DOCTORAL THESIS

Application of Electroencephalographic Signal Based Measures for Early Detection of Depression Symptoms in Occupational Health

Toomas Põld

TALLINNA TEHNIKAÜLIKOOL
TALLINN UNIVERSITY OF TECHNOLOGY
TALLINN 2021

TALLINN UNIVERSITY OF TECHNOLOGY
DOCTORAL THESIS
61/2021

Application of Electroencephalographic Signal Based Measures for Early Detection of Depression Symptoms in Occupational Health

TOOMAS PÕLD

TALLINN UNIVERSITY OF TECHNOLOGY
School of Information Technologies, Department of Health Technologies
Curriculum: School of Science
This dissertation was accepted for the defence of the degree 27/10/2021

Supervisor: Prof. Maie Bachmann, PhD
School of Information Technologies
Department of Health Technologies
Tallinn University of Technology
Tallinn, Estonia

Co-supervisor: Dr. Jaanus Lass, PhD
School of Information Technologies
Department of Health Technologies
Tallinn University of Technology
Tallinn, Estonia

Opponents: Dr. Anastassia Rodina-Theocharaki, PhD
Lab of Medical Physics and Digital Innovation
School of Medicine, Aristotle University of Thessaloniki
Thessaloniki, Greece

Dr. Carolina Murd, PhD
Chronic Diseases Department
National Institute for Health Development
Tallinn, Estonia

Defence of the thesis: 17/12/2021, Tallinn

Declaration:
Hereby I declare that this doctoral thesis, my original investigation and achievement, submitted for the doctoral degree at Tallinn University of Technology, has not been submitted for doctoral or equivalent academic degree.

Toomas Põld

----
signature

European Union
European Regional
Development Fund

Investing
in your future

ISSN 2585-6898 (publication)
ISBN 978-9949-83-771-7 (publication)
ISSN 2585-6901 (PDF)
ISBN 978-9949-83-772-4 (PDF)
Printed by Koopia Niini & Rauam

TALLINNA TEHNIKAÜLIKOOL
DOKTORITÖÖ
61/2021

Elektroentsefalograafilisel signaalil põhinevate indikaatorite kasutamine depressiooni sümptomite varaseks avastamiseks töötervishoius

TOOMAS PÕLD

TALTECH KIRJASTUS

Contents

List of publications

The current thesis is based on the following publications referred to in the text by their Roman numerals I – IV.

I **Põld, T**.; Päeske, L.; Bachmann, M.; Lass, J.; Hinrikus, H. (2019). Assessment of Objective Symptoms of Depression in Occupational Health Examination. Journal of Occupational and Environmental Medicine, 61 (7), 605−609. DOI: 10.1097/JOM.0000000000001622.

II **Põld, T.;** Päeske, L.; Hinrikus, H.; Lass, J.; Bachmann, M. (2021). Long-term stability of resting state EEG-based linear and nonlinear measures. International Journal of Psychophysiology, 159, 83−87. DOI: 10.1016/j.ijpsycho.2020.11.013.

III **Põld T**.; Bachman M.; Orgo L.; Kalev K.; Lass J.; Hinrikus H. (2018). EEG Spectral Asymmetry Index Detects Differences Between Leaders and Non-leaders. EMBEC 2017, NBC 2017. IFMBE Proceedings, 65: Joint Conference of the European Medical and Biological Engineering Conference (EMBEC) and the Nordic-Baltic Conference on Biomedical Engineering and Medical Physics (NBC), Tampere, 11-15 June 2017. Ed. Eskola H., Väisänen O., Viik J., Hyttinen J. Singapore: Springer, 17−20. DOI: 10.1007/978-981-10-5122-7_5.

IV **Põld, T.;** Bachmann, M.; Päeske, L.; Kalev, K.; Lass, J.; Hinrikus, H. (2019). EEG Spectral Asymmetry Is Dependent on Education Level of Men. In: Lhotska, L.; Sukupova, L.; Lacković, I.; Ibbott, G. (Ed.). World Congress on Medical Physics and Biomedical Engineering 2018 (405−408). Singapore: Springer. (IFMBE Proceedings; 68/2). DOI: 10.1007/978-981-10-9038-7_76.

Author's contribution to the publications

Contributions to the papers in this thesis are (Publications I-IV):

I designing and conducting of the experimental study;
recruitment of volunteers and evaluation of their health condition;
application of depression questionnaires;
interpreting data;
writing the manuscript;

II recruitment of subjects and monitoring their health condition;
estimating mental state of the participants;
conducting the experimental study;
interpreting data;
writing the manuscript;

III recruitment of subjects;
interpreting data;
writing the manuscript;

IV recruitment of subjects;
interpreting data;
writing the manuscript.

Introduction

Depression is a leading cause of disability and a burden of disease affecting a remarkable part of population of working age (WHO 2020). During last decades, depression has become a common mental disorder worldwide and it is in rise with a prevalence in developed countries [Whiteford et al., 2010; Wittchen et al., 2011; WHO Europe 2019]. The COVID 19 pandemic contributes to the additional rise of depression [Ettman et al., 2020; Salari et al., 2020; Troyer et al., 2020].

The work stress caused by psychosocial factors in the work environment can contribute to the development of depression [Madsen et al.; 2017; Netterstrøm et al., 2008]. Work stress is increasing today due to increasingly complicated tasks and high demand in the work environment [Stansfeld and Candy, 2006; Madsen et al., 2017]. High work stress and depression are causing professional inefficacy and burnout [Saijo et al., 2014; Golonka et al., 2019]. Early detection of depression is essential to prevent burnout and subsequent depression in employees.

Mental state of employees during implementing their everyday duties is an important factor determining the quality of their work (Goetzel et al., 2018). Potential mental disorders present a crucial risk factor for professionals of high personal responsibility as policemen, pilots, military specialists etc. Exposure to stressful working conditions can have direct influence on safety and health of employees and their beneficiaries (Landsbergis et al., 2011; Hsu Sandy et al., 2016). Therefore, monitoring of mental state during regular occupational health examination is highly important to prevent accidents and unexpected events.

Today, the diagnosis of mental disorders is based on the evaluation of subjective symptoms by a general practitioner, an occupational physician or a psychiatrist, using questionnaires and interviews. The commonly accepted assessment tools for depression are based on questionnaires that classify various self-declared subjective symptoms [Hamilton, 1960; Williams, 1988; Cusin et al., 2010; Fried, 2017]. No other objective measures exist in clinical practice.

Early detection of depression is complicated due to the lack of commonly accepted tools developed to reveal signs of depression, which would appear before the self-declared subjective symptoms related to already ongoing depression. There is a high demand for the low-cost objective methods suitable to screen employees for early depression.

Mental disorders, including depression, are expected to have underlying alterations in brain physiology and restructured dynamics of brain bioelectrical activity. During years, several studies have demonstrated specific features of depression in the electroencephalographic (EEG) signal [Knott et al., 2001; Hinrikus et al., 2009; Leuchter et al., 2012; Ahmadlou et al., 2012; Hosseinifard et al., 2013; Fingelkurts and Fingelkurts, 2015). Statistically significant differences have been confirmed in various EEG-based measures between the groups of depressive and healthy subjects. EEG-based non-invasive and cost-effective methods seem promising to carry out the evaluation of depression in occupational health examinations.

However, the high diversity of EEG measures between individuals makes it difficult to estimate depression symptoms. The feasibility of EEG-based indication of early symptoms of depression for an individual was first reported in **Publication I**. The results indicated that the applied EEG measures, spectral asymmetry index SASI and Higuchi’s fractal dimension detect the change of the EEG signal in depression for a larger number of participants compared to the scores of depression questionnaires HAM-D and EST- Q- D.

The temporal stability of the EEG measures that point to the depression is important to assure the reliability of the performed evaluations. Caused by physiological processes, high natural variability of EEG takes place even in the healthy brain. However, today data are available supporting the long-term stability of EEG bands' power and related linear measures [Gasser et al., 1985; Salinsky et al., 1991; Kondacs et al., 1999; Allen et al., 2004]. Only few data are available about the stability of EEG nonlinear measures [Gudmundsson et al., 2007]. Detailed investigation of long-term stability for different linear and nonlinear EEG measures has been performed in **Publication II**. The results provide new knowledge about the temporal stability of the EEG measures and indicate that the stability of nonlinear measures is even higher than linear measures.

The high diversity of EEG measures between individuals is related to the dependence of EEG on various factors (Veldhuizen et al., 1993; Marciani et al., 1994; Nikulin and Brismar, 2005; Purdon et al., 2015; Orgo et al., 2016; Meyers et al., 2021).

Work stress can be considered as a specific factor affecting human brain and changing brain bioelectric oscillations. Consequently, it is expected that the EEG measures of persons on more responsible positions (leaders) differ from the EEG measures of the persons having lower responsibility and lower stress (non-leaders). This novel hypothesis has been supported by the experiment in **Publication III**: The EEG of leaders has higher beta and gamma power compared to non-leaders.

Learning process causes alteration in human brain (Dehaene and Changeux, 2000; Frank et al., 2015). Consequently, human EEG is related to the level of education. This novel hypothesis has been supported by the experiment in **Publication IV**. The EEG gamma power for men with the tertial level of education is higher compared to men having secondary education.

The results of **Publication III** and **Publication IV** suggest that the levels of occupational position and education are the factors to be taken into account using EEG markers for the detection of depression symptoms.

The results of the Thesis have demonstrated the advantage of the easy-to-use novel EEG-markers for detection of persons with probability of depression, pointing to the need for future larger studies.

Other related publications

- Uudeberg, T., Päeske, L., Põld, T., Lass, J., Hinrikus, H., & Bachmann, M. (2020). Long-Term Stability of EEG Spectral Asymmetry Index – Preliminary Study. In: Henriques J., Neves N., de Carvalho P. (eds) XV Mediterranean Conference on Medical and Biological Engineering and Computing – MEDICON 2019. MEDICON 2019. IFMBE Proceedings, 76. Springer, Cham. doi: 10.1007/978-3-030-31635-8_33
- Päeske, L., Bachmann, M., Põld, T., de Oliveira, S. P. M., Lass, J., Raik, J., & Hinrikus, H. (2018). Surrogate Data Method Requires End-Matched Segmentation of Electroencephalographic Signals to Estimate Non-linearity. Frontiers in Physiology, 9, 1350. doi: 10.3389/fphys.2018.01350

Abbreviations

DFA	Detrended Fluctuation Analysis
EEG	Electroencephalography
EST-Q-D	Emotional State Questionnaire for Depression
fMRI	Functional Magnetic Resonance Imaging
HAM-D	Hamilton Depressive Rating
HFD	Higuchi's Fractal Dimension
ICC	Intraclass Correlation Coefficient
IHAS	Interhemispheric Asymmetry
KFD	Katz Fractal Dimension
MDD	Major Depressive Disorder
MEG	Magnetoencephalography
MRI	Magnet Resonance Imaging
PET	Positron Emission Tomography
SASI	Spectral Asymmetry Index
SL	Synchronization Likelihood
SPECT	Single Photon Emission Computed Tomography

1 Resting-state electroencephalography

Electroencephalography (EEG) is a non-invasive method for recording bioelectrical activity of the brain using electrodes located on scalp. The resting-state EEG has several applications in clinical practice and a wide use in neurophysiology, psychophysiology, psychology, and other research fields (Niedermeyer and Lopes da Silva, 1993; Michel and Murray, 2012).

Neuronal oscillations and synchronization of the oscillations constitute the bases of brain activity (Nunez 1995; Buzsáki and Draguhn, 2004). The brain dynamics is determined by neuronal oscillations. Therefore, the recorded EEG signal is oscillating by its nature.

Brain ejectrical oscillations are related to various physiological processes, physical activity, emotions, etc. To reduce the impact of various factors on the EEG and the level of its natural variability, the resting-state EEG is most commonly used for diagnostic purposes, employing eyes-closed situation to minimize visual input data. However, the EEG signal shows high level of natural variability even in these conditions. Figure 1 presents a typical EEG signal recorded in the Biosignal Processing Laboratory of Tallinn University of Technology.

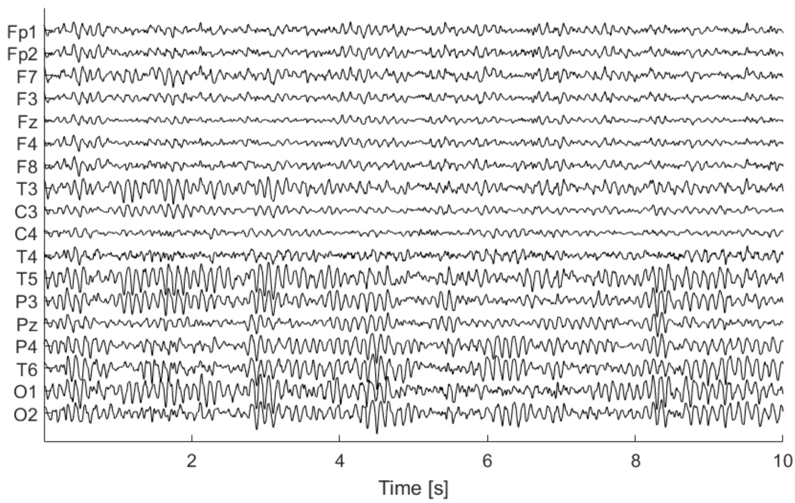

Figure 1. An example of recorded eyes-closed resting-state EEG signal at Cz as reference.

EEG signal has no deterministic shape, seems irregular, and contains nonlinearity (Friston, 2000; Breakspear and Terry, 2002; Stam, 2005; Rodríguez-Bermudez and Garcíia Laencin, 2015).

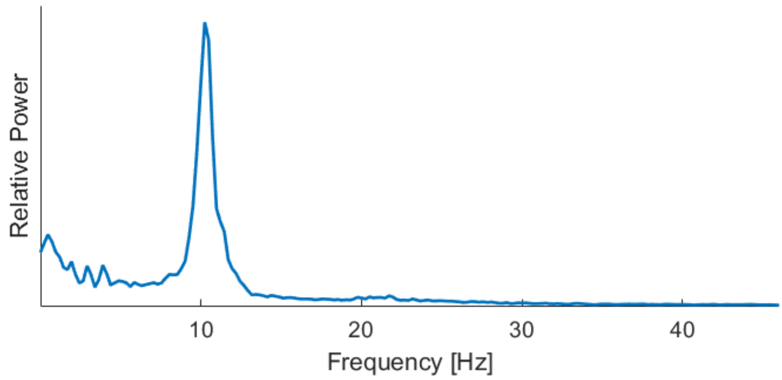

Figure 2. Spectrum of eyes-closed resting-state EEG.

The spiking frequencies of single neurons reach 1–2 kHz. The bandwidth of oscillatory frequencies of neuronal networks is about 0.5–500 Hz (Buzsáki and Draguhn, 2004). The spectrum of the eyes-closed resting-state EEG signal contains frequency components at different brain oscillation frequencies with maximum at about 10 Hz (Figure 2). Traditionally, the spectrum of EEG is divided to the following frequency bands: delta 0.5–4 Hz, theta 4–8 Hz, alpha 8–13 Hz, beta 13–30, and gamma 30–45 Hz. Maximum power of eyes-closed EEG occurs in the alpha band.

The position of EEG electrodes on scalp is determined by the internationally standardized 10–20 system covering all brain regions: frontal (F), central (C), temporal (T), parietal (P), and occipital (O) (Figure 3) (Homan et al., 1987; Malmivuo and Plonsey, 1995).

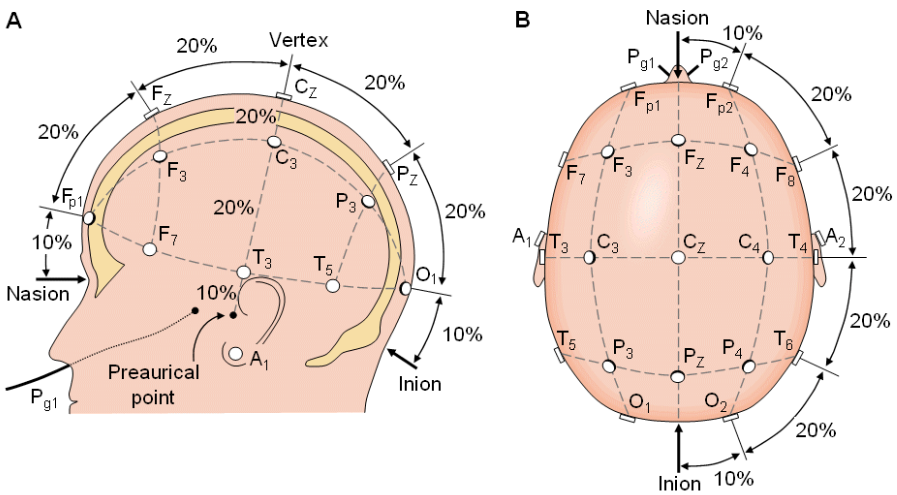

Figure 3. The international 10-20 system for placement of electrodes (Malmivuo and Plonsey, 1995).

Resting-state EEG has several advantages over other brain imaging methods (MRI, fMRI, PET, SPECT):

- The source of EEG are neuronal bioelectric processes in the brain. Other brain imaging methods provide information only about the structure of the brain or the intensity of cerebrovascular processes.
- EEG provides high temporal resolution up to milliseconds sufficient for detection of neuronal processes in real time. Other methods have lower temporal resolution.
- EEG is a non-invasive, patient friendly and easy to apply method. Other methods may be more inconvenient for patients and are complicated to apply.
- EEG equipment can be portable.
- EEG equipment and procedure are less expensive than other methods.

However, the resting-state EEG has some principal limitations and disadvantages:

- EEG can get information only from the brain cortex not from deeper structures.
- EEG has low spatial resolution. The neuronal oscillations from larger cortical areas contribute to the signal in a scalp channel.
- EEG signal is complex and requires special analysis for interpretation.

2 Detection of depression

2.1 EEG-based measures for detection of depression

EEG has been successfully applied in anaesthesia, epilepsy studies, sleep medicine, and other clinical areas, but is not in clinical use to evaluate depression nor other mental disorders. Still, many various EEG-based linear and nonlinear measures have been successfully used for discrimination between the groups of healthy and major depressive disorder (MDD) subjects in research studies (Knott et al., 2001; Allen et al., 2004; Sun et al., 2008; Hinrikus et al., 2009; Ahmadlou et al., 2012; Bachmann et al., 2013; Bachmann et al., 2018; Lee et al., 2018; Newson and Thiagarajan, 2019; Mahato and Paul, 2020).

2.1.1 Linear EEG measures

Linear EEG measures provide for the estimation of depression symptoms based on the analyses of EEG frequency band powers and their combinations (Knott et al., 2001; Bachmann et al., 2018; Lee et al., 2018; Newson and Thiagarajan, 2019; Mahato and Paul, 2020). Compared to nonlinear EEG measures, linear measures have lower computational load.

Power of an EEG frequency band is the simplest linear measure widely used in quantitative EEG. EEG frequency band power employs an EEG signal from a single EEG channel and a single frequency band. Several studies have reported depression-related alterations in the powers of different EEG frequency components. Increased alpha, beta and gamma band power have been shown to be specific for depression EEG and are successfully applied for discrimination between the groups of depressive and healthy persons (Knott et al., 2001; Bachmann et al., 2018; Lee et al., 2018).

Interhemispheric asymmetry (IHAS) presents the difference between the powers of two symmetric EEG channels from different hemispheres. IHAS is calculated as

$$IHAS = \frac{L - R}{L + R},$$

where L indicates the power of a selected frequency band for an EEG channel from the left hemisphere and *R* for the symmetric EEG channel from the right hemisphere.

IHAS employs EEG signals from two EEG channels of different hemispheres of the same frequency band.

EEG alpha IHAS has been successfully applied to differentiate between the groups of depressive and healthy subjects (Henriques and Davidson, 1991; Knott et al., 2001; Allen et al., 2004; Mathersul et al., 2008). In the majority of cases, depressed patients show decreased left frontal activation compared to healthy controls. However, some researchers have expressed criticism regarding IHAS (Debener et al., 2000; van der Vinne et al., 2017).

Spectral asymmetry index (SASI) describes the asymmetry of the EEG spectrum by comparing powers in the selected frequency bands higher and lower than the central alpha frequency band in spectrum maximum. SASI is calculated as

$$SASI = \frac{HFB - LFB}{HFB + LFB},$$

where *HFB* indicates the power in the frequency band, which is higher than the alpha band and *LFB* indicates the power in the frequency band, which is lower than the alpha band.

The boundary frequencies of the bands are determined by a method described in the previous study (Hinrikus et al., 2009). The lower frequency band is close to the traditional theta frequency band and higher band close to the beta band. This procedure excludes the EEG alpha band from the calculations of SASI. SASI, as a measure of spectral asymmetry, employs two different frequency bands from a single channel EEG signal.

SASI provides good classification accuracy between the groups of depressed and healthy persons (Hinrikus et al., 2009; Bachmann et al., 2013; Bachmann et al., 2017; Bachmann et al., 2018).

The results indicated that the SASI values were higher for depression and lower for healthy persons.

2.1.2 Nonlinear EEG measures

EEG signal is complex, chaotic and nonlinear in nature (Friston, 2000; Breakspear and Terry, 2002; Stam, 2005; Robets and Robinson, 2012; Rodríguez-Bermudez and Garcíıa Laencin, 2015). Therefore, the linear measures, which take into account only linear combinations of signals, have limited capability of describing the signal features and hence also the brain activity. On the other hand, nonlinear measures can well describe the features of a complex signal. It is suggested that nonlinear methods enable us to analyse a larger spectrum of features of the signal preserving the signal’s initial properties.

Higuchi’s fractal dimension (HFD) describes the self-similarity of the signal (Higuchi, 1988). HFD has demonstrated good quality while classifying between the groups of depressive and healthy persons (Ahmadlou et al., 2012; Bachmann et al., 2013; Bachmann et al., 2018; Čukić et al., 2020a; Čukić et al., 2020b).

Detrended fluctuation analysis (DFA) describes temporal dynamics and variability of EEG fluctuations (Peng et al., 1995; Hu et al., 2001). DFA has also been successfully applied for discrimination between the groups of depressive and healthy persons (Leisted et al., 2007; Lee et al., 2007; Hosseinifard et al., 2012; Bachmann et al., 2017; Bachmann et al., 2018).

HFD and DFA are calculated for a signal in a single EEG channel employing all EEG frequency bands.

Various other nonlinear measures (Katz fractal dimension, entropy measures, etc.) have been used in other studies for the detection of depression; however, those studies have not been shown to be more efficient or advantageous in classification accuracy nor in computational load compared to HFD (Ahmadlou et al., 2012; Čukić et al., 2020a; 2020b).

None of the EEG measures have been used for the detection of depression symptoms at the level of individuals.

2.1.3 Reliability of EEG measures

The application of EEG measures for diagnostic purposes requires temporal stability of the measures and reliability of the scores. Emotions, physiological processes, life events, and other factors cause alterations in healthy human EEG (Sammler et al., 2007; Harmon-Jones et al., 2010; Orgo et al., 2015; Saifudinova et al., 2015). Therefore, the estimation of the stability of EEG-based markers is important.

Many researchers have investigated the temporal stability of EEG frequency band powers. The frequency band powers have demonstrated high stability for long time periods, up to 12 years (Gasser et al., 1985; Salinsky et al., 1991; Kondacs and Szab´o, 1999; Corsi-Cabrera et al., 2007; Rogers et al., 2016; Tenke et al., 2018). Good reliability of IHAS has also been demonstrated (Allen et al., 2004; Stewart et al., 2010; Gold et al., 2013), while no information about the stability of SASI is available.

In addition, data available about the stability of nonlinear measures are scarce. The entropy measures have indicated lower reliability compared to EEG band power measures (Gudmundsson et al., 2007). To the best of our knowledge, the temporal stabilities of HFD and DFA have not been investigated before.

2.2 Depression questionnaires

The Hamilton Depression Rating Scale (HAM-D) is the most widely used tool for clinician-administered assessment of depression (Hamilton, 1960). Initially, the HAM-D was designed to be used as a clinical interview with a depressed patient to measure treatment outcome (Hamilton, 1967, Williams, 1988). The HAM-D has been a golden standard over half a century. Despite that, some criticism about the retest reliability and validity of the test has been expressed (Bagby et al., 2004).

The HAM-D is a psychometric test based on subjective symptoms of patients. HAM-D is applicable at the individual level. However, the HAM-D is not designed to evaluate symptoms of depression in healthy persons.

The Emotional State Questionnaire for depression (EST-Q-D) is based on self-rated subjective symptoms (Aluoja et al., 1999). The EST-Q-D has been designed to distinguish between different groups of population and validate discriminating groups of healthy persons and patients. The authors underline that “As no diagnostic interview was used in the population sample, we could not determine the exact cut-off points of subscales for screening purposes. “(Aluaoja et al., 1999).

EST-Q-D is designed for differentiation between groups, patients and healthy or within healthy people. The questionnaire is not validated for differentiation at the individual level.

3 Aims of the thesis

Today we have no psychometric tests to differentiate between subjective symptoms nor EEG-based measures to evaluate objective symptoms of depression on subjects at an individual level.

The general goal of the Thesis is to demonstrate the potential of the EEG measures to detect the symptoms of depression on different groups of subjects reliably and earlier than in other methods.

The aim of the Thesis research is as follows:

- compare various EEG-based measures and psychometric tests for the detection of symptoms of depression in seemingly healthy people one by one at an individual level (**Publication I**);
- evaluate the temporal reliability of the EEG-based measures (**Publication II**);
- evaluate the impact of the level of responsibility on EEG measures (**Publication III**);
- evaluate the impact of the level of education on EEG measures (**Publication IV**).

4 Experimental studies

4.1 Methods

4.1.1 Participants

Participants were recruited among the persons from different institutions passing occupational health examination in the Qvalitas Medical Centre. In total, 125 healthy volunteers were recruited for the study. According to their declarations as well as medical and biochemical examinations, the recruited participants were healthy. The average age of the group was 41.04 (median 41.00 years) with a standard deviation of 8.66 years. Table 1 presents the data for the participants.

*Table 1. Main data of the participants (**Publication I**).*

Qualities	Subgroup	Number of participants	Percentage %
Gender	Male	49	39.2
	Female	76	60.8
Age	> 41 years	62	49.6
	< 41 years	63	50.4
Education	Higher/Tertiary	99	79.2
	Secondary	26	20.8
	Primary	0	0

Three years after the first study described in Publication I, the participants were invited to the follow-up study. Out of 49, 17 subjects agreed to participate in the second study; other 32 did not respond to the invitation. The group consisted of twelve female and five male individuals of average age 42.3±5.4 years during the first and 45.2±5.4 during the second study (**Publication II**). A group of 82 persons, 27 males and 55 females, mean age 40.2 years (Standard deviation of age 7.6) participated in the study described in **Publication III**. According to their occupational position and duties, 45 subjects were leaders (average age 40.7) and 37 subjects were non-leaders (average age 39.6).

The age-matched groups of 30 participants having tertiary education and 16 participants having secondary education were recruited for the analysis in **Publication IV**.

The studies were conducted in accordance with the Declaration of Helsinki, as revised in 2013. All studies were formally and prospectively approved by the Tallinn Medical Research Ethics Committee. All participants were informed about the aim and protocol of the studies and they signed a written informed consent before inclusion in the study groups.

4.1.2 Procedures, methods, equipment

All participants filled in the self-report Emotional State Questionnaire (Aluoja et al., 1999) subscale for depression (EST-Q-D) before the EEG recording. The depressive subscale score 11 was the threshold to indicate depressive symptoms (Aluoja et al., 1999).

Depressive symptoms were evaluated by an experienced clinician using 17-item Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1960). The following scale of scores was applied: mild depression 7 to 14, moderate depression 14 to 18, severe depression 19 to 22, and very severe depression higher than 22 **(Publication I).**

Cadwell Easy II EEG (Kennewick, WA, USA) device was used for recording the 18-channel resting-state eyes-closed EEG for seven minutes. The electrodes were located according to the international 10-20-electrode position system. Electrode Cz was selected as a reference. **(Publication I, II, III, IV)**

The raw EEG signals of 0.3-70 Hz frequency were stored at the sampling frequency of 400 Hz. An experienced EEG specialist evaluated visually the quality of the recorded EEG signals.

4.1.3 EEG analyses

The artefact-free EEG segments (duration 5 min) were used in the analysis. Linear and nonlinear EEG measures were calculated in 18 EEG channels for each participant using MATLAB (The MathWorks, Inc. Massachusetts, USA).

Table 2 presents the EEG measures calculated in the studies.

Table 2. EEG measures calculated in Publications.

	Publ. I	**Publ. II**	**Publ. III**	**Publ. IV**
Theta power (4-7 Hz)		**X**		**X**
Alpha power (8-13 Hz)		**X**		**X**
Beta power (14-30 Hz		**X**		**X**
Gamma power (30-47 Hz)		**X**		**X**
IHAS		**X**		
SASI	**X**	**X**	**X**	**X**
HFD (4-47 Hz)	**X**	**X**		
DFA (4-47 Hz)		**X**		

4.1.4 Statistics

The Pearson correlation coefficients between the different measures and data of participants were calculated in Microsoft Excel (Microsoft Corporation, Redmond, WA) software (**Publication I**). The intraclass correlation coefficient (ICC) was used to evaluate the reliability of the EEG scores in two recording sessions. MATLAB (The MathWorks, Inc. Massachusetts, USA) was used for calculations of ICC(A,1) by a two-way mixed random model (McGraw and Wong, 1996) (**Publication II**).

The Student's t test with post-hoc Bonferroni correction was performed to evaluate statistical significance between different groups (age, gender, marital status, educational level, leadership) (**Publication I, Publication II, Publication III,**) and measures in the first and the second recording sessions (**Publication IV**).

4.2 Results

4.2.1 Assessment of different measures of depression (Publication I)

Figure 4 presents the rate of participants with symptoms of depression indicated by various measures. The EEG measures indicate depressive symptoms for 55% (HFD) to 65% (SASI) and the psychometric tests for 29% (EST-Q-D) to 45% (HAM-D) of the subjects.

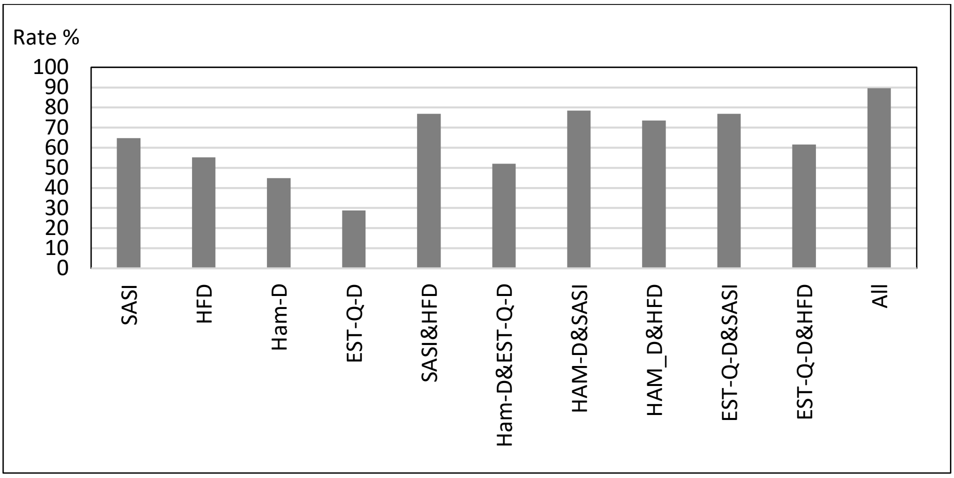

*Figure 4. The rate of participants with signs of depression (**Publication I**).*

The Pearson correlation coefficients calculated between different measures are presented in Table 3 (**Publication I**). Moderate correlation occurs between the psychometric tests HAM-D and EST-Q-D as well as EEG-based measures SASI and HFD. The psychometric tests and EEG-based measures do not correlate.

*Table 3. Correlation coefficients between the calculated EEG measures and the results of psychological tests (**Publication I**).*

	SASI	HFD	HAM-D	EST-Q-D
SASI		**0.48**	0.04	-0.04
HFD	**0.48**		0.01	-0.16
HAM-D	0.04	0.01		**0.66**
EST-Q-D	-0.04	-0.16	**0.66**	

4.2.2 Temporal reliability of EEG measures (Publication II)

Figure 5 presents the average values of the EEG-based measures in two sessions. The level of relative change between the values in two sessions is presented in Table 4. All single channel EEG measures using a single frequency band (spectral band relative powers, HFD and DFA) indicate very high stability within 2.4% over three years. The highest stability was shown by nonlinear measures HFD 0.2% and DFA 0.5%. The single-channel measure SASI, employing signals from two frequency bands, indicates lower stability of 11.8%. The IHAS, which uses signals from a single band but from two channels from different hemispheres, is much more unstable compared to single-channel measures. The differences between the sessions appear statistically insignificant for all measures ($p > 0.005$).

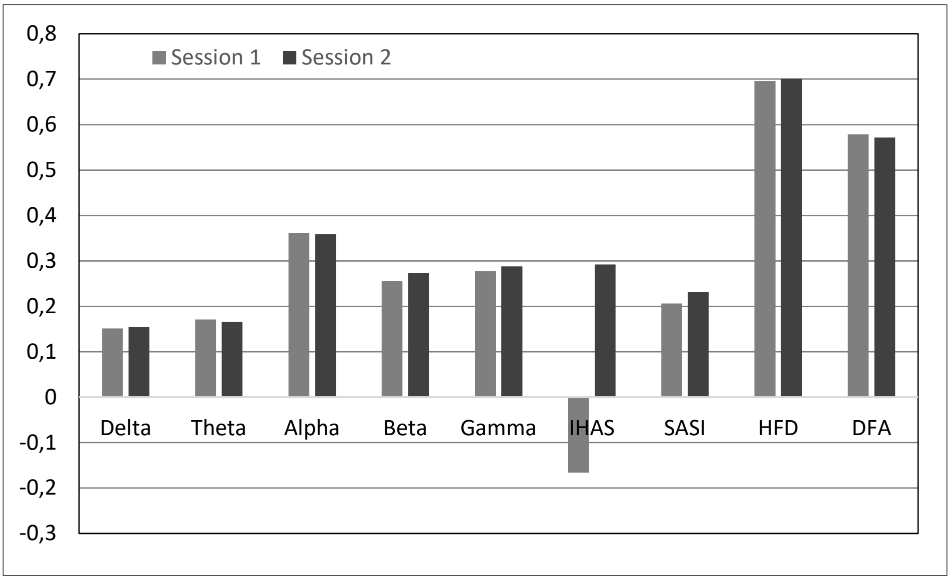

Figure 5. The mean values, averaged over 18 EEG channels and all 17 participants of the EEG measures: delta, theta, alpha, beta, and gamma bands relative powers, interhemispheric asymmetry index (IHAS), spectral asymmetry index (SASI), Higuchi fractal dimension (HFD) (the value -!) and detrended fluctuation analysis (DFA) (according to the data in Table 1, ***Publication II****).*

Table 4. Relative change between two sessions in single-channel EEG measures averaged over 18 EEG channels and 17 participants (data from Table 1 ***Publication II****).*

	Delta	Theta	Alpha	Beta	Gamma	SASI	IHAS	HFD	DFA
%	1.0	1.2	0.7	2.3	2.4	11.8	236.2	0.2	0.5

Table 5. Intra-class correlation coefficients averaged over all frequency bands and channels (according to the data in Table 2 and Table 3 ***Publication II****).*

Delta	Theta	Alpha	Beta	Gamma	SASI	IHAS	HFD	DFA
0.84	0.84	0.88	0.83	0.83	0.82	0.38	0.82	0.84

Table 5 presents the ICC values between the two sessions. The ICC values are higher 0.8 and statistically significant for all single-channel EEG measures Delta, Theta, Alpha, Beta, Gamma, SASI, HFD, and DFA. The ICC for IHAS is much lower.

4.2.3 Impact of professional responsibility on EEG (Publication III)

Figure 6 presents the values of SASI averaged over the groups of leaders with higher responsibility and non-leaders with lower level of responsibility. Statistically significant difference between the leaders and non-leaders indicates increased SASI for leaders.

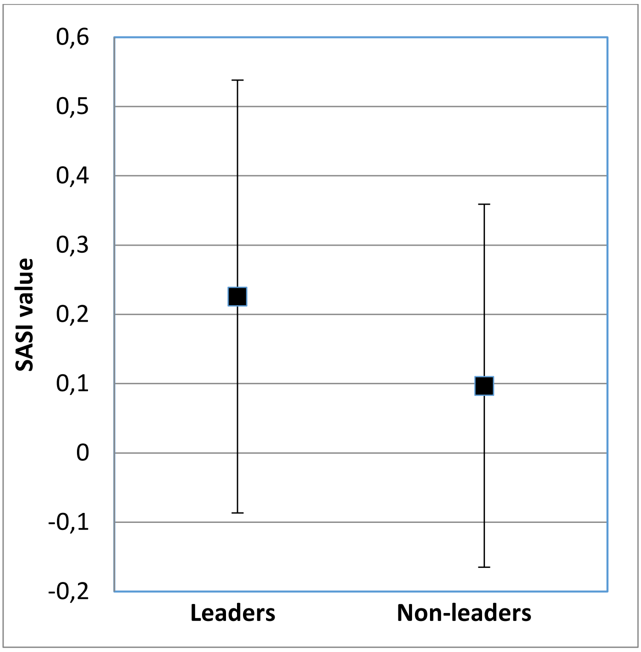

*Figure 6. Calculated SASI values averaged over the subgroup of leaders (n=45) and non-leaders (n=37); vertical bars denote standard deviation (**Publication III**).*

4.2.4 Impact of educational level on EEG (Publication IV)

The bars in Figure 7 demonstrate the level of SASI for men at different educational levels. The rise of SASI with the level of education is statistically significant in the majority of brain regions.

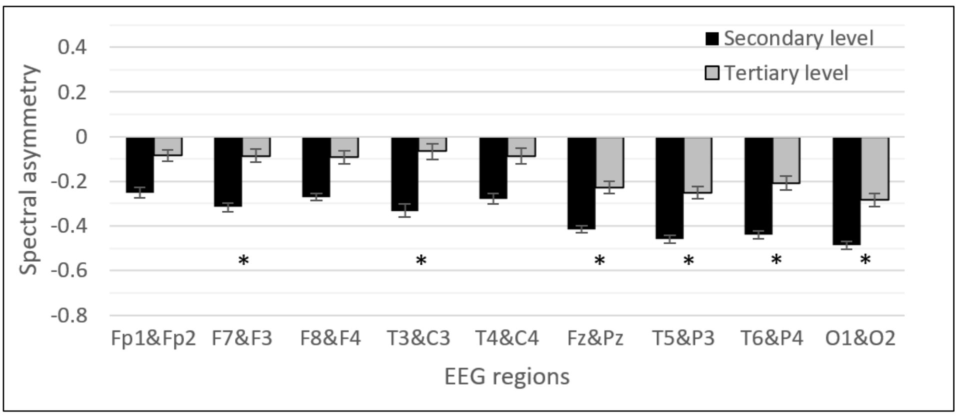

*Figure 7. Mean and standard error of SASI averaged over the group of men having secondary education (n= 16) and group of men having tertiary education (n=30) in 9 brain regions. Vertical bars represent standard error, asterisk statistically significant difference (p<0.05) (**Publication IV**).*

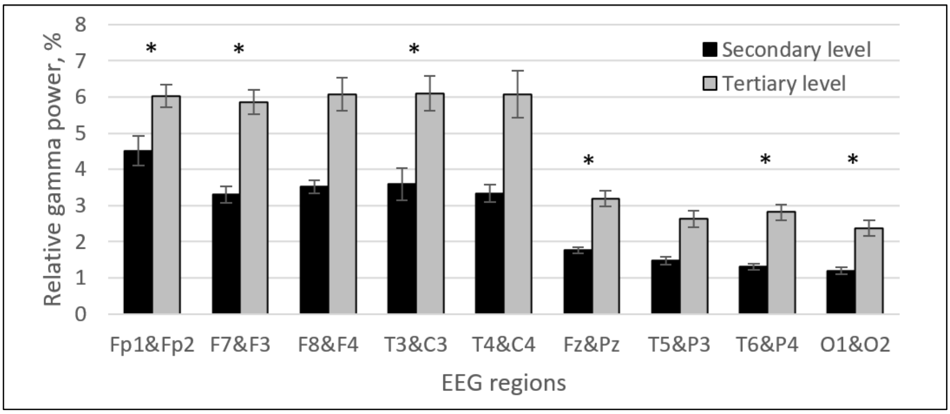

*Figure 8. Mean and standard error of the relative gamma power for the group of men having secondary education and group of men having tertiary education in 9 brain regions. Asterisks show statistically significant differences (p<0.05) (**Publication IV**).*

4.3 Discussion

4.3.1 The rate of depression symptoms

The share of participants with depression signs indicated by EEG measures as well as psychometric tests in **Publication I** are much higher than 7.1%, the number indicated in medical statistics among adults (NIMH, 2017). The share of depression symptoms indicated by ECT-Q 28.8% in **Publication I** is higher than the prevalence among Estonian population 11.1% (Aluoja et al., 2004).

