NEUROMODULATORY EFFECT OF BILATERAL RHYTHMIC TACTILE
STIMULATION ON RECOGNITION MEMORY

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ABSTRACT

NEUROMODULATORY EFFECT OF BILATERAL RHYTHMIC TACTILE STIMULATION ON RECOGNITION MEMORY

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Over two decades, Saccade Induced Retrieval Enhancement (SIRE), referring to memory performance enhancement with alternating left-right horizontal eye movements, gained a lot of popularity among cognitive science researchers. A similar effect can optionally be realized by bilateral tactile stimulation (BLS). Although the mechanism behind the SIRE effect hasn't been conclusively revealed yet, there have been two alternative explanations: the interhemispheric interaction hypothesis and the top-down attentional hypothesis. Main purpose of this thesis is to investigate the neuromodulatory effects of bilateral tactile stimulation on face recognition memory tasks based on these hypotheses. EEG data were acquired while twenty-one university students performed a recognition memory task. Behavioral analyses revealed that subjects under BLS yield more conservative response biases. EEG results showed that the N100 ERP component is modulated by BLS. Moreover, through EEG coherence analysis, there is some indication that BLS induces an increase in interhemispheric connectivity within the delta frequency band in the frontal regions and a decrease within the gamma band in the parietal regions.

Keywords: recognition memory, inter-hemispheric interaction, top-down attentional control, N100, coherence

ÖZ

İKİ TARAFLI RİTMİK DOKUNSAL UYARANLARIN TANIMA BELLEĞİ ÜZERİNDEKİ NÖROMODÜLER ETKİSİ

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Son yıllarda, belirli aralıklarla yatay göz sekme hareketi yapıldıktan sonra kişilerin bellek performansındaki artma fenomeni pek çok bilişsel araştırmacının ilgisini çekmeye başlamıştır. Bu fenomen Göz Sekmesine bağlı geri getirme geliştirmesi (SIRE) olarak adlandırmaktadır. SIRE etkisinin ardındaki mekanizma kesin olarak bilinmemekle birlikte, interhemisferik etkileşim hipotezi ve yukarıdan aşağıya dikkat hipotezi olmak üzere iki olası açıklama vardır. Bu tezin temel amacı, sözü geçen iki hipoteze dayalı olarak, iki taraflı dokunsal uyarılmanın yüz tanıma belleği görevi üzerindeki nöromodülatör etkilerini araştırmaktır. Bu doğrultuda yirmi bir üniversite öğrencisine tanıma belleği görevleri uygulanmış ve denekler tanıma belleği görevlerini gerçekleştirirken EEG verileri kaydedilmiştir. Davranışsal analizler, deneklerin iki taraflı dokunsal uyaran ile etkileşim halinde olduklarında daha muhafazakâr tepki yanlılıklarına sahip olmalarıyla sonuçlanırken, EEG sonuçları, N100 ERP bileşeninin iki taraflı dokunsal uyaran tarafından modüle edildiğini gösterdi. Ayrıca, EEG koherans analizinde, iki taraflı dokunsal uyaranın frontal bölgelerde delta frekans bandında interhemisferik koheransını arttırdığına ve parietal bölgelerde ise gama frekans bandında azalttığına dair birtakım bulgular elde edilmiştir.

Anahtar Sözcükler: tanıma belleği, interhemisferik etkileşim, yukarıdan aşağıya dikkat kontrolü, N100, koherans

To My Wife

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LIST OF ABBREVIATIONS

EEG   Electroencephalography
ERP   Event Related Potential
BLS   Bilateral Stimulation
LTM   Long-term memory
STM   Short-term memory
SIRE   Saccade-induced retrieval enhancement
PTSD   Post-traumatic stress disorder

CHAPTER 1

INTRODUCTION

1.1. Memory and SIRE

All humans must encounter a myriad of information in every second, every minute, from birth to death. Throughout every epoch of human history, the question of how we perceive things surrounding our environment, including ourselves, how we have representations of those perceptions, and how we can still have those representations even when we learned them in our childhood remained to hide its mysteries even today's world.

Humankind's adventure of understanding our mental faculties has never come to an end from ancient times till today's modern world. Cognitive scientists had great deals of explanations, theories, and experimentation based on the models that they developed in the last century. Especially after the computer revolution in the mid-1950s, modern information processing technology opened new doors for comprehending the hidden mechanism of one of the primary mental concepts, which is memory.

In 1968, Atkinson and Shiffrin understood the importance of developing computer technologies, and they established a model based on computational theoretical aspects of information processing units of computer devices. Insights and the terminology of that model exceed the limits of computer-mind metaphor and become the basic building blocks for developing any memory model, even today. It allowed the researchers to conduct empirical research on memory to a great extent. Although their model compartmentalizes memory basic memory units (sensory, short-term, and long-term memory) and basic processes (storage, retrieval, and encoding), Tulving (1972) proposed a new model by elaborating the compartments of long-term memory. He realized that long-term memory is far from being a single unit by highlighting that it has different subsystems, and every subsystem has its own distinctive process. Accordingly,

he suggests dividing long-term memory processes according to whether they require unconscious knowledge (procedural), whether they reflect common knowledge such as knowing the 'capital of Turkey' (semantic), and whether they deal with personal events and experiences (episodic). At the beginning of the 1970s, Craik and Lockhart (1972) stated 'level of processing' model considered encoding factors based on 'process' instead of 'structures' unlike previous models.

