both go types. Results shows that there are no differences in total error rates between study groups. Similarly like in ANOVA test, the unbalanced group sizes might be the reason. However, there are still some interesting visual results between the study groups. Total error rates between study groups split by emotions are presented in Figure 9.

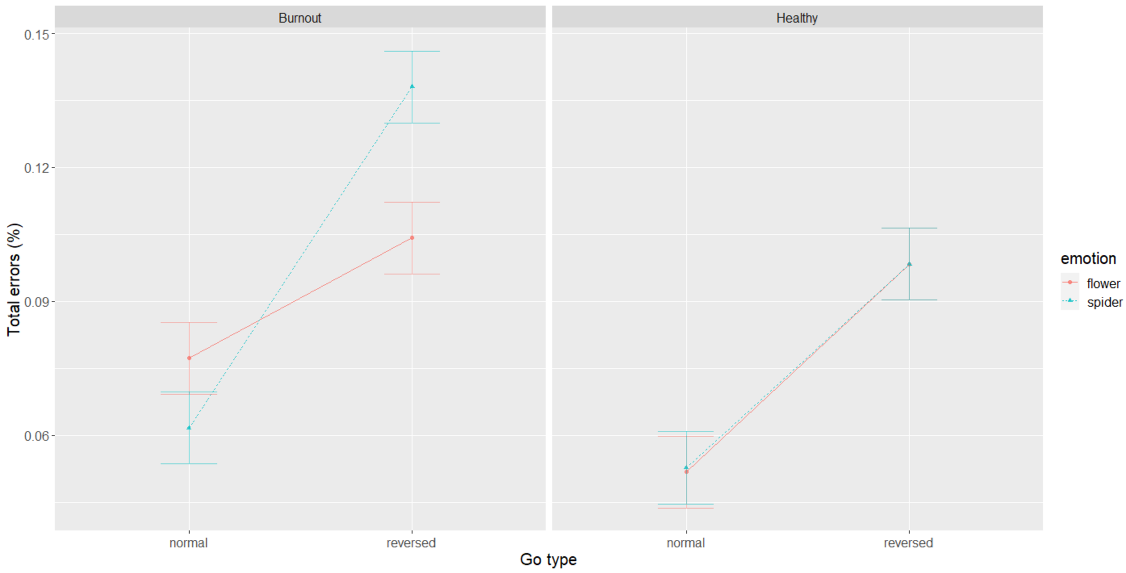

Figure 9. *Total error rates between study groups, divided by emotional distractor go type.*

When looking at Figure 9, the emotional distractor does not have an impact on total error rates in the healthy subjects, but the reversed trial type increases the total error rate. Interesting differences occur in the burnout group. The total error rate with negative emotional distractor is less than the neutral total error rate in the regular trial type but greater in the reversed trial type. The phenomenon could be explained with the Yerkes–Dodson law. Burnout subject's mean total error rate is over doubled with the negative emotional distractor when compared between reversed trial type and regular trial type. This phenomena of the seemingly altered impact of emotional stimuli on EF performance due to burnout is further studied using a subtraction score described later.

Next the incorrect responses were analyzed. The results of regression analysis on incorrect responses are presented in Table 7. The visual presentation of mean incorrect response rates between study groups is presented in Figure 10.

