Effect of CBASP therapy on the neurophysiological responses to pictures of neutral faces in depression An event-related potential study

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Tämä pro gradu -tutkielma tarkastelee masentuneiden ja terveiden koehenkilöiden tunnetiedon käsittelyn eroja. Tarkoituksena on selvittää, onko masentuneiden ja terveiden koehenkilöiden välillä eroa kasvonilmeiden välittämän tunnetiedon käsittelyssä aivoissa, ja vaikuttaako kognitiivisbehavioraalinen CBASP-psykoterapia aivovasteisiin.

Tutkimuksen 42 koehenkilöstä 32 oli masentuneita ja 10 terveitä. Masentuneet koehenkilöt jaettiin sattumanvaraisesti terapiaryhmään ja tavanomaisen hoidon ryhmään. Tutkimusmenetelmänä käytettiin EEG-aineiston ERP-analyysia. EEG-aineistosta tarkasteltiin kasvokuvien esittämiseen liittyvää aivoaktivaatiota. Keskiarvot kasvokuvien aiheuttamista vasteista laskettiin ryhmittäin ja jokaiselta koehenkilöltä erikseen. Pääasiallinen tarkastelun kohde oli vasteet neutraaleille kasvokuville, kun niitä edelsi a) neutraali b) iloinen c) surullinen ilme. Näitä kolmea kategoriaa tarkasteltiin vasemman ja oikean näköaivokuoren päällä olevalta kanavalta kahdessa eri aikaikkunassa. Varsinainen tilastollinen analyysi tehtiin toistomittausten varianssianalyysilla.

Tuloksista havaittiin ensimmäisessä aikaikkunassa (80-160 millisekuntia) oikeassa aivopuoliskossa olevan korkeammat vasteet kuin vasemmassa sekä masentuneilla että kontrolleilla. Oikealla puolella kontrolleilla oli korkein vaste neutraali-neutraali pareihin. Masentuneilla ilmeiden välillä ei ollut eroa. Jälkimmäisessä huipussa masentuneilla oli oikealla puolella korkeammat vasteet, kontrolleilla eroa ei ilmennyt. Masentuneilla oli korkeammat vasteet kaikkiin ilmeisiin oikeassa kuin vasemmassa aivopuoliskossa. Interventiovaikutus havaittiin tavanomaisen hoidon ryhmässä: jälkimittauksessa vasteet laskivat. CBASP-terapia nosti ensimmäisessä aikaikkunassa oikeassa aivopuoliskossa amplitudit samalle tasolle kuin kontrolleilla. Jälkimmäisessä huipussa (200-350 millisekuntia) oikealla puolella CBASP-ryhmän vasteet nousivat kontrolleja korkeammaksi.

Terapialla saattaa olla vaikutusta jälkimmäiseen aikaikkunaan, joka liitetään tietoiseen ärsykkeen tarkasteluun. Terapia näyttää estävän amplituditasojen laskun, joka on nähtävissä tavanomaisen hoidon ryhmässä, ja joka saattaa viitata patologiseen muutokseen masennuksessa. Tutkimuksen pienen otoskoon vuoksi saattaa olla, että terapia- ja tavanomaisen hoidonryhmiin valikoitui lähtökohtaisesti erilaisia koehenkilöitä, minkä vuoksi terapiaryhmän vasteet muistuttavat



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1. INTRODUCTION

1.1 Depression

Depression is one of the most common psychiatric disorders in Finland. The prevalence of depression in one year is estimated to be approximately 5 % of the population. The lifelong prevalence of depression varies in different countries, but in Finland it is estimated to be approximately 10-15 % of the population. Thus, the impacts of depression are significant to the public health, for instance causing expenses by being the reason of many disability pensions (Isometsä et al. 2014).

In the diagnostic systems ICD-10 and DSM-V, depression is categorized under mood disorders together with bipolar disorder. Depression is divided into many groups depending on its severity and recurrence. The most common symptoms of depression are depressed mood, loss of interest or satisfaction, exhaustion, loss of self-appreciation or self-confidence, unconscionable self-criticism or unjustified feel of guilt, recurrent thoughts of death or self-harm or parasuicidal behavior, indecisiveness or inability to concentrate, psychomotoric agitation or slowness, sleep disorders or changes in appetite and weight.

Depression is also characterized by a negativity bias, which is an increased responsiveness to affectively negative stimuli, and memorizing negative stimuli (Fales et al. 2008). The origin of the bias is yet unknown. It's hypothesized to derive either from impaired cognitive control of affective information or increased bottom-up responses to stimuli containing emotional information which disturb the cognitive control mechanisms (Fales et al. 2008). Another characteristic called mood congruency has been studied. According to Leppänen et al. (2004), mood congruency hypothesis means that depressed mood may enhance the processing of mood congruent material, which in this case might pictures of depressive and sad facial expressions, and impair the processing of mood incongruent, for instance happy and pleasant, material.

1.2 Treatment of depression

Depression is commonly treated either by medication, psychotherapy or the combination of these two. According to Reinecke and Davison (2006), outcome studies have shown that both medication and psychotherapy are effective in the treatment of depression. There are different kinds of psychotherapies hypothesizing causes of depression differently and also concentrating on different depressive symptoms. One of the most common type of psychotherapy is cognitive-behavioral therapies (CBT). According to Roth (2005), cognitive-behavioral therapies have been shown to be efficient in treating moderate and severe depression. Psychotherapies can be delivered as individual treatments or group treatments, both of which have their strengths and weaknesses. In group treatments, the group lessens the feeling of despair and enhances empowerment. Other group participants enable model learning and give the participant a sense of different ways to solve problems (Kokko, Karila 2014).

According to Schatzberg et al. (2005), there are significant differences in the treatment responses: a proportion of depressed patients do not respond to either medication or psychotherapy. In their research they noticed that those who do not respond to nefazodone medication respond to psychotherapy and vice versa. This may not be generalized to other medicines and psychotherapies; however, individual differences must be noted in choosing the treatment to ensure the response.

1.3 Cognitive Behavioral Analysis System of Psychotherapy (CBASP)

One model of cognitive-behavioral group therapy is CBASP, which stands for Cognitive Behavioral Analysis System of Psychotherapy (McCullough 2003). It is a model of psychotherapy designed by James McCullough in the 1980s. CBASP is designed for the treatment of chronically depressed adults. CBASP is based on the cognitive behavioral treatment tradition of depression, created originally by Aaron T. Beck. The main idea of cognitive behavioral treatment is that the thought processes of the depressed are disturbed. The individuals with depression have distorted negative

views of themselves, their world and their future. These areas are known as the cognitive triad, and the distortion of the triad leads to depressive feelings (Beckham et al. 1986). According to McCullough (2003), the behavior and speech of individuals with depression is primitive, which is keeping them disconnected from the environment. This makes them unresponsive to environmental consequences and feedback. CBASP draws from the work of Jean Piaget, who constructed the model of the cognitive development of children. One of Piaget's developmental stages is the preoperational stage, which is characterized by egocentrism and a person using their existing viewpoints to explain causation. The stage is apparent in children aged from 2 to 7. The main principle of McCullough's CBASP therapy is that chronic depression leads the depressed person to think and act like a preoperational child in the social and interpersonal area.