The memory type that was investigated in this study is episodic memory. The traditional ways of investigating episodic memory in laboratory settings are free recall, cued recall, and recognition memory tests. In this thesis, behavioral and EEG data that was acquired by the former and present members of the METU Neurosignal Lab was analyzed in the context of the saccade-induced memory enhancement research program. The episodic memory paradigm that is used is a recognition memory test.

The main subject in this thesis is whether there is any effect of bilateral tactile stimulation on episodic memory and related brain areas. Throughout this goal, theoretical framework and analyses were done based on saccade-induced retrieval enhancement literature.

To understand saccade-induced retrieval enhancement, it would be better first to mention EMDR. EMDR, which is applied by using bilateral stimulation (BLS), is an innovative method for dealing with psychological disorders, especially mood-related ones. Standardized and structured methods of EMDR (Shapiro, 1989) have come to compete with other traditional psychotherapy techniques, such as cognitive and behavioral therapy (CPT), in terms of alleviating the symptoms. This method allows therapists to deal with symptoms of post-traumatic stress disorder patients who are characterized by emotionally dense traumatic memories. The main reason for episodic memory problems in post-traumatic stress disorder is that it breaks the transformation process from episodic memories to semantic memory.

After the promising results of EMDR in terms of retrieving traumatic episodic memories, which is the biggest problem in the therapeutic setting for PTSD patients (because patients couldn't retrieve those episodic memories, these traumatic memories aren't integrated into semantical memory), for last two decades, cognitive researchers started to investigate whether horizontal left-right alternating eye movements that are used in EMDR for facilitating the traumatic episodic memory retrieval could also enhance memory retrieval abilities outside of the therapeutic setting in healthy individuals. Following the first study (Christman, 2003) that found engaging voluntary horizontal saccadic eye movement prior to a task increased memory performance, this memory-enhancing phenomenon was replicated in many different experimental settings and by many different researchers. This phenomenon was later called Saccade-Induced Retrieval Enhancement (SIRE).

There are two main neuromodulatory explanations of the SIRE phenomenon: the Interhemispheric Interaction hypothesis and the (Christman, 2003) Top-Down Attentional Control hypothesis (Lyle, 2008). While interhemispheric interaction theory asserts that memory performance enhancement is caused by the increasing interhemispheric communication induced by saccadic horizontal eye movements, top-down attentional control theory argues that the reason for occurring SIRE effect is that eye movements increase the activation of frontoparietal brain areas that are responsible for top-down attention modulation, then these increased attentional controls catalyze the boost on the cognitive tasks. Although behavioral evidence supports both theories, more neuroimaging evidence still needs to be.

The typical independent variables of any SIRE research paradigm are stimulation type and subjects' handedness status. In the standard SIRE experiment, subjects are exposed to stimulation before the cognitive tasks, mainly in memory tasks. The stimulus used in this research paradigm could differ in terms of their modalities (visual, auditory, tactile). Considering the two theories that most studies are based on, visual stimulation was the most popular. However, in 2013, Nieuwenhuis conducted a recognition memory experiment using bilateral tactile stimulation. Furthermore, the SIRE effect was observed in tactile and visual stimulation, not auditory stimulation. These results were consistent with the interhemispheric interaction hypothesis. Since bilateral tactile and visual stimulations have only a contralateral effect on the brain; bilateral auditory stimulation also has ipsilateral and contralateral projections.

In this thesis, behavioral and EEG data come from an experiment that used bilateral tactile stimulation during memory retrieval. This experimental design had two novel benefits that differ from the other SIRE neuroimaging studies (Göktepe, 2017; Göktepe et al., 2017; Göktepe & Özkurt, 2020). This is the first experiment in which tactile stimulation was used as bilateral stimulation. Since EEG data were acquired during the memory retrieval, not before, like other SIRE studies, it allowed analyzing the direct effect of bilateral stimulation during the retrieval. In this thesis, my primary purpose was to investigate the behavioral and EEG data based on the two aforementioned theories.

The organization of the thesis is as follows; in Chapter 2, theoretical frameworks in the literature that are used in the thesis are explained (signal detection model of recognition memory and saccade-induced retrieval enhancement); in Chapter 3, methods and experimental procedures are explained; in Chapter 4 results are demonstrated; in Chapter 5, results are discussed based on the literature.

CHAPTER 2

LITERATURE REVİEW

2.1. Memory

Memory is not only one of the most studied topics of our cognitive sciences but also is a fundamental part of our everyday experiences from birth till the end of our lives. Human's ability to remember the past is, besides, to allow us to know who we are and what we do, providing to construct our personality and plan our future actions.

Cognitive psychologists have explained memory based on the learning process of information regarding three stages: encoding is the initial acquisition of sensory information; storage is keeping that acquired information over time; retrieval refers to accessing information from storage when there is a need (Melton, 1963). However, there is no one type of memory according to the proposed models of memory. From a wider perspective, the basic distinction between memory types is sensory memory, short-term memory (STM), and long-term memory (LTM) in terms of storage properties (Atkinson &Shiffrin, 1968). Fundamental differences between STM and LTM are based on their way of storing, storage capacity, