IMPROVING READING ABILITIES IN DYSLEXIA WITH NEUROFEEDBACK AND MULTI-SENSORY LEARNING

by

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IMPROVING READING ABILITIES IN DYSLEXIA WITH MULTI-SENSORY AND NEUROFEEDBACK

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Keywords: Brain-computer interfaces, neurofeedback, multi sensory learning, dyslexia, multi-scale entropy, TILLS, Auto Train Brain

Abstract

Developmental dyslexia is a subtype of specific learning disabilities. There are several methods for improving learning abilities, including neurofeedback and multi-sensory learning methods. As past work has shown, applying neurofeedback can improve spelling, reading, writing skills, normalizing fear, and anxiety of children with dyslexia. Multi-sensory learning methods utilize hearing (audition), reading (vision), seeing (vision), and touching (tactile/ kinaesthetic) simultaneously and proven to be useful for children with dyslexia. Neurofeedback focuses on normalizing the synaptic connections in the cortex, while multi-sensory learning focuses on using different parts of the brain to help with the learning process. Neurofeedback with multi-sensory learning (MSL) experiences in helping people with dyslexia was investigated in this research. Auto Train Brain is multi-sensory learning and neurofeedback based mobile application to improve the cognitive functions of children with dyslexia. It reads qEEG signals from EMOTIV EPOC+ and processes these signals aand provides feedback to a child to improve the brain signals with visual and auditory cues. The major contribution of this thesis is that it presents the first study that combines neurofeedback with multi-sensory learning principles. Moreover Auto Train Brain has a novel neurofeedback technique from 14- electrode channels. Auto Train Brain was applied to 16 subjects with dyslexia more than 60 times for around 30 minutes. 4 of them also received special education. The control group consisted of 14 subjects with dyslexia (mean age: 8.59) who did not have remedial teaching with Auto Train Brain, but who did continue special education. The TILLS test, which is a new neuropsychological test to diagnose dyslexia, was applied to both groups at the beginning of the experiment and after a 6-month duration from the first TILLS test. Comparison of the pre- treatment and post-treatment TILLS test results indicate that applying neurofeedback and multi-sensory learning method concurrently is feasible for improving reading abilities of people with dyslexia. Reading comprehension of the experimental group improved more than that of the control group statistically significantly.

NÖROGERİBİLDİRİM VE ÇOKLU DUYULU ÖĞRENME İLE DİSLEKSİDE OKUMA BECERİLERİNİN ARTIRILMASI

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Özet

Gelişimsel disleksi, özgül öğrenme güçlüğünün bir alt grubudur. Dislekside öğrenmeyi kolaylaştırıcı çeşitli yöntemler bulunmaktadır, nörogeribildirim ve çoklu duyulu öğrenme metodları bunlardan ikisidir. Bazı araştırmalarda gösterildiği üzere, nörogeribildirim disleksili çocukların heceleme, okuma ve yazma becerilerini iyileştirebilir, korku ve kaygılarını kontrol etmeyi öğretebilir. Çoklu duyulu öğrenme metodu, disleksili çocukların işitme, okuma, görme ve dokunma duyularını bir arada kullanarak onların öğrenmesine yardımcı olur. Nörogeribildirim, beyindeki sinaps bağlantılarını güçlendirirken, çoklu duyulu öğrenme beynin farklı bölgelerini öğrenme aşamalarında kullanmayı hedefler. Bu tezde, nörogeribildirim ve çoklu duyulu öğrenme deneyimlerinin disleksiye fayda sağlayıp sağlamadığı incelenmiştir. Bu tez kapsamında geliştirilen Auto Train Brain, disleksili çocukların bilişsel performanslarını artırmak için, nöro geribildirim ve çoklu duyu prensiplerine göre hazırlanmış bir cep telefonu uygulamasıdır. Auto Train Brain sisteminde, 14 kanallı EMOTIV EPOC+ EEG başlığından gelen sinyaller okunur, işlenir, görsel ve işitsel olarak disleksili çocuğa geribildirim olarak sunulur. Auto Train Brain, ortalama yaşları 8.56 olan 16 disleksili çocuğa 60 kez 30'ar dakika uygulanmıştır. 4 denek eş zamanlı olarak özel eğitim almıştır. Kontrol grubu, 8.59 yaş ortalamasına sahip 14 disleksili

çocuktan oluşmaktadır. Bu çocuklar, Auto Train Brain ile eğitim almamış, sadece özel eğitime devam etmişlerdir. Disleksiyi teşhis etmekte kullanılan yeni bir test olan TILLS testi, deneylerin başında ve 6 ay sonra hem disleksili gruba hem de kontrol grubuna uygulanmıştır. Deney öncesi ve sonrası ölçülen TILLS testi sonuçlarını karşılaştırdığımızda, Auto Train Brain eğitiminin etkili sonuç ürettiği izlenmiştir. Auto Train Brain eğitimi, özel eğitime nazaran okuduğunu anlamayı daha çok artırmıştır. Bu tezin ana katkısı, nörogeribildirim ve çoklu duyulu öğrenmeyi aynı anda kullanan Auto Train Brain'in etkin bir çözüm olduğunu göstermiş olmasıdır.

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Chapter 1

Introduction

Dyslexia is a neurological disorder which is primarily developmental. Developmental dyslexia is categorized as a subtype of learning disabilities. The primary root cause of dyslexia is in the phonological component of language. Spelling abilities, reading abilities and reading comprehension are affected. Reading abilities also affect the vocabulary and knowledge [1]. The posterior and the anterior of the left hemisphere are weakly connected [2]. This disorder affects both children and adults. These people find it difficult to understand the relationship between graphemes and phonemes, they don't analyze the sounds correctly and manipulate sounds, and they slowly identify the words [3].

In the literature, computer-based multi-sensory learning methods are used for improving the writing and reading abilities of people with dyslexia. According to [4], a computer-based multi-sensory learning program strengthens memory via visual and auditory associations between graphemes and phonemes, and improves the writing abilities of people with dyslexia. People with dyslexia must learn correspondences between phonemes and graphemes, and they rapidly name the letters and words correctly. As more senses are involved in the learning process, rapid naming and memory strengthen. Orton-Gillingham (O-G) approach, a multi-sensory learning method designed for people with dyslexia, has proven that a multi-sensory approach improves the reading abilities of dyslexics [5]. People with dyslexia have difficulty in shifting their attention from visual to auditory or vice versa [6,7]. Therefore, any dyslexia training software should take into account the asymmetric shifts of cross-modal attention.

Quantitative EEG is the analysis of the digitized EEG which is the measurement of electrical patterns at the surface of the scalp. qEEG neurofeedback is a type of neurofeedback based on the digitized EEG. Electroencephalography (EEG) reveals periodic variations in electrical activity within the brain, that has been characterized as combinations of four frequency bands or components; which are delta (4 Hz), theta (between 4-8 Hz), alpha (between 8-12 Hz), and beta-1 and beta-2 (between 12-35 Hz) and gamma(above 35 Hz). While the state of consciousness is the primary reason for one frequency being dominant over the other, subtle variations in these components frequently indicate underlying disorders. For the people with dyslexia, an increase in theta relative power according to their age has been found extensively. In the literature, higher amounts of delta band power and lower amounts of alpha band power in people with dyslexia compared to typically developing healthy children of the same age have been reported. Most of the children with learning disabilities show EEG patterns that are more common for younger healthy children, which shows brain maturation delay. Other groups of children with learning disabilities show different EEG activity [8].

Various researchers have shown that people with dyslexia have slow waves at FC5 and F7, and they do not desynchronize fast wave activity (Beta-1) during a reading task in areas related to Broca's area and the Angular gyrus [9], as well as the left parieto-occipital area (P7, O1) [10]. Dyslexic children have increased slow activity at the right temporal and parietal (P8 and T8) regions of the brain [3]. Dyslexia may also be comorbid with ADHD, meaning that slow activity in the frontal lobes may be high. There is a symmetric hyper-coherence for the delta and theta bands at T3 and T4 and a specific right-temporal hyper-coherence for the alpha and beta bands [3]. Bi-hemispheric (at T3 and T4) hyper-coherence manifests in the slow waves (delta and theta) bands, while hypo-coherence can be found between P7- O1 in the slow brain waves (delta, theta, and alpha bands) [11], meaning that left-hemispheric dominance is not established yet. Therefore, any dyslexia training software should improve the left hemispheric dominance.

In neurofeedback applications, EEG signals of a user will be read and sent to the computer to be processed. The processed qEEG signal is presented to the user as visual and auditory cue in real time. The user learns to gain voluntary control over neural signals upon continuous usage. The age-matched brain activity is rewarded wheras slow brain waves are penalized [12]. Neurofeedback has been used for treating attention-deficit/hyperactivity disorder, autism, depression, migraines, seizures, sleep disorders, and anxiety attacks [12].

There are many different types of neurofeedback:

- qEEG neurofeedback
- Coherence training neurofeedback
- Hemoencephalography (HEG) neurofeedback
- HPN Ultra Low Power Neurofeedback
- Interactive Metronome® (IM)
- 3D Neurofeedback (QEEG LoRETA neurofeedback)

Although there has been much separate research about qEEG neurofeedback and multi-sensory learning methods for people with dyslexia, none of the research has combined the best parts of these methods and come up with a seamless, fully automated version of both methods which will provide an effective way of improving the learning abilities of people with dyslexia. Neurofeedback is based on visual and auditory cues, which provides the basis of a multi-sensory approach for people with dyslexia who cannot read and write yet. By applying neurofeedback, slow brain waves are reduced to the degree that the brain is ready for learning new information about lexemes and graphemes. Then, an alphabet teaching system that combines lexemes with graphemes should be presented. The system should connect the visual representations of lexemes with phonemes in a seamless way, and this process should be repeated many times as there are cross-modal processing differences of people with dyslexia in order to make it a permanently acquired ability. Computers can handle repetitive tasks very efficiently and can repeat the same procedure to a dyslexic child. This new solution should provide replicable results and allow an application to any subtypes of dyslexia.

1.1 Scope

Our first objective in this thesis was to design and implement an end-to-end system for improving reading performance of dyslexic children by using neurofeedback and multi-sensory learning. This requires:

- The development of experimental scenarios for stimulating the appropriate neural mechanisms in the subject,
- The design of algorithms for information extraction from the collected EEG data,
- The design and implementation of the Android mobile software,
- The design of the mobile user interface which is ergonomic and ease to use
- Combining the neurofeedback component with a multi-sensory learning experience which is suitable for 7-10-year-old dyslexics,
- The demonstration of the effectiveness of the Android Mobile application through experiments on dyslexic subjects.

Auto Train Brain is developed within the scope of this thesis and it becomes a patented software (patent number: PCT/TR2017/050572) specifically designed for dyslexic children[13–15]. In the solution, a system and method for improving reading ability are implemented, the system relies on a distinctive protocol of multi-sensory learning and EEG biofeedback. An application on a mobile phone for improving reading ability is provided. The software includes a multi-sensory application which contains pictures and audition of letters, words and text. Before the training or concurrently with the training, EEG signals are read from a sufficient number of electrodes (1-14), and these EEG signals are translated to auditory and visual feedback to improve the 'user's brain performance. If this app is used a sufficient number of times, the 'user's reading speed is increased, and the error rate during reading is reduced. The software contains norm data collected from healthy people and people with learning disabilities. This data is used for determining thresholds. In other words, the threshold values for EEG signals are set with norm data collected from healthy people and people with learning disabilities. Therefore, the 'subject's performance can be statistically compared to that of an extensive population database (Quantitative Electroencephalograph; qEEG).

1.2 Motivation

Dyslexia is described as brain maturation delay or incomplete lateralization during brain maturation. There are many subtypes of learning disabilities, brain mapping of people with dyslexia show variations in many electrodes compared with that of healthy normal people. In the literature, one or two electrode-based neurofeedback methods are applied to children with dyslexia. Finding the electrode place on the scalp that needs treatment is done with brain mapping and the decision is taken by a therapist manually. The duration of the treatment may be too long for people with dyslexia because many different brain regions are affected. We have invented a novel neurofeedback algorithm to apply neurofeedback from 14 channels simultaneously. Simultaneous neurofeedback from many channels may reduce the neurofeedback treatment time for dyslexia. With 14-channel neurofeedback, we would like to improve the brain maturation as a whole and enhance the lateralization of the brain naturally. 14-channel neurofeedback enables us to apply the neurofeedback to different subtypes of learning disabilities. It takes 2-3 months to improve the brain maturation with neurofeedback only. These children should catch up with the school at the same time. Multi-sensory learning, which is effective for people with dyslexia, does not attempt to change the structure of the brain, but improves the perceptual processes with multi-sensory input. Right after neurofeedback session which reduces the slow brain waves with visual and auditory cues, the child is ready to acquire some academic skills, like learning the alphabet. We have proposed an alphabet teaching method in the app which is multi-sensory, that matches graphemes with phonemes and provides a strong base to learn reading and spelling.

1.3 Contributions

Our main contribution and goal of this thesis was to design, implement, and evaluate experimental protocols and real-time information extraction and neurofeedback protocols to increase the involvement of people with dyslexia with the main aim of improving the efficacy of the reading process. Some of the motivating questions for this thesis are listed as follows:

1. Does neurofeedback training together with multi-sensory learning improve

reading comprehension and spelling abilities of dyslexic children?

2. Does novel neurofeedback method of Auto Train Brain from 14-channels provide an effective neurofeedback method for dyslexia?

3. Can Auto Train Brain efficiently improve the reading abilities of children who are 7-10 years old?

Our contribution to this research is to understand the possible positive effects of the Auto Train Brain training and compare the treatment effects with those of special education, Orton Gilligam method and neurofeedback alone.

For this purpose, first, we have designed a neurofeedback system which infers the resting state of the subject. Secondly, we have built a complete neurofeedback system that can control slow brain waves of the subject. Moreover, we have developed new procedures for the use of this system in improving the reading abilities of dyslexic children. Therefore the main contributions are summarized as follows:

- We have built neurofeedback and multi-sensory learning-based Android Mobile application which uses EMOTIV EPOC+ headset to read EEG signals from 14 electrodes.

- We have proposed a new neurofeedback approach that enables detecting slow brain waves in the left and right brain and reduces them in parallel.

- We have built an online alphabet teaching system with multi-sensory learning methods to investigate the positive effects of the designed Android Mobile Phone application after neurofeedback session.

1.4 Outline

Chapter 2 presents the necessary background and literature review about the medical background for dyslexia, neurophysiology of brain and EEG signal processing by presenting a survey and literature review about published works, methods, and results.

In Chapter 3, we have described the mobile solution components and explained the proof-of-concept experiments we have conducted with the preliminary version of the app written with Python.

In Chapter 4, we have explained the experiments conducted on the healthy subjects. The first experiment is about the prediction who will respond more to neurofeedback training with the resting state qEEG, the second experiment is about improving reading abilities with multi-sensory learning experience.

In chapter 5, we have described complexity, entropy, coherence concepts to measure the healthiness of brain and explained in detail how Auto Train Brain app has improved entropy and coherence of a 14-year-old dyslexic boy. Then, we have explained that we have measured the multi-scale entropy of children with dyslexia (7-10 years old) and compared that with age-matched typically developing norm group. We have applied neurofeedback with multi-sensory learning to children with dyslexia and reported the changes in multi-scale entropy.

In chapter 6, we have reported the improvements in reading abilities of children with dylexia after neurofeedback and multi-sensory learning in dyslexia. We have compared the results with that of children with dyslexia who continued special education only.

In chapter 7, we have summarized all the experiments and findings. We have presented what should be done as future work.

Chapter 2

Background

This chapter intends to describe how developmental dyslexia develops and the basic concepts about neurophysiology of brain and EEG signal processing by presenting a survey about published articles.

2.1 Medical background on dyslexia

2.1.1 Definition of dyslexia

Although IQ is measured as normal or above normal, some people face difficulty in reading, writing, learning mathematics, and learning other tasks in general. This situation is called a specific learning disability (özgül öğrenme güçlüğü). If the difficulty is in reading, it is called as dyslexia (okumada güçlük) ; if the difficulty is in writing, it is called as dysgraphia (yazmada güçlük) ; if the difficulty is in learning mathematics, it is called as dyscalculia (aritmetikte güçlük), and if the difficulty is in physical coordination of tasks, it is called as dyspraxia (koordinasyonda güçlük). One or more learning difficulties may exist at the same time [16–19].

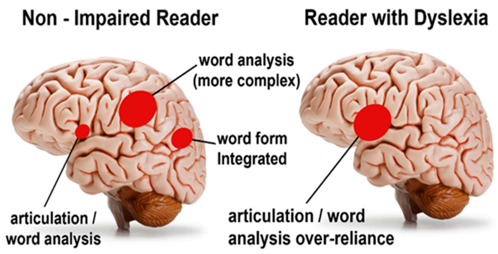

Figure 2.1: Dyslexic brain, taken from Understanding Dyslexia - Cognitive Development Learning Centre, cognitive.com.sg

During brain maturation process some neural functions are lateralized to the left brain (lateralization). A minicolumn can be thought of as a computational unit of cerebral cortex, which has inputs and outputs. Neocortex formation is affected by the addition of minicolumns within the neocortex [20]. As these minicolumns are widespread, the abnormalities in their presence and patterns, which are called minicolumnopathy, changes the functioning of the brain; these minicolumnopathies change brain gyrification and volume [21]. Hence, any brain training system targeted at people with dyslexia should aim to improve these short connections to reduce their symptoms. Minicolumns form "weak linkages" within canonical circuits, in this way they adapt to the environmental demands [20]. During the maturation phase, the brain adapts the visual and language systems to form a reading system [22]. However, in people with dyslexia, left hemispheric dominance is not established yet. Current studies showed that dyslexic group may have a deficit in their functional connectivity targeting the left angular gyrus [23,24]. As a result, a less efficient reading circuit manifests itself as a weaker phonologic processing or awareness. Hence, any brain training system targeted at people with dyslexia should aim to increase the efficiency of the reading circuits by improving short-distance connections in the left hemisphere.

2.1.2 Genetic disposition of dyslexia

Dyslexia has genetic roots. The existence of dyslexia in a family span longer than a person's lifetime. Dyslexic parents and offspring tend to be similar to each other for genetic reasons [25].

2.1.3 Maternal excess androgens due to PCOS affects fetal brain development during pregnancy

Polycystic Ovary Syndrome is an autoimmune-related endocrine syndrome, which increases the androgen/ testosterone levels in a woman's blood. It also increases the risk of metabolic syndrome, type 2 diabetes and hypothyroidism. PCOS is related with excess androgens and increase the risk of ASD (Autism Spectrum Disorder) in the offspring[26]. N. Geschwind and A. M. Galaburda (1987) has shown that genetic origin as well as an aberrant immune system could thus affect the developing brain

[27].

2.1.4 Dyslexia is a disconnection syndrome between posterior and anterior language areas

Broca's area are activated during the rhyming task and temporal and parietal lobes are activated during the short-term memory task for the typically developing individuals. In people with dyslexia, these areas including the left insula are not activated properly. The posterior and the anterior language areas seem to be disconnected [2].

2.1.5 High cortisol levels of the mother affect the hippocampus of fetus

Women with PCOS have high cortisol levels in their blood. Cortisol influences neuronal excitability which affects the neuronal functioning, through a reduction of long-term hippocampal potentiation. Stress is known to impact on learning and memory processes. Neurocircuitry, underlying memory contextualization processes, is sensitive to cortisol [28].

2.1.6 Minicolumnopathies exist, subcortical learning and hippocampus are also affected as well as cortex in dyslexia

Minicolumnopathies affect the brain formation and lateralization, and these are the basis for significant alterations in the brain connectivity and functioning [20]. In dyslexia, subcortical learning regions and hippocampus are also affected[29].

2.1.7 Double deficit theory (deficiency in the formation of cortex)

The authors of [30] propose the double deficit hypothesis. In people with dyslexia, the left parietal and frontal as well as the right cerebellar lobule VI are affected. Double-deficit subtype cause more severe impairments in reading. Phonological awareness is related with the left parietal and frontal regions wheras naming speed is related with the right cerebellar lobule.

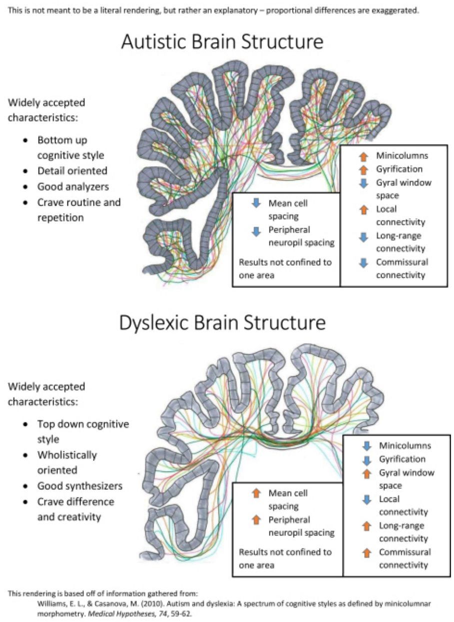

Figure 2.2: Autism versus dyslexia, Williams & Casanova, 2010

2.1.8 Dyslexia is the result of autoimmune system problems

The researchers reported that there are more immune and autoimmune-related problems at dyslexic children [31]. In people with dyslexia, thyroxine is measured high compared with typically developing children [32].

The gut barrier is the most complex as it performs various functions in addition to the barrier function and most important of that is the digestion and absorption of food. In the gut, there exists a complicated symbiotic relationship between host and gut microbiota. On many diseases, gut equilibrium is disturbed to develop dysbiosis. The reasons of dysbiosis are stress, dietary changes, use of antibiotics, and steroids. Dysbiosis is also associated with various liver diseases like gastrointestinal infections, inflammatory bowel disease, cancer, irritable bowel syndrome, food intolerance and allergy, obesity and metabolic syndromes, small intestinal bacterial overgrowth, liver diseases [33, 34]. Gut microbiota is implicated in the following diseases:

- Obesity
- Diabetes
- Metabolic syndromes
- Rheumatoid disorders

- Alcoholic fatty liver disease
- Heart disease
- Periodontitis
- behavior and motor activities
- schizophrenia
- dyslexia
- autism
- Many mood disorders.

2.1.9 Summary of the medical literature research

- Dyslexia has genetic roots. Dyslexic parents and offsprings tend to resemble each other for genetic reasons, and not due to cultural transmission.
- Due to fatty acid deficiency which is genetic, maternal immune system may be affected by leaky gut and dysbiosis. Furthermore, a fatty acid deficiency increases the chance of gut permeability and blood-brain permeability. There is a gut dysbiosis which is usually linked to leaky gut, which is dysfunctioning of the gut barrier. This problem triggers the autoimmune response and allergies.
- Maternal autoimmune diseases like PCOS, diabetes, and hypothyroidism affect the formation of the fetus brain due to elevated testosterone and cortisol levels. High cortisol levels affect the functioning of the hippocampus and introduce the minicolumnopathies in the primarily male fetus. The female fetus is probably protected by the estrogen produced in ovaries.
- Maternal autoimmune response creates problems in neurogenesis, neuronal migrations, and neuronal communications in perinatal period.
- Abnormal lateralization problems, reduced brain volume, and abnormal gyrification exist. The interhemispheric connectivity is high, the corpus callosum is more comprehensive than usual.

- Subcortical learning systems (like hippocampus) may get affected.
- In dyslexia, left hemispheric dominance is not established yet.
- Dyslexic children have allergies and autoimmune problems. Due to an autoimmune response, the microglial cells may get activated in the brain, especially in the frontal lobe (chronic inflammation).
- The Broca area (F7 and FC5) and the Wernicke area (T7, P7, O1) in the left hemisphere are mostly affected. The right Temporal and Parietal areas (FC6, P8, T8) may also get affected.

2.2 Introduction to brain neurophysiology

Typically, EEG is recorded after the subjects close their eyes and relax. Brain patterns form sinusoidal wave shapes. Brain waves are categorized into five groups:

Delta (1 Hz up to 4 Hz). It tends to be the highest in amplitude and the slowest waves and very difficult to store in EEG signals. During sleep state, it is seen in adults, whereas the babies have it during the day time.

Theta (4 Hz to 7 Hz). Theta during eyes open situation is seen generally in young children. It is mostly seen in learning disabilities and ADHD, ASD.

Alpha (7 Hz to 13 Hz). Alpha wave is seen in the posterior regions of the head on both sides; it increases when eyes are closed and reduces with eyes opening or mental exertion.

Beta (4 Hz to about 30 Hz). The prefrontal cortex produces beta during semantic and decision making tasks. Beta activity is closely linked to motor behavior and increased with motion. Low-amplitude beta is associated with cognitive abilities.

Gamma (30–100 Hz). Gamma rhythms are thought to represent consciousness, which is produced by binding of different populations of neurons together into a network to carry out a specific cognitive or motor function.

2.2.1 EEG biofeedback

The brain waves of a person are presented to himself in order to change and correct the frequency bands into desired amplitudes by repetitive visual and auditory

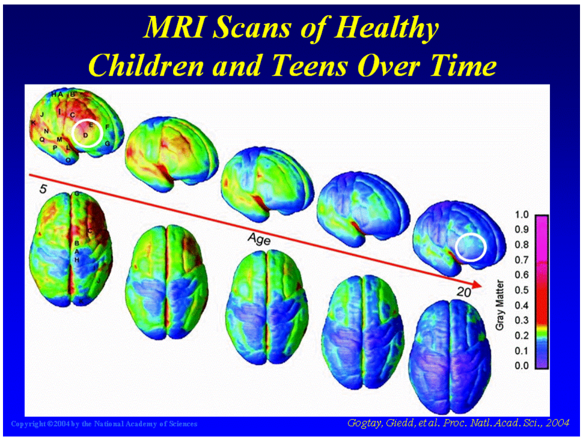

Figure 2.3: Brain development phases

stimuli. It is suggested that brain training system may help a subject to modify his brain wave activity. The person is aware of the right direction of the training. There is research that subjects can improve their mental performance, normalize behavior, and stabilize mood through a positive or negative feedback loop. Neurofeedback is applied successfully for ADHD, depression, epilepsy, and alcoholism.

2.2.2 Coherence

As dyslexia is a disconnection syndrome, coherence calculations are essential in diagnosing the syndrome. Coherence is defined as a measure of the amount of association or coupling between the brain signal recorded from two different electrodes. Coherence is analogous to a Pearson product-moment correlation. Coherence is necessary to understand the degree of relationship between two living systems over a long period. Coherence is dependent on the phase delay between the two-time series. In dyslexia, coherence measures show two different things. Interhemispheric coherence between T3 and T4 in dyslexia is high (hyper-coherence), meaning that the left hemispheric dominance is not established yet. Moreover, the coherence within the same intrahemisphere is low (hypo-coherence) shows the disconnection syndrome between Broca's area and Wernicke area. The aim of neurofeedback should be to normalize the coherence.

2.2.3 EEGLAB

EEGLAB is a toolbox which has an interactive interface in Matlab in order to process the .edf EEG recorded from different systems. It is possible to do independent component analysis (ICA), artifact rejection by eye, filtering, brain mapping, and visualization. In our project, EEG of dyslexic children during resting state eyes closed are recorded to be analyzed with Sample entropy and MSE. These data had artifacts by nature. EEGLAB is used for artifact removal, choosing AF3 through AF4 channels EEG information from data, and storing the cleaned data as .csv files.

2.2.4 EMOTIV EPOC+

Dyslexia is a disconnection syndrome which affects more than one part of the brain. Although there was research which only focuses on F7 and T3 (Broca Area) in order to conduct neurofeedback to improve the spelling of dyslexic children, our choice was to apply neurofeedback from more than one channel at the same time in order to reduce the slow brain waves that can be found in different parts of brain. So we had to choose a device which can read EEG signals from at least eight channels to implement our solution. Another requirement was that the device should be reliable enough to be used on children who are 7-10 years old. There were very few products in the market which can provide solutions to these requirements. EMOTIV EPOC+ was one of them. The study [?] has proven that EMOTIV EPOC+ captures the real EEG. The features are

Signals

- 14 channels: AF3, F7, F3, FC5, T7, P7, O1, O2, P8, T8, FC6, F4, F8, AF4
- References: In the CMS/DRL noise cancellation configuration P3/P4 locations

2.3 Treatment options for dyslexia

2.3.1 Neurofeedback on dyslexia

Dyslexic group was better performing during a visual search task than a phonological processing task and here are differences in task-related alpha desynchronization and theta inhibition compared with control group [10].

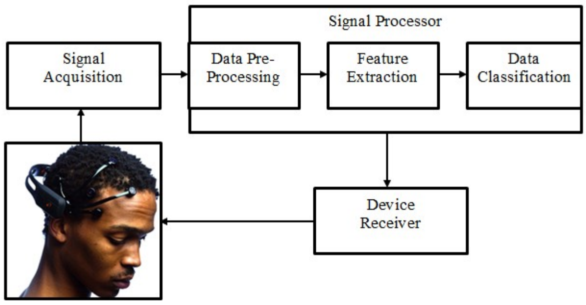

Figure 2.4: EMOTIV learning system

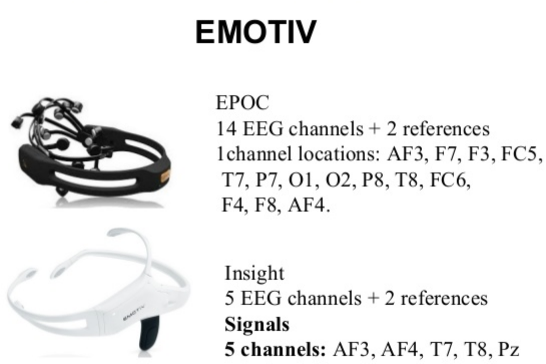

Figure 2.5: EMOTIV EPOC+

Neurofeedback protocol of increasing low beta activity at T3 (left mid-temporal area) has proven helpful in improving reading speed and comprehension. Twelve dyslexic individuals are treated and improved at least 2-grade levels by 30-35 sessions [35]. Theta/beta neurofeedback on Chinese dyslexic children was proven to be effective [36]. Reducing theta at F7 and T3 improved the spelling abilities but not reading [37]. Coherence protocols on people with dyslexia also improved reading and phonological awareness [11, 38]. Neurofeedback applied at sensorimotor area is more effective than Fernald's methods [39].

Study [8] has reported that follow-up assessments show that the efficacy of neurofeedback lasts and even improves 2-month after the training program.

2.3.2 GAPS diet treatment for dyslexia

Dr. Natasha Campbell-McBride has invented the GAPS diet in 2004 and used this diet to improve the cognitive abilities of autistic, ADHD, and dyslexic children. According to the inventors, GAPS is a syndrome which is caused by inadequate con-

Figure 2.6: 32-channel neurofeedback

sumption of proper foods. Unhealthy food choices affect the balance of gut microbiota. Although the genetic disposition of these conditions has, the gut microbiota of the mother may affect the child's formation of the digestive system after birth. Mothers who have GAPS syndrome, as well as their children, may show characteristics that attribute to severe behavioral and neurological disorders, and by proper diet, this condition is reversible. When there is an immune system deficit, the gut releases toxins into the bloodstream, and then these toxins go to the brain, causing a lack of nutrients, starting microglial activation. When a mother has immune system problems and gut dysbiosis, this condition is transferred to the child upon birth. The child may also have autoimmune responses which affect the formation of the brain.

GAPS diet first focuses on detoxifying the person and brain, so that gut dysbiosis is healed. Healing the gut dramatically heals the body and brain. If the dyslexic child has autoimmune problems and allergies, leaky gut is a possibility. Together with neurofeedback, the diet should be applied in order to strengthen the immune system [40]. The child should be on a diet for years in order to reach a reasonably excellent health condition. Neurofeedback requires less time than the diet to see the effectiveness, but to make the result of neurofeedback permanent, a diet is necessary to follow for a certain amount of time or the rest of the child's life.

2.3.3 Multi-sensory learning for dyslexia

In the literature, there is research about using computer-based multi-sensory learning methods to improve the cognitive abilities of people with dyslexia. According to [4], a computer-based multi-sensory learning program strengthens memory by improving associations between phonemes and graphemes. Orton-Gillingham (O-G) approach, which is a multi-sensory learning method designed for people with dyslexia have proven that a multi-sensory approach improves the reading abilities of dyslexics[5]. People with dyslexia have cross modal attention shift problems [7]. Perceptual learning improves the audiovisual sensory integration and binds the stimuli to be perceived as the same part of the environment [41].

Although there has been much separate research about qEEG neurofeedback and multi-sensory learning methods for people with dyslexia, none of the research has combined the best parts of these methods and come up with a seamless, fully automated versions of both methods which will provide an effective way of improving literacy skills of people with dyslexia. Neurofeedback is based on visual and auditory cues, which provides the basis of a multi-sensory approach for those of people with dyslexia who can not read and write yet. By applying neurofeedback, slow brain waves are reduced to the degree that the brain is ready for learning new information about lexemes and graphemes. Then, an alphabet teaching system which combines lexemes with graphemes should be presented. The system should connect the visual representations of lexemes with phonemes in a seamless way, and this process should be repeated many times as there are crossmodal processing differences of people with dyslexia in order to make it a permanently acquired ability. Computers can handle repetitive tasks very efficiently and can repeat the same procedure to a dyslexic child. This new solution should provide replicable results and could be applied to different subtypes of dyslexia.

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Chapter 3

Mobile Solution Components & Proof-of-Concept Experiments

In this chapter, we have described the mobile solution components and explained the proof-of-concept experiments we have conducted with the preliminary version of the app written with Python.

3.1 Overview

Before developing our extensive study on many participants to be described later in this thesis, we performed some preliminary experiments with a small number of healthy and dyslexic participants. These preliminary experiments enabled us to improve our approach before launching the main study. Our preliminary experiments were guided by the following observations about dyslexia.

- 1-channel neurofeedback on Broca area was indeed effective in solving reading difficulties. However in dyslexia, there is a "disconnection syndrome" . Neurofeedback protocol should be combined with improving coherence as well. There were coherence based neurofeedback protocols in the literature, but these procedures can not be implemented with EMOTIV EPOC+ as we can only read frequency band brain signals. The solution should be based on frequency band neurofeedback, but at the same time, it should improve coherence and reduce disconnectivity.

- There were many subtypes of dyslexia, any electrode location (F7, FC5, T7, P7, O1, O2) where theta band power is above thresholds may be symptoms of reading disabilities, which made a single solution to all of these problems impossible.

- The presence of high anxiety, and fear (right frontal areas) in dyslexic people suggested that more than one regions of the brain should be treated with neurofeedback.

- Some children with dyslexia have also attentional deficits (dyslexia is comorbid with ADHD most of the time), so the solution should address the need for ADHD as well. In the literature, SMR neurofeedback was applied to improve ADHD, which was different from the treatment of dyslexia.

- Some children with dyslexia have impulsivity and motivational issues which may be due to ADHD.

- Some children with dyslexia have clumsiness and difficulty in self-care issues (related with P8).

- Dyslexia has similar roots with autism where low-gamma and high gamma can be measured at the scalp, which shows the brain maturation delay and aberrant neuronal connectivity. We need a neurofeedback protocol which improves the gamma bands as well.

- Learning disabilities have different subgroups. In one subgroup, the auditory abilities are higher than the visual abilities; in the other subgroup, the visual abilities are better than the auditory abilities. Attentional shifting differences should be improved with the proposed protocols.

- In some dyslexia subgroups, there is an asymmetry between the left and the right visual cortex which may also be another cause of reading difficulties.

- Neurofeedback during 3D computer game was effective for people with dyslexia. Dyslexics have natural tendency to play computer games.

Usually, a therapist first records EEG, and by comparing EEG with that of normative databases, they decide where to apply neurofeedback for how many sessions to improve which power bnd values and repeats the same procedure at least 10-20 times. The protocols commonly used for neurofeedback are reducing theta at F7 and T3, reducing theta at T8 and P8, improving coherence between T3 and T4, reducing beta-1 at F7. Although considerable time is spent on reducing delta/theta signals on Broca area (2-3 months), we need to apply neurofeedback to many areas of the brain with individualized trainings sequentially. Moreover, there was not any research in the literature, whether working on one electrode channel for a long time had adversary effects on the other parts of the brain. This situation has led to think that neurofeedback should be applied at more than one electrode channels during a session. If we process the slow brain waves in parallel, then the total time required would be reduced and also the side effects would be minimized. As a first attempt, we have decided to take the average of all slow brain waves (namely theta) at 14 electrode channels and attempt to reduce this with neurofeedback. However, our experimental analysis has shown that the brain is capable of processing more detailed feedback given based on slow signals measured from each electrode. This enabled us to shape our unique neurofeedback protocol, which aims to reduce the highest slow brain signal above threshold in left and right hemisphere.

Neurofeedback was coupled with visual and auditory tasks beforehand, reported effective in improving reading. However, a reading/learning alphabet task is not given just after the neurofeedback session. Our hypothesis is reducing the slow brain waves before attempting to teach the alphabet to a dyslexic child would be more effective. Just after the neurofeedback session, the child's brain would be more receptive to embrace the alphabet letters and match the phonemes with lexemes.

Our hypothesis is

- Neurofeedback should be applied at more than 1-electrode channels at a time, reducing theta brain waves in parallel
- After neurofeedback session, a session for matching lexemes and phonemes makes learning more effective
- For hyperactivity, there needs to be a separate neurofeedback protocol

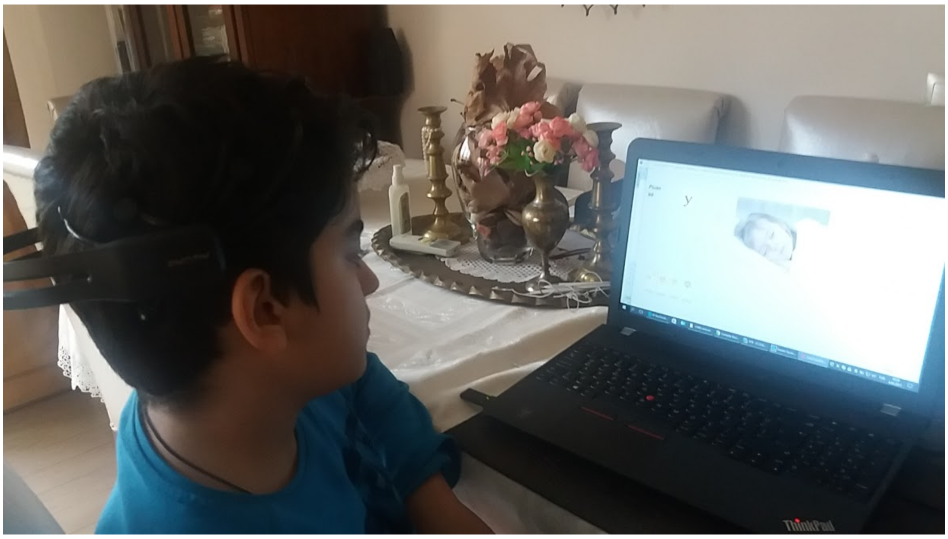

Figure 3.1: The computer based training program which couples neurofeedback with Multi Sensory learning

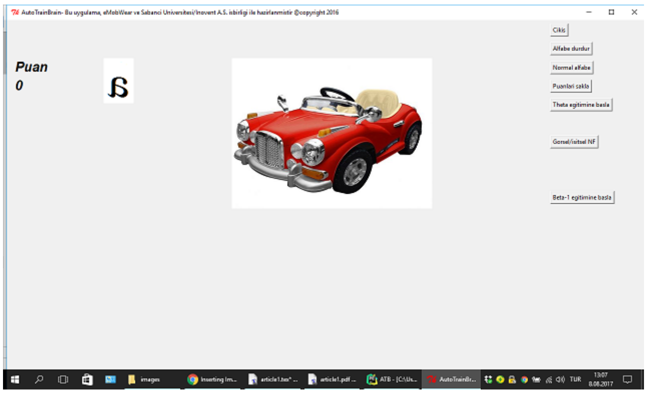

Figure 3.2: The computer based training program to teach distorted letters

3.2 Proof-of-concept experiments

Our first solution has been implemented with Python.

The EEG headset we have chosen is EMOTIV EPOC+ as it has 14-channel electrodes, and the company provides a free SDK to develop Python and Java programs. Our first solution is designed in such a way that it is possible to apply neurofeedback alone, or together with multi-sensory learning. We have received the Ethical Approval to test our solution to healthy subjects at Sabancı University. The PROJ 102 students helped us to conduct experiments. There were 22 participants in the experiment (14 men, eight women). They were aged between 19-20. The IQ mean:131,31 and standard deviation:17,32. The participants' name is not recorded

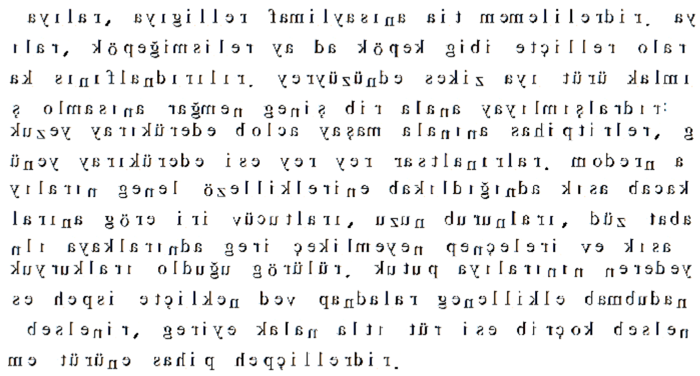

Figure 3.3: "Ayılar" text

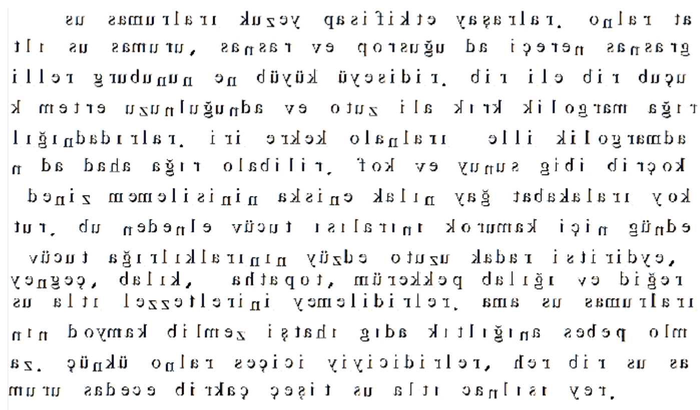

Figure 3.4: "Susamuru" texts

during the experiment. They were given IDs.

- The participant reads a text (either "bears" or "sea otters"). His voice is recorded.
- He does training to learn new letters with MSL or NF-MSL
- The participant reads the other text (either "bears" or "sea otters"). His voice is recorded.

The measurement is done as follows:

- reading errors before (errorbefore)
- number of wpm (oneminuteB)
- reading errors after (errorafter)
- number of wpm (oneminuteA)

- wordsreadonemin = (oneminuteA - errorafter) - (oneminuteB - errorbefore)

The results: Human beings can handle neurofeedback during reading tasks, and this influences their success rate in a better way even for the first time.

Applied T-Test for statistical significance

- NF-MSL is significantly superior ($p < 0{,}001$)
- MSL is significantly superior ($p < 0{,}001$)
- NF-MSL is better than MSL, but $p=0{,}26$(more than 1 session necessary)

*Control group: (read Bears text, then Sea Otters Text afterward without training)

Difficulties faced

- EEG Norm data (thresholds) for different ages were non-existent
- In the literature review, different protocols (reducing theta, reducing theta/ beta ratio, increasing Beta-1, coherence training) were found.
- Needed empirical justification/experiment about what happens in the brain during learning (with EMOTIV) to decide on NF protocols
- Need to do research more on distinguishing good learners from bad learners

3.3 Solution Components

3.3.1 Android Mobile Application

Dyslexic children have a natural tendency to use computers and tablets as they have visual to auditory attention shifting problem. They favor visual sensory inputs over auditory and can not switch between sensory input types very quickly. This makes them addicted to computer games. It is irony to use tablets or mobile phones for the treatment of dyslexia. However, this provides an easy and cost-effective solution which could be applied at home.

Smartphones and tablets are widely used in modern societies; we aimed to create a compact mobile phone application which has neurofeedback and a multi-sensory learning component. Android Developer Studio is a free IDE to write down Java programs which can be executable on Android.

3.3.2 MEAN Stack web server application

Mobile software is coupled with web sites and web applications. Java programs talk to the server-side and pass data to be stored on cloud databases. For our mobile software, it has been decided to use MEAN stack as it is based on JavaScript and easy to build web applications. The MEAN stack has the following components:

- MongoDB, which is a NoSQL database
- Express.js, which is a web application framework that runs on Node.js
- Angular.js or Angular, which is a JavaScript MVC framework that runs in-browser JavaScript engines
- Node.js, which is an execution environment for event-driven server-side and networking applications

3.3.3 HTTP communication & Bluetooth Low Energy

The communication between the mobile Java software and the webserver is accomplished using HTTP communication.

In research laboratories, EEG cap is connected with the computer through wired communication. 32-64 wired cables which connect the electrodes placed on the scalp to the analog amplifier creates an uncomfortable environment for a child to sit still until the neurofeedback session is completed. Our main aim was to create a more comfortable environment for a child to receive neurofeedback sessions. Hence, wireless communication was a good option. EMOTIV PRO+ headset connects with the Java software through Bluetooth Low Energy, which provides a seamless infrastructure for transferring data from headset to mobile software. Wireless communication improves user satisfaction and the adoption of the software. Bluetooth Low Energy does not interfere with brain signals and does not have any side effects on human health.

3.3.4 Wireless communication

There are seamless EEG signals which are coming from EMOTIV PRO+ headset during a neurofeedback session. Our aim was to transfer the EEG signals read from the headset to the cloud database as fast as possible. Mobile phones have either wi-fi or GPRS connection, which enables to store EEG data at the cloud. Wireless communication makes the training more comfortable for a child if compared with neurofeedback sessions at the psychiatrist.

3.3.5 Mongo DB

MongoDB is a database program which is also called noSQL, where it is possible to store a large amount of data. It is a preferred web site database management system nowadays. Mobile phone software uses MongoDB quite well. MongoDB uses JSON format and documents. The system is reliable, and the service provided by mlab.com is free for startups. It provides a cost-effective solution. MongoDB provides high availability and very scalable. It can run on multiple servers, balancing the load, it can duplicate data to keep the system up and to run. Ad hoc queries are possible with a web-based user interface. There is no need for running programs to implement search queries. MapReduce can be used for batch processing of data and aggregate operations.

3.4 Our Solution- Auto Train Brain

Our solution combines neurofeedback (presenting one's brain signals to himself/herself) with multi-sensory learning experience on Android mobile phone and uses EMOTIV EPOC+ in order to read EEG signals. The mobile phone application is developed with Java on Android Studio IDE using Android SDK and EMOTIV Community SDK. It connects with EMOTIV EPOC+ through Bluetooth (BLE) connection. The data is written to MongoDB, which is hosted on mLab (www.mlab.com). The back end server is written with MEAN stack and deployed to AWS.

There is a dev/test and production versions of the software.

Auto Train Brain product functionalities:

- application works with EMOTIV EPOC+ 14 channel electrode system
- communicates with EMOTIV through Bluetooth (BLE)
- logs all brain signals on the mobile phone
- gives neurofeedback which will improve learning skills
- teaches the alphabet to 7-10-year-old children whose learning skills are not well
- provide feedback on progress
- no side or adversary effects

The application

- has been tested on many numbers of people (more than 1500 people) with success.
- is based on many years of research on Brain-Machine Interfaces, neurofeedback, and multi-sensory learning experiences.
- is developed using the MEAN stack.
- is developed with Java on Android 6.0.1.

The Android (Java) Mobile phone application connects with EMOTIV EPOC+ (14 channels) on Bluetooth and enhances learning abilities upon 20-40 sessions of usage. It is the first mobile application in the world which requires no prior knowledge about neurofeedback.

3.4.1 The data model of Auto Train Brain

The data model that has been implemented in Auto Train Brain has 3 tables. The “user” table contains the information about the users of the system.

- id : the unique id of the user
- dateStr : the date on which the record is created

- username : the username
- password : the password of the user
- gender : the gender of the user
- birthDate : the birth date of the user
- maxSession : the maximum session available for the user
- subscriptionEndDate : the subscription end date
- subscriptionStartDate : the subscription start date

The “activity” table contains the information about the neurofeedback activity of the user per channel.

- id : the unique id of the user
- dateStr : the date on which the record is created
- username : the username
- session : the session number of the user
- channel : the channel the data belongs to
- gamma : the gamma frequency band value
- beta2 : the beta2 frequency band value
- beta1 : the beta1 frequency band value
- alpha : the alpha frequency band value
- theta : the theta frequency band value

The “activitySummary” table contains the summarized data about the neurofeedback activity of the user.

- id : the unique id of the user
- dateStr : the date on which the record is created

- username : the username
- session : the session number of the user
- score : total scores collected during neurofeedback session
- avggamma : the average gamma frequency band value
- avgbeta2 : the average beta2 frequency band value
- avgbeta1 : the average beta1 frequency band value
- avgalpha : the average alpha frequency band value
- avgtheta : the average theta frequency band value
- sessionDuration : the duration of the session
- sessionEndDate : the session end date
- sessionStartDate: the session start date

3.4.2 The Android app activities in Auto Train Brain

The Android Mobile phone application contains the following activities.

- LoginActivity : This activity controls the login process of the user with a username and a password.
- MainActivity : This activity controls the neurofeedback session after the login.
- ShowReportActivity : This activity shows the brain waves after each neurofeedback session.

EMOTIV Community SDK is imported and used in the application.

3.4.3 The web client/ server interface of Auto Train Brain

The web interface contains both server and client implementations. The full MEAN stack implementation has been performed. The web interface has viewer-controller-modeller implementation. HTML codes are used for the viewer. The controller part is written with Angular Java Script.

The server api runs on Express framework and Node.js. The java script server api of Auto Train Brain contains the following implementations.

- atbActivity : This server api consists of the java scripts to write data to activity table.
- atbActivitySummary : This server api consists of the java scripts to write data to activitySummary table.
- atbUser : This server api consists of the java scripts to write data to user table.

The java script client api contains the following implementations.

- atbActivityCtrl.js and atbActivityView.html : These are the implementations for the viewer and controller of atbActivity.
- atbActivitySummaryCtrl.js and atbActivitySummaryView.html : These are the implementations for the viewer and controller of atbActivitySummary.
- atbUserCtrl.js and atbUserView.html : These are the implementations for the viewer and controller of atbUser.

Chapter 4

Trainings on Healthy Subjects

In this chapter, we have explained the experiments conducted on the healthy subjects. The first experiment is about predicting who can benefit more from the neurofeedback, the second experiment is about improving reading abilities with multi-sensory learning experience.

4.1 Can we infer who will respond positively to neurofeedback with qEEG?

4.1.1 Introduction

In the literature, neurofeedback has been applied to ADHD successfully, but it is still at "possibly efficacious" state. More than 60 percent of the subjects benefit from it. It is not well known under which conditions neurofeedback positively affects the subjects. In this research, we wanted to investigate whether we can infer who will respond to neurofeedback by looking at EEG patterns.

4.1.2 Materials and Methods

Subject and Experimental data

21 subjects (6 healthy and 15 diagnosed patients) have participated in this experiment. Their ages range from 8(eight) to 81 (eighty one). 8 of them are males, 5 of them are females. ADHD, dyslexia, and autism are developmental brain conditions and they have the same root causes, and are mostly comorbid. The subjects have used AutoTrainBrain many times in order to improve their cognitive abilities.

Throughout the experiments, eMotiv EPOC+ headset is used. Internal sampling rate in the headset is 2048 samples per second per channel, which is downsampled to 128 samples per second per channel.

Study Design

Each participant has used AutoTrainBrain many times. Their EEG is recorded and sent to a database. For all analyses in this study, all of the 14-channel EEG data are recorded during the experiments and decomposed into theta (between 4-8 Hz), alpha (between 8-12 Hz), beta-1 (between 12-16 Hz), beta-2 (between 16-25 Hz), gamma (between 25-45 Hz) bands. The feature set includes the gender, age, and the EEG band power values before neurofeedback from 14 channels.

Measuring performance

Measuring : the difference between the average theta band power measured before neurofeedback and the average theta band power measured after neurofeedback session. Average theta band power means that we read N numbers of theta band powers measured from scalp in a session and sum these numbers and divide by N. average theta band powers = sum(theta band powers read)/ N.

4.1.3 Results

Theta at the left DLPFC, electrode FC5) at resting state infers who will respond to neurofeedback with AutoTrainBrain. The resting state absolute theta brain powers at the left DLPFC before the experiment demonstrated a high Pearson correlation (0.78) with the measure ($P<0.001$). We have checked whether the data has a normal distribution first. The data are normalized by taking logarithm of both independent (Theta, FC5) and dependent variables (measure) and a linear regression model is created (the independent variable is the ln(avgThetaFC5), the dependent variable is the logarithm of the difference of average theta powers before and after neurofeedback. The output of the regression model is compared with the actual data using ANOVA. The result is statistically significant ($P<0.001$). Non-parametric tests are also applied: Two related samples (Wilcoxon test) are applied to pairs (theta,FC5, measure), and the two tailed significance is 0.014. In other words, the higher the amplitude of the theta brain waves measured at the left Dorsolateral Prefrontal Cortex (electrode FC5) at resting state, the more effective AutoTrainBrain for reducing the slow brain waves with neurofeedback. The data are clustered using K-Means algorithm to see who has responded more to neurofeedback and observed that the clusters 2, where theta power at FC5 is greater than 3.60 are the ones who will respond to neurofeedback more. It means 7/21 people respond to neurofeedback significantly more than the others. The clinical and psychometric tests have not been applied to subjects after the experiment. The theta power at the right Dorsolateral Prefrontal Cortex (electrode FC6) during resting state is the second most important area which can be used to predict who will respond more to neurofeedback (Pearson correlation: 0.79, $P<0.001$). The relationship between the measure and the other electrode theta band powers at resting state are not statistically significant. Age and gender do not have high correlation with responding to neurofeedback.

4.2 Improving reading abilities with multi-sensory learning experience

4.2.1 Introduction

Reading, writing, and arithmetic abilities are essential for academic success. University students already passed many exams throughout their school lives by the time they reach university education. However, some of these students. If the WISC-R test shows there is a significant discrepancy between verbal IQ and performance IQ, this may show the specific learning disabilities (SLD); however, there are many specific learning disability cases which cannot be shown by these tests alone [42]. The findings in the article suggest that IQ tests are not particularly useful for determining learning disabilities. Instead, achievement (reading, arithmetic, writing) test scores are more useful diagnostic tools.

They are learning to read starts with learning the phonemes and graphemes [43]. The relation between an alphabet symbol and it is sound should be unique in order to retrieve the information correctly later on when needed during reading. Reading speed is based on how a person quickly retrieves the information about the symbol and its sound(phonics). This reading process involves both short term and long term memory.

Although IQ is normal or above average, 5% of people in many societies may not perform well in reading, writing and arithmetic, and in learning in general [44, 45]. There is a great deal of research about specific learning disabilities in the literature which show that specific learning disabilities are mostly developmental [46–48]. The research conducted in this area suggests abnormal lateralization of prefrontal attentional control processes [49]. This finding is by the (scarce) evidence that reading disabilities involve a deviant structural asymmetry of the frontal lobe [50].

In the literature, it has been further shown that slow brain waves in the Broca's area (F7 and FC5) in the left hemisphere have a high correlation with linguistic learning disabilities [51–56]. These studies have been completed using laboratory EEG equipment with 32 or 64 electrodes. In our study, we measured the EEG signals of subjects with a lightweight EMOTIV EPOC+ headset with 14 electrodes before, during, and after a learning task. Although many researchers are questioning its use for research purposes, several types of research have demonstrated that EMOTIV EPOC+ headset captures the real EEG data [57–59]. In order to collect data from many children, EMOTIV EPOC+ provides a user-friendly and ergonomic interface and can integrate with both desktop and mobile phone applications and be used at home. Shortly, with this new technology, it can be possible to apply neurofeedback to young children at home without disturbing them much and without lowering their self-esteem.

Turkish is an orthographic language, meaning that the words are read as they are written. This feature makes reading easier for many people, yet there are learning disabilities in Turkey. There have been little research [**?**, 60–62] conducted about specific learning disabilities in Turkey, and to our knowledge, there is no research conducted about the Turkish language which correlates learning disabilities with EEG data.

Our research was conducted with University students, who have already passed many difficult exams and been compared with other members of society(children and older adults). They are expected to have more learning abilities due to their age and level of maturity of their brain. If we can correlate their learning abilities with EEG signals, we may do the same for other disadvantaged members of society in a similar way.

4.2.2 Materials and Methods

Subjects and Experimental data

Seventeen University students (mean age: 20.58, standard deviation: 2.39 ; 10 men, 7 women) are volunteered to participate in this study. All subjects' native language was Turkish; they have learned reading without any problem in elementary school. However, they were naive to the alphabet formed with distorted Turkish letters and the computer-based training task. Throughout the experiments, EMOTIV EPOC+ headset is used.

Study Design

Experimental group performed a letter print learning task. The goal of the task was learning the name of new letters, which are distorted 180 degrees in the y-axis (See Figure 3.5). Before the experiments, the EEG signals in the "resting state" are measured for each subject for five minutes, and the data is stored in .csv files. The programs are written with Python and uses the Community SDK provided by EMOTIV to communicate with EMOTIV EPOC+ headset. The EMOTIV standard procedures do artifact removal and conversion from Analog to Digital signal. During the experiments, EEG is recorded, and after the experiment, another five minutes of resting,"eyes open" state EEG signals are recorded.

Graphemes learning task

The task involved showing distorted letters on the screen together with a picture which starts with the letter shown and the phonics of letter (See Figure 3.6). Throughout the experiments, subjects are shown 29 distorted Turkish letters, repeated three times. In each repetition, there are slight differences in the order of pictures and sounds which are shown on the screen. In the first round, the picture and sound are shown at the same time, in the second round, the picture is shown one second before the sound, in the third round, the picture is shown one second after the sound.

Measuring performance of reading speed and number of errors

Before the experiments, subjects are asked to read A text written with distorted letters, and the voice is recorded (See Figure 3.5). The following measures are calculated:

- The number of wpm (pre-training)
- The number of errors done (pre-training)

After the experiments, subjects also read another text written with distorted letters, and the voice is recorded.

- The number of wpm (post-training)
- The number of errors done (post-training)

The final performance score is calculated by taking the difference between the post-training performance and the pre-training performance.

Relation of Resting-state the Broca Area: Resting-state absolute value of theta brain waves have a high correlation with the level of letter print learning performance.

The analysis of data is done with SPSS, and a linear regression model is created. The independent variable is the average of theta absolute powers at F7 and FC5; the dependent variable is the difference between the correctly read words in one-minute after-training and that before training. The output of the regression model is compared with the actual data using ANOVA.

The sample size for the experiment is calculated by using this formula $n = (Z_{\alpha/2}\sigma/E)^2$ where Z-score is taken as 1.96 for 95% confidence interval, the standard deviation of theta is 0.68 and E=0.1 and the calculated sample size is 8.35.

4.2.3 Results

The resting-state absolute theta brain powers at the Broca area (F7 and FC5) demonstrated a high correlation (0.66) with the measured learning performance ($P<0.05$). We created a linear regression model with the independent variable of the average of absolute theta brain powers at F7 and FC5 and the dependent variable of a learning performance measure which can be decided as the difference between the number of wpm after training and the number of wpm before training.

In other words, the slower the brain waves measured in the Broca area (F7 and FC5) at a resting state in the brain, the less useful the computer-based training of distorted letters is for learning performance.

In this study, we investigated the correlation of the resting-state theta band powers at the Broca area EEG activity with the measured learning performance. We created distorted new letters for the healthy subjects to learn using a computer-based multi-sensory application. We measured the resting-state brain powers with EMOTIV EPOC+ before the experiment (5 mins), during the experiment and after the experiment (5 mins). Some of the subjects showed that learning performance increases throughout the task, while others did not show any increase. We checked for the presence of a correlation of a learning performance with any of the brain powers measured before, during, and after the experiment. Based on this, we noticed that the resting state theta band powers at the Broca area have a high correlation with learning performance. We then created a linear regression model, and the output of this regression model was compared with the actual data using ANOVA. The result is statistically significant ($P<0.05$).

We conclude that, shortly, it will be possible to apply neurofeedback with EMOTIV EPOC+ headset to increase the reading abilities of the children at home. Shortly, the outcome of this research will be used to decide on which band powers and which electrodes to train with neurofeedback to increase the reading abilities of Turkish speaking children with EMOTIV EPOC+ at home.

Some of the participants who did not perform well in the experiment were already very good readers of distorted text before training. That means the training influenced their rapid automatic naming of letters in the wrong way, and it created ambiguity for some participants. Whether the children with specific learning disabilities have the same ambiguity in rapid automatic naming of letters would seem to be a logical area for further research.

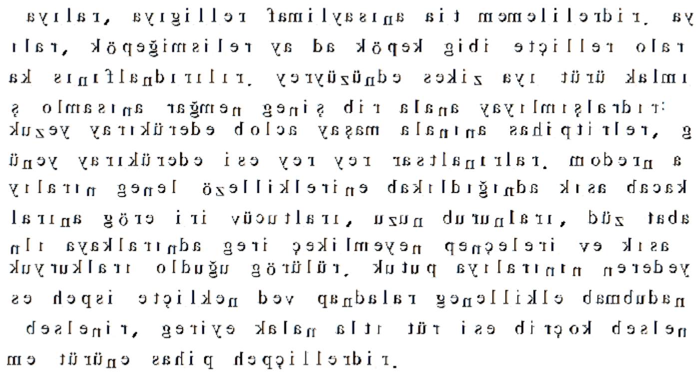

Figure 4.1: The text written with distorted Turkish letters

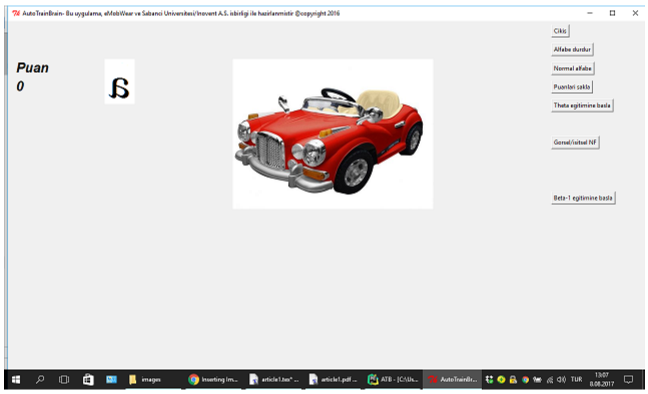

Figure 4.2: The computer based training program to teach distorted letters

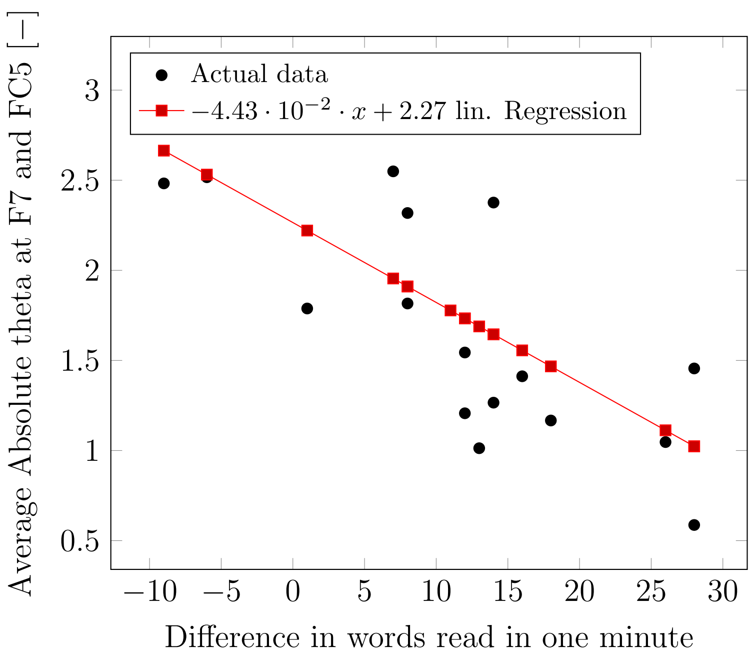

Table 4.1: Learning performance measures

ID	Age	Sex	error pre-training	error post training	Oneminute-pre	Oneminute-post	Words read one minute
307	19	Erkek	3	1	14	40	28
304	19	Kadin	3	2	49	75	28
5000	20	Erkek	4	1	42	65	26
5005	18	Kadın	7	1	18	31	18
5002	20	Kadın	6	5	31	46	16
302	22	Kadın	4	2	24	36	14
5006	20	Erkek	0	2	0	16	14
5004	19	Erkek	4	2	25	36	13
2002	20	Erkek	4	1	31	40	12
5009	20	Erkek	3	0	31	40	12
5001	20	Kadın	7	5	42	51	11
308	18	Erkek	0	0	30	38	8
303	27	Kadin	3	2	49	56	8
5003	20	Erkek	3	3	45	52	7
2001	25	Erkek	1	3	37	40	1
306	20	Erkek	1	0	50	43	-6
301	23	Kadın	2	2	43	32	-9

Table 4.2: Theta at Broca area

ID	Words read in one minute	Avg theta (F7)	Avg theta(FC5)	Average of theta at F7 and FC5
307	28	1,346621	1,564475	1,455548
304	28	0,821042	0,352808	0,586925
5000	26	1,233911	0,860058	1,0469845
5005	18	0,75083	1,582611	1,1667205
5002	16	2,077955	0,746231	1,412093
302	14	0,440884	2,090648	1,265766
5006	14	2,873486	1,878642	2,376064
5004	13	1,463205	0,562709	1,012957
2002	12	1,038742	1,374948	1,206845
5009	12	2,15392	0,934102	1,544011
5001	11	3,144928	2,957646	3,051287
308	8	1,571115	2,060929	1,816022
303	8	2,549321	2,086834	2,3180775
5003	7	3,630647	1,467857	2,549252
2001	1	0,915747	2,660747	1,788247
306	-6	3,537321	1,495707	2,516514
301	-9	2,6577	2,307136	2,482418

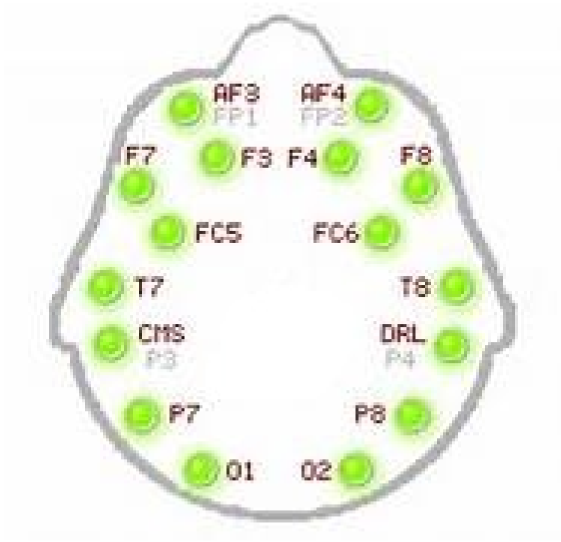

Figure 4.3: The 10-20 numbering system of EMOTIV EPOC electrodes

Chapter 5

Changes in Complexity of People with Dyslexia

In this chapter, we have explained in detail how Auto Train Brain app has improved the entropy and the coherence of a 14-year-old dyslexic boy. Then, we have explained that we have measured the multi-scale entropy of children with dyslexia (7-10 years old) and compared that with age-matched typically developing norm group. We have applied neurofeedback with multi-sensory learning to children with dyslexia and reported the changes in multi-scale entropy.

5.1 Improving entropy and coherence with 14-channel neurofeedback system

After we have proven that EMOTIV EPOC+ measures the correct EEG data and slow brain waves in Broca area determines the ability in reading, we have decided to rewrite the algorithm in Android Java to have a mobile application which is more user friendly for children.

We have improved our algorithm by rewriting it on the Android Mobile Platform, and we have revised the neurofeedback algorithm. We have categorized the 14 electrode channels into the right and left the brain and applied neurofeedback on either left or right brain. We aim to reduce theta, and we reward the subject when he reduces the maximum theta, which can be found on either left or right hemisphere. We always aim to reduce the slow brain waves at the channel where we find the maximum theta each time. This will ensure the maximization of the effectiveness of neurofeedback.

Also, we have decided to separate the sessions of neurofeedback from multi-sensory learning, although we have reached the positive results in the first experiment. Because theta increases in reading-intensive tasks at the frontal lobes if the workload is high, which shows the usage and formation of working memory. Therefore, it may not always be feasible to reduce theta during a semantic learning task. Instead, we first apply neurofeedback in a 10-20 min session, and then we teach the alphabet to the child.

We have decided to test the 14-channel newly proposed neurofeedback protocol on a child with dyslexia. Before the neurofeedback session, we have recorded the raw EEG data, conducted neurofeedback on both left and right hemisphere for 20 mins in total moreover then recorded the raw EEG data after neurofeedback and compared the results.

AutoTrainBrain is a patented software application specially designed for children with dyslexia. According to the solution, a system and method for improving reading ability and cognitive functions is proposed, the system relying on a distinctive protocol of multi-sensory learning and EEG biofeedback. The EEG biofeedback protocol is specially designed for learning disabilities, and the EEG biofeedback system integrated with multisensory learning provides a powerful and robust tool for improving reading ability. The EEG biofeedback system is easily usable and does not require theoretical knowledge (Figure 5.1 and Figure 5.2).

Figure 5.1: The usage of AutoTrainBrain

A single user software module/application on a Mobile phone for improving reading ability and cognitive functions, in general, is provided. Before the training or concurrently with the training, EEG signals are read from a sufficient number of electrodes (1-14). If this software is used a sufficient number of times, the user's reading speed is increased, and the error rate during reading is reduced, moreover,

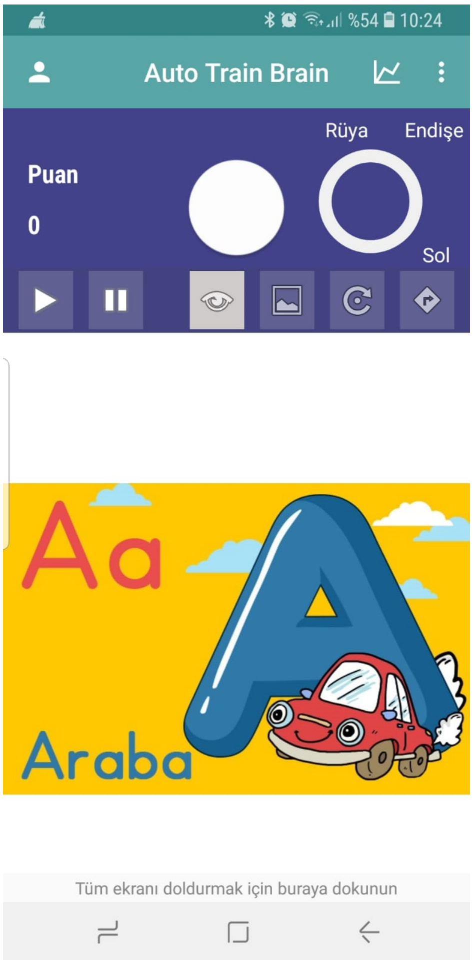

Figure 5.2: AutoTrainBrain Software User Interface

the cognitive functions are improved. The software contains norm data collected from healthy people. This data is used for determining thresholds during neurofeedback to eliminate the side effects.

5.1.1 Materials and Methods

Subject and Experimental data

A child with dyslexia at the age of 14 is participated in this study. Throughout the experiments, EMOTIV EPOC+ headset is used.

Study Design

The main goal of the experiment is to reduce the theta band power. Before the experiment, the raw EEG signals in the resting state are measured using EMOTIV PRO software, and the data is stored in .edf files. During the neurofeedback session, EEG data is recorded, and after the experiment, another two minutes of resting state raw EEG signals are recorded using EMOTIV PRO software. AutoTrainBrain software is written with Android Java and uses the Community SDK provided by EMOTIV to communicate with EMOTIV EPOC+ headset. The EMOTIV standard procedures do artifact removal and conversion from Analog to Digital signal.

Raw EEG Data Analysis

The analysis is conducted by comparing the before neurofeedback raw EEG resting state, eyes closed recordings with that of the after neurofeedback session and those of the across sessions. The .edf data is filtered by using a bandPass FIR filter (1-50Hz). The artifacts are removed manually by using EEGLAB's data rejection options. The raw EEG signals collected from each electrode channel are segmented into 2-second sliding windows. For each 2-second EEG segment, the spectral entropy and related Alpha Band (8-13 Hz) Absolute Power are calculated. As seen in Figure 5.3, 60 short segments are constructed for 2- minute recorded session, and the statistics are plotted as an error bar graph. For power spectral density calculations, Burg method is applied, and the AR model rate is calculated with ARfit algorithm.

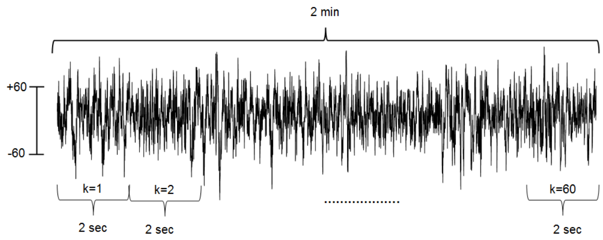

Figure 5.3: The raw EEG data segmentation

5.1.2 Results

- If we compare the entropy (based on Burg method) calculated with EEG recordings before the first neurofeedback session with that after the first neurofeedback session, there are entropy increases in almost all channels (Figure 5.4).

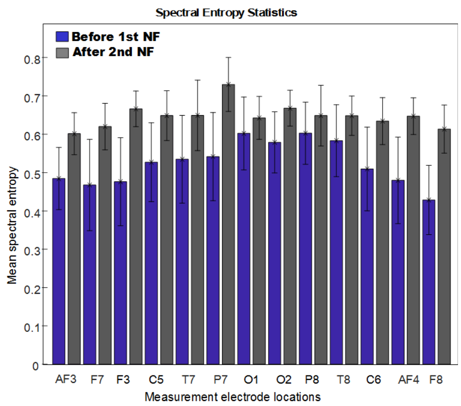

Figure 5.4: Spectral entropy based on Burg Method (Session 1)

- After the 9th neurofeedback session, the entropy/complexity increase compared with that at the first neurofeedback session is retained. In the 9th session, the difference between entropy/complexity increase before and after the neurofeedback is lowered. It means the cognitive improvement is permanent (Figure 5.5).

- If we compare the Alpha Band Power (8-13 Hz) over total EEG (0-30 Hz)(Alpha Band Relative Power) calculated with EEG recordings before the first neurofeedback session with that after the first neurofeedback session, Alpha Band Relative Power is increased in almost all channels (Figure 5.6).

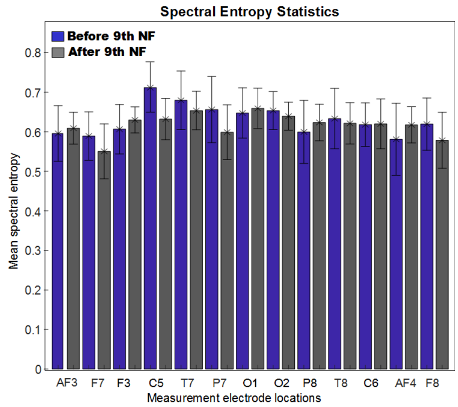

Figure 5.5: Spectral entropy based on Burg Method (Session 9)

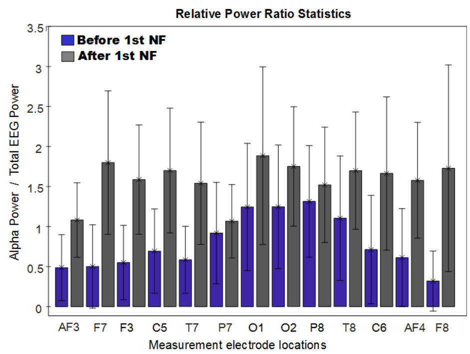

Figure 5.6: Single channel Alpha Relative Power increase (Session 1)

After the 9th neurofeedback session, the increase in Alpha Band Relative Power compared with that at the first neurofeedback session is retained. In the 9th session, the increase in Alpha Band Relative Power before and after neurofeedback is lowered. It means the cognitive improvement is permanent (Figure 5.7).

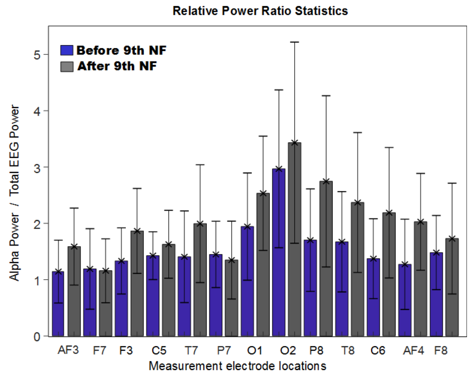

Figure 5.7: Single channel Alpha Relative Power increase (Session 9)

- If we compare the coherence calculated with EEG recordings before the first neurofeedback session with that after the first neurofeedback session, there are coherence increases in almost all channels (Figure 5.8).

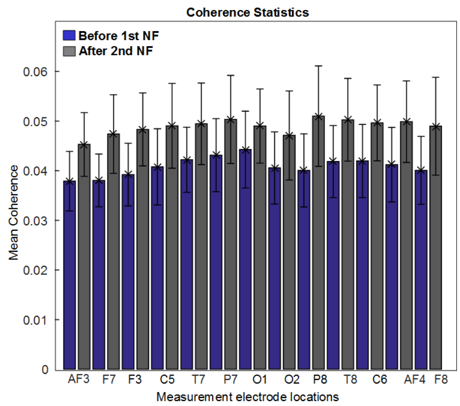

Figure 5.8: Increase in coherence (Session 1)

After the 9th neurofeedback sessions, the increase in coherence compared with that at the first neurofeedback session is retained. In the 9th session, the increase in coherence before and after neurofeedback is lowered. It means the cognitive improvement is permanent (Figure 5.9).

- The increase in both entropy/ complexity, coherence and Alpha Band Relative

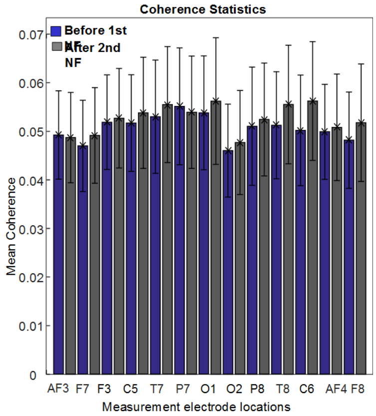

Figure 5.9: Increase in Coherence (Session 9)

Power show that the active neurons in the cortex are increased with neurofeedback and this increase is recorded more in the right hemisphere. Before the neurofeedback session and after the neurofeedback session, the performance increase is determined in the frontal lobes, which are mainly responsible for organization, managerial, and motor functions. Other performance increases are also found in Occipital and Parietal regions.

5.2 Changes in complexity due to Auto Train Brain in people with dyslexia: A multi-scale entropy analysis

We aimed to investigate the complexity of EEG signals across multiple time scales in people with dyslexia and the positive effects of special neurofeedback and multi-sensory learning treatment, namely Auto Train Brain. We investigated the resting state "eyes closed" EEG, using MSE in children with dyslexia during pre- and post-treatment with Auto Train Brain. We then compared the results of the experimental group with those of typically developing (TD) children of the age-matched group. Our hypotheses are as follows:

1. The complexity of EEG signals in people with dyslexia is lower than that of typically developing children.

2. Neurofeedback and multi-sensory learning improve the complexity in people

with dyslexia.

Nonlinear EEG analyses has been used to diagnose brain disorders. Abnormal neural connectivity can be tracked as abnormal complexity in EEG analyses [63]. Sample entropy is a refinement of the approximate entropy introduced by Pincus [64–66]. Recently Costa [67] introduced multiscale entropy, which is an extension of sample entropy to multiple time scales. In [68], the authors have demonstrated that autism also has aberrant neuronal connectivity, which is reflected as high or low complexity [69, 70]. In [71], applying multiscale entropy methodology, it was shown that for Alzheimer's disease, although the entropy values are similar for lower temporal scales, they are higher than those of healthy controls at higher temporal scales. MSE estimations demonstrate the underlying pathology. The higher complexity at higher temporal scales in MSE indicates that there is a greater number of slow signals (theta and delta) measured, which is the marker for neurodegeneration as in Alzheimer's disease. Although the study in [72] compares the AppEn of people with dyslexia with that of typically developing norm group, there are no studies which investigate temporal complexitys in dyslexia. It is known that dyslexics' entropy is lower than non-dyslexics meaning that higher long-range connectivity than the TD norm group should be expected.

Auto Train Brain is a patented software specifically designed for dyslexic children [13–15]. Within this software application, a system and method for improving reading ability and cognitive functions is proposed.

In the present study, our contribution is to investigate the complexity of EEG signals in people with dyslexia and the positive effects of the Auto Train Brain treatment. We investigated resting state "eyes closed" EEG, an activity using MSE in people with dyslexia pre- and post-treatment with Auto Train Brain, and compared the results with those of healthy children of the same age group.

5.2.1 Materials and Methods

Participants

16 children with dyslexia (Mage=8.56, SD=1.36) and 20 typically developing (TD) healthy children (Mage=8.55, SD=1.45) voluntarily participated in this study

(Table 5.1). The participants were recruited with advertisements randomly. The child neurologist physically examined the participants and approved their participation in the experiment. The experimental group met DSM-V criteria for dyslexia, as assessed by psychologists and psychiatrists beforehand. The experimental group consisted of randomly picked, 7-10-year-old children with dyslexia, who were patients seen in Ankara University the Faculty of Medicine. In the experimental group, there were comorbid situations such as EEG anomalies, ADHD disorder, and giftedness. The socio-economic situation of the experimental group was low to the middle class; they were residents of Ankara. The socio-economic situation was measured with a survey which includes questions about education level, income, occupation, and residence.

The control group (TD norm group) consisted of randomly chosen age-matched healthy children who didn't have any known diseases and didn't have any reading or writing problems. The control group resided in Izmir; the socio-economic situation of the control group was low to the middle class.

As Auto Train Brain training system will be available and be used for all types of dyslexia at home without any provision, we haven't set any inclusion/exclusion criteria except being officially diagnosed with dyslexia for the experimental group.

Neurofeedback treatment protocol and multi-sensory learning method

Auto Train Brain is a mobile application that uses neurofeedback and multi-sensory learning principles. It is used with the EMOTIV EPOC+ headset. It is a non-invasive solution, offers continuous brain performance improvement for both adults and children without any side-effects. It reads QEEG from 14 channels, processes these signals, and provides real-time visual and auditory, online neurofeedback. Auto Train Brain is a patented software (patent number: PCT/TR2017/050572) specifically designed for people with dyslexia. Within this software application, a system and method for improving reading ability and cognitive functions is proposed. The system relies on a distinctive protocol of multi-sensory learning and EEG neurofeedback. The EEG neurofeedback protocol is explained below:

1. Reduce theta waves at Broca area in the brain if above the threshold;

2. Reduce theta waves at Wernicke area in the brain if above the threshold;
3. Find the channels with the maximum absolute power of theta waves at the left hemisphere and reduce absolute theta for those channels; and
4. Find the channels with the maximum absolute power of theta waves at the right hemisphere and reduce absolute theta for those channels.

The EEG neurofeedback system integrated with multi-sensory learning (visual and auditory) provides a powerful and robust tool for improving reading ability. The EEG neurofeedback system is easy to use and does not require technical expertise. A positive reward is a green arrow on the screen, negative feedback is a red arrow and a "beep" sound. With a positive reward, the score displayed on the screen is increased. If the slow brain waves of the subject are above the norm threshold, a red arrow is presented on the screen and the subject is asked to try to turn it to a green arrow. After the neurofeedback session, a phoneme-grapheme matching alphabet teaching system is presented. One of the significant differences between the currently available neurofeedback systems and Auto Train Brain is that it combines neurofeedback with multi-sensory learning principles.

Reading speed

The reading speed of the children was measured by recording the number of wpm when they read different pages from an age-matched children's book. In normal children, Words Correct Per Minute increases from an average of 51 words per minute at the beginning of second grade to 71 words per minute at the beginning of third grade [73]. Lower reading speed compared with the age-matched norm group may be a sign of learning disability.

Study Design, Behavioral Assessments, and Training Sessions

The experimental group with their parents commuted to the Ankara University Faculty of Medicine 3 times a week. In the first interview, all participants filled out questionnaires, and a psychologist applied the 1.5-hour TILLS test to the subjects. Before the first session, the EEG of the subjects was recorded with EMOTIV PRO software for 2 minutes during resting state. The reading speed of the dyslexic children was measured. The subjects were asked to read an age-appropriate book for 1 minute and their voices were recorded.

The participants came to the sessions with their parents, while the parents were waiting in the waiting room, only the participant was taken to the room. There were 0.5 meters between the participant and the mobile phone screen. The psychologist just stayed with the participant to make sure he/ she was using the mobile app correctly, but no guidance or encouragement was provided. There was no one else in the room and the door of the room was closed. There was a distance of 1 meter between the psychologist and the participant. The psychologist in the room was neutral to the participant, not friendly or empathetic. In the first session, the participant was told to focus on the arrow he saw on the application screen and, if he/she saw a red arrow, he/she was asked to try to turn it to green with brainpower. No additional information about the experimental procedure was provided to the participant.

Before the 10th session, the child neurologist examined the children and checked for any side effects. All participants were given 60 sessions of neurofeedback training during 12 consecutive weeks. A standard neurofeedback protocol for reducing slow brain waves was applied to the experimental group for 10 minutes in the left brain and 10 minutes in the right brain. After neurofeedback, the participants received 10-minute multi-sensory learning of the alphabet with Auto Train Brain. The participants who completed the 60th session, were told that the experiment was completed. An appointment was made for the 2nd TILLS test exactly 6 months after the first TILLS test. At the end of the sixth month, the TILLS test was performed again. A 1-minute reading test was applied and the voice of the participant was recorded. The eyes closed resting-state EEG was taken for 2 minutes.

Since the children in the control group were healthy, the TILLS test which measures the learning disability was not performed, reading speed was not measured and only one EEG measurement (eyes closed resting-state for 2 minutes) was taken within the framework of our Ethics Committee approval. EEG changes in healthy children over time was not observed in our experiment. However, multiscale entropy changes by age for healthy children was investigated in [74].

Raw EEG data processing and multiscale entropy calculations

At the start and the end of the full training period, we measured eyes closed resting-state raw EEG data for 2 minutes with the EMOTIV PRO software. Eyes closed resting-state gives the necessary information about the brain's developmental issues for dyslexia [75]. The collected raw EEG data from 14 channels were processed using Matlab and EEGLAB.The artifacts were manually removed by using EEGLAB's data rejection options. Further, the independent component analysis was performed. MSE was calculated for 60-s epoch for each group EEG data. The number of samples (N) was set to N = 128*60 = 7680. SampEn parameters were set to m=2 and r=0.25*standard deviation of the EEG signal [63]. As in this study, we have created 40 temporal scales to analyze complexity[67].

MSE method describes the degree of complexity in a time series at 40 temporal scales [67]. Irregularity is measured by SampEn. SampEn is the negative of the logarithmic conditional probability that two sequences of m consecutive data points which are similar to each other will remain similar at the next point $(m+1)$ in the dataset (N). Considering the EEG time series $(x_1, x_1, ...x_N)$ as observations of a variable x, dynamic SampEn is defined as $h_{samp}(r, m, N) = log_e[C_{m+1}(r)/C_m(r)]$,where C_m(r)={number of pairs (i,j) with $|x_i^m - x_j^m| < r$, i $\neq$ j}/{number of all probable pairs, i.e.,$(N-m+1)(N-m)$}. Here, x^m is a vector of m sample time series of (N-m) length, and $|x_i^m - x_j^m|$ denotes the distance between x_i^m and x_j^m in the space of m, and r is the filter for measuring consistency.

We first embedded the time series into an m dimensional space as a vector $x_i^m = \{x_i, x_{i+1}, ..., x_{i+m-1}\}$ and counted the points that stay around x_i^m within distance r. Then, we summed up all counts to produce the numerator of $C_m(r)$, a measure of correlation by its definition. -$\log_e[C_m(r)]$ is the information content, and the difference in information content for vectors of length m and m+1, $h_{samp}(r, m, N) = (-log_e[C_m(r)]) - (-log_e[C_{m+1}(r)]$, defines the rate of information content loss.

For the extension to 40 time scales, the original EEG time series $(x_1, x_1, ...x_N)$ was coarse grained by a scale factor(SF) τ, with non-overlapping windows as follows:

$y_j^{(\tau)} = (1/\tau)\Sigma_{i=(j-1)\tau+1}^{j\tau} x_i, 1 \leq j \leq N/\tau$

Then, the SampEn was calculated for each series $y^{(\tau)}$. For the coarse-grained time series at SF, τ =1, the time series $y^{(1)}$ was identical to the original time series [63].

Statistical analysis

For the experimental group, multiscale entropy of the raw EEG data (14 channels, pre- and post-), the overall TILLS test descriptive points (pre- and post-), reading speed (pre- and post-), and band power values (pre- and post-) were calculated and compared.

For the control group, multiscale entropy of the raw EEG data (14 channels, one time only) were calculated.

SampEn values at each temporal scale factor log-transformed to approximate a normal distribution. The alpha significance level was 0.05. Greenhouse-Geisser adjustment was applied to the degrees of freedom for all the statistical analyses of this research.

For MSE analyses, independent t-tests were performed to assess the significant main effect for group and group-by-SF-interaction between the TD norm group and the experimental group (i.e., pre- and post-treatment). Additionally, repeated measures analysis of variance, with treatment (dyslexia: pre-treatment vs. post-treatment) and SF (40 scales). By comparing the data from Session 1 of the experimental group and the TD norm group, we aimed to find the differences within the experimental group before treatment; by comparing the data from Session 60 and Session 1 of the experimental group, we aimed to find the treatment effects within the experimental group; and by comparing the data from Session 60 of the experimental group and the TD norm group, we aimed to find the differences within the experimental group after treatment.

We have checked the normality of data for reading speed (skewness = -1.167, kurtosis = 1.351) and the TILLS test results (skewness = 0.439, kurtosis = -0.399). Based on these findings, we haven't assumed a normal distribution. Reading speed were analyzed with a Wilcoxon Signed-Ranks Test, which is a non-parametric test and does not assume a normal distribution.

We also performed band power analysis. The open eye resting-state within a 2-minute frequency band data was recorded with Auto Train Brain before and after treatment. Repeated measures analysis of variance, with treatment (dyslexia: pre-treatment vs. post-treatment) and the frequency band data both in absolute powers and relative powers as within-subject factors were used to assess the effect of Auto Train Brain training.

Lastly, associations between changes in the TILLS test results, changes in the number of wpm, and changes in complexity were explored using correlation analysis.

Comparison of MSE between the experimental and the TD norm group

MSE at SF1 of the TD norm group ranged from 0.48 to 1.79 (M = 1.51, SD = 0.33). The near-horizontal curve from SF1 to SF40 indicated that this group had more slow waves than fast waves as expected in TD children. In the experimental group, MSE at SF1 ranged from 1.04 to 1.76 (M = 1.41, SD = 0.22). Before treatment, the experimental group's mean complexity was lower than that of the TD norm group, especially at SF1, t (496.836) = 5.793, p<.001, d=0.47 and between SF12, t (445.831) = 2.228, p =.026, d=0.22 and SF36, t (396.752) = 4.962, p<.001, d=0.54 (Figure 5.10, Table 5.2).

Further, the treatment with Auto Train Brain significantly increased the complexity in all channel locations that exceeded that of the TD norm group between SF2, t (539.568) = -2.055, p =.040, d= 0.20 and SF10, t (435.575) = -2.889, p =.004, d=0.34. Only the complexity between SF32, t (516.654) = 4.108, p<.001, d=0.30 and SF36, t (519.423) = 2.217, p =.027, d=0.15 remained dissimilar (Figure 1, Table 2). The complexity at lower temporal scales of the experimental group exceeded that of the TD norm group, and the complexity of the experimental group became similar at medium to higher temporal scales to that of the TD norm group after treatment in all channel locations (Figure 5.10).

Pre- vs. post-treatment MSE changes in the experimental group

Applying Auto Train Brain from 14 channels created complexity improvements for the experimental group at all temporal scales except SF38 and SF40 in all channel locations (Table 5.1, Figure 5.11). There was a significant effect of time on children with dyslexia; for SF1, Wilks' Lambda = .785, F (1, 220) = 60.391, p<.001, Eta=0.78. Table 5.1 summarizes MSE repeated measures analysis of variance results for pre- and post-treatment of the experimental group.

The primary outcome of the experiment was the comparison of MSE between the experimental group and the TD norm group, and the analysis of MSE changes in the experimental group after neurofeedback and multi-sensory learning. The rest of the results presented below were secondary.

Reading speed, the TILLS test results, band power changes in the experimental group

A Wilcoxon Signed-Ranks Test showed that the post-test scores in reading speed (Mdn = 64) were significantly higher than the pre-test scores in reading speed (Mdn = 44), Z= 3.41, $p<.001$, r =.85. A Wilcoxon Signed-Ranks Test showed that the post-test TILLS scores (Mdn = 23) were not significantly higher than the pre-test TILLS scores (Mdn = 18), Z= 1.94, $p<.052$, r=.48.

To alleviate the effects of comorbidity in our analysis, data from the 8 participants without any comorbidity were analyzed with a Wilcoxon Signed-Ranks test. The test showed that the post-test reading speed scores of the experimental group without any comorbidity (Mdn = 69) were significantly higher than the pre-test scores of the same experimental group (Mdn = 47), Z= 2.37, $p<.018$, r= .84. Similarly, a Wilcoxon Signed-Ranks Test showed that the post-test TILLS scores of the experimental group without any comorbidity (Mdn = 23) were significantly higher than the pre-test TILLS scores of the same experimental group (Mdn = 15), Z= 2.25, $p<.024$, r = .80. The effect size in the TILLS test results for pure dyslexia (r=.80) was higher than that for dyslexia with comorbid situations (r= .48).

Absolute band power values were reduced by each neurofeedback session, and the intermediate results were not included. The short-term neurofeedback effects were temporary; after 60 sessions, there were no significant changes between pre- and post-treatment in either absolute band power values (theta, alpha, beta1, beta2, gamma) or relative band power values (relative theta, relative alpha, relative beta1, relative beta2, relative gamma) for the experimental group. Although it was not found to be statistically significant, relative gamma values tended to be reduced at electrode T8 location and increased at electrode T7 location, positioned over the temporal lobe (Figure 5.12).

5.2.2 Discussion

In this study, we reported the first research of complexity calculated through MSE from the EEG of children with dyslexia. The main finding of this study, MSE of the children with dyslexia had significantly lower complexity over medium to high temporal scales compared to that of the TD norm group, supported our hypothesis.

Long-distance dynamic temporal complexity is reflected as high or low complexity at higher temporal scales in MSE. Lower complexity at higher temporal scales means that there is less difference between the brain's two hemispheres. This situation indicates that children with dyslexia use both hemispheres equally, whereas, in the TD norm group, the left-brain dominance was already established.

The complexity at lower temporal scales in MSE was heterogeneous for the experimental group. Some participants in the experimental group had less complexity at lower temporal scales than that of the TD norm group, and some had more. This situation might indicate that children with dyslexia may have minicolumnopathies. Inflammation is also known to increase complexity at lower temporal scales meaning gamma brain waves [76]. In general, ASD and dyslexia have opposite characteristics which were described in [21], but MSE of children with dyslexia resembles that of children with atypical ASD, as described in [68].

One of our hypotheses was that the complexity of the experimental group would be improved with training. Indeed, after 60 sessions of Auto Train Brain training, the complexity of the experimental group improved and became similar to that of the TD norm group. As we have only measured the complexity of the TD norm group once at the beginning of the experiment and we have not measured the maturation effect, we investigated previously published research to predict the maturation-related changes in a TD norm group in 6 months. Other research reported that healthy children who are 8-10 years old improve MSE at SF1 (lower temporal scales) approximately by 0.02 in 6 months, whereas MSE at higher temporal scales decreases slightly [74]. After including the maturation effect of the TD norm group, we can deduce that MSE of the experimental group improved up to the level of MSE of the TD norm group both in lower and medium temporal scales in 6 months. In our experiments, we have not observed any adverse side effects on the experimental group. Auto Train Brain system as a whole provided safe neurofeedback for 7-10-year old children in our study.

This study implies that reducing slow brain waves with Auto Train Brain also tends to reduce fast waves which are recorded above normal. This may be due to the relaxing effect of neurofeedback. However, this requires further investigation. Previous research demonstrated that people with dyslexia benefit from neurofeedback applications. In [35], they applied neurofeedback protocols to people with dyslexia to decrease delta and theta at Cz, to increase beta-1 at T3, and to decrease coherence at delta and theta range. Their research showed at least two levels of increase in reading levels. In [38], they applied neurofeedback protocols to people with dyslexia to decrease delta and theta at T3 and F7, as well as to increase beta-1 at T3 and F7. They reported no significant changes in band powers, but hyper-coherence in theta and delta bands. Reading times and reading mistakes were reduced due to the treatment. Follow up assessments showed that reading improvements were sustained. Applying neurofeedback to dyslexia (delta down at T3-T4, beta down at F7 and C3, coherence training in the delta, alpha and beta ranges) was shown useful for spelling but not reading in [37], although other previous studies reported increases in raising reading grade levels [77]. In [11], they performed coherence neurofeedback on the participants with dyslexia: the most common hypo-coherence was the occipito-parietal lobes to the frontal-temporal lobes. The second most common hypo-coherence was the parietal to medial-temporal connections. Hypo-coherence has been reported on the delta, theta, and alpha bands. Trained with coherence neurofeedback, the reading performances of people with dyslexia improved. Our research differs from previous research because we have applied 14-channel neurofeedback and measured the improvements in training by complexity calculations through MSE.

The recent findings confirm the findings of the previous NF studies under strict control and randomized conditions [78–85]. Notwithstanding, the above-mentioned studies have reported success in training subjects to manipulate activity in specific, targeted brain regions, and such training has been shown to enable changes in behavioral measures or clinical symptoms. Our research was different from the studies mentioned above since our control group consisted of healthy children. Our future work will include a control group of children with dyslexia.

In another study that combines NF protocol with game-based cognitive training, neurofeedback was applied to 31 dyslexic children and it has been reported that both intelligence and attention improved [82]. In our study, we combined a neurofeedback protocol with multi-sensory learning. Our goal was to make the training robust and more effective. While our study assesses the overall impact of the Auto Train Brain training system, which includes a novel neurofeedback protocol and multi-sensory learning, it would be of definite interest to assess the impacts of the neurofeedback protocol and multi-sensory learning components separately.

5.2.3 Limitations of the study

The first limitation of the study is the number of participants.

The second limitation of the study is the existence of comorbid situations such as EEG anomalies, ADHD, giftedness, and CP in the experimental group. In this study, we have observed that for children with dyslexia who had comorbid brain situations such as EEG anomalies and giftedness, the positive effect of Auto Train Brain is limited. The existence of comorbidity in the experimental group also affected our statistical analysis. To overcome the comorbidity effects, we have not assumed normal distributions, log-transformed the entropy calculations, and used non-parametric tests. Furthermore, we repeated the statistical analysis with the subset of the participants who had pure dyslexia. Having comorbid situations in our experimental group, however, helped to understand to which subsets of dyslexia with comorbid situations Auto Train Brain training should be targeted.

The third limitation of the study is the possibility of placebo effects. As described by [86], children that are given one-on-one interactions and specialized interventions may improve their functioning based solely on the social and environmental impact of those interventions. Because no alternative intervention for the control group was provided, placebo effects may represent a significant source of improvement in the experimental group.

The fourth limitation of the study is maturation effects. All children have significant brain changes throughout the developmental period. Therefore, maturation is likely to have some impact on MSE changes over 6 months (duration between the pre- and post- EEG measurements in this study).

We conclude that children with dyslexia have lower complexity compared with that of the TD norm group and Auto Train Brain training improves the complexity in 60 sessions of usage.

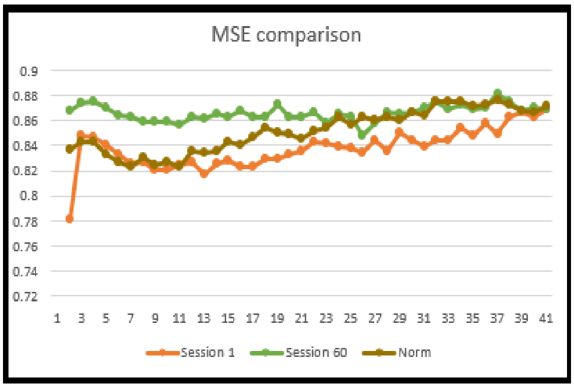

Figure 5.10: MSE Pre- and post- training analysis

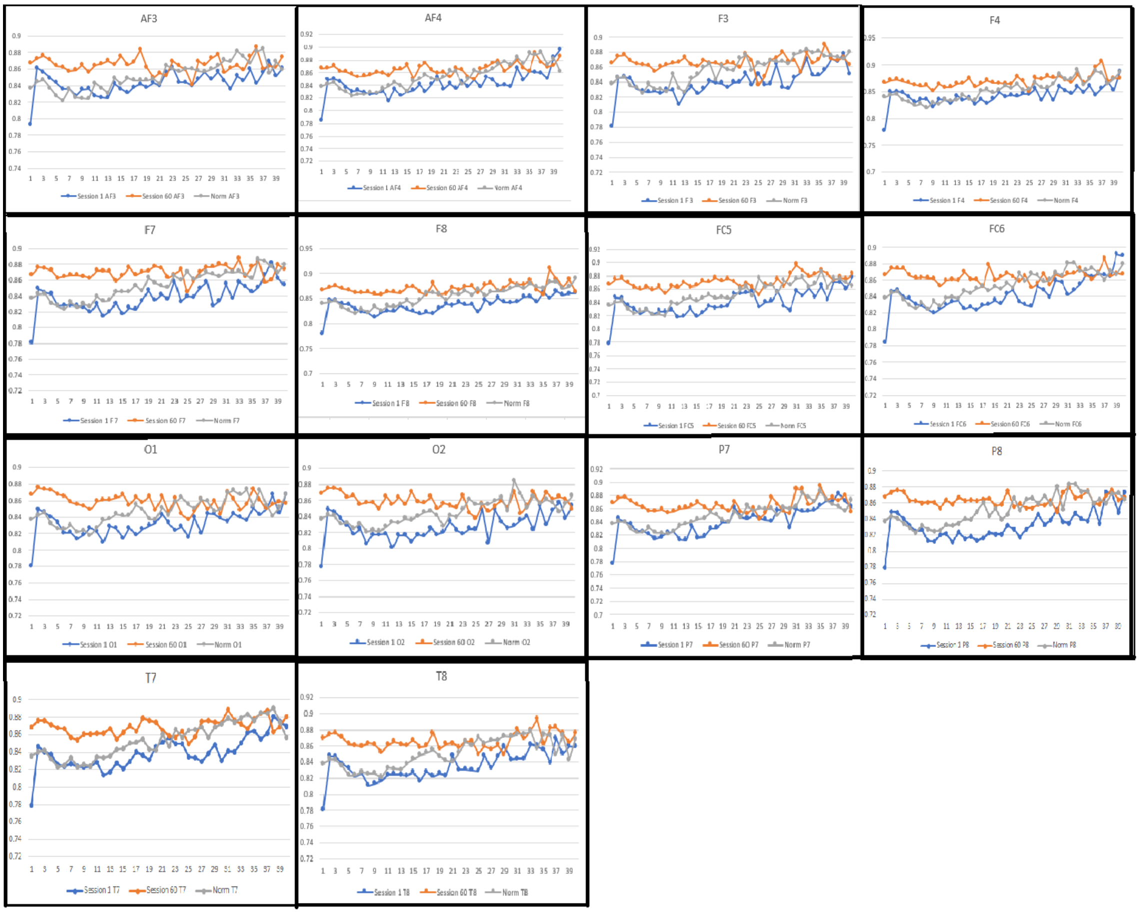

Figure 5.11: MSE Pre- and post- training analysis

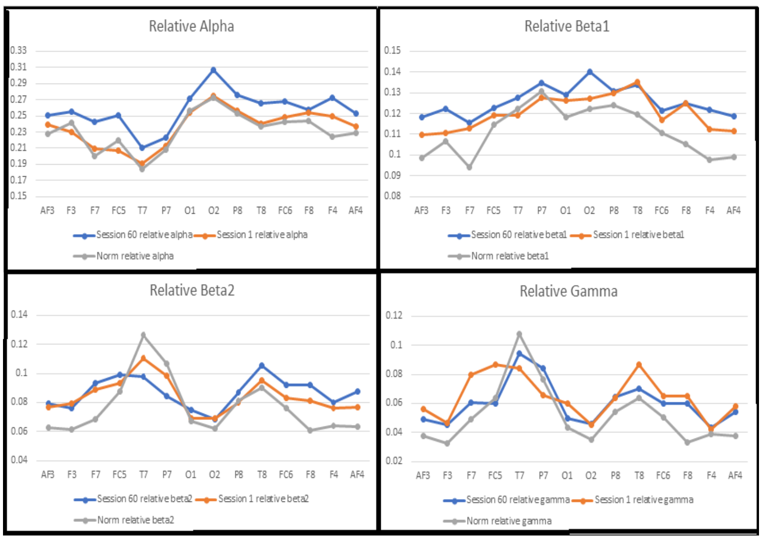

Figure 5.12: Relative Alpha, Pre- and post- training analysis

***Table 5.1** -Demographic features of the experiment group, comparison of TILLS test results and reading speed, pre- and post- treatment*

Subjects	Comorbidity	Sp.Edu	Gender	Age	C-section	Breastfeed	Left Hand	SES	TILLS pre	TILLS Post	Wpm pre-	Wpm post-	Complexity pre-	Complexity post-
Subject1		YES	F	9	NO	0	YES	Low	40	46	51	101	0.71	0.78
Subject2	ADHD	YES	M	7	NO	3	NO	Low	20	32	25	60	0.95	0.93
Subject3	EEG abnormality	NO	M	9	NO	30	YES	Low	20	10	20	40	0.73	0.98
Subject4		NO	M	10	NO	4	NO	Low	16	24	54	90	0.98	0.65
Subject5		NO	M	10	YES	6	NO	Middle	15	19	31	63	0.76	0.85
Subject6	ADHD	NO	M	7	YES	6	NO	Middle	13	18	0	28	0.7	0.87
Subject7		YES	M	9	YES	18	NO	Low	11	24	44	70	0.76	0.97
Subject9		NO	M	7	NO	30	NO	Middle	20	35	61	93	0.79	0.97
Subject8	CP, gifted	YES	M	8	YES	13	YES	Middle	42	45	45	60	0.89	0.84
Subject10		NO	M	10	NO	24	NO	Middle	9	13	58	68	0.73	0.93
Subject11	Gifted	NO	M	8	YES	30	NO	Low	41	40	65	82	0.78	0.87
Subject12		NO	M	11	NO	24	NO	Low	4	4	41	60	0.69	0.88
Subject13	EEG abnormality	NO	M	9	YES	0	NO	Low	21	19	52	72	0.81	0.89
Subject14		NO	M	6	NO	6	NO	Middle	15	23	0	0	0.67	0.72
Subject15	Gifted	NO	M	9	NO	6	NO	Middle	30	26	61	65	0.66	0.91
Subject16	EEG abnormality	NO	M	8	NO	24	NO	Low	7	8	0	10	0.77	0.84

