Graduate thesis

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

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EEG in clinical practice

A pilot study of relationships between delta band activity and level of function in a children and adolescents psychiatry population

Graduate thesis in Clinical Psychology

Supervisor: Stig Hollup

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Preface and acknowledgement

It all started with a biology class in year 2016. Mr. Hollup was the leader of the course. At first this man made me provoked and almost angry. But after a little while I got very impressed over his big knowledge and critical thinking. It is Mr. Hollups engagement and generosity that have led me to this thesis. The knowledge about EEG and how this can be helpful in clinical settings I would never have received if I had not met Mr. Hollup. Now in year 2020, I am forever grateful for all time spent in the lab, all interesting discussions and all knowledge Mr. Hollup has given me.

I also want to thank my family for your support during this time, and for all your help, especially my sister Malin. A big thanks to Peter Zehentbauer who let me takes part of your EEG-records. Thank you all!

Abstract

Today, investigation of psychiatric disorder is assessed by clinical interviews, rating scales, behavioral observations and development history. Clinical neuropsychology does not only comprehend the relationship between the brain and behavior, but also consulting and clinical intervention. Many psychological disorders share symptoms, which is a challenge in the field of psychiatry (Gillberg, 2010). One could argue that we need more objective measures that investigate the biology that include our psyche, so that we can differentiate why the person has the symptoms that he or she has. One tool for this could be electroencephalography (EEG). In this study delta frequency brain waves were examined in a population of 117 (7 to 17 years old) children and adolescents by the use of EEG. The delta frequency was examined in the conditions eyes closed, eyes opened, and visual continuous performance test (VCPT). A psychologist, specialist in clinical psychology, made a severity rating of functionality of all the subjects included in the study. The results showed that presence of delta activity indicated a higher grade of disability in the subjects participating in this study. This indicates that increased delta activity corresponds with greater disabilities in-group level and that the higher amplitude in the delta activity, the greater disabilities in individuals. Further research with an improved research design, a more appropriate control group together with a more standardized classification of functionality is recommended.

Keywords: EEG, delta frequency, connectivity, biology, functionality

Sammendrag

I dag blir utredning av psykiatrisk lidelse vurdert ved kliniske intervjuer, vurderingsskalaer, atferdsobservasjoner og utviklingshistorie. Klinisk nevropsykologi beskriver ikke bare forholdet mellom hjerne og atferd, men inkluderer også rådgivning og klinisk intervensjon. Mange psykologiske lidelser deler symptomer, noe som er en utfordring innen psykiatrien (Gillberg, 2010). Man kan hevde at vi trenger mer objektive tiltak som undersøker biologien som inkluderer psyken vår, slik at vi kan forstå hvorfor personen har symptomene som han eller hun har. Et verktøy for dette kan være elektroencefalografi (EEG). I denne studien ble hjernebølgenes deltafrekvens undersøkt i en populasjon på 117 (7 til 17 år gamle) barn og unge ved bruk av EEG. Deltafrekvensen ble undersøkt under forholdene lukkede øyne, øyne åpnet og visuell kontinuerlig ytelsestest (VCPT). En psykolog, spesialist i klinisk psykologi vurderte graden av funksjonalitet hos forsøkspersonene inkludert i studien. Resultatene viste at tilstedeværelsen av deltaaktivitet indikerte en høyere grad av funksjonsnedsettelse hos forsøkspersonene som deltok i denne studien. Dette indikerer at økt deltaaktivitet tilsvarer større funksjonsnedsettelser i gruppenivå og jo høyere amplitude i deltaaktiviteten desto større funksjonshemninger hos individer. For å bekrefte disse funnene anbefales videre forskning med forbedret forskningsdesign, en mer passende kontrollgruppe sammen med en mer standardisert klassifisering av funksjonsnivå.

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List of Abbreviations

A:	Animal (in the Visual Continuous Performance Task)
ADHD:	Attention Deficit Hyperactivity Disorder
ASD:	Autism Spectrum Disorder
BA:	Brodmann Area
BSS:	Blind Source Separation
CNS:	Central Nervous System
EC:	Eyes Closed
ECG:	Electrocardiography
EEG:	Electroencephalography
EO:	Eyes Opened
H:	Human (in the Visual Continuous Performance Task)
HBI:	Human Brain Institute
HCP:	Human Connectome Project
Hz:	Hertz
ICA:	Independent Component Analysis
LORETA:	Low-Resolution Brain Electromagnetic Tomography
Mdn:	Median
MEG:	Magnetoencephalography
MR:	Magnetic Resonance
MRI:	Magnetic Resonance Imaging
P:	Plant (in the Visual Continuous Performance Task)
PCA:	Principal Component Analysis
PSP:	Post-Synaptic Potential
qEEG:	Quantitative Electroencephalography
SOBI:	Second-Order Blind Inference
VCPT:	Visual Continuous Performance Task

1. Introduction

Clinical neuropsychology is based on the knowledge of both normal brain development and brain function, and how different disorders, damages/lesions and diseases affect it. Clinical neuropsychology is "an applied science that examines the impact of both normal and abnormal brain functioning on a broad range of cognitive, emotional and behavioral functions" (Board of Directors, 2007).
Today, investigation of psychiatric disorder is assessed by clinical interviews, rating scales, behavioral observations and development history. Clinical neuropsychology does not only comprehend the relationship between the brain and behavior, but also consulting and clinical intervention. Many psychological disorders share symptoms, which is a challenge in the field of psychiatry (Gillberg, 2010).

While deciding which diagnostic category any given patient may fall into, how certain can we be in the absence of objective measures? The author's point of view is that all kinds of psychology have a fundament in biology and the brain. The importance of biology is a topic in psychological investigation that is not getting a lot of attention. The diagnostic guidelines are today mainly based on behavioral symptoms. Do we not already know that persons can have the same symptoms but with different causes? Do we not need more objective measures that investigate the biology that include our psyche, so that we can differentiate why the person has the symptoms that he or she has? One tool for this could be electroencephalography (EEG). By the use of EEG human brain waves and the activity can be measured and one can see how the brain is working. Analyses of the EEG can give information about when the brain waves are deviant, which can tell us something about the function of the person of interest. Brain waves of the slowest frequency, called delta waves, indicate the greatest disturbance of function (Hess, 1977).

During a research scholarship (made by the author, not published) a tendency of a pattern of temporal delta activity was found in a population of children and adolescents from the child and psychiatry system in Nordfjordeid and south Sunnmøre, Norway. This tendency/pattern will in this graduate thesis be examined further. EEG measures from another population of children and adolescents from the child and psychiatry system in Nordfjordeid and south Sunnmøre have been studied. The aim of present study is to examine if significant delta deviances correlate with the amount of difficulties within the subjects and between groups, and if higher amplitudes in the delta activity are correlated with greater disabilities.

This work is an attempt to shed light on the importance of neurobiology in the assessment of psychiatric disorders and how this may help us to both, easier and more precisely come to a conclusion regarding the cause of the symptoms, and therefore also psychiatric diagnosis and treatment.

This thesis will start with a general introduction including a presentation of the theoretical and empirical research on the neurobiological and functional properties of quantified EEG (qEEG) measures. Thereafter the results of the study will be presented and discussed.

1.1 Basic investigation in child and adolescent psychiatry

In Norway, children and adolescents with psychological problems are being referred to the child and adolescent psychiatry system.

According to the Norwegian national clinical guidance (Helsedirektoratet) the basic psychological investigation in the child and adolescent psychiatry system should be the same for all children and adolescents, where resources, symptoms and function should be mapped. The main focus should be on the child's or youth's own difficulties or disorders, and life situation (e.g., stress, stresses in or around the family and caregiver). The basic investigation should provide the basis and direction (or hypotheses) for any possible specific or extended further investigation, differential diagnostic assessment, and of course diagnostic assessment (Helsedirektoratet, 2019).

Sometimes it might seem like the diagnostic assessment gets bigger importance than the actual problem of the child. The author's point of view is that the focus should be on finding a cause of the problems, and from that come to a conclusion about what interventions that can help the child, or the adolescent, in the best way possible.

1.1.2 Clinical interview/mapping. Mapping should include the patient's life situation, psychological and somatic medical history (also within family), risk factors for suicide, substance use (also within family), living habits, violence, abuse and other traumatic experiences, somatic status, drug use, and other possible elements (Helsedirektoratet, 2019).

1.1.3 Differential diagnostic assessment. A differential diagnostic assessment involves mapping and investigation about how symptoms can be understood to exclude other diseases / disorders as a cause, and to include concomitant diseases / disorders in further investigation and treatment. A multidisciplinary team makes these considerations. The person who is in charge for

the patient must ensure that a doctor in the specialist health service considers the need for supplementary examinations based on the referral, the patient's symptoms and what examinations have been done at the general practitioner. Symptoms, age, gender, past illnesses, genetics, and ethnicity will impact the somatic assessment. Other medical examinations such as blood tests, MRI (magnetic resonance imaging) of the brain, EEG, and ECG (electrocardiography) may be relevant, as well as neuropsychological tests (Helsedirektoratet, 2019).

1.1.4 Diagnostic assessment. For diagnostics, a structured assessment tool / interview should be used that covers the categories within the ICD-10 F-chapter. Diagnostic assessments should have been made on all axes in the multi-axial classification system. The possible causes of the patient's difficulties should be considered, whether there are sustaining factors and their consequences for the recommended treatment. It is also recommended to use relevant and validated self-filling forms if appropriate (Helsedirektoratet, 2019).

Diagnostic assessment today is mostly based on symptoms and there are few, or none, objective measures to assess different psychiatric disorders. A major challenge for clinicians is the big amount of co-existence of disorders and sharing of symptoms across disorders. This is actually rather a rule than an exception in child psychiatry and developmental medicine today (Gillberg, 2010). Development of more objective measures and biomarkers that correlate with grade of function and symptoms across disorders might make it easier to understand the symptoms and make the treatment more specific and effective. One tool in the research field that can give us objective measures is EEG.

1.2 EEG

In 1875, Richard Caton recorded electrical activity from the cerebral cortex in a monkey, but it was not until 1929 that a German psychiatrist, Hans Berger, first made similar recordings in humans (Purves et al., 2012). Since then electroencephalography (EEG), has been crucial in the diagnosis and management of epilepsy. Several paroxysmal phenomena are associated with particular types of seizure disorders. Abnormalities shown in the EEG recording provides support for the diagnosis, and the EEG record is therefore also instrumental in epilepsy classification. During the years it has been found that the EEG is useful in the investigation of neurological disorders other than epilepsy (Rowan & Tolunsky, 2003). The EEG provides clues that may support a presumed diagnosis and sometimes it can reveal

surprising findings. The EEG provides additional and often crucial information in a wide variety of neurological disorders, like attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) to mention a few. For example, research suggests that high levels of theta and/or reduced levels of beta are typical for patients with ADHD (Barkley, 1998; Barry, Clarke & Johnstone, 2003; Chabot, di Michele & Prichep, 2005; Monastra, 2008; Monastra et al., 1999; Monastra, Lubar, Linden, 2001; Quintana, Snyder, Purnell, Aponte & Sita, 2007; Snyder & Hall, 2006; Snyder, Hall, Cornwell & Quintana, 2006; Snyder et al., 2008).

The EEG records electrical activity from the cerebral cortex. Most of what is recorded is electrical fields that originate from neurons (Rowan & Tolunsky, 2003). The electrical fields are developed by ionic currents, generated by bioelectrical processes at network level (da Silva, 2013). The electrocortical activity is measured in microvolts (μV), and therefore it must be amplified by a factor of 1 000 000 in order to be displayed in a write-out or a computer screen (Rowan & Tolunsky, 2003). There are a number of possible sources that the recorded electrical field can originate from, including action potentials, post-synaptic potentials and chronic neuronal depolarization. Action potentials are unlikely candidates, since they induce a brief (1 ms or less) local current in the axon with a very limited potential field. A more likely candidate and generator of the EEG are post-synaptic potentials (PSPs), since they are longer (10-200 ms) and have a much greater field (Rowan & Tolunsky, 2003). When there is a synchronic activation of a big number of neurons, the fields that are recorded are shown in the EEG as brain waves, or brain oscillations, and brain oscillations are therefore the fundamentals in the EEG recording.

Analysis of the EEG signals is helpful in various clinical applications, like classifying sleep stages, predicting epileptic seizures, measuring depth of anesthesia, monitoring and detection of brain injury, and detection of abnormal brain states. Visual inspection of the EEG signals is an empirical science that requires a considerable amount of clinical and neurological knowledge. Because monitoring and visual interpretation is very subjective and does not lend itself to statistical analysis, alternative methods are used to quantify information carried by an EEG signal (Tong & Thakor, 2009). Before analysis there is a need for artifact correction.

1.2.1 Artifact correction. When an EEG is recorded there are often some signal distortions to be seen, also called artifacts. Artifacts can be seen in many different forms and have diverse causes. The artifacts can be patient or technical

related. Examples of patient related artifacts can be any minor body movement, eye blinks, pulse, muscle tension, eye movements or sweating for mention a few. Technical related artifacts could for example be impedance fluctuation, cable movements, broken wire contacts, too much or too little electrode paste and so forth (Teplan, 2002). The major underlying artifact problem is though the enormous amplification required to record the brain waves (Rowan & Tolunsky, 2003).

Artifact correction can be done by using the software WinEEG, but at the same time a trained expert also needs to inspect the recording manually to make sure that the signals that the program excludes really are artifacts, and not actually unusual signals from the brain.

Blind source separation. The isolation and removal of artifacts and noise that contaminate the cortical signal is a significant challenge for EEG research (Fitzgibbon, Powers, Pope & Clark, 2007). It is common practice to manually reject contaminated data before analysis. This process is requiring considerable effort and time and can result in unacceptable data loss when there is a high degree of contamination.

An alternative to rejecting contaminated data is to correct or remove the artifact or noise. A class of algorithms, called blind source separation (BSS), has been prominent in the artifact/noise correction literature. "BSS is the process of recovering the source signals from a linear mixture of measured signals" (Fitzgibbon et al., 2007, s. 232). Each source signal is identified/classified as being either brain or artifact/noise, which allows removal of artifact signals without distortion of the desired brain signals.

The choice of BSS algorithm is primarily determining the quality of the source separation. The measure (or statistic) that is used to assess the degree of separation (or independence) of the signals is the key difference between the various BSS algorithms. Some BSS algorithms have been applied specifically to artifact removal from EEG including principal component analysis (PCA), second-order blind inference (SOBI), and independent components analysis (ICA) (Fitzgibbon et al., 2007). "ICA refers to a group of algorithms that recover statistically independent signals from a linear mixture using high-order statistics as the measure of independence" (Fitzgibbon et al., 2007, s. 233). ICA can effectively separate both artifact and noise from cortical sources in the EEG data.

1.2.2 QEEG. Quantitative electronencephalography (qEEG) is a quantification of the raw EEG-record. Technological advances have increased the ability to read brain activity data from the entire head simultaneously. The measurements applied by the qEEG, improve the determination of spatial structures and localize areas with brain activity or abnormality (Teplan, 2002). Statistical analysis can also be performed to generate the patient´s spectral map of frequencies, amplitude and their relative power (Legarda, McMahon, Othmer, & Othmer, 2011).

Once the artifact correction is done, further analyses are possible. For most people that use EEG in a clinical or research setting, qEEG starts at this point (Duffy, Hughes, Miranda, Bernad & Cook, 1994). By using data analyzing programs (for example WinEEG software) one can do a number of different analyses that will now be explained further.

Spectral analysis and mapping. Spectral analysis is an analysis that many clinicians start their analysis procedure with. The results are often used for topographic brain mapping represented with color maps in 2D and 3D to enhance visualization (Teplan, 2002), which is shown in figure 1.

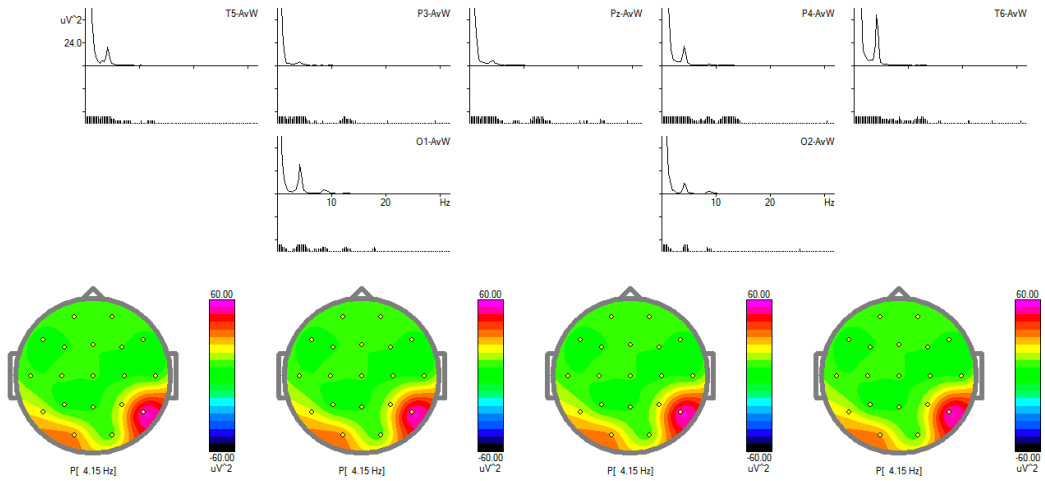

Figure 1. Topographic brain mapping represented with color maps.

When spectra are compared to the reference database, WinEEG depicts significant deviances in certain electrodes. The deviances are shown as “bars” indicating a statistical deviance and p-values. These statistical deviances can show up at only one, a few, or several electrodes, which are also shown in figure 1. The neuronal generators of the EEG components cannot be deduced by electrode

positioning. A more useful approach that has been proved to improve the spatial resolution of the scalp-recorded EEG is the application of source localization (Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002).

Source localization. To estimate the intracortical electrical sources, or the neuronal generators, there are several analyses that can be used. Two of the main analyses used will now be explained further.

Independent component analysis (ICA). EEG data collected from any point of the human scalp includes brain activity from a large area of the brain, because of the distance between the skull and the brain and their different resistivities (Makeig, Bell, Jung, & Sejnowski, 1996). ICA, mentioned in previous section, can reveal interesting information about where the recorded activity on the scalp actually is generated, by giving access to the independent components of the brain activity (Hyvärinen & Oja, 2000).

LORETA. Low-resolution brain electromagnetic tomography analysis (LORETA) is functional imaging based on electrophysiology and neuroanatomy (Pascual-Marqui et al., 2002). This analysis method is used to estimate the three-dimensional intracortical current density distribution. LORETA identifies the cerebral generators of the pathogenesis or the deviances that is shown in the EEG data (Saletu, Anderer, & Saletu-Zyhlarz, 2010). LORETA has good spatial resolution and adequately measures all of the Brodmann areas (BAs).

1.3 Brain oscillations

The term "brain oscillations" refers to the electrical activation that is generated in rhythmic and/or repetitive forms in the brain. This activity is generated spontaneously and in response to stimuli by neural tissue in the central nervous system (CNS) (Başar, 2013). The oscillations are shown in different frequencies and are measured in Hertz (Hz, wave per second) in the brain and represent different mental states. Traditionally frequencies are divided into five frequency bands, which are delta, theta, alpha, beta, and gamma oscillations. All these frequencies are present in the human brain during a day.

1.3.1 Beta, alpha and theta oscillations. Beta activity is characterized by frequencies of 14 to 30 Hz. This activity is rhythmic and present in the background of most EEG records. Beta activity is prominent when awareness and concentration are increased (Rowan & Tolunsky, 2003).

Another rhythmic frequency is defined at 8 to 13 Hz and is called alpha oscillations. This activity is in fact the principal background feature of the normal adult EEG. The alpha rhythm is typically recorded in awake subjects with their eyes closed (Rowan & Tolunsky, 2003). This rhythm is often called the resting rhythm. It represents a resting state in the brain, or the absence of cognitive processes.

Theta activity is characterized by frequencies of 4 to 7 Hz and is usually present in the waking EEG. It is suggested that theta present simply early drowsiness. Theta activity can be related to "daydreaming" and increased ability in creativity, visualization and imagination. Diffuse theta activity is common in children (Rowan & Tolunsky, 2003).

1.3.2 Gamma oscillations. Gamma activity is considered to be involved in information processing on a higher level, like more complex cognitive operations. It is proposed to bind multiple features of an object, which are coded in a distributed manner in the brain, and is modulated by cognitive processes such as attention and memory (Herrmann & Dermiralp, 2005). The empirical data about gamma oscillations are still weak, since the equipment use is challenging.

1.3.3 Delta oscillations. The delta rhythm is defined at 0.5 to 4 Hz, and these waves are normally not present in the adult waking, resting record (Rowan & Tolunsky, 2003). In some research it is found that the delta activity band can go up to over 4 Hz. A 2.5 Hz to 4.5 Hz delta wave is actually one of the most frequently observed normal delta slow activity in the waking EEG record of children. This activity is commonly located in the occipitoparietal or occipitotemporal regions (Scher, 2017). Developmental studies show that delta percentage gradually decreases and faster rhythms increase with age (Gasser, Verleger, Bächer, & Sroka, 1988; Harmony, Marosi, Díaz de León, Becker, & Fernández, 1990; John et al., 1980; Matoušek & Petersén, 1973). A large amount of delta activity after 4 or 5 years of age indicates cerebral dysfunction (Rowan & Tolunsky, 2003).

Delta rhythms are typically seen when a person is in deep dreamless sleep, and if seen in awaking recordings it's normally present drowsiness. Focal delta activity is also proved to be a reliable indicator of localized disease of the brain and is considered a marker of pathological condition or brain sufferance (Rowan & Tolunsky, 2003). Several studies has also found that slow wave activity, particularly delta activity, marks pathological brain abnormality resulting from neurological damage, such as tumor, cerebral infarct, contusion, subdural hematoma or local

infection (e.g., De Jongh et el., 2001; Gloor, Ball, & Schaul, 1977; Tanaka, Kimura, Yoshinaga, Tomonaga, &, Mizoguchi, 1998; Vieth, Kober, Ganslandt, Möller, & Kamada, 1999; Vieth, Kober, Kamada, & Ganslandt, 1998). When investigating how neurosurgical treatment of patients with brain tumors influences brain activity, a study found reduced delta activity after surgical treatment (De Jongh et al., 2003). They also found persistent focal delta activity near lesion or edema borders. Thus, delta was recorded also when the tissue of the tumor was removed. This finding suggests that the pathological source of the delta activity is the possibly a bit damaged tissue around the tumor, rather than the tumor itself (De Jongh et al., 2003). The assumption that abnormal slow-wave activity is correlated with a dysfunctional state of neuronal tissue (Elbert, 1998; Lewine & Orrison, 1995; Rockstroh, Fehr, Kissler, Wienbruch, & Elbert, 2001) is therefore confirmed by the findings from De Jongh et al. (2003). A border between normal and seriously damaged brain tissue characterize "dysfunctional" (De Weerd, Veldhuizen, Veering, Poortvliet, & Jonkman, 1988; Kamada et al., 2001), which can be due to local deficit in cerebral oxygen metabolism and blood flow (Nagata, Tagawa, Hiroi, Shishido & Uemura, 1989), or other mechanisms that may lead to a disrupted afferentation of neural networks from their major input source.

Further evidence of the link between delta activity and brain damage comes from studies of neurological or psychiatric patients affected by Alzheimer's disease, mild cognitive impairment, aphasia, dyslexia, schizophrenia or depression (e.g., Babiloni et al., 2006; Hensel, Rockstroh, Berg, Elbert, & Schönle, 2004; Meinzer et al., 2004; Penolazzi, Spironelli, & Angrilli, 2008; Szelies, Mielke, Kessler, & Heiss, 2002; Wienbruch et al., 2003). Increased delta activity has also been found in patients with disorders like ASD, ADHD, Angelman syndrome and epilepsy (Brigo, 2011; Shephard et al., 2018; Sidorov et al., 2017). The slow wave activity has been related to the extent of cognitive impairment in all these studies, and the abnormal delta activity has been considered a distinct marker of altered brain functioning (e.g., Hensel et al., 2004, Penolazzi et al., 2008).

Studies have suggested that delta activity can be shown in other settings as well. For example Harmony et al. (1996) found that delta activity is a sign of internal concentration during the performance of mental tasks.

1.4 The Brain

The brain can be divided into three main parts; the forebrain, midbrain and hindbrain. The largest part of the brain is the forebrain, and it contains the cerebral cortex with its two hemispheres. The forebrain also contains a number of other structures, which are placed beneath the cortex, also called subcortical structures. The cerebral cortex is the outer surface of the brain and is a thin layer of gray matter, which mostly contains cell bodies (Brodal, 2001).

1.4.1 Lobes of the brain. The cortex, and each hemisphere, is often divided into the frontal, parietal, temporal, and occipital lobes, which all are associated with different functions. These areas of the brain are so big that several different functions are located in each lobe (Brodal, 2001).

The frontal, parietal and occipital lobes. The frontal lobe is, as its name provides, located in the forward part of the brain and can be divided into three distinct functional zones. These zones are the motor cortex, premotor cortex, and prefrontal cortex that are involved in motor control, reasoning, language and emotion. The motor cortex is the part of the frontal lobe that is involved in planning and coordinating movement, and the premotor cortex selects movement. Another part of the frontal lobe is the prefrontal cortex, which represents higher-level cognitive functioning, or executive functions. In the frontal lobe one also finds Broca's area that is involved in language production (Kolb & Wishaw, 2009).

The parietal lobe is located behind the frontal lobe and can be divided into three different functional zones. One zone is responsible for somatosensory processes, one for movement, and one for spatial cognition. Lesions in this lobe can therefore produce problems with tactile function, guiding limb movements, and spatial cognition (Kolb & Wishaw, 2009).

The occipital lobe is located at the back of the skull, and the main function of the lobe is perception of visual stimuli. Primary visual cortex is located in this lobe and represents the beginning of visual processing. A variety of deficits can emerge when damage to the occipital lobe is seen. Deficits can be ranged from blindness in all or part of the visual field to problems with the perception of color, form, and movement (Kolb & Wishaw, 2009).

The temporal lobe. On the side of the head the temporal lobe is located, and it´s responsible for hearing, emotions, memory and some aspects of language. In this lobe one can find the auditory cortex, which is essential in processing auditory

information. The sounds we hear first enter an area within the superior temporal gyrus, which also are located in the temporal lobe. The primary auditory cortex can then process the auditory information (the sounds) into meaningful units, like words or sentences (Patel, Biso & Fowler, 2020).

The Wernicke's area, which also is located in the temporal lobe, is important for speech comprehension, and specially for processing written and spoken language (Patel et al., 2020). Several critical brain structures including the hippocampus and the amygdala are also located in the temporal lobe and are involved in memory and emotion functions. Hippocampus is responsible for the formation of new memories, and the conversion from short-term to long-term memories. We know that the hippocampus closely communicates with the structure amygdala, which is essential for processing emotions.

The temporal lobe is also involved in processing visual stimuli. The responsible parts of the lobe primary allow us to recognize objects like faces, locations and landscapes (Patel et al., 2020).

1.4.2 Brodmann areas. Brodmann areas refer to 52 regions of the cerebral cortex. The German neurologist Korbinian Brodmann identified these areas in 1909. The Brodmann areas form the basis of "localization" of function in the cerebral cortex, and are used to designate cortical functional regions, such as area 17 for visual cortex, area 4 for motor cortex, and so forth. See figure 2 for an overview of Brodmann Areas.

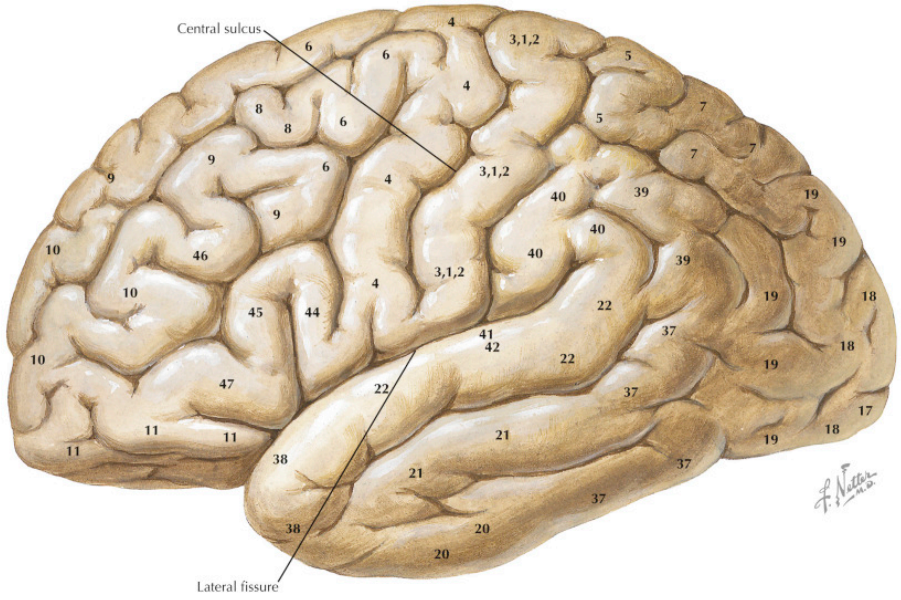

Figure 2. The figure shows an overview of Brodmann areas.

The Brodmann areas are often shown on a map of the brain surface, but each Brodmann area is continued through the depth of the cerebral cortex. The classification is based on the fact that the cortex is composed of six cellular layers, the density and architecture of which vary from region to region (Brodmann, 2007).

This nomenclature is used by neurologists and neurosurgeons, and Brodmanns mapping of functional areas of the brain must be one of the most used figures in neurobiological publishing (Brodmann, 2007).

Since this thesis is investigating activity in the temporal area of the brain, these BA's will now be explained further.

Temporal Brodmann areas. The Brodmann areas that are located in the temporal regions of the brain according to Brodmann (2007) himself are 36, 37, 38, 20, 21, 22, 52, 41 and 42. The temporal Brodmann areas are shown in figure 3.

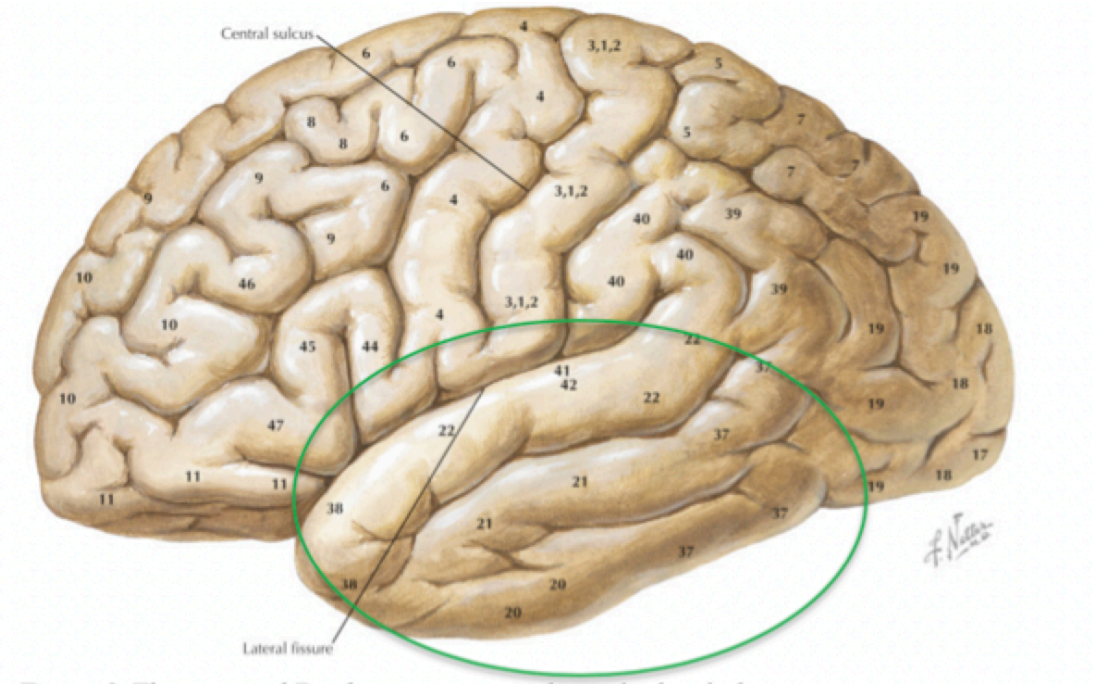

Figure 3. The figure shows the temporal Brodmann areas, which is marked with a green circle.

BA36 is a part of the perirhinal cortex, which is involved in visual perception and memory. The perirhinal cortex also facilitates the recognition and identification of environmental stimuli (Murray, Bussey & Saksida, 2007). BA37 is also called the occipitotemporal area since it is placed near the occipital lobe (Brodmann, 2007). One part of BA37 is the fusiform gyrus, also called the medial occipitotemporal gyrus

(Gray, 1981). The function is not fully understood, but it has been linked to several neural pathways related to recognition. It is considered a key structure for functionally-specialized computations of high-level vision such as object recognition, face perception, and reading (Weiner & Zilles, 2016). BA38 is located at the anterior end of the temporal lobe, also known as the tempopolar area (Brodmann, 2007). The function of this area is not fully known, but it is considered to be involved with binding complex, highly processed perceptual inputs to visceral emotional responses (Ding, van Hoesen, Cassell & Poremba, 2009).

BA20 mainly consists of the inferior temporal gyrus (Brodmann, 2007), which is responsible for receiving information, and is part of a region essential in recognizing patterns, faces and objects (Creem & Proffitt, 2001). BA21 is situated approximately in the middle temporal gyrus (Brodmann, 2007), which has been connected with processes as different as accessing word meaning while reading, recognition of known faces, and contemplating distance (Acheson & Hagoort, 2013). BA22 is part of the superior temporal gyrus (together with BA41 and BA42) (Brodmann, 2007), and is often known as a part of Wernicke's area. This is an important area for the processing of speech so that it can be understood as language (Geschwind, 1970). The other part of Wernicke's area is BA39. Lesions in this part have been connected to dyslexia and semantic aphasia (Kantha, 1992).

Another Brodmann area of the temporal lobe is BA52, also known as the parainsular area (Brodmann, 2007), which is considered to be involved in the processing of somatosensory, visual, and motor stimuli (Baker et al., 2018). It also plays a role in internal regulatory processes (Baker et al., 2018).

BA41 is also known as the anterior transverse temporal area, and is connected and placed beside BA42 in the temporal lobe. BA 42 is also called the posterior transverse temporal area (Brodmann, 2007). Brodmann areas 41 and 42 are both parts of the primary auditory cortex (Moerel, de Martino, & Formisano, 2014), and are found on the posterior superior temporal gyrus (Brodmann, 2007). The main functions of these areas are processing auditory stimulus (Moerel et al., 2014).

The complexity of the brain is fundamental, but awareness of the connectivity between different areas of the brain can be one part in better understanding the functionality of the brain regarding cognition and behavior.

1.4.3 Connectivity. There has been an increase in recognizing connections and interactions among distributed brain areas as the basis for cognitive operations

and diverse behaviors (Mišić & Sporns, 2016). Brain connectivity refers to a pattern of connectivity between distinct units within the nervous system. Generally patterns discussed are anatomical links (or "anatomical connectivity"), statistical dependencies (or "functional connectivity"), or causal interactions ("effective connectivity") (Sporns, 2007). Neural activity can be seen as neural codes, and is constrained by connectivity. Therefore, it is important to consider the connectivity when analyzing EEG records. Brain connectivity is crucial to clarifying how neurons and neural networks process information (Sporns, 2007). A simplified overview can be seen in figure 4.

A project that aims to study brain connectivity and function with a genetically-informative design in individuals is the Human Connectome Project (HCP). This project is using (four) MR-based modalities plus MEG (magnetoencephalography) and EEG in the design, and behavioral and genetic data will also be acquired from the subjects included in the project (Van Essen et al., 2012). This project, which can lead to a deeper understanding of human brain connectivity and its variability, can provide valuable insights into what makes the individuality in humans and what accounts for great diversity of behavioral capacities and repertoires in healthy individuals. It can also provide a great baseline of knowledge for future studies of brain connectivity during development and aging, and in a great number of neurodevelopmental, neuropsychiatric and neurological disorders (Van Essen et al., 2012).

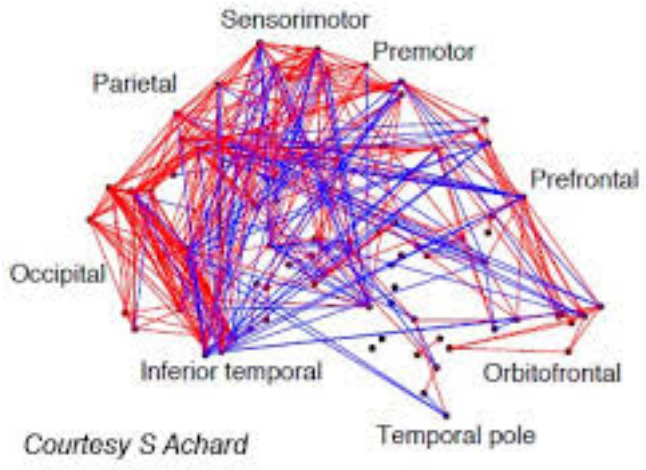

Figure 4. The figure shows a simplified overview of brain connectivity.

1.5 Importance of this study

The diagnostic classification system with it´s symptom based criteria makes it difficult to actually be aware/sure of the etiology of the difficulties the patient experiences. Since overlaps in symptoms between diagnoses also are high, this also makes it difficult to provide a correct diagnosis and treatment. Children often have complex difficulties, and the symptoms can therefore satisfy several diagnoses in the diagnostic systems (Thapar, Pine, Scott, Snowling & Taylor, 2017). For example, children with depression often have problems with anxiety, and vice versa. Also, children with ADHD and behavioral disorders have depression and anxiety more often than other children. Children with developmental disorders may have multiple disorders at the same time, and these may occur together with neurological disorders (Gillberg, 2010).

The big amount of symptom overlap in psychiatric disorders is a problem that the field wants to solve. By bringing clinical data together with an EEG uptake we believe that this study can contribute with a suggestion to a beginning of a solution. An objective measure like EEG can bring a wider understanding in the brain's functionality and connection to cognition and behavior in humans (with psychiatric difficulties). This may help us be able to say something about etiology and causality regarding the symptoms across disorders. Further we think that this study will show that EEG and the analyses connected to it can be helpful in predicting diagnoses and treatment.

1.6 Aim of the study and hypotheses

The main objective of the present study is to investigate whether delta brain activity deviances represent higher disabilities in children and adolescents in the child and adolescent psychiatry system, and if these deviances are interesting in clinical settings. This objective is based on the delta activity research that often is connected to brain damage (Rowan & Tolunsky, 2003). The investigation in this study is based on two hypotheses:

1. If there is increased delta activity, this will correspond with greater disabilities in subjects at group level.
2. If the amplitude in the delta activity is higher there will be greater disabilities in individuals.

2. Method

2.1 Subjects

In this study, one hundred and seventeen (7 to 17 years old) were examined. 27.4 % were females (32), and 72.6 % (85) were males. The subjects were patients and part of the child and adolescent psychiatry in the county of Nordfjordeid and south Sunnmøre, Norway. The subjects were given oral consent in participating in research. No identificational information was shown, and all EEG-recordings were anonymised.

The database used for normal controls were the Human Brain Institute (HBI) database which includes children and adolescents, that were matched in age with the patients. The children and adolescents in the database were healthy with no psychiatric diagnosis, learning disability, developmental disorder or brain injury. The same procedures and equipment were used for both patients and controls when EEG was recorded.

2.2 Apparatus

2.2.1 EEG. The EEG was recorded using a digital amplifier from Mitsar (St. Petersburg, Russia), which is a PC-controlled 19-channel electroencephalographic system. The electrode caps used were made by Electro-Cap (Electrocap International Inc.) and utilized tin (Sn) electrodes. The electrodes were placed on the scalp according to the 10-20 international standard montage system. Reference electrodes were placed on the ear lobes, and the ground electrode was placed at Fpz (Klem, Lüders, Jasper, & Elger, 1999). The impedance was kept below 10 kOhm, by using conductive gel. The input signals were filtered between 0.5 and 50 Hz, and digitized at a sampling rate of 250 Hz.

EO/EC. At first the EEG was recorded in two resting conditions; 180 seconds with eyes opened (EO), and 180 seconds with eyes closed (EC). These conditions were used both for analyzing and for making the subjects comfortable before the testing condition (VCPT). They were also used to check for anything unusual in the signal or the recording. The subjects were seated in a comfortable chair placed around 100 cm from a computer screen, with a visual angle for the images of 4,5 degrees.

VCPT. Afterwards, the visual continuous performance task was performed. This is a Go/NoGo-task that can be used to assess the subjects' capacity for sustained attention and response control (Mestanikova et al., 2015). The software tool PsyTask (Mitsar Ltd.) was used when presenting the stimuli for the VCPT task (Mueller,

Candrian, Kropotov, Ponomarev & Baschera, 2010). The VCPT lasted for 20 minutes, including 400 trials altogether. The VCPT was divided into 4 blocks, and each block lasted for 5 minutes (100 trials). Between every block the subjects were given a short break to promote a continuous performance and to reduce task-related tiredness.

Three categories of visual stimuli were presented: 20 pictures of animals, 20 pictures of plants, and 20 pictures of humans. The 400 trials were divided into four categories with 100 trials in each condition. Each condition was composed of a picture pairing, including animal-animal (Go trials), animal-plant (NoGo trials), plant-plant (Ignore trials), or plant-human (Novel trials) pairings. In the plant-human condition a novel sound at 60 dB was presented simultaneously with the picture of a human. Every picture was shown for 100 ms, followed by an inter-stimulus interval of 1000 ms, and the inter-trial interval was 3500 ms between pairings. The two pictures presented in the Ignore and the Go trials were identical, and there was an equal probability of each condition being presented in each block.

The subjects were instructed to press a button as fast as possible to the second image in the Go condition. In the NoGo condition the subjects were instructed to withhold a response to the second picture, and the other two conditions, Ignore and Novel, they were instructed to ignore. The task is illustrated in figure 5.

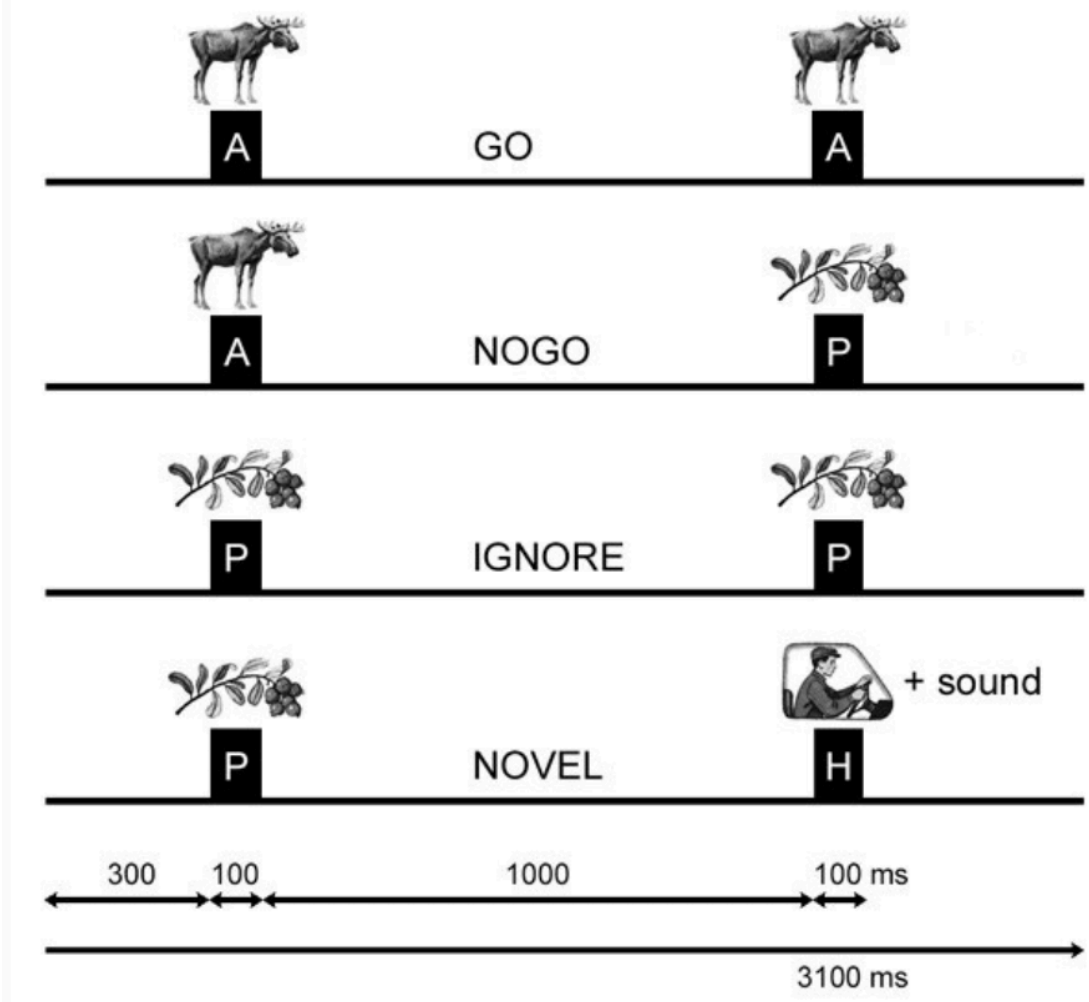

Figure 5. Schematic representation of the VCPT Go/NoGo task. A, P and H refer to the stimulus-pictures of animals, plants and humans. "Go trials" required the subject to press a button as fast as possible, "NoGo trials" required the subject to suppress the prepared response, "Ignore" and "Novel trials" required no response. In the "Novel trials" the picture of a human were coupled with a novel sound.

2.3 Procedure

2.3.1 Severity rating. The psychologist, specialist in clinical psychology, that took the EEG record of the patients within the two selected groups, the "delta group" and the "no delta group", made a severity rating of functionality. This psychologist had knowledge of the patients over time and he made a subjective clinical assessment that led to a classification. The psychologist was classifying the patients' levels of function in 3 classes, class 1, 2 and 3. 1 = no or easy problems (no actions required), 2 = moderate problems with a clear diagnosis (some actions required), and 3 = serious

and long-standing problems with a high degree of facilitation at home and at school (major actions required).

2.3.2 QEEG analysis. Quantitative data were obtained by using the Mitsar WinEEG software 2.115.83.

Artifact correction. Before the EEG was analyzed, the EEG raw data were artifact corrected. This procedure includes removing artifacts that disturbs the data, such as eye blinks and muscle tension. The WinEEG program was used when the artifact was performed, by implementing an independent component analysis (ICA) on the raw EEG. The ICA constructs a set of templates, and some of these templates correspond with artifacts. Eye-blink artifacts were corrected by zeroing the activation curves of individual ICA components corresponding to eye blinks (Vigário, 1997). Subtracting the artifact templates from the raw EEG made this correction. In addition, epochs within the filtered EEG with an excessive absolute amplitude or excessive faster, or slower, frequency activity were marked and excluded from further analysis. The rejection threshold was set at 50 μV for slow (0-1 Hz) and fast waves (above 30 Hz). The raw EEG was also manually inspected to verify artifact removal.

Power spectra analysis. To examine the brain frequency delta band activity within the patient group, power spectra analysis was performed. In addition, individual power spectra analysis was performed to compensate for group variance. The subjects with increased significant delta activity in all three conditions (compared to the HBI database) in the EEG record were selected for further analyses. The raw EEG was visually inspected to make sure that EEG artifacts didn't cause the deviant brain activity. To eliminate potential errors due to skull thickness and impedance, relative power (%) was preferred over absolute power (Benninger, Matthis, & Scheffner, 1984).

The selected "delta group" was examined with the spectral ICA and then exported to LORETA to position-estimate the qEEG activity found in all three conditions.

2.3.3 Source analysis. The analyses used for source analysis were ICA and LORETA.

ICA. Independent component analysis was performed on all individuals in the "delta group". If the delta activity deviance wasn't confirmed by ICA, those subjects were excluded from further analyses. The proposed generator(s) of the delta activity

were noted, and the positions were written down. After this procedure the records were exported to LORETA to estimate the cortical current density distribution.

LORETA. The Brodmann areas found by LORETA were written down to conduct a detailed investigation of which Brodmann area displayed deviant brain activity in the delta group.

2.4 Statistical analyses

Statistical analyses were performed in the Mitsar WinEEG 2.115.83 and the SPSS 26.0 software package. Mitsar WinEEG 2.115.83 was used to estimate the statistical significance of the deviances in EEG parameters, found by comparing the power spectra`s and ICA files with the normative database. Statistical significance was accepted at the level of $p < .05$.

2.4.1 QEEG and source analysis. Mitsar WinEEG 2.115.83 was used when performing power spectra analysis, and to estimate statistical significance for qEEG deviations. The patients' brain activity was examined and compared to the HBI normative database. This was displaying significant deviances for all patients' power spectra. Additionally, the patients' individual significant deviances compared to the normative database, was evaluated to examine tendencies among the patients and to compensate for group variance/tendencies within the patient group.