According to McCullough (2003), individuals with depression are unable to disengage themselves from the present moment and tend to evaluate social-interpersonal events negatively. Individuals with depression are seeing their own distortedly negative view of the world and the current situation as the only one possible, reflecting a negative past and a hopeless future. Individuals with depression are highly sensitive to emotional behavior of other people. This is seen both on behavioral level and neuropsychological level. According to McCullough (2003), the emotional sensitivity of depressed persons is similar to that of children in preoperational developmental stage. Chronically depressed patients are, according to McCullough (2003), unable to generate and feel true empathy. CBASP is designed to help individuals with depression move beyond a preoperational worldview and help them function better in social situations.

According to Kokko and Karila (2014), the group model of CBASP concentrates on two main themes. Activation of functioning is one part. It aims to lessen passivity and improve mood by increasing functionality. Another part of the CBASP therapy is the social interaction. In therapy sessions patients think how their own behavior affects their relationships and outcomes in social situations. People with depression often behave and think in such ways in social situations that leave them unsatisfied and disappointed. Sociality is a remarkable part of the human life and helping people to thrive in relationships and social situations is critical in the treatment of chronic depression (Kokko, Karila 2014).

CBASP has been practiced both as a group therapy and as an individual therapy. According to McCullough (2003), the efficacy of the therapy has been studied more with individuals. According to Schoepf and Neudeck (2011), CBASP has been shown to be efficient in treating patients with

major depressive disorder. The group therapy has been studied also. According to Sayegh (2012), the group treatment given for 20 sessions significantly reduced the symptoms of depression in the chronically depressed. There was improvement in psychosocial functioning, trusting in relationships and in social skills.

Efficacy of CBASP has been studied both in the symptomatology and neurology level. Klein et al. (2014) studied the efficacy of CBASP with functional magnetic resonance imaging (fMRI) measurements before and after a 12-week intervention. An increased activity in amygdala was found, resulting in the researchers carefully suggesting that CBASP might increase the patients' capability to interact with their interpersonal environment and relationships. The studied group, however, was small and included no control group, so it is not certain that the amygdala activity resulted from the therapy.

1.4 Processing of emotional information in depression

As is noted in McCullough's CBASP therapy, individuals with depression tend to have negative cognitions about the world. Vanderhasselt et al. (2011) have noted that depression is also characterized by impaired ability of disengaging from negative stimuli. They studied the ability of individuals diagnosed with major depressive disorder to disengage from negative emotional stimuli. They hypothesized that depressed patients have less control over negative stimuli. In their study, participants were shown happy or sad faces (from Karolinska Institute Emotional Faces), preceded by a cue word instructing participants to press a button corresponding to the expressed emotion or button opposite to the expressed emotion. They noted that the participants with depression responded more slowly than the control group on trials that required disengaging from negative faces.

According to Fales et al. (2008), the negativity bias causes individuals with depression to get stuck in negative information, which occurs also in emotional information processing in general. Research has found that brain areas which are involved in emotion processing function differently in depressed individuals. These include the amygdala and ventromedial prefrontal cortex. These areas might be involved in the perception, evaluation and response to emotion inducing stimuli.

Amygdala and ventromedial prefrontal cortex are normally deactivated during cognitive processing. When a person experiences anxiety, sadness, fear, these areas activate. Depressed individuals show hyperactivity of the amygdala when processing emotional information and stimuli (Fales et al. 2008).

There appears to be lateralization to some extent of emotional facial expression perception; however, the results in different studies have been contradictory. There are two significant theories. Borod et al. (1998) presented the right hemisphere hypothesis, which suggests that the right hemisphere is responsible for processing emotions. The valence-specific hypothesis, which was proposed by Ahern and Schartz, suggests that the left hemisphere is responsible for positive emotion processing while the right hemisphere is important in processing negative emotions (Adolphs, 2001; Wedding & Stalans, 1985). Killgore and Yurgelun-Todd (2007) suggested that aspects of both hypotheses may be present simultaneously and that they might be different perspectives to emotional information processing, which is a complex system of neural networks. Considering individuals with depression, it was found in a study comparing healthy controls and depressed subjects in recognition of facial expressions that the depressed showed a reduced hemispheric asymmetry and impairment in right hemisphere performance (Mikhailova et al., 1996).

According to Leppänen and Milders (2004), there may be functional abnormalities in emotion processing in depression, and depressed patients may therefore attribute valence to stimuli that are normally interpreted as neutral. In their study, they examined the recognition of different facial expressions in patients with depression. The patients and controls had to respond quickly and recognize faces with happy, sad or neutral emotions. Researchers found out that depressed were as accurate as controls at recognizing happy and sad faces. Controls recognized neutral faces as accurately as happy and sad faces, but depressed patients recognized neutral faces less accurately than either happy or sad faces. People with depression were also slower to recognize neutral faces than controls. This may suggest that, unlike control subjects, individuals with depression might not perceive neutral faces as unambiguous signals of emotional neutrality.

Suslow, Junghanns and Adolt (2001) had a contradictory result in their study compared to Leppänen and Milders. In their study participants had to recognize faces with happy, sad or neutral faces from a crowd, and their reaction time was tested. Suslow et al. (2001) found out that depressed individuals did not recognize neutral faces any slower than nondepressed controls. However, Leppänen and Milder's result might have more support, as they note other studies have

had similar findings, and therefore depression might impair recognition of neutral faces.

1.5 Attention and emotional information processing

According to Mogg and Bradley (2005), some studies have found that depressed patients have an attentional bias in information processing towards negative information. The attentional bias is not present in all stimuli, but predominantly in stimuli containing material relevant to self. This has been tested with modified Stroop tests, where negative self-descriptive words are presented. The participants with depression have shown attentional bias towards negative words when they have an opportunity to process negative word content relative to their own experiences. This means for instance, that the words are primed with self-descriptive negative schemas and ideas. The bias is not, however, always present.

According to Lichtenstein-Vidne et al. (2016) there is evidence of an attentional negativity bias, which is, according to the authors, a key factor in initiating and maintaining depression on the cognitive level of the disorder. They also mention that the strongest evidence of attentional negativity bias comes from emotional Stroop tests. In emotional Stroop tests the participants need to name the color of an emotional word and disregard its semantic meaning. Individuals with depression take a longer time to name the color of negative words, compared to words with no affective valence. It is unclear whether the negativity emotional bias appears and arises at the level of perception, at the level of response selection or whether it reflects an effort to try to suppress the negative emotional information.

However, according to Lichtenstein-Vidne et al. (2016), the evidence of the negativity emotional bias in Stroop tests represents emotional distraction inside the focus of attention, which is task-relevant, or a required part of the task. It is unclear whether people with depression would exhibit a bias towards task-irrelevant information, or information not associated with the ongoing task. Task-irrelevant material is often presented outside the center of attention. In real life situations, most of the information is not presented in the center of the retina.

Surguladze et al. (2005) measured in their study the fMRI responses in happy and sad emotional faces in depressed individuals. They found differences in the neural responses in right

and left fusiform gyri, which are areas associated with facial recognition and in right putamen. These areas had increases in neural responses to expressions of happiness in control subjects and decreases in depressed individuals. The results of their study suggest increases in neural responses in regions associated with processing of emotional stimuli to sad, but not happy facial expressions in depressed individuals. The results may be associated with attentional biases in individuals with depression and suggest a potential neural basis for the negative cognitions and social dysfunction in major depression.

In a study of Leppänen et al. (2004) they studied accuracy and speed in the recognition of neutral, happy, and sad facial expressions in depressed patients and healthy controls. The depressed individuals and controls were equally accurate at recognizing happy and sad faces, but they differed in the recognition of neutral faces. Controls recognized neutral faces as accurately as happy and sad faces, while depressed individuals recognized neutral faces less accurately than either happy or sad faces. Results showed a generally slower emotion recognition performance for the depressed than the controls. Leppänen et al. (2004) suggested that depression especially affected the processing of emotionally neutral faces.

1.6 Affective priming

In a study of Hietanen and Astikainen (2013), the ERP responses to facial expressions were studied. The main target of the study was to examine the affective congruency effect, that is, whether the priming or preceding emotional picture affects the response to the emotional picture shown after the prime. They examined especially the N170 response, which is a face sensitive ERP response. The results showed that the affective congruency effect is present in the N170 responses. The researchers also found that the P1 amplitudes recorded in the left hemisphere were larger for happy faces after incongruent, in which the priming emotional picture was not the same as the target picture, than after congruent primes.

Therefore, according to Hietanen and Astikainen (2013), the face-sensitive N170 response amplitudes showed an affective priming effect. The N170 amplitudes to happy faces were larger when presented after positive than negative primes, whereas the N170 amplitudes to sad faces were

larger when presented after negative than positive primes. In addition to N170, priming effects were also found in later brain responses. Facial expression recognition was found to be faster and more accurate when the context was congruent rather than incongruent with the facial expression, which advocates the affective congruency effect. However, the priming effect in this behaves differently from a typical priming effect. In semantic priming, for instance, the brain responses after the congruent priming word are smaller than after a non-congruent prime, suggesting that less resources are needed to process the word. The N170 might, however, work differently than the responses for semantic priming.

1.7 Studying depression with EEG

Depression can be studied with brain imaging techniques, one of which is electroencephalography (EEG). A point of interest in depression research may be for example biomarkers, which aid the study of mental disorders by connecting measurable neurological phenomena to the underlying biological processes. According to Baskaran et al. (2012), biomarkers are indications of pharmacological response that are quantifiable and precise. According to Baskaran et al. (2012), biomarkers may be used in predicting treatment response. They may help finding a suitable treatment for depression for each individual.

The processing of facial information in the brain can be followed by focusing on different event-related potentials. They are measured as averaged EEG components. In facial information processing several different ERPs can be extracted. They are measured by the time they appear after the onset of the stimulus, or as latency. Typical ERP components evoked by visual face stimuli are P1, N170, P2 and P3. The letter indicates the direction (positive or negative amplitude) and the number indicates the latency (Luck 2005). P1 is the first peak appearing after stimulus onset and it is associated with directing of attention. N170 reflects the neural processing of faces, and it is a negative peak which appears about 130-200 milliseconds after stimulus presentation. P2 appears between 150 and 270 milliseconds P3 appears at 200-500 and they are thought to reflect more conscious stimulus evaluation (Zhang et al. 2016; Dai et al. 2016).

Chen et al. (2014), compared N170 responses to emotional faces in patients with first or recurrent major depressive disorder. Patients with first major depression disorder had lower N170 amplitudes and longer latencies when identifying happy, neutral, and sad faces, compared to control group. Patients with recurring depression had lower N170 amplitudes and longer latencies when identifying happy and neutral faces, but higher N170 amplitudes and shorter latencies when identifying sad faces, compared to first MDD patients.

In an ERP study of Dai and Feng (2010) major depressive disorders patients, depression in remission patients and nondepressed controls were compared in a word valence evaluation task. MDD participants had a smaller N1 amplitude for negative words in bilateral hemispheres compared with depressed participants in remission and nondepressed controls. They also had a smaller P1 amplitude for positive words in both hemispheres compared with other groups. Researchers also noted that depressed participants and those in remission showed enhanced negativity in N450 over the parietal regions for negative words than the control group.

In the study of Zhang et al. (2016) unconscious emotional processing in depression was studied with EEG. They conducted an experiment in which they showed either sad and neutral faces or happy and neutral faces. In recognizing happy faces, the depressed showed a smaller response in happy than in neutral trials. In the sad faces, depressed showed a larger response in sad than in neutral trials. According to the researchers, the abnormality in the responses suggests that the unconscious emotional processing is biased towards mood-congruent stimuli in individuals with depression. Individuals with depression might process happy stimuli insufficiently, and might avoid careful processing of neutral faces in sad, mood congruent material (Zhang et al. 2016; Leung et al. 2009).

1.8 Research questions

This thesis is based on the data of the Psychological Group Interventions for Depression: Systemic and Neurophysiological Correlates of Treatment Effect research project (PsySysNe). In the PsySysNe project, the goal was to study the efficacy of CBASP therapy in treatment of depression. Importance of this thesis arises from the need to create efficient treatments for depression. Chronic

depression causes a lot of pain and frustration and the effects of depression on the psychosocial wellbeing and social functioning are tremendous. Deficits in social functioning may be a remarkable part of the disorder and to improve the wellbeing of individuals suffering from depression is critical. People with depression might not demand efficient treatments for themselves, since depression is characterized by feelings of inferiority, low self-esteem and self-appreciation.

The PsySysNe research project aims to research possible neuroimaging biomarkers and systemic and neurophysiological changes in body in depression, which can be used for diagnostical purposes and estimating treatment efficiency. As depression is a common psychiatric disorder, it is critical to find efficient and cost-effective treatments for it. To ensure ample treatment for depression, the costs of the treatments must be within the resources of the public health system. CBASP therapy has been studied, but not enough to measure the efficacy and effectiveness for it to be implemented to the Finnish healthcare system.

The goal of this study is to examine the processing of emotional information of individuals with depression. As stated above, individuals with depression tend to be preoccupied with negative ideas and thoughts. People with depression also react differently to negative emotions compared to healthy people with no depression. In my study, I examine how the brain of individuals with depression processes emotional information by comparing reactions to neutral facial expressions presented after priming with negative, positive or neutral faces. After examining the differences in participants with depression and control participants, I examine whether the CBASP treatment affects the information processing of the depressed and whether the CBASP therapy changes the emotional information processing responses in depressed towards to those of healthy controls.

The facial expressions used for the analysis of the brain responses are neutral faces. Most studies researching emotional information processing in depression have been examining tasks containing different emotions (Leppänen, Milders 2004). This study might be able to give new information on how emotional priming and negativity bias affect emotional information processing in such cases where both primes and targets are shown. The PsySysNe project experiment included also emotional primes, which have been studied before (i.e. Valkonen and Vacker, 2015).

The CBASP treatment is to lessen the exuberant focusing in negativity of depressed patients and help them to manage to interact in social situations. Both the recognition of other's feelings and reacting to them is essential in social behavior. The CBASP therapy concentrates on interpersonal skills and social cognition, among other points of interest. The negativity bias might cause people

with depression concentrate more on the sad emotional information which might cause the responses to be different in the neutral faces too.

Therefore, the research questions are:

- 1) Are there differences in the neural basis emotional processing between depressed participants and healthy controls in the event-related potentials in neutral targets following emotional primes?
- 2) Does CBASP affect the neural basis of emotional information processing more than treatment as usual (TAU)?

Based on the research question two hypotheses are set. It is hypothesized that controls and depressed have differences in the emotional information processing. The difference is seen in the form of negativity bias, or depressed having difficulties in detaching from negative emotional information. It is also hypothesized that CBASP will affect the neural basis of emotional information processing more than TAU.

2. METHODS

2.1 Research project

This master's thesis is based on the data from the study project Psychological Group Interventions for Depression: Systemic and Neurophysiological Correlates of Treatment Effect (PsySysNe). The study was conducted in collaboration with University of Jyväskylä/Jyväskylä Centre for Interdisciplinary Brain Research, Kuopio University Hospital and Central Finland Healthcare District. The project is funded by the government of Finland. The ethical approval for the study had been applied for and received from the University of Eastern Finland Committee of Research Ethics. The research project aims to study the efficacy of CBASP therapy in moderate and severe depression, compared to the usual treatment. In addition to studying the efficacy of CBASP therapy,

the PsySysNe project studies if the psychosocial treatments cause neurophysiological changes in the participants.

2.2 Participants

The participants chosen to the project were patients of the Psychiatric Center of Kuopio University Hospital and the Psychiatric Department of Central Finland Health District. The participants were informed about the study project by the personnel of the psychiatric departments. If the personnel regarded the patient as suitable for the study in terms of inclusion criteria the patients were given the research handout and they underwent an evaluation visit. The participants with depression were divided randomly to either a psychotherapy group, or treatment as usual group.

Inclusion criteria for depressed participants were one of the following: 1) moderate or difficult depression that has lasted at least two years, 2) "double depression", consisting of both moderate or difficult depression and dysthymia, which includes persistent depression-like mild symptoms, 3) moderate or difficult depression that has lasted at least two years and had been recurrent with only partial recovery between depressive episodes. Exclusion criteria were psychotic depression, bipolar disorder, current substance abuse and severe cognitive, motor, visual or auditory deficits. Structured Clinical Interview for DSM-IV was conducted for depressed participants to ensure eligibility. The Montgomery-Åsberg depression scale was used in the Structured Clinical Interview. After the interview the participants were asked to sign a paper of conduct. For the EEG part of the study, participants willing to participate in the EEG measurements filled in a background information questionnaire to assess their suitability for the EEG method. The participants were then interviewed by the person conducting the measurements to ensure their suitability. Exclusion criteria for the EEG measurements were epilepsy, head injuries or encephalopathy and developmental neurocognitive disorders. The ages of the participants ranged between 18 to 65 years. Controls were recruited via an e-mail list for people interested in participating in brain research.

There were 42 participants chosen for this thesis, 10 of which are healthy controls and 32 depressed patients. Left-handed participants were excluded, also those participants in the depression group with no after therapy measurements. In the original PsySysNe project, there were also people

who participated in a befriending group, which intended to study a social support effect. However, they were not chosen for this thesis as their amount in the after measurements was small. Participants with depression were divided into two groups. 21 of the depressed underwent CBASP therapy and 11 treatment as usual (TAU), which included medication and supportive visits with a psychiatric nurse. The duration of CBASP therapy was 20 weeks and a single therapy session lasted 2 hours, and the total amount of therapy visits was 20. The TAU also lasted 20 weeks.

2.3 Experiment

The research project included an EEG analysis of an emotional picture processing paradigm, alongside with other measurements to participants. The other experiments studied rhythmic resting state activity and event related potentials during listening tasks. Participants also took part in a linguistic/non-linguistic skills assessment by using Wechsler Adult Intelligence Scale (WAIS-II) similarities and block design. The measurements were conducted before and after the therapy, or in the TAU group after the treatment as usual. EEG responses to emotional faces were measured both with depressed participants and healthy controls. The presented pictures included emotional and neutral female and male faces derived from the Karolinska Directed Emotional Faces (KDEF). The KDEF pictures were controlled in their other visual elements, for example by using soft lightning, shooting expressions in multiple angles, using uniform shirt colors, using grid to center participants face during shooting, and positioning of eyes and mouths in fixed image coordinates during scanning (More information of the paradigm can be found in page About KDEF. Karolinska Directed Emotional Faces. http://www.emotionlab.se/sites/default/files/About%20KDEF.pdf.) Example of the pictures is attached in the attachment page.

During the experiment participants were shown the emotional face photographs on a high definition television screen while sitting in a comfortable chair in a dimly lit laboratory room, where a button pressing apparatus was placed on a small table on the side of their right hand. The placement of the chair, the television screen and the button were kept constant for all the participants in all groups. The researchers were in a separate observation room next door to the participant, receiving constant video and audio monitoring of the participant.

The faces shown to participants were arranged in prime-target pairs. There was a prime picture, which was either a happy face, sad face or neutral face. After that participants were shown a neutral face, and the prime-target pairs appeared in these combinations: neutral face after a happy prime (labeled hneu), neutral face after a neutral prime (labeled nneu), or a neutral face after a sad prime (labeled sneu). The abbreviations are used later in this thesis. The primes and targets appeared in random pairs and there was no specific order which of the primes appeared first. The prime was shown for 1000 milliseconds (ms), followed by a black screen for 700 milliseconds, after which the neutral face was presented for 1000 milliseconds.

The research setting included also target pictures. In the target pictures, white screen with a black question mark appeared sporadically. The participants were instructed to answer which was the gender of the person in the photograph presented prior to the question screen by pressing a button. Participants pressed a button with the tag "male" for photographs of male faces with their index finger and a button with the tag "female" for female faces with their middle finger. After pressing the button, the experiment continued by another set of photographs. The purpose of question marks was to ensure that the participants' attention was directed toward the monitor.

During the task, EEG data was recorded with a 128-channel Geodesic sensor net and the Net Station program version 4.2.1 on an Apple Mac computer. Electrode impedance was kept below $50k\Omega$ by maintaining the moisture levels of the electrode sponges in between experiments.

According to previous studies, hemispheric differences in emotional information processing may be important (Chen et al. 2014, Mikhailova et al. 1996). Therefore in the analysis two channels from different hemispheres were chosen to study the interhemispheric differences. The two channels are P7, or 58 from the parietal lobe in left hemisphere and P8, or 96 from the parietal lobe in right hemisphere. The numbers channels are derived from the 128-channel EEG cap, implying that the different channels measure responses from different parts of the brain. The letter P implies the lobe the electrode is measuring data from, in this case from parietal lobe. It is important to note that EEG method is mainly designed to study temporal differences, not spatial differences.

2.4 EEG data analysis

The data from the participants was analyzed with MEGGIE, a program created by University of Jyväskylä for studying MEG and EEG data (Heinilä et al. 2013). The first part in the data analysis was to preprocess the data, which was done with the help of the MEGGIE interface in the same manner for all participants. The preprocessing included filtering and cleaning the data by excluding bad channels and eye blinks.

The first step in data preprocessing was to combine the data files from three parts to a complete file with a python script.

The second step in data preprocessing was filtering the raw data. The signal was digitally filtered with a 40 Hz low pass filter and with 1 Hz high pass filter. The filtering helped the detection of eye blinks, movement artifacts, cardiac artifacts and bad channels. The third step was to choose the bad channels, chosen visually and with the help of PsySysNe research records and previous records by Sandra Naumann (Naumann 2015). Noisy channels were excluded to ensure that the results would be as accurate as possible. The comparison channels P7 and P8 (58 and 96 in the 128 Channel Geodesic Sensor Net) were not bad in any of the datasets. The fourth step was choosing the eye blink channel. The eye blinks were visible especially in channel 8. Channels 17 and 11 were used in some cases if the channel 8 was unusually noisy. The MEGGIE default options were used for blink detection; 1 Hz low pass, 10 Hz high pass, 10 second filter length and 5 second start time. Eye blink projections were implemented on the data.

2.5 Data epoching and averaging

After the preprocessing was done to all the data, epochs were created to identify the event-related potentials. Epochs were created in the MEGGIE interface. The time window was locked to stimulus onset from 200 milliseconds pre-stimulus to 500 milliseconds post stimulus. EEG signals with larger than 300µv amplitude were rejected. The datasets included 99 pieces of neutral primes after happy faces (hneu) and neutral primes after sad faces (sneu) and 117 pieces of neutral faces after neutral primes (nneu).

After the epoching the averages were created for each of the participants in each of the

categories in both hemispheres. From these averages the two peaks in two time windows were chosen for the statistical analysis. Each participant belonged to a group; controls, and depressed which in the before measures were labeled as depressed and in the after measures CBASP and TAU. Each participant had data from the two hemispheres and three categories in the both hemispheres. Also, grand averages for the different groups were created.

2.6 Statistical analysis

Statistical analysis was done in IBM SPSS Statistics 24. The analysis method chosen was repeated measures multivariate analysis of variance (repeated ANOVA). There were three different kinds of ANOVAs that were made, aiming to answer the research question. In the ANOVAs when the Mauchly's test of sphericity indicated that the assumption of sphericity had been violated, the corrected p-value was used.

In the first repeated ANOVA the point of interest was to research differences in depressed and controls. It was used to measure if there is a difference in the ERP responses to the neutral target faces in depressed and controls, measured before the therapy. Dependent measure was amplitude (measured in microvolts). Independents measures (within-subject factors) were the facial expression (labeled as category, which included hneu or neutral primed with happy, nneu or neutral primed with neutral and sneu or neutral primed with sad) and channel (P7 and P8). Between-subject factor was diagnosis, which divided the participants in two groups, in which 0 = controls and 1 = depressed.

The second ANOVA was used to study the efficacy of the intervention. It was used to measure if there are differences in the responses between CBASP and TAU groups. Dependent measure was amplitude (measured in microvolts). Independent measures (within-subject factors) were the facial expression (category) intervention (labeled before and after) and channel (P7 and P8). Between-subject factor was group, which divided the participants in two groups in which 1 = TAU, 2 = CBASP.

The third ANOVA was used to measure if there are differences ERP responses to the neutral target faces in CBASP and TAU, and whether the responses of the CBASP group resemble those of

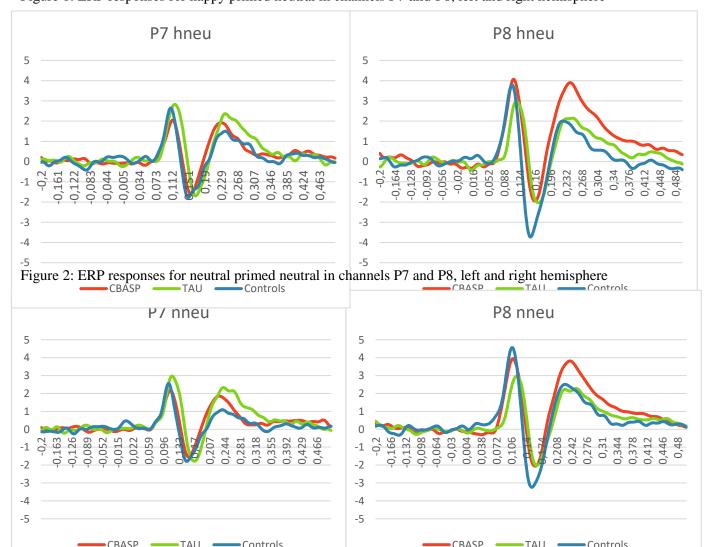
the controls. Dependent measure was amplitude, measured in microvolts. Independent measures (within-subject factors) were the facial expression (category) and channel (P7 and P8). Between-subject factor was group, which divided the participants in three groups in which 0 = controls, 1 = TAU, 2 = CBASP. Only the values from the after measurements were used for this ANOVA.

3. RESULTS

3.1 Average graphs

The graphs drawn from the averaged data over all participants (grand averages) in different groups are shown in the figures 1, 2 and 3. The graphs are drawn for each condition in both channels, one graph showing all the grand averages for each group in different conditions and channels. The Y axis is showing the amplitude in microvolts (μV) and the X axis is showing the time in milliseconds.

Figure 1: ERP responses for happy primed neutral in channels P7 and P8, left and right hemisphere



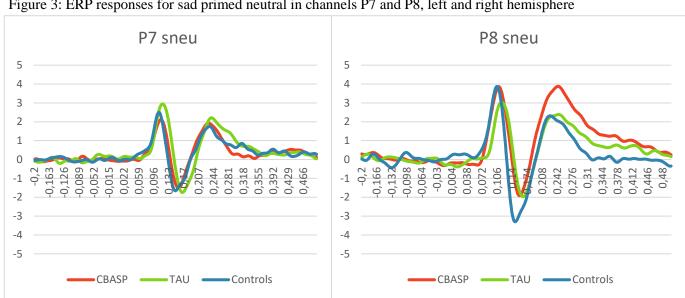


Figure 3: ERP responses for sad primed neutral in channels P7 and P8, left and right hemisphere

3.2 Max values

Maximum amplitude values were collected for each category in each channel separately for all individuals. There are two positive peaks in each of the conditions, the first peaking in 80-160

milliseconds and the second in 200-350 milliseconds. The first positive peak resembles most likely the P1 peak and the second positive peak is most likely the P2 peak. In between the positive peak is a N170 negative peak, but it will not be analyzed in this thesis. The analysis will be done for the positive peaks P1 and P2. There were some participants whose max values for the second peak were in 180-190 milliseconds, and these true max values were used for those participants. Also for couple participants the max values of the second peak were in 350-360 milliseconds, and these values were used for those participants. The peaks are analyzed separately and will be later be labeled as P1 and P2 for their onset time. Labels early and late peak and first and second time window will also be used.

