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The Evolution of Reaction Time Latencies in Attention Bias Modification Training against Anxiety and Depression

Elias Kvamme

Department of Computer Science

Faculty of Technology, Art and Design

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4 Abstract

Depression disorder is one of the most prevalent mental illnesses in the world. Its societal and economic burden on the world society is huge, and therefore the need for good treatment methods is of great importance.

Attention Bias Modification Training (ABM) is an interesting way of treating patients with depression and anxiety. Studies have shown that a bias against the negative is having a crucial role in both developing and keeping a depression disorder. Several researchers have proved that depressed patients tend to have a focus and attention against negative information. (Beck, 2008; Disner et al., 2011; Gotlib & Joormann, 2010; Peckham et al., 2010)

Using a dot-probe task, 321 patients have gone through ABM training over a 14-day period, with a total of 28 sessions. The scope of this thesis is to find key factors amongst the patients that can predict the effect of the training. The information provided for each patient was the age, gender, Brain-Derived Neurotrophic Factor (BDNF) allele and depression severity before and after the training period, using both the Hamilton scale and Beck's Depression Inventory.

The findings that were made was that it was in particular two main factors that were the best predictor for if the training would have the desired effect or not. These two factors were the age of the patients as well as the severity of the depression. The younger participants tended to have a higher improvement rate than the older participants. This might be due to the decreased plasticity in the older participants' brains. The analysis also indicates that the younger patients that had a positive effect of the training showed improvement already after the first week of training. This hypothesis would be interesting to pursue further.

The participants with more severe depression had a much higher rate of improving their illness. The median pre-training Hamilton score for the ones that improved was 10, while the non-improving participants had a median pre-training Hamilton score of 6.5.

5 Introduction

During the Covid-19 pandemic, there have been a lot of researchers proclaiming the effect the intrusive restrictions have on people's well-being, and especially their mental health. A study published in the Public Health Journal followed a little over 2300 Brazilian adults during the first year of the pandemic. In 2015 Brazil was ranked first and fifth in the world when it came to the prevalence of anxiety disorder and depression. During the study, the researchers found an increase in participants reporting moderate or severe depression and anxiety of as much as 6.6 and 7.4 times, respectively (Feter et al., 2021). This is a very significant increase, given that Brazil already has one of the highest densities of people suffering from depression and anxiety in the world. The significant increase corresponds well with studies from other countries such as the United States of America and Norway (Rosenberg et al., 2021; Ulset et al., 2021)

This thesis will research the evolution of reaction time latencies in attention bias modification training against anxiety and depression. I will also try to find clear markers amongst the patients to help determine who will have an effect from the treatment and find out how early in the treatment process it is possible to say if it is giving a positive effect or not. The scope of the thesis will be the patients undergoing the positive training. The question about the effect on the Positive training compared to placebo training can be found in these papers. (Bø et al., 2021; Jonassen et al., 2019; Kraft et al., 2019)

6 Background

6.1 Depression disorder

6.1.1 History

Considering the long history of medicine, depression disorder is a relatively new medically described condition. The first mention of what was then called “mood disorder” can be found in the “Diagnostic and Statistical Manual of Mental Disorders – First edition” (DSM-I) published in 1952. Here it was said that the reasons for the mood disorder were either organic or reactive. This was continued to the next version of the DSM, DSM-II, which came in 1968. The publisher grouped the mood disorder into two main groups, as either neurotic or psychotic. The mood disorder was in other words either a brain disease, a physical, curable disease, or it was a chronic disease of the mind. The reactive, neurotic version of the disease was said to be cured by removing the cause. If the patient on the other hand was placed in the other category, the general assumption of the therapists was that there was no hope for this patient, and he would be placed in an institution on a permanent basis. (Boland & Keller, 2002)

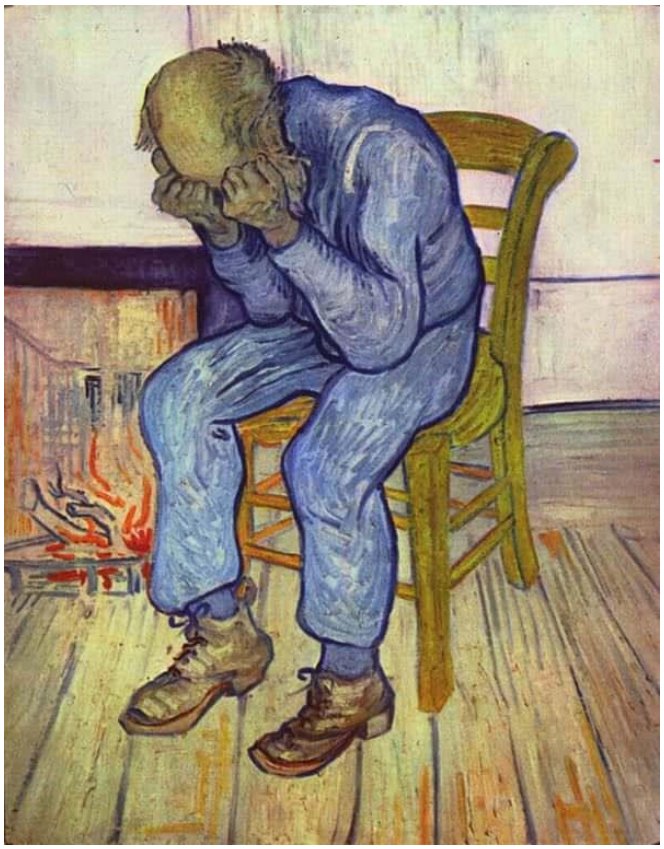


Figure 1 van Goch, V. (1890). At Eternity’s Gate. https://www.vincentvangogh.org/at-eternitys-gate.jsp#prettyPhoto

This was the leading practice up until there came a new version of the Diagnostic and Statistical Manual of Mental Disorders, namely the DSM-III. This was published in the American Psychiatric Association (APA) in 1980. In this version the thought of not differentiating the patients as completely curable or completely lost, but treating everyone with the main focus of reducing the symptoms was emphasized. There was also launched a more universal diagnostic tool for diagnosing the patient more correctly based on meeting some clear diagnostic criteria. It also came with a set of exclusion criteria that should not be present in a diagnosed patient. The thought of having a more systemized way of diagnosing depression is important and having specific markers to look for is crucial in the work done on the field today. (Richards, 2011) Another improvement on the DSM-III versus the DSM-II was that in addition to include all psychiatric illnesses, it contained information on what was the typical symptoms of the illnesses as well as the occurrence, the course of the disease and differential diagnosis.(Malt, 2020)

Through the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders that were published in 2000, the term that is used today, Major Depressive Disorder (MDD) was thoroughly described. (Richards, 2011) In 2013 the latest version as of today was published. In the DSM-V, the main changes are that there is no longer a distinction between psychiatric diagnoses for adults, youths and children.

6.2 Prevalence

Depression disorder is a widespread illness that is affecting millions worldwide. The Worlds Health Organization (WHO) states that depressive disorder is one of the most common diseases in the world. Studies has shown that in the entrance of the new millennium there were a prevalence of depression disorder at a rate of 16 per 100'000 males and 25 per 100'000 females each year on a worldwide basis. (Üstün et al., 2004)

In the 1990's the World Bank introduced the term DALY, which stands for Disability-Adjusted-Life-years and is a way of measuring the burden of a disease in a population as well as the effect on measures done in order to cease or decrease the burden. The purpose of having this measure was so that it should be possible to lay a foundation for comparing the effect different diseases has on different populations and over time in a population. (Stoltenberg, 2020) After the introduction of DALY, the WHO published a study called the Global Burden of Disease (GBD). This study was made so that politicians and researchers worldwide could be informed on what diseases were the most prevalent and burdensome on the population. This was done so that it would be easier to prioritize the most acute problems for further research and political initiatives on an international scale. (Murray et al., 1996) The study shed a light on the enormous burden depression disorder put on the society. Taking up 3.7% of the total disability-adjusted life-years (DALY), depression disorder was ranked as the fourth highest burden-causing disease in the world. Üstün et al. writes that the WHO does a follow-up study in 2001 called the Global Burden of Disease for the year 2000 (the GBD 2000) which shows that the DALY of depression is worsening, now accounting for 4.4%. They conclude that "These data on the burden of depression worldwide represent a major public health problem that affects patients and society." (Üstün et al., 2004) A study only 5 years newer concludes that the DALY of depression in Europe is as high as 6%. (Sobocki et al., 2006)

Around the turn of the millennium Kessler et al. reported a 12-month prevalence of 6.6% amongst adults in the United States. A 12-month prevalence of depression disorder means the amount of people having experienced a depression in the last 12 month. The lifetime prevalence reported, that is the amount of people having experienced depression throughout their life, was as high as 16.2% (Kessler et al., 2003) This is an increase from an earlier study by Kessler et al. from the early 90s that resulted in a prevalence of 14.9%. (Kessler et al., 1994) The reason for the increase could be due to several things. One

explanation could be that the general population got it worse, or another explanation could be, as suggested by Richard, that people throughout the years got more and more open to talk about their emotions. (Richards, 2011) There is no secret that there has been a culture of not talking about feelings in the past. In many ways it could be argued that the society still has a way to go before these things become easy enough to talk about.

When it comes to distinguish the prevalence amongst gender, there is no doubt that depression illness is far more common amongst females. As stated earlier the general prevalence in the world per year is 16 per 100'000 males and 25 per 100'000 females. In Europe, the same study concludes that there are even more females with depression disorder, at the rate of 27 per 100'000 females every year. (Üstün et al., 2004)

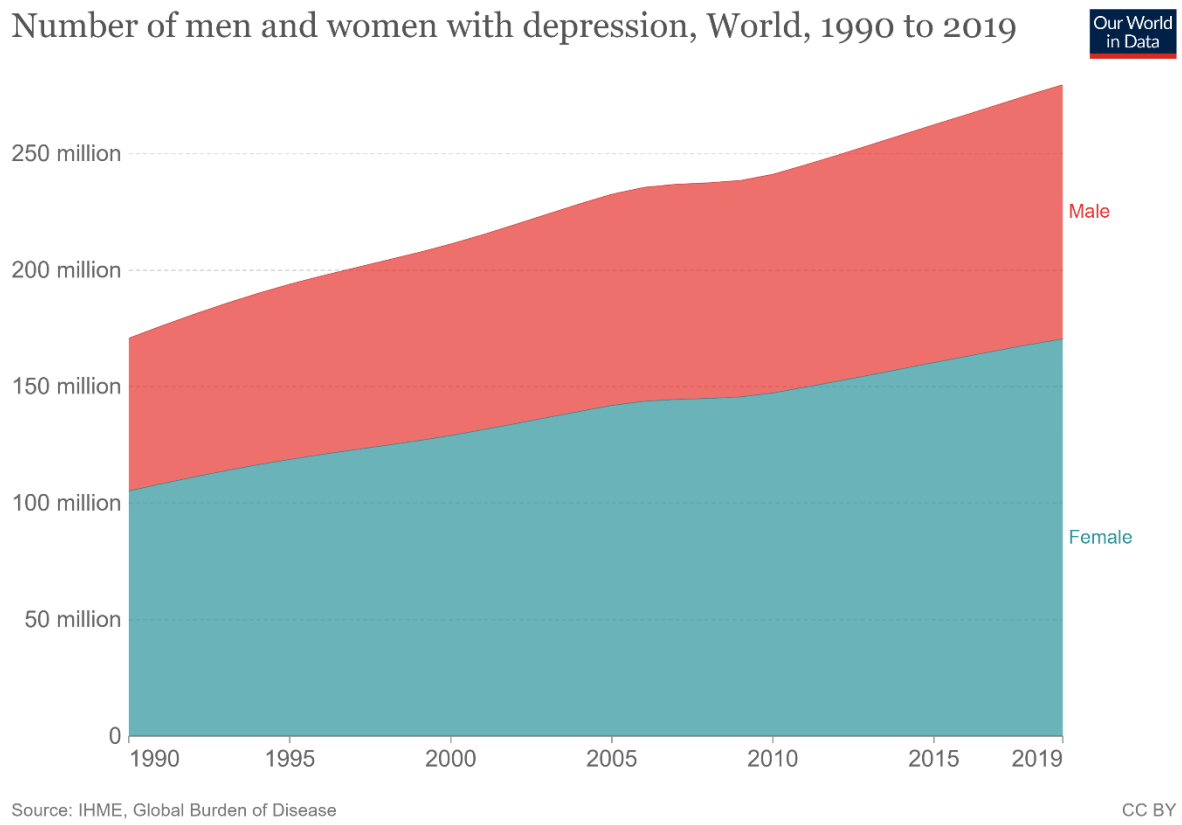


Figure 2 Graph showing the increase in number of men and women with depression disorder in the world from 1990 to 2019. (Dattani et al., 2021)

As clearly displayed Figure 2 above, there is a huge overweight of females suffering from depression disorder. Something that is interesting to see is that even though the females have been overrepresented amongst patients with depressive disorder the last 30 years, the slope showing number of males with depression is steeper than the one showing the

number of females. This means that the number of males with depression disorder is increasing faster than number of females, and if this trend is going to continue the skewed distribution between the genders will cease.

Early studies from the 90s on the duration of a depression episode shows an average duration of 6 months. A study by Eaton et al. that were written in 2008 shows an average duration of a depression disorder episode of three months. This is a significant decrease in duration in just a decade. (Eaton et al., 2008) The halving in duration suggest that depressed humans gets faster and better help that before. This could be due to a more awareness around the issue, as well as more knowledge amongst the therapists. Depression disorder is not only more common amongst women, but several studies also suggest that the average duration of a depression episode is longer amongst women as well. Even though the episodes amongst females are statistically longer than amongst men, there is nothing that suggests that the recovery time of the depression itself is different amongst females and males. (Eaton et al., 2008)

In 2018 Grace Lim et al. published a review article named “Prevalence of Depression in the Community from 30 Countries between 1994 and 2014” in the Scientific Reports Journal. Amongst the topics discussed in the article, the evolution of the depression disorder throughout those 20 year is interesting to investigate. Even though, as stated earlier, the duration of a depression disorder seems to have halved from the 90s, there is unfortunately no doubt that the depression disorder is a growing problem in the world. Looking into the studies published between 1994 to 2003 the aggregate prevalence reported was 9.8% with a 95% CI from 6.7% to 14.1%. Comparing to the studies published between 2004 and 2014, which reported an aggregate prevalence of 15.4% with a 95% CI from 12.9% to 18.3%, it is clear that the prevalence has had a significant growth over the years. (Lim et al., 2018)

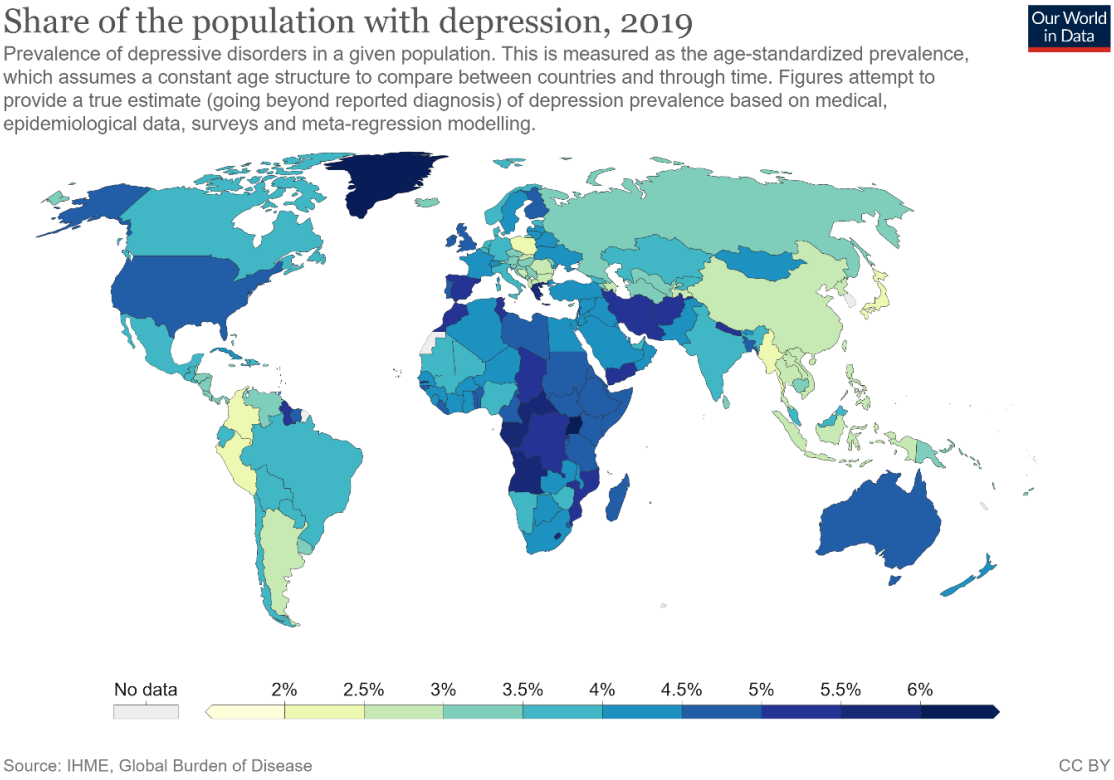


Figure 3 Map of the world showing the share of the population with depression in each country in 2019 (Dattani et al., 2021)

In Figure 3 there is a map showing the share of population with depression in each country in 2019. This gives us a good visualisation on where in the world the highest density of depressed persons is located. Taking a quick peek, you can see that the countries with highest density are the African countries south of Sahara, in the middle east and the western countries in Europe and America. These findings will be commented later.

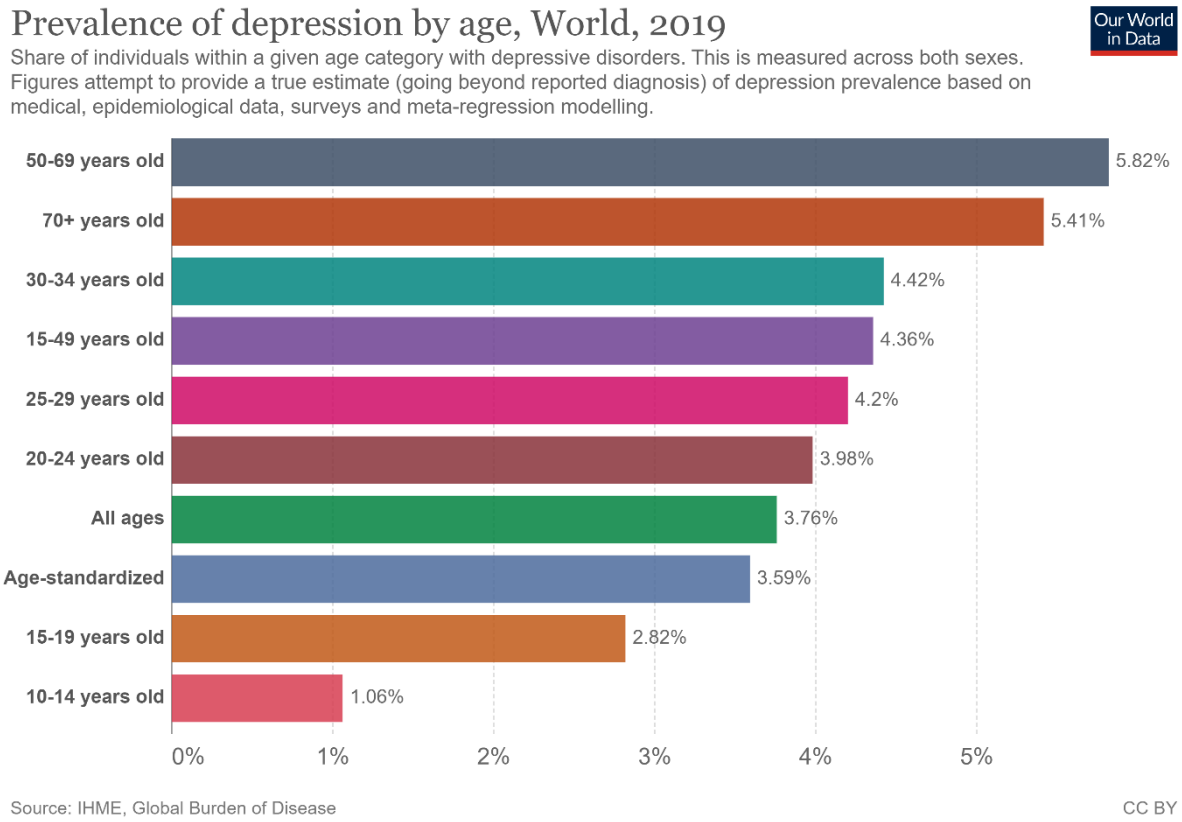


Figure 4 Bar chart showing the prevalence of depression in the world in 2019 by age (Dattani et al., 2021)

Looking at Figure 4, one can see that the prevalence of depression is highest amongst the elderly above 50 years. This contrasts with statistics from Norway, as can be seen in Figure 5, where the prevalence is clearly highest amongst young adults. This is interesting and might have something to do with the living standards in Norway, compared to other countries. One might speculate that it can have something with the fact that while the elderly in Norway grew up in a poor country and have experienced an enormous change in the standard of living. With the oil money and everything that came with it, they have had experienced a whole new way of life compared to their parents, with good caring facilities and good pension schemes. The young people in Norway have more or less always had what they need and way more but is growing up in a society highly focused on social status and high achieving careers. This might be some of the reason that the young people in Norway have the highest prevalence of depression, while the elderly has a much lower prevalence, especially compared to elderly in the rest of the world.

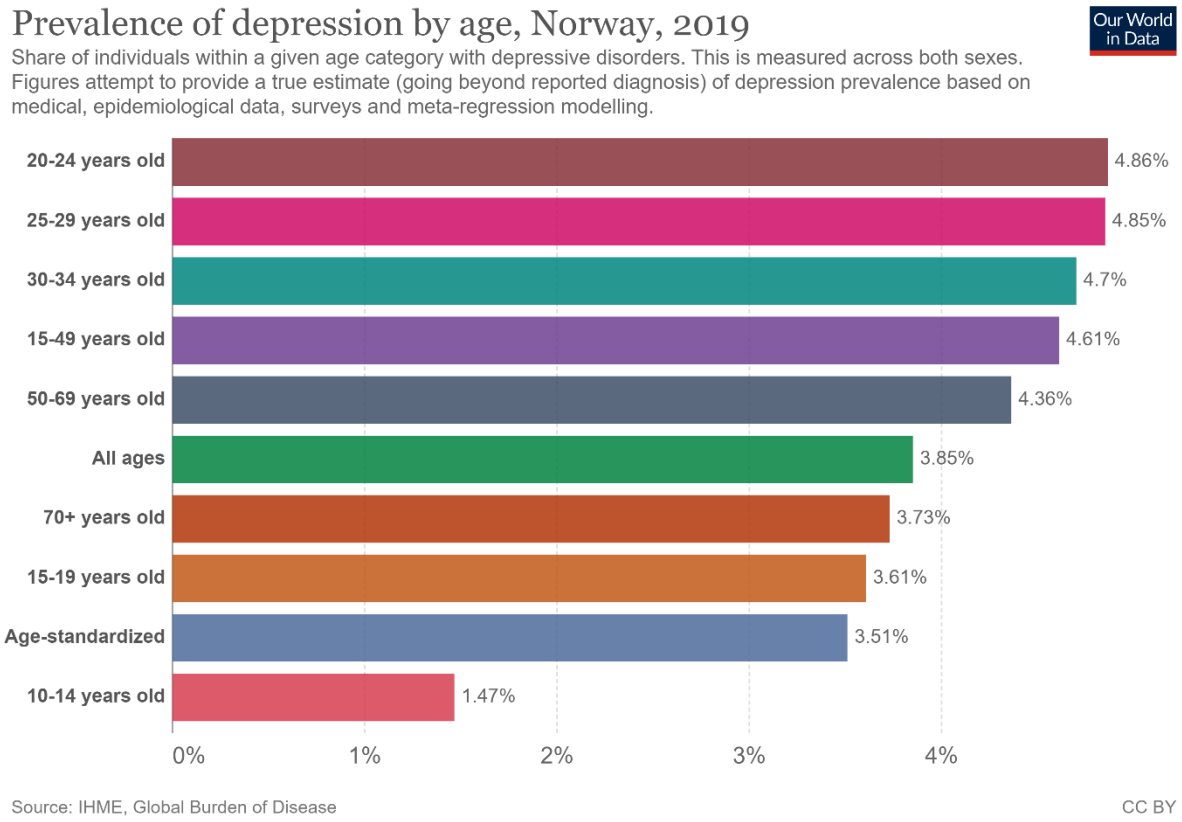


Figure 5 Bar chart showing prevalence of depression by age in Norway 2019 (Dattani et al., 2021)

The prevalence on depression is not only different amongst the different genders and age groups. There is also a great difference when taking the Human Development Index (HDI) into account. The HDI is an index developed by the United Nations (UN) which by looking at the living standard, expected life length and education level of the inhabitants in a country gives the country a score between 0 and 1. There are four categories in the HDI. These are "very high human development", "high human development", "medium human development" and "low human development". The categories contain countries that score between 1.0-0.8, 0.79-0.70, 0.69-0.55 and 0.54-0.0 respectively.(United Nations Development Programme et al., 2020) Lim et al. has studied the prevalence on depression in countries in these HDI categories.(Lim et al., 2018) To no surprise, the countries from the "very high human development" category have the lowest prevalence of depression amongst their inhabitants. The average prevalence in these countries, which includes countries such as Norway (HDI #1), Hong Kong (HDI tied #3), United states (HDI #17) and Russia (HDI #52) is 9.8%. (Lim et al., 2018; United Nations Development Programme et al., 2020)

A bigger surprise was maybe that on a strong number two came the countries from the

lowest HDI tier, the ones with a “low human development”. These countries include the likes of Rwanda (HDI #160), Afghanistan (HDI #169), Eritrea (HDI #180) and Niger (HDI #189).(United Nations Development Programme et al., 2020) The average prevalence were only slightly higher, scoring an 11.5% prevalence. It would be interesting to get some insight into what the reason is that the once who, objectively, has it hardest in life when it comes to the criteria set by the UN, have such a low prevalence of depression compared to others that are better educated, lives longer and has a completely different living standard. Maybe there is something in the expression “money can’t buy you happiness” or maybe it should be changed to “money isn’t the only way to happiness” considering the “very high human development” countries are, in fact, on top.

The countries with “high human development” scores second last in the depression prevalence study by Lim et al. With a depression prevalence of 19.2%, this is a significantly higher percentage compared to the depression prevalence in “very high human development” countries and “low human development” countries. Countries that come in the “high human development” HDI category are countries like Iran (HDI tied #70), China (HDI #85), Indonesia (HDI tied #107) and Egypt (HDI #116) (United Nations Development Programme et al., 2020)

The countries that without doubt has the highest prevalence of depression disorder according to the review study written by Lim et al. is the countries in the “medium human development” HDI category. These are the countries that scores between 0.55 and 0.69 on the HDI scale which goes from 0 to 1 where 0 is the worst possible and 1 in the best possible. Countries in this category includes India (HDI #131), Ghana (HDI #138), Congo (HDI #149) and Pakistan (HDI #154). (United Nations Development Programme et al., 2020) The prevalence of depression disorder in these countries are as high as 29.2%. (Lim et al., 2018)This means that almost a third of the population in these countries has suffered from depression. Considering that India, with its almost 1.4 billion inhabitants per 2020 (The World Bank, 2020) , is a part of the “medium human development” category, the amount of people who is suffering from depression in the world is so high it is hard to imagine.

It must be taken into consideration that the review made by Lim et al. has an overweight of studies from countries in the two higher HDI tiers. With a total of 59 studies from these tiers, and a participant number of about 866’000 there is a lot more data here than from countries

from the two lower HDI tiers. There are reviewed a total of 9 studies from these tiers, containing a participant number of 30’727. (Lim et al., 2018) This provides an uncertainty to the numbers that should not be overlooked.

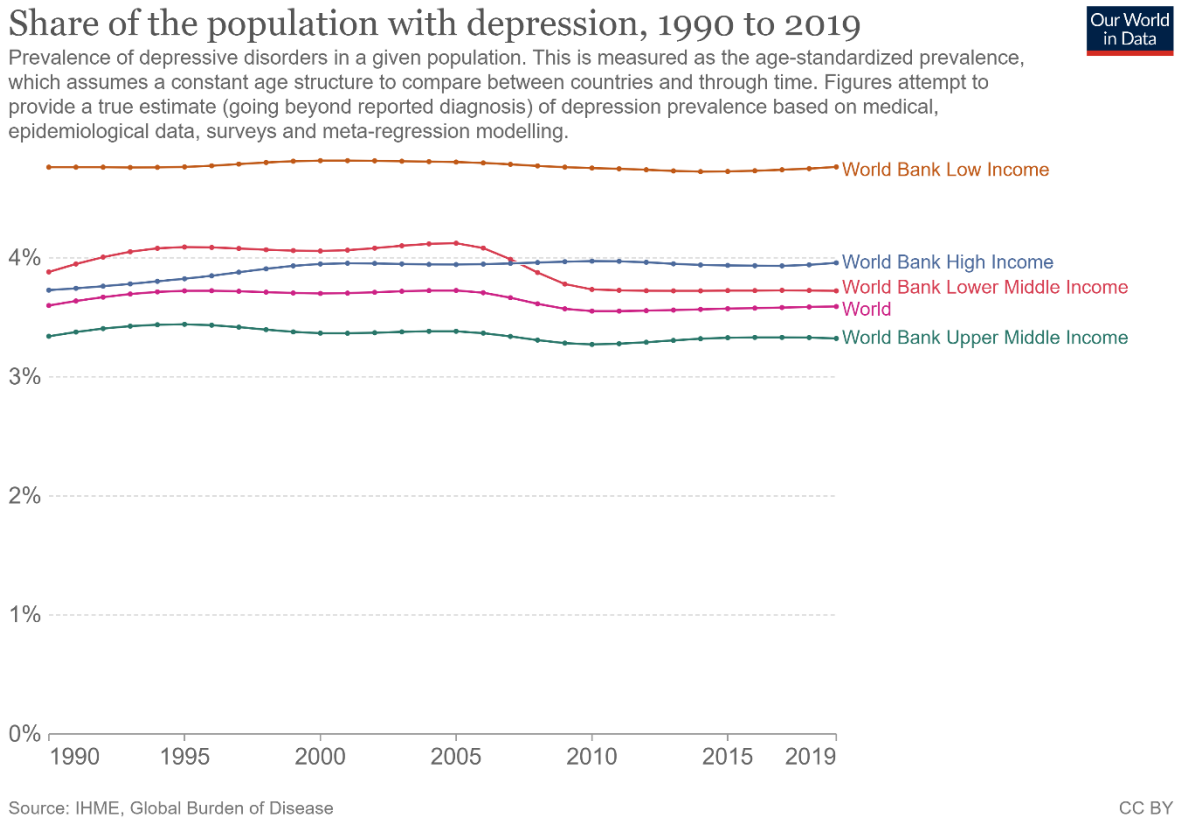


Figure 6 Graph showing the share of population with depression grouped in economic tiers from 1990 to 2019 (Dattani et al., 2021)

Comparing the numbers from the HDI to numbers from countries divided into the World Bank Income categories, it is possible to see that there is a difference in living in a country with high income and living in a country with a very high HDI. Where the very high HDI countries scored lowest on depression prevalence, the figure above is placing the high-income countries in second place when it comes to highest prevalence of depression.

To sum it all up, there are no doubt that with almost 300 million (ref Figure 2) persons suffering from depression worldwide, this is a huge societal problem that should be focused a lot more on. The impacts of having so many people sick from something as unnecessary as depressions are way too big to not being dealt properly with.

6.2.1 Diagnosing depression disorder

When it comes to diagnosing Major Depression Disorder there are several well-implemented

methods of doing so. The most widely used are the Diagnostic and Statistical Manual for Mental Disorders, fifth version (DSM-5) and the International Classification of Diseases 10th revision. To be diagnosed with having Major Depression Episode there are a requirement of at least five symptoms that the patient needs to experience in a two-week period. Of these five symptoms, one of them must be either having a depressed mood, or having the feeling that nothing is fun, and that you feel no pleasure in anything, called anhedonia. These two symptoms are classified as the primary symptoms. Some of the secondary symptoms of a Major Depression Disorder is having insomnia, which is having trouble sleeping, concentration issues, being suicidal, and experiencing changes in weight or appetite. The others are the feeling of guilt or worthlessness, experiencing having no energy, also known as fatigue and having trouble with psychomotor retardation or agitation. (Tolentino & Schmidt, 2018) In this diagnostic tool you either have the symptoms or not, there are no weighting how much of each the patient are experiencing the symptoms.

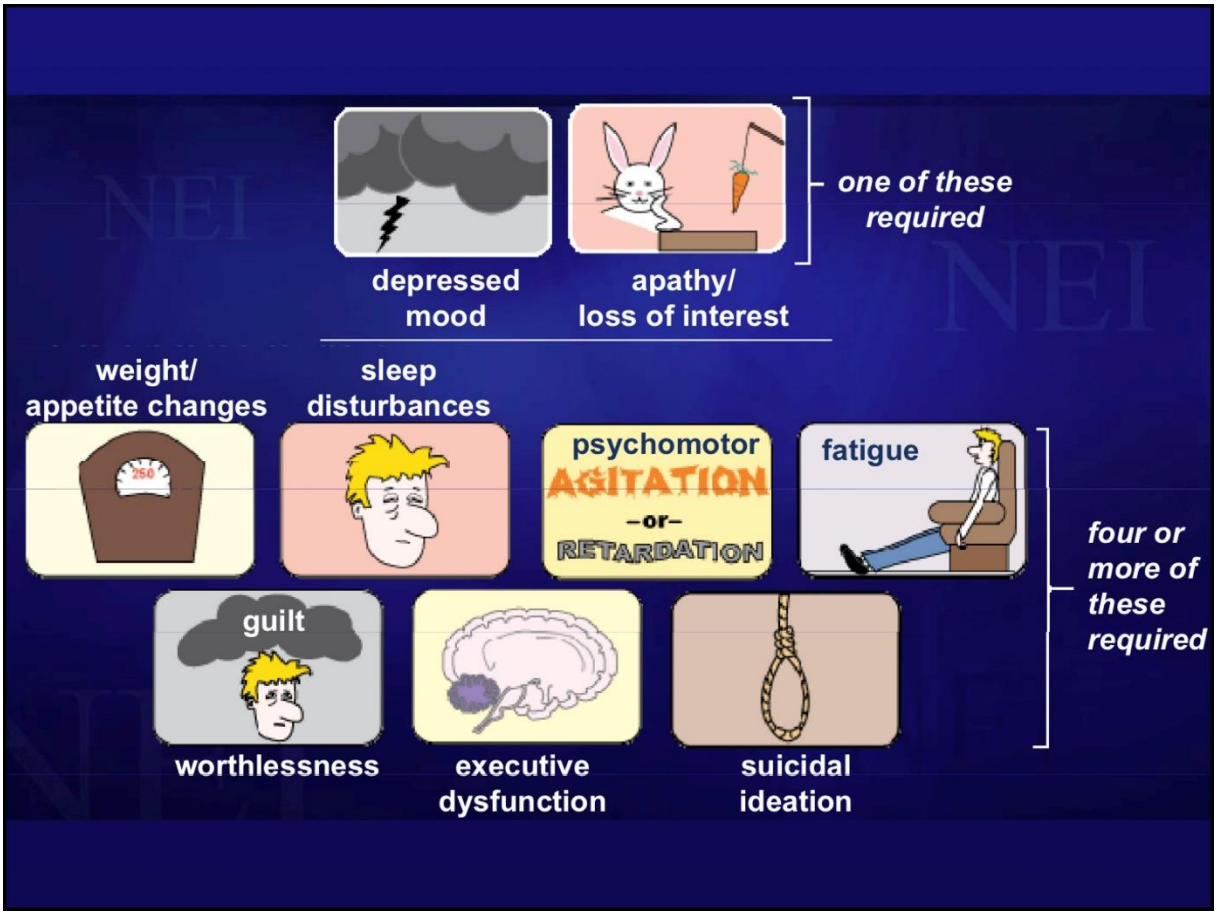


Figure 7 Symptom dimensions of a major depressive episode. In addition to depressed mood and agitation, ≥4 other symptoms are required to make the diagnosis of major depressive disorder. This indicates that there are many types of major depression, and that treatment needs to be individualized to the specific symptoms present.

A weakness in this way of diagnosing depression is that it is classifying the depression disorder as unidimensional. This opposed to other studies that shows that a depression disorder is better described if the symptoms are separated into two distinct categories: somatic and non-somatic symptoms. (Helzer et al., 2006; Smolderen et al., 2009) This way of dividing the symptoms is supported by studies that suggests that there are several subtypes of depression (Rantala et al., 2018; van Loo et al., 2012) While some studies has shown the correlation between factors such as age, psychosis, cognitive dysfunction, suicidality and unemployment and the severity of the depression, there has earlier not been shown any similar correlation regarding the primary and secondary symptoms in the DSM-model. Neither were there any suggestions that the degree of the symptoms gives any form for indication to the severity of the depression. Tolentino and Schmidt published a journal article in the journal Frontiers in Psychiatry in 2018 suggesting otherwise, and substantiates the claim that the somatic DSM symptoms, including insomnia, fatigue, change in appetite and concentration issues are linked to a moderate depression. They also suggest that non-somatic, cognitive symptoms such as suicidality, depressed mood, feelings of worthlessness and anhedonia corresponds to a more severe form for depression. (Tolentino & Schmidt, 2018)

While the DSM only diagnose the patient to either have a Major Depression Episode or not, the International Classification of Diseases rev 10 (ICD-10) diagnoses the patient with either a mild, moderate or severe depression. (Smith-Nielsen et al., 2018) This is done by determining how many of the defined most common symptoms for depression, usually 10, the patient has. To be diagnosed with mild or moderate depression, the patient must have at least 2 core symptoms and 2-3 or 4-5 associated symptoms, respectively. If the patient has 3 core symptoms and 5-7 other symptoms associated with depression, they are diagnosed with severe depression. (Smith-Nielsen et al., 2018)

When the patient is diagnosed with Major Depression Disorder, the next step is to find out how severe the depression is. One of the most widespread used clinical-rated scales for determining the grade of depression amongst patients already diagnosed with depression is the Hamilton Rating Scale for Depression (HAM-D). This way of grading the depression were

introduced as early as 1960 by the famous psychiatrist Max Hamilton. (Bech, 2009)

There are several versions of the HAM-D. The one Hamilton himself published back in 1960 consisted of 21 symptoms that were screened for. The symptoms were then graded on a score from either 0 to 2 or 0 to 4. These symptoms were everything from depressed mood, feelings of guilt and suicidal thoughts to loss of weight, genital symptoms and hypochondriasis. The rest of the symptoms can be seen in Figure 8 in the furthermost left column. Even though Hamilton presented 21 different symptoms to determine the severity of the depression disorder, he recommended only using the first 17, as the last four were either not very common, or not proved to have anything to do with the severity of the depression.(Carrozzino et al., 2020)

Table 1. Items of the most widely used HAM-D versions

Number	Items	Range of scores													
		Hamilton [2] $HAM\text{-}D_{21}$ unstructured version with ratings only	Hamilton [2, 3] $HAM\text{-}D_{17}$ unstructured version with ratings only	Bech et al. [13, 14] $HAM\text{-}D_{6}$ unstructured version with ratings only	Miller et al. [21] $MiHRSD_{25}$ structured version with structured interview	Bech et al. [18] $HAM\text{-}D_{23}$ structured version with anchor points and item definitions	Williams [22] $SIGH\text{-}D_{21}$ structured version with structured interview	Potts et al. [24] $SI\text{-}HDRS_{17}$ structured version with structured interview	Gelenberg [11] $HAM\text{-}D_{27}$ unstructured version with ratings only	Williams et al. [26] $SIGH\text{-}SAD_{29}$ structured version with structured interview	Moberg et al. [27] $HAM\text{-}D_{24}$ structured version with structured interview	Morriss et al. [19] $HDRS_{17}$ structured version with semi-structured interview and anchor points	Timmerby et al. [20] $HAM\text{-}D_{6}$ structured version with semi-structured interview and anchor points
1	Depressed mood	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4
2	Feelings of guilt	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–3	0–4	0–4	0–4	0–4
3	Suicide	0–4	0–4	–	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	–
4	Insomnia, early	0–2	0–2	–	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	–
5	Insomnia, middle	0–2	0–2	–	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	–
6	Insomnia, late	0–2	0–2	–	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	–
7	Work and interests	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4
8	Psychomotor retardation	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4
9	Psychomotor agitation	0–2	0–2	–	0–2	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	–
10	Anxiety, psychic	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4
11	Anxiety, somatic	0–4	0–4	–	0–4	0–4	0–4	–	0–4	0–4	0–4	0–4	0–4	–
12	Somatic symptoms, GI	0–2	0–2	–	–	0–2	0–2	–	0–2	0–2	0–2	0–2	0–4	–
13	Somatic symptoms, general	0–2	0–2	–	–	0–2	0–2	0–4	0–2	0–2	0–2	0–2	0–2	–
14	Genital symptoms	0–2	0–2	–	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	–
15	Hypochondriasis	0–4	0–4	–	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	0–4	–
16	Loss of weight	0–2	0–2	–	0–2	0–2	0–3	–	0–2	0–2	0–2	0–3	0–2	–
17	Insight	0–2	0–2	–	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	0–2	–
18	Diurnal variation	0–2	–	–	0–2	–	0–2	–	0–2	–	–	0–2	–	–
19	Depersonalization/derealization	0–4	–	–	–	–	0–4	–	0–4	0–4	0–4	0–4	–	–
20	Paranoid symptoms	0–4	–	–	–	–	0–3	–	0–3	0–3	0–3	0–3	–	–
21	Obsessive/compulsive	0–2	–	–	–	–	0–2	–	0–2	0–3	0–2	0–2	–	–
22	Tiredness and pains	–	–	0–2	0–2	0–4	–	0–2	–	0–2	–	–	–	0–2
23	Distinct quality of mood	–	–	–	0–2	–	–	–	–	–	–	–	–	–
24	Lack of reactivity	–	–	–	0–2	–	–	–	–	–	–	–	–	–
25	Worthlessness	–	–	–	0–4	–	–	–	–	–	0–4	–	–	–
26	Helplessness	–	–	–	0–4	–	–	–	–	–	0–4	–	–	–
27	Hopelessness	–	–	–	0–4	–	–	–	–	–	0–4	–	–	–
28	Loss of appetite	–	–	–	0–2	–	–	0–2	–	–	–	–	–	–
29	Weight gain	–	–	–	0–2	–	–	–	0–2	0–2	–	–	–	–
30	Loss of interest	–	–	–	0–2	–	–	–	–	–	–	–	–	–
31	Insomnia, general	–	–	–	–	0–4	–	–	–	–	–	–	–	–
32	Retardation (motor)	–	–	–	–	0–4	–	–	–	–	–	–	–	–
33	Retardation (verbal)	–	–	–	–	0–4	–	–	–	–	–	–	–	–
34	Retardation (intellectual)	–	–	–	–	0–4	–	–	–	–	–	–	–	–
35	Retardation (emotional)	–	–	–	–	0–4	–	–	–	–	–	–	–	–
36	Loss or gain of weight	–	–	–	–	–	–	0–2	–	–	–	–	–	–
37	Fatigue	–	–	–	–	–	–	–	0–4	0–4	–	–	–	–
38	Social withdrawal	–	–	–	–	–	–	–	0–4	0–1	–	–	–	–
39	Appetite increase	–	–	–	–	–	–	–	0–2	0–3	–	–	–	–
40	Carbohydrate craving	–	–	–	–	–	–	–	0–3	0–3	–	–	–	–
41	Hypersomnia	–	–	–	–	–	–	–	0–4	0–4	–	–	–	–
42	Increased eating	–	–	–	–	–	–	–	–	0–3	–	–	–	–
43	Diurnal variation type A	–	–	–	–	–	–	–	–	0–2	–	–	–	–
44	Diurnal variation type B	–	–	–	–	–	–	–	–	0–2	–	–	–	–

HAM-D, Hamilton Rating Scale for Depression; GI, gastrointestinal.

Figure 8 List of different versions of the HAM-D rating scale, and the similarities and differences. From "The Hamilton Rating Scales for Depression: A Critical Review of Clinimetric Properties of Different Versions" by Carrozzino et al.*, 2020, Psychotherapy and Psychosomatics, 89(3), p. 135, DOI: 10.1159/000506879.*

As seen in the figure above, there are 12 different versions of the Hamilton Rating Scale that are widely used. There is a lot of similarities between them, and the main difference is the items, or symptoms, and whether or not the versions are structured or unstructured. The differences in symptoms are both that new symptoms are added or removed, and a difference in how each symptom is scored. The HAM-D_6 unstructured version with ratings only, published by Bech et al., and the HAM-D_6 structured version with semi-structured interview and anchor points published by Timmerby et al. are shortened versions of the original Ham-D_{21} rating scale that only uses 6 core symptoms of depression. On the other side there are versions with as many as 36 items. (Carrozzino et al., 2020)

The other thing that differs the different version is as mentioned whether they are structured or unstructured. A HAM-D is categorized as unstructured when the rating scale is based on the scoring points alone. Max Hamilton stated that the best way to measure the severity of the depression was to solely base the evaluation on rating points, as the process of interviewing the patient depended "entirely on the skill of the interviewer in eliciting the necessary information" (Hamilton, 1960) meaning that when rating the patient the only dependency were the clinicians expertise of judging the ratings, not the interviewing skills additionally, which may not always be the primary skill of every academically focused doctors.

6.2.2 Depression costs

It is no secret that healthcare is expensive, and most illnesses costs the society time, money and reduced working capacity. Depression disorder is no exception, as it is not only causing the patient misery and torment, but it also has a serious economic impact on the world's population. As depression disorder often is a chronic recurring disease, the patient will need treatment several times throughout its lifetime. The fact that it also causes many absent workdays and often early retirement is other factors that causes burden on the society (Kleine-Budde et al., 2012) A study made by Kleine-Budde et al in 2012 uses data from a German health insurance company to find the annual cost to the society per patient with depression. In this study, containing data from in excess of 117'000 German patients, the authors found that the mean cost per patient on depression-specific costs were 458.9 Euros per year. It was also clear that the severity of the disease, as well as age, gender and area of living had a significant influence on the depression-specific costs. (Kleine-Budde et al., 2012)

As Germany is a highly industrial country with, to my knowledge, prices above the worlds average, it would probably not be completely right to assume that the number of 458.9 Euros per patient per year is applicable to use as an average price in the world. Assuming that the average price per patient per year is in fact 458.9 Euros, and that there are about 300 million humans in the world suffering from depression disorder (Figure 2), this will make up 137.67 billion Euros every year.

6.3 Anxiety disorder

6.3.1 History

"Generalized anxiety disorder (GAD) is a mental disorder in which a person is often worried or anxious about many things and finds it hard to control this anxiety." (MedlinePlus Medical Encyclopedia et al., n.d.)

This mental illness has had many different interpretations over the course of history. In the beginning of the modern psychiatry, it was known under the name *panophobia*, which can be translated to "the fear of everything". This term was used from late 1700 to the middle of 1800. As the condition were reported to come in paroxysmal attacks (symptoms comes very sudden in a short period, like for example a spasm) there were a broad understanding that GAD and panic attacks were part of the same illness. (Crocq, 2017)

Developing the understanding of mental illnesses further, George Beard introduced a new category to diagnose mental illnesses in the second half of 1800 which he called *Neurasthenia*. The term translates to weak nerves and is a condition describing a mechanical weakness in the nerves. It was believed to be a result of overstimulating the central nerve system, resulting in nerve fatigue. Beard argued that this was a result of the constant, high tempo in the modern day-to-day life. (Beard, 1880) Later, there were some that speculated that Americans were extra receptive to get neurasthenia, and therefore started calling it "Americanitis." (Daugherty, 2015) Beard meant that panophobia could be one of the outcomes from neurasthenia and wrote in his treatise that "There is a manifestation of morbid fear which is not uncommon, and to which we might perhaps give the term pantaphobia, or fear of everything." (Beard, 1880) Although the anxiety diagnose were taken further by Sigmund Freud already before the turn of the 19th century, the diagnose neurasthenia was included as late as in the ICD-10 (International Classification of Diseases, by World Health Organization), which is the predecessor of today's ICD-11. Even though the work of the ICD-11 were started in 2007, it wasn't official in effect until 1. Jan 2022, meaning that it is first this year that neurasthenia is no longer an official diagnose. (Harrison et al., 2021)

As stated above, Sigmund Freud took the diagnose panophobia further by introducing the term *Anxiety Neurosis* in his article "On the grounds for detaching a particular syndrome from neurasthenia under the description 'Anxiety Neurosis'" published in 1895. He believed

that this anxiety neurosis was a result of “sexual excitation that could not find discharge in coitus.” (Crocq, 2017)

6.3.2 Prevalence

As the depression disorder and anxiety disorder is closely connected, there is no surprise that the prevalence of anxiety is in many ways connected to depression as well. In this chapter data from Institute for Health Metrics and Evaluation (IHME), Global Burden of Disease will be commented by the help of maps and graphs gathered from *Our World in Data.* (Dattani et al., 2021) It is of great importance to spend some time looking at the prevalence of depression and anxiety in order to understand and find markers to what the common factors amongst the patients are.

6.3.2.1 Geographic

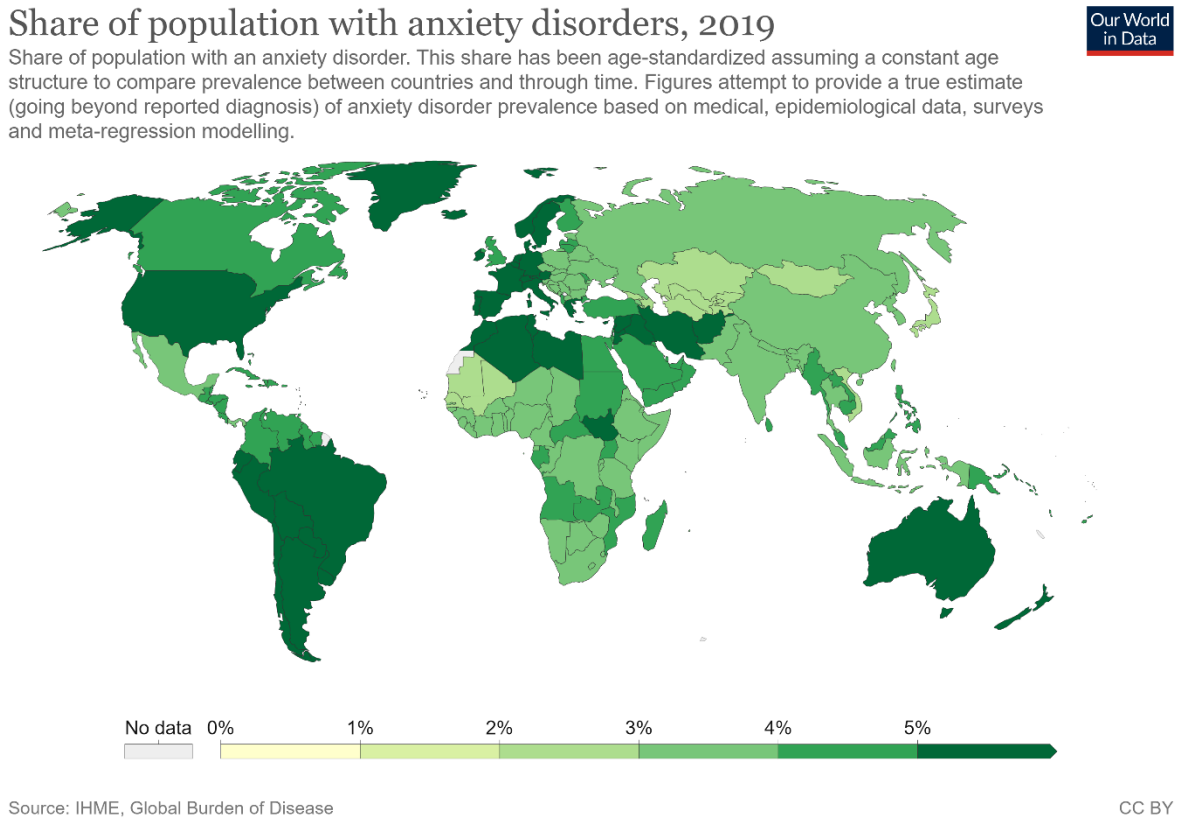


Figure 9 Map of the world showing the share of population with anxiety disorders in 2019

In the map above, the share of population with anxiety disorders in 2019 per country is displayed. As with depression disorder, the anxiety disorder is highly prevalent in Southern America, as well as in the western countries such as United States, Australia and the western part of Europe. The northern part of Africa, as well as countries in the Middle East is also

having a high prevalence of anxiety disorders.

6.3.2.2 DALY

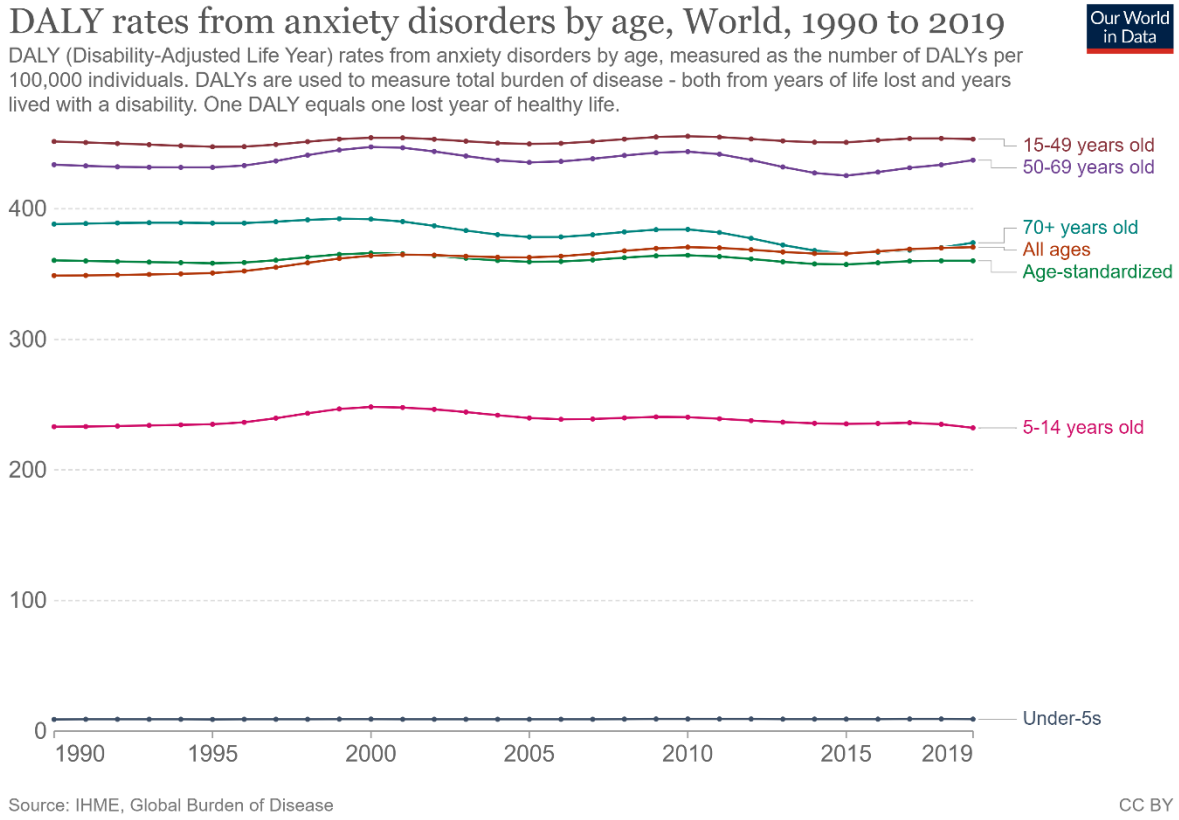


Figure 10 Graph showing DALY rates from anxiety disorders by age in the World from 1990 to 2019

Disability Adjusted Life Years or DALY is, as stated in the depression chapter, the World Bank's way of measuring disease burden and the effect on measures done against the burdens. In Figure 10 above the DALY rates from anxiety disorders in the World, grouped by age, from 1990 to 2019 is displayed. Looking at the graph, you can see that the disease burden has been more or less stable the last thirty years. Overall, on all ages, the DALY has increased a little, but there has been no change in the positions between the age group, with young people between 15 and 49 has a slightly higher disease burden than the 50-69 group. Even though the disease burden amongst children and young teens are about half of the burden amongst the adults, the number is still very high.

Looking at the figure below, the rate of disease burden from anxiety disorders between 1990 and 2019 is grouped geographically. Looking at the different continents, you can see that both Asia and Africa have a rate of disease burden which is lower than the average in the world.

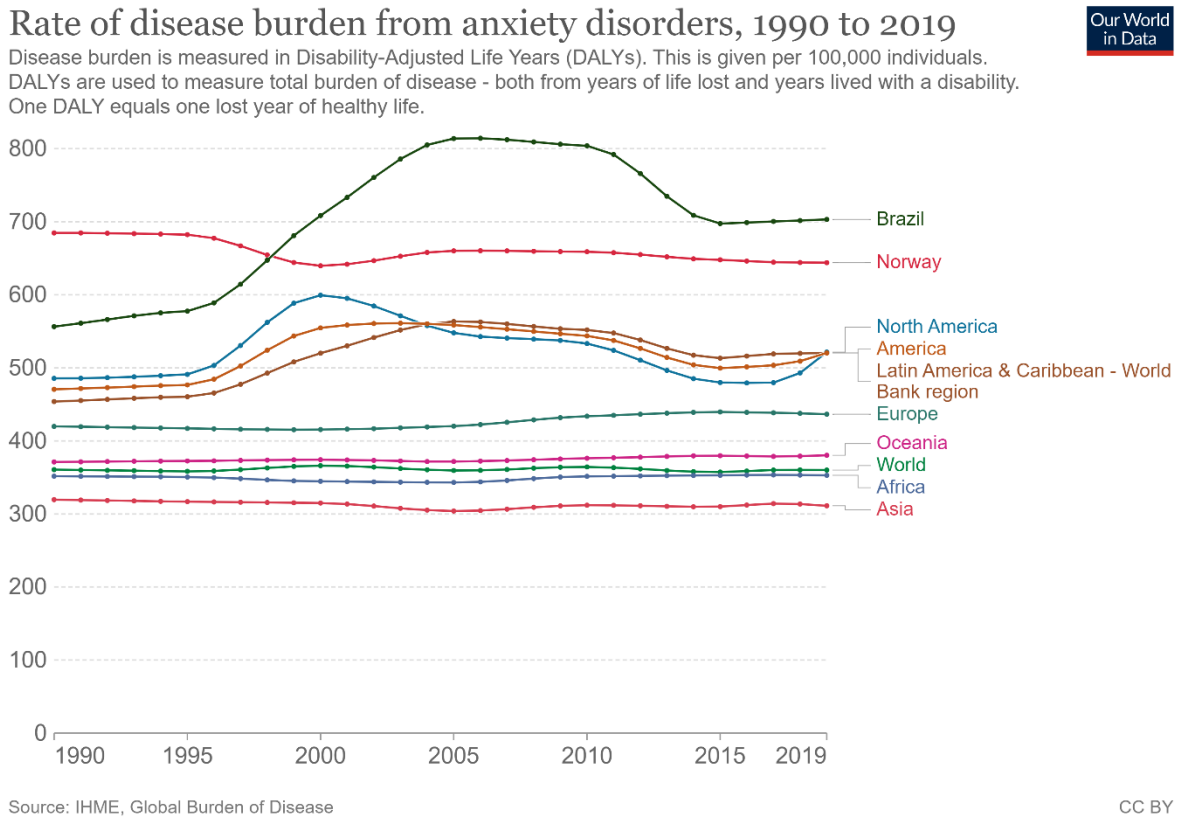


Figure 11 Graph showing the DALY rate of disease burden from anxiety disorders from 1990 to 2019 grouped geographically

While Africa and Oceania have a DALY rate almost at the World average, both Europe and especially North and South America has a significantly higher anxiety disease burden than the rest of the world. On interesting thing that is worth noticing is that while the DALY rate in Europe, Oceania, Africa and Asia has had a stable evolvement throughout the last thirty years, the Americans, both northern and southern, has had a wavier evolvement. As Brazil was mentioned in the introduction as a country with high prevalence of both depression and anxiety, it is interesting to see how the country is compared to the rest of the world. As seen in the graph, there was a significant increase in disease burden in Brazil in the decade from ’95 to ’05, before being reduced and evened out the last 15 years. But as Feter et al. stated, the number of participants in their study reporting moderate or severe anxiety increased as much as 7.4 times during the first year of the Covid-19 Pandemic, which would make the graph make a significant leap upwards from the already high number. (Feter et al., 2021) Comparing the evolution of anxiety’s disease burden in Norway compared to the rest of the world is interesting as well. Here in Norway, the DALY is actually slowly decreasing, and has more or less done so the last thirty years. But as with Brazil and the United States, there are

studies suggesting that the impact of the pandemic has been huge in the rest of the world as well, and that the DALY rates most likely has had an increase the last years. (Rosenberg et al., 2021; Ulset et al., 2021)

6.3.2.3 Gender

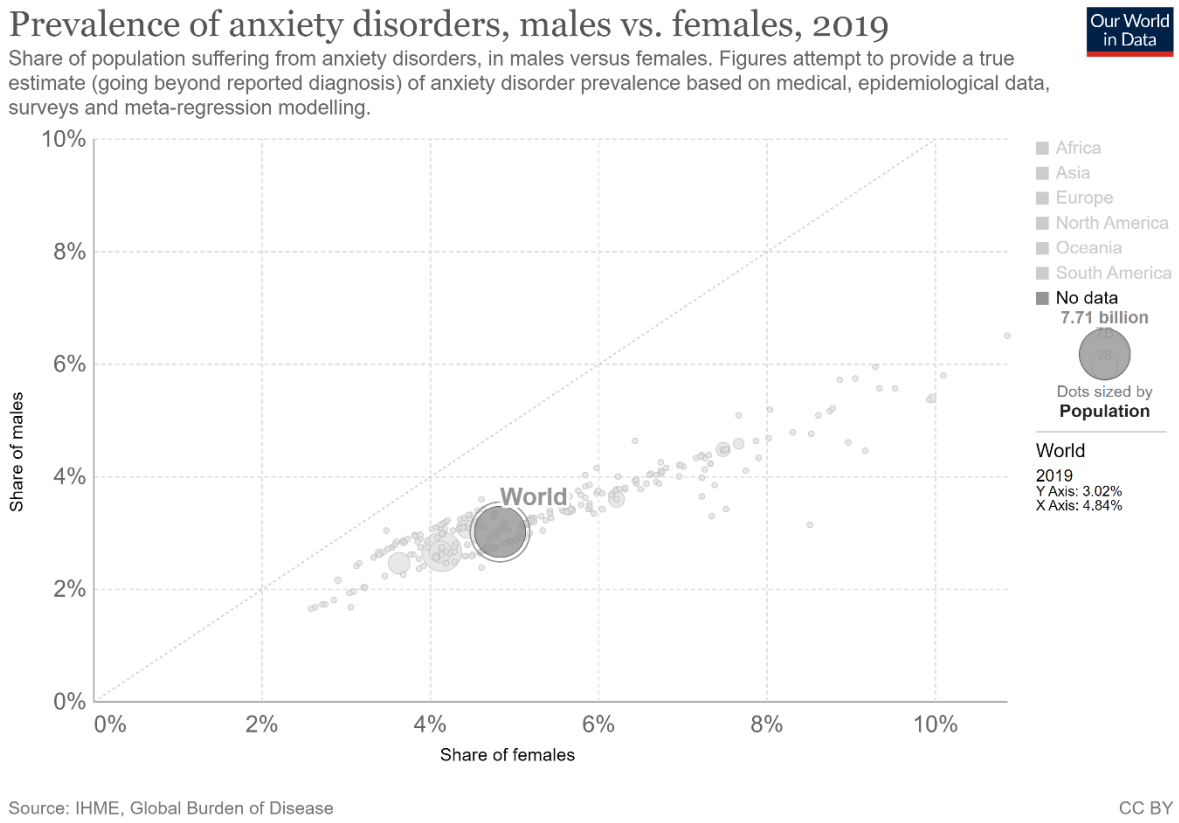


Figure 12 Graph showing the share of population suffering from anxiety disorders, males versus females, in 2019

The figure above is showing the prevalence of anxiety disorders amongst the gender's male and female in the world. The large circle "World" shows the percentage of males and females and is clearly placed in the downside of the diagonal line that represent an even distribution between men and women. This figure shows that in the whole world 3.02% of all males and 4.84% of all women are suffering from anxiety. The other smaller circles are not tagged with names but are different countries and continents throughout the world. Thus, there are no country or continent in the world where there are more men than women than has anxiety disorder. This is, as stated earlier, something that we find amongst persons with depression disorder as well.

In the figure below, we can see the number of people with anxiety disorders in the world from 1990 to 2019 divided into genders. There are as we can see just above 300 million

people in the world suffering from anxiety disorder, and the trend is clearly that the number is just going up, with an increase of almost 50% the last thirty years from just below 200 million in 1990 to 300 million in 2019. Another interesting fact is that the slope of number of males with anxiety is steeper than the slope showing number of females with depression. This is something that we saw in the depression graph as well. If this trend is continuing the number of males will by time catch up with the females.

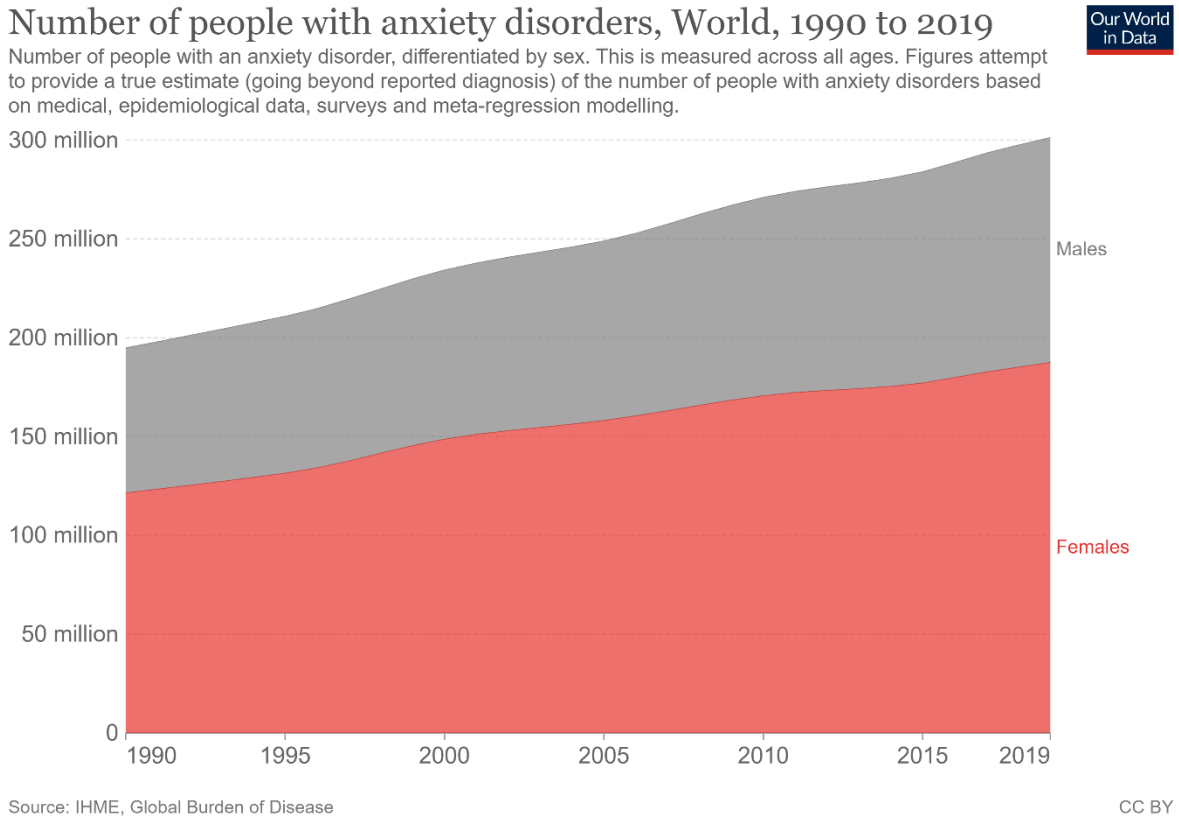


Figure 13 Graph displaying the evolution of number of people in the world with anxiety disorders from 1990 to 2019 categorized by gender

6.3.2.4 Age

In the DALY segment above, we looked at the disease burden of anxiety disorder roughly divided by age. In the figure below, the evolution of prevalence of anxiety disorders by age in the world from 1990 to 2019 is displayed in a finer grouping of age categories. Looking away from the large "15-49 years olds" group and seeing more on the smaller groups, it is the people in their early thirties and in their late career years that has the highest prevalence of anxiety. This corresponds well with the finding on depression as well. It is also worth mention that even though the prevalence amongst people between

5 and 14 years is clearly smaller than the rest of the population, except the even younger children, there are a prevalence of about 2.5%. This means that as many as one in 40 small children is suffering from this disease. Even higher is the group of children between 10 and 14 years old with a prevalence on about 3.5%, which corresponds to every 1 in 28 children, or one in every class, is having an anxiety disorder.

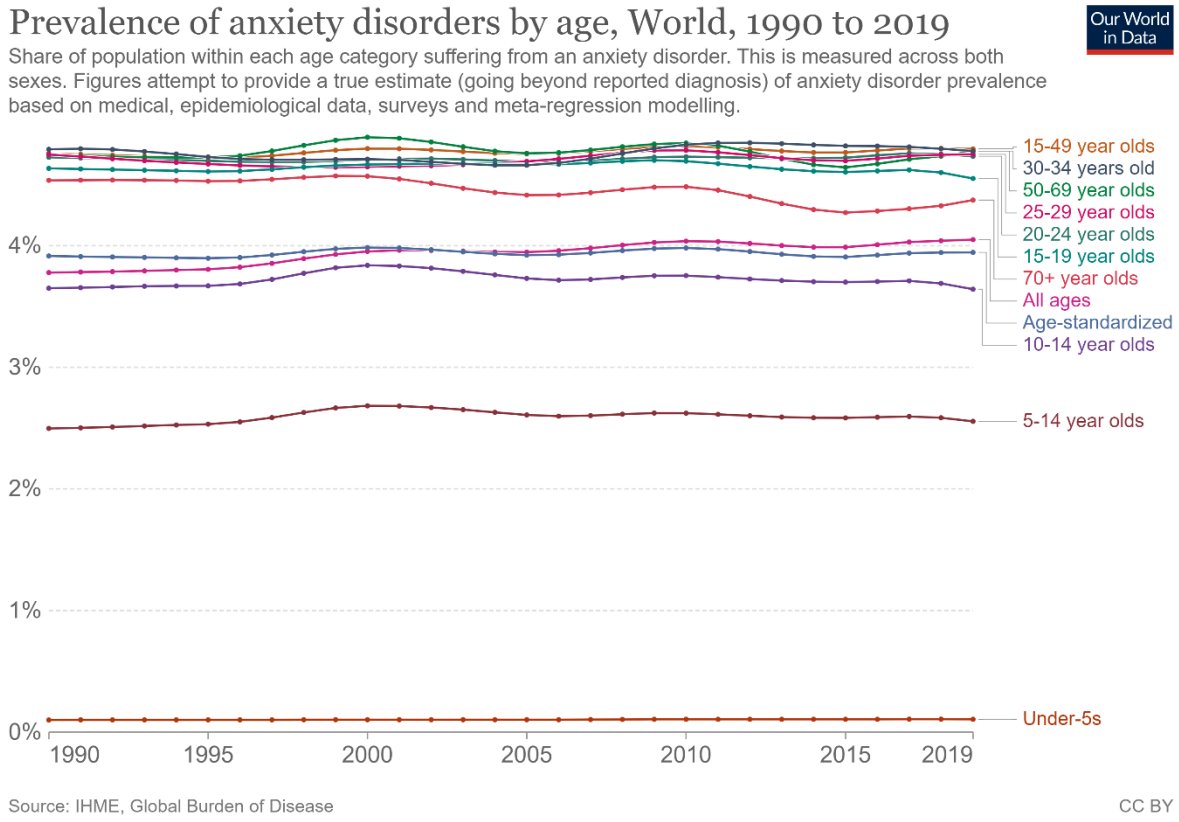


Figure 14 Graph displaying the evolution of prevalence of anxiety disorders by age in the world from 1990 to 2019