The unexpectedly high share of depression symptoms can be explained by various reasons.

- The participants with mild depression (32% from HAM-D scores) are probably not accounted in medical statistics. However, the rate of moderate and severe scores, in total 12.8%, still exceeds the expected 7.1% or 11.1%.
- The volunteers who agreed to participate in the study might have had already some feelings of stress or even depression.
- The rate of depression depends on the character of the work: industrial workers have reported the rate of 6.9 – 16.2% at the rate for population 10.45% (Wulsin et al., 2014). The EST-Q test has indicated difference in the rates between Estonian general population 11.1% (Aluoja et al., 2004) and Estonian medical students 30.6 % (Eller et al., 2006).
- The major part, 79.2% of the participants in the study, have higher education and their position involves high responsibility. The EEG measures indicating depression increase with the level of education and responsibility (**Publication III, Publication IV**).
- The subset of population not having subjective depression symptoms has been out of medical reach as there are no clinical measures to assess early changes in EEG.

4.3.2 Comparison of different measures

The EEG measures are associated with a remarkable increase in the rate of symptoms of depression, 55% (HFD) to 65% (SASI), compared to the rate of subjective symptoms of depression, 29% (EST-Q-D) to 45% (**Publication I**). These results could be interpreted as the ability of the EEG measures to reveal depression not yet detectable by subjective feelings.

The correlation between SASI and HFD, indicating different features of the EEG signal, is equal to 0.48 (**Publication I)**.

A moderate correlation of 0.66 occurs between HAM-D and EST-Q-D scores, despite similar questions used the questionnaires (**Publication I)**. The discordances between the ratings assessed by patients and clinicians have been also mentioned in several other studies (Domken et al., 1994; Enns et al., 2000; Cusin et al., 2010). The correlation of 0.4, even lower than in the current study, has been previously reported (Enns et al., 2000).

Very low correlation is observed between the EEG measures and depression questionnaires in the current study (**Publication I)**. However, a good correlation of 0.7 between the SASI and HAM-D has been found previously in the study on inpatients (Hinrikus et al., 2009). The low correlation between the EEG measures and depression for healthy people can be partly caused by psychological factors: people do not reveal or accept being depressed themselves or intend to present better status for the employers.

4.3.3 Reliability of EEG measures

The characteristic regularity can be noticed in the results of **Publication II**: the reliability depends on the number of channels and frequency bands used for the calculation of the measure. Good stability within 2.4% (Table 4) and high ICC values 0.82 or higher (Table 5) are indicated for all EEG single-channel and single-band measures (relative powers of frequency bands, nonlinear HFD and DFA) over a three-year interval. Nonlinear measures HFD and DFA indicated the highest stability within 0.5%. The single-channel measure SASI, employing signals from two frequency bands, indicates lower stability of 11.8%. The IHAS, the calculation of which requires signals from two channels of different hemispheres, demonstrates the lowest stability 236.2% and ICC value 0.36.

Several previous studies have demonstrated high stability of the EEG bands power and strong correlation (typically higher than 0.8) has been reported in time intervals between sessions from hours to twelve years (Gasser et al., 1985; Salinsky et al., 1991; Kondacs and Szab´o, 1999; Corsi-Cabrera et al., 2007; Rogers et al., 2016; Tenke et al., 2018). The results of **Publication II** are in accordance with the earlier studies.

The IHAS is the only EEG measure demonstrating remarkable trend of changes between two sessions and lower ICC values. The IHAS has the highest interhemispheric asymmetry ICC value 0.6 in alpha and gamma band frontal channels F7-F8 (Table 3, **Publication II**). The stability of frontal alpha asymmetry is shown to be decreasing in time, within months (Allen et al., 2004). The stability of resting frontal asymmetry for two weeks, four months and twelve years has been reported (Allen et al., 2004; Stewart et al., 2010). The ICC value 0.6 related to the three-year period in the current study is in compliance with the stronger correlation over four months 0.86 (Allen et al., 2004). The IHAS, using signals from two channels of different hemispheres, depends on the spatial stability of EEG power distribution. The higher instability of IHAS might be related to the topographic instability of EEG powers reported earlier (Burgess and Gruzelier, 1993).

4.3.4 Impact of professional responsibility and educational level on EEG measures

The higher levels of responsibility and education, which often go hand in hand, both cause a significant increase in the SASI value (**Publication III** and **Publication IV**). The increase in relative gamma power occurs in **Publication IV**.

The increase of SASI, according to formula (2), can be related to the increase in higher (beta) or decrease in lower (theta) frequency band power. Whereas increasing gamma power appears in **Publication IV**, most probably the increase in the higher frequency band power is evident. Consequently, the higher level of responsibility and education of persons both are related to the increase in higher EEG spectrum frequencies. The rise in higher EEG frequencies, beta and gamma power, is probably related to increasing mental and cognitive workload (Spironelli et al., 2008; Werkle-Bergner et al., 2009; So et al., 2017).

However, the increased SASI, relative beta and gamma power are also indicators of depression (Sun et al., 2008; Hinrikus et al., 2010; Bachmann et al., 2018). Therefore, the impact of professional responsibility and education on EEG needs to be considered in the classification of depression.

4.3.5 Limitations and future perspectives

Despite the fact that the results of the Theses support the understanding that EEG-based measures are applicable and may be useful for early detection of depressive symptoms, there are limitations of the study. The main limitation is the small number of participants in each group. Further much wider research is required to confirm these preliminary results.

The main challenge is the absence of commonly approved rating scores for EEG measures to discriminate between depression symptoms. The rating scores used in this study have been assessed previously in independent groups; however, the base for rating remains still limited. The extent of the investigations needed for the development of a commonly approved rating scale for EEG measures reaches beyond the current study, being too large for solution by a single research group. Further large-scale investigations are required to implement EEG-based measures for early detection of depression symptoms in occupational health examinations.

Conclusions

The results of the Thesis have demonstrated the advantage of the easy-to-use novel EEG-markers for detection of persons with high probability of depression, pointing to the need for future larger studies for the purpose of occupational health and screening of population.

1. The rate of subjects indicating symptoms of depression in healthy people detected by the EEG measures SASI and HFD is much higher than the rate of subjects indicating symptoms according to the depression questionnaires HAM-D and EST-Q-D (**Publication I**). This result supports the hypothesis that the changes in EEG signals seem to be detectable before the subjective symptoms have become evident.
2. The observed high stability of EEG measures over three years confirms their reproducibility, and thus – feasibility for the detection of depression symptoms. The original finding is that the nonlinear HFD provides better stability than the frequency band powers (**Publication II**).
3. The results demonstrated an unexpected regularity: the reliability of a measure decreases with the increasing number of channels and frequency bands used for the calculation of the measure (**Publication II**): This finding supports the preferable application of the single-channel measures.
4. The original finding is that the level of professional responsibility and education causes a significant increase in the SASI value and relative gamma power (**Publication III, Publication IV**). These factors should be considered in the evaluation of depressive symptoms.

The results of the Thesis support the prospect of using EEG-based measures in clinical practice. However, further large-scale investigations are required to implement EEG-based measures for early detection of depression symptoms in occupational health examination.

References

Ahmadlou, M.; Adeli, H; Adeli, A. (2012). Fractality analysis of frontal brain in major depressive disorder. Int J Psychophysiol. 85(2):206–11. doi: 10.1016/j.ijpsycho.2012.05.001.

Allen, J.J.B.; Urry, H.L.; Hitt, S.K.; Coan, J.A. (2004). The stability of resting frontal electroencephalographic asymmetry in depression. Psychophysiology 41: 269–280.

Aluoja, A.; Shlik, J.; Vasar V. et al. (1999). Development and psychometric properties of the Emotional State Questionnaire, a self-report questionnaire for depression and anxiety. Nord J Psychiatry. 53(6), 443–449. doi: 10.1080/080394899427692.

Aluoja, A.; Leinsalu, M.; Shlik, J.; Vasar, V.; Luuk, K. (2004). Symptoms of depression in the Estonian population: Prevalence, sociodemographic correlates and social adjustment. J Affect Disord 78:27–35

Bachmann, M.; Lass, J.; Suhhova, A.; Hinrikus, H. (2013). Spectral Asymmetry and Higuchi's Fractal Dimension Measures of Depression Electroencephalogram. Comput Math Methods Med, Volume 2013.

Bachmann, M.; Lass, J.; Hinrikus, H. (2017). Single channel EEG analysis for detection of depression. Biomed Signal Process Control, 31:391–397.

Bachmann, M.; Päeske, L.; Kalev, K.; Aarma, K.; Lehtmets, A.; Ööpik, P.; Lass, J.; Hinrikus,H. (2018) Methods for classifying depression in single channel EEG using linear and nonlinear signal analysis. Comput Methods Programs Biomed. 155:11–17. doi: 10.1016/j.cmpb.2017.11.023.

Balconi, M.; Pozzoli, U. (2009). Arousal effect on emotional face comprehension: Frequency band changes in different time intervals, Physiology & Behavior, 97(3-4):455-62. doi: 10.1016/j.physbeh.2009.03.023.

Breakspear, M.; Terry, J.R. (2002) Detection and description of non-linear interdependence in normal multichannel human EEG data. Clin. Neurophysiol. 113(5):735-53. doi: 10.1016/s1388-2457(02)00051-2.

Burgess, A.; Gruzelier, J. (1993). Individual reliability of amplitude distribution in topographical mapping of EEG. Electroencephalogr. Clin. Neurophysiol. 86, 219–223.

Buzsáki, G.; Draguhn, A. (2004) Neuronal oscillations in cortical networks. Science 304:1926–1929

Corsi-Cabrera, M.; Galindo-Vilchis, L.; Del-Rio-Portilla, Y.; Arce, C.; Ramos-Loyo, J.; (2007). Within-subject reliability and inter-session stability of EEG power and coherent activity in women evaluated monthly over nine months. Clin. Neurophysiol. 118, 9–21.

Čukić, M.; Stokić, M.; Simić, S.; Pokrajac, D. (2020a). The successful discrimination of depression from EEG could be attributed to proper feature extraction and not to a particular classification method. Cognitive Neurodynamics, Springer Verlag 2020. DOI: 10.1007/s11571-020-09581-x

Čukić, M.; Stokić, M.; Radenković, S.; Ljubisavljević, M.; Simić, S.; Savić, D. (2020b) Nonlinear analysis of EEG complexity in episode and remission phase of recurrent depression. Int J Methods Psychiatr Res, 29(2):e1816. doi: 10.1002/mpr.1816.

Cusin, C.; Yang, H.; Yeung, A.; Fava, M. (2010) Rating Scales for Depression. In Handbook of Clinical Rating Scales and Assessment in Psychiatry and Mental Health. Ed. Lee Baer Mark A. Blais. New York: Humana Press, 2010. Pages 7–35.

Debener, S.; Beauducel, A.; Nessler, D.; Brocke, B.; Heilemann, H.; Kavser, J. (2000) Is resting anterior EEG alpha asymmetry a trait marker for depression? Findings for healthy adults and clinically depressed patients. Neuropsychobiology 41: 31–37.

Dehaene, S.; Changeux, JP. (2000) Reward-dependent learning in neuronal networks for planning and decision making. Prog Brain Res. 2000;126:217–29. doi: 10.1016/S0079-6123(00)26016-0.

Domken, M.; Scott, J.; Kelly, P. (1994) What factors predict discrepancies between self and observer ratings of depression? J Affective Dis. 31: 253–259.

Eller, T.; Aluoja, A.; Vasar, V.; Veldi, M. (2006) Symptoms of anxiety and depression in Estonian medical students with sleep problems. Depression and Anxiety 23:250–256.

Enns, MW.; Larsen, DK.; Cox, BJ. (2000) Discrepancies between self and observer ratings of depression. The relationship to demographic, clinical and personality variables. J Affective Dis. 60:33–41.

Ettman, C.K.; Abdalla, S.M.; Cohen, G.H.; Sampson, L.; Vivier, P.M.; Galea, S. (2020) Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic. JAMA Netw Open, 3(9), p. e2019686

Fingelkurts, A.A.; Fingelkurts, A.A. (2015) Altered structure of dynamic electroencephalogram oscillatory pattern in major depression. Biol Psychiatry. 77(12):1050–60. doi: 10.1016/j.biopsych.2014.12.011.

Fingelkurts, A.A.; Fingelkurts, A.A.; Rytsälä, H.; Suominen, K.; Isometsä, E.; Kähkönen, S. (2006). Composition of brain oscillations in ongoing EEG during major depression disorder. Neurosci Res, 56(2):133–144.

Fingelkurts, A.A.; Fingelkurts, A.A.; Rytsälä, H.; Suominen, K.; Isometsä, E.; Kähkönen, S. (2007). Impaired functional connectivity at EEG alpha and theta frequency bands in major depression. Hum Brain Mapp, 28(3):247–261.

Frank, M.J.; Gagne, C. ; Nyhus,E. ; Masters, S.; Wiecki, T.V.; Cavanagh, J.F.; Badre, D. (2015) fMRI and EEG Predictors of Dynamic Decision Parameters during Human Reinforcement Learning. J Neurosci. 35(2):485–494. doi: 10.1523/JNEUROSCI.2036-14.2015

Fried, EI. (2017). The 52 symptoms of major depression: Lack of content overlap among seven common depression scales. J Affect Disord. 208:191–197. doi: 10.1016/j.jad.2016.10.019.

Friston, K.J. (2000) The labile brain. I. Neuronal transients and nonlinear coupling. Philos Trans R Soc Lond B Biol Sci. 355(1394):215–36. doi: 10.1098/rstb.2000.0560.

Gasser, T.; Bächer, P.; Steinberg, H. (1985). Test-retest reliability of spectral parameters of the EEG. Electroencephalogr. Clin. Neurophysiol. 60, 312–319.

Goetzel, R.Z. ; Roemer, E.C. ; Holingue, C. et al. (2018) Mental health in the workplace: a call to action proceedings from the mental health in the workplace – Public Health Summit. J Occup Environ Med. 60(4):322–330. doi: 10.1097/JOM.0000000000001271.

Golonka, K.; Mojsa-Kaja, J.; Blukacz, M.; Gawłowska, M.; Marek, T. (2019). Occupational burnout and its overlapping effect with depression and anxiety. Int J Occup Med Environ Health. 32(2):229–244. doi: 10.13075/ijomeh.1896.01323.

Gold, C.; Fachner, J.; ErkkilØa, J. (2013). Validity and reliability of electroencephalographic frontal alpha asymmetry and frontal midline theta as biomarkers for depression," Scandinavian Journal of Psychology, 54(2): 118–126.

Gudmundsson, S.; Runarsson, T.P.; Sigurdsson, S.; Eiriksdottir, G.; Johnsen, K. (2007). Reliability of quantitative EEG features. Neurophysiol. 118, 2162–1271.

Hamilton, M. (1960). A rating scale for depression. J Neurol Neurosurg Psychiatry. 23: 56–62.

Hamilton, M. (1967). Development of a rating scale for primary depressive illness. Br J Soc Clin Psychol 6(4): 278–296.

Harmon-Jones, E.; Gable, P.A.; Peterson, C.K. (2010) The role of asymmetric frontal cortical activity in emotion-related phenomena: A review and update. Biological Psychology. 84(3): 451–463.

Henriques, J.B.; Davidson, R.J. (1991) Left frontal hypoactivation in depression. J Abnorm Psychol 100:535–545.

Higuchi, T. (1988) Approach to an irregular time series on the basis of the fractal theory. Phys D Nonlinear Phenom.31:277–283.

Hinrikus, H.; Suhhova, A.; Bachmann, M.; Aadamsoo, K.; Võhma, U.; Lass, J.; Tuulik, V. (2009) Electroencephalographic spectral asymmetry index for detection of depression. Med Biol Eng Comput. 47(12):1291–9. doi: 10.1007/s11517-009-0554-9.

Hinrikus, H.; Suhhova, A.; Bachmann, M.; Aadamsoo, K.; Võhma, Ü.; Pehlak, H.; Lass, J. (2010) Spectral features of the EEG in depression. Biomedizinische Technik / Biomedical Engineering 55(3): 155–161.

Homan, R.W.; Herman, J.; Purdy, P. (1987) Cerebral location of international 10-20 system electrode placement Electroencephalogr Clin Neurophysiol. 66(4): 376–82. doi: 10.1016/0013-4694(87)90206-9.

Hosseinifard, B.; Moradi, M.H.; Rostami, R. (2013) Classifying depression patients and normal subjects using machine learning techniques and nonlinear features from EEG signal. Comput Methods Programs Biomed. 109(3):339–45. doi: 10.1016/j.cmpb.2012.10.008.

Hu, K.; Ivanov, P.C.; Chen, Z.; Carpena, P.; Stanley, H.E. (2001). Effect of trends on detrended fluctuation analysis. Phys. Rev. E Stat. Nonlinear Soft Matter Phys. 64, 011114.

Newson, J.J.; Hunter, D.; Thiagarajan, T.C. (2020) The Heterogeneity of Mental Health Assessment. Front Psychiatry. 11: 76. doi: 10.3389/fpsyt.2020.00076.

Landsbergis, P.A.; Dobson, M.; LaMontagne, A.D.; Choi, B.K.; Schnall, P.; Baker, D.B. (2011). Occupational Stress in Occupational and environmental health, Edited by Levy B S, Wegman D H, Baron S L, Sokas R K. 6th edition, Oxford University Press, New York, 14:296–312.

Knott, V.; Mahoney, C.; Kennedy, S.; Evans, K. (2001). EEG power, frequency, asymmetry and coherence in male depression. Psychiatry Res, 106: 123–140.

Kondacs, A.; Szabó, M. (1999). Long term intra-individual variability of the background EEG in normals. Clin. Neurophysiol. 110, 1708–1716. doi: 10.1016/s1388-2457(99)00122-4.

Lee, J.-S.; Yang, B.-H.; Lee, J.-H.; Choi, J.-H. ; Choi, I.-G. ; Kim, S.-B. (2007). Detrended fluctuation analysis of resting EEG in depressed outpatients and healthy controls. Clin Neurophysiol, 118(11):2489–2496. doi: 10.1016/j.clinph.2007.08.001.

Lee, P.F.; Kan, D.P.X.; Croarkin, P; Phang, C.K.; Doruk, D. (2018). Neurophysiological correlates of depressive symptoms in young adults: A quantitative EEG study. J Clin Neurosci. 47:315–322.

Leistedt, S.; Dumont, M.; Lanquart, J.-P.; Jurysta, F.; Linkowski, P. (2007). Characterization of the sleep EEG inacutely depressed men using detrended fluctuation analysis, Clin.Neurophysiol. 118:940–950.

Leuchter, A. F.; Cook, I. A.; Hunter, A. M.; Cai, C.; Horvath, S. (2012). Resting-state quantitative electroencephalography reveals increased neurophysiologic connectivity in depression. PLoS One. 2012;7(2):e32508. doi: 10.1371/journal.pone.0032508.

Mahato, S.; Paul, S. (2020). Classification of Depression Patients and Normal Subjects Based on Electroencephalogram (EEG) Signal Using Alpha Power and Theta Asymmetry. J Med Syst, 44(1).

Madsen, I.E.H.; Nyberg, S.T.; Magnusson Hanson, L.L.; Ferrie, J.E.; Ahola, K.; Alfredsson, L.; Batty, G.D.; et al. (2017) IPD-Work Consortium. Job strain as a risk factor for clinical depression: systematic review and meta-analysis with additional individual participant data. Psychol Med. 2017;47(8):1342–1356. doi: 10.1017/S003329171600355X.

Malmivuo, J.; Plonsey, R. (1995). Bioelectromagnetism - Principles and Applications of Bioelectric and Biomagnetic Fields, Oxford University Press, New York, 1995. http://www.bem.fi/book/

Marciani, M.G.; Maschio, M.; Spanedda, F.; Caltagirone, C.; Gigli, G.L.; Bernardi, G. (1994). Quantitative EEG evaluation in normal elderly subjects during mental processes: age-related changes. Int J Neurosci 76(1-2):131–40. doi: 10.3109/00207459408985998

Mathersul, D.; Williams, L.; Hopkinson, P.; Kemp, A. (2008). Investigating models of affect: relationships among EEG alpha asymmetry, depression, and anxiety. Emotion 8:560–572.