Table 1: Means and standard deviations for amplitude, first time window (P1)

	Intervention	Group	Mean	Std. Deviation	N
Left neutral after happy	Before	Controls	3,256157712	2,851518246	10
		Depressed	3,231086869	1,997675404	32
	After	TAU	3,774149267	2,763432982	11
		CBASP	2,613928438	1,597771496	21
Left neutral after					
neutral	Before	Controls	3,04308763	2,942262334	10
		Depressed	3,335196254	1,866966385	32
	After	TAU	3,98009141	3,310950048	11
		CBASP	2,580653997	1,680006714	21
Left neutral after sad	Before	Controls	3,066685879	2,72438989	10
		Depressed	3,206009354	1,987130346	32
	After	TAU	3,922201672	2,859124045	11
		CBASP	2,608460391	1,633505124	21
Right neutral after					
happy	Before	Controls	4,439848853	3,526362265	10
		Depressed	4,692792821	1,912595821	32
	After	TAU	3,576460201	1,654003523	11
		CBASP	4,924132579	3,455590561	21
Right neutral after					
neutral	Before	Controls	5,352288876	3,266419542	10
		Depressed	4,677644699	1,877038072	32
	After	TAU	3,488349873	1,65032393	11
		CBASP	4,795737623	3,312656919	21
Right neutral after sad	Before	Controls	4,511223227	3,340272544	10
-		Depressed	4,596800077	2,059311566	32
	After	TAU	3,702757382	1,526098709	11
		CBASP	4,900088939	3,155913832	21

Table 2: Means and standard deviations for amplitude, second time window (P2)

	Intervention	Group	Mean	Std. Deviation	N
Left neutral after happy	Before	Controls	2,251499	1,294980556	10
		Depressed	2,457512	1,40881761	32
	After	TAU	3,035757	1,656594568	11
Left neutral after happy		Depressed	2,457512	1,40881761	32

		CBASP	2,365835	1,27236404	21
Left neutral after					
neutral	Before	Controls	2,051539	1,328091971	10
		Depressed	2,40586	1,571229111	32
	After	TAU	2,777826	1,801184963	11
		CBASP	2,305935	1,109041695	21
Left neutral after sad	Before	Controls	2,597388	0,875329486	10
		Depressed	2,405322	1,538198012	32
	After	TAU	2,620206	1,690256255	11
		CBASP	2,297027	1,099902222	21
Right neutral after					
happy	Before	Controls	2,525673	1,271256957	10
		Depressed	3,905146	2,558945427	32
	After	TAU	2,60668	1,762708922	11
		CBASP	4,706331	3,488621145	21
Right neutral after					
neutral	Before	Controls	3,02845	1,624713911	10
		Depressed	3,861716	2,477073466	32
	After	TAU	2,750522	1,783081182	11
		CBASP	4,593179	3,320474453	21
Right neutral after sad	Before	Controls	2,771312	1,225344721	10
		Depressed	3,985317	2,594886771	32
	After	TAU	2,851813	1,807817079	11
		CBASP	4,708905	3,56990405	21

3.3 Repeated ANOVA

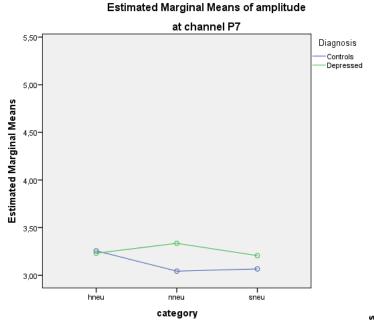
3.3.1 The differences between the depressed and controls before the intervention in P1

In P1, which occurred between 80-160 milliseconds, main effect of both channel (F(1, 41) = 18,738, p < 0,001) and category (F(2, 40) = 3,767, p < 0,05) was significant. The responses in the

right hemisphere were higher than in the left hemisphere. Neutral faces after neutral primes yielded the highest amplitudes. The interaction effect between channel, category and diagnosis was also significant (F(1, 40) = 3,714, p < 0,05). Therefore, depressed group and control group were measured separately. When the data was split by diagnosis, the main effect of channel was significant both in controls (F(1, 9) = 16,453, p < 0,01), and in depressed participants (F(1, 29) = 14,272, p <0,001). In both depressed and control participants, the amplitudes were higher in right hemisphere than in left hemisphere.

After that the channels were tested separately. No significant effects were found in the left hemisphere. In the right hemisphere the main effect of category was significant, (F(2, 40) = 3,533, p < 0,05). Also the interaction effect of category and diagnosis was significant in the right hemisphere (F(2, 40) = 3,989, p < 0,05), responses for nneu being higher for controls than for depressed.

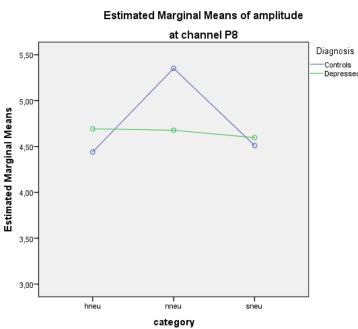
Figure 4: The differences between the depressed and controls before the intervention, P1 left and right hemisphere



0,05), right hemisphere yielding higher amplitudes. Also the interaction between channel, category and diagnosis was

3.3.2 The differences between the depressed and controls before the intervention in P2

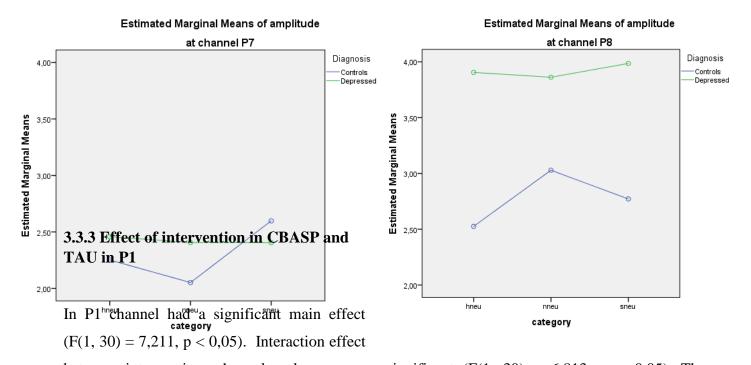
In P2, occurring from 200 to 350 milliseconds, the main effect of channel was significant (F(1, 40) = 6,992, p <



significant (F(2, 40) = 3,687, p < 0,05). The amplitudes were higher in depressed participants than in controls in both channels, except for the neutral faces after sad primes category in the left hemisphere, in which the amplitudes were higher in controls.

When the data was split by diagnosis, a significant main effect of channel was found in depressed (F(2, 30) = 8,815, p < 0,001). No significant effects were found in controls. When only category was set as within-subject factor, in the left hemisphere interaction between category and diagnosis was significant (F(2, 40) = 3,128, p < 0,05). Controls had higher responses for sneu, depressed had higher responses for hneu and nneu than controls.

Figure 5: The differences between the depressed and controls before the intervention, P2 left and right hemisphere

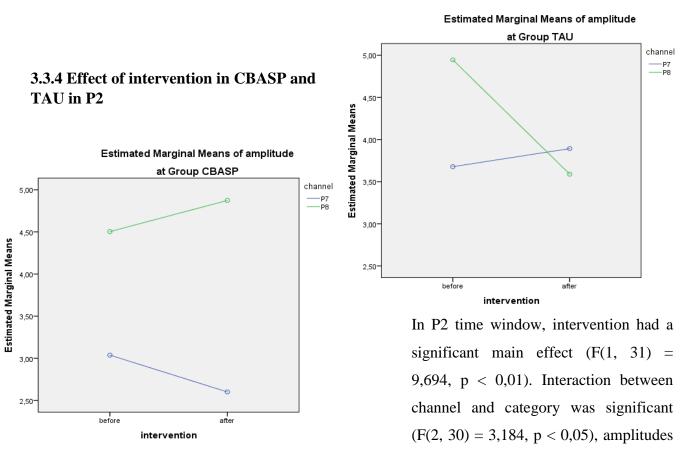


between intervention, channel and group was significant (F(1, 30) = 6,813, p < 0,05). The

differences were seen especially in the right hemisphere.