To position estimate the cortical source of the deviant delta activity, ICA for all patients were individually exported to LORETA.

2.4.2 Non-parametric tests. This study includes categorical data that are not expected to fulfill the assumption of normality. When wanting to use a statistical test to evaluate a hypothesis but the conditions for using a parametric test not are met, we need to use non-parametric tests (Field, 2013). Ranking the data by using non-parametric tests can be less powerful than parametric tests, but this statement is only valid if the assumption of normality is met (Field, 2013). In this case, we have a sample size in which the sampling distribution is assumed to be non-normal. Therefore, non-parametric test statistics are used for analysis.

2.4.3 Pearson's Chi Square Test. To examine potential relationships between disability grade and presence of delta activity, a Pearson's Chi-Squared Test was used. For Pearson's Chi-Square Test, Cramer's V was used as effect size. The effect size is an objective and standardized measure of the magnitude of the observed effect. It measures the strength of the relationships between two variables and indicates the size of any observed effects. According to Cohen, .07 is a small effect, .21 is a

medium effect, and .35 is a large effect (Field, 2013) for the degrees of freedom relevant in this study. Effect size for Pearson's Chi-Squared Test, Cramer's *V* can be seen in table 1.

Table 1

Effect size for Pearson's Chi-Squared Test, Cramer's V

Degree of freedom	Effect size		
	Small	Medium	Large
1	0.10	0.30	0.50
2	0.07	0.21	0.35
3	0.06	0.17	0.29
4	0.05	0.15	0.25
5	0.04	0.13	0.22

2.4.4 Mann Whitney U-test. The non-parametric equivalent of the independent *t*-test (Field, 2013) was used to compare the amplitude of the delta activity with the disability grade of the subjects in the group with delta activity. For Mann Whitney U Test Pearson's correlation coefficient *r* was used as effect size, and according to Cohen, $r = .10$ is a small effect, $r = .30$ is a moderate effect, and $r = .50$ is a large effect (Field, 2013).

3. Results

3.1 Analysis

3.1.1 QEEG analysis. After artifact correction was made, spectral analysis was made on the one hundred and seventeen subjects. When compared with the normative database 60.00 % of the subjects (69) were revealed with significant deviances ($p < .05$) in the delta frequency band in one of three conditions. Of these, 26 subjects were revealed with significant deviances in the delta frequency band in all three conditions (eyes opened, eyes closed, and visual continuous performance test) in the EEG recording. After independent component analysis of the spectral analyses in the delta group 4 patients were excluded, since the delta activity deviance wasn't

confirmed by ICA. This made the delta group to 22 subjects (7-14 years old). The 22 subjects that still remained were included in further analyses.

A control group of 22 patients (7-16 years old) without any delta activity in any conditions were randomly selected. In the group with delta activity (n=22) 9.1% were females (2), and 90.9% were males. In the group without delta activity (n=22) 36.4 % were females (8), and 63.6 % were males.

Spectral analysis was made in the EC condition. Only the EC condition was selected for further analysis due to the visual system activity present in the two other conditions. This showed that 95.5 % of the 22 subjects showed significant deviances in the delta frequency band at frontal sites (Fz, Fp1, Fp2, F1, F2, F3, F4, F7, F8), 54.5 % of the 22 subjects showed significant deviances in the delta frequency band at central sites (Cz, C3, C4), 54.5 % of the 22 subjects showed significant deviances in the delta frequency band at parietal sites (Pz, P3, P4), 59.1 % of the 22 subjects showed significant deviances in the delta frequency band at temporal sites (T3, T4, T5, T6), and 31.8 % of the 22 subjects showed significant deviances in the delta frequency band at occipital sites (O1, O2). This classification was made due to the lobes of the brain and the electrode placement division in the electro cap used during the EEG recording. See table 2 for descriptives. When examining the highest amplitude in the EC condition, 31.8 % of the 22 subjects had the highest amplitude in the delta frequency band at frontal sites, 0.0 % at central sites, 22.7 % at parietal sites, 36.4 % at temporal sites, and 9.1 % at occipital sites (see table 3). An example of the most common pattern is shown in Figure 6.

Table 2

Number of subjects (and percentage) with significant deviances in the delta frequency band in the different cerebral regions in the eyes closed condition

Cerebral region	n	%
Frontal	21	95.5
Central	12	54.5
Parietal	12	54.5
Temporal	13	59.1
Occipital	7	31.8

Table 3

Number of subjects (and percentage) with the highest amplitude in the delta frequency band in the different cerebral regions in the eyes closed condition

Cerebral region	n	%
Frontal	7	31.8
Central	0	0.0
Parietal	5	22.7
Temporal	8	36.4
Occipital	2	9.1

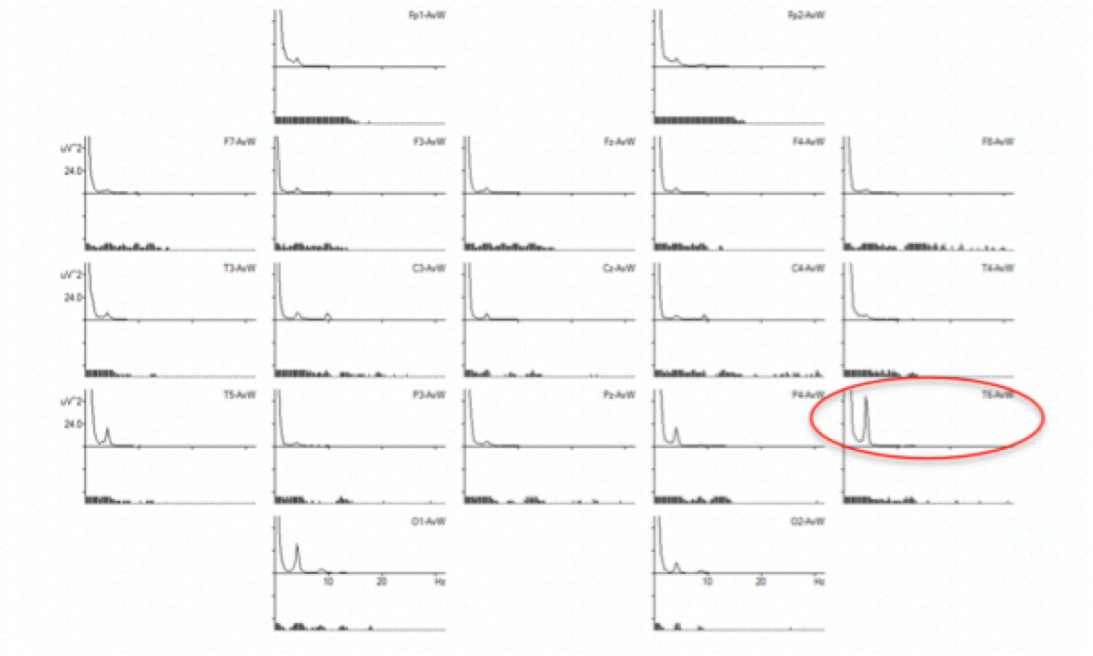

Figure 6. One subject's spectra of significant deviances compared to the normative database, representing the typical temporal delta finding in this study.

3.1.2 Source analysis. By giving access to the independent components of the brain activity, ICA revealed interesting information about where the recorded activity on the scalp actually was generated. Source analysis indicated that 22 of the original 26 subjects deviances found in the spectral analysis could be verified by ICA. All the 22 subjects´ ICA files were exported to LORETA. LORETA showed activation in Brodmann areas 9, 31, 32, 40, 42, and 22 and/or 39. 9.1 % of the subjects showed that the deviances were generated from BA 9, 9.1 % from BA 31, 9.1 % from BA 32, 9.1

% from BA 40, 4.5 % from BA 42, and 59.1 % from BA 22 and/or 39 (see table 4). This is also illustrated in figure 7.

Table 4

Percentage of subjects with significant deviances in Brodmann areas in the eyes closed condition
(n = 22)

Brodmann area	Percentage (%)
9	9.1
31	9.1
32	9.1
40	9.1
42	4.5
22/39	59.1

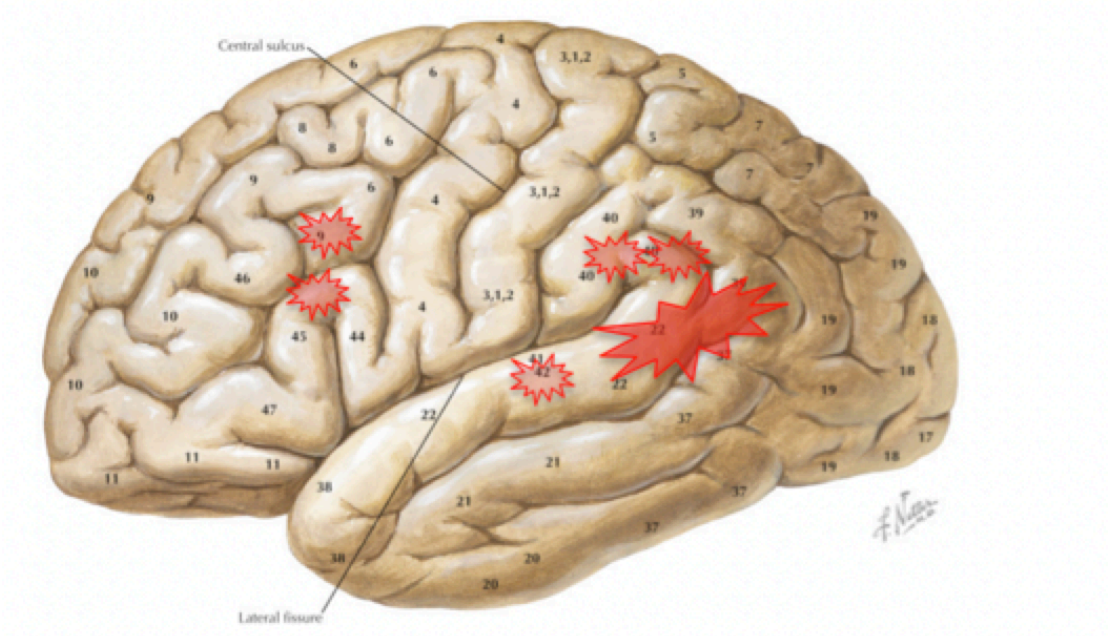

Figure 7. The figure illustrates cortical positions of the Brodmann areas displaying deviant brain activity in the delta frequency band.