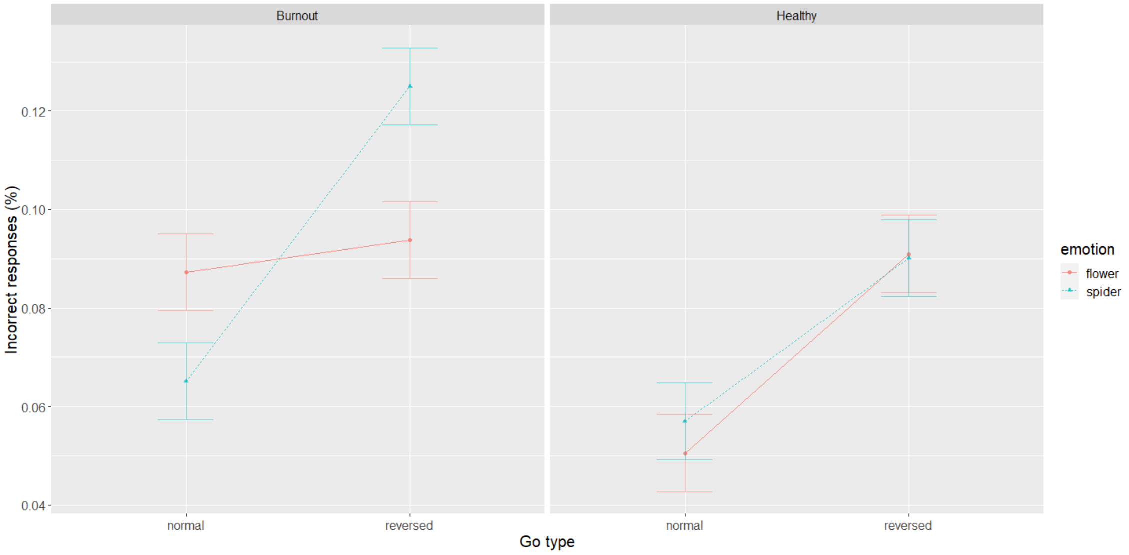

Figure 10. *Incorrect error rates between study groups, divided by emotional distractor and go type*

When inspecting Figure 10 it can be seen that the reversed trial type increases the incorrect response rate in both groups. The emotional distractor seems not to have an effect on the incorrect response rate in the healthy subjects as the error rates between the emotional distractors are similar in both trial types. Differences between the emotional distractors are visible with the subjects with burnout. Contrary to the hypothesis, the subjects are giving more incorrect responses on average with the neutral distractor in the regular trial type. In the reversed trial type, the subjects are making more errors with the negative emotional distractor. Similarly like in case of total error rates, this could be explained with Yerkes–Dodson law.

There was a significant three-way interaction between group, emotion and go type in incorrect response type. Two-way interactions are not studied separately because they are included in the three-way interaction. In order to find out which parameters are causing the significance, the data is split and the sub datasets are analyzed separately. First data was stratified by group to see if there are any significant differences between the groups. Results of the regression model after the data is stratified by group are presented in Table 9.

*Table 9. Results of the regression analysis on incorrect responses when the data was stratified by study groups. Significant results are marked with a *.*

	Healthy	*Burnout*
Emotion (negative)	1.14 (0.87 - 1.50)	0.72 (0.49 - 1.06)
Go type (reversed)	1.98 (1.48 - 2.65)*	1.09 (0.70 - 1.68)
Emotion (spider) x Go type (reversed)	0.86 (0.57 - 1.30)	1.96 (1.07 - 3.61)*

The results show that the reversed trial type significantly increases the incorrect response rate with the healthy subjects. (*OR = 1.98, CI = 1.48 - 2.65*). With burnout subjects there is a significant interaction between emotion and go type (*OR = 1.96, CI = 1.07 - 3.61*). Therefore, from the data only burnout subjects are selected and the remaining data was stratified by emotion and go type for further analysis. The results are presented in Table 10.

*Table 10. Results of the regression analysis on incorrect responses when the data including only subjects with burnout was stratified by go type and emotion. Significant results are marked with a *.*

	Stratified by emotion		*Stratified by go type*	
	Neutral	*Negative*	*Regular*	*Reversed*
Go type (reversed)	1.09 (0.71 - 1.68)	2.14 (1.40 - 3.28)*	-	-
Emotion (negative)	-	-	0.71 (0.48 - 1.05)	1.40 (0.88 - 2.21)

The results show that the burnout subjects are giving twice as many incorrect responses in the reversed trial type when the emotional distractor is spider compared to the regular trial type (*OR = 2.14, CI = 1.40 - 3.28*). When the data is stratified by emotion there are no significant differences between the emotional distractors in regular and reversed trial types. The results shows again that the subjects with burnout are making less incorrect responses with negative distractor in the regular trial and more in reversed trial. These results can be similarly explained with Yerkes-Dodson law like in total errors.

6.5 Correlation analysis of BRIEF-A, BBI-15 and Executive reaction time test

For the correlation analyses the absolute value was taken from the subtraction between emotional distractors in both regular (absΔERT Regular) and reversed (absΔERT Reversed) RT within each subject. For the different error types, same procedure was done. By doing so, the magnitude independent of direction of the emotional effect on RTs and error rates can be analyzed.

absΔERT Regular correlated negatively with the behavioral regulation index (BRI) and global executive composite (GEC) score of the BRIEF-A questionnaire before p-value adjustment. After the p-value adjustment, the correlations were no longer statistically significant (*Appendix I*). Better results were obtained with the absΔERT Reversed index. absΔERT Reversed correlated with three BRIEF-A questionnaire indicis after the p-value was corrected for multiple comparisons. The significant correlations were obtained from the Initiate, Working Memory and metacognition index (MI) (*Appendix I: Initiate 0.60 (0.004/0.046), Working Memory 0.54 (0.011/0.046) and MI 0.56 (0.009/0.046)*).

Total errors, incorrect and IncorrectR error types correlated with the certain BRIEF-A indicis before the p-value adjustment. All significances disappeared after the adjustment (*Appendix II*). Correlations between absΔERT Regular, absΔERT Reversed, ΔERT Regular and ΔERT Reversed indicis and BBI-15 indicis are presented in Table 11.

*Table 11. Results of correlation analyses between reaction time results and BBI-15. The results are presented as follows first the correlation coefficient is presented, then inside the brackets first non-adjusted p-value followed by adjusted p-value. Statistically significant results are marked with a *.*

	absΔERT Regular	*absΔERT Reverse*	*ΔERT Regular*	*ΔERT Reversed*
Score	-0.46 (0.034/0.034)*	0.44 (0.041/0.082)	-0.31 (0.166/0.222)	0.15 (0.498/0.768)
Exhaustion	-0.53 (0.014/0.022)*	0.53 (0.013/0.051)	-0.18 (0.429/0.429)	0.07 (0.742/0.768)
Cynicism	-0.53 (0.017/0.022)*	0.38 (0.094/0.125)	-0.40 (0.066/0.154)	0.07 (0.768/0.768)
Self-esteem	-0.56 (0.01/0.022)*	0.29 (0.207/0.207)	-0.40 (0.077/0.154)	0.08 (0.723/0.768)

absΔERT Regular significantly correlates even after the adjustment with every BBI-15 indicis (*Score*: *-0.46 (0.034/0.034), Exhaustion: -0.53 (0.014/0.022), Cynicism: -0.53 (0.017/0.022) and self-esteem: -0.56 (0.01/0.022)*). absΔERT Reversed correlates only with Total score and Exhaustion indicis before the adjustment but not after. In Table 11 it can be seen that the correlation between mean absolute RT in reversed trial type and exhaustion index was almost significant after the adjustment. None of the error types correlated with the BBI-15 questionary before or after the adjustment. Correlations between total errors and Total score and total errors and self-esteem were closing to significant level. The results are presented in Table 12.

*Table 12. Results of correlation analyses between error results and BBI-15. The results are presented as follows first the correlation coefficient is presented, then inside the brackets first non-adjusted p-value followed by adjusted p-value. Statistically significant results are marked with a *.*

	Total score	*Exhaustion*	*Cynicism*	*Self esteem*
Total errors	0.41 (0.056/0.112)	0.24 (0.294/0.294)	0.31 (0.161/0.215)	0.45 (0.056/0.112)
Incorrect responses	0.25 (0.272/0.272)	0.29 (0.272/0.272)	0.39 (0.083/0.272)	0.27 (0.253/0.272)
IncorrectR responses	-0.07 (0.764/0.776)	-0.2 (0.385/0.776)	0.06 (0.776/0.776)	-0.15 (0.528/0.776)
Miss responses	0.15 (0.515/0.822)	-0.05 (0.822/0.822)	0.08 (0.717/0.822)	0.17 (0.484/0.822)
MissR responses	0.3 (0.179/0.358)	0.11 (0.623/0.623)	0.47 (0.03/0.122)	0.24 (0.313/0.417)
Commission error	-0.06 (0.780/0.849)	0.18 (0.425/0.849)	0.04 (0.849/0.849)	-0.31 (0.168/0.672)

Based on the results, it seems that the error rates of different error types are not that efficient parameter for assessment of burnout. However, it has to be kept in mind that there were only 6 patients with burnout. Correlation analyses was also performed between BRIEF-A and BBI-15 results. The results are presented in Table 13.

*Table 13. Correlation analysis results between BBI-15 and BRIEF-A questionnaires. The results are presented as follows first the correlation coefficient is presented, then inside the brackets first non-adjusted p-value followed by adjusted p-value. Statistically significant results are marked with a *.*

	Total score	*Exhaustion*	*Cynicism*	*Self-esteem*
Inhibit	0.52 (0.013/0.020)*	0.68 (0.001/0.002)*	0.56 (0.008/0.014)*	0.31 (0.172/0.192)
Shift	0.59 (0.003/0.006)*	0.67 (0.001/0.002)*	0.44 (0.039/0.047)*	0.48 (0.026/0.035)*
Emotional control	0.68 (0.001/0.002)*	0.79 (0.000/0.000)*	0.60 (0.003/0.006)*	0.52 (0.015/0.021)*
Self-monitoring	0.39 (0.080/0.091)	0.65 (0.002/0.003)*	0.40 (0.074/0.087)	0.18 (0.442/0.482)*
Initiate	0.68 (0.001/0.002)*	0.76 (0.000/0.000)*	0.55 (0.009/0.015)*	0.47 (0.028/0.036)*
Working memory	0.69 (0.001/0.002)*	0.48 (0.024/0.033)*	0.63 (0.002/0.004)*	0.72 (0.000/0.001)*
Plan	0.62 (0.002/0.004)*	0.55 (0.006/0.011)*	0.74 (0.000/0.001)*	0.61 (0.002/0.005)*
Task monitoring	0.66 (0.001/0.002)*	0.46 (0.030/0.037)*	0.59 (0.004/0.007)*	0.48 (0.027/0.035)*
Organization of materials	0.16 (0.487/0.520)	0.09 (0.690/0.690)	0.09 (0.684/0.690)	0.15 (0.527/0.550)
BRI	0.76 (0.000/0.000)*	0.90 (0.000/0.000)*	0.68 (0.000/0.002)*	0.67 (0.001/0.002)*
MI	0.65 (0.001/0.003)*	0.64 (0.001/0.003)*	0.52 (0.017/0.024)*	0.54 (0.014/0.021)*
GEC	0.83 (0.000/0.000)*	0.74 (0.000/0.000)*	0.68 (0.000/0.002)*	0.72 (0.000/0.001)*

Despite the fact that in the statistical analyses the burnout status did not reveal statistically significant differences between the study groups, the correlation analysis between BRIEF-A and BBI-15 shows that the subjects with burnout are facing more difficulties in EFs.

6.6 Experiences from remote Executive reaction time test

Remote EF assessment was successfully conducted. Data collection was easy as the results of the ERT test were automatically sent to the NBS server, where it could be downloaded for the analysis. In most of the cases subjects were able to install required software with the instructions they were provided. Only one subject required further assistance. Subject was using rather old computer and the problem was fixed when the subject used another computer. At the moment, NBS only provides a version of the Package Player for Windows operating system. One subject did withdraw from the study because there was not compatible version for macOS devices. Based on experiences from this study it is possible to instruct the subjects how to perform the ERT test only with the written instructions. 23 subjects gave reliable data while 3 were stated as outliers. In the laboratory environment the test could have been interrupted and subjects could have been reinstructed. In remote assessment it must be ensured with other methods that the subjects understand the instructions. For that reason, the practice test was also included for the ERT test. The practice test needs to be further developed because e.g. there was one subject who answered every reversed trial type incorrectly. Either the passage threshold of 60 % has to be increased or a separate indicator for passage in reversed trials needs to be set in the future tests. When the test is used in repeated testing the learning effect needs to be addressed. Learning effect could be controlled by increasing the number of trials in the practice test.

As remote test setup was a success it could be also a good idea to provide a phone compatible version from the ERT test. In the future the instructions could be given also in the video format so that the users would have the option to choose suitable option for the instructions. So that even more broad population could have the access for the ERT test, the test could have different versions e.g. for color blind or blind people. The variation of the negative emotional distractor image could possibly increase the effect as it might diminish potential habituation to the emotional stimuli.

7. CONCLUSIONS

In general, the remote test setup was a success. The subjects were able to execute the ERT test remotely with the given written instructions without major problems and the data was easily obtained from the NBS server. The remote setup allowed collecting data outside the laboratory in their home or working environments. Three persons had to be excluded from the analysis due to unreliable data. Subjects probably misunderstood the instructions. Thus, for the future the instructions, ERT test and practice test needs to be slightly modified. Greatest issue in terms of understanding ERT test instructions occurred with one of the subjects who had answered every reversed trial type incorrectly. This indicates that the passage limit in the ERT pretest has to be increased from 60 % or separate minimum performance criteria for reversed trial type has to be set.

One of the aims of this thesis was to make the ERT test more demanding of EFs in order to make the test even more sensitive to subtle EF impairments. For that reason, a new reversed trial type was designed and implemented into the test. The results shows that the reversed trial type was more demanding for the subjects as it significantly increased RTs, total error rates and incorrect rates. This indicates that the subjects are processing information for longer periods and therefore they engage more EF. Burnout status increased the RTs but the increment was not statistically significant. Burnout status neither had a statistically significant effect on error rates. This is most likely due to the small burnout group size with only 6 subjects with burnout. Therefore, more subjects with burnout are required to get more reliable results.

Regression analyses reveal that the emotional distractors are affecting more subjects with burnout than without. Subjects with burnout were able to control their emotion-attention interaction in the regular trial type but the reversed trial type burdens their EFs too much leading to a reduced emotional control and greater impact of emotional stimuli. Therefore, it seems that emotional distractors affect EFs more in reversed trial type and to those subjects who have burnout.

absΔERT Reversed correlated with various BRIEF-A and BBI-15 indices even after the p-value correction. This is another evidence that the reversed trial type was a successful addition to the ERT test. absΔERT Regular were significantly correlating with each BBI-15 indicis. Therefore, absΔERT Regular holds promise as a biomarker in burnout assessment. Even though, there were no objective differences in the general performance measures of EF in the ERT test between subjects with and without burnout, the correlation between BBI-15 and BRIEF-A reveals that the subjects with burnout are experiencing more difficulties in EFs. In conclusion, remotely executed ERT test has potential to be used as a feasible and efficient assessment tool of EF reflecting more generally brain health and wellbeing.

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APPENDIX I

Table 14. Results of correlation analysis between the BRIEF-A and absΔERT *on RTs. The results are presented as follows first the correlation coefficient is presented, then inside the brackets first non-adjusted p-value followed by adjusted p-value. Significant results are marked with a *.*

	absΔERT Regular	*absΔERT Reversed*	*ΔERT Regular*	*ΔERT Reversed*
Inhibit	-0.12 (0.628/0.754)	0.46 (0.038/0.076)	-0.29 (0.203/0.753)	0.23 (0.325/0.721)
Shift	-0.17 (0.454/0.682)	0.10 (0.648/0.648)	0.10 (0.665/0.831)	-0.16 (0.481/0.721)
Emotional control	-0.30 (0.190/0.398)	0.49 (0.022/0.066)	-0.21 (0.360/0.753)	0.35 (0.107/0.721)
Self-monitoring	-0.08 (0.733/0.800)	0.24 (0.298/0.357)	-0.17 (0.454/0.753)	-0.13 (0.578/0.770)
Initiate	-0.29 (0.199/0.398)	0.60 (0.004/0.046)*	-0.07 (0.750/0.831)	0.05 (0.827/0.902)
Working memory	0.01 (0.949/0.949)	0.54 (0.011/0.046)*	-0.16 (0.499/0.753)	-0.01 (0.953/0.953)
Plan	-0.38 (0.092/0.368)	0.29 (0.183/0.244)	-0.30 (0.173/0.753)	-0.09 (0.688/0.826)
Task monitoring	-0.24 (0.285/0.489)	0.33 (0.140/0.210)	-0.15 (0.502/0.753)	0.33 (0.134/0.721)
Organization of materials	0.14 (0.554/0.739)	0.21 (0.353/0.385)	-0.01 (0.949/0.949)	0.26 (0.258/0.721)
BRI	-0.52 (0.020/0.219)	0.38 (0.079/0.136)	-0.22 (0.333/0.753)	0.18 (0.438/0.721)
MI	-0.33 (0.156/0.398)	0.56 (0.009/0.046)*	-0.07 (0.762/0.831)	0.22 (0.341/0.721)
GEC	-0.47 (0.036/0.219)	0.46 (0.033/0.076)	-0.19 (0.399/0.753)	0.18 (0.446/0.721)