6.3.2.5 *Economy*

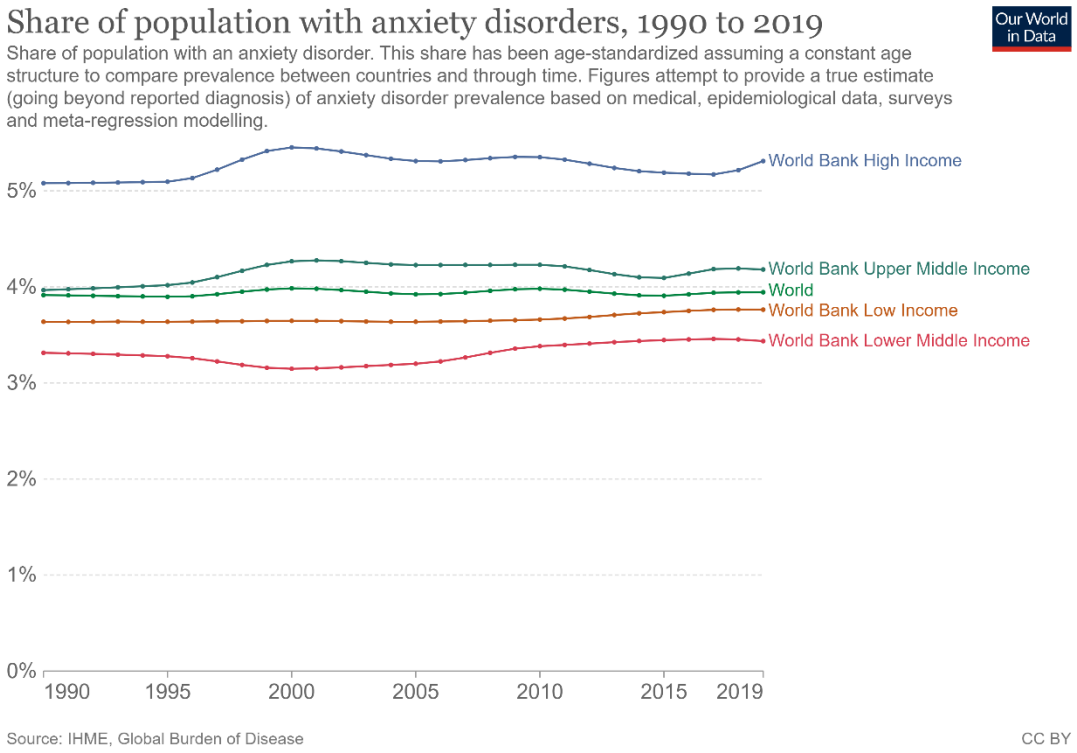
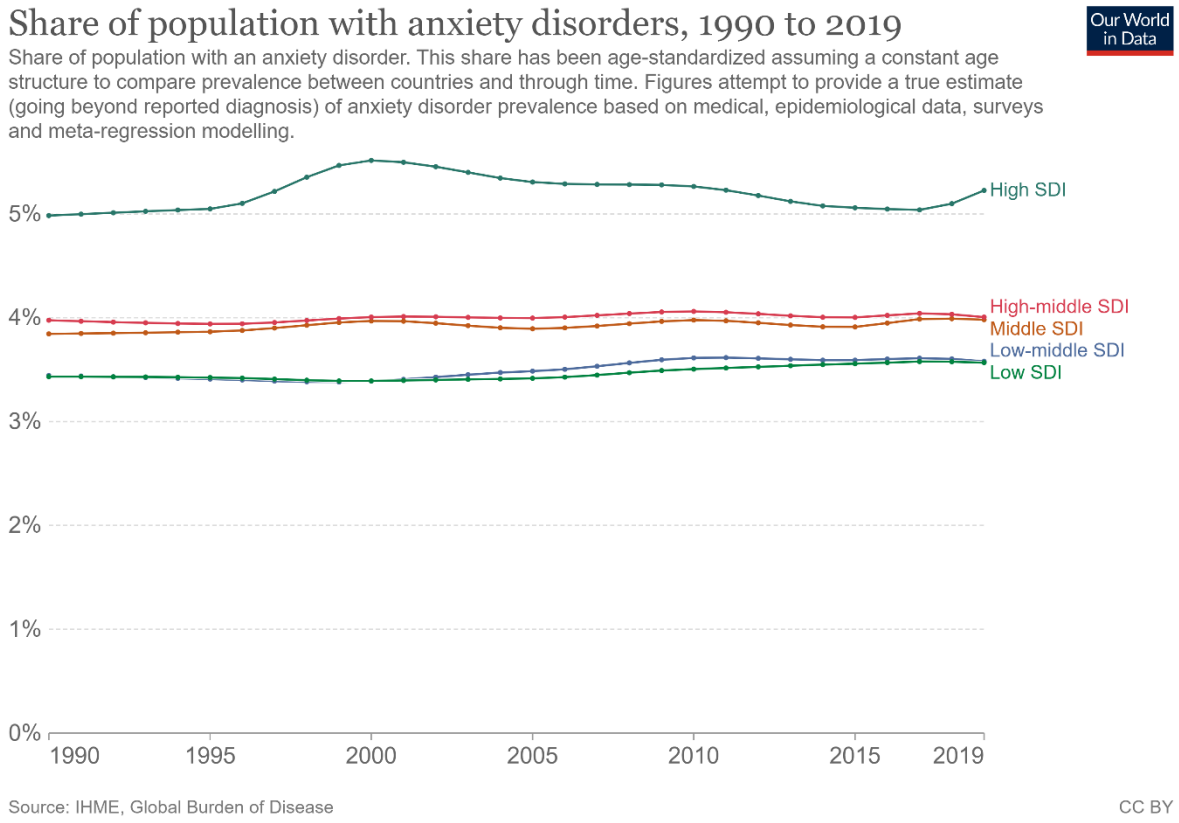


Figure 15 Graph displaying the evolution of the share of population with anxiety disorders from 1990 to 2019 based on the World Bank's Economy groupings.

In Figure 15 above, the share of population with anxiety disorders from 1990 to 2019 is divided into the World Bank Income Categories “World Bank High Income”, “World Bank Upper Middle Income”, “World Bank Lower Middle Income” and “World Bank Low Income”. As was possible to see in the world map in Figure 9, it is the wealthiest countries that has the highest prevalence of anxiety disorder, by a significant amount as well. It is interesting to see that it is the two lowest income categories that has the lowest prevalence of anxiety. That might suggest that money is not all that matters in the world.

6.3.2.6 SDI



As with the World Bank Income Categories, we find many of the same things here in the table above showing the evolution of the share of population with anxiety disorders from 1990 to 2019 based on the Sustainable Development Index. The countries in the "World Bank High Income" category are as usual high on the Sustainable Development Index as well, and we can see that the countries with the highest prevalence of anxiety is the ones in the "High SDI" category. The prevalence of anxiety amongst SDI categories is actually complete reverse of what one might think. Here are the lowest SDI categories the ones with the lowest prevalence, and all the categories from lowest to highest SDI corresponds to their level of prevalence.

6.3.2.7 Summary

To sum up the findings of what is the "typical" Anxiety patient, it will be a woman in her early thirties. Most likely coming from a country high on the SDI scale, as well as in the highest tier regarding the World Bank's Income classification, preferably in the American continent.

6.3.3 Impact

Anxiety disorder's economic impact on society is, like with Depression disorder, very high. In

a review article from 2020 by Konnopka et al. they found that the total cost of Anxiety Disorder amongst the countries in The Organisation for Economic Co-operation and Development (OECD) were as high as 118 billion USD in direct costs and 122 billion USD in indirect costs, making a grand total of 240 billion USD. This high number is of course making it a no-brainer to find the best ways of treatment and prevention.(Konnopka et al., 2020)

6.4 Treatment

6.4.1 Attention Bias Modification Training

So, what is Attention Bias Modification Training, and what has been done so far on this subject?

Individuals who are suffering from anxiety and depression is tending to focus more on the negative aspects of life. Studies has shown that a bias against the negative, a negative attentional bias, is having a crucial role in both developing and keeping a depression disorder. Several researchers have proved that depressed patients tend to have a focus and attention against negative information. (Beck, 2008; Disner et al., 2011; Gotlib & Joormann, 2010; Peckham et al., 2010) There has been found evidence that even having a mother that is showing negative attention biases gives girls, both previously suffering from depression, but also girls who never has had a depressive episode, has a higher risk of (re)developing depression disorder. This suggests that, as stated above, that negative attention biases are not only a sign of bad mood and depression, but also a factor that could trigger and develop a depressive disorder. This means that negative attention bias is not only a marker for depression, but also a vulnerability factor. (Yang et al., 2015)

MacLeod et al. wanted to explore this further. They conducted a study that used a probe detection task that tried to train the subjects into getting a bias against preferring negative words over neutral ones. After a period of attention bias training, they did some stress tests on the subjects. The results were conclusive that the ones having trained their attention bias towards the negative words responded more negative, with a higher level of depression and anxiety related factors to the applied stress. (MacLeod et al., 2002) This seminal study is important in the way that it shows that the attention bias is in fact trainable, making it possible to train the selective attention in a positive way.

Another study from 2009 by Wells and Beevers were using a similar approach. Instead of using neutral and negative words, they wanted to try to change the attention towards the positive, rather than towards the negative. In this way, they did not try to prove that the attention bias could be modified, and that it could cause depression, but rather see if this could be used as a treatment method for helping patients suffering from depression disorder get better. Instead of using words they used sad and neutral faces. The training process presented the sad faces as negative and induced a selective processing of the faces that were

neutral. A probe detection task works in the way that when a dot probe replaces a negative loaded image or word, a person with anxiety or depression will respond quicker than if it is replacing a positive or neutral image or word. The purpose of the training is to alter this reaction time so instead of reacting fastest to the negative biased stimuli, it will get the patient to react faster towards the neutral or positive stimuli. The participants completed four sessions of training during a period of 14 days. After the training period, the participants that had completed the training had a significant lower attention bias towards negative stimuli. They also had a clear change for the better when it came to depressive symptoms compared to before starting the study and compared to the placebo contenders. (Wells & Beevers, 2009)

Several studies in the past have shown promising results, and in this thesis some of the data will be analysed further to see if more specific markers and traits for improvement can be found. (Bø et al., 2021; Jonassen et al., 2019; Kraft et al., 2019)

7 Method

The objective in this thesis is to do a deep dive into the data gathered from the patients going through the Attention Bias Modification Training against anxiety and depression to see if it is possible to get a clearer understanding of who this training would be the most effective on.

7.1 Datasets

The data consists of three sets of data. The biggest dataset contains just under 823’000 rows of information of the training the patients has gone through. This data has the following information:

- Participant ID
- Date
- Time
- Session Number Today (The participants had two sessions a day)
- Cumulative Session Number
- Stimulus Type, which in all cases were faces
- Training Type (this was either neutral or positive; placebo or not placebo)
- List Used
- Trial Number (Each session consists of 96 trials)
- Negative Stimulus (Which face was shown as negative stimulus)
- Positive Stimulus (Which face was shown as positive stimulus)
- Pair Type (Could either be negative/neutral, negative/positive or neutral/positive)
- Location of Positive Stimulus (whether the positive stimulus was on top or bottom)
- Probe Type (whether the probe was one or two dots)
- Probe Location (whether the probe was on top or bottom)
- Stimulus Presentation Duration (the stimulus lasted either 500ms or 1000ms)
- Response (The participant should respond to the probe type with either a ‘m’ or a ‘z’, regarding the probe type)
- Response Accuracy (Whether the response from the participant was correct or not)
- Reaction Time (The time the participant used to respond to the stimulus)

The next dataset is a bit smaller and contains computed Attention Bias Index (ABI) and Adjusted Attention Bias Index (ABI_{adj}). The computation of the ABI is explained by Jonassen et al. in their paper *Effects of Attentional Bias Modification on residual symptoms in depression: A randomized controlled trial* from where the data is retrieved: "Attentional biases (AB) was calculated as the difference in reaction time in milliseconds (RT) between trials in which the probe replaced the relatively more negative face vs. the more positive face ([(SUM (more positive face in upper screen position - locus of probe in lower screen position, more positive face in lower screen position, locus of probe upper screen position) – SUM(more positive face in upper screen position - locus of probe in upper screen position, more positive face in lower screen position - locus of probe in lower screen position)]/2.). Thus, a more positive score reflects a greater bias towards the more positive stimuli." (Jonassen et al., 2019)

This is the same as we can see in Equation 1 . If we say that T is the reaction time recorded a given day, we can classify the response time to whether or not the probe was placed in the positive location, and we get two T's. $T^{(s)}$ is the reaction time where the probe was placed on the same spot as the positive stimulus and $T^{(d)}$ is the reaction time where the probe was placed in the different spot than the positive stimulus. In the equation p is the absolute value of $T^{(d)}$ and q is the absolute value of $T^{(s)}$.

$$AB = \sum_{i=1}^{p} \tau_i^{(d)} - \sum_{i=1}^{q} \tau_i^{(s)}$$

Equation 1 Computation of Attention Bias Index

To get a number that is more comparable, the authors has adjusted the ABI, and created the ABI_{adj} using Equation 2.

$$AB_{adj} = \frac{1}{p}\sum_{i=1}^{p} \tau_i^{(d)} - \frac{1}{q}\sum_{i=1}^{q} \tau_i^{(s)}$$

Equation 2 Computation of Adjusted Attention Bias Index

Thus, the second dataset contains the ABI and ABI_{adj} for each day the participant is doing the training, as well as information about the training type (placebo or not) and how many trials where conducted the given day.

The third dataset is considerably smaller, containing only a row for 250 of the participants. Nevertheless, this contains all the personal data needed for being able to do the data analysis. This dataset has the following information for every participant:

- Participant ID
- BDNF_2 (Whether or not the patient has a Met allele of the neurotrophin Brain-Derived neurotrophic factor)
- BDNF_3 (Shows if the patient has 0, 1 or 2 number of Met alleles)
- Intervention (Placebo or positive training)
- BDI pre sum (Becks Depression Inventory, self-scoring scale for determining the presence and severity of depressive symptoms. Pre sum before ABM training)
- BDI post sum (BDI sum after ABM training
- BDI 1 month sum (BDI sum one month after ended training.
- Hamilton 1 month sum (Hamilton score one month after ABM training)
- Age
- Sex
- MDD recurrent no current (Whether or not the patient has had recurrent Major Depressive Disorder, but are not having one right now)
- MDD single no current (Whether or not the patient has had an MDD but are not having one right now.)
- Hamilton pre sum (Hamilton score before ABM training)
- Hamilton post sum (Hamilton score after ABM training
- Hamilton difference pre post (The difference in Hamilton score after and before ABM training)
- Hamilton pre 1 month (The difference in Hamilton score after one month of ended training and before training.)

7.2 Analysis

7.2.1 Orange

There was spent a whole lot of time trying to analyse these datasets using a software called Orange. Using component based visual programming and scripting in python, Orange is a data mining and machine learning suite which is open source. (Demšar et al., 2013) The idea

of using Orange as a data analysis program in this thesis were that it was a good way of testing its potential and limits and were stressed by the supervisors that it was preferable to try and use it. Since it is based on visual programming, with widgets connected to perform a workflow, it is thought that it is an easy entry for students with no, or little, programming experience. Figure 16 shows a typical workflow in the Orange program. Here it is possible to see a file that is being loaded in the file widget. This file is then sent to be displayed as a data

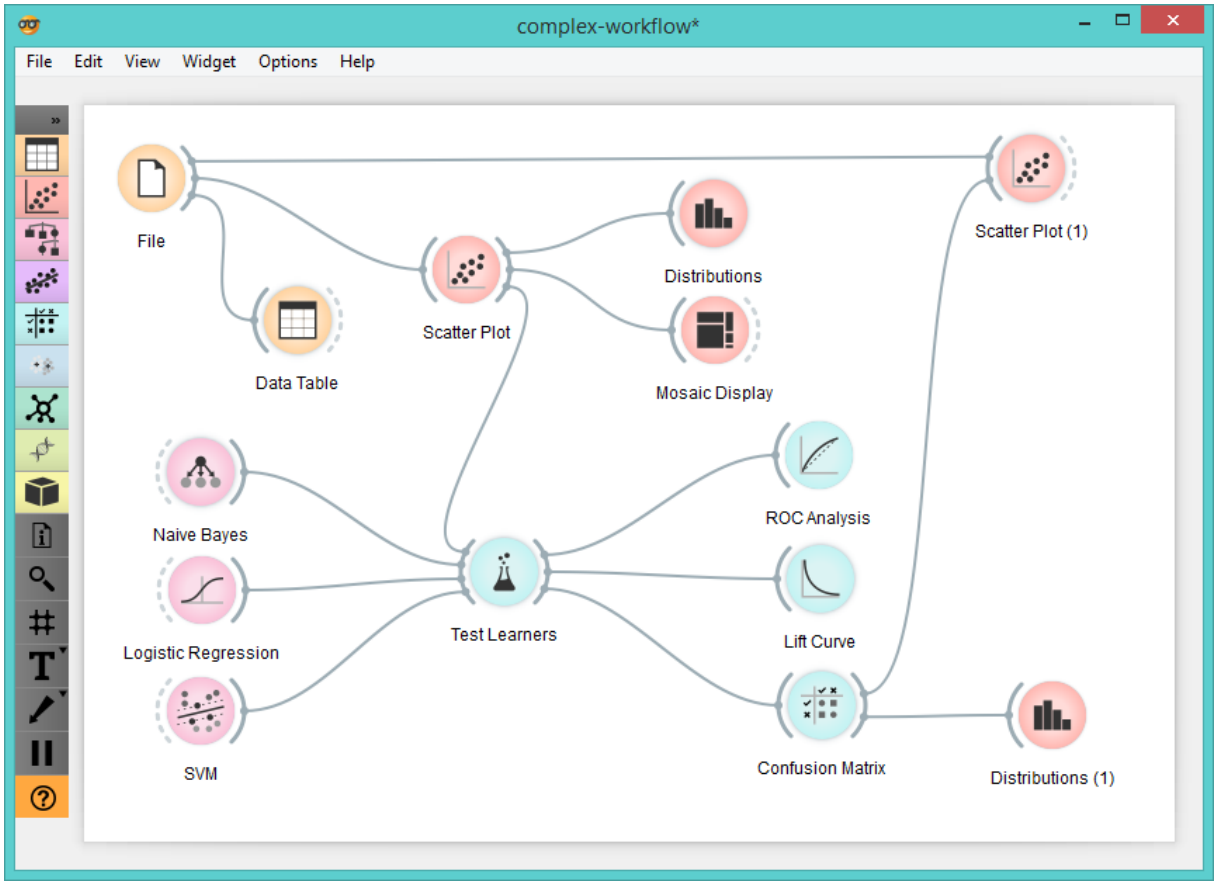


Figure 16 Displaying a typical workflow in Orange. By Vijolica9 - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=42219515

table and two scatter plots. Using naive bayes, logistic regression and SVM on the data from one of the scatter plots the software can use learning to perform different analysis and send the result further in the workflow to for example a new scatter plot or a bar chart showing distributions.

As shown in the figure, Orange is a very easy and straight forward software that can be good to use on some occasions. For this particular task, performing processing and analysis on huge dataset, Orange was not able to handle the amounts of data. This led to constant

crashing and frustration of not being able to perform the desired analyses. Due to this fact, the used software on the analysis were changed from Orange to the more well documented and used MATLAB.

7.3 MATLAB

After switching over to MATLAB, the pre-processing and data analysis could get started. The first part of the analysis was to get an overview over the data and understand what was possible to gather from it.

7.3.1 Training data

From the first data set, containing all training data, the following parameters were singled out as the most important one for analysing the data:

- Participant ID
- Cumulative Session number
- Training Type
- Trial Number
- Reaction Time
- Training Category

These numbers were used to get the mean and median reaction time from each session. Using a singular spectrum analysis (SSA) function in MATLAB called trenddecomp() on the mean and median reaction time for each participant, it was possible to get the long-term trend (LT) of the reaction time throughout the training period. Using the curve fitter application in MATLAB, the method curvefitter() was made and tweaked. Using this method, it was possible to retrieve a value for each participants reaction time slope. This was also done with the data form the first and second week separately.

7.3.2 ABM Index data

From the second dataset containing ABM data the first thing that was being done was to create a new table with some more data. This dataset contained, amongst other information, the Adjusted Attention Bias Index (ABI_{ajd}) from each day of training for each participant. Using the same method as with the reaction time data, the long-term trend of the ABI_{ajd} data was calculated and the slope data, both mean and median slope, was computed and added to the new table. As the ABM data did not contain any information on the participant other

than the participant ID this was added to the new table as well. This participant information was the age, the sex and the information on whether or not the participant had a Met allele of the neurotrophin Brain-Derived neurotrophic factor. (BDNF) Information regarding if the training type was positive or placebo were added as well. At the end, a new column containing a Boolean value stated if the participant had experienced an improvement in the ABI_{ajd} or not. The upper parts of the table are displayed in the figure below.

	1 ParticipantID	2 GroupCount	3 Median_ABM_Slope	4 Mean_ABM_Slope	5 Training Type	6 AGE	7 SEX	8 BDNF	9 ABM_Improvement
1	101	14	-0.7641	-0.7641	1	65	1	1	0
2	103	15	0.6023	0.6023	0	51	1	0	1
3	104	11	-7.7724	-7.7724	1	49	0	1	0
4	201	14	1.4313	1.4313	1	61	1	1	1
5	202	16	0.0065	0.0065	0	43	1	0	1
6	204	15	0.4900	0.4900	0	32	1	1	1
7	205	15	1.4328	1.4328	0	33	0	1	1
8	206	14	0.4461	0.4461	0	50	0	0	1
9	207	12	0.6460	0.6460	1	50	1	0	1
10	208	13	-0.2043	-0.2043	0	47	1	0	0
11	210	15	-0.0717	-0.0717	0	28	0	0	0
12	301	16	0.0866	0.0866	0	46	0	1	1
13	303	15	-0.1290	-0.1290	0	60	0	0	0
14	304	13	-0.4114	-0.4114	0	44	0	0	0
15	305	14	-0.0637	-0.0637	1	35	1	1	0

Figure 17 Figure displaying the upper parts of the ABM Info table created to do the ABM analysing on.

After creating the new table with more ABI_{ajd} information, it was time to do some analysing, to see if it was possible to find some common factors and markers amongst the patients that improved versus the patients that did not have an effect of the training.

The patients were grouped based on improvement in ABI_{ajd} and if the training type was positive or placebo. In these groups the mean and median age was computed, the number of females and males in each group were counted as well as adding a column with the percentage of males contra females in the group and a column with the overall percentage of males for comparison. The number of participants with the Val and Met allele of BDNF was added as well as two columns containing the percentage of Met alleles in each group and percentage of Met alleles in all the patients.

After doing these calculations, the participants were split into three age groups. These groups were participants from 18 to 36 years, 37 to 54 years and participants from 55 to 72 years old. When the participants were separated into these groups, the same calculations were done on a group level, so that the average and mean age, gender information and BDNF information were gathered on each group and placed together into a new table. This

was done so it would be even more clear how the age impacted the outcome of the training.

As well as doing the analysis on an age grouped level, the same calculations were also done with respect to time. The ABM Info table that was used to do the analyse were split into two, with one containing the ABI_{ajd} data of the participants from the first week of training, and the second containing the ABI_{ajd} data of the participants from the second week of training. Having the information from each week of training it was possible to do the same analyse that was being done on the dataset as a whole on the two weeks of training. The outcome of this analysis was gathered and placed in a new table containing the ABI_{ajd} analysis on the whole period as well as the ABI_{ajd} analysis on each week's data.

The purpose of doing the analysis with respect to time is that in every treatment method it is important to know and determine how early in a treatment process it is possible to see whether or not the treatment is having a positive impact on the patient. Even though this treatment process only lasted for 14 days, there are other treatment methods for other diseases that takes much longer time before the healthcare professional can confirm or deny its effect on the patient. For instance, my wife did go through a Botox treatment for chronic migraine for which it took 6-9 months to confirm that it did not work after all. This displays the importance of always manage to confirm a positive effect of a treatment as early as possible in the treatment process

7.3.3 Patient information data

From the last dataset, the one having information on age, sex, Hamilton and BDI scale score before, during and after the training it was possible to look more into what separated the participants that the training was effective on. The following parameters were singled out as the most important for analysing the data:

- Participant ID
- BDNF_2
- Age
- Sex
- Intervention
- BDI pre sum
- BDI pre post sum

- Hamilton pre sum
- Hamilton pre post sum

Using these parameters, it was possible to analyse what were the common factors amongst the ones getting better. Using the Hamilton pre post sum, there was made a comparison between the ones having a negative pre post sum, i.e., the ones that got a lower score on the Hamilton scale after finishing the training as opposed to before the training, with the ones having no or a positive change on the Hamilton scale. The parameters that were looked on was the mean and median age, the mean and median Hamilton score before training, sex and BDNF factor. This was made so that it would be possible to say anything about whether or not these factors would have an impact on the ABM training outcome. The table containing the Hamilton analysis grouped the participants in groups based on whether or not they improved their Hamilton score, meaning the score got lower and the severity of the depression lowered, and if their training type were positive or placebo.

After doing the analysis on the patients as a whole group, the participants were divided into the same groups based on age as in the ABI_{adj} analysis with one group for the participants between 18 and 36 years, one group for the participants between 37 and 54 years and one group for the participants between 55 and 72 years old.

	1 AGE_Category	2 Ham_Improvement	3 Training type
1	Age 18-36	0	0
2	Age 18-36	0	1
3	Age 37-54	0	0
4	Age 37-54	0	1
5	Age 55-72	0	0
6	Age 55-72	0	1
7	Age 18-36	1	0
8	Age 18-36	1	1
9	Age 37-54	1	0
10	Age 37-54	1	1
11	Age 55-72	1	0
12	Age 55-72	1	1

Figure 18 Table displaying the way the participants in the Hamilton analysis were grouped based on age, improvement, and training type

The same analysis that was done regarding improvement on the patients Hamilton scale, were made on the BDI scale as well.