The data was split by group because of the interaction effect. In TAU there was a significant interaction between intervention and channel (F(1,10) = 5,085, p < 0,05). In the left hemisphere, no significant effects were found. In the right hemisphere in TAU group intervention had a significant main effect (F(1, 10) = 9,112, p < 0,05). Mean amplitudes were smaller after the intervention. In CBASP group there was a significant main effect of channel (F(1, 20) = 12,534, p < 0,01). Amplitudes were higher in the right hemisphere. No significant effects were found in CBASP when channels were measured separately.

Figure 6: The effect of intervention in CBASP and TAU in P1

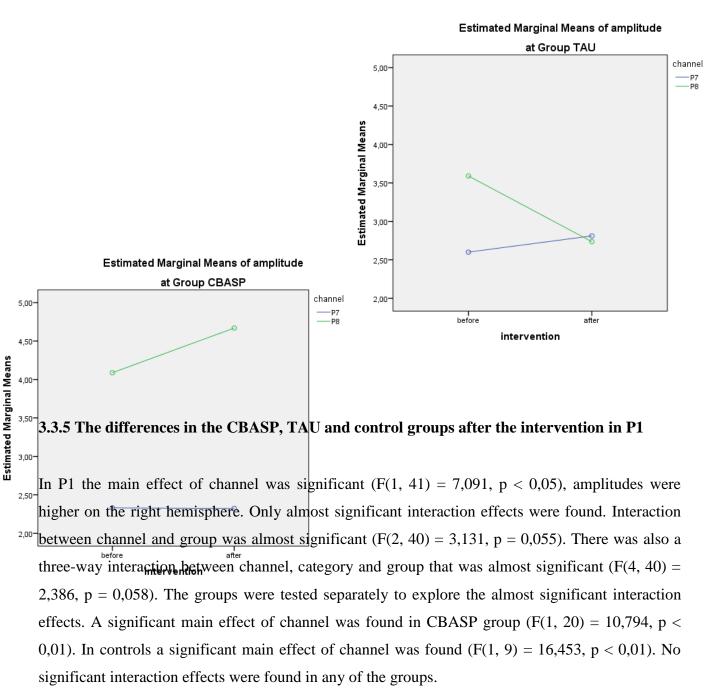


being higher for all categories in the right hemisphere than the left hemisphere. For CBASP group, differences in amplitude levels in the hemispheres was visible before and after the intervention. In TAU group the differences were not visible in the after measurement.

When the channels were measured separately, no significant results were found in either

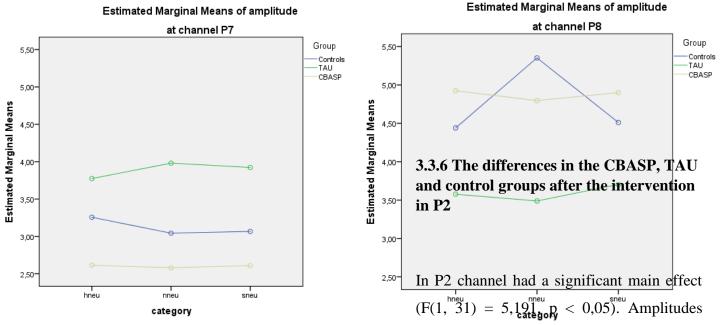
hemisphere.

Figure 7: The effect of intervention in CBASP and TAU in P2



In sum in the right hemisphere amplitudes for controls and CBASP were on the same level, while amplitudes for TAU were lower. In the left hemisphere amplitudes for TAU were the highest. When the channels were tested separately, no significant results were found for either channel.

Figure 8: The differences in the CBASP, TAU and control groups after the intervention, P1 left and right hemisphere



were higher in the right hemisphere than in the left hemisphere. There was also a significant three-way interaction between channel, category and group (F(4, 28) = 2,775, p < 0,05).

The groups were split to explore the significant interaction effect. In TAU the interaction between channel and category was significant (F(2, 19) = 4,504, p < 0,05). The responses for neutral faces after happy primes were higher in the left hemisphere than right.

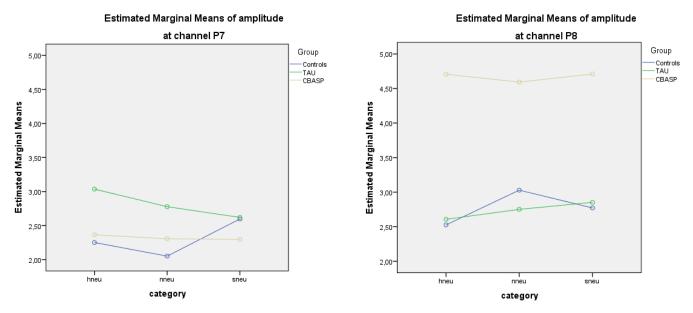
When channels were tested separately, in the left hemisphere the interaction between category and group was significant (F(4, 28) = 3,232, p < 0,05). Controls had higher responses to

neutral faces after sad primes than the other groups. Amplitudes in the categories were higher in CBASP group for the other categories except for the neutral faces after sad primes. No significant results were found in the right hemisphere.

Figure 9: The differences in the CBASP, TAU and control groups after the intervention, P2 left and right hemisphere

4. DISCUSSION

This study was conducted to explore the differences in emotional information processing in



depressed and healthy individuals and to study the if the CBASP therapy changed the emotional information processing in depressed towards to healthy individuals. The emotional information processing was studied by using neutral facial expression occurring after either happy, neutral or sad expression. From the responses two time windows with positive peaks were chosen for the repeated multivariate analysis of variance, P1, associated with processing of visual stimulus, which onset was 80-160 milliseconds after the stimulus and P2, associated with more conscious evaluation, which onset was 200-350 milliseconds after the stimulus.

The first research question was to see if there are differences between depressed participants and non-depressed controls in the processing of neutral faces after emotional expressions. The aim

of this question was to test the hypothesis that depressed individuals have difficulties in detaching from negative emotional information. The difference was seen on the hemispheric level, as in both time windows the responses were higher in the right hemisphere than the left hemisphere. This was expected, as the right hemisphere is the typical hemisphere for facial information processing. The variance was, however, larger in the groups in the latter time window. In the facial expressions controls had a significantly higher response to neutral primed neutral faces in the right hemisphere in the early P1 peak.

In sum, the results from comparison between depressed patients and controls in general reveled that in P1 in right hemisphere (channel P8) responses were stronger than left hemisphere (channel P7) responses both in control and depressed subjects. Group differences were evident in the right hemisphere, where categories differed for control subjects, seen as stronger responses to neutrally primed neutral faces, but not for participants with depression. The results indicate no differences in categories in the left hemisphere. The interaction between category and diagnosis implies that in the right hemisphere the responses for faces were different in depressed and controls. Controls had a higher response to neutral faces after neutral primes than to other faces. In depressed participants, the categories did not differ in the right hemisphere.

For the later P2 peak, the results showed that the right hemisphere (channel P8) responses where stronger than left hemisphere (channel P7) responses, but only in depressed subjects. Also for this later peak, the group differences emerged mainly in the right hemisphere, seen as stronger responses in depressed subjects for all categories.

In addition to general group differences we tested the effect of intervention in the two different intervention types, CBASP and TAU. The results indicate that in P2, the second time window, CBASP therapy increased the amplitudes on the right hemisphere. In P1 the therapy also increased the amplitude in the right side, but only to the level of controls. In P2 the amplitudes for controls did not rise, so for the CBASP group amplitudes continued to rise over the level of controls. Both in P1 and P2 the right hemisphere was more dominant in the CBASP group, compared to the left side. The P2 is the event-related potential a participant can consciously alter more than P1. The effect of therapy can be seen in the two time windows. For the CBASP group the responses in P2 are similar to the responses of control group in P1. CBASP alters the responses in the right and left hemisphere, but can be seen in the amplitudes not decreasing. A change happened

also in the TAU group but in that the responses are decreasing in the right hemisphere. The change in TAU group might mean a change in their depression.

In sum the right hemisphere, specialized in facial recognition had higher amplitudes than the left. A change in amplitudes was only seen in TAU group. Intervention did not cause change to happen in CBASP group. In TAU, a change can be seen in the right hemisphere even though the group did not undergo the treatment. In P2 the change was similar in the as P1. The amplitudes for TAU group in the right hemisphere decreased below the level of left hemisphere after the intervention. The amplitudes on the left side in TAU group increased after the intervention. In CBASP group amplitudes on the left side stayed stable after the intervention, right side rising a bit. Overall the amplitudes in TAU group in the hemispheres were more adjacent than in the CBASP group.

To further study the second research question differences in the CBASP, TAU and control groups after the intervention were tested. Although there were no significant intervention effects in the CBASP group, amplitudes in channels had similar changes in controls and CBASP groups. Both in control and CBASP group amplitudes in channel were lower before the intervention and higher after the intervention. TAU group had no significant main effects. In TAU group the left hemisphere yielded higher amplitudes than the right. In the right hemisphere responses for CBASP were similar to controls, even though the second ANOVA showed no change occurring in the group. TAU differed from the other groups in the left hemisphere being the dominating one.

All in all, the results are surprising, as intervention effects were expected to happen in the CBASP group, not in the TAU group. It may be, however, that the intervention effect, amplitudes decreasing in the after measurement, observed in TAU group is related to a pathological change associated with depression. The therapy might cause the amplitude levels of the CBASP group to stay stable on the levels of controls' in the P1 peak and rise them over the controls' level in the P2 peak. This might be due to the psychotherapy's ability to modify the conscious information processing which the P2 peak is associated with.

In this study, the differences in emotional information processing were seen more clearly in the hemispheric level, not necessarily in the facial expression level, which was anticipated in the introduction. The hemispheric differences have been seen in previous studies. Kayser et al. (2000) found that especially the P3 responses peaking at 330 milliseconds were larger in the right

hemisphere than in the left hemisphere electrodes in participants with depression. In this study, similar results were found in the P2 peak.

The hypotheses set in the introduction were not entirely correct. The hypothesized negativity bias was not present in the results. There were differences between depressed and controls in hemispheric level and in controls having stronger responses for neutral primed neutrals than depressed in right hemisphere in the first time window. The therapy was effective in preventing the possibly pathological change seen in the TAU group, but to ensure the nature of the change it would have been useful to study the depression scale scores in the groups.

Many studies presented in the introduction differ in their methods compared to this thesis. For example, the studies of Leppänen and Milders (2004) and Suslow et al. (2001), presented in the introduction, included neutral faces. However, the experiments demanded the participants to recognize neutral faces accurately and quickly. In this experiment the participants only had to watch the faces and occasionally press a target button to ensure their attention. The results of this study might therefore be different if another type of experiment had been conducted.

In the introduction the negativity bias was presented and highlighted, as it has been noted to be a significant part of depression. In this study the negativity bias was not seen. It must be noted, however, that all the negativity bias might be most visible in facial pictures with negative valence. In this study, all the studied faces were neutral so the differences in the responses to the faces in different groups are not surprisingly smaller, and, in many cases, not significant.

An interesting and important question is what makes a treatment effective for some but not for others. In this thesis no demographics of the participants were included so it is hard to speculate whether the participants responding to the psychotherapy had something in common. The study by Schatzberg et al. (2005) presented in the introduction studied CBASP therapy, and the result was that CBASP nonresponders seem to respond to medication and vice versa. The researchers also speculated whether people not responding for cognitive-behavioral therapy responded to an interpersonal or psychoanalytic psychotherapy. In this study, results might have been different if different participants had been in different groups. As at the moment there is no way of knowing what will work for whom beforehand, it is important to ensure treatment possibilities and provide psychotherapy for those who do not respond for medication.

The strength of this study was that a psychotherapy model was studied. More psychotherapies, which are both efficient in terms of outcomes and cost-effective, are needed. A

group model psychotherapy enables multiple patients to get treatment at the same time. Psychotherapy is often time-consuming and may take a long time and efficacy must be ensured so that the patient will get beneficial treatment and resources are used well. Based on this thesis it seems as the psychotherapy had some effect in the P2 peak, but it cannot be regarded as an intervention effect. It might be said, however, that undergoing the CBASP therapy prevented the possibly pathological change seen in the treatment as usual group.

Another benefit of the study was to use neutral faces instead of faces with emotional content. The approach was different from many other studies and may offer ecological validity. In real-life conversations, facial expressions vary fast and a situation in which a neutral face is presented in conversation after a face with emotional valence is plausible.

A weakness of the study was the small sample size. Only 42 participants were used for the study, and only 21 of the studied underwent the CBASP therapy. Also the size of the TAU group was only 11 participants. A change in the mean amplitudes occurred in the TAU group, even though the group did not go through any specific treatment. No after measures were available for the controls, and it was only hypothesized that no change would happen in their responses to emotional information. As intervention effects occurred only in the TAU group, but nevertheless the controls and the CBASP group appeared similar, it might be that the TAU and CBASP groups were different per se.

For later studies, not only amplitudes, but also the latencies of the ERP components should be studied. Studying the latencies might give confirmation for these results or might reveal distinct results. For studies researching the effective factors in CBASP psychotherapy, the befriending element implemented in the research project should be examined. That might give new insight on how the psychotherapy delivers the change; by giving the participants new ways to solve problems or by giving the social support of the group. Also for later studies researching not only the neurophysiological responses but also the depression scale scores might reveal new information of the efficacy of the therapy.

It is not sure what exactly is causing the change, or in this case, preventing the decrease of the amplitudes in the CBASP group participants. It might be due to focus on social interaction prominent in the therapy. CBASP group helps participants to interact in social situations and interpersonal relationships by helping them learn new ways to act and think.

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6. ATTACHMENTS

Figure 10: An example of the experiment with a happy-neutral prime-target pair.

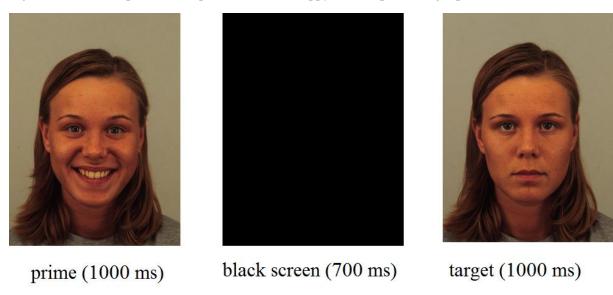


Figure 11: The 128-Channel Geodesic Sensor Net. Channels 58 and 96 or P7 and P8 are the parietal lobes in the visual cortex in the left and right hemispheres