APPENDIX II

Table 15. Results of correlation analysis between the BRIEF-A and absΔERT *on different error types. The results are presented as follows first the correlation coefficient is presented, then inside the brackets first non-adjusted p-value followed by adjusted p-value. Significant results are marked with a *.*

	absΔTotal errors	*absΔIncorrect responses*	*absΔIncorrectR responses*	*absΔMiss responses*	*absΔMissR responses*	*absΔCommission errors*
Inhibit	0.12 (0.616/0.865)	0.48 (0.032/0.127)	-0.51 (0.022/0.261)	0.17 (0.463/0.794)	0.25 (0.295/0.895)	0.22 (0.338/0.965)
Shift	0.47 (0.042/0.501)	-0.12 (0.609/0.609)	-0.31 (0.167/0.502)	0.27 (0.244/0.765)	0.16 (0.496/0.895)	0.13 (0.568/0.965)
Emotional control	0.10 (0.649/0.865)	0.19 (0.415/0.498)	-0.38 (0.087/0.405)	-0.14 (0.547/0.821)	0.12 (0.613/0.895)	-0.16 (0.488/0.965)
Self-monitoring	0.19 (0.423/0.846)	0.52 (0.016/0.118)	-0.20 (0.390/0.937)	-0.23 (0.313/0.765)	-0.13 (0.574/0.895)	0.31 (0.165/0.965)
Initiate	-0.02 (0.945/0.945)	0.24 (0.298/0.397)	0.01 (0.963/0.963)	0.20 (0.383/0.765)	0.07 (0.781/0.895)	0.32 (0.144/0.965)
Working memory	0.32 (0.174/0.846)	0.53 (0.020/0.118)	0.03 (0.891/0.963)	0.22 (0.343/0.765)	0.22 (0.349/0.895)	0.20 (0.408/0.965)
Plan	0.19 (0.403/0.846)	0.27 (0.225/0.338)	-0.06 (0.799/0.963)	0.01 (0.974/0.974)	0.11 (0.624/0.895)	0.02 (0.921/0.965)
Task monitoring	-0.03 (0.897/0.945)	0.32 (0.150/0.300)	0.13 (0.561/0.962)	0.25 (0.267/0.765)	0.05 (0.821/0.895)	0.10 (0.654/0.965)
Organization of materials	-0.21 (0.357/0.846)	-0.13 (0.561/0.609)	0.01 (0.954/0.963)	0.25 (0.283/0.765)	0.08 (0.750/0.895)	-0.01 (0.965/0.965)

BRI	0.15 (0.508/0.865)	0.37 (0.112/0.268)	-0.37 (0.101/0.405)	-0.07 (0.773/0.970)	0.03 (0.899/0.899)	-0.03 (0.903/0.965)
MI	-0.04 (0.872/0.945)	0.30 (0.193/0.331)	0.04 (0.867/0.963)	0.03 (0.905/0.974)	0.18 (0.448/0.895)	0.05 (0.818/0.965)
GEC	0.23 (0.328/0.846)	0.44 (0.050/0.149)	-0.16 (0.491/0.962)	0.05 (0.808/0.970)	0.18 (0.427/0.895)	0.23 (0.307/0.965)