7.4 Ethical Aspects

The datasets provided in this thesis is completely anonymized, with no other connection to the participants than their participant ID. The trial the patients participated in was retrospectively registered at ClinicalTrials.gov, with ID: NCT02658682 in January 2016. The participants handed in written informed consent before enrolment, and the study was conducted in accordance with the Helsinki Delcaration and the ethical principles for Nordic Psychologist and approved by regional committees for medical and health research ethics. (Jonassen et al., 2019)

8 Results

8.1 Attention Bias Index

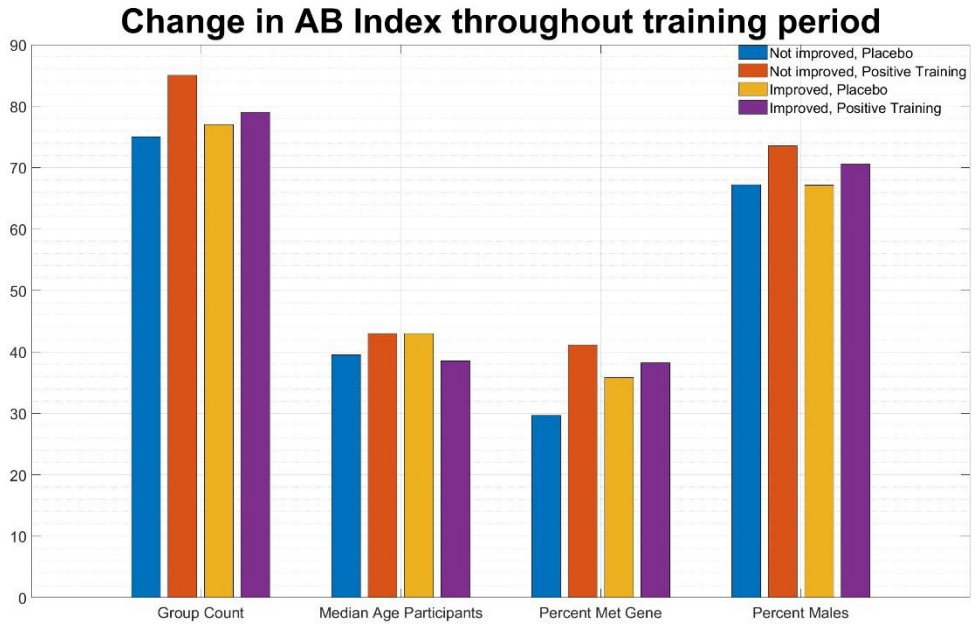


Figure 19 Bar chart displaying change in AB Index Throughout the Training Period

In regards of finding what was the common factors amongst the patients that responded positive to the Attention Bias Modification Training by improving the Adjusted Attention Bias Index (ABI_{adj}) three key factors has been singled out. These are the age, the gender and the version of BDNF alleles. In the figure above, a bar chart is showing these factors grouped in four. As visible in the chart legend, the four groups are the ones that improved their AB Index while undergoing positive training, the ones that improved their AB Index while undergoing placebo training, the ones that did not improve their AB Index while undergoing positive training and last, the ones that did not improve their AB Index while undergoing placebo training. In addition to the key factors, the number of patients in each group is displayed as well.

Comparing the people undergoing positive training, it is clear that the ones improving their AB Index is younger than the ones who doesn't. The median age amongst the improving participants is, as can be seen at more precise in Table 1, is 38.5 years while the median age of the not improving participants are 43 years.

Looking at the BDNF factor with Met and Val alleles, the patients going through the positive training and is improving their AB Index has a lower percentage of the Met gene, meaning a

higher share of the Val gene. Here is the percentage of the Met version 38.24% amongst the positive training patients that improved versus a 41.18% of the Met version amongst the positive training patients that did not improve their AB Index during the training period.

The last factor in the bar chart is the gender. As can be seen in Table 1 below, the average percentage of males in the positive training group is 72.1%. In the group of participants undergoing the positive training and are having a positive effect regarding AB Index, the percentage of males is lower than in the positive training group that did not have a positive effect regarding the AB Index. The percentage of males in the two groups are 70.6% and 73.5% respectively.

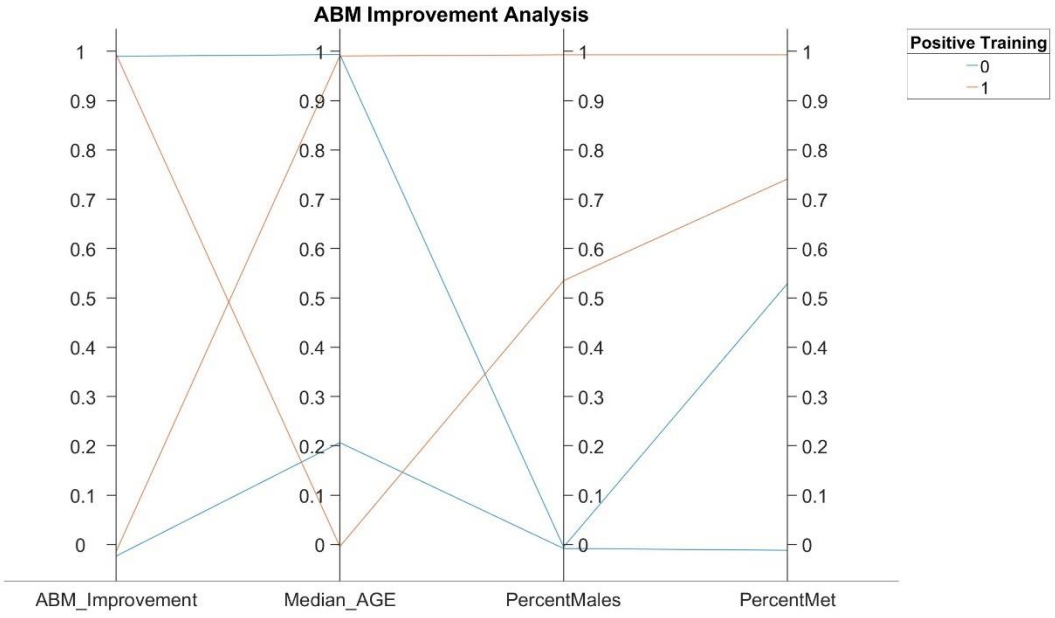


Figure 20 Parallel Plot of the AB Index improvement

In the figure above, the same key factors are displayed in a parallel plot that shows the results relative to each other. In this plot the two blue lines are the placebo groups, with one starting on a positive AB Index improvement, and one on the not improvement. The same goes for the orange line, in which the two positive training groups are shown. In this parallel plot, the difference in age on the two positive training groups are seen as the biggest difference, with the gender as second biggest difference and the BDNF factor as the closest.

Table 1 AB Index Improvement Analysis Table

ABI_{ajd} Improvement	Positive Training	Group count	Mean Age	Median Age	Female	Male	Percent Males	Total Percent Males	Val	Met	Percent Met	Total Percent Met
0	0	75	41.0781	39.5	21	43	67.1875	67.1756	45	19	29.6875	33.8244
0	1	85	42.6029	43	18	50	73.5294	72.0588	40	28	41.1765	39.7059
1	0	77	40.9254	43	22	45	67.1642	67.1756	43	24	35.8209	33.8244
1	1	79	40.1176	38.5	20	48	70.5882	72.0588	42	26	38.2353	39.7059

8.2 Hamilton

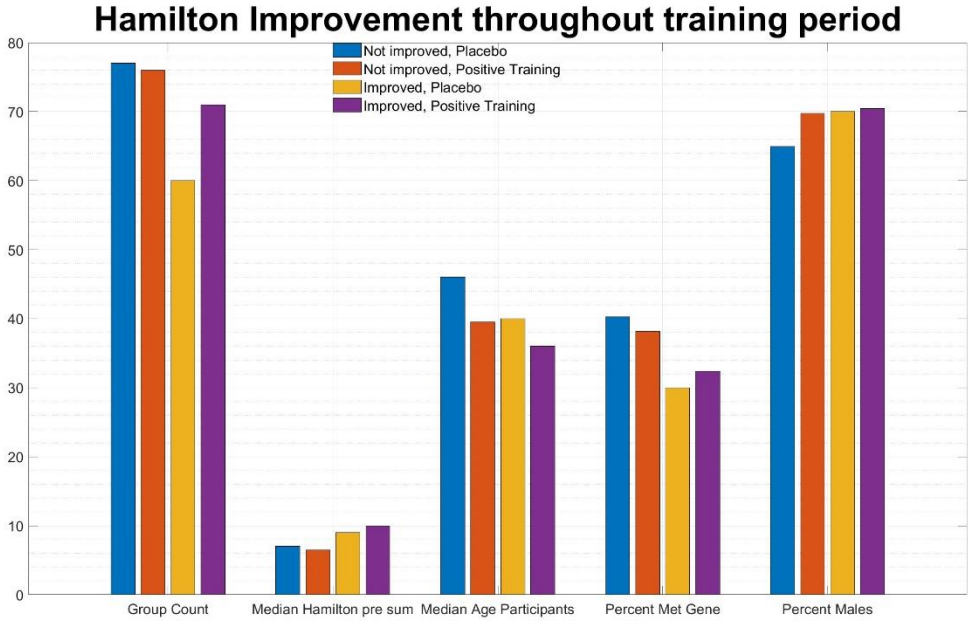


Figure 21 Bar Chart Displaying Characteristics with Patients with Respect to the Hamilton Scale Throughout the Training Period

The bar chart above is displaying the key factors looked at in the Hamilton improvement analysis, with the same groupings as in the AB Index analysis. These groups are the ones with positive training, and improvement on the Hamilton scale after ended training compared to before starting, the ones with positive training but no improvement, the ones with placebo training and improvement in the Hamilton scale and least, the ones with placebo training and no improvement on the Hamilton scale. The key factors to look at in the Hamilton analysis is the Median Hamilton pre sum, meaning the mean sum the participants in each group had before starting the Attention Bias Modification training, the median age, the percentage of the Met variant of BDNF and the percentage of males in each group. For more exact numbers, see Table 2 below.

Starting with the pre training median Hamilton sum, it is a big gap between the positive training participants that are improving and the ones that aren't improving their Hamilton score. For the group with an improved Hamilton rating, the median pre sum is as high as 10 while for the group that did not improve, their median pre sum was down on 6.5 (Mean sum was 11.4 and 7.5 respectively).

Looking at the median age of the participants, it is a clear connection to the AB Index results.

Here we can see that the median age of the participants undergoing positive training and are experiencing an improvement in their depression severity using the Hamilton scale are 36 years while the ones in the positive training group that did not improve, the median age are a bit higher, with 39.5 years.

The BDNF factor of the percentage of participants having the Met allele is similar to the AB Index as well. Here has the positive training patients with no improvement a higher amount of the Met gene than the positive training patients with an improvement on the Hamilton scale. The percentage of the Met allele is 38.2 % and 32.4% respectively.

Looking at the gender distribution of the groups, the positive training, Hamilton improvement group is actually having a higher percentage of males than the positive training group that did not improve. But as can be seen in the parallel plot below, the difference here is marginal, with 69.7% males amongst the positive training group that did not improve, and 70.4% males amongst the positive training group that did improve their Hamilton Score.

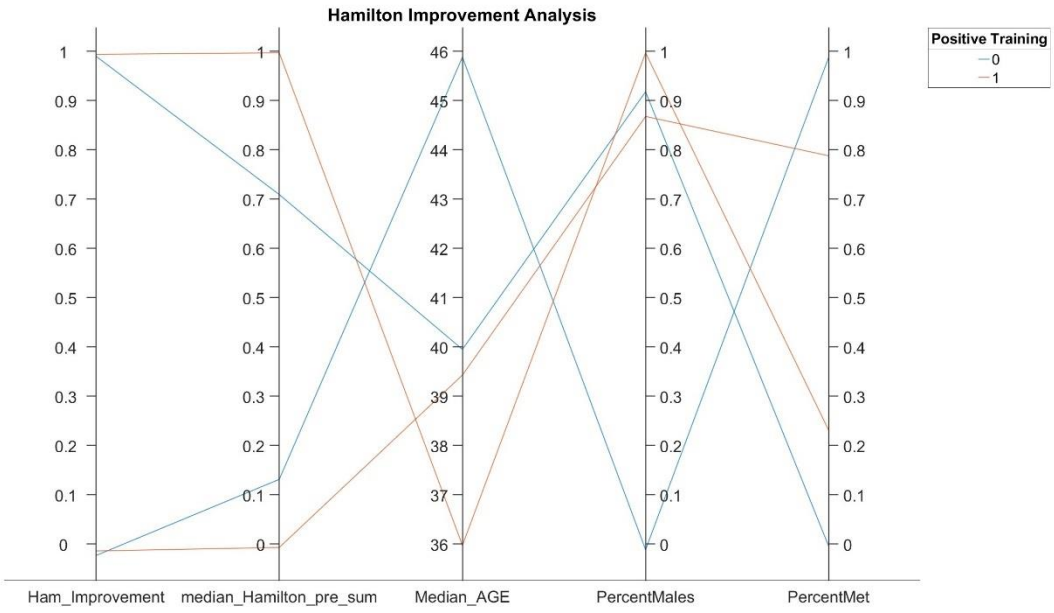


Figure 22 Parallel Plot of the Hamilton Improvement Analysis

When looking at the parallel plot of the Hamilton Improvement Analysis above, it is displayed clearly that the most important factor, or the factor that has the biggest difference amongst improvement or not in the positive training groups, are the median Hamilton score the

participants had before beginning their Attention Bias Modification training. The age scale in this plot differs from the rest of the scales, and from the age scale on the AB Index parallel plot, with the reason being unknown as the same code is being used to create both plots. The difference in age is nevertheless clearly displayed. As stated above, it is clear to see the small difference in gender percentage, while the BDNF factor has a larger difference and influence in the Hamilton Analysis than in the AB Index analysis.

Table 2 Hamilton Scale Improvement Analysis Table

Ham Improvement	Positive Training	GroupCount	Mean Age	Median Age	Val	Met	Percent Met	Total Percent Met	Mean Hamilton Pre-Sum	Median Hamilton Pre-Sum	Female	Male	Percent Males	Total Percent Males
0	0	77	42,53	46	46	31	40,26	35.77	7,22	7	27	50	64,94	67.15
0	1	76	42,13	39,5	47	29	38,16	35.37	7,53	6,5	23	53	69,74	70.07
1	0	60	40,6	40	42	18	30	35.77	9,35	9	18	42	70	67.15
1	1	71	37,90	36	48	23	32,39	35.37	11,41	10	21	50	70,42	70.07

8.3 BDI

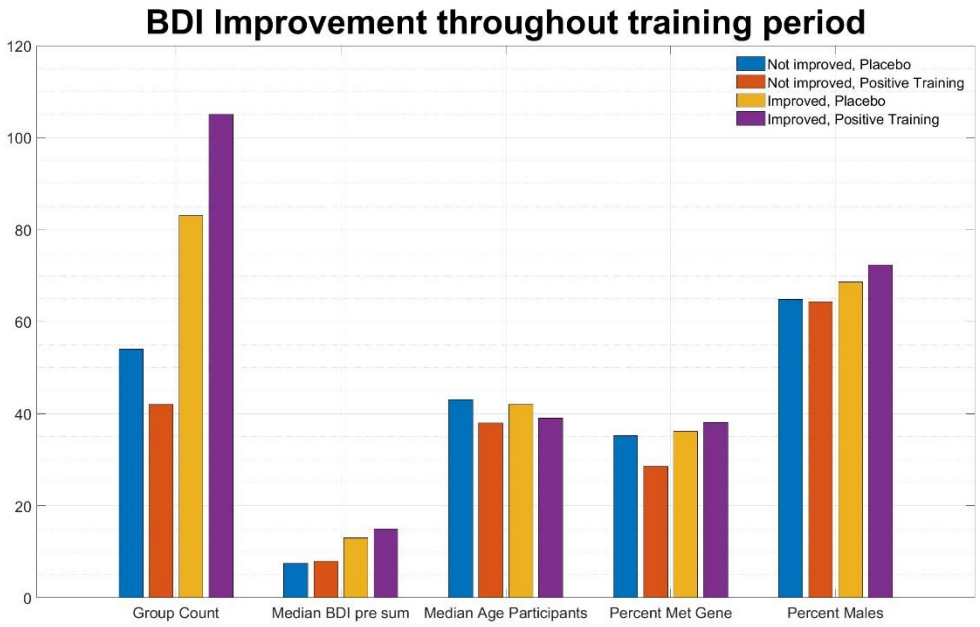


Figure 23 Bar Chart Displaying Characteristics with Patients with Respect to the BDI Scale Throughout the Training Period

Being a little more familiar with the plots, there is no need to dig as deep in them as earlier. The details are as usual in the table below. The key takeaways from the BDI Improvement analysis are as following:

- As with the Hamilton scale, the median pre sum has a lot of influence on the improvement. With a median pre sum of the positive, improved group of 15 on the BDI scale contra the positive, not improved group's 8 on the BDI scale, this is a clear indicator that this is a key factor looking for patients with great change of improvement using Attention Bias Modification Training
- The age is a lot closer on the BDI scale than with the Hamilton scale, and the median age of the positive, improved patients is actually higher than the age of the ones that did not improve their BDI score. Their score is 39 and 38 respectively.
- Regarding BDI scale, the improved patients with positive training had a higher percentage of the Met gene than the positive training patients that did not improve their score. The percentage is 38.1% and 28.6% respectively.
- The percentage of males having a positive outcome of the positive training is higher

than the percentage of males not having a positive outcome of the positive training. The percentage is 72.4% and 64.3% respectively.

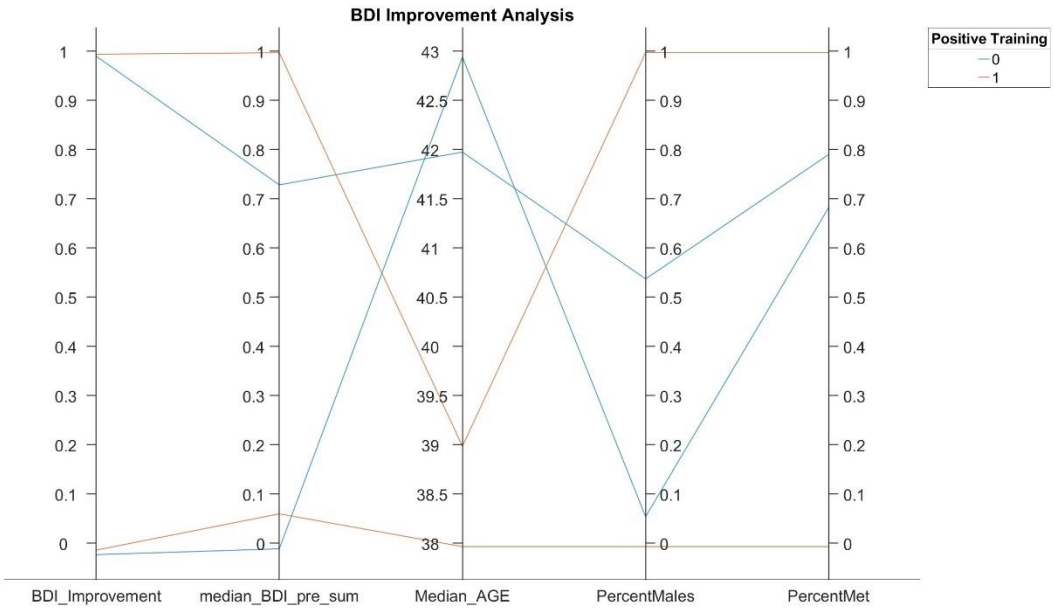


Figure 24 Parallel Plot of the BDI Improvement Analysis

The parallel plot of the BDI Improvement Analysis above shows that regarding improving on the self-reported BDI scale, the age has the least to say in whether or not the patient is having a positive training outcome of the Attention Bias Modification training. Based on the plot above, it is the gender and BDNF factor that has about equally large impact, with the median BDI pre sum right behind.

Table 3 BDI Scale Improvement Analysis Table

BDI Improvement	Positive Training	GroupCount	Mean Age	Median Age	Val	Met	Percent Met	Total Percent Met	Mean BDI Pre-sum	Median BDI Pre-sum	Female	Male	Percent Males	Total Percent Males
0	0	54	41,91	43	35	19	35,19	35,77	10,85	7,5	19	35	64,81	67,15
0	1	42	39,26	38	30	12	28,57	35,37	12,33	8	15	27	64,29	70,07
1	0	83	41,54	42	53	30	36,14	35,77	15,40	13	26	57	68,67	67,15
1	1	105	40,42	39	65	40	38,10	35,37	16,35	15	29	76	72,38	70,07

8.4 Grouping Patients based on their Age

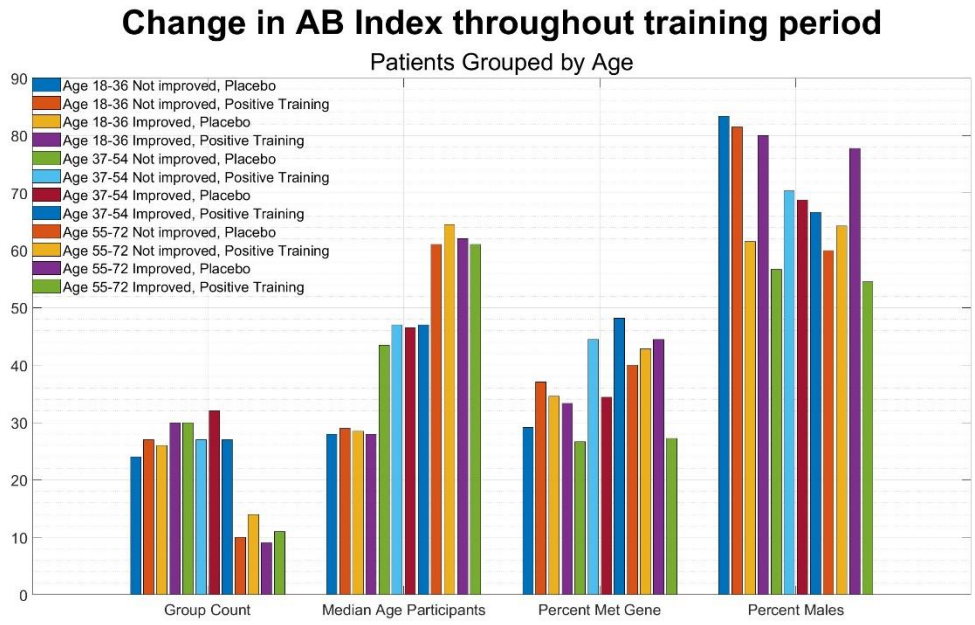


Figure 25 Bar chart displaying change in AB Index Throughout the Training Period, Grouped by Age

In the bar chart above, Figure 25, the patients are grouped into three groups, based on their age. The corresponding table, Table 4, can be found in Appendix A. As seen in the legend, the groups are patients from 18-36, 37-54 and 55-72 years old. Starting with the last key factor, the gender, the chart is showing that in all the age groups, the ones in the positive training that are improving their AB Index throughout the training, have a lower fraction of males than the corresponding positive training group that did not improve their AB Index.

Regarding the BDNF factor, both the youngest and oldest age group has a lower fraction of the Met gene amongst the positive training group that did improve their ABI than the positive training group that didn't. In the middle age group, the positive training group that improved has a higher prevalence of the Met gene than the positive training group that did not improve.

Looking at the median age of the patients in the positive training group that are improving their AB Index, they are younger than the corresponding group that are not improving in both the youngest and oldest age group, and the same in the middle age group.

An interesting takeaway from the age-based analysis can be seen in the group count. As can be seen, it is only the youngest age group that has more patients in the positive training

group that are improving than not. In the middle age group, the amount is the same, while amongst the oldest patients, there are more patients in the positive training group that are not improving than patients that are improving.

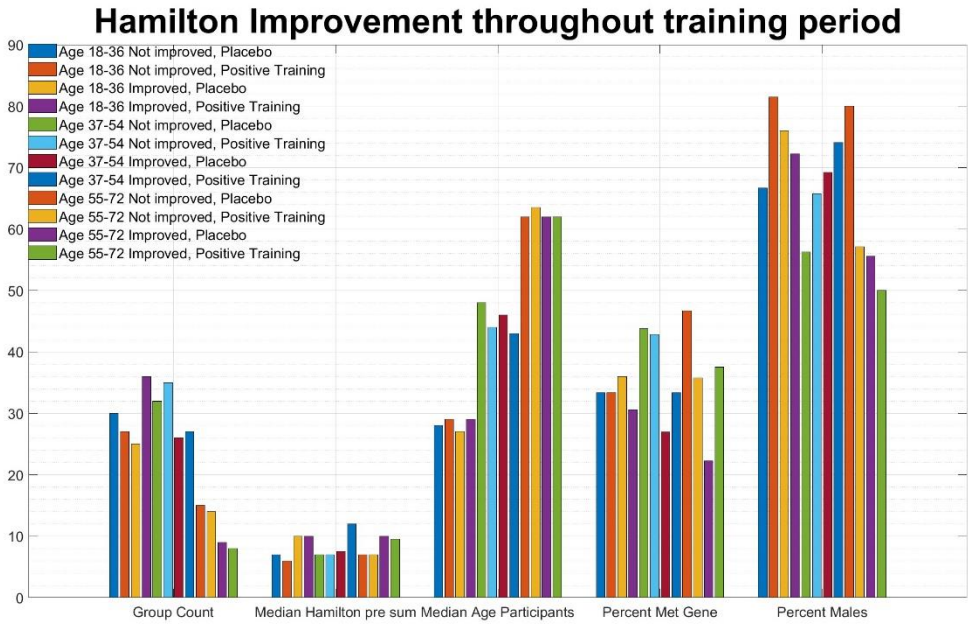


Figure 26 Bar Chart Displaying Characteristics with Patients with Respect to the Hamilton Scale Throughout the Training Period Grouped by Age

The Hamilton improvement bar chart above is built in the same way as the previous AB Index bar chart, with the participants divided into three main groups, based on their age, and then divided further into four subgroups based on training method and improvement. The corresponding table, Table 5, can be found in Appendix A.