Table 5.2 - Statistical Analysis of the experimental group versus TD norm group, the experimental group pre- and post- trainings

Scale Factor	Dyslexia Session 1 versus TD norm group			Dyslexia Session 60 versus TD norm group			Dyslexia Session 1 versus Session 60				
SF	t	df	Sig. (2-tailed)	t	df	Sig. (2-tailed)	Wilks' Lambda	F	Hypotheses df	Error df	Sig.
1	5.793	496.836	.000	.720	525.855	.472	.785	60.391	1.000	220.000	.000
2	-.687	491.083	.492	-2.055	539.568	.040	.978	4.945	1.000	220.000	.027
3	-.394	496.980	.694	-2.559	564.204	.011	.960	9.264	1.000	220.000	.003
4	-.935	474.653	.350	-3.075	521.024	.002	.945	12.794	1.000	220.000	.000
5	-.719	485.922	.472	-3.629	528.745	.000	.914	20.689	1.000	220.000	.000
6	-.318	489.817	.750	-3.941	493.621	.000	.869	33.090	1.000	220.000	.000
7	.464	485.955	.643	-2.237	524.367	.026	.901	24.208	1.000	220.000	.000
8	.383	479.649	.702	-3.247	470.912	.001	.836	43.007	1.000	220.000	.000
9	.878	457.436	.381	-2.940	483.871	.003	.751	72.855	1.000	220.000	.000
10	-.141	434.643	.888	-2.889	435.575	.004	.829	45.304	1.000	220.000	.000
11	1.109	436.970	.268	-1.732	444.132	.084	.779	62.321	1.000	220.000	.000
12	2.228	445.831	.026	-1.893	425.046	.059	.663	111.700	1.000	220.000	.000
13	1.253	413.126	.211	-1.980	431.734	.048	.693	97.665	1.000	220.000	.000
14	1.964	430.760	.050	-1.053	436.643	.293	.717	86.895	1.000	220.000	.000
15	2.223	444.988	.027	-1.645	420.588	.101	.603	144.906	1.000	220.000	.000
16	2.976	455.920	.003	-.494	451.834	.621	.681	103.189	1.000	220.000	.000
17	3.194	435.303	.002	.663	475.423	.508	.751	72.861	1.000	220.000	.000
18	2.761	438.452	.006	-.920	443.547	.358	.610	140.490	1.000	220.000	.000
19	2.259	443.600	.024	-.220	455.056	.826	.756	70.943	1.000	220.000	.000
20	1.348	455.328	.178	-1.154	486.870	.249	.818	48.892	1.000	220.000	.000
21	1.254	438.518	.211	-.576	474.473	.565	.845	40.452	1.000	220.000	.000
22	2.034	463.053	.042	1.177	481.358	.240	.914	20811.000	1.000	220.000	.000
23	3.611	482.447	.000	.916	544.774	.360	.794	57.248	1.000	220.000	.000
24	2.898	497.337	.004	.845	560.605	.398	.831	44.894	1.000	220.000	.000
25	4.560	498.949	.000	3.579	578.481	.000	.918	19.578	1.000	220.000	.000
26	2.860	496.367	.004	2.073	585.324	.039	.888	27.729	1.000	220.000	.000
27	4.380	490.920	.000	.848	585.988	.397	.728	81.996	1.000	220.000	.000
28	1.848	468.830	.065	.399	569.292	.690	.918	19.732	1.000	220.000	.000
29	4.034	440.273	.000	2.176	551.408	.030	.895	25.684	1.000	220.000	.000
30	4.026	429.044	.000	.944	573.611	.346	.874	31.769	1.000	220.000	.000
31	6.241	453.263	.000	1.813	520.783	.070	.727	82.750	1.000	220.000	.000
32	5.587	411.244	.000	4.108	516.654	.000	.874	31.785	1.000	220.000	.000
33	3.814	447.728	.000	3.271	542.470	.001	.953	10.730	1.000	220.000	.001
34	4.091	450.196	.000	2.438	555.709	.015	.877	30.728	1.000	220.000	.000
35	2.778	446.473	.006	2.179	520.101	.030	.948	12.100	1.000	220.000	.001
36	4.962	396.752	.000	2.217	519.423	.027	.804	53.597	1.000	220.000	.000
37	1.515	485.902	.131	.961	576.585	.337	.945	12.751	1.000	220.000	.000
38	.073	437.005	.942	.852	550.581	.395	.997	0.731	1.000	220.000	.394
39	.649	475.718	.517	.974	550.083	.330	.975	5.702	1.000	220.000	.018
40	.443	443.189	.658	1.519	547.633	.129	1.000	0.039	1.000	220.000	.843

Chapter 6

Efficacy of neurofeedback and multi-sensory learning in dyslexia

In the present research, we performed a clinical trial in which the effects of qEEG neurofeedback and multi-sensory learning training were studied. The following research question is addressed:

1. Does simultaneous neurofeedback training together with multi-sensory learning improve the reading abilities of children with dyslexia who are 7-10 years old?

Our contribution to this research is to research the positive effects of the Auto Train Brain and compare the effect size of neurofeedback and multi-sensory learning with that of special education and other proven methodologies for dyslexia in the literature. The primary endpoint of the experiment was set to 60 sessions of Auto Train Brain training to be completed in 6 months when the reading abilities of both groups would be evaluated in terms of the TILLS test descriptive scores. A priori power calculation was not registered. We presented a priori power calculation in the limitations of the study.

6.1 Materials and Methods

6.1.1 Participants

36 individuals applied to participate in the experiment (Figure 6.2). Four of them were excluded due to their ages. 32 participants from Ankara, İzmir, and Kocaeli were included to participate in the experiment. The participants met DSM-V criteria

for dyslexia, as assessed by psychologists and psychiatrists beforehand. The child neurologist physically examined the participants and approved their participation in the experiment. The participants resided in the different cities of Turkey, and those who would be assigned to the experimental group were expected to come to the Ankara University Faculty of Medicine during the experiment. Therefore, those who resided in Ankara or were willing to come to Ankara were assigned to the experimental group primarily. The experimental group and the control group were matched based on age and the first TILLS test descriptive scores (Table 6.1, Figure 6.2). There were 16 participants with dyslexia (Mage= 8.56, SD = 1.36) in the experimental group and 14 participants with dyslexia (Mage= 8.59, SD=0.94) in the control group. The experimental group had dyslexia, and there were comorbid situations such as EEG anomalies, cerebral palsy, ADHD, and giftedness. The socio-economic situation of the experimental group was low to the middle class; they were mostly residents of Ankara. The experimental group took 60 sessions of Auto Train Brain 3 times a week, 4 of them received special education concurrently.

At the start of the experiment, the control group had 16 participants. However, two of them left the study to get neurofeedback training at a psychiatrist's office. The control group resided in İzmir and Kocaeli; the socio-economic situation of the control group was low to the middle class. The control group was more homogeneous than the experimental group and had dyslexia only. The participants in the control group received special education provided by the rehabilitation centers according to the Special Learning Difficulty Support Training Program, prepared by the Special Education and Rehabilitation Center at the Ministry of Education in Turkey. The support training program includes a) Preparation for learning (300 lesson hours) b) Reading and writing (250 lesson hours) c) Mathematics (200 lesson hours). The control group received 3-hour special education per week during 6 months.

The socio-economic situation was measured with a survey filled out by the parents of the children. The survey includes questions about education level, income, occupation, and residence.

6.1.2 Neurofeedback treatment protocol and multi-sensory learning method

Auto Train Brain is a mobile application that uses neurofeedback and multi-sensory learning principles. It is used with the EMOTIV EPOC+ headset. It is a non-invasive solution, offers continuous brain performance improvement for both adults and children without any side-effects. It reads qEEG from 14 channels, processes these signals, and provides online, real-time visual and auditory neuro-feedback. Within this software application, a system and method for improving learning ability are proposed. The EEG neurofeedback protocol is explained below:

1. Reduce theta waves at Broca area in the brain if above the threshold;
2. Reduce theta waves at Wernicke area in the brain if above the threshold;
3. Find the channels with the maximum absolute power of theta waves at the left hemisphere and reduce absolute theta; and
4. Find the channels with the maximum absolute power of theta waves at the right hemisphere and reduce absolute theta.

The positive reward is a green arrow on the screen, negative feedback is a red arrow and a "beep" sound. With a positive reward, the score displayed on the screen is increased. If the slow brain waves of the subject are above the norm threshold, a red arrow is presented on the screen and the subject is asked to turn it to a green arrow with brainpower online real-time. A typical neurofeedback session lasts 20 minutes. After the neurofeedback session, a phoneme-grapheme matching alphabet teaching system is presented. One of the significant differences between the currently available neurofeedback systems and Auto Train Brain is that it combines neurofeedback with multi-sensory learning principles. Moreover, the neurofeedback protocol has a novel approach, as the above-mentioned, which assumes that establishing new weak linkages between disconnected brain areas improves the reading process upon 60 or more uses.

6.1.3 Study Design, Behavioral Assessments, and Training Sessions

The participants in the experimental group with their parents commuted to the Ankara University Faculty of Medicine 3 times a week. In the first interview, all participants filled out questionnaires, and a psychologist applied the 1.5-hour TILLS test to the participants. The experimental group came to the sessions with their parents, while the parents were waiting in the waiting room, only the participant was taken to the room. There were 0.5 meters between the participant and the mobile phone screen. The psychologist just stayed with the participant to make sure the participant was using the mobile app correctly, but no guidance or encouragement was provided. There was no one else in the room and the door of the room was closed. There was a distance of 1 meter between the psychologist and the participant. The psychologist in the room was neutral to the participant, not friendly or empathetic. In the first session, the participant was told to focus on the arrow he saw on the application screen and, if he saw a red arrow, he was asked to turn it to green with brainpower. No additional information about the experimental procedure was explained to the participant. Before the 10th session, the child neurologist examined the children and checked for any side effects. All participants were given 60 sessions of neurofeedback training during 12 consecutive weeks. A standard neurofeedback protocol for reducing slow brain waves was applied to the experimental group for 10 minutes in the left brain and 10 minutes in the right brain. After neurofeedback, the participants received 10-minute multi-sensory learning of the alphabet with Auto Train Brain. The participants who completed the 60th session were told that the experiment was completed. An appointment was made for the second TILLS test exactly 6 months after the first TILLS test. At the end of the sixth month, the TILLS test was performed again. The control group received a TILLS test at the beginning of the experiment and after 6 months. They have not received any training with Auto Train Brain. Instead, they continued special education.

6.1.4 Statistical Analysis

The variables were the TILLS test descriptive scores and the TILLS subtests' scores (pre- and post-treatment) for both groups (Table 6.2). This design allows for a multivariate repeated measures analysis of variance that was applied for a comparison of both groups about the subtests of the TILLS test. There were two factors in our experiment, namely time (there were two levels for the factor "time" , the time at which the first TILLS test was conducted and the time at which the second TILLS test was conducted), and the factor "group". The significant interaction effects (group X time) were determined. The alpha significance level was set to 0.05. We have checked the normality of data for the TILLS test results (skewness = 0.439, kurtosis = -0.399), and validated that the data were normally distributed. Mauchly's test did not indicate any violation of sphericity.

6.2 Results

Multivariate repeated measures of ANOVA indicated that there was no significant group-by-time interaction in the TILLS test descriptive scores [F (1, 28) = 0.729, p= .400; Table 6.3]. However, a significant main effect of time was identified for the TILLS test descriptive scores [F (1,28) = 11.972, p=.002; Table 6.4]. Between subject groups, the TILLS descriptive scores did not differ statistically significantly [F (1, 28) = .384, p=.540; Table 6.4]. We have repeated the analysis excluding the four participants who also continued special education from the experimental group. Multivariate repeated measures of ANOVA indicated that there was no significant group-by-time interaction in the TILLS test descriptive scores [F (1, 23) = 2.117, p= .159]. However, a significant main effect of time was identified for the TILLS test descriptive scores [F (1,23) = 5.694, p=.0026]. Between subject groups, the TILLS descriptive scores did not differ statistically significantly [F (1, 23) = 2.683, p=.115]. Our results indicated that we have reached our primary endpoint for this experiment. Auto Train Brain training improved the reading abilities of the experimental group up to the level of the control group who only received special education. The rest of the statistical results about the subtests of the TILLS test which were presented below were secondary.

There was no significant group-by-time interaction in the subtests of phonemic awareness [F(1, 28)=0.779, p=.385; Table 6.3], story retelling [F(1, 28)=0.010, p=.920; Table 6.3], nonword spelling [F(1, 27)=0.018, p=.894; Table 6.3]. However, a significant main effect of time was identified for phonemic awareness [F (1, 28) =4.749, p=.038; Table 6.4], story retelling [F (1, 28) = 6.482, p=.017; Table 6.4], nonword spelling [F (1, 28) = 8.660, p=.007; Table 6.4]. Between subject groups, the scores in these subtests did not differ statistically significantly. Both Auto Train Brain and special education improved phonemic awareness, story retelling, nonword spelling (Table 4). We have repeated the analysis excluding the four participants who continued special education from the experimental group. There was no significant group-by-time interaction in the subtests of phonemic awareness [F (1, 23) = 0.202, p=.657] and nonword spelling [F (1, 23) = 0.181, p=.674]. However, a significant main effect of time was identified for phonemic awareness [F (1, 23) = 4.708, p=.041] and nonword spelling [F (1, 23) = 4.447, p=.046]. Between subject groups, the scores in these subtests did not differ statistically significantly. Both Auto Train Brain and special education improved phonemic awareness and nonword spelling.

There was a significant group-by-time interaction in the subtests of reading comprehension [F (1, 27)=5.711, p=.024; Table 6.3], vocabulary awareness [F(1, 28) = 4.684, p=.039; Table 6.3], social communication [F (1, 28) = 5.845, p=.022; Table 6.3], digit span forward [F(1, 28) = 5.758, p= .023; Table 6.3], digit span backward [F(1, 28) = 4.443, p= .044; Table 6.3]. For the experimental group, the simple effect of time in the subtests of reading comprehension [F (1, 14) = 4.98, p=.042; Table 6.5] was statistically significant. Post-hoc tests indicated that Auto Train Brain training improved reading comprehension statistically significantly more than that of special education. The experimental group progressed from m = 3.06 (SD = 4.22) to 5.20 (SD = 4.41), a 70% improvement, whereas the control group regressed from m = 7.12 (SD = 3.18) to m = 6.36 (SD = 4.22), a -10% improvement (Table 6.2). We have repeated the analysis excluding the four participants who continued special education from the experimental group. There was a significant group-by-time interaction in the subtests of reading comprehension [F (1, 23) =5.973, p=.023], vocabulary awareness [F (1, 23) = 6.680, p=.017], social communication [F (1, 23) = 6.067, p=.022], digit span forward [F (1, 23) = 4.590, p= .043], digit span backward [F (1, 23) = 5.601, p= .027]. For the experimental group, the simple effect of time in the subtests of reading comprehension [F (1, 10) = 5.252, p=.045] was statistically significant. Post-hoc tests indicated that Auto Train Brain training improved reading comprehension statistically significantly more than that of special education. The experimental group progressed from m = 2.86 (SD = 4.29) to 5.20 (SD = 5.41), an 81% improvement.

For the control group, the simple effect of time in the subtests of vocabulary awareness [F (1, 13) =9.69, p=.008; Table 6.6], social communication [F (1, 13) =5.430, p=.037; Table 6.6], digit span forward [F (1, 13) =9.75, p=.008; Table 6.6], and digit span backward [F (1, 13) =8.576, p=.012; Table 6.6] were statistically significant. Post-hoc tests showed that special education improved vocabulary awareness, social communication, digit span forward, and digit span backward scores more than those of Auto Train Brain training.

No adversity was reported for any of the participants except for short-lived headaches after treatment in rare conditions.

6.3 Discussion

Our research indicated that Auto Train Brain improves the reading abilities of children with dyslexia in 60 sessions up to the level achieved by special education in 6 months. So, we find support to our hypothesis. Auto Train Brain and special education improved phonemic awareness and nonword spelling at a similar level. Auto Train Brain improved reading comprehension more than that of special education. Special education improved vocabulary awareness, social communication, digit span forward, and digit span backward more than that of Auto Train Brain which did not cause any side effects on children. Neurofeedback and multi-sensory learning solution are feasible to train children with dyslexia at home reliably. Therefore, we find support to our hypothesis. This is a pilot study with only 30 participants. In the near future, there needs another experiment to be designed for the definitive conclusion. Our experimental group consisted of children with dyslexia with comorbid situations and the effect size was 0.23 (16 people). When we excluded the subjects with comorbidities and those who also continued special education from analysis, the effect size of Auto Train Brain was increased to 0.66 (6 people). The effect size of Auto Train Brain is larger than that of Orton-Gillingham method and the neurofeedback study (Breteler et al., 2010). The effect size of Auto Train Brain for people with dyslexia without any comorbidities who also continued special education was 0.88 (2 people). These results showed that Auto Train Brain's effect size was the largest for people with dyslexia without any comorbidities who also continued special education (Table 6.7). This research also revealed that the activity and effectiveness of Auto Train Brain will be carried to a higher level with special training materials to be added to the later versions.

In this research, it is important to reveal that Auto Train Brain is as effective as special education, because the rehabilitation of children with dyslexia with online education at home is paved the way. Due to the fact that rehabilitation centers were closed during the pandemic period, these children could not receive any education for a very long time. Considering that the pandemic may continue in the upcoming period, online education may remain the only training option.

Previous research indicated that people with dyslexia benefit from neurofeedback applications. In the study [35], the researchers applied neurofeedback protocols to people with dyslexia to decrease theta at Cz, to increase beta-1 at T3, to decrease coherence at delta and theta range and their research showed at least two levels of increase in reading levels. In the study [38], they applied neurofeedback protocols to people with dyslexia to decrease theta at T3 and F7, to increase beta-1 at T3 and F7. They reported no significant changes in band powers, but hyper-coherence in theta and delta bands were reduced as well as reading time and reading mistakes were reduced due to the treatment. Follow up assessments showed that reading improvements were permanent. Applying neurofeedback to dyslexia (delta down at T3-T4, beta down at F7 and C3, coherence training inboth slow and fast band powers) was shown useful for spelling but not reading [37] although other previous studies reported increases in raising reading grade levels [77]. Coherence neurofeedback training has been performed on the participants with dyslexia: the most common hypo-coherence was the occipitoparietal lobes to the frontotemporal lobes. The second common hypo-coherence was the parietal to medial temporal connections. Hypo-coherence has been reported on the delta, theta, and alpha bands.

Trained with coherence neurofeedback, the reading performances of people with dyslexia improved [11]. One of the significant differences between the currently available neurofeedback systems and Auto Train Brain is that the latter combines neurofeedback with multi-sensory learning principles. The neurofeedback protocol also has a novel approach; it is applied from 14 channels. Establishing new weak linkages in disconnected areas improves the reading process upon 60 or more uses. In general, the more neurofeedback is applied, the more permanent and positive are the results achieved. Auto Train Brain is designed for use at home reliably, which extends the treatment period for the end-user and makes it more convenient to use for both children and parents.

6.3.1 Limitations of the study

The first limitation of the study is the number of participants. It would have been better if we had more participants in the experiment. We made a priori power calculation to predict the sample size using G*power. We set the effect size as 0.63, that was calculated from the pre- and post- TILLS descriptive scores of the experimental group who did not have comorbidities, set alpha value as 0.05, set power (1-beta) as 0.95, set T-Test and RCT as input parameters. The sample size for both groups was calculated as 67. So, this study can be considered as a pilot study.

The second limitation of the study is the existence of comorbid situations such as EEG anomalies, ADHD, giftedness, and CP in the experimental group. The control group consisted of people with pure dyslexia and was more homogenous than the experimental group. For people with dyslexia who had comorbid brain conditions like EEG anomalies and giftedness, the positive effect of Auto Train Brain is limited. Gifted children with dyslexia have less slow brain waves than those of the norm group; therefore, it was hard to apply neurofeedback protocols, since we aim to reduce the slow brain waves down to norm threshold. These results indicate that comorbid brain conditions reduce the positive effect of Auto Train Brain. The theta/gamma high group of children with dyslexia benefit more. As people with dyslexia who have comorbid brain conditions did not improve much in the experimental group, we can conclude that comorbid brain conditions present in the experimental group compared with pure dyslexia in the control group do not affect the outcome of the experiment.

The third limitation of the study is the possibility of placebo effects. As described by [86], children that are given one-on-one interactions and specialized interventions may improve their functioning based solely on the social and environmental impact of those interventions. Because no alternative intervention for the control group was provided, placebo effects may represent a significant source of improvement.

The fourth limitation of the study is that 4 participants of the experimental group also continued special education. We have repeated the statistical analysis by excluding these participants and showed that the results are also valid for this subgroup. Future work will include adding special education practices to Auto Train Brain (especially memory, listening and speaking exercises, and vocabulary awareness) and introduce new games for improving the cognitive abilities that currently neither Auto Train Brain nor special education touches (such as writing words and sentences). Moreover, future work can address whether using Auto Train Brain will help improving other brain conditions like dysgraphia, dyscalculia, dyspraxia, anxiety, autism, and mental retardation.

Table 6.1: *Demographic information about the experimental (n=16) and the control group (n=14)*

Participants	Comorbidity	Spec.Edu.	Gender	Age	C-section	Breastfeeding	Left hand	SES	TILLS pre	TILLS post
Experiment1		YES	F	9	NO	0	YES	Low	40	46
Experiment2	ADHD	YES	M	7	NO	3	NO	Low	20	32
Experiment3	EEG abnormality	NO	M	9	NO	30	YES	Low	20	10
Experiment4		NO	M	10	NO	4	NO	Low	16	24
Experiment5		NO	M	10	YES	6	NO	Middle	15	19
Experiment6	ADHD	NO	M	7	YES	6	NO	Middle	13	18
Experiment7		YES	M	9	YES	18	NO	Low	11	24
Experiment9		NO	M	7	NO	30	NO	Middle	20	35
Experiment8	CP, gifted	YES	M	8	YES	13	YES	Middle	42	45
Experiment10		NO	M	10	NO	24	NO	Middle	9	13
Experiment11	Gifted	NO	M	8	YES	30	NO	Low	41	40
Experiment12		NO	M	11	NO	24	NO	Low	4	4
Experiment13	EEG abnormality	NO	M	9	YES	0	NO	Low	21	19
Experiment14		NO	M	6	NO	6	NO	Middle	15	23
Experiment15	Gifted	NO	M	9	NO	6	NO	Middle	30	26
Experiment16	EEG abnormality	NO	M	8	NO	24	NO	Low	7	8
Control1		YES	M	8	YES	6	NO	Middle	15	30
Control2		YES	M	9	NO	24	NO	Middle	23	31
Control3		YES	F	8	YES	9	NO	Low	28	33
Control4		YES	M	9	YES	6	YES	Low	14	19
Control5		YES	F	7	YES	19	YES	Middle	5	34
Control6		YES	M	7	NO	7	YES	Middle	9	17
Control7		YES	M	10	NO	6	YES	Middle	24	24
Control8		YES	M	9	YES	24	NO	Middle	30	33
Control9		YES	M	10	YES	0	YES	Middle	34	31
Control10		YES	M	10	YES	24	NO	Low	22	34
Control11		YES	F	8	YES	12	NO	Middle	32	33
Control12		YES	M	9	YES	9	NO	Middle	30	33
Control13		YES	F	9	YES	4	YES	Low	18	15
Control14		YES	F	8	YES	6	NO	Low	15	16
Experiment		YES:4	Female:1	*M*=8.56	NO:10	*M*=11.1	YES:3	Low:9	*M*=20.25	*M*=24.12
		NO: 12	Male:15		YES :6		NO:13	Middle:7		
Control		YES:14	Female:5	*M*= 8.59	NO:3	*M*= 13.9	NO:8	Low:5	*M*=20.88	*M*=27.36
		NO :0	Male:9		YES:11		YES:6	Middle :9		

Table 6.2: *Pre- and post- TILLS test results for experimental group and control group*

	Control group (n=14)				Experimental group (n=16)			
	pre-scores		post-scores		pre-scores		post-scores	
TILLS	M	SD	M	SD	M	SD	M	SD
Descriptive scores	20.88	8.67	27.36	7.44	20.25	12.02	23.88	8.63
Vocabulary awareness	5.00	2.09	7.57	2.71	5.19	3.35	5.75	2.61
Phonemic awareness	4.82	3.83	7.43	4.78	4.94	4.09	5.88	4.63
Story retelling	4.29	1.90	5.43	3.11	4.88	2.39	6.06	3.13
Nonword repetition	6.76	4.21	7.79	5.28	4.00	3.93	4.88	5.12
Nonword spelling	6.53	3.94	8.21	3.36	6.87	3.66	8.67	3.81
Listening comprehension	5.59	3.62	6.86	4.02	3.75	3.66	4.94	3.88
Reading comprehension	7.12	3.18	6.36	4.22	3.06	4.22	5.20	4.41
Following directions	8.06	3.90	9.07	4.03	8.63	4.81	9.19	3.95
Delayed story retelling	4.76	1.44	5.79	3.64	5.06	2.32	5.38	3.61
Nonword reading	8.00	3.59	9.21	3.19	6.27	4.65	7.47	3.11
Reading fluency	0.41	0.80	0.29	0.61	0.53	0.99	0.60	0.59
Written expression -Disc.	3.00	2.06	2.14	1.96	2.87	2.50	3.67	2.96
Written expression -Sen.	4.88	5.02	3.79	1.76	4.60	5.00	5.07	1.70
Written expression – Words	2.71	3.50	2.21	3.29	3.27	4.03	2.80	3.90
Social communication	3.12	2.20	5.21	3.51	5.31	4.11	5.00	3.42
Digit span forward	8.18	2.46	9.71	3.12	5.63	2.31	5.88	3.09
Digit span backward	7.41	3.00	9.71	3.22	7.00	3.04	7.06	3.11

Table 6.3: *Repeated measures of ANOVA results, multivariate tests (group X time), interaction effects*

TILLS	Wilks' Lambda	F	Hypotheses df	Error df	Sig.	Eta
Descriptive points	0.975	0.729	1	28	0.400	0.025
Vocabulary awareness	0.857	4.684	1	28	0.039*	0.143
Phonemic awareness	0.973	0.779	1	28	0.385	0.027
Story retelling	1.000	0.010	1	28	0.920	0
Nonword repetition	0.998	0.06	1	28	0.809	0.002
Nonword spelling	0.999	0.018	1	27	0.894	0.001
Listening comprehension	0.999	0.015	1	28	0.903	0.001
Reading comprehension	0.825	5.711	1	27	0.024*	0.175
Following directions	0.992	0.237	1	28	0.63	0.008
Delayed story retelling	0.980	0.584	1	28	0.451	0.020
Nonword reading	0.993	0.188	1	27	0.668	0.007
Reading fluency	0.997	0.091	1	27	0.766	0.003
Written expression -Disc.	0.906	2.791	1	27	0.106	0.094
Written Expression – Sen.	0.980	0.556	1	27	0.462	0.020
Written expressions- Word	0.992	0.226	1	27	0.638	0.008
Social communication	0.827	5.845	1	28	0.022*	0.173
Digit span forward	0.829	5.758	1	28	0.023*	0.171
Digit span backward	0.863	4.443	1	28	0.044*	0.137

*$p < 0.05$.

Table 6.4: *Repeated measures of ANOVA results, within subject effects (time) and between subject effects (group)*

	Within subject effects					Between subject effects				
TILLS	F	Hypo. df	Error df	Sig.	Eta	F	Hypo. df	Error df	Sig.	Eta
Descriptive points	11.972	1	28	0.002**	0.300	0.384	1	28	0.540	0.014
Vocabulary awareness	11.121	1	28	0.002**	0.284	0.595	1	28	0.447	0.021
Phonemic awareness	4.749	1	28	0.038*	0.145	0.461	1	28	0.503	0.016
Story retelling	6.482	1	28	0.017*	0.188	0.694	1	28	0.412	0.024
Nonword repetition	1.353	1	28	0.254	0.046	4.259	1	28	0.048*	0.132
Nonword spelling	8.66	1	28	0.007**	0.243	0.076	1	27	0.785	0.003
Listening comprehension	3.422	1	28	0.075	0.109	2.421	1	28	0.131	0.08
Reading comprehension	1.059	1	27	0.313	0.038	3.725	1	27	0.064	0.121
Following directions	2.043	1	28	0.164	0.068	0.074	1	28	0.787	0.003
Delayed story retelling	1.94	1	28	0.175	0.065	0.002	1	28	0.968	0
Nonword reading	1.497	1	27	0.232	0.053	2.633	1	27	0.116	0.089
Reading fluency	0.012	1	27	0.914	0	0.426	1	27	0.519	0.016
Written expression -Disc.	0.059	1	27	0.81	0.002	0.592	1	27	0.448	0.021
Written Expression – Sen.	0.006	1	27	0.941	0.000	0.297	1	27	0.590	0.011
Written expressions- Word	1.461	1	27	0.237	0.051	0.056	1	27	0.815	0.002
Social communication	3.536	1	28	0.07	0.112	1.288	1	28	0.266	0.044
Digit span forward	10.361	1	28	0.003**	0.27	13.392	1	28	0.001*	0.324
Digit span backward	5.058	1	28	0.033*	0.153	3.652	1	28	0.066	0.115

*p < 0.05. **p < 0.01.

Table 6.5: *Repeated measures of ANOVA results for the experimental group, the simple effect of time*

TILLS	Wilks' Lambda	F	Hypotheses df	Error df	Sig.	Eta
Descriptive scores	0.768	4.533	1	15	0.050*	0.232
Vocabulary awareness	0.924	1.226	1	15	0.286	0.076
Phonemic awareness	0.863	2.372	1	15	0.144	0.137
Story retelling	0.819	3.304	1	15	0.089	0.181
Nonword repetition	0.764	4.623	1	15	0.048*	0.236
Nonword spelling	0.74	4.916	1	14	0.044*	0.260
Listening comprehension	0.897	1.723	1	15	0.209	0.103
Reading comprehension	0.737	4.985	1	14	0.042*	0.263
Following directions	0.951	0.775	1	15	0.392	0.049
Delayed story retelling	0.973	0.423	1	15	0.525	0.027
Nonword reading	0.918	1.258	1	14	0.281	0.082
Reading fluency	0.999	0.012	1	14	0.914	0.001
Written expression -Disc.	0.942	0.859	1	14	0.370	0.058
Written expression -Sen.	0.959	0.604	1	14	0.45	0.041
Written expression -Words	0.984	0.234	1	14	0.636	0.016
Social communication	0.979	0.319	1	15	0.580	0.021
Digit span forward	0.958	0.652	1	15	0.432	0.042
Digit span backward	0.999	0.011	1	15	0.918	0.001

*p < 0.05. **p < 0.01.

Table 6.6: *Repeated measures of ANOVA results for the control group, the simple effect of time*

TILLS	Wilks' Lambda	F	Hypotheses df	Error df	Sig.	Eta
Descriptive scores	0.647	7.106	1	13	0.019*	0.353
Vocabulary awareness	0.573	9.688	1	13	0.008**	0.427
Phonemic awareness	0.835	2.562	1	13	0.133	0.165
Story retelling	0.804	3.172	1	13	0.098	0.196
Nonword repetition	0.984	0.210	1	13	0.655	0.016
Nonword spelling	0.774	3.802	1	13	0.073	0.226
Listening comprehension	0.885	1.683	1	13	0.217	0.115
Reading comprehension	0.918	1.163	1	13	0.300	0.082
Following directions	0.916	1.190	1	13	0.295	0.084
Delayed story retelling	0.904	1.384	1	13	0.260	0.096
Nonword reading	0.974	0.351	1	13	0.564	0.026
Reading fluency	0.984	0.210	1	13	0.655	0.016
Written expression -Disc.	0.847	2.349	1	13	0.149	0.153
Written expression -Sen.	0.985	0.196	1	13	0.665	0.015
Written expression -Words	0.883	1.728	1	13	0.211	0.117
Social communication	0.705	5.430	1	13	0.037*	0.295
Digit span forward	0.571	9.750	1	13	0.008**	0.429
Digit span backward	0.603	8.576	1	13	0.01*	0.397

*p < 0.05. **p < 0.01.

Table 6.7: *The comparison of the effectiveness of the dyslexia training programs in the literature*

Dyslexia training program	Effect size	Dyslexia	Comorbid	Group size
AutoTrainBrain with special education	0.88	Yes	No	2
AutoTrainBrain	0.66	Yes	No	6
Orton Gillingham	0.43	Yes	No	77
Special education	0.35	Yes	No	14
Neurofeedback (Breteler et al., 2010)	0.3	Yes	No	19
AutoTrainBrain	0.23	Yes	Yes	16

Chapter 7

Conclusion

7.1 Summary

In this thesis, extensive research was conducted to survey the causes and the treatment options of dyslexia. The major academic contribution of this thesis is the combination of neurofedback and multi-sensory learning in a novel protocol for improving the reading abilities of children with dyslexia. For this purpose, a mobile application with these functionalities and integrated with a wireless EEG system was developed and successfully tested. We conducted randomized controlled trial with 30 children with dyslexia. The application was tested on more than 2500 healthy individuals to date, and more than 100 children with dyslexia, ADHD, autism, CP and MR without any side effects or harm, and the results were positive.

The EEG neurofeedback system integrated with multi-sensory learning (visual and auditory) provides a powerful and robust tool for improving reading ability. The EEG neurofeedback system is easy to use and does not require technical expertise. One of the significant differences between the currently available neurofeedback systems and Auto Train Brain is that the latter combines neurofeedback with multi-sensory learning principles. The neurofeedback protocol also has a novel approach; it is applied from 14 channels. Establishing new weak linkages in disconnected areas improves the reading process upon 60 or more uses. In general, the more neurofeedback is applied, the more permanent and positive are the results achieved. Auto Train Brain is designed for use at home reliably, which makes it more convenient to use for both children and parents. We have observed in the experiments that the training did not cause any adverse side effects for children with dyslexia. EMOTIV headset provided a reliable and effective measurement system for dynamic complexity. Auto Train Brain system as a whole provided safe neurofeedback for children who are 7-10 years old.

Our experiment showed that Auto Train Brain improves the reading abilities of dyslexic children up to the level of special education in 60 sessions of usage. Auto Train Brain and special education improved phonemic awareness and nonword spelling in a similar level. Auto Train Brain improved reading comprehension more than that of special education. Special education improved vocabulary awareness, social communication, digit span forward, and digit span backward more than that of Auto Train Brain. This is a pilot study with only 30 subjects. Further work with a larger number of participants is needed to strengthen the results of our study.

7.2 Future Work

Combined 14-channel neurofeedback and multi-sensory learning method can improve the reading abilities of children with dyslexia. Our study has shown that Auto Train Brain improves the cognitive abilities of people with dyslexia up to the level of special education.

Auto Train Brain software may potentially improve the cognitive abilities of children with autism. We have a case report on autism [87]. The only condition is that people with autism would be able to wear the EMOTIV headset without any resistance. Our next aim is to develop an ergonomic and cost effective headset which is easily wearable by children with autism and dyslexia. The new headset should also process delta frequency band and has at least 8 electrodes. The raw EEG data should be read as well astheir conversion into frequency bands. We think that qEEG neurofeedback from Delta band will make the training more effective.

This study has some implications for future research. New games that improve memory, listening, speaking and vocabulary awareness may be added to Auto Train Brain to increase efficacy. The future work will also address whether using Auto Train Brain will help improving other brain conditions like dysgraphia, dyscalculia, dyspraxia, anxiety, autism, and mental retardation.

Figure 7.1: ATB Clinical trials 1

Figure 7.2: ATB Clinical trials 2

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