Meyers, J.L.; Chorlian, D.B.; Bigdeli, T.B.; Johnson, E.C.; Aliev, F.; Agrawal, A.; Almasy, L.; Anokhin, A.; Edenberg, H.J.; Foroud, T.; Goate, A.; Kamarajan, C.; Kinreich, S.; Nurnberger, J.; Pandey, A.K.; Pandey, G.; Plawecki, M.H.; Salvatore, J.E.; Zhang, J.; Fanous, A.; Porjesz, B. (2021) The association of polygenic risk for schizophrenia, bipolar disorder, and depression with neural connectivity in adolescents and young adults: examining developmental and sex differences. Transl Psychiatry. 11(1):54. doi: 10.1038/s41398-020-01185-7.

Michel, C.M.; Murray, M.M. (2012) Towards the utilization of EEG as a brain imaging tool. Neuroimage. 61(2):371–85. doi: 10.1016/j.neuroimage.2011.12.039.

Mumtaz, W.; Ali, S.S.A.; Yasin, M.A.M.; Malik, A.S. (2018). A machine learning framework involving EEG-based functional connectivity to diagnose major depressive disorder (MDD). Med Biol Eng Comput. 56:233–246.

Mumtaz, W.; Xia, L.; Ali, S.S.A.; Yasin, M.A.M.; Hussain, M.; Malik, A.S. (2017). Electroencephalogram (EEG)-based computer-aided technique to diagnose major depressive disorder (MDD). Biomed Signal Process Control, 31: 108–115. doi: 10.1016/j.bspc.2016.07.006.

Netterstrøm, B.; Conrad, N.; Bech, P.; Fink, P.; Olsen, O.; Rugulies, R.; Stansfeld, S. (2008) The relation between work-related psychosocial factors and the development of depression. Epidemiol Rev. 30:118–32. doi: 10.1093/epirev/mxn004.

Hsu Sandy, H.-J.; Chen, D.-R.; Cheng, Y.; Su, T.-C. (2016) Association of psychosocial work hazards with depression and suboptimal health in executive employees. J Occup Environ Med 58:728–736.

Newson, J.J.; Thiagarajan, T.C. (2019) EEG Frequency Bands in Psychiatric Disorders: A Review of Resting State Studies. Front. Hum. Neurosci., 09 January 2019. doi: 10.3389/fnhum.2018.00521.

Newson, J.J.; Hunter, D.; Thiagarajan, T.C. (2020) The Heterogeneity of Mental Health Assessment. Front. Psychiatry, 27 February 2020. doi: 10.3389/fpsyt.2020.00076.

Niedermeyer, E.; Lopes da Silva, F. (1993): 'Electroencephalography, Basic Principles, Clinical Applications and Related Fields' (William & Wilkins, Baltimore, 1993).

NIMH (2017) Mental health information, Depression. https://www.nimh.nih.gov/health/statistics/major-depression.shtml

Nunez, P.L. (1995) Neocortical Dynamics and Human EEG Rhythms. Oxford University Press, New York.

Olbrich, S.; Tränkner, A.; Chittka, T.; Hegerl, U.; Schönknecht, P. (2014). Functional connectivity in major depression: Increased phase synchronization between frontal cortical EEG-source estimates. Psychiatry Res, 222(1-2):91–99.

Orgo, L.; Bachmann, M.; Lass, J.; Hinrikus, H. (2015) Effect of Negative and Positive Emotions on EEG Spectral Asymmetry. 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). 8107–8110, doi: 10.1109/EMBC.2015.7320275.

Orgo, L.; Bachmann, M.; Kalev, K.; Järvelaid, M.; Hinrikus, H. (2016). Brain Functional Connectivity in Depression: Gender Differences in EEG. IEEE - EMBS Conference on Biomedical Engineering and Science, Kuala Lumpur, 4-8 December 2016. IEEE, 270−273. doi: 10.1109/IECBES.2016.7843456.

Nikulin, V.V.; Brismar, T. (2005) Long-range temporal correlations in electroencephalographic oscillations: Relation to topography, frequency band, age and gender. Neuroscience. 130(2):549–58. doi: 10.1016/j.neuroscience.2004.10.007.

Peng, C.K.; Havlin, S.; Stanley, H.E.; Goldberger, A.L. (1995). Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time seires. Chaos 5:82–87.

Purdon, P.L.; Pavone, K.J.; Akeju, O.; Smith, A.C.; Sampson, A.L.; Lee, J.; Zhou, D.W.; Solt, K.; Brown, E.N. (2015) The Ageing Brain: Age-dependent changes in the electroencephalogram during propofol and sevoflurane general anaesthesia. Br J Anaesth. 115 Suppl1:i46–i57. doi: 10.1093/bja/aev213.

Roberts, J. A.; Robinson, P.A. (2012). Quantitative theory of driven nonlinear brain dynamics. Neuroimage, 62(3):1947–1955.

Rodríguez-Bermudez, G.; Garcíıa Laencin, P.J. (2015). Analysis of EEG signalsusing nonlinear dynamics and chaos: a review. Appl. Math. Inf. Sci. 9, 1–13. doi: 10.12785/amis/090512.

Rogers, J.M.; Johnstone, S.J.; Aminov, A.; Donnelly, J.; Wilson, P.H. (2016). Test-retest reliability of a single-channel, wireless EEG system. Int. J. Psychophysiol. 106: 87–96.

Saijo, Y. ; Chiba, S.; Yoshioka, E.; Kawanishi, Y.; Nakagi, Y.; Itoh, T.; Sugioka, Y.; Kitaoka-Higashiguchi, K.; Yoshida, T. (2014) Effects of work burden, job strain and support on depressive symptoms and burnout among Japanese physicians. Int J Occup Med Environ Health. 27(6):980-92. doi: 10.2478/s13382-014-0324-2.

Saifudinova, M.; Bachmann, M.; Lass, J.; Hinrikus, H. (2015). Effect of Coffee on EEG Spectral Asymmetry. IFMBE Proc, vol. 51, World Congress on Med. Phys. & Biomed. Eng., Toronto, Canada, 2015, 1030–1033. doi: 10.1007/978-3-319-19387-8_251.

Salari, N.; Hosseinian-Far, H.; Jalali, R.; Vaisi-Raygani, A.; Rasoulpoor, S.; Mohammadi, M.; Rasoulpoor, S.; Khaledi-Paveh, B. (2020). Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: A systematic review and meta-analysis. Global Health, 16:57. doi: 10.1186/s12992-020-00589-w.

Salinsky, M.C.; Oken, B.S.; Morehead, L. (1991). Test–retest reliability in EEG frequency analysis. Electroencephalogr. Clin. Neurophysiol. 79:382–392.

Sammler, D.; Grigutsch, M.; Fritz, T.; Koelsch, S. (2007) Music and emotion: Electrophysiological correlates of the processing of pleasant and unpleasant music. Psychophysiology. 44(2):293–304.

Shim, M.; Im, C.-H.; Kim, Y.-W.; Lee, S.-H. (2018). Altered cortical functional network in major depressive disorder: A resting state electroencephalogram study. Neuroimage Clin. 19:1000–1007.

Siu, A.L.; et al. (2016). Screening for depression in adults: US Preventive Services Task Force recommendation statement. JAMA, 315(4):380–387. doi: 10.1001/jama.2015.18392.

So, W.K.Y.; Wong, S.W.H.; Mak J.N.; Chan, R.H.M. (2017) An evaluation of mental workload with frontal EEG. PLoS ONE 12(4): e017494.

Spironelli, C.; Penolazzi, B.; Angrilli, A. (2008) Dysfunctional hemispheric asymmetry of theta and beta EEG activity during linguistic tasks in developmental dyslexia. Biological psychology. 77(2):123–131. https://doi.org/10.1016/j.biopsycho.2007.09.009 PMID: 17997211 34.

Stam, C.J. (2005) Nonlinear dynamical analysis of EEG andMEG: review of an emerging field. Clinical Neurophysiology. 116(10):2266–2301.

Stansfeld, S.; Candy, B. (2006) Psychosocial work environment and mental health--a meta-analytic review. Scand J Work Environ Health. 32(6):443–462.

Stewart, J.L.; Bismark, A.W.; Towers, D.N.; Coan, J.A.; Allen, J.J.B. (2010). Resting frontal EEG asymmetry as an endophenotype for depression risk: sex-specific patterns of frontal brain asymmetry. J. Abnorm. Psychol. 119, 502–512.

Sun, Y.; Li, Y.; Zhu, Y.; Chen, X.; Tong, S. (2008) Electroencephalographic differences between depressed and control subjects: an aspect of interdependence analysis. Brain Res Bull 76:559–564.

Tenke, C.E.; Kayser, J.; Alvarenga, J.E.; Abraham, K.S.; Warner, V.; Talati, A.; Weissman, M.M.; Bruder, G.E. (2018). Temporal stability of posterior EEG alpha over twelve years. Clin. Neurophysiol. 129:1410–1417. doi: 10.1016/j.clinph.2018.03.037.

Troyer, E.A.; Kohn, J.N.; Hong, S. (2020). Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. Brain Behav Immun. 87:34–39.

van der Vinne, N.; Vollebregt, M.A.; van Putten, M.J.A.M.; Arns, M. (2017). Frontal alpha asymmetry as a diagnostic marker in depression: Fact or fiction? A meta-analysis. Neuroimage Clin. 16:79–87.

Veldhuizen, R. J.; Jonkman, E. J.; Poortvliet, D.C. (1993). Sex differences in age regression parameters of healthy adults--normative data and practical Implications. Electroencephalogr Clin Neurophysiol. 86(6):377–84.

Werkle-Bergner, M.; Shing, Y.L.; Müller, V.; Li, S.C.; Lindenberger, U. (2009) EEG gammaband synchronization in visual coding from childhood to old age: evidence from evoked power and inter-trial phase locking. Clinical Neurophysiology 120(7):1291–1302.

Whiteford, H.A.; Ferrari, A.J.; Degenhardt, L.; Feigin, V.; Vos, T. (2010) The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010. PLoS One. 2015;10:e0116820.

Williams, J.B. (1988) A structured interview guide for the Hamilton Depression Rating Scale. Arch Gen Psychiatry 45(8):742–747.

Wittchen, H.U.; Jacobi, F.; Rehm, J., et al. (2011) The size and burden of mental disorders and other disorders of the brain in Europe. Eur Neuropsychopharmacol. 21(9):655–679. doi: 10.1016/j.euroneuro.2011.07.018. PMID: 21896369.

WHO Europe, 2019. Mental health: Fact sheet https://www.euro.who.int/__data/assets/pdf_file/0004/404851/MNH_FactSheet_ENG.pdf

WHO, 2020. Depression. https://www.who.int/news-room/fact-sheets/detail/depression

Wulsin, L.; Alterman, T.; Timothy-Bushnell, P.; Li, J.; Shen, R. (2014). Prevalence rates for depression by industry: a claims database analysis. Soc Psychiatry Psychiatr Epidemiol. 49:1805–1821.

Acknowledgements

I am sincerely thankful to everyone who has been helping and contributing to the work of my Thesis. There are a number of people behind this work who deserve to be acknowledged and thanked.

I would like to express my deep gratitude to my supervisor professor Maie Bachmann for her patient guidance, constructive suggestions, immense knowledge and kind support.

I am very grateful to my supervisor Jaanus Lass for his valuable guidance and positive support that made this work possible.

I am very grateful to Professor Emeritus Hiie Hinrikus for her valuable guidance and positive support that made this work possible.

My grateful thanks are extended to my co-authors Laura Päeske and Kaia Kalev for fruitful co-operation and contribution.

Abstract

Application of electroencephalographic signal based measures for early detection of depression symptoms in occupational health

Depression is a leading cause of disability and a burden of disease that involves a remarkable part of working age population. During last decades, depression has become a common mental disorder worldwide and it is in rise with a predominance in developed countries. The work stress caused by psychosocial factors in the work environment can contribute to the development of depression among employees.

Today, the diagnosis of mental disorders is based on the evaluation of subjective symptoms by a general practitioner, an occupational physician or a psychiatrist using questionnaires and interviews. No other easy-to-use objective measures exist in clinical practice.

Early detection of depression symptoms is required to prevent burnout and subsequent depression of employees.

The general aim of the Thesis is to demonstrate the potential of the EEG-based measures to detect depression symptoms on different groups of subjects reliably and earlier than by other methods.

The aim of the Thesis is as follows:

- compare various EEG-based measures and psychometric tests for the detection of symptoms of depression in seemingly healthy people at an individual level;
- evaluate the temporal reliability of the EEG-based measures;
- evaluate the impact of the level of responsibility on the EEG measures;
- evaluate the impact of the level of education on the EEG measures.

The results of the Thesis have demonstrated the advantage of the easy-to-use novel EEG-markers for detection of persons with high probability of depression, pointing to the need for future larger studies for the purpose of occupational health and screening of population.

- The rate of subjects indicating symptoms of depression in seemingly healthy people detected by the EEG measures SASI and HFD is much higher than the rate of subjects indicating symptoms according to the depression questionnaires HAM-D and EST-Q-D.
- The observed high stability of the EEG measures over three years suggests that they are feasible for the detection of depression symptoms.
- The results demonstrated an unexpected regularity: the reliability of a measure decreases with the number of channels and frequency bands used for the calculation of the measure. This finding supports the preferable application of the single-channel measures.
- The level of professional responsibility and education causes a significant increase in the SASI value and relative gamma power. These factors should be considered in the evaluation of the depressive symptoms.

The results of the Thesis support the prospect of using EEG-based measures in clinical practice. However, further large-scale investigations are required to implement EEG-based measures for early detection of depression in occupational health examination.

Lühikokkuvõte

Elektroentsefalograafilisel signaalil põhinevate indikaatorite kasutamine depressiooni sümptomite varaseks avastamiseks töötervishoius

Pingeline töö ja kiire elutempo põhjustavad vaimseid pingeid. Vaimsed pinged tekitavad stressi, krooniline stress võib kasvada üle depressiooniks, mis juba oluliselt mõjutab elu kvaliteeti, töövõimet ja võib olla isegi fataalne. Töötervishoius pööratakse siiani töötajate vaimsele tervisele suhteliselt vähe tähelepanu.

Depressioon on haiguskoormuse ja töövõimetuse üks peamisi põhjuseid tööealise elanikkonna hulgas. Viimaste aastakümnete jooksul on depressioon muutunud kogu maailmas sagedaseks psüühikahäireks, mis on eriti levinud arenenud riikides. Töökeskkonna psühhosotsiaalsete tegurite põhjustatud tööstress võib aidata kaasa depressiooni tekkele töötajate seas. Hetkel jätkuvalt kestev COVID-19 pandeemiast tingitud kriis on veelgi võimendanud depressiooni avaldumist.

Täna põhineb psüühikahäirete diagnoosimine perearsti, töötervishoiu arsti või psühhiaatri poolt subjektiivsete sümptomite hindamisel küsimustike ja intervjuude abil. Muid objektiivseid indikaatoreid kliinilises praktikas täna ei kasutata, mistõttu võib väliste tundemärkideta kulgev depressioon jääda mõnikord märkamata.

Aju koordineerib ja juhib kogu inimese elutegevust. Meeleolu muutus või vaimne pinge on otseselt seotud muutustega ajutegevuses. Aju neuronite bioelektriliste võnkumiste sagedus muutub vaimse koormuse ja pingega. Sellepärast on peanahalt salvestatav aju neuronite bioelektrilisi võnkumisi kirjeldav elektroentsefalograafiline (EEG) signaal sobiv meetod aju seisundi ja vaimsete häirete avastamiseks ja kirjeldamiseks.

Aju töös esinevate kõrvalekallete varajane avastamine on vajalik töötajate läbipõlemise ja sellele järgneva depressiooni vältimiseks või õigeaegseks raviks. Eriti oluline on see sellistel ametitel, kus depressioon võib mõjutada teiste turvalisust nagu näiteks lennunduses, nii pilootidel kui lennujuhtidel, politseinikel, sõjaväelastel.

Doktoritöö tõstatab esmakordselt probleemi EEG kasutamisest töötervishoius töötajate vaimse pinge ja depressiooni varaseks avastamiseks. Doktoritöö peamine eesmärk on demonstreerida EEG-põhiste mõõdikute potentsiaali tuvastada depressioonile viitavaid tunnuseid usaldusväärselt ja varem, kui seni kasutatud meetodite puhul.

Doktoritöö alameesmärgid:

- Võrrelda näiliselt tervete inimeste depressioonisümptomite tuvastamiseks erinevaid EEG-põhiseid mõõdikuid ja psühhomeetrilisi teste individuaalsel tasandil.
- Hinnata EEG-põhiste mõõdikute ajalist usaldusväärsust.
- Hinnata tööalase vastutuse taseme mõju EEG-põhistele mõõdikutele.
- Hinnata haridustaseme mõju EEG-põhistele mõõdikutele.

Väitekirja tulemused näitavad uute lihtsalt kasutatavate EEG-põhiste tunnuste rakendamise eeliseid tuvastamaks isikud, kes vajavad süvendatud kliinilist uuringut:

- EEG-põhiste mõõdikutega SASI ja HFD näidatud objektiivsete depressiooni-sümptomitega inimeste osakaal tervete hulgas on kõrgem kui depressiooni küsimustikega HAM-D ja EST-Q-D näidatud depressioonisümptomitega inimeste osakaal.

- Kolme aasta jooksul täheldatud EEG-põhiste mõõdikute kõrge stabiilsus võimaldaks nende rakendatavust depressiooni sümptomite tuvastamiseks.
- Tulemused näitasid ootamatut seaduspärasust: mõõtmise usaldusväärsus väheneb mõõtmise arvutamiseks kasutatud kanalite arvu ja sagedusribade arvu kasvuga. See leid toetab ühekanaliliste meetmete eelistatavat rakendamist.
- Kõrgema ametialase vastutuse ja hariduse taseme puhul on SASI väärtus ja suhteline gammavõimsus oluliselt suuremad. Seda asjaolu tuleb depressiooni sümptomite hindamisel arvestada.

Väitekirja tulemused osutavad võimalusele kasutada EEG-põhiseid mõõdikuid kliinilises praktikas. EEG-põhiste mõõtmiste rakendamine depressiooni sümptomite varajaseks avastamiseks töötervishoius eeldab täiendavaid ulatuslikke uuringuid.

Appendix 1

Publication I

Põld, T.; Päeske, L.; Bachmann, M.; Lass, J.; Hinrikus, H. (2019). Assessment of Objective Symptoms of Depression in Occupational Health Examination. Journal of Occupational and Environmental Medicine, 61 (7), 605−609. DOI: 10.1097/JOM.0000000000001622

Assessment of Objective Symptoms of Depression in Occupational Health Examination

Toomas Põld, MD, Laura Päeske, MS, Maie Bachmann, PhD, Jaanus Lass, PhD, and Hiie Hinrikus, DSc

Objective: The aim of the study was to assess early symptoms of depression in regular occupational health examination using the objective measures based on electroencephalographic (EEG) signal analysis. **Methods:** The study was performed on 125 volunteer participants. The resting-state EEG signal was recorded for 7 minutes. The spectral asymmetry index (SASI) and Higuchi fractal dimension (HFD) were calculated in EEG channel P_z. Parallel, the participants were subjected to two psychological tests, observer-rated HAM-D and self-rated EST-Q-D. **Results:** The SASI revealed depressive symptoms for 64.8%, HFD for 55.2%, HAM-D for 44.8%, and EST-Q-D for 28.8% of participants. Combination of two different measures indicated depression symptoms up to 78.4% of participants. **Conclusion:** The results of this study confirm the feasibility of indication of early symptoms of depression applying EEG-based objective measures.

Keywords: depression symptoms, early detection, electroencephalography, Higuchi fractal dimension, occupational stress, psychological tests, spectral asymmetry index

Mental disorders contribute to 56.7% of disability-adjusted life-years, peaking in early adulthood for mental and substance use disorders and including remarkable part of working age population.[1] Depression has become a common mental disorder during last decades with a prevalence rate of 7% in developed countries.[1–3] The development of depression has been suggested to be related to work stress, caused by psychosocial factors in the work environment.[4–8] The work stress due to high demand and low control may precipitate clinical depression among employees. Mental disorders of workers and specialists may increase the risk of accidents especially in the cases of high personal responsibility (pilots, policemen, military specialists, etc). Therefore, early detection of depression symptoms is expected to be beneficial to prevent further and more serious mental disorder and possible related accidents. Despite that, regular examination of depression symptoms has still not become common in occupational health examination.

Clinical interview and psychological tests have been used in monitoring of depression symptoms in clinical practice, as well as in studies in work environment.[4–8] Tests and interviews as subjective measures, based on self-feeling, enable revealing only symptoms evident in the developed stage of depression. The detection of possible alterations in underlying physiology, foremost in brain behavior, can provide objective information about depression symptoms and provide early detection of disorders. Alterations in human brain bioelectric activity are expected to be able to detect specific to mental disorders changes in brain bioelectric processes before the subjective symptoms become evident.

Electroencephalography (EEG) is a tool suitable for noninvasive cost-effective monitoring the state of the brain including depression.[9–12] Many special studies on depression EEG have demonstrated that depression causes significant alterations in various EEG parameters between preselected groups of depressive and healthy subjects.[10–14] To the best of our knowledge, no EEG analysis based evaluation of depression has been performed for individual persons.

The aim of the current study is to assess early symptoms of depression of employees in occupational health examination. For this purpose, objective measures, based on EEG signal analysis, have been used and subjective measures, based on psychological tests, explored for comparison.

To assess objective depression symptom for individuals, two measures based on EEG analysis, the linear spectral asymmetry index (SASI) and the nonlinear Higuchi fractal dimension (HFD), were calculated.[10,15] For comparison, two psychological tests were used for evaluation of subjective symptoms: the Hamilton Depressive Rating Scale HAM-D, assessed by a medical doctor, and the Emotional State Questionnaire for depression EST-Q-D, based on self-rated symptoms.[16,17]

METHODS

Participants

In the current study, the volunteers from different institutions passing occupational health examination were invited to participate. As a result, 125 volunteers without declared depression episodes nor other mental disorders were selected for the study. According to the results of performed medical and biochemical examinations, the selected participants were healthy. The participants were asked to fulfill the questionnaire and declare their habits and health condition. Average age of the group was 41.04 (median 41.00 years) with standard deviation of 8.66 years. Selected participants had a higher or secondary level of education and were employed as managers, specialists, engineers, etc. Unfortunately, none from the group of pilots accepted the invitation to participate in the study. The demographic factors of the selected group of participants are presented in Table 1. The participants were asked to abstain from alcohol for 24 hours and from coffee for 2 hours before the EEG recordings.

All participants have been informed about the aim and procedures of the study and have signed written informed consent. The study was conducted in accordance with the Declaration of Helsinki and formally approved by the Tallinn Medical Research Ethics Committee.

Procedures, Methods, and Equipment

All participants underwent a clinical test by the medical doctor based on the 17-item Hamilton Depression Rating Scale

From the Centre of Biomedical Engineering, Department of Health Technologies, Tallinn University of Technology, Tallinn, Estonia (Dr Põld, Dr Päeske, Dr Bachmann, Dr Lass, Hinrikus); and Qvalitas Medical Centre, Tallinn, Estonia (Dr Põld).

This study was financially supported by the Estonian Ministry of Education and Research under institutional research financing IUT 19-2 and by the Estonian Centre of Excellence in IT (EXCITE) 2014-2020.4.01.15-0018 funded by the European Regional Development Fund.

The authors declare no conflict of interest.

Supplemental digital contents are available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal's Web site (www.joem.org).

Address correspondence to: Maie Bachmann, PhD, Centre of Biomedical Engineering, Department of Health Technologies, Tallinn University of Technology, Ehitajate tee 5, 19086 Tallinn, Estonia (maie@cb.ttu.ee)

DOI: 10.1097/JOM.0000000000001622

TABLE 1. Data of the Group of Participants

Qualities	Subgroup	Number of Participants	Percentage %
Gender	Male	49	39.2
	Female	76	60.8
Age	>41 years	62	49.6
	<41 years	63	50.4
Education	Higher	99	79.2
	Secondary	26	20.8
	Primary	0	0
Marital status	Married	74	59.2
	Single	51	40.8
Smoking	Yes	19	15.2
	No	106	84.8

(HAM-D) for determining depressive symptoms.[16] In addition, the participants completed themselves the self-report Emotional State Questionnaire (EST-Q) subscale for depression EST-Q-D.[17]

The EEG recordings were performed in a quiet dimly lit room, and no special conditions were provided. During an EEG recording, a subject was lying in a relaxed position with blocked ears and closed eyes. The resting-state EEG was recorded for 7 minutes using the Cadwell Easy II EEG (Kennewick, WA) equipment. The international 10 to 20-electrode position classification system was applied for recordings of the 18-channel EEG. The quality of the recorded EEG signals was evaluated by an experienced EEG specialist and only artefact-free segments were selected for analysis. The raw signals in frequency band 0.3 to 70 Hz were stored at the sampling frequency of 400 Hz.

The single-channel EEG signal has been demonstrated being sufficient for separation between depressive and healthy subjects and the best differentiation ability has occurred in parietal-central EEG channels.[14] In the current study, the EEG signal in channel P_z was selected for analysis with C_z as a reference.

ANALYSIS

In the case of objective EEG measures, there are still no commonly accepted indicators, recommended criteria nor validated scores for the assessment of depressive symptoms. Therefore, the measures and gradation scores developed and successfully applied for differentiation between the groups of depressive and healthy subjects in previous studies have been selected for analysis in this study.[10,13,14]

The selected linear measure SASI has demonstrated good differentiation ability between depressive and healthy subjects.[10,14] The SASI indicates the balance of energy in the EEG spectrum at the frequencies higher and lower than the spectrum maximum and has been calculated according to the published algorithms[10] (see details in Supplemental Digital Content, http://links.lww.com/JOM/A564). The SASI value of 0.1 as the selection criteria between depressive and healthy subjects has been demonstrated to provide the classification accuracy of about 77%.[10,14] Therefore, the SASI score higher than 0.1 was selected to indicate depressive symptoms in this study.

The nonlinear measure HFD has been selected as a method providing good differentiation between depressive and healthy subjects and requiring less computational power compared with other nonlinear methods.[11,14] The HFD evaluates the fractal dimension of the EEG signal waveform and has been calculated according to the original algorithms.[15] The classification accuracy of 77% has been achieved using HFD for differentiation between depressive and healthy subjects, whereas the threshold value of HFD appeared equal to 1.3.[14] In the current study, HFD scores higher than 1.3 have been selected for indication of depressive symptoms.

In the case of clinical HAM-D test, the following gradation has been applied: mild depression score 7 to 14; moderate depression score 14 to 18; severe depression score 19 to 22; very severe depression score higher 22.[16] The depressive subscale score higher than 11 indicates depressive symptoms in the case of self-reported EST-Q-D test.[17]

STATISTICS

Correlation coefficients, coincidences, and combinations of decisions between the results achieved applying different methods were calculated in Microsoft Excel (Microsoft Corporation, Redmond, WA) software.

The possible dependences of depressive symptoms on gender, age, educational level, and marital status were evaluated. For this purpose, the Student t test with post-hoc Bonferroni correction for multiple comparisons ($n = 4$) was performed for the assessment of statistical significance between the participants with and without depressive symptoms.

RESULTS

Table 2 presents the number of participants with depression symptoms indicated by various objective (SASI and HFD) or subjective (HAM-D and EST-Q-D) measures and demographic factors of the participants with depressive symptoms.

The SASI reveals the highest and EST-Q-D the lowest number of participants with depression symptoms. The EEG measures indicate depressive symptoms for 55% to 65% of the participants in the group, whereas the psychological tests only for 29% to 45% of them.

The coincidences between SASI and HFD reach 81% (56 cases from 69 indications by HFD). The coincidences of indications by HAM-D and EST-Q-D reach 80.5% (29 cases from 36 indications by EST-Q-D). The coincidence of indications by HAM-D and EST-Q-D, based on similar questions, is not higher than in the case of HAM-D and SASI describing principally different behavior of the EEG signal.

TABLE 2. Numbers and Demographic Factors of Participants with Depression Symptoms Indicated by Various Measures

	Score	Number	Rate %	Female %	Aver. Age, years	Age <41%	P with Age	Higher Educ. %
SASI	>0.1	81	64.8	60.5	41.9	44.4	>0.1	81.5
HFD	>1.3	69	55.2	65.2	43,5	31.9	<0.01	84.0
HAM-D								
Mild	7–13	40	32					
Moderate	14–18	8	6.4					
Severe	19–22	8	6,4					
Very severe	>22	0	0					
Total	>7	56	44.8	66.1	41.2	44.6	>0.1	83.9
EST-Q-D	>11	36	28.8	69.4	43.1	33.3	>0.1	77.8

TABLE 3. Correlation Coefficients Between the Calculated EEG Measures and the Results of Psychological Tests

	SASI	HFD	HAM-D	EST-Q-D
SASI		0.48	0.04	−0.04
HFD	0.48		0.01	−0.16
HAM-D	0.04	0.01		0.66
EST-Q-D	−0.04	−0.16	0.66	

The rates of female participants with depressive symptoms, indicated by different measures, are lightly higher than the whole group, with the exception of SASI. The average age of participants with depressive symptoms is higher than the whole group: the minimal rise occurs in the case of HAM-D (0.2 years) and maximal in the case of HFD (2.5 years). The prevalence of participants younger than 41 years decreases with depression symptoms. The percentage of participants with higher education increases with depression symptoms in the case of three measures and decreases only in the case of the subjective EST-Q-D test. The difference between the participants with and without depressive symptoms appeared statistically significant only for age factor in the case of HFD. No other factors (gender, education, marital status) differed significantly for participants with and without depressive symptoms.

Table 3 presents correlation coefficients between the results achieved using different measures. The moderate correlation is evident between the measures of the same origin, the EEG-based SASI and HFD, as well as the psychological tests HAM-D and EST-Q-D. However, very low correlation has been detected between the measures of different origin, tests, and EEG measures. The trend of negative correlation has been indicated between self-rated EST-Q-D and objective measures SASI and HFD.

Table 4 presents the data about correlation between the scores of depression symptoms indicated by different measures and demographic factors. Moderate correlation with age was detected only in the case of EEG measures. Low correlation occurs in the case of all other measures.

Figure 1 presents the rate of participants with depressive symptoms indicated by various measures and their combinations. The graphs demonstrate that the objective EEG measures SASI and HFD reveal depressive symptoms in larger number of participants than the subjective tests HAM-D and EST-Q-D. The evaluation of depressive symptoms based on two different measures result in much higher numbers of participants with depressive symptoms. The combination of two objective measures indicated depression symptoms for 76.8% and subjective measures for 52% of participants. The combinations of objective and subjective measures indicated depressive symptoms up to 78.4% of participants. Taking into account all four measures, the depression symptoms appeared for 89.6% of participants.

TABLE 4. Correlation Coefficients Between the Depression Symptoms Indicated by EEG Measures or Psychological Tests and Demographic Factors

	SASI	HFD	HAM-D	EST-Q-D
Gender	−0.06	0.06	0.05	0.07
Age	0.30	0.36	0.04	0.05
Education	0.05	0.09	0.07	−0.06
Marriage	0.08	0.20	0.07	0.17
Smoking	−0.08	−0.06	−0.01	0.01

DISCUSSION

Rate of Depression Symptoms

The results of the study show that the rate of participants with depression symptoms, indicated by EEG measures, as well as psychological tests, presented in Table 2 and Fig. 1 are much higher than 7%, the expected rate in developed countries based on medical statistics.[1,2]

A possible reason is that the remarkable number of participants with mild depression are probably not taken into account in medical statistics. The HAM-D scores, based on subjective symptoms, show that the main part of participants (32%) have only symptoms of mild depression. However, even the indicated rate about 12.8% for moderate and severe depression symptoms is higher than the rate of depression disorder of 7% from population according to medical statistics.

The higher rate of participants with depressive symptoms in this study might be related to the procedure of the selection of participants: the volunteers interested in participation would have already some feelings of stress or even depression.

The nature of work should also be taken into account. The rate of clinical depression among industrial workers has been indicated ranging from 6.9% to 16.2% (population rate

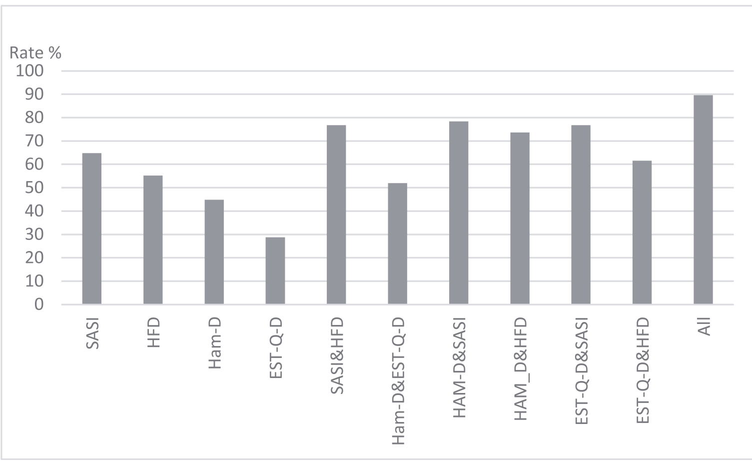

FIGURE 1. The rate of participants with depression symptoms indicated by a single measure and by the combinations of measures.

10.45%).[18] In the current study, the major part of participants have higher educational level and their employment positions are related to responsibility and leadership, probably causing higher level of stress and related depression symptoms.[19,20]

The part of population with depressive symptoms assessable only by objective EEG measures has been out of attention and not considered in medical statistics.

Objective and Subjective Measures

The rate of participants with depressive symptoms indicated by objective EEG measures SASI and HFD is 55% to 65% (combining both 76.8%), much higher than the rate of participants indicated by psychological tests HAM-D and EST-Q-D about 29% to 45% (combining both 52%) (Table 2, Fig. 1). The increased rate can be explained by the different nature of the measures. The alterations in brain physiology related to depression can occur before the subjective feelings appear. The achieved results support the ability of the EEG-based measures to indicate depression symptoms not yet accompanied by subjective self-feeling. The objective EEG measures, describing the behavior of brain physiology, enable early evaluation of depression symptoms undetectable by psychological tests.

The correlation between SASI and HFD, indicating different features of the EEG signal, is equal to 0.48 (Table 3). To the best of our knowledge, no data about correlation between various depression EEG measures have been reported earlier. The coincidence of indications by two objective EEG measure 81% is equal to this for HAM-D and EST-Q-D tests (80.5%). The high coincidence of indication of depression symptoms using objective EEG measures suggests good connectivity with underlying neurophysiological processes.

It seems surprising that only moderate correlation of 0.66 occurs between HAM-D and EST-Q-D ratings (Table 3), based on similar questions. This finding suggests that the results of self-rating differ from the ratings assessed by an observer. The similar discordances of the ratings assessed by patients and clinicians have been also mentioned in several other studies.[21–23] The correlation of 0.4 between HAM-D and self-reported test scores, even lower than in the current study, has been observed.[23] The lowest detection ability with self-rating EST-Q-D test could be related to psychological factors: the people do not reveal or accept being depressed themselves or intend to present better status for the employers.

The low correlation was observed between the depression symptoms evaluated by measures of different origin, psychological tests, and EEG (Table 3). Keeping in mind only moderate correlation between the indications of depression symptoms based on similar questions HAM-D and EST-Q-D, it is not surprising, because the early symptoms of depression, revealed by EEG measures, have not been identified by psychological tests. Unfortunately, it is impossible to compare our results with other studies, because to the best of our knowledge, there are still no publications on the topic.

It is remarkable that the relationship between objective EEG measures and self-rated psychological test EST-Q-D indicates trend of negative correlation. Possible psychological aspects of correlation between objective and subjective symptoms need further investigation.

Demographic Factors

The impact of demographic factors on the indication of depressive symptoms was not revealed in this study, except for some effect of age on the EEG measures.

The alteration of the EEG signal with age during life span is known in neurophysiology. In the current study, the swift of average age for the participants with depressive symptoms is maximal in the case of HFD measure, about 2.5 years. Moderate correlation with age and significant differences were detected in this case. Slightly lower swift 2.1 years appeared for EST-Q-D, but no correlation nor significant differences were detected. On the contrary, some correlation with age is evident for SASI despite minimal swift of average age with depressive symptoms. Keeping in mind these aspects, the revealed age correlation is rather related to the alterations of depression symptoms than to the alteration of EEG with age. Still, the stability of EEG with age requires further investigation to clarify the necessity of age correction for the EEG measures.

Limitations and Future Perspectives

The first promising results achieved in this study suggest that the EEG-based objective measures are applicable and would be prospective for early detection of depressive symptoms. The main limitation of the study is small group of participants. Further and much wider research is needed for confirming these preliminary results and implementing the methodology of early assessment of objective depression symptoms in occupational health examination.

The main problem in applying objective EEG measures for early detection of depressive symptoms is the absence of commonly approved rating scores for these measures. Despite the rating scores used in this study that have been assessed previously in independent groups, the base for rating is still limited. Only large-scale investigations can result in commonly approved rating scores. The dimensions of the problem of ratings based on EEG measures are definitely too large for being solved by a single research group or institution. Further large-scale investigations are required to implement EEG-based measures for early detection of depression symptoms in occupational health examination.

CONCLUSION

The results of this study confirm the feasibility of indication of early symptoms of depression applying EEG-based objective measures. The rates of participants with objective depression symptoms, indicated by EEG measures, are higher than expected according to the results of subjective psychological tests. Early detection of depression symptoms of employees in occupational health monitoring will benefit to the effectiveness of improving mental health in their professional activity and avoiding related accidents.

The high rate of participants with depressive symptoms needs special attention. Keeping in mind the importance of the problem, this study is dedicated to initiate discussion and further research on the development of methodology for assessment of objective symptoms of mental disorders in occupational health examination.

REFERENCES

1. Whiteford HA, Ferrari AJ, Degenhardt L, et al. The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010. *PLoS One*. 2015;10:e0116820.
2. World Health Organization. The Global Burden of Disease: 2004 Update. Geneva: WHO Press; 2008, 153 p. Available at: http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf. Accessed September 15, 2018.
3. Wittchen HU, Jacobi F, Rehm J, et al. ECNP/EBC Report 2011 The size and burden of mental disorders and other disorders of the brain in Europe. *Eur Neuropsychopharmacol*. 2010;21:655–679.
4. Goetzel RZ, Roemer EC, Holingue C, et al. Mental health in the workplace: a call to action proceedings from the mental health in the workplace - public health summit. *J Occup Environ Med*. 2018;60:322–330.
5. Stansfeld S, Candy B. Psychosocial work environment and mental health: a meta-analytic review. *Scand J Work Environ Health*. 2006;32:443–462.
6. Netterstrøm B, Conrad N, Bech P, et al. The relation between work-related psychosocial factors and the development of depression. *Epidemiol Rev*. 2008;30:118–132.
7. Madsen IE, Nyberg ST, Magnusson Hanson LL, et al. IPD-Work Consortium Job strain as a risk factor for clinical depression: systematic review and meta-analysis with additional individual participant data. *Psychol Med*. 2017;47:1342–1356.

8. Hsu Sandy H-J, Chen D-R, Cheng Y, Su T-C. Association of psychosocial work hazards with depression and suboptimal health in executive employees. J Occup Environ Med 2016; 58:728–736.
9. Knott V, Mahoney C, Kennedy S, Evans K. EEG power, frequency, asymmetry and coherence in male depression. *Psychiatry Res*. 2001;106:123–140.
10. Hinrikus H, Suhhova A, Bachmann M, et al. Electroencephalographic spectral asymmetry index for detection of depression. *Med Biol Eng Comput*. 2009;47:1291–1299.
11. Hosseinifard B, Moradi MH, Rostami R. Classifying depression patients and normal subjects using machine learning techniques and nonlinear features from EEG signal. *Comput Methods Programs Biomed*. 2013;109:339–345.
12. Fingelkurts AA, Fingelkurts AA. Altered structure of dynamic electroencephalogram oscillatory pattern in major depression. *Biol Psychiatry*. 2015;77:1050–1060.
13. Bachmann M, Lass J, Hinrikus H. Single channel EEG analysis for detection of depression. *Biomed Signal Process Control*. 2017;31:391–397.
14. Bachmann M, Päeske L, Kalev K, et al. Methods for classifying depression in single channel EEG using linear and nonlinear signal analysis. *Comput Methods Programs Biomed*. 2018;155:11–17.
15. Higuchi T. Approach to an irregular time series on the basis of the fractal theory. *Phys D Nonlinear Phenom*. 1988;31:277–283.
16. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56–62.
17. Aluoja A, Shlik J, Vasar V, et al. Development and psychometric properties of the Emotional State Questionnaire, a self-report questionnaire for depression and anxiety. *Nord J Psychiatry*. 1999;53:443–449.
18. Wulsin L, Alterman T, Timothy-Bushnell P, et al. Prevalence rates for depression by industry: a claims database analysis. *Soc Psychiatry Psychiatr Epidemiol*. 2014;49:1805–1821.
19. Põld T, Bachman M, Orgo L, et al. EEG Spectral Asymmetry Index Detects Differences Between Leaders and Non-leaders. In: Eskola H, Väisänen O, Viik J, Hyttinen J, editors. EMBEC & NBC 2017. EMBEC 2017, NBC 2017. IFMBE Proceedings 65. Singapore: Springer. p. 17–20.
20. Põld T, Bachmann M, Päeske L, et al. EEG spectral asymmetry is dependent on education level of men. In: Lhotska L, Sukupova L, Lacković I, Ibbott G, editors. World Congress on Medical Physics and Biomedical Engineering 2018. IFMBE Proceedings 68(2). Singapore: Springer. p. 405–408.
21. Cusin C, Yang H, Yeung A, Fava M. Rating scales for depression. In: Baer L, Blais MA, editors. *Handbook of Clinical Rating Scales and Assessment in Psychiatry and Mental Health*. New York: Humana Press Pages; 2010. p. 7–35.
22. Domken M, Scott J, Kelly P. What factors predict discrepancies between self and observer ratings of depression? *J Affective Dis*. 1994;31: 253–259.
23. Enns MW, Larsen DK, Cox BJ. Discrepancies between self and observer ratings of depression. The relationship to demographic, clinical and personality variables. *J Affective Dis*. 2000;60:33–41.

Appendix 1 (Continued)

Publication II
Põld, T.; Päeske, L.; Hinrikus, H.; Lass, J.; Bachmann, M. (2021). Long-term stability of resting state EEG-based linear and nonlinear measures. International Journal of Psychophysiology, 159, 83–87. DOI: 10.1016/j.ijpsycho.2020.11.013.

International Journal of Psychophysiology 159 (2021) 83–87

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Long-term stability of resting state EEG-based linear and nonlinear measures

Toomas Põld [a,b], Laura Päeske [a], Hiie Hinrikus [a], Jaanus Lass [a], Maie Bachmann [a,*]

[a] Tallinn University of Technology, School of Information Technologies, Department of Health Technologies, Centre for Biomedical Engineering, Tallinn, Estonia
[b] Qvalitas Medical Centre, Tallinn, Estonia

A R T I C L E I N F O

Keywords:
EEG
Linear measure
Spectral asymmetry
Nonlinear measure
Fractal dimension
Intraclass correlation

A B S T R A C T

This preliminary study is aimed to evaluate the stability of various linear and nonlinear EEG measures over three years on healthy adults. The linear measures, relative powers of EEG frequency bands, interhemispheric (IHAS) and spectral (SASI) asymmetries plus nonlinear Higuchi's fractal dimension (HFD) and detrended fluctuation analyses (DFA), have been calculated from the resting state eyes closed EEG of 17 participants during two sessions separated over three years. Our results indicate that the stability is highest for the nonlinear (HFD and DFA) and the linear (relative powers of EEG frequency bands) EEG measures that use the signal from a single EEG channel and frequency band, followed by the SASI employing signals from a single channel and two frequency bands and lowest for the IHAS employing signals from two channels. The result support the prospect of using EEG-based measures in clinical practice.

1. Introduction

Growing interest in applications of electroencephalographic (EEG) methods for diagnostic purposes in clinical practice has raised an important problem of long-term stability of the EEG measures. Linear and nonlinear EEG measures have been successfully applied to differentiate between the groups of healthy persons and those with mental disorders in preclinical studies (Knott et al., 2001; Allen et al., 2004; Ahmadlou et al., 2012; Hosseinifard et al., 2013; Bachmann et al., 2017; Bachmann et al., 2018; Čukić, 2019). Linear measures, based on EEG power analysis, as absolute and relative powers of different EEG frequency bands, frontal alpha asymmetry and spectral asymmetry, have been shown to provide good sensitivity (Knott et al., 2001; Coan and Allen, 2003; Hinrikus et al., 2009). More specific nonlinear measures describing temporal dynamics of EEG, as fractality, complexity and entropy, are expected to provide higher classification ability compared to linear measures at various machine learning techniques (Ahmadlou et al., 2012; Hosseinifard et al., 2013). On the other hand, comparable classification accuracy of linear and nonlinear methods has been reported (Bachmann et al., 2018).

EEG-based measures are still not validated for diagnostic purposes in clinical practice. Today, questionnaires, based on heterogeneous subjective symptoms declared by a person, are commonly accepted assessment tools in the evaluation of mental disorders in clinical practice (Hamilton, 1960; Cusin et al., 2010).

Applications of EEG measures in clinical practice presume long-term stability of the measures and reliability of the scores. Stability of a linear measure, frontal alpha asymmetry has been reported (Allen et al., 2004). High temporal stability of EEG spectral band powers for healthy participants has been reported decades ago (Gasser et al., 1985; Salinsky et al., 1991; Kondacs and Szabó, 1999). High stability of various linear EEG measures and reliability of the scores for healthy participants has been demonstrated in recent studies (Gevins et al., 2011; Gevins et al., 2012; Cannon et al., 2012; Ip et al., 2018; Tenke et al., 2018). Only limited results about stability of nonlinear EEG features are available (Dünki et al., 2000; Gudmundsson et al., 2007).

Due to a good stability of EEG measures, it can be presumed that declinations of the scores are related to brain disorders. Our previous preliminary study has been aimed to assess early symptoms of depression in regular occupational health examination using resting state EEG based indicators, spectral asymmetry index and Higuchi's fractal dimension, parallel to depression questionnaires (Põld et al 2019). The results of the study, performed on 125 healthy volunteers, are unexpected: the rate of individuals with depression symptoms discovered by

* Corresponding author at: Tallinn University of Technology, School of Information Technologies, Department of Health Technologies, Centre for Biomedical Engineering, 5 Ehitajate Rd, Tallinn 19086, Estonia.
E-mail address: maie.bachmann@taltech.ee (M. Bachmann).

https://doi.org/10.1016/j.ijpsycho.2020.11.013
Received 14 May 2020; Received in revised form 21 November 2020; Accepted 23 November 2020
Available online 1 December 2020
0167-8760/

the EEG-based measures (55–65%) is much higher compared to the rate discovered by the questionnaires (36–56%) (Põld et al., 2019). Therefore, the question rises concerning the reliability of scores and stability of the applied EEG measures.

This preliminary study is aimed to evaluate the long-term stability of the EEG-based measures specific for depression symptoms on healthy individuals by employing various linear and nonlinear EEG measures. Two sessions of evaluation, combined with regular occupational health examinations separated for three years, have been performed. To support the validity of the study consisting only two sessions, several EEG measures of previously confirmed high stability have additionally been included in the study.

Three groups of resting EEG measures have been selected for the investigation. Firstly, EEG delta, theta, alpha, beta and gamma band relative powers have been selected as the measures of confirmed stability (Gasser et al., 1985; Salinsky et al., 1991; Kondacs and Szabó, 1999). Secondly, interhemispheric and spectral asymmetries, based on the combination of EEG powers, have been included as the measures previously successfully used for differentiation between the groups of depressive and healthy subjects (Allen et al., 2004; Hinrikus et al., 2009; Põld et al., 2019). From these two, the frontal alpha asymmetry has been reported having high stability (Allen et al., 2004). Thirdly, two nonlinear measures, Higuchi fractal dimension (HFD) and detrended fluctuation analyses (DFA) have been selected as the measures successfully used by several authors for classification depression (Ahmadlou et al., 2012; Hosseinifard et al., 2013; Bachmann et al., 2018).

2. Methods

2.1. Participants

The participants for this study were invited among the persons from different institutions passing regular occupational health examination at the medical center. The people were asked to declare their habits and health condition and fulfill the questionnaire. The selected participants were healthy according to the self-reported questionnaires as well as to the medical and biochemical examinations performed in the medical center. They were free of current depression episode and previous history of depression, other mental disorders and brain injuries.

Finally, the selected group of 17 participants passed two sessions three years apart. The group consisted of twelve female and five male individuals of average age 42.3 ± 5.4 during the first and 45.2 ± 5.4 during the second session. All selected participants were right-handed and non-smoking. Selected participants had higher education and were employed as specialists, managers, editors, etc.

The study was conducted in accordance with the Declaration of Helsinki as revised in 2013 and formally approved by the Tallinn Medical Research Ethics Committee. All participants were informed about the aim and procedures of the study and they signed the written informed consent.

2.2. Procedures, methods and equipment

The study comprised of two sessions 3 ± 0.3 years apart. Each session included identical procedures: resting eyes closed EEG recording.

The EEG recordings were performed in a quiet dimly lit room. The participants were asked to abstain from alcohol for 24 h and from coffee for 2 h before the EEG recordings. During the recording, the participant was lying in a relaxed position with blocked ears.

The 18-channel resting state eyes closed EEG was recorded for 7 min using the Cadwell Easy II EEG (Kennewick, WA, USA) device. The electrodes were located according to the international 10-20-electrode position classification system. The signal from channels O1, O2, Pz, P4, P8, C4, T8, P7, P3, C3, Fz, F4, F8, T7, F3, FP2, F7, FP1 were recorded. Cz reference was used following our previous study (Põld et al., 2019). The raw EEG signals of 0.3–70 Hz frequency were stored at the sampling frequency of 400 Hz.

2.3. EEG analyses

The EEG was segmented into 20.48-second segments and an experienced EEG specialist visually evaluated the quality of the recorded EEG segments and selected the first 15 artefact-free segments for further analysis – 5 min and 7 s in total. The linear and nonlinear measures were calculated for 20.48-second segments, after which the median of all the segments was calculated. The following explains how different measures were calculated for those segments.

To calculate EEG delta, theta, alpha, beta and gamma band relative powers, the power spectral density of the EEG signal was estimated by Welch's method. The signal segments were once more divided into overlapping epochs (50%), with the length of 1024 data points. Epochs were extracted through a Hanning window and Fast Fourier Transform (FFT) was applied (Bachmann et al., 2018). EEG powers in delta (2–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (30–47 Hz) frequency bands were computed by integrating the power spectral density at the frequencies within the boundary frequencies of the EEG spectral bands. For relative band power the outcome was divided by the total power.

The interhemispheric asymmetry (IHAS) describes the balance between EEG powers in the symmetric channels of different hemispheres. The IHAS was calculated according to formula $(L\text{-}R)/(L + R)$ were L and R are EEG powers in the symmetric channels of left and right hemisphere consequently. IHAS was calculated for O1-O2, P3-P4, P7-P8, C3-C4, T7-T8, F3-F4, F7-F8, Fp1-Fp2 pairs of channels.

The spectral asymmetry index (SASI) describes the balance between EEG powers at the EEG spectrum frequency bands higher and lower than the spectrum maximum in alpha frequency band in a single EEG channel. SASI was calculated according to formula $(T\text{-}B)/(T + B)$, where T and B are EEG theta and beta band powers consequently. The calculation algorithm was adjusted to an individual alpha maximum frequency (Hinrikus et al., 2009; Bachmann et al., 2017).

Higuchi fractal dimension (HFD) describes self-similarity of EEG as the fractal dimension of time series directly in the time domain. HFD was calculated according to published algorithm at the parameter $kmax = 50$ (Higuchi, 1988).

Detrended fluctuation analyses (DFA) describes temporal dynamics and variability of EEG. DFA was calculated according to the published algorithms (Peng et al., 1995; Hu et al., 2001; Bachmann et al., 2018).

The EEG measures were calculated in 18 EEG channels for each participant using MATLAB (The MathWorks, Inc. Massachusetts, USA).

2.4. Statistics

The mean values M, standard deviations SD and the coefficients of variations $CV = SD/M$ were calculated for the measures in the first and the second session. The two-tailed paired Student's *t*-test was performed to evaluate, whether the values of measures calculated in the first and the second recording sessions were statistically different. According to the post-hoc Bonferroni correction for multiple comparisons (in total 11 measures) the confidence level of 0.005 was considered statistically significant.

Test-retest reliability was assessed with intraclass correlation values (ICC) for EEG scores at both timepoints (two recording sessions). MATLAB (The MathWorks, Inc. Massachusetts, USA) was used for calculations ICC(A,1) by a two-way mixed random model (McGraw and Wong, 1996).

3. Results

The quantitative parameters for the scores in two sessions and the differences between these are presented in Table 1.

All EEG measures employing signal from a single channel (the EEG

Table 1
Mean values (M), standard deviation (SD), coefficient of variation (CV) for all score in first and second sessions, absolute (Dif) and relative (RDif %) difference and uncorrected *p*-values between two sessions for the scores.

	Delta	Theta	Alpha	Beta	Gamma	IHAS	SASI	HFD	DFA
M 1	0.152	0.171	0.362	0.259	0.039	−0.024	0.202	1.697	0.580
M 2	0.154	0.168	0.359	0.262	0.040	0.032	0.226	1.700	0.577
SD 1	0.062	0.062	0.153	0.091	0.027	0.147	0.291	0.049	0.156
SD 2	0.068	0.051	0.180	0.100	0.022	0.148	0.272	0.053	0.171
CV 1	0.408	0.365	0.423	0.357	0.687	6.199	1.442	0.029	0.269
CV 2	0.441	0.303	0.502	0.38	0.556	4.671	1.219	0.031	0.296
Dif	0.002	−0.003	−0.003	0.003	0.001	0.056	0.024	0.003	−0.003
SD-d	0.027	0.025	0.086	0.058	0.019	0.083	0.134	0.018	0.045
RDif %	1.01	1.86	−0.72	1.15	2.28	236.2	11.89	0.18	−0.49
p	0.76	0.42	0.87	0.76	0.73	0.02	0.39	0.58	0.38

spectral band relative powers, SASI, HFD and DFA) indicate high stability within 12% between the two sessions. The interhemispheric asymmetry index (IHAS), employing data from two channels from different hemispheres, is much more unstable compared to single-channel measures. For all measures the differences between the sessions appear statistically insignificant ($p > 0.005$).

There is no uniform trend of average changes for single-channel EEG measures: Theta, Alpha and DFA indicated some decrease, the other five measures an increase in the second session. Due to small alterations, the directions of changes are rather random. IHAS demonstrated the remarkable trend of increase in the second session.

The intraclass correlation values (ICC) in 18 EEG channels for the single-channel EEG measures are presented in Table 2. The values for all measures in all EEG channels are positive. The ICC values indicate some decrease moving from occipital to frontal area for all measures, except relative alpha power. The higher ICC values occur in parietal channels for all single-channel measures.

Table 3 presents calculated ICC values for interhemispheric asymmetry in eight pairs of EEG channels in different EEG frequency bands. The ICC values vary strongly between brain areas and EEG frequency bands. The higher ICC values are observed for EEG interhemispheric alpha and gamma asymmetry in temporal T7-T8 and frontal F7-F8 channel pairs.

Data from Table 2 show that the ICC values are high and statistically significant for all single-channel measures Delta, Theta, Alpha, Beta, Gamma, SASI, HFD and DFA in many EEG channels. The ICC values are much lower and partly statistically insignificant in the case of interhemispheric asymmetry in Table 3.

Table 3
The calculated intra-class correlation coefficients for the EEG interhemisperic asymmetry in different frequency bands. Statistically significant correlation marked in bold.

	Delta	Theta	Alpha	Beta	Gamma
O1-O2	**0.66**	**0.90**	**0.53**	**0.50**	**0.53**
P3-P4	−0.12	0.04	**0.40**	**0.40**	**0.40**
P7-P8	0.23	0.14	**0.48**	0.30	**0.48**
C3-C4	0.06	0.06	**0.36**	0.28	**0.36**
T7-T8	0.28	**0.46**	**0.59**	0.24	**0.59**
F3-F4	0.25	**0.47**	0.38	**0.43**	0.38
F7-F8	0.26	**0.54**	**0.60**	0.40	**0.60**
FP1-FP2	0.26	0.35	0.10	0.25	0.10

4. Discussion

The results demonstrate good stability within 12% and high ICC values for all EEG single-channel measures: relative powers of frequency bands, SASI, nonlinear HFD and DFA measures between two sessions over three-year interval (Tables 1, 2). The reliability (assessed via ICC) of interhemispheric asymmetry IHAS containing data from two channels from different hemispheres is much lower (Tables 1, 3). The alterations between the two sessions for HFD, DFA and SASI (Table 1) are smaller than the differences between the groups of healthy and depressive subjects, calculated following the identical method in our previous study (Bachmann et al., 2018).

The stability of EEG bands power has been proved earlier in several studies and strong correlation (typically higher than 0.8) reported in time intervals between sessions from hours to twelve years (Gasser et al.,

Table 2
The calculated intraclass correlation values (ICC) between two sessions for the EEG measures in a single EEG channel and for questionnaires, for all coefficients $p < 0.05$ and the values over average for a measure are marked in bold.

	Delta	Theta	Alpha	Beta	Gamma	SASI	HFD	DFA
O2	**0.93**	0.76	0.87	**0.87**	**0.82**	0.78	**0.92**	**0.91**
O1	**0.90**	0.80	0.82	**0.83**	**0.87**	0.82	**0.86**	**0.93**
PZ	**0.84**	0.81	**0.90**	**0.87**	**0.82**	0.77	0.81	**0.85**
P4	**0.86**	0.78	0.86	**0.86**	**0.93**	**0.86**	**0.89**	**0.92**
P8	**0.90**	**0.90**	0.87	**0.88**	**0.89**	**0.92**	**0.95**	**0.87**
C4	**0.88**	**0.83**	0.76	**0.88**	0.50	**0.88**	**0.84**	0.84
T8	**0.92**	**0.89**	**0.89**	**0.91**	0.67	**0.86**	0.81	**0.92**
P7	**0.91**	**0.90**	0.86	**0.89**	**0.91**	**0.88**	**0.92**	**0.93**
P3	**0.89**	**0.86**	0.87	**0.90**	**0.92**	**0.85**	**0.90**	0.78
C3	0.71	**0.86**	0.80	**0.94**	**0.92**	**0.87**	0.79	0.77
FZ	0.78	**0.85**	**0.93**	0.81	**0.98**	**0.89**	**0.86**	0.78
F4	0.76	0.80	**0.91**	**0.88**	0.68	**0.88**	**0.84**	0.77
F8	0.78	0.80	**0.91**	0.81	0.72	**0.85**	**0.82**	0.82
T7	**0.85**	**0.86**	**0.90**	0.83	0.42	0.76	0.65	**0.90**
F3	0.64	**0.86**	**0.94**	0.81	**0.94**	**0.87**	**0.87**	0.80
FP2	0.71	0.70	0.86	0.65	**0.89**	0.81	0.61	0.69
F7	0.80	0.82	**0.89**	0.77	0.69	0.78	0.71	**0.84**
FP1	0.75	0.76	0.87	0.61	**0.87**	0.80	0.58	0.74
Mean	0.82	0.82	0.87	0.83	0.80	0.84	0.81	0.84

1985; Salinsky et al., 1991; Kondacs and Szabó, 1999; Corsi-Cabrera et al., 2007; Rogers et al., 2016; Tenke et al., 2018). The results of the current study about EEG delta, theta, alpha, beta and gamma powers stability are in good agreement with the previously reported data and support the reliability of achieved results.

The stability of resting frontal asymmetry during two weeks, four months and twelve years have been reported (Allen et al., 2004; Stewart et al., 2010). In the current study, the highest interhemispheric asymmetry ICC value 0.6 was observed in alpha and gamma band frontal channels F7-F8 (Table 3). The stability of frontal alpha asymmetry is decreasing in time with months (Allen et al., 2004). The ICC value 0.6 related to three-year period in the current study, is in accordance with the stronger correlation over four months 0.86 (Allen et al., 2004). IHAS is the only EEG measure demonstrating remarkable trend of changes between two sessions (Table 1) and lower ICC values (Table 3). Unlike other EEG measures in the current study that are calculated in a single channel, IHAS, incorporating signals from two channels and hemispheres, depends not only on temporal but also on spatial stability of EEG power distribution. The higher instability of IHAS might be related to topographic instability of EEG powers (Burgess and Gruzelier, 1993). The reliability of coherence between different brain areas has been reported lower compared to EEG frequency band powers and nonlinear measures also by other researchers (Gudmundsson et al., 2007).

The changes in SASI level between two sessions (12%) were higher than for EEG bands relative powers (max 2.38%), but ICC values higher 0.8 were observed for SASI in the majority of channels. This result is in agreement with the preliminary study reporting the good stability of SASI over 15 months (Uudeberg et al., 2020).

Nonlinear measures, HFD and DFA, demonstrate the stability comparable to that of EEG frequency bands' powers. To the best of our knowledge, no earlier investigations for the temporal stability of HFD and DFA have been performed. The investigation of entropy measures in 10 sessions over two months has demonstrated the lower reliability compared to EEG power measures (Gudmundsson et al., 2007). The correlation coefficient (14 days and 5 years later) of a specific nonlinear measure, the so-called Grassberger-Procaccia correlation dimension, has been reported being much less ($r = 0.55$) compared to linear measure ($r = 0.84$) (Dünki et al., 2000).

In the current study, the stability is comparable for nonlinear measures (HFD and DFA), and EEG bands relative powers, somewhat lower for SASI and much lower for IHAS. Such result differs from the conclusions of an earlier study, where the reliability of EEG features has been reported the highest for EEG bands power parameter, followed by entropy and complexity measures (Gudmundsson et al., 2007). The measure, involving information from different channels (coherence between channels), has been reported as the least stable (Gudmundsson et al., 2007). This has been followed by IHAS in the current study. On the other hand, the higher relative variations and instability of IHAS and SASI are related to the low value of mean, close to zero, in the case of IHAS.

The best reliability of the EEG scores (except IHAS) calculated using reference Cz occurs in parietal channels (Table 2).

The main limitations for this preliminary study are the small number of sessions and relatively small number of participants. It has been complicated to recruit volunteers among persons passing regular occupational health examination, especially involving the same persons after the three-year period determined by the interval between the regular health examination. Further investigations involving larger numbers of participants and sessions are required to confirm the interesting results of this preliminary study. It is crucial to differentiate between the natural variability of EEG measures in healthy state and the declinations related to the mental disorder at an individual level.

5. Conclusions

The high stability of single-channel EEG measures and the reliability of the scores over three years support the prospective to use EEG-based objective measures for diagnostic purposes. Our results indicate that the stability is the highest for the nonlinear (HFD and DFA) and linear (relative powers of EEG frequency bands) measures that use the signal from a single EEG channel and frequency band, followed by the SASI employing signals from a single channel and two frequency bands and lowest for the IHAS employing signals from two channels.

Declaration of conflicting interests.

The Authors declare that there is no conflict of interest.

Acknowledgement

This study was financially supported by the Estonian Centre of Excellence in IT (EXCITE) funded by the European Regional Development Fund.

References

Ahmadlou, M., Adeli, H., Adeli, A., 2012. Fractality analysis of frontal brain in major depressive disorder. Int. J. Psychophysiol. 85, 206–211.
Allen, J.J.B., Urry, H.L., Hitt, S.K., Coan, J.A., 2004. The stability of resting frontal electroencephalographic asymmetry in depression. Psychophysiology 41, 269–280.
Bachmann, M., Lass, J., Hinrikus, H., 2017. Single channel EEG analysis for detection of depression. Biomedical Signal Processing and Control 31, 391–397.
Bachmann, M., Päeske, L., Kalev, K., Aarma, K., Lehtmets, A., Ööpik, P., Lass, J., Hinrikus, H., 2018. Methods for classifying depression in single channel EEG using linear and nonlinear signal analysis. Comput. Methods Prog. Biomed. 155, 11–17.
Burgess, A., Gruzelier, J., 1993. Individual reliability of amplitude distribution in topographical mapping of EEG. Electroencephalogr. Clin. Neurophysiol. 86, 219–223.
Cannon, R.L., Baldwin, D.R., Shaw, T.L., Diloreto, D.J., Phillips, S.M., Scruggs, A.M., Riehl, T.C., 2012. Reliability of quantitative EEG (qEEG) measures and LORETA current source density at 30 days. Neurosci. Lett. 518, 27–31.
Coan, J. A., Allen, J. J. B., 2003. The state and trait nature of frontal EEG asymmetry in emotion. In K. Hugdahl and R. J. Davidson (Eds.), The Asymmetrical Brain, 2nd ed., Cambridge, MA, MIT Press, pp. 565–615.
Corsi-Cabrera, M., Galindo-Vilchis, L., Del-Rio-Portilla, Y., Arce, C., Ramos-Loyo, J., 2007. Within-subject reliability and inter-session stability of EEG power and coherent activity in women evaluated monthly over nine months. Clin. Neurophysiol. 118, 9–21.
Čukić, M., 2019. Novel Approaches in Treating Major Depressive Disorder (Depression). Nova Science Publishers, Inc, NY. ISBN: 978-1-53614-382-9.
Cusin, C., Yang, H., Yeung, A., Fava, M., 2010. Rating scales for depression. In Handbook of Clinical Rating Scales and Assessment in Psychiatry and Mental Health. Ed. Lee Baer Mark A. Blais. New York: Humana Press, pp. 7–35.
Dünki, R.M., Schmid, G.B., Stassen, H.H., 2000. Intraindividual specificity and stability of human EEG: comparing a linear vs a nonlinear approach. Methods Inf. Med. 39, 78–82.
Gasser, T., Bächer, P., Steinberg, H., 1985. Test-retest reliability of spectral parameters of the EEG. Electroencephalogr. Clin. Neurophysiol. 60, 312–319.
Gevins, A., Smith, M.E., McEvoy, L.K., Ilan, A.B., Chan, C.S., Jiang, A., Sam-Vargas, L., Abraham, G., 2011. A cognitive and neurophysiological test of change from an individual's baseline. Clin. Neurophysiol. 122, 114–120.
Gevins, A., McEvoy, L.K., Smith, M.E., Chan, C.S., Sam-Vargas, L., Baum, C., Ilan, A.B., 2012. Long-term and within-day variability of working memory performance and EEG in individuals. Clin. Neurophysiol. 123, 1291–1299.
Gudmundsson, S., Runarsson, T.P., Sigurdsson, S., Eiriksdottir, G., Johnsen, K., 2007. Reliability of quantitative EEG features. Neurophysiol. 118, 2162-1271.
Hamilton, M., 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62.
Higuchi, T., 1988. Approach to an irregular time series on the basis of the fractal theory. Physica D 31, 277–283.
Hinrikus, H., Suhhova, A., Bachmann, M., Aadamsoo, K., Võhma, U., Lass, J., Tuulik, V., 2009. Electroencephalographic spectral asymmetry index for detection of depression. Med. Biol. Eng. Comput. 47, 1291–1299.
Hosseinifard, B., Moradi, M.H., Rostami, R., 2013. Classifying depression patients and normal subjects using machine learning techniques and nonlinear features from EEG signal. Comput. Methods Prog. Biomed. 109, 339–345.
Hu, K., Ivanov, P.C., Chen, Z., Carpena, P., Stanley, H.E., 2001. Effect of trends on detrended fluctuation analysis. Phys. Rev. E Stat. Nonlinear Soft Matter Phys. 64, 011114.
Ip, C.T., Ganz, M., Ozenne, B., Sluth, L.B., Gram, M., Viardot, G., l'Hostis, P., Danjou, P., Knudsen, G.M., Christensen, S.R., 2018. Pre-intervention test-retest reliability of EEG and ERP over four recording intervals. Int. J. Psychophysiol. 134, 30–43.
Knott, V., Mahoney, C., Kennedy, S., Evans, K., 2001. EEG power, frequency, asymmetry and coherence in male depression. Psychiatry Res. 106, 123–140.
Kondacs, A., Szabó, M., 1999. Long term intra-individual variability of the background EEG in normals. Clin. Neurophysiol. 110, 1708–1716.
McGraw, K.O., Wong, S.P., 1996. Forming inferences about some intraclass correlation coefficients. Psychol. Methods 1 (1), 30–46.

Peng, C.K., Havlin, S., Stanley, H.E., Goldberger, A.L., 1995. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time seires. Chaos 5, 82–87.

Põld, T., Päeske, L., Bachmann, M., Lass, J., Hinrikus, H., 2019. Assessment of Objective Symptoms of Depression in Occupational Health Examination. J. Occup. Environ. Med. 61 (7), 605–609. https://doi.org/10.1097/JOM.0000000000001622.

Rogers, J.M., Johnstone, S.J., Aminov, A., Donnelly, J., Wilson, P.H., 2016. Test-retest reliability of a single-channel, wireless EEG system. Int. J. Psychophysiol. 106, 87–96.

Salinsky, M.C., Oken, B.S., Morehead, L., 1991. Test–retest reliability in EEG frequency analysis. Electroencephalogr. Clin. Neurophysiol. 79, 382–392.

Stewart, J.L., Bismark, A.W., Towers, D.N., Coan, J.A., Allen, J.J.B., 2010. Resting frontal EEG asymmetry as an endophenotype for depression risk: sex-specific patterns of frontal brain asymmetry. J. Abnorm. Psychol. 119, 502–512.

Tenke, C.E., Kayser, J., Alvarenga, J.E., Abraham, K.S., Warner, V., Talati, A., Weissman, M.M., Bruder, G.E., 2018. Temporal stability of posterior EEG alpha over twelve years. Clin. Neurophysiol. 129, 1410–1417.

Uudeberg, T., Päeske, L., Põld, T., Lass, J., Hinrikus, H., Bachmann, M., 2020. Long-term stability of EEG spectral asymmetry index – preliminary study. IFMBE Proc. 76, 276–281.

Appendix 1 (Continued)

Publication III

Põld T.; Bachman M.; Orgo L.; Kalev K.; Lass J.; Hinrikus H. (2018). EEG Spectral Asymmetry Index Detects Differences Between Leaders and Non-leaders. EMBEC 2017, NBC 2017. IFMBE Proceedings, 65: Joint Conference of the European Medical and Biological Engineering Conference (EMBEC) and the Nordic-Baltic Conference on Biomedical Engineering and Medical Physics (NBC), Tampere, 11-15 June 2017. Ed. Eskola H., Väisänen O., Viik J., Hyttinen J. Singapore: Springer, 17−20. DOI: 10.1007/978-981-10-5122-7_5.

EEG Spectral Asymmetry Index Detects Differences Between Leaders and Non-leaders

T. Põld[1, 2], M. Bachman[1], L.Orgo[1], K. Kalev [1, 3], J. Lass[1] and H. Hinrikus[1]

[1] Centre for Biomedical Engineering, Department of Health Technologies, Tallinn University of Technology, Tallinn, Estonia
[2] Qvalitas Medical Centre, Tallinn, Estonia
[3] Centre for Biorobotics, Department of Computer Systems, Tallinn University of Technology, Tallinn, Estonia

Abstract— **The aim of the study was to find an objective indicator for evaluation of occupational stress. For this purpose, the electroencephalographic (EEG) spectral asymmetry index (SASI) was applied to estimate the differences between leaders and non-leaders. The experiments were performed on a group of 82 healthy volunteers who were divided into two subgroups of leaders and non-leaders taking into account whether their position comprised the leadership role or not. The resting eyes closed EEG signal was recorded and the signal in channel Pz was selected for calculation of SASI. The results indicated higher SASI values for the subgroup of leaders when compared to non-leaders and the difference between the subgroups was statistically significant. Higher SASI values could indicate increased psychological stress in leaders group and SASI could be a promising method in occupational health analysis.**

Keywords— **EEG, Spectral Asymmetry index, stress, leaders, non-leaders.**

I. Introduction

Today, mental disorders, as stress and depression, are a leading cause of burden of disease in high- and middle-income countries and projected to take the first place in the world in 2030 [1]. The problems of stress and mental disorders have become important in labour force nowadays and, consequently, needs more attention in occupational health. Exposure to stressful working conditions can have direct influence on work safety and health [2]. However, the diagnosis of stress, depression and other mental disorders are based on the evaluation of the intensity of subjective symptoms by psychiatrists using questionnaires. No objective criteria exist in clinical practice. It is highly important to have an inexpensive objective measure for screening workers and early detection of stress.

The brain behaviours and its mental state are related to its bioelectric activity determined by neuronal oscillations. The unperturbed brain is a complex system of numerous self-governed oscillations. The properties of neuronal oscillators are the result of the physical architecture of neuronal networks and the limited speed of neuronal communication due to axon conduction and synaptic delays [3]. The oscillations are a prominent feature of neuronal processes and the synchronization of the oscillations is a likely mechanism for cerebral integration for neural communication [4, 5]. Therefore, the spectrum of the resting electroencephalographic (EEG) signal is determined by the state of the brain. Consequently, EEG methods can be highly promising in early detection of mental disorders including occupational stress.

EEG is potentially an effective tool for assessing matters of mental and psychological concerns in occupational health. Diagnostics criteria can be developed based on EEG methods for General Practitioner to start an early treatment and, if necessary, to isolate workers whose occupation entails high responsibility as leaders, pilots, police and security workers etc. However, to the best of our knowledge, currently there are no EEG based methods approved in the occupational health practice.

In our previous studies we proposed a new EEG method, spectral asymmetry index (SASI), to evaluate depression [6, 7]. SASI can be easily calculated from a resting EEG single channel signal. The principle of SASI bases on the presumption of balance between the powers of EEG frequency bands in unperturbed brain. Disturbances in the brain state alter the balance between the powers of special EEG frequency bands selected higher and lower than the spectrum maximum (alpha band) and result in the alterations of symmetry of the EEG spectrum described by SASI. Therefore, SASI, as an inexpensive objective measure, can be promising also for detection of mental disorders other than depression.

We have shown, that in addition to detecting declination in the balance of spectral powers caused by depression [6], SASI detects also declination caused by external physical stressor, microwave radiation, or chemical stressor, coffee [8, 9]. The results of our previous study indicate that SASI provides a good discrimination between the effects of negative, neutral and positive emotions on human EEG related to possible psychological stress [10]. Reliability of linear SASI method has been compared to nonlinear Higuchi's fractal dimension method and SASI demonstrated good sensitivity for detection of characteristic features of depression in a single-channel EEG [11]. Therefore, SASI is expected to be a promising indicator also for detection of occupational stress and might be used as a method for assessment of mental health during routine screening of workers. Accord-

H. Eskola et al. (eds.), *EMBEC & NBC 2017*,
IFMBE Proceedings 65,
DOI: 10.1007/978-981-10-5122-7_5

ingly, the applicability of SASI for detecting the effect of various occupational stressors should be investigated.

In this study the sensitivity of SASI for detecting the effect of an occupational stressor related to leadership is analyzed.

II. Methods and equipment

A. Subjects

The experiments were carried out in Qvalitas Medical Center on a group of healthy volunteers. The group initially consisted of 86 subjects. However, 4 subjects were removed, because of the lack of artefact-free EEG segments. The analyzed group consisted of 82 persons, aged between 25 and 59 years (27 male and 55 female). The mean age was 40.2 (std 7.6). The volunteers were asked to answer questions about their occupational position and duties. According to the results of the questions, the group was divided into two subgroups of subjects, who declared themselves as leaders (45 subjects, average age 40.7) or non-leaders (37 subjects average age 39.6).

All subjects reported being non-smoking and right handed. At least 1.5 hours before the experiment they did not had any caffeinated drinks and up to 8 hours before no alcoholic beverages.

The experiments were conducted with the mutual understanding and written consent of each subject.

B. Experiment procedure and EEG recording equipment.

The experimental study was performed according to the recording protocol identical for all subjects: eyes closed resting EEG recorded for 7 minutes. During the EEG recording subject was lying in a relaxed position with eyes closed and ears blocked. The room was dimly but no other special conditions were provided.

The Cadwell Easy II EEG (Kennewick, WA, USA) measurement equipment was used for the EEG recordings. The 18-channel EEG was recorded according to the international 10-20-electrode position classification system (common reference Cz). Raw signals in frequency band 0.3-70 Hz were stored at sampling frequency 400 Hz. The notch filter was applied at 50 Hz.

C. EEG analysis

For further analysis, the channel Pz was chosen as proven effective while differentiating depressive subjects from controls [12]. The visually checked artefacts-free EEG segments of 10 seconds duration were selected from the EEG signal. First 30 of the segments (5 minutes) were used in further analysis. SASI was calculated for each of those segments and the results were averaged over 30 segments.

The algorithm for calculation of SASI is based on relative differences between the powers of two EEG frequency bands selected higher and lower than the alpha band located in spectrum maximum.

Calculation of SASI comprises of four main steps:

1. *Computing of power spectral density of the recorded EEG signal in channel Pz.* The power spectral density s_n for a subject n was calculated by means of Welch's averaged periodogram method. The signal was divided into overlapping epochs (50%), with the length of 1024 samples and extracted through a Hanning window.

2. *Selection of boundary frequencies of the lower and higher specific EEG frequency bands.* At first, the frequency with the maximum spectral power in the region of alpha band 8-13 Hz was estimated. Thereafter, the parabolic approximation was applied to the spectrum of the EEG central frequency band within the width of the band $2B$. The maximum point of the fitted parabola fc was taken as a centre of the central band.

The frequency limits for the lower and the higher specific frequency bands were related to the estimated central band and determined as follows:

- the lower frequency band from $F1 = (fc - B - 4)$ Hz to $F2 = (fc - B)$ Hz;
- the higher frequency band from $F3 = (fc + B)$ Hz to $F4 = (fc + B + 24)$ Hz.

The width of the excluded from calculation central band $2B = 4$ Hz was determined as the width of traditional alpha band.

3. *Calculation of the EEG signal power in the selected bands*. The EEG signal powers W_{ln} and W_{hn} in the lower and in the higher EEG frequency bands respectively were calculated for each subject n as

$$W_{\ln} = \sum_{f=F1}^{F2} s_n \; ; \qquad W_{hn} = \sum_{f=F3}^{F4} s_n \; . \tag{1}$$

4. *Calculation of the spectral asymmetry index as a combination of the EEG powers in the selected bands*. The spectral asymmetry index for a subject n was calculated as

$$SASI_n = \frac{W_{hn} - W_{\ln}}{W_{hn} + W_{\ln}} \tag{2}$$

The EEG analysis was performed using MatLab software.

D. Statistics

The Student t-test was performed to evaluate differences between subgroups of leaders and non-leaders. The confidence level 0.05 was selected for evaluation.

III. RESULTS AND DISCUSSION

Figure 1 presents the calculated values of SASI averaged over all subjects within the subgroups of leaders and non-leaders. The average SASI is higher for leaders.

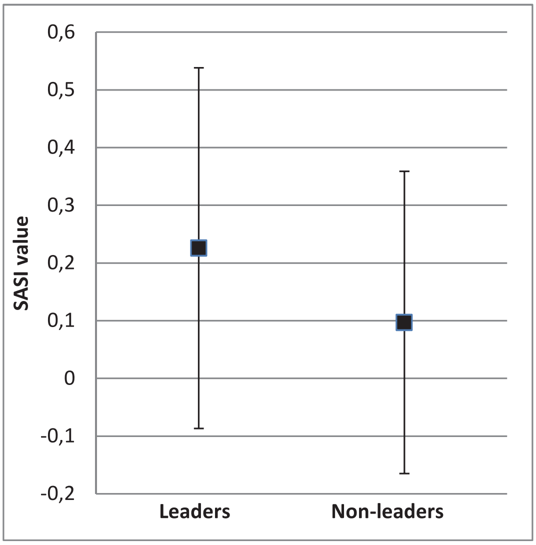

Fig. 1 Calculated SASI values averaged over the subgroup of leaders (n=45) and non-leaders (n=37); vertical bars denote standard deviation.

Despite of relatively high standard deviation, the difference of SASI values between two subgroups is statistically significant, $p = 0.04$. Relatively high standard deviation can be related to the diversity of subgroups: the character of declared leaderships and the levels of duties varied.

In this study, the higher SASI values are indicated for leaders compared to non-leaders. The leadership position is expected to be connected to higher level of responsibilities and duties and is considered as a possible occupational stressor. The similar trend of enhancement of SASI values has been reported in our previous studies with external microwave radiation exposure as physical stressor [8]. The SASI values increase also for subjects with major depression [6]. The opposite direction of SASI was indicated in our study with coffee as a chemical stressor [9]. We can suggest that the SASI values differentiate various characters, negative or positive, of the stressors: depression, microwave radiation and leadership responsibility can be considered as negative and coffee as positive stressor.

The increase of SASI value, according to the formula (2), is caused by the enhancement of the EEG power in higher frequency band W_{hn} or decrease of the power in lower frequency band W_{ln}. Our previous investigations of SASI indicated dominant impact of the higher frequency band to discrimination between healthy and depressive subjects [13]. Consequently, the indicated increase of SASI values is expected to exhibit increased beta power for the leaders. The EEG data have been reported having a significant increase in absolute EEG power in alpha and beta bands in workers with higher chemical exposure [14]. Increased SASI in depression is in a good agreement with the findings reported by other authors where relative beta was found to be greater for depressive patients compared to controls [15, 16].