Looking at the group count, you can see that it is only the youngest group that are experiencing a higher number of patients improving their Hamilton score amongst the positive training groups.

The trend seen at the previous charts looking at the patient group as a whole with a higher median Hamilton pre sum amongst the positive training groups that are improving are found on age-group level as well. This is a clear trend in all age groups.

Regarding the BNDF allele factor, both the youngest and the middle age group are having a higher amount of the Val allele contra the Met allele in the positive training groups that are improving contra the positive training groups that are not improving their Hamilton score. Amongst the oldest patients in the study, the ones that are going

through positive training and improving their score is having a higher amount of the Met allele.

Both the youngest and oldest age group is having a higher number of women amongst them in the positive training groups that are improving their depression severity looking at the Hamilton scale, than the positive training groups that are not improving their score. This is in contrast to the middle age groups where there are a greater overweigh of males amongst the positive training group that are improving than the ones that are not getting a lower Hamilton score.

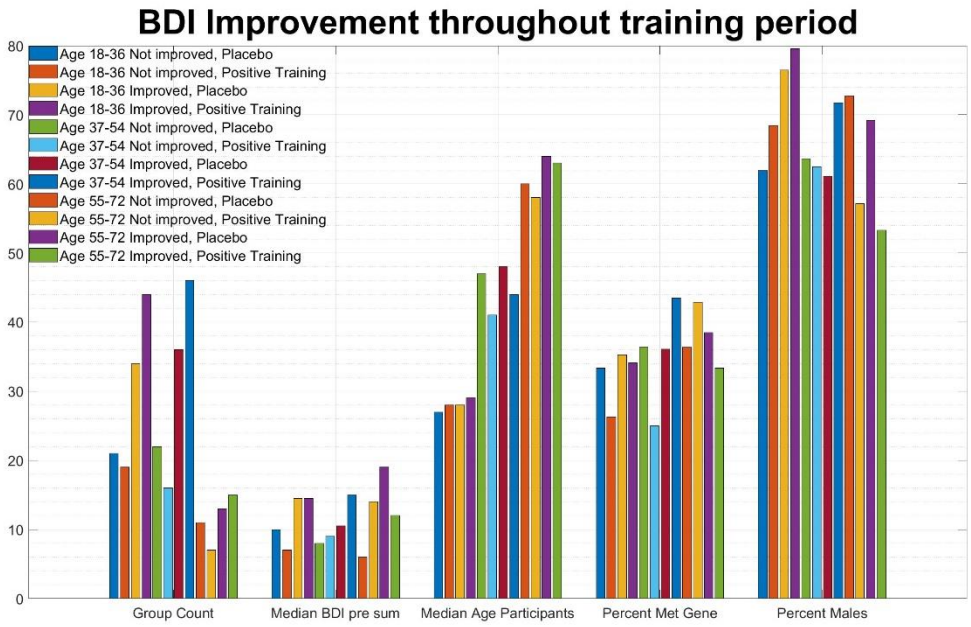


Figure 27 Bar Chart Displaying Characteristics with Patients with Respect to the BDI Scale Throughout the Training Period Grouped by Age

The figure above is displaying the BDI Improvement Analysis with the patients grouped into age group as is being done with the AB Index and Hamilton analysis as well. The corresponding table, Table 6, can be found in Appendix A.

In this analysis the group count of each age group stands out from the other two age-group analyses. Here are all three age groups is having a clear overweight of patients that are doing the positive training and improving their BDI score, with respect to the ones that are going through the positive training without improving their score.

Looking at the Median BDI pre sum, both the youngest and middle age group are having a significant higher BDI pre sum amongst the positive training groups that are improving contra

the ones in the positive training groups that aren't. The oldest, on the other hand, is having a lower median BDI pre sum.

As with the BDI pre sum, the youngest and middle age group is having similar results on the BDNF factor. Here, the positive training participants in both groups that are improving is having a higher percentage of the Met gene than the corresponding participants that are not improving their BDI score. Once again, the eldest are the ones that are standing out, with their positive training participants that are improving their BDI score having a significantly lower amount of the Met allele amongst themselves.

The story repeats itself when looking at the gender distribution amongst the positive patients that are improving their depression severity regarding the BDI scale. Once again, the youngest and middle age group are having similar results with a clear overweight of male distribution amongst themselves, while in the corresponding positive training group amongst the oldest, the percentage of females are higher amongst the ones that are improving their BDI score.

8.5 Other results

The slope calculations made on the reaction time in general can be done using the MATLAB code found in Appendix B. Due to its size and poorer relevance comparing to the AB Index calculations, it is not included in the thesis. An Excel file of the table will be handed in.

The same goes for the time analysis on the same data. The slope results for the first week only can be found amongst the handed in files, or by running the provided MATLAB code in Appendix B.

Table 7 in Appendix A is showing the results of the AB Index with calculations been done on data from the first week, data from the second week and the two weeks as a whole. Table 8 in Appendix A is showing the number of participants in the positive training group and in the placebo group that improved their AB Index from the first to the second week, the number of participants that worsened their AB Index from the first to the second week and the number of participants that did not experience any change in the AB index during the training period. As well as the number of participants, the percentage of these outcomes in each training group are displayed.

9 Discussion

In this thesis, the importance of being able to single out key factors amongst the patients that have a positive outcome of the Attention Modification Bias training is being addressed. From the datasets provided, the information of each patient is the following:

- Age
- Gender
- BDNF Factor
- Training Type
- Hamilton score
- Beck's Depression Inventory (BDI)
- Attention Modification Index
- Training result

Looking at the results from the analysis, there are especially two factors that seems to stick out in almost every analyse. This is the age factor and the factor saying something about the degree of the depression, the Hamilton score and the score on Beck's Depression Inventory.

9.1 Age

It is a clear trend that the participants undergoing the positive Attention Bias Training and are improving either their Attention Bias Index, their Hamilton score or their BDI score is younger than the ones that are not improving. There may be several reasons for this. The most plausible explanation to this is linked up with the difference in the human brain's plasticity of young and old people. Noack et al. is arguing in their paper "Cognitive plasticity in adulthood and old age: Gauging the generality of cognitive intervention effects" that even though both younger and older people is capable of learning and adapting, changes in brain activation due to cognitive training is having different causes. Park and Bischof supplement by stating that while the brain activation change in young people is mostly due to actual plasticity and an increase in their intrinsic neural capacity, the effects in the elderly are more due to the brains experience and ability to strategically use its resources. Throughout years of experience, the elderly brains learn to use their knowledge to effectively deploy its resources in the most effective way. (Noack et al., 2009; Park & Bischof, 2013) This can explain why the younger patients is having a higher improvement rate in their training than

the oldest ones.

The relative short time frame of two weeks may also have an impact on the gap in results between the young and the old. It is interesting to see the results from the analysis that were done on the AB Index data respective to time. In Table 7, the AB Index results from the first and second week are separated. Looking at the age of the positive training group that has an improvement of the AB Index on the training period as a whole, the median age is 38.5 versus 43 years amongst the positive training group without improvement. If we look at the AB Index improvement from the first week of training only, the median age of the ones that are improving are 38 years while the ones that are not improving are 41 years. This is in accordance with the overall impression that it is the youngest patients that are getting the most positive outcome of the training. Looking at the AB Index improvement on the second week on the other hand, the tables has turned. Here is the median age of the participants that are not improving their AB Index 38 years while the median age of the participants that are improving their AB Index in the second week are 39. This might suggest that in general, the young people that are getting a better AB Index score during the two weeks of training is experiencing this improvement already in the first week. The young patients that do not get better the first week, might not get better at all, while the elderly people, that might have less plasticity and ability to adapt as quickly as the youngest, is not experiencing their improvement in AB Index before the end of the training period. This is an interesting hypothesis that it might be interesting to investigate more closely to see if this is the case.

Looking at the bar chart in Figure 25, displaying the AB improvement analysis grouped by age, the group count in the youngest age group substantiates the hypothesis that the Attention Bias Training is having a better effect on the young patients. From this group, the number of patients that are improving their AB Index is 30, while 27 patients from this positive training group are not improving their BDI score. The middle age group is having a tie, with 27 patients improving, and 27 patients not improving. Amongst the oldest age group there are more patients that are not improving than the ones that are improving. Here 11 patients are improving while 14 is not improving their AB score.

9.2 Depression Severity

The factor that is without doubt the most significant looking at these analyses is the scores on the different scales measuring depression severity. In both the Hamilton and Beck's

Depression Inventory analyses, the patients that are getting better during the Attention Bias Modification Training is much harder affected by the depression than the ones that are not improving their depression severity. The reason for why this is the case is not completely clear, but it might be possible to think that for instance a decrease on the BDI scale from 16 to 14, is easier to manage than a decrease from 4 to 2, which even though both are a two-point improvement, the first one is a 12.5% improvement while the last is a 50% improvement. Whatever the reason might be, there is still no doubt that the severity of the depression is the biggest contributor to whether or not the patient will have a positive effect of the Attention Bias Modification Training.

9.3 Gender

Looking at the distribution on the genders, it is small changes, but there is relative more females than males that are improving their AB Index, while there is relative more males than females that are improving their Hamilton and BDI score. On an age-based group level, the gender distribution on the improvement of AB Index is similar in all age groups, with relative more females than males that are improving. Looking at the Hamilton scale it is the middle age group that is dragging the relative number of males to the top, while both amongst the young and old age group, there are relatively more females than males amongst the patients that improve their Hamilton score. Regarding the BDI scale, both the youngest and the middle age group has a relative number of males amongst them with about 10 percent point (68.4 vs 79.5 and 62.5 vs 71.7 respectively) more males in the improvement group than in the group that did not improve. Amongst the oldest age group, there are relatively more females amongst the patients that are getting better.

With this in mind it is not easy to pinpoint a very clear favour in one gender direction. While the women are the ones that are improving their AB Index the most, there are overall, even though only slightly, males that are improving most on their depression severity.

9.4 BDNF

Regarding the BDNF factor, the ones with the Val allele is doing it better on the Attention Bias Index overall and amongst the youngest and oldest age group, with the largest relative number of patients with the Val allele amongst the oldest patients.

Looking at the Hamilton and BDI analyse, the highest relevant amount of the Met allele

overall and amongst the age groups is complete opposite of each other. While there are relatively more patients with the Val allele amongst the patients that are improving their Hamilton score both overall and in the two youngest age groups, there are relatively more patients with the Met allele amongst the same groups in the BDI analyse.

This makes it hard to determine what factor, Met or Val, that are having the most promising results in the Attention Bias Modification training, and must be studied further before any conclusion can be made.

9.5 Placebo

There has been done studies on this dataset that are addressing the validation of the training method comparing the Placebo and Positive Training methods and is therefore not been taken in as a scope of this thesis. For more in-depth information on the double-blind study, please refer to Bø, Jonassen and Kraft's studies. (Bø et al., 2021; Jonassen et al., 2019; Kraft et al., 2019)

10 Conclusion

It has been interesting to dive deep into the large datasets provided with all the information that laid hidden within them. The focus in the thesis has not been whether or not the Attention Bias Modification Training is working or not, as this has been addressed earlier. (Bø et al., 2021; Jonassen et al., 2019; Kraft et al., 2019)The focus has on the other hand been on finding key factors and markers amongst the patients that has gone through the Positive Training and improved their depression disease.

Some of the findings from the analysis has been very clear, while others are harder to conclude on, and needs to be researched further before a final conclusion. The two key factor that stood out the most was without doubt the depression severity, measured on both the Hamilton scale and Beck's Depression Inventory, and the age of the participating patient. It is a clear trend that the more severe the depression is, the better effect has the training on the patient. With a median Hamilton score of 10 and BDI score of 15 amongst the participants that improved their severity, this is much higher than the median Hamilton score of 6 and BDI score of 8 amongst the patients that did not improve their condition.

Regarding the patients age, it became quicky clear that the younger patients had a higher improvement rate. This might be due to the fact that a younger brain has more plasticity than an older brain, and therefore might be more able to change the attention bias. The results also suggested that the youngest people got their effect of the training during the first week, while the older patients needed the two weeks of training to improve. This hypothesis needs further investigation to be completely confirmed.

When it came to the gender and BDNF factor, it was harder to see clear indications that the one was more responsive to the treatment than the other.

10.1 Further work

As stated above, it would be interesting to either confirm or deny the hypothesis that the younger patients that got better, did so already during the first week of training. This would make the training period for those that did not have an effect of the training shorter, meaning spending less time on a treatment method that is not working on the patient.

Another factor that would be interesting to look further into is the Hamilton and BDI scores one month after the training period and compare them to the scores that was taken right after the training period ended. This would be helpful to see if some patients got better with time, or if the effect of the training was short term or long term. In order to be able to validate a long-term effect, the patients should have a follow up later as well, for example after 6 and 12 months, to see if they still had a positive effect of the training.

It would also be interesting to do these tests in a hybrid EEG – fNIRS study, to see better the actual effects the attention bias modification training is having on the patient's brain.

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12 Appendix A – Tables

Table 4 AB Index analysis grouped based on the participant's age

AGE Category	ABM Improvement	Positive Training	GroupCount	Mean Age	Median Age	Female	Male	Percent Males	Total Percent Males	Val	Met	Percent Met	Total Percent Met
Age 18-36	0	0	24	28,29	28	4	20	83,33	72	17	7	29,17	32
Age 18-36	0	1	27	28,56	29	5	22	81,48	80,70	17	10	37,04	35,09
Age 37-54	0	0	30	44,1	43,5	13	17	56,67	62,90	22	8	26,67	30,65
Age 37-54	0	1	27	45,93	47	8	19	70,37	68,52	15	12	44,44	46,30
Age 55-72	0	0	10	62,7	61	4	6	60	68,42	6	4	40	42,11
Age 55-72	0	1	14	63,29	64,5	5	9	64,29	60	8	6	42,86	36,00
Age 18-36	1	0	26	27,88	28,5	10	16	61,54	72	17	9	34,62	32,00
Age 18-36	1	1	30	27,63	28	6	24	80	80,70	20	10	33,33	35,09
Age 37-54	1	0	32	45,81	46,5	10	22	68,75	62,90	21	11	34,38	30,65
Age 37-54	1	1	27	45,22	47	9	18	66,67	68,52	14	13	48,15	46,30
Age 55-72	1	0	9	61,22	62	2	7	77,78	68,42	5	4	44,44	42,11
Age 55-72	1	1	11	61,64	61	5	6	54,55	60	8	3	27,27	36

Table 5 Hamilton analysis grouped based on the participant's age

AGE Category	Ham Improvement	Positive Training	GroupCount	Mean Age	Median Age	Val	Met	Percent Met	Total Percent Met	Mean Hamilton Pre-sum	Median Hamilton Pre-sum	Female	Male	Percent Males	Total Percent Males
Age 18-36	0	0	30	27,47	28	20	10	33,33	34,55	7,8	7	10	20	66,67	70,91
Age 18-36	0	1	27	28,70	29	18	9	33,33	31,75	7,11	6	5	22	81,48	76,19
Age 37-54	0	0	32	47,28	48	18	14	43,75	36,21	6,84	7	14	18	56,25	62,07
Age 37-54	0	1	35	44,09	44	20	15	42,86	38,71	7,46	7	12	23	65,71	69,35
Age 55-72	0	0	15	62,53	62	8	7	46,67	37,5	6,87	7	3	12	80	70,83
Age 55-72	0	1	14	63,14	63,5	9	5	35,71	36,36	8,5	7	6	8	57,14	54,55
Age 18-36	1	0	25	27,32	27	16	9	36	34,55	9,8	10	6	19	76	70,91
Age 18-36	1	1	36	28,47	29	25	11	30,56	31,75	10,97	10	10	26	72,22	76,19
Age 37-54	1	0	26	45,69	46	19	7	26,92	36,21	8,96	7,5	8	18	69,23	62,07
Age 37-54	1	1	27	43,59	43	18	9	33,33	38,71	11,93	12	7	20	74,07	69,35
Age 55-72	1	0	9	62,78	62	7	2	22,22	37,5	9,22	10	4	5	55,56	70,83
Age 55-72	1	1	8	61,13	62	5	3	37,5	36,36	11,63	9,5	4	4	50	54,55

Table 6 BDI analysis grouped based on the participant's age

AGE Category	BDI Improvement	Positive Training	GroupCount	Mean Age	Median Age	Val	Met	Percent Met	Total Percent Met	Mean BDI Pre-sum	Median BDI Pre-sum	Female	Male	Percent Males	Total Percent Males
Age 18-36	0	0	21	27,29	27	14	7	33,33	34,55	11,14	10	8	13	61,90	70,91
Age 18-36	0	1	19	28,26	28	14	5	26,32	31,75	13,47	7	6	13	68,42	76,19
Age 37-54	0	0	22	46,27	47	14	8	36,36	36,21	11,45	8	8	14	63,64	62,07
Age 37-54	0	1	16	42,5	41	12	4	25	38,71	9,31	9	6	10	62,5	69,35
Age 55-72	0	0	11	61,09	60	7	4	36,36	37,5	9,09	6	3	8	72,73	70,83
Age 55-72	0	1	7	61,71	58	4	3	42,86	36,36	16,14	14	3	4	57,14	54,55
Age 18-36	1	0	34	27,47	28	22	12	35,29	34,55	15,56	14,5	8	26	76,47	70,91
Age 18-36	1	1	44	28,70	29	29	15	34,09	31,75	16,59	14,5	9	35	79,55	76,19
Age 37-54	1	0	36	46,75	48	23	13	36,11	36,21	14,5	10,5	14	22	61,11	62,07
Age 37-54	1	1	46	44,35	44	26	20	43,48	38,71	16,33	15	13	33	71,74	69,35
Age 55-72	1	0	13	63,92	64	8	5	38,46	37,5	17,46	19	4	9	69,23	70,83
Age 55-72	1	1	15	62,73	63	10	5	33,33	36,36	15,73	12	7	8	53,33	54,55

Table 7 AB Index analysis grouped based on the Training Periods

Time Category	ABM_Improvement	Positive Training	Group Count	Mean Age	Median Age	Female	Male	Percent Males	Total Percent Males	Val	Met	Percent Met	Total Percent Met
Whole Period	0	0	75	41,078125	39,5	21	43	67,1875	67,17557252	45	19	29,6875	32,82442748
Whole Period	0	1	85	42,6029412	43	18	50	73,52941176	72,05882353	40	28	41,1764706	39,70588235
Whole Period	1	0	77	40,9253731	43	22	45	67,1641791	67,17557252	43	24	35,8208955	32,82442748
Whole Period	1	1	79	40,1176471	38,5	20	48	70,58823529	72,05882353	42	26	38,2352941	39,70588235
First Week	0	0	67	42,45	40	18	42	70	70,33898305	41	19	31,6666667	30,50847458
First Week	0	1	88	41,4459459	41	22	52	70,27027027	70,14925373	43	31	41,8918919	42,53731343
First Week	1	0	70	42,1724138	43	17	41	70,68965517	70,33898305	41	17	29,3103448	30,50847458
First Week	1	1	73	39,3833333	38	18	42	70	70,14925373	34	26	43,3333333	42,53731343
Last Week	0	0	73	41,8923077	43	19	46	70,76923077	69,84126984	37	28	43,0769231	44,44444444
Last Week	0	1	73	39,7966102	38	18	41	69,49152542	69,74789916	43	16	27,1186441	30,25210084
Last Week	1	0	65	43,7377049	44	19	42	68,85245902	69,84126984	33	28	45,9016393	44,44444444
Last Week	1	1	72	41,2666667	39	18	42	70	69,74789916	40	20	33,3333333	30,25210084

Table 8 Table displaying AB Index Evolvement throughout the two weeks of training showing a positive or negative evolvement from the first to second week, both Positive Training and Placebo

	Improvement Last Week	Placebo Improvement Last Week	Decrease Last Week	Placebo Decrease Last Week	No Change	Placebo No Change	Total Positive Training	Total Placebo
Number	46	35	46	32	69	70	161	137
Percentage of total	28,57	25,55	28,57	23,36	42,86	51,09	100	100

13 Appendix B – MATLAB Code

13.1 Main()

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% This is the Main File of the MATLAB files.
% It is being used to gather all the files and compute the calculations
% and analysis
%
%
% One important thing to note, is that the training type, either positive
% training or Placebo is noted a little different throughout the files
% It is either referenced to as "Training Type" "Intervention" or "Placebo"
% with a boolean 0 or 1. The biggest issue here is that the value 1 is
% ALWAYS a positive training, and 0 is ALWAYS Placebo, even though this is
% not very logical when the column name is Placebo.
%
% Also, even though it says BNDF all over, it is BDNF that is the correct
% term for Brain Derived Neurotropic Factor. This is due to a typing error
% in the datatable provided.
%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%




%imports all user data

ImportDatatable;
BNDF_Import;
ImportAB_Dataset;

% BNDF_Table = sortrows(BNDF_Table,{'Intervention','Ham_pre_post'},"ascend");

%Creates a copy for different computations
dataCopy = FullDataset;


%Removes the data that aren't complete
dataCopy(dataCopy.TrainingCategory=="303",:) = [];
dataCopy(dataCopy.TrainingCategory=="306",:) = [];
dataCopy(dataCopy.TrainingCategory=="308",:) = [];
dataCopy(dataCopy.TrainingCategory=="dager",:) = [];
dataCopy(dataCopy.TrainingCategory=="etter",:) = [];
dataCopy(dataCopy.TrainingCategory=="hjemme (uf",:) = [];
dataCopy(dataCopy.TrainingCategory=="hjemme ufu",:) = [];
dataCopy(dataCopy.TrainingCategory=="naa",:) = [];
dataCopy(dataCopy.TrainingCategory=="uke",:) = [];



%Creates a copy of this and removes the unwanted categories
WashedDataset = dataCopy;
usedDataset =
WashedDataset(:,["ParticipantID","TrainingCategory","CumulativeSessionNumber","Tri
alNumber","ReactionTime"]);

%Creates table with only participantID and placebo info
```

```
PlaceboTable = My_Functions.getPlaceboInfo(WashedDataset);

%Defines functions for removing outliers, and computing mean and median
prefunc = @rmoutliers;
meanfunc = @mean;
medianfunc = @median;
slopefunc = @findSlopeValue;


%removing outliers and computing mean and median of each training session,
%combining the two datasets in the end.
preprosDataset =
varfun(prefunc,usedDataset,"GroupingVariables",["ParticipantID","TrainingCategory"
,"CumulativeSessionNumber"],"InputVariables","ReactionTime");
medianFullDataset =
varfun(medianfunc,preprosDataset,"GroupingVariables",["ParticipantID","TrainingCat
egory","CumulativeSessionNumber"],"InputVariables","rmoutliers_ReactionTime");
GjennomsnittFullDataset =
varfun(meanfunc,preprosDataset,"GroupingVariables",["ParticipantID","TrainingCateg
ory","CumulativeSessionNumber"],"InputVariables","rmoutliers_ReactionTime");
ComputedTable = join(medianFullDataset,GjennomsnittFullDataset);

%Create table with slopedata based on reaction time
slopeTable = My_Functions.findSlopeValue(ComputedTable);
slopeTable = My_Functions.addPlaceboColumnToTable(slopeTable,PlaceboTable);

%Create table with slopedata based on reaction time first week of training
firstWeekSlope = ComputedTable(ComputedTable.CumulativeSessionNumber < 15,:);
firstWeekSlope = My_Functions.findSlopeValue(firstWeekSlope);
firstWeekSlope =
My_Functions.addPlaceboColumnToTable(firstWeekSlope,PlaceboTable);


%Create table with slopedata based on ABM adjusted data
ABM_Info = My_Functions.findABMSlope(ABdataset,PlaceboTable,BNDF_Table);

%Create table with analysed ABM data
ABM_Analysis = My_Functions.ABM_Analysis(ABM_Info);

%Create table with slopedata and analysed ABM data based on first and last week of
%training combined with data for whole period
ABM_Analysis_timewise =
My_Functions.ABM_Analysis_basedOnTime(ABdataset,PlaceboTable,BNDF_Table);

%Do ABM and BNDF calculations on group level based on age (18-36,37-54,55-72)
[ABM_Age, BNDF_Ham_Age, BNDF_BDI_Age] =
My_Functions.CalculateBasedOnAge(ABM_Info,BNDF_Table);
```

13.2 My_Functions()

```
classdef My_Functions
    methods(Static)

        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        % BDNF Analysis function
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        function [BNDF_BDI_Info, BNDF_Ham_Info] = BNDF_analysis(BNDF_Table)