3.1.3 Pearson's Chi-Square Test. A chi-square test of independence was performed to examine the relation between disability grade and presence of delta activity. The relation between these variables was significant, x^2 (2, N = 44) = 10.305, p = .006. Presence of delta activity indicated a higher grade of disability, which can

be seen in figure 8. The effect size for this finding, Cramer's *V*, was large, .484 (Field, 2013). Table 5 shows the distribution of disability grade and presence of delta activity.

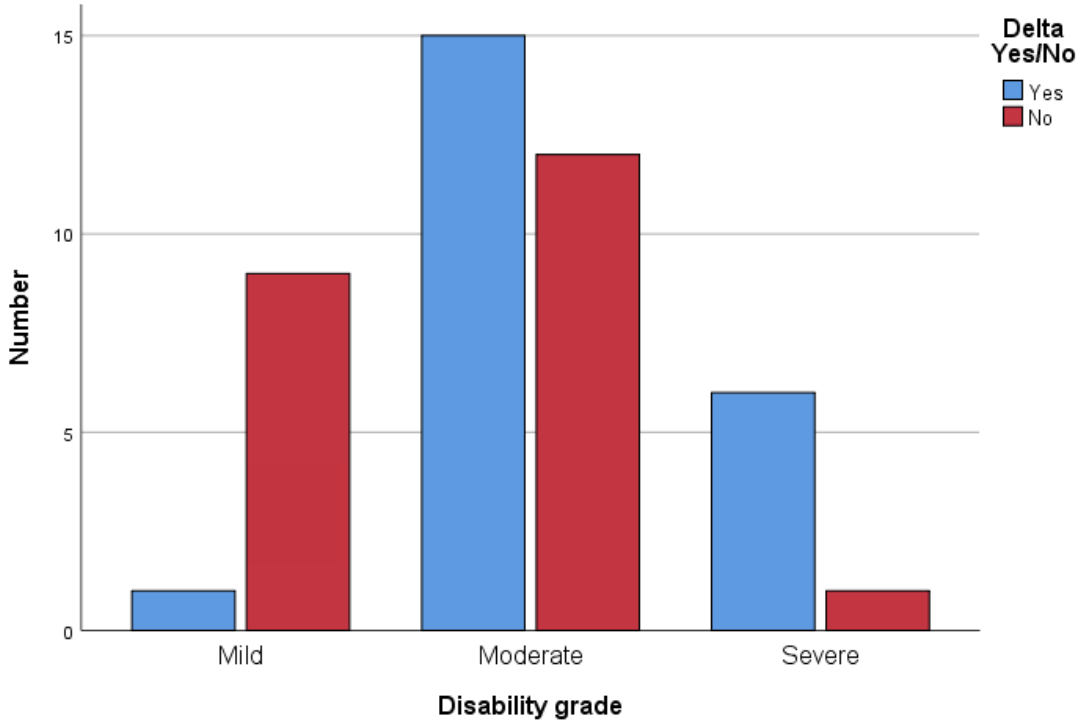

Figure 8. Bar-chart showing the relation between disability grade and presence of delta activity.

Table 5

Results from the Chi-Square Test showing distribution of disability grade and presence of delta activity

Delta present	Disability grade						
	1 (n = 10)		2 (n = 27)		3 (n = 7)		*p-level*
	n	%	n	%	n	%	
Yes	1	10.0	15	55.6	6	85.7	.006
No	9	90.0	12	44.4	1	14.3	.006

3.1.4 Mann-Whitney U Test. The amplitude of delta activity was greater in the higher disability grade (grade 3) (*Mdn* = 4.75) than in the lower disability grade (grade 1 or 2) (*Mdn* = 1.50), which can be seen in figure 9. A Mann-Whitney test

indicated that this difference was significant (U = 16.5, z = -2.33, p = 0 .02). The effect size for this finding, Pearson's correlation coefficient r, was moderate to large, .496 (Field, 2013).

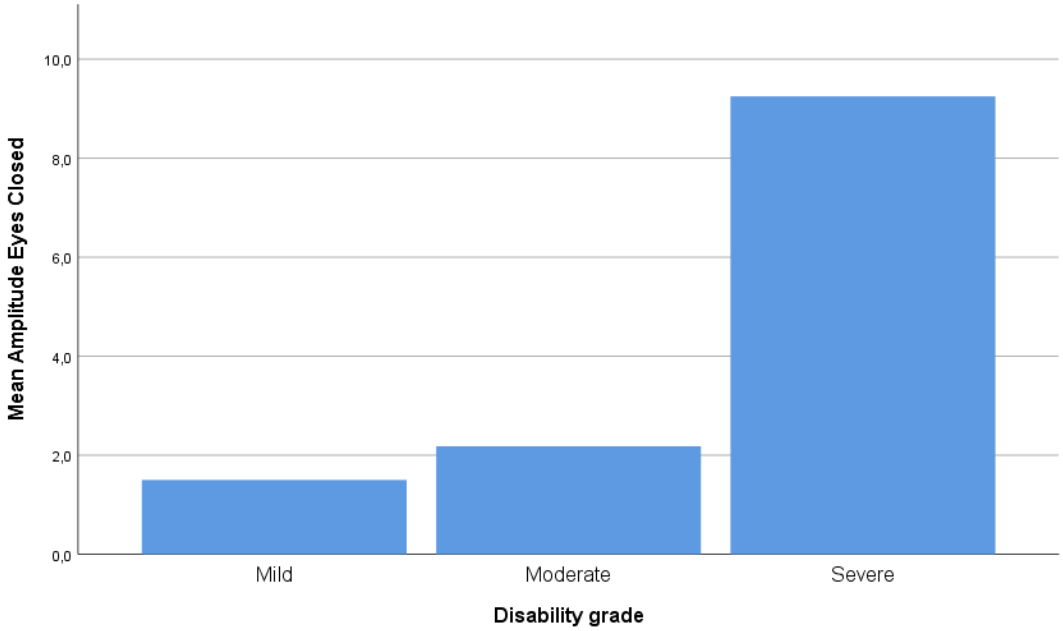

Figure 9. Bar-chart showing mean amplitude in the eyes closed condition in the different disability grades.

4. Discussion

The purpose of this study was to examine and report delta activity deviances in spectral analysis in relation to disabilities causing impaired daily functioning in a sample of one hundred and seventeen children and adolescents (age 7-17) referred to the child and adolescent psychiatry system in Nordfjordeid and south Sunnmøre, Norway. First in this section, the results and the delta activity will be discussed. Second the use of, and the challenges in clinical application of EEG, qEEG and source localization will be provided for discussion. Third, a more general discussion on methodological issues will be addressed. Finally, a section with discussion about limitations and implications of the present study including further recommendations will follow.

4.1 Results and delta activity

As mentioned in previous sections, delta activity is one of the most frequently observed activities in the waking EEG record of children. By using qEEG the delta

activity was shown to be significantly higher when compared with the norm database. This implicates that these children and adolescents had a larger amount of delta activity than the average population. A large amount of delta activity after 4 or 5 years of age indicates cerebral dysfunction (Rowan & Tolunsky, 2003). Several studies have also found that slow delta activity marks pathological brain abnormality resulting from neurological damage (e.g., De Jongh et al., 2001; Gloor et al., 1977; Tanaka et al., 1998; Vieth et al., 1999; Vieth et al., 1998). These and similar findings could implicate that the subjects included in this study have some kind of micro damage in the brain, which leads to the higher amount of delta activity. On the other hand, other studies have shown that delta activity can be a sign of internal concentration during the performance of mental tasks (Harmony et al., 1996). This finding could explain the higher degree of delta activity during the VCPT condition, but since the subjects included in this study also had significant higher degrees of delta activity in the resting conditions (EO and EC), this explanation is not very likely.

An increased delta activity correlates with several psychiatric disorders. Alzheimer's disease, schizophrenia, depression, ASD and ADHD are some of the disorders, to mention a few. Most of these disorders share symptoms and this is a challenge in the field of psychiatry (Gillberg, 2010). One thing these disorders do have in common is the increased delta activity. One could argue that the delta activity can tell us something about functionality, and the delta activity might explain the difficulties and symptoms the patients with the different disorders experience. The localization of the delta activity in a specific brain area will then most likely explain the typical symptoms of impairment.

4.1.1 Temporal delta activity. In this study one main focus was to examine and try to understand the temporal delta activity found in a previous study. The EEG record gives us a representation of the brain activity on the scalp. We know that just because we see an activity in one area of the scalp it doesn't mean that the activity is generated from that specific area. The source localization of the activity is therefore extremely important. We will come to different conclusions about assumed symptoms and difficulties in an individual if we think we found a deviation in the frontal area in the brain or the temporal area in the brain. This was actually the case in this study. In many subjects we found the delta deviations in frontal sites, but after source analyses

we could conclude that the delta activity were generated in temporal areas, often BA 22/39. So what does this temporal delta activity tell us?

We can only assume what the temporal delta will represent, since research about temporal delta activity is insufficient. One assumption though, is that the delta activity represents a micro damage in the neuronal tissue. This tissue will, because of the damage, be dysfunctional and give the individual typical symptoms of damage in this specific area. In this case, the temporal lobe will give the subject problems in auditory information into meaningful units, problems with emotions, memory and some aspects of language (Patel et al., 2020). Even more specific in this study we found deviances in BA22/39. BA22 and BA39 together represent Wernicke's area, which is an important area for the processing of speech, and therefore can be understood as language (Geschwind, 1970). Damage in this area has been connected to dyslexia and semantic aphasia (Kantha, 1992), which will be assumed to be typical problems for the subjects in this study. It might not be that simple though. As already mentioned in previous sections, connectivity plays an important role in the function of the human brain and as the basis for cognitive operations and diverse behaviors (Mišić & Sporns, 2016). The connectivity will under this assumption lead to inaccurate input and output from the dysfunctional area to other important structures and areas of the brain. This can result in incorrect processing of information in the brain, which can lead to several different difficulties for the subject in question. The symptoms shown in the subject will then depend on which area that generates the delta activity, and which areas this first area is connected to.

However, in this study, we have only been exploring the delta activity. There is a possibility that other deviances shown in the EEG record could better explain the symptomatology and the functionality of the subjects in question. This and the statistical analyses used in this study make it therefore difficult to say something about causality. Unfortunately, to examine all deviances in the population was beyond the scope of this study.

4.2 The EEG recording

The EEG has the advantages that it is a well-proven method of measurement that has been used in medicine for decades. Several previous studies have been published and there are a lot of comparing data. Another advantage is that there is extremely good time resolution at the millisecond level by measuring the actual electric field generated by the instantaneous nerve activation and EEG has not the

indirect effect on hemoglobin level and blood volume as in hemodynamic methods. The EEG equipment is relatively inexpensive compared with other devices and techniques. Furthermore, EEG equipment is mobile and can be used in more places compared to other methods studying brain function. Additionally, the method is completely non-invasive and can be applied repeatedly to patients, children and adults, with virtually no risk or limitation (Teplan, 2002).

The main disadvantage of EEG recording is the poor spatial resolution (Srinivasan, 1999). The received signal is the sum of the electric field that is produced of a large number of neurons. One single electrode has the spatial resolution in the order of five square centimeter of the cortex, which means hundreds of thousands of neurons. Several neighboring electrodes can therefore pick up strong electrical activity. To compensate for the poor spatial resolution the use of the source localization methods, used in this study, becomes extremely important.

However, some studies have criticized the LORETA method (de Peralta-Menendez & Gonzalez-Andino, 1998; de Peralta-Memendez & Andino, 2000; Kincses, Braun, Kaiser & Elbert, 1999; Michel et al., 1999). They state that LORETA is incapable of localizing sources. Pascual-Marqui (1999) demonstrated the falsehood of the statement. One argument was that the criticism was based on an incorrectly programmed algorithm of their author's own making.

These controversies may indicate that we should be careful about drawing any conclusions in localization only on the LORETA method. It is important to include the clinical picture in understanding the individual`s problems and their emergence. An even better alternative to LORETA may be the somewhat newer method s-LORETA (Pascual-Marqui et al., 2002), which is therefore recommended in future studies. The lack of access to s-LORETA in this study is the reason why this study used the LORETA method.

4.2.1 Connectivity. When trying to understand abnormalities in the brain and their causes one has to consider the brain's complexity, and how the brain communicates and are connected in different networks. If there is a dysfunction in one area of the brain, this may have major consequences on behavior and functionality that is not directly connected to that area. This is because of the brain's different neural networks and the connectivity will be affected. We think that this issue needs to be addressed in future studies. A promising tool for studying this problem will be the Human Connectome Project mentioned in previous section.

4.3 Limitations, implications and recommendations

4.3.1 Methodological issues. There are some methodological issues in the present study that need to be addressed. One concern regarding the design is the possibility of confirmation bias. Since the author was looking only for deviances in the delta frequency band this may have influenced the results. Though, the inclusion criteria were strict, as only subjects with delta activity present in all three EEG conditions were included. Therefore, we do not think this has impacted the ending result.

4.3.2 Subjects and control group. First of all, we need to ask ourselves if the subjects in the study can represent a general child and adolescent psychiatry population. The subjects in this study are from an area in rural Norway. To be sure of the answer of that question one would need further similar studies with other subjects from different national areas.

The lack of a suitable control group is a relevant limitation of this study. It would have been more appropriate if the subjects had been compared to a gender-matched healthy control group from Norway. In this study, the control group used was the HBI normative database, which provided a reasonable foundation for comparison. Nevertheless, this database has some statistical limitations. There is a lack that no records of the standard deviations exist in the database. The only statistical information obtained is the average mean for the whole group, but no single values. This makes it impossible for us to make analyses for comparisons on an individual level. Therefore, we had to rely on the internal t-test engine of the WinEEG software when looking for significant deviances between the subjects and controls in the HBI database.

4.3.3 Variables. The lack of control regarding possible confounding third variables that could have influenced the qEEG data, and consequently the result, is another concern in this study. Many variables may influence the VCPT-results, such as sight/vision, medication, time of the day, and comorbid disorders. Moreover, frequency band definitions vary somewhat across studies, which affect the cut-off point for frequency band ranges. This can for example lead to that low alpha can be reported as theta whereas high theta can be reported as low alpha. In this study we decided to include up to 4,5 Hz in the delta frequency band because of the shown distribution of the delta frequency in the spectral analysis.

Moreover, the classification of the severity grade of function made by the

psychologist was a subjective classification. The grade of action required was though included in the classification. The psychologist made a clinical assessment of the subjects, which was not a standardized method. On the other hand, it was the same psychologist that made the classification for all subjects, which reduces the risk of inter-observer variation. This will anyway make it somewhat difficult with an exact replication in further studies. In future studies we recommend to use some standardized methods in the classification process.

5. Conclusion

The main objective of this study was to investigate whether delta brain activity deviances represent higher disabilities in children and adolescents in the child and adolescent psychiatry system, and if these deviances are interesting in clinical settings. The results showed that presence of delta activity indicated a higher grade of disability in the subjects participating in this study. This supports the hypothesis that increased delta activity will correspond with greater disabilities in-group level. The other hypothesis was also supported since the result showed that the higher amplitude in the delta activity the greater disabilities in the individuals.

The limitations of this study have been addressed. Further research with an improved research design, a more appropriate control group together with a more standardized classification of clinical symptoms and functionality is recommended. Despite the limitations of this study it is possible to claim that increased delta activity plays an important role in the functionality of children and adolescents. EEG together with source localization can be helpful in understanding the brain's functionality and connection to cognition and behavior in humans. This may also help us be able to say something about etiology and causality regarding the symptoms across disorders, and be helpful in predicting diagnoses and treatment.

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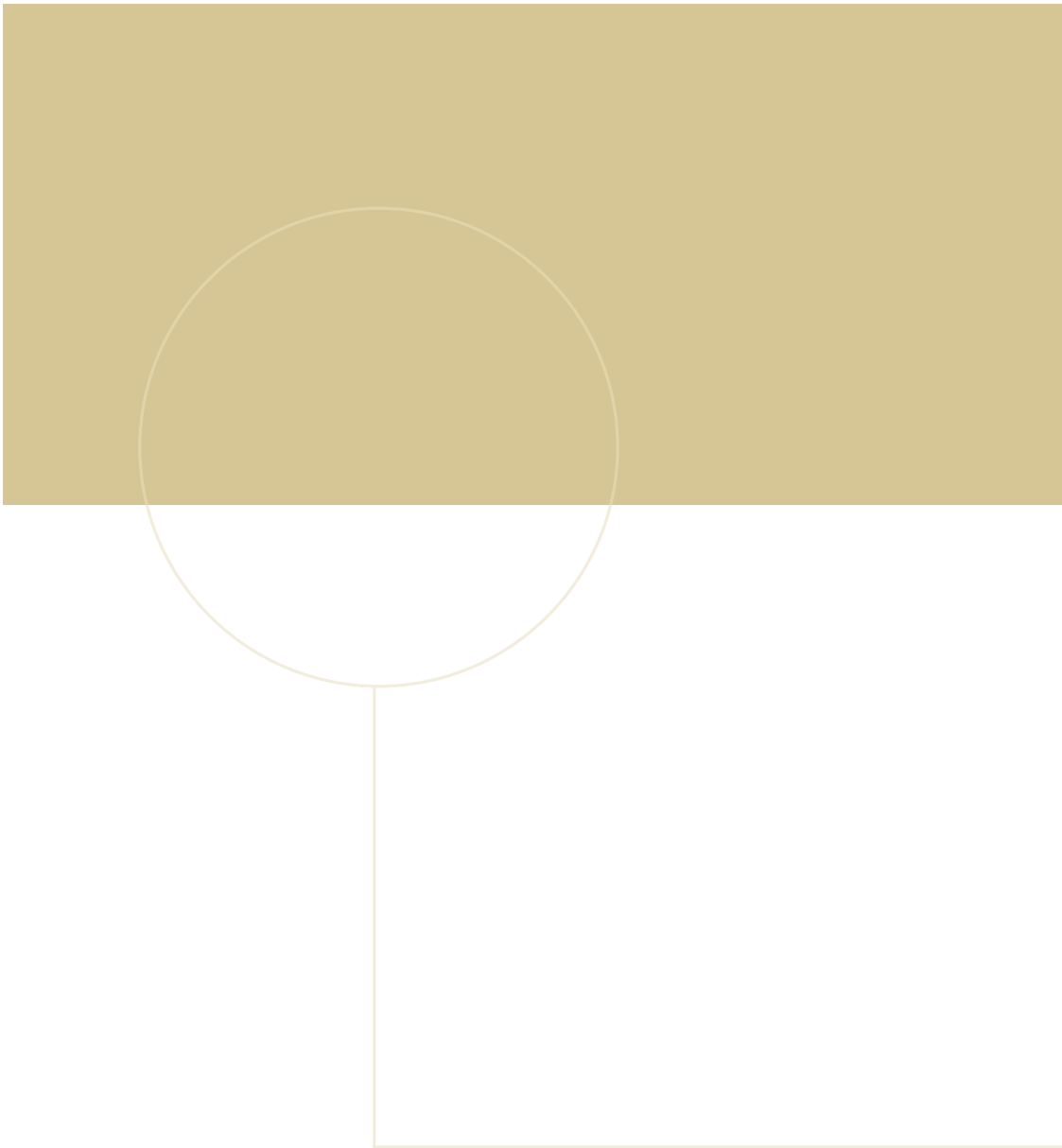

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