The enhanced SASI can be related to some factors other than leadership responsibility, for example increased intellectual activity or educational level. The further investigations are required to clarify the limitations of SASI in applications for detecting occupational stress.

IV. COMPLIANCE WITH ETHICAL REQUIREMENTS

A. Statement of Informed Consent

The experiments were conducted with the understanding and the written informed consent of each human subject. Complete anonymity of recorded EEG signals and the results of analysis was guaranteed.

B. Statement of Human and Animal Rights

The study was in accordance with the ethical standards and formally approved by the Tallinn Medical Research Ethics Committee. The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000 and 2008.

V. CONCLUSIONS

The current study suggests that SASI provides detection of psychological stress factors related to leadership duties. Our previous studies reported that SASI is sensitive to physical and chemical stressors. Therefore, SASI as a simple objective measure is promising for application in occupational health.

Acknowledgment

The research was funded partly by the Estonian Ministry of Education and Research under institutional research financing IUT 19-2 and by Estonian Centre of Excellence in IT (EXCITE) funded by European Regional Development Fund.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. World Health Organization (2008) The global burden of disease: 2004 update. WHO Press Geneva Availabe: http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004 update_full.pdf
2. Levy B S, Wegman D H, Baron S L, Sokas R K et al (2011) Occupational and environmental health. 6th edition. Oxford University Press, New York 14:296-312
3. Nunez P. L (1995) Neocortical Dynamics and Human EEG Rhythms. Oxford University Press, New York
4. Buzsáki G, Draguhn A (2004) Neuronal oscillations in cortical networks. Science 304:1926–1929
5. Schnitzler A, Gross J (2005) Normal and pathological oscillatory communication in the brain. Nature Rev Neurosci 6:285–296
6. Hinrikus H, Suhhova A, Bachmann M et al. (2009) Electroencephalographic spectral asymmetry index for detection of depression. Med Biol Eng Comp 47:1291–1299
7. Hinrikus H, Bachmann M, Lass J et al (2012) Method and device for diagnosing a mental disorder by measuring bioelectromagnetic signals of the brain. US8244341B1
8. Bachmann M, Lass J, Suhhova A et al (2014) Spectral asymmetry index and Higuchi's fractal dimension for detecting microwave radiation effect on electroencephalographic signal. Proc Est Acad Sci 63:234 – 239
9. Saifudinova M, Bachmann M, Lass J et al (2015) Effect of Coffee on EEG Spectral Asymmetry. IFMBE Proc, vol. 51, World Congress on Med. Phys. & Biomed. Eng., Toronto, Canada, 2015, pp 1030-1033
10. Orgo L, Bachmann M, Lass J et al (2015) Effect of Negative and Positive Emotions on EEG Spectral Asymmetry. Proc 37th Annual International Conference of the IEEE EMBS, Milan, Italy, 2015, pp 8107–8110
11. Bachmann M, Lass J, Suhhova A et al (2013) Spectral asymmetry and Higuchi's fractal dimension measures of depression electroencephalogram. Comput Math Methods Med 2013:251638 DOI 10.1155/2013/251638
12. Bachmann M, Lass J, Hinrikus H (2017) Single channel EEG analysis for detection of depression. Biomed Signal Process Control 31:391-397
13. Hinrikus H, Suhhova A, Bachmann M et al (2010) Spectral features of EEG in depression. Biomed Tech 55:155–161
14. Matikinen E, Forsman-Grönholm L, Pfäffli P et al (1993) Nervous system effects of occupational exposure to styrene: a clinical and neurophysiological study. Environ Res 61:84-92
15. Knott V, Mahoney C, Kennedy S et al (2001) EEG power, frequency, asymmetry and coherence in male depression. Psyhiatry Research: Neuroimaging 106:123 – 140
16. Sun Y, Li Y, Zhu Y et al (2008) Electroencephalographic differences between depressed and control subjects: an aspect of interdependence analysis. Brain Res Bull 76:559-564

Enter the information of the corresponding author:

Author: Toomas Põld
Institute: Qvalitas Medical Centre
City: Tallinn 11312
Street: Pärnu mnt.102C
Country: Estonia
Email: toomas.pold@qvalitas.ee

Appendix 1 (Continued)

Publication IV

Põld, T.; Bachmann, M.; Päeske, L.; Kalev, K.; Lass, J.; Hinrikus, H. (2019). EEG Spectral Asymmetry Is Dependent on Education Level of Men. In: Lhotska, L.; Sukupova, L.; Lacković, I.; Ibbott, G. (Ed.). World Congress on Medical Physics and Biomedical Engineering 2018 (405−408). Singapore: Springer. (IFMBE Proceedings; 68/2). DOI: 10.1007/978-981-10-9038-7_76.

EEG Spectral Asymmetry is Dependent on Education Level of Men

Toomas Põld[1, 2], Maie Bachman[1], Laura Päeske[1], Kaia Kalev[1], Jaanus Lass[1] and Hiie Hinrikus[1]

[1] Tallinn University of Technology, Ehitajate tee 5, 12616 Tallinn, Estonia
[2] Qvalitas Medical Centre, Pärnu mnt 102C, 11312 Tallinn, Estonia
toomas.pold@qvalitas.ee

Abstract. An objective indicator based on the asymmetry of electroencephalographic (EEG) signal spectrum has been shown promising for screening of population to discover occupational stress. However, the factors other than stress affect the EEG spectrum. The aim of the current study is to investigate the role of education level on EEG signals' band relative powers. For this purpose, 18-channel resting eyes-closed EEG was recorded from 30 men having Bachelor or higher education (tertiary education) and 16 men declaring to have lower, upper or post-secondary education (secondary education). For those signals, relative theta, alpha, beta and gamma powers were calculated. The results indicated increase in relative gamma power for the subgroup of men having tertiary education compared to the subgroup of men having secondary education. No significant alterations were revealed in other relative band powers. Higher relative gamma power of men having higher level of education could be related to the higher cognitive load in their everyday life, as widespread gamma activation has been previously demonstrated during cognitive tasks. The results of the current study suggest that the level of education is one of the factors to be taken into account in EEG based evaluation of occupational stress or mental disorders.

Keywords: EEG, education, relative band power

1 Introduction

The problems of stress and mental disorders have become important in labour force nowadays and, consequently, need more attention also in occupational health. One in five people at the workplace experience a mental health condition. This statistic is predicted to worsen if early intervention and awareness is continuously avoided [1]. Exposure to stressful working conditions can have direct influence on safety and health [2]. Currently the diagnosis of stress, depression and other mental disorders are based on the evaluation of the intensity of subjective symptoms by general practitioner, occupational physician or psychiatrist using questionnaires and interview – no objective criteria exist in clinical practice. As a result, it is highly important to have an inexpensive objective measure to screen employees for early detection of stress.

The brain behaviour and its mental state are related to its bioelectric activity determined by neuronal oscillations. The oscillations are a prominent feature of neuronal processes and the synchronization of the oscillations is a likely mechanism for cerebral integration for neural communication [3, 4]. Therefore, the spectrum of the resting electroencephalographic (EEG) signal is determined by the state of the brain. Consequently, EEG methods can be highly promising in early detection of mental disorders including occupational stress. For example, a method, spectral asymmetry index, has been shown to differentiate depression from controls [5]. Spectral asymmetry index was also elevated for the group of leaders compared to non-leaders [6]. However, EEG, and therefore different objective parameters calculated from EEG, indicate changes also in variation of normal conditions or under consumption of different substances, like coffee [7], which need to be taken into account while studying stress or different brain disorders. What is more, Veldhuizen et al. [8] found significant gender differences for the temporal theta power for healthy subjects, while Orgo et al. [9] demonstrated significant differences in synchronization likelihood between EEG male and female major depressive disorder. In addition, Marciani et al. [10] concluded that young subjects indicate more pronounced fast activity compared to elderly subjects, while some studies have indicated changes in EEG depending on the cognitive load [10]. Cognitive load can be indirectly related to the subjects' education level.

As it is shown, several factors other than mental disorders or stress are capable of changing the EEG relative band powers.

Current study aims to identify whether EEG relative band powers differ for men having tertiary or secondary education. The results would give valuable information about the dependence of EEG on the level of education that is important in EEG-based estimation of occupational stress and explains whether and how the education level could be revealed in spectral asymmetry of the EEG signal.

2 Methods

2.1 Subjects

The experiments were carried out in Qvalitas Medical Center on a group of healthy volunteers. The group consisted of 46 subjects: 30 subjects having tertiary education with the mean age of 42.1 and standard deviation of 9.4 years and 16 subjects having secondary education with the mean age of 37.6 and standard deviation 7.5. The age difference between two education levels of interest were statistically compared ($p>0.05$) to exclude the influence of age on the results.
At least 1.5 hours before the experiment the subjects did not consume any caffeinated drinks and up to 8 hours before no alcoholic beverages.

2.2 Experiment procedure and EEG recording equipment

The experimental study was performed according to the recording protocol identical for all subjects: eyes closed resting EEG recorded for seven minutes. During the EEG recordings, subjects were lying in a relaxed position with eyes closed and ears blocked. The room was dimly lit but no other special conditions were provided.

The Cadwell Easy II EEG (Kennewick, WA, USA) measurement equipment was used for the EEG recordings. The 18-channel EEG was recorded according to the international 10-20-electrode position classification system (common reference Cz). Raw signals in frequency band 0.3-70 Hz were stored at sampling frequency 400 Hz. The notch filter was applied at 50 Hz.

2.3 EEG analysis

The visually checked artefacts-free EEG segments with the duration of ten seconds were selected from the EEG signal. First 30 of the segments (five minutes) were used in further analysis. Spectral asymmetry and also the relative theta, alpha, beta and gamma band powers were calculated for each of those segments, to clarify, which part of the EEG spectrum is responsible for alterations in EEG spectral asymmetry.

The spectral asymmetry was calculated as relative difference between powers of EEG bands at frequencies higher and lower than the central alpha band. In spectral asymmetry, the alpha band was excluded from the calculations.

To calculate the EEG segments' relative band powers, the power spectral density was estimated by means of Welch's averaged periodogram method for each subject's EEG channels. The signal was divided into overlapping epochs (50%), with the length of 2048 samples and extracted through a Hanning window. Afterwards, the average of relative powers were computed for theta (3.5-7.5 Hz), alpha (7.5-12.5 Hz), beta (12.5-30 Hz) and gamma (30-46 Hz) bands. Next the relative band powers and also the spectral asymmetry were averaged over all channels and the difference in those parameters between groups with secondary and tertiary education was evaluated using the Mann-Whitney statistical test. The confidence level of 0.05 was selected for evaluation. In case any of the parameters gave significant difference between the two groups, those parameters were re-evaluated for group differences in nine more specific brain regions, each comprising of two nearby channels: Fp1&Fp2, F7&F3, F8&F4, T3&C3, T4&C4, Fz&Pz, T5&P3, T6&P4, O1&O2.

All the EEG data processing was performed using MATLAB (The Math-works, Inc.).

3 Results

The groups with different education levels were not statistically significantly different considering the age ($p>0.05$). We found statistically significant difference between the group of men having tertiary education compared to the group of men having secondary education in spectral asymmetry values averaged over all channels ($p<0.05$). Therefore, also the difference between the groups in nine more specific brain regions was studied (Figure 1). As can be seen all the posterior regions and also left anterior regions indicate statistically significant increase in spectral asymmetry in case of tertiary education.

While calculating the relative band powers of theta, alpha beta and gamma band averaged over all channels for group of males with tertiary and secondary education, only the relative gamma band power indicated statistically significant difference ($p<0.05$) between the groups. Therefore, only the behaviour of relative gamma band power was studied in more specific brain regions. Figure 2 presents the average relative gamma band powers for the group of men having secondary education and group of men having tertiary education in nine brain regions. The results indicate increased relative gamma power for the group of men having tertiary education compared to group of men having secondary education in all regions. The increase was statistically significant in all regions, except F8&F4 ($p=0.08$) and T5&P3 ($p=0.07$) indicating increase close to statistical significance, and T4&C4 indicating non-significant increase. In other words, it can be generalized that all brain regions, except left fronto-central region, indicate increased relative gamma band power for men with tertiary education compared to men with secondary education.

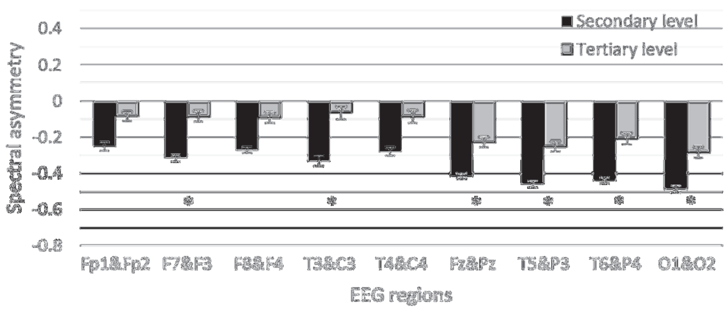

Fig. 1. Mean and standard error of the spectral asymmetry values for the group of men having secondary education and group of men having tertiary education in 9 brain regions. Asterisk represent statistically significant difference ($p<0.05$).

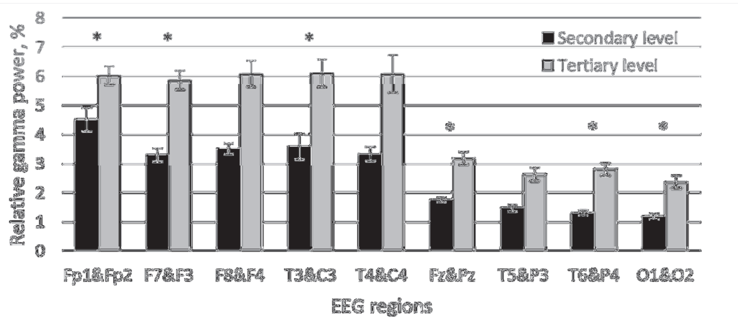

Fig. 2. Mean and standard error of the relative gamma power for the group of men having sec-

ondary education and group of men having tertiary education in 9 brain regions. Asterisk represent statistically significant difference ($p<0.05$).

4 Discussion

The results indicated significant increase in spectral asymmetry for men with tertiary education compared to men with secondary education. While clarifying which EEG frequency band is responsible for those differences, it was revealed that only relative gamma power is able to differentiate those groups. As relative gamma power in combination with spectral asymmetry gave good results while classifying depressive disorder [11], the education level of subjects needs to be considered in future studies to better classify mental disorders. Higher relative gamma power of men having higher level of education could be related to the higher cognitive load in their everyday life, as widespread gamma activation has been previously demonstrated during cognitive load [12].

Considering the current results, one has to keep in mind that the study included only men. Additional study is needed to understand how variations in education level reveal in women's EEG, as there have been found significant sex differences in theta power [8]. In addition, the research of mental health charity Mind reveals that men are twice as likely to suffer work-related mental health problems compared to women [1].

The results of the current study suggest that the level of education is one of the factors to be taken into account in EEG based evaluation of occupational stress or mental disorders.

5 Conclusions

The results of the performed study indicate that men with tertiary education have increased relative gamma band power compared to men with secondary education, influencing also the EEG spectral asymmetry. The level of education is one of the factors to be taken into account in EEG based evaluation of stress or mental disorders.

Acknowledgment

This study was financially supported by the Estonian Ministry of Education and Research under institutional research financing IUT 19-2 and by the Estonian Centre of Excellence in IT (EXCITE) funded by the European Regional Development Fund.

Compliance with ethical requirements

The experiments were conducted with the understanding and the written informed consent of each human subject. Complete anonymity of recorded EEG signals and the results of analysis was guaranteed.

The study was in accordance with the ethical standards and formally approved by the Tallinn Medical Research Ethics Committee. The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000 and 2008.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Mamo, E. Men more likely to suffer work-related mental health issues https://www.openaccessgovernment.org/men-work-related-mental-health-issues/36371/ (2017) last accessed 2018/02/02
2. Levy, B. S., Wegman, D. H., Baron, S. L., Sokas, R. K. et al.: Occupational and environmental health. 6th edition. Oxford University Press, New York, 14, 296-312 (2011).
3. Buzsáki, G., Draguhn, A.: Neuronal oscillations in cortical networks. Science 304, 1926–1929 (2004).
4. Schnitzler, A., Gross, J.: Normal and pathological oscillatory communication in the brain. Nature Rev Neurosci 6, 285–296 (2005).
5. Hinrikus, H., Suhhova, A., Bachmann, M. et al.: Electroencephalographic spectral asymmetry index for detection of depression. Med Biol Eng Comp 47, 1291–1299 (2009).
6. Põld T., Bachman M., Orgo L., Kalev K., Lass J., Hinrikus H.: EEG Spectral Asymmetry Index Detects Differences Between Leaders and Non-leaders. In: Eskola H., Väisänen O., Viik J., Hyttinen J. (eds) EMBEC & NBC 2017. EMBEC 2017, NBC 2017. IFMBE Proceedings, vol 65, pp.17-20, Springer, Singapore (2018).
7. Saifudinova M., Bachmann M., Lass J., Hinrikus H.: Effect of Coffee on EEG Spectral Assymmetry. In: Jaffray D. (eds) World Congress on Medical Physics and Biomedical Engineering, June 7-12, 2015, Toronto, Canada. IFMBE Proceedings, vol 51, pp. 1030-1033 Springer, Cham (2015).
8. Veldhuizen, R. J., Jonkman, E. J., Poortvliet, D. C.: Sex differences in age regression parameters of healthy adults--normative data and practical Implications. Electroencephalogr Clin Neurophysiol. 86(6), 377-84 (1993).
9. Orgo, L., Bachmann, M., Kalev, K., Hinrikus, H., Järvelaid, M.: Brain functional connectivity in depression: Gender differences in EEG. 2016 IEEE EMBS Conference on Biomedical Engineering and Sciences (IECBES), pp. 270-273. Kuala Lumpur (2016)
10. Marciani, M. G., Maschio, M., Spanedda, F., Caltagirone, C., Gigli, GL., Bernardi, G.: Quantitative EEG evaluation in normal elderly subjects during mental processes: age-related changes. Int J Neurosci. 76(1-2), 131-40 (1994).
11. Bachmanna, M., Päeske, L., Kalev, K., Aarmaa, K., Lehtmets, L., Ööpik, P., Lass, J., Hinrikus, H.: Methods for classifying depression in single channel EEG using linear and non-

linear signal analysis. Computer Methods and Programs in Biomedicine, 155, pp. 11-17 (2018).

12. Werkle-Bergner, M., Shing, Y.L., Müller, V., Li, S.C., Lindenberger, U.: EEG gamma-band synchronization in visual coding from childhood to old age: evidence from evoked power and inter-trial phase locking. Clinical Neurophysiology 120(7), 1291-1302 (2009).

Curriculum vitae

Personal data

Name:	Toomas Põld
Date of birth:	21.12.1961
Place of birth:	Kohtla-Järve, Estonia
Citizenship:	Estonian

Contact data

E-mail:	tpf@hot.ee

Education

1995–1997	University of Tartu
1994–1995	University of Bergen, Norway
1992–1993	University of Helsinki
1982–1992	University of Tartu
1969–1980	Jõhvi High School

Language competence

Estonian	Mother tongue
Russian	Fluent
English	Average
Finnish	Average

Professional employment

1993–1997	Ministry of Social Affairs, physician-consultant
1993–2013	Tallinn University, Lecturer
1997–2009	Tallink, Ship's doctor, doctor in Charge
2009–	Qvalitas Medical Centre, doctor in Charge
2011–	Aviomedical Centre, aviomedicine physician (AME)

Elulookirjeldus

Isikuandmed

Nimi:	Toomas Põld
Sünniaeg:	21.12.1961
Sünnikoht:	Kohtla-Järve, Eesti
Kodakondsus:	Eesti

Kontaktandmed

E-post:	tpf@hot.ee

Hariduskäik

1995–1997	Tartu Ülikool
1994–1995	Bergeni Ülikool, Norra
1992–1993	Helsinki Ülikool, Soome
1982–1992	Tartu Ülikool
1969–1980	Jõhvi Keskkool

Keelteoskus

Eesti keel	Emakeel
Vene keel	Kõrgtase
Inglise keel	Kesktase
Soome keel	Kesktase

Teenistuskäik

1993–1997	Sotsiaalministeerium, arst-konsultant
1993–2013	Tallinna Ülikool, Lektor
1997–2009	Tallink, Laevaarst, Peaarst
2009–	Qvalitas Arstikeskus, Peaarst, Töötervishoiu arst
2011–	Eesti Lennumeditsiini keskus, Lennundusarst

ISSN 2585-6901 (PDF)
ISBN 978-9949-83-772-4 (PDF)