        %Creates variables to compute percentage of gender and BDNF
            rows = height(BNDF_Table);
            NumberOfMalesPositive = 0;
            NumberOfMalesPlacebo = 0;
            NumberOfFemalesPositive = 0;
            NumberOfFemalesPlacebo = 0;
            NumberOfMetPositive = 0;
            NumberOfMetPlacebo = 0;
            NumberOfValPositive = 0;
            NumberOfValPlacebo = 0;

            for row=1:rows
                if BNDF_Table.SEX(row) == "1"
                    if BNDF_Table.Intervention(row) == "1"
                        NumberOfMalesPositive = NumberOfMalesPositive + 1;
                    elseif BNDF_Table.Intervention(row) == "0"
                        NumberOfMalesPlacebo = NumberOfMalesPlacebo + 1;
                    end
                elseif BNDF_Table.SEX(row) == "0"
                    if BNDF_Table.Intervention(row) == "1"
                        NumberOfFemalesPositive = NumberOfFemalesPositive + 1;
                    elseif BNDF_Table.Intervention(row) == "0"
                        NumberOfFemalesPlacebo = NumberOfFemalesPlacebo + 1;
                    end
                end

                if BNDF_Table.BDNF_2(row) == "1"
                    if BNDF_Table.Intervention(row) =="1"
                        NumberOfMetPositive = NumberOfMetPositive + 1;
                    elseif BNDF_Table.Intervention(row) == "0"
                        NumberOfMetPlacebo = NumberOfMetPlacebo + 1;
                    end
                elseif BNDF_Table.BDNF_2(row) == "0"
                    if BNDF_Table.Intervention(row) =="1"
                        NumberOfValPositive = NumberOfValPositive + 1;
                    elseif BNDF_Table.Intervention(row) == "0"
                        NumberOfValPlacebo = NumberOfValPlacebo + 1;
                    end
                end
            end

            % Not all participants has all information, so is creating the
            % percentage based on the participants that has, excluding the
            % other from the percentage computation

            ParticipantsWithSpecifiedGenderPlacebo = NumberOfFemalesPlacebo +
NumberOfMalesPlacebo;
            ParticipantsWithSpecifiedGenderPositive = NumberOfFemalesPositive +
NumberOfMalesPositive;
```

```
            MalePercentageTotalPlacebo =
NumberOfMalesPlacebo/ParticipantsWithSpecifiedGenderPlacebo*100;
            MalePercentageTotalPositive =
NumberOfMalesPositive/ParticipantsWithSpecifiedGenderPositive*100;
            ParticipantsWithSpecifiedBNDFPlacebo = NumberOfValPlacebo +
NumberOfMetPlacebo;
            ParticipantsWithSpecifiedBNDFPositive = NumberOfValPositive +
NumberOfMetPositive;
            MetPercentageTotalPlacebo =
NumberOfMetPlacebo/ParticipantsWithSpecifiedBNDFPlacebo*100;
            MetPercentageTotalPositive =
NumberOfMetPositive/ParticipantsWithSpecifiedBNDFPositive*100;


            %
            % Hamilton analysis
            %

            %Calculate the mean age, grouped by Hamilton improvement and
            %Training type
            BNDF_Ham_Info_age_mean =
varfun(@(x)mean(x,'omitnan'),BNDF_Table,"InputVariables","AGE","GroupingVariables"
,["Ham_Improvement","Intervention"]);
            BNDF_Ham_Info_age_mean.Properties.VariableNames{4} = 'Mean_AGE';

            %Creates colums with number of males and females in each group
            gendertest =
varfun(@countcats,BNDF_Table,"InputVariables","SEX","GroupingVariables",["Ham_Impr
ovement","Intervention"]);
            BNDF_Ham_Info_age_mean.Female(1) = gendertest.countcats_SEX(1);
            BNDF_Ham_Info_age_mean.Female(2) = gendertest.countcats_SEX(3);
            BNDF_Ham_Info_age_mean.Female(3) = gendertest.countcats_SEX(5);
            BNDF_Ham_Info_age_mean.Female(4) = gendertest.countcats_SEX(7);
            BNDF_Ham_Info_age_mean.Male(1) = gendertest.countcats_SEX(2);
            BNDF_Ham_Info_age_mean.Male(2) = gendertest.countcats_SEX(4);
            BNDF_Ham_Info_age_mean.Male(3) = gendertest.countcats_SEX(6);
            BNDF_Ham_Info_age_mean.Male(4) = gendertest.countcats_SEX(8);

            %Computes the percentage of males in each row, providing the
            %total percentage of males in the training type group
            rows = height(BNDF_Ham_Info_age_mean);

            for row = 1:rows
                tot =
BNDF_Ham_Info_age_mean.Male(row)+BNDF_Ham_Info_age_mean.Female(row);
                percentage = BNDF_Ham_Info_age_mean.Male(row)/tot*100;

                BNDF_Ham_Info_age_mean.PercentMales(row) = percentage;
                if BNDF_Ham_Info_age_mean.Intervention(row) == "1"
                    BNDF_Ham_Info_age_mean.TotalPercentMales(row) =
MalePercentageTotalPositive;
                elseif BNDF_Ham_Info_age_mean.Intervention(row) == "0"
                    BNDF_Ham_Info_age_mean.TotalPercentMales(row) =
MalePercentageTotalPlacebo;
                end
            end

            %Same procedure as with the gender above, now with the BDNF
            %factor
```

```
            bndf =
varfun(@countcats,BNDF_Table,"InputVariables","BDNF_2",'GroupingVariables',["Ham_I
mprovement","Intervention"]);
            BNDF_Ham_Info_age_mean.Val(1) = bndf.countcats_BDNF_2(1);
            BNDF_Ham_Info_age_mean.Val(2) = bndf.countcats_BDNF_2(3);
            BNDF_Ham_Info_age_mean.Val(3) = bndf.countcats_BDNF_2(5);
            BNDF_Ham_Info_age_mean.Val(4) = bndf.countcats_BDNF_2(7);
            BNDF_Ham_Info_age_mean.Met(1) = bndf.countcats_BDNF_2(2);
            BNDF_Ham_Info_age_mean.Met(2) = bndf.countcats_BDNF_2(4);
            BNDF_Ham_Info_age_mean.Met(3) = bndf.countcats_BDNF_2(6);
            BNDF_Ham_Info_age_mean.Met(4) = bndf.countcats_BDNF_2(8);

            for row = 1:rows
                tot =
BNDF_Ham_Info_age_mean.Met(row)+BNDF_Ham_Info_age_mean.Val(row);
                percentage = BNDF_Ham_Info_age_mean.Met(row)/tot*100;

                BNDF_Ham_Info_age_mean.PercentMet(row) = percentage;
                if BNDF_Ham_Info_age_mean.Intervention(row) == "1"
                    BNDF_Ham_Info_age_mean.TotalPercentMet(row) =
MetPercentageTotalPositive;
                elseif BNDF_Ham_Info_age_mean.Intervention(row) == "0"
                    BNDF_Ham_Info_age_mean.TotalPercentMet(row) =
MetPercentageTotalPlacebo;
                end
            end


            %Computes the mean and median Hamilton pre-sum and the median
            %age, before joining the tables together to a single table.

            BNDF_Ham_Info_age_median =
varfun(@(x)median(x,'omitnan'),BNDF_Table,"InputVariables","AGE","GroupingVariable
s",["Ham_Improvement","Intervention"]);
            BNDF_Ham_Info_age_median.Properties.VariableNames{4} = 'Median_AGE';
            BNDF_Ham_Info_age =
join(BNDF_Ham_Info_age_mean,BNDF_Ham_Info_age_median);
            BNDF_Ham_Info_age =
movevars(BNDF_Ham_Info_age,"Median_AGE","After","Mean_AGE");


            BNDF_Ham_Info_HamPre_mean =
varfun(@(x)mean(x,'omitnan'),BNDF_Table,"InputVariables","Hamilton_pre_sum","Group
ingVariables",["Ham_Improvement","Intervention"]);
            BNDF_Ham_Info_HamPre_mean =
renamevars(BNDF_Ham_Info_HamPre_mean,"Fun_Hamilton_pre_sum","mean_Hamilton_pre_sum
");
            BNDF_Ham_Info_HamPre_median =
varfun(@(x)median(x,'omitnan'),BNDF_Table,"InputVariables","Hamilton_pre_sum","Gro
upingVariables",["Ham_Improvement","Intervention"]);
            BNDF_Ham_Info_HamPre_median =
renamevars(BNDF_Ham_Info_HamPre_median,"Fun_Hamilton_pre_sum","median_Hamilton_pre
_sum");


            BNDF_Ham_Info_HamPre =
join(BNDF_Ham_Info_HamPre_mean,BNDF_Ham_Info_HamPre_median);
            BNDF_Ham_Info = join(BNDF_Ham_Info_age,BNDF_Ham_Info_HamPre);
```

```
            %Small adjustments in column placement

            BNDF_Ham_Info =
movevars(BNDF_Ham_Info,"Female","After","median_Hamilton_pre_sum");
            BNDF_Ham_Info = movevars(BNDF_Ham_Info,"Male","After","Female");
            BNDF_Ham_Info = movevars(BNDF_Ham_Info,"PercentMales","After","Male");
            BNDF_Ham_Info =
movevars(BNDF_Ham_Info,"TotalPercentMales","After","PercentMales");

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%
            % BDI Analysis
            %
            % This is the same as the Hamilton analysis, only with the BDI
            % information
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%

            BNDF_BDI_Info_age_mean =
varfun(@(x)mean(x,'omitnan'),BNDF_Table,"InputVariables","AGE","GroupingVariables"
,["BDI_Improvement","Intervention"]);
            BNDF_BDI_Info_age_mean.Properties.VariableNames{4} = 'Mean_AGE';

            gendertest =
varfun(@countcats,BNDF_Table,"InputVariables","SEX","GroupingVariables",["BDI_Impr
ovement","Intervention"]);
            BNDF_BDI_Info_age_mean.Female(1) = gendertest.countcats_SEX(1);
            BNDF_BDI_Info_age_mean.Female(2) = gendertest.countcats_SEX(3);
            BNDF_BDI_Info_age_mean.Female(3) = gendertest.countcats_SEX(5);
            BNDF_BDI_Info_age_mean.Female(4) = gendertest.countcats_SEX(7);
            BNDF_BDI_Info_age_mean.Male(1) = gendertest.countcats_SEX(2);
            BNDF_BDI_Info_age_mean.Male(2) = gendertest.countcats_SEX(4);
            BNDF_BDI_Info_age_mean.Male(3) = gendertest.countcats_SEX(6);
            BNDF_BDI_Info_age_mean.Male(4) = gendertest.countcats_SEX(8);

            rows = height(BNDF_BDI_Info_age_mean);

            for row = 1:rows
                tot =
BNDF_BDI_Info_age_mean.Male(row)+BNDF_BDI_Info_age_mean.Female(row);
                percentage = BNDF_BDI_Info_age_mean.Male(row)/tot*100;

                BNDF_BDI_Info_age_mean.PercentMales(row) = percentage;
                if BNDF_BDI_Info_age_mean.Intervention(row) == "1"
                    BNDF_BDI_Info_age_mean.TotalPercentMales(row) =
MalePercentageTotalPositive;
                elseif BNDF_BDI_Info_age_mean.Intervention(row) == "0"
```

```
                    BNDF_BDI_Info_age_mean.TotalPercentMales(row) =
MalePercentageTotalPlacebo;
                end
            end

            bndf =
varfun(@countcats,BNDF_Table,"InputVariables","BDNF_2",'GroupingVariables',["BDI_I
mprovement","Intervention"]);
            BNDF_BDI_Info_age_mean.Val(1) = bndf.countcats_BDNF_2(1);
            BNDF_BDI_Info_age_mean.Val(2) = bndf.countcats_BDNF_2(3);
            BNDF_BDI_Info_age_mean.Val(3) = bndf.countcats_BDNF_2(5);
            BNDF_BDI_Info_age_mean.Val(4) = bndf.countcats_BDNF_2(7);
            BNDF_BDI_Info_age_mean.Met(1) = bndf.countcats_BDNF_2(2);
            BNDF_BDI_Info_age_mean.Met(2) = bndf.countcats_BDNF_2(4);
            BNDF_BDI_Info_age_mean.Met(3) = bndf.countcats_BDNF_2(6);
            BNDF_BDI_Info_age_mean.Met(4) = bndf.countcats_BDNF_2(8);

            for row = 1:rows
                tot =
BNDF_BDI_Info_age_mean.Met(row)+BNDF_BDI_Info_age_mean.Val(row);
                percentage = BNDF_BDI_Info_age_mean.Met(row)/tot*100;

                BNDF_BDI_Info_age_mean.PercentMet(row) = percentage;
                if BNDF_BDI_Info_age_mean.Intervention(row) == "1"
                    BNDF_BDI_Info_age_mean.TotalPercentMet(row) =
MetPercentageTotalPositive;
                elseif BNDF_BDI_Info_age_mean.Intervention(row) == "0"
                    BNDF_BDI_Info_age_mean.TotalPercentMet(row) =
MetPercentageTotalPlacebo;
                end


            end


            BNDF_BDI_Info_age_median =
varfun(@(x)median(x,'omitnan'),BNDF_Table,"InputVariables","AGE","GroupingVariable
s",["BDI_Improvement","Intervention"]);
            BNDF_BDI_Info_age_median.Properties.VariableNames{4} = 'Median_AGE';
            BNDF_BDI_Info_age =
join(BNDF_BDI_Info_age_mean,BNDF_BDI_Info_age_median);
            BNDF_BDI_Info_age =
movevars(BNDF_BDI_Info_age,"Median_AGE","After","Mean_AGE");


            BNDF_BDI_Info_BDIPre_mean =
varfun(@(x)mean(x,'omitnan'),BNDF_Table,"InputVariables","BDI_pre_sum","GroupingVa
riables",["BDI_Improvement","Intervention"]);
            BNDF_BDI_Info_BDIPre_mean =
renamevars(BNDF_BDI_Info_BDIPre_mean,"Fun_BDI_pre_sum","mean_BDI_pre_sum");
            BNDF_BDI_Info_BDIPre_median =
varfun(@(x)median(x,'omitnan'),BNDF_Table,"InputVariables","BDI_pre_sum","Grouping
Variables",["BDI_Improvement","Intervention"]);
            BNDF_BDI_Info_BDIPre_median =
renamevars(BNDF_BDI_Info_BDIPre_median,"Fun_BDI_pre_sum","median_BDI_pre_sum");
            BNDF_BDI_Info_BDIPre =
join(BNDF_BDI_Info_BDIPre_mean,BNDF_BDI_Info_BDIPre_median);
            BNDF_BDI_Info = join(BNDF_BDI_Info_age,BNDF_BDI_Info_BDIPre);
```

```
            BNDF_BDI_Info =
movevars(BNDF_BDI_Info,"Female","After","median_BDI_pre_sum");
            BNDF_BDI_Info = movevars(BNDF_BDI_Info,"Male","After","Female");
            BNDF_BDI_Info = movevars(BNDF_BDI_Info,"PercentMales","After","Male");
            BNDF_BDI_Info =
movevars(BNDF_BDI_Info,"TotalPercentMales","After","PercentMales");

        end

        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        % AB Index slope function
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

        function[ABM_Info] = findABMSlope(ABdataset,PlaceboTable,BNDF_Table)

            abmdata = ABdataset;

            %Removes the data that are too small for comutation -> less than 6
values
            B = groupcounts(abmdata,"ParticipantID");

            ParticipantIDCategory2small = B(B.GroupCount < 6,"ParticipantID");

            removerows = ParticipantIDCategory2small;

            for row = 1 : height(removerows)
                removethis = removerows{row,"ParticipantID"};
                abmdata(abmdata.ParticipantID == removethis,:) = [];
            end

            %Compute LT values, to get a trendline for each participant
            trendfunc = @trenddecomp;
            MedianLT_Table =
varfun(trendfunc,abmdata,"GroupingVariables","ParticipantID","InputVariables","Adj
ustedAB");
            abmdata.medianLT = MedianLT_Table{:,"trenddecomp_AdjustedAB"};

            MeanLT_Table =
varfun(trendfunc,abmdata,"GroupingVariables","ParticipantID","InputVariables","Adj
ustedAB");
            abmdata.meanLT = MeanLT_Table{:,"trenddecomp_AdjustedAB"};


            % Gets the mean and median slope variable and combines them
            % into a single table
            fitfunc = @My_Functions.createFit;
            MedianSlopeTable =
rowfun(fitfunc,abmdata,"GroupingVariables","ParticipantID","InputVariables",["Date
","medianLT"],"SeparateInputs",true,"OutputVariableNames","Median_ABM_Slope");
            MeanSlopeTable =
rowfun(fitfunc,abmdata,"GroupingVariables","ParticipantID","InputVariables",["Date
","meanLT"],"SeparateInputs",true,"OutputVariableNames","Mean_ABM_Slope");

            ABM_Info = join(MedianSlopeTable,MeanSlopeTable);

            %Adds placebo column to ABM_Slope table
            % NB - placebo = 0 means placebo, placebo = 1 means positive
```

```
            % training

            ABM_Info =
My_Functions.addPlaceboColumnToTable(ABM_Info,PlaceboTable);

            ABM_Info = My_Functions.getPersonaliaToTable(ABM_Info,BNDF_Table);

            rows = height(ABM_Info);

            for row = 1:rows
                abm_improvement = ABM_Info.Median_ABM_Slope(row);
                if abm_improvement > 0
                    ABM_Info.ABM_Improvement(row) = 1;
                else
                    ABM_Info.ABM_Improvement(row) = 0;
                end
            end

        end

        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        %  Slope function
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

        function[slopefitness] = findSlopeValue(ComputedTable)

            hjemmeTable = ComputedTable;

            %Removes the data that aren't "hjemme" to get the data from the
            %home training
            hjemmeTable(hjemmeTable.TrainingCategory=="pre",:) = [];
            hjemmeTable(hjemmeTable.TrainingCategory=="post",:) = [];

            %Removes the data that are too small for comutation -> less than 6
values
            B = groupcounts(hjemmeTable,"ParticipantID");

            ParticipantIDCategory2small = B(B.GroupCount < 6,"ParticipantID");

            removerows = ParticipantIDCategory2small;

            for row = 1 : height(removerows)
                removethis = removerows{row,"ParticipantID"};

                hjemmeTable(hjemmeTable.ParticipantID == removethis,:) = [];
            end


            %Compute LT values, to get a trendline for each participant
            trendfunc = @trenddecomp;
            MedianLT_Table =
varfun(trendfunc,hjemmeTable,"GroupingVariables","ParticipantID","InputVariables",
"median_rmoutliers_ReactionTime");
            hjemmeTable.medianLT =
MedianLT_Table{:,"trenddecomp_median_rmoutliers_ReactionTime"};
```

```
            MeanLT_Table =
varfun(trendfunc,hjemmeTable,"GroupingVariables","ParticipantID","InputVariables",
"mean_rmoutliers_ReactionTime");
            hjemmeTable.meanLT =
MeanLT_Table{:,"trenddecomp_mean_rmoutliers_ReactionTime"};


            % Gets the mean and median slope variable and combines them
            % into a single table
            fitfunc = @My_Functions.createFit;
            MedianSlopeTable =
rowfun(fitfunc,hjemmeTable,"GroupingVariables","ParticipantID","InputVariables",["
CumulativeSessionNumber","medianLT"],"SeparateInputs",true,"OutputVariableNames","
MedianSlope");
            MeanSlopeTable =
rowfun(fitfunc,hjemmeTable,"GroupingVariables","ParticipantID","InputVariables",["
CumulativeSessionNumber","meanLT"],"SeparateInputs",true,"OutputVariableNames","Me
anSlope");

            slopeTable = join(MedianSlopeTable,MeanSlopeTable);
            slopefitness = slopeTable;

        end


        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        %  Placebo function for getting Placebo Info
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%


        function[PlaceboTable] = getPlaceboInfo(WashedDataset)
                        PlaceboTable =
WashedDataset(:,["ParticipantID","TrainingCategory","TrainingType"]);
            %Removes the data that aren't "hjemme"
            PlaceboTable(PlaceboTable.TrainingCategory=="pre",:) = [];
            PlaceboTable(PlaceboTable.TrainingCategory=="post",:) = [];

            %Creates table with only ParticipantID and TrainingType
            PlaceboTable =
groupsummary(PlaceboTable,["ParticipantID","TrainingCategory","TrainingType"]);
            PlaceboTable = PlaceboTable(:,["ParticipantID","TrainingType"]);

            % NBNBNBNB!
            % Substitues Trainingtypes 'control' and 'positive' for boolean
            % 1 and 0, where 1 is POSITIVE TRAINING and 0 is PLACEBO
            %
            rows = height(PlaceboTable);
            for row = 1:rows
                if PlaceboTable.TrainingType(row) == "control"
                    PlaceboTable.Placebo(row) = 0;
                elseif PlaceboTable.TrainingType(row) == "positive"
                    PlaceboTable.Placebo(row) = 1;
                end
            end
            PlaceboTable = PlaceboTable(:,["ParticipantID","Placebo"]);
        end
```

```
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        %  Function for adding a Training Type row to given Table
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

        function[TableWithPlaceboColumn] =
addPlaceboColumnToTable(TableWithoutPlaceboColumn,PlaceboTable)
            rows = height(TableWithoutPlaceboColumn);
            for row = 1:rows
                ParticipantID = TableWithoutPlaceboColumn.ParticipantID(row);
                TableWithoutPlaceboColumn.Placebo(row) =
PlaceboTable{PlaceboTable.ParticipantID == ParticipantID,"Placebo"};
            end
            TableWithPlaceboColumn = TableWithoutPlaceboColumn;
        end


        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        %  Function for getting Gender, Age and BDNF factor to table
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        function[Table_sex_age_BNDF] = getPersonaliaToTable(ABM_Info,BNDF_Table)
            rows = height(BNDF_Table);
            for row = 1:rows
                ParticipantID = BNDF_Table.ParticipantID(row);
                isthere = ismember(ParticipantID,ABM_Info.ParticipantID);

                if isthere == 1
                    ABM_Info.AGE(row) = BNDF_Table{BNDF_Table.ParticipantID ==
ParticipantID,"AGE"};
                    ABM_Info.SEX(row) = BNDF_Table{BNDF_Table.ParticipantID ==
ParticipantID,"SEX"};
                    ABM_Info.BNDF(row) = BNDF_Table{BNDF_Table.ParticipantID ==
ParticipantID,"BDNF_2"};
                end
            end
            rows = height(ABM_Info);
            for row = 1:rows
                if ABM_Info.AGE(row) == 0
                    ABM_Info.AGE(row) = nan;
                end
            end

            Table_sex_age_BNDF = ABM_Info;
        end


        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        %  Function for Doing the AB Index Analysis
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

        function[ABM_Analysis_Table] = ABM_Analysis(ABM_Info)

            %
            % For more details, see the BDNF analysis, which is based on
```

```
            % the same code
            %
            rows = height(ABM_Info);
            NumberOfMalesPositive = 0;
            NumberOfMalesPlacebo = 0;
            NumberOfFemalesPositive = 0;
            NumberOfFemalesPlacebo = 0;
            NumberOfMetPositive = 0;
            NumberOfMetPlacebo = 0;
            NumberOfValPositive = 0;
            NumberOfValPlacebo = 0;

            for row=1:rows
                if ABM_Info.SEX(row) == "1"
                    if ABM_Info.Placebo(row) == 1
                        NumberOfMalesPositive = NumberOfMalesPositive + 1;
                    elseif ABM_Info.Placebo(row) == 0
                        NumberOfMalesPlacebo = NumberOfMalesPlacebo + 1;
                    end
                elseif ABM_Info.SEX(row) == "0"
                    if ABM_Info.Placebo(row) == 1
                        NumberOfFemalesPositive = NumberOfFemalesPositive + 1;
                    elseif ABM_Info.Placebo(row) == 0
                        NumberOfFemalesPlacebo = NumberOfFemalesPlacebo + 1;
                    end
                end

                if ABM_Info.BNDF(row) == "1"
                    if ABM_Info.Placebo(row) ==1
                        NumberOfMetPositive = NumberOfMetPositive + 1;
                    elseif ABM_Info.Placebo(row) == 0
                        NumberOfMetPlacebo = NumberOfMetPlacebo + 1;
                    end
                elseif ABM_Info.BNDF(row) == "0"
                    if ABM_Info.Placebo(row) ==1
                        NumberOfValPositive = NumberOfValPositive + 1;
                    elseif ABM_Info.Placebo(row) == 0
                        NumberOfValPlacebo = NumberOfValPlacebo + 1;
                    end
                end
            end

            ParticipantsWithSpecifiedGenderPlacebo = NumberOfFemalesPlacebo +
NumberOfMalesPlacebo;
            ParticipantsWithSpecifiedGenderPositive = NumberOfFemalesPositive +
NumberOfMalesPositive;
            MalePercentageTotalPlacebo =
NumberOfMalesPlacebo/ParticipantsWithSpecifiedGenderPlacebo*100;
            MalePercentageTotalPositive =
NumberOfMalesPositive/ParticipantsWithSpecifiedGenderPositive*100;
            ParticipantsWithSpecifiedBNDFPlacebo = NumberOfValPlacebo +
NumberOfMetPlacebo;
            ParticipantsWithSpecifiedBNDFPositive = NumberOfValPositive +
NumberOfMetPositive;
            MetPercentageTotalPlacebo =
NumberOfMetPlacebo/ParticipantsWithSpecifiedBNDFPlacebo*100;
            MetPercentageTotalPositive =
NumberOfMetPositive/ParticipantsWithSpecifiedBNDFPositive*100;
```

```
            ABM_Info_age_mean =
varfun(@(x)mean(x,'omitnan'),ABM_Info,"InputVariables","AGE","GroupingVariables",[
"ABM_Improvement","Placebo"]);
            ABM_Info_age_mean.Properties.VariableNames{4} = 'Mean_AGE';



            gendertest =
varfun(@countcats,ABM_Info,"InputVariables","SEX",'GroupingVariables',["ABM_Improv
ement","Placebo"]);
            ABM_Info_age_mean.Female(1) = gendertest.countcats_SEX(1);
            ABM_Info_age_mean.Female(2) = gendertest.countcats_SEX(3);
            ABM_Info_age_mean.Female(3) = gendertest.countcats_SEX(5);
            ABM_Info_age_mean.Female(4) = gendertest.countcats_SEX(7);
            ABM_Info_age_mean.Male(1) = gendertest.countcats_SEX(2);
            ABM_Info_age_mean.Male(2) = gendertest.countcats_SEX(4);
            ABM_Info_age_mean.Male(3) = gendertest.countcats_SEX(6);
            ABM_Info_age_mean.Male(4) = gendertest.countcats_SEX(8);

            rows = height(ABM_Info_age_mean);

            for row = 1:rows
                tot = ABM_Info_age_mean.Male(row)+ABM_Info_age_mean.Female(row);
                percentage = ABM_Info_age_mean.Male(row)/tot*100;

                ABM_Info_age_mean.PercentMales(row) = percentage;
                if ABM_Info_age_mean.Placebo(row) == 1
                    ABM_Info_age_mean.TotalPercentMales(row) =
MalePercentageTotalPositive;
                elseif ABM_Info_age_mean.Placebo(row) == 0
                    ABM_Info_age_mean.TotalPercentMales(row) =
MalePercentageTotalPlacebo;
                end

            end

            bndf =
varfun(@countcats,ABM_Info,"InputVariables","BNDF",'GroupingVariables',["ABM_Impro
vement","Placebo"]);
            ABM_Info_age_mean.Val(1) = bndf.countcats_BNDF(1);
            ABM_Info_age_mean.Val(2) = bndf.countcats_BNDF(3);
            ABM_Info_age_mean.Val(3) = bndf.countcats_BNDF(5);
            ABM_Info_age_mean.Val(4) = bndf.countcats_BNDF(7);
            ABM_Info_age_mean.Met(1) = bndf.countcats_BNDF(2);
            ABM_Info_age_mean.Met(2) = bndf.countcats_BNDF(4);
            ABM_Info_age_mean.Met(3) = bndf.countcats_BNDF(6);
            ABM_Info_age_mean.Met(4) = bndf.countcats_BNDF(8);

            for row = 1:rows
                tot = ABM_Info_age_mean.Met(row)+ABM_Info_age_mean.Val(row);
                percentage = ABM_Info_age_mean.Met(row)/tot*100;

                ABM_Info_age_mean.PercentMet(row) = percentage;
                if ABM_Info_age_mean.Placebo(row) == 1
                    ABM_Info_age_mean.TotalPercentMet(row) =
MetPercentageTotalPositive;
                elseif ABM_Info_age_mean.Placebo(row) == 0
                    ABM_Info_age_mean.TotalPercentMet(row) =
MetPercentageTotalPlacebo;
```

```
            end

        end

        ABM_Info_age_median =
varfun(@(x)median(x,'omitnan'),ABM_Info,"InputVariables","AGE","GroupingVariables"
,["ABM_Improvement","Placebo"]);
        ABM_Info_age_median.Properties.VariableNames{4} = 'Median_AGE';
        ABM_Info_age = join(ABM_Info_age_mean,ABM_Info_age_median);
        ABM_Info_age = movevars(ABM_Info_age,"Median_AGE","After","Mean_AGE");

        ABM_Analysis_Table = ABM_Info_age;
    end


    %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    %
    %  Function for doing the AB Index Analysis based on time
    %
    %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

    function[ABM_Analysis_table_Timewise] =
ABM_Analysis_basedOnTime(ABdataset, PlaceboTable, BNDF_Table)

        ABM_Info =
My_Functions.findABMSlope(ABdataset,PlaceboTable,BNDF_Table);
        ABM_Analysis = My_Functions.ABM_Analysis(ABM_Info);

        rows = height(ABM_Analysis);
        for row = 1:rows
            ABM_Analysis.TimeCategory(row) = "Whole Period";
        end
        ABM_Analysis.TimeCategory = categorical(ABM_Analysis.TimeCategory);


        ABM_Info_firstWeek = ABdataset(ABdataset.Date < 8,:);
        ABM_Info_firstWeek =
My_Functions.findABMSlope(ABM_Info_firstWeek,PlaceboTable,BNDF_Table);
        ABM_Analysis_firstWeek =
My_Functions.ABM_Analysis(ABM_Info_firstWeek);

        rows = height(ABM_Analysis_firstWeek);
        for row = 1:rows
            ABM_Analysis_firstWeek.TimeCategory(row) = "First Week";
        end
        ABM_Analysis_firstWeek.TimeCategory =
categorical(ABM_Analysis_firstWeek.TimeCategory);


        ABM_Info_lastWeek = ABdataset(ABdataset.Date > 7,:);
        ABM_Info_lastWeek =
My_Functions.findABMSlope(ABM_Info_lastWeek,PlaceboTable,BNDF_Table);
        ABM_Analysis_lastWeek = My_Functions.ABM_Analysis(ABM_Info_lastWeek);

        rows = height(ABM_Analysis_lastWeek);
        for row = 1:rows
            ABM_Analysis_lastWeek.TimeCategory(row) = "Last Week";
        end
```

```
            ABM_Analysis_lastWeek.TimeCategory =
categorical(ABM_Analysis_lastWeek.TimeCategory);



            ABM_Analysis_table_Timewise =
[ABM_Analysis;ABM_Analysis_firstWeek;ABM_Analysis_lastWeek];


        end



        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        %  Function for doing the AB Index and BDNF analysis on age-level
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

        function[ABM_Age, BNDF_Ham_Age, BNDF_BDI_Age] =
CalculateBasedOnAge(ABM_Info, BNDF_Table)


        Young_ABM = ABM_Info(ABM_Info.AGE<37,:);
        Mid_ABM = ABM_Info((ABM_Info.AGE>36 & ABM_Info.AGE<55),:);
        Old_ABM = ABM_Info(ABM_Info.AGE > 54,:);

        Young_ABM = My_Functions.ABM_Analysis(Young_ABM);
        Mid_ABM = My_Functions.ABM_Analysis(Mid_ABM);
        Old_ABM = My_Functions.ABM_Analysis(Old_ABM);


        rows = height(Young_ABM);

        for row = 1:rows
            Young_ABM.AGE_Category(row) = "Age 18-36";
            Mid_ABM.AGE_Category(row) = "Age 37-54";
            Old_ABM.AGE_Category(row) = "Age 55-72";
        end

        Young_ABM = movevars(Young_ABM,"AGE_Category","Before","ABM_Improvement");
        Mid_ABM = movevars(Mid_ABM,"AGE_Category","Before","ABM_Improvement");
        Old_ABM = movevars(Old_ABM,"AGE_Category","Before","ABM_Improvement");

        ABM_Age = [Young_ABM;Mid_ABM;Old_ABM];

        ABM_Age.AGE_Category = categorical(ABM_Age.AGE_Category);
        ABM_Age = sortrows(ABM_Age,["ABM_Improvement", "AGE_Category"]);



        Young_BNDF = BNDF_Table(BNDF_Table.AGE<37,:);
        Mid_BNDF = BNDF_Table((BNDF_Table.AGE>36 & BNDF_Table.AGE<55),:);
        Old_BNDF = BNDF_Table(BNDF_Table.AGE>54,:);

        [Young_BNDF_BDI, Young_BNDF_Ham] = My_Functions.BNDF_analysis(Young_BNDF);
        [Mid_BNDF_BDI, Mid_BNDF_Ham] = My_Functions.BNDF_analysis(Mid_BNDF);
        [Old_BNDF_BDI, Old_BNDF_Ham] = My_Functions.BNDF_analysis(Old_BNDF);
```

```
        rows = height(Young_BNDF_Ham);
        for row = 1:rows
            Young_BNDF_Ham.AGE_Category(row) = "Age 18-36";
            Mid_BNDF_Ham.AGE_Category(row) = "Age 37-54";
            Old_BNDF_Ham.AGE_Category(row) = "Age 55-72";

            Young_BNDF_BDI.AGE_Category(row) = "Age 18-36";
            Mid_BNDF_BDI.AGE_Category(row) = "Age 37-54";
            Old_BNDF_BDI.AGE_Category(row) = "Age 55-72";

        end

        Young_BNDF_Ham =
movevars(Young_BNDF_Ham,"AGE_Category","Before","Ham_Improvement");
        Mid_BNDF_Ham =
movevars(Mid_BNDF_Ham,"AGE_Category","Before","Ham_Improvement");
        Old_BNDF_Ham =
movevars(Old_BNDF_Ham,"AGE_Category","Before","Ham_Improvement");


        Young_BNDF_BDI =
movevars(Young_BNDF_BDI,"AGE_Category","Before","BDI_Improvement");
        Mid_BNDF_BDI =
movevars(Mid_BNDF_BDI,"AGE_Category","Before","BDI_Improvement");
        Old_BNDF_BDI =
movevars(Old_BNDF_BDI,"AGE_Category","Before","BDI_Improvement");

        BNDF_Ham_Age = [Young_BNDF_Ham;Mid_BNDF_Ham;Old_BNDF_Ham];
        BNDF_Ham_Age.AGE_Category = categorical(BNDF_Ham_Age.AGE_Category);
        BNDF_Ham_Age = sortrows(BNDF_Ham_Age,["Ham_Improvement", "AGE_Category"]);


        BNDF_BDI_Age = [Young_BNDF_BDI;Mid_BNDF_BDI;Old_BNDF_BDI];
        BNDF_BDI_Age.AGE_Category = categorical(BNDF_BDI_Age.AGE_Category);
        BNDF_BDI_Age = sortrows(BNDF_BDI_Age,["BDI_Improvement", "AGE_Category"]);

        end

        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
        %
        %  Tweaked autogenerated MATLAB function for doing the slope
        %  calculations
        %
        %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%


        function [sloperesult] = createFit(CumulativeSessionNumber, LT)
            %CREATEFIT1(CUMULATIVESESSIONNUMBER,LT)
            %  Create a fit.
            %
            %  Data for 'TrainingSlope' fit:
            %      X Input: CumulativeSessionNumber from participant301hjemme
            %      Y Output: LT
            %  Output:
            %      Fitresult : a fit object representing the fit.
            %      Gof : structure with goodness-of fit info.
            %
            %  See also FIT, CFIT, SFIT.
```

```
            %  Auto-generated by MATLAB on 05-Apr-2022 12:08:09


            %% Fit: 'TrainingSlope'.
            [xData, yData] = prepareCurveData( CumulativeSessionNumber, LT );

            % Set up fittype and options.
            ft = fittype( 'poly1' );

            % Fit model to data.
            [fitresult, gof] = fit( xData, yData, ft );

            sloperesult = fitresult.p1;

            % % Plot fit with data.
            % Figure('Name', 'TrainingSlope' );
            % h = plot( fitresult, xData, yData );
            % Legend( h, 'LT vs. CumulativeSessionNumber', 'TrainingSlope',
'Location', 'NorthEast', 'Interpreter', 'none' );
            % % Label axes
            % xlabel( 'CumulativeSessionNumber', 'Interpreter', 'none' );
            % ylabel( 'LT', 'Interpreter', 'none' );
            % grid on
        end



    end
end
```

13.3 ImportDatatable;

```
%% Import data from text file
% Script for importing data from the following text file:
%
%    filename:
C:\Users\elias\OneDrive\OsloMet\Master\Masteroppgave\Koding\dataset.csv
%
% Auto-generated by MATLAB on 04-May-2022 10:49:07

%% Set up the Import Options and import the data
opts = delimitedTextImportOptions("NumVariables", 24);

% Specify range and delimiter
opts.DataLines = [1, Inf];
opts.Delimiter = ",";

% Specify column names and types
opts.VariableNames = ["ParticipantID", "MM", "DD", "YYYY", "hh", "mm", "ss",
"SessionNumberToday", "CumulativeSessionNumber", "StimulusType", "TrainingType",
"ListUsed", "TrialNumber", "NegativeStimulus", "PositiveStimulus", "PairType",
"LocationOfPositiveStimulus", "ProbeType", "ProbeLocation",
"StimulusPresentationDuration", "Response", "ResponseAccuracy", "ReactionTime",
"TrainingCategory"];
opts.VariableTypes = ["double", "double", "double", "double", "double", "double",
"double", "double", "double", "categorical", "categorical", "double", "double",
"string", "string", "categorical", "categorical", "categorical", "categorical",
"double", "categorical", "double", "double", "categorical"];

% Specify file level properties
opts.ImportErrorRule = "omitrow";
opts.MissingRule = "omitrow";
opts.ExtraColumnsRule = "ignore";
opts.EmptyLineRule = "read";

% Specify variable properties
opts = setvaropts(opts, ["NegativeStimulus", "PositiveStimulus"],
"WhitespaceRule", "preserve");
opts = setvaropts(opts, ["StimulusType", "TrainingType", "NegativeStimulus",
"PositiveStimulus", "PairType", "LocationOfPositiveStimulus", "ProbeType",
"ProbeLocation", "Response", "TrainingCategory"], "EmptyFieldRule", "auto");

% Import the data
FullDataset =
readtable("C:\Users\elias\OneDrive\OsloMet\Master\Masteroppgave\Koding\dataset.csv
", opts);


%% Clear temporary variables
clear opts
```

13.4 BDNF_Import;

```
%% Import data from text file
% Script for importing data from the following text file:
%
%    filename:
C:\Users\elias\OneDrive\OsloMet\Master\Masteroppgave\Koding\BNDF.csv
%
% Auto-generated by MATLAB on 11-Apr-2022 12:27:53

%% Set up the Import Options and import the data
opts = delimitedTextImportOptions("NumVariables", 16);

% Specify range and delimiter
opts.DataLines = [2, Inf];
opts.Delimiter = ",";

% Specify column names and types
opts.VariableNames = ["ParticipantID", "BDNF_2", "BDNF_3", "Intervention",
"BDI_pre_sum", "BDI_post_sum", "BDI_1month_sum", "Hamilton_1month_sum", "AGE",
"SEX", "MDD_recurrent_no_current", "MDD_single_no_current", "Hamilton_pre_sum",
"Hamilton_post_sum", "Ham_pre_post", "Ham_pre_1month"];
opts.VariableTypes = ["double", "categorical", "categorical", "categorical",
"double", "double", "double", "double", "double", "categorical", "categorical",
"categorical", "double", "double", "double", "double"];

% Specify file level properties
opts.ExtraColumnsRule = "ignore";
opts.EmptyLineRule = "read";

% Import the data
BNDF_Table =
readtable("C:\Users\elias\OneDrive\OsloMet\Master\Masteroppgave\Koding\BNDF.csv",
opts);

% Create table with the non-placebo Participants
nonplacebo_BNDF_Table = BNDF_Table(BNDF_Table.Intervention == '0',:);

%Create binary category for Hamilton Improvement
rows = height(BNDF_Table);  %Changed from non_placebo
for row = 1:rows
    if BNDF_Table.Ham_pre_post(row) < 0       %Changed from non_placebo
        BNDF_Table.Ham_Improvement(row) = 1;   %Changed from non_placebo
    else
        BNDF_Table.Ham_Improvement(row) = 0;   %Changed from non_placebo
    end
end

%Create binary category for BDI Improvement
rows = height(BNDF_Table);      %Changed from non_placebo
for row = 1:rows
    BNDF_Table.BDI_pre_post(row) = BNDF_Table.BDI_post_sum(row) -
BNDF_Table.BDI_pre_sum(row);   %Changed from non_placebo
    if BNDF_Table.BDI_pre_post(row) < 0    %Changed from non_placebo
        BNDF_Table.BDI_Improvement(row) = 1;%Changed from non_placebo
    else
        BNDF_Table.BDI_Improvement(row) = 0;  %Changed from non_placebo
    end
end
```

```
BNDF_Table = movevars(BNDF_Table,"BDI_pre_post","After","BDI_post_sum");
%Changed from non_placebo

%Get table with some BNDF analysis
[BNDF_BDI_Info, BNDF_Ham_Info] = My_Functions.BNDF_analysis(BNDF_Table);
%Changed from non_placebo


%% Clear temporary variables
clear opts
```

13.5 ImportAB_Dataset;

```
%% Import data from text file
% Script for importing data from the following text file:
%
%    filename:
C:\Users\elias\OneDrive\OsloMet\Master\Masteroppgave\Koding\AB_dataset.csv
%
% Auto-generated by MATLAB on 11-Apr-2022 12:35:48

%% Set up the Import Options and import the data
opts = delimitedTextImportOptions("NumVariables", 7);

% Specify range and delimiter
opts.DataLines = [2, Inf];
opts.Delimiter = "\t";

% Specify column names and types
opts.VariableNames = ["ParticipantID", "TrainingType", "ConditionType",
"TrainingSetLength", "Date", "AdjustedAB", "ABIndex"];
opts.VariableTypes = ["double", "categorical", "categorical", "double", "double",
"double", "double"];

% Specify file level properties
opts.ExtraColumnsRule = "ignore";
opts.EmptyLineRule = "read";

% Specify variable properties
opts = setvaropts(opts, ["ParticipantID", "TrainingType", "ConditionType"],
"EmptyFieldRule", "auto");

% Import the data
ABdataset =
readtable("C:\Users\elias\OneDrive\OsloMet\Master\Masteroppgave\Koding\AB_dataset.
csv", opts);


%% Clear temporary variables
clear opts
```

13.6 Plots

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%
% Code for making the plots. Be aware that some of the Variable Names has
% been changed manually, and might need some change. This will come up as
% Error messages.
%
% A typical message can be that the vaiable Median Hamilton Pre-sum doesn't
% exist. Then this might need to be changed to something like
% median_hamilton_pre_sum. The program will suggest variable name, so it is
% possible to see what is right.
%
%
%
%
%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
%
% p =
parallelplot(ABM_Analysis,"GroupVariable","Placebo","CoordinateVariables",["
ABM_Improvement","Median_AGE","PercentMales","PercentMet"],
LegendTitle="Positive Training",Title="ABM Improvement Analysis")
%
%
```

```
HamPlot = parallelplot(BNDF_Ham_Info,"GroupVariable","Positive
Training","CoordinateVariables",["Ham Improvement","Median Hamilton Pre-
sum","Median Age","Percent Males","Percent Met"],"LegendTitle","Positive
Training","Title","Hamilton Improvement Analysis")
```

```
x = categorical(["Group Count","Median Hamilton pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
x = reordercats(x,["Group Count", "Median Hamilton pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
y = BNDF_Ham_Info{1:end,["GroupCount", "Median Hamilton Pre-sum","Median
Age","Percent Met","Percent Males"]}
bar(x,y.')
title("Hamilton Improvement throughout training period","FontSize",35);
legend({'Not improved, Placebo', 'Not improved, Positive Training',
'Improved, Placebo', 'Improved, Positive
Training'},"FontSize",15,Box="off");
grid on
grid minor
```

```
BDIPlot = parallelplot(BNDF_BDI_Info,"GroupVariable","Positive
Training","CoordinateVariables",["BDI Improvement","Median BDI Pre-
sum","Median Age","Percent Males","Percent Met"],"LegendTitle","Positive
Training","Title","BDI Improvement Analysis")
```

```
x = categorical(["Group Count", "Median BDI pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
x = reordercats(x,["Group Count", "Median BDI pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
y = BNDF_BDI_Info{1:end,["GroupCount", "Median BDI Pre-sum","Median
Age","Percent Met","Percent Males"]}
bar(x,y.')
title("BDI Improvement throughout training period","FontSize",35);
legend({'Not improved, Placebo', 'Not improved, Positive Training',
'Improved, Placebo', 'Improved, Positive
Training'},"FontSize",15,"Box","off");
grid on
grid minor
```

```
ABM_Plot_Timewise =
parallelplot(ABM_Analysis_timewise,GroupVariable="Positive
Training",CoordinateVariables=["ABM_Improvement","Median Age","Percent
Males","Percent Met","Time Category"],LegendTitle="Positive
Training",Title="ABM Analysis Containing information on training period as
whole, as well as first and last week")
```

```
%stack = stackedplot(ABM_Plot_Timewise,BDIPlot)
```

```
%bar(categorical(table_data{1:7, 1}), table_data{1:7, 2:4});
x = categorical(["Group Count", "Median Age Participants","Percent Met
Gene","Percent Males"]);
x = reordercats(x,["Group Count", "Median Age Participants","Percent Met
Gene" ,"Percent Males"]);
y = ABM_Analysis{1:end,["GroupCount",
"Median_AGE","PercentMet","PercentMales"]}
bar(x,y.')
title("Change in AB Index throughout training period","FontSize",35);
legend({'Not improved, Placebo', 'Not improved, Positive Training',
'Improved, Placebo', 'Improved, Positive
Training'},"FontSize",15,Box="off");
grid on
grid minor
% bar(ABM_Analysis.Mean_AGE)
%bar(categorical(ABM_Analysis{["Median_AGE","PercentMales","TotalPercentMet"
]}),ABM_Analysis{2:end,["Median_AGE","PercentMales","PercentMet"]});
```

```
x = categorical(["Group Count", "Median Age Participants","Percent Met
Gene","Percent Males"]);
x = reordercats(x,["Group Count", "Median Age Participants","Percent Met
Gene" ,"Percent Males"]);
y = ABM_Age{1:end,["GroupCount", "Median Age","Percent Met","Percent
Males"]}
bar(x,y)
title("Change in AB Index throughout training period","FontSize",35);
subtitle("Patients Grouped by Age");
legend({'Age 18-36 Not improved, Placebo', 'Age 18-36 Not improved, Positive
Training', 'Age 18-36 Improved, Placebo', 'Age 18-36 Improved, Positive
Training','Age 37-54 Not improved, Placebo', 'Age 37-54 Not improved,
Positive Training', 'Age 37-54 Improved, Placebo', 'Age 37-54 Improved,
Positive Training','Age 55-72 Not improved, Placebo', 'Age 55-72 Not
improved, Positive Training', 'Age 55-72 Improved, Placebo', 'Age 55-72
Improved, Positive Training'},"FontSize",15,Box="off");
grid on
grid minor
```

```
x = categorical(["Group Count", "Median Age Participants","Percent Met
Gene","Percent Males"]);
x = reordercats(x,["Group Count", "Median Age Participants","Percent Met
Gene" ,"Percent Males"]);
y = ABM_Analysis_timewise{1:end,["Group Count", "Median Age","Percent
Met","Percent Males"]}
bar(x,y)
title("Change in AB Index throughout training period,
timewise","FontSize",35);
legend({'Not improved, Placebo', 'Not improved, Positive Training',
'Improved, Placebo', 'Improved, Positive
Training'},"FontSize",15,Box="off");
grid on
grid minor
```

```
x = categorical(["Group Count", "Median Hamilton pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
x = reordercats(x,["Group Count", "Median Hamilton pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
y = BNDF_Ham_Age{1:end,["GroupCount", "Median Hamilton Pre-sum","Median
Age","Percent Met","Percent Males"]}
bar(x,y.')
title("Hamilton Improvement throughout training period","FontSize",50);
legend({'Age 18-36 Not improved, Placebo', 'Age 18-36 Not improved, Positive
Training', 'Age 18-36 Improved, Placebo', 'Age 18-36 Improved, Positive
Training','Age 37-54 Not improved, Placebo', 'Age 37-54 Not improved,
Positive Training', 'Age 37-54 Improved, Placebo', 'Age 37-54 Improved,
Positive Training','Age 55-72 Not improved, Placebo', 'Age 55-72 Not
```

```
improved, Positive Training', 'Age 55-72 Improved, Placebo', 'Age 55-72
Improved, Positive Training'},"FontSize",15,Box="off");
grid on
grid minor
```

```
x = categorical(["Group Count", "Median BDI pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
x = reordercats(x,["Group Count", "Median BDI pre sum", "Median Age
Participants", "Percent Met Gene", "Percent Males"]);
y = BNDF_BDI_Age{1:end,["GroupCount", "Median BDI Pre-sum","Median
Age","Percent Met","Percent Males"]}
bar(x,y.')
title("BDI Improvement throughout training period","FontSize",35);
legend({'Age 18-36 Not improved, Placebo', 'Age 18-36 Not improved, Positive
Training', 'Age 18-36 Improved, Placebo', 'Age 18-36 Improved, Positive
Training','Age 37-54 Not improved, Placebo', 'Age 37-54 Not improved,
Positive Training', 'Age 37-54 Improved, Placebo', 'Age 37-54 Improved,
Positive Training','Age 55-72 Not improved, Placebo', 'Age 55-72 Not
improved, Positive Training', 'Age 55-72 Improved, Placebo', 'Age 55-72
Improved, Positive Training'},"FontSize",15,Box="off");
grid on
grid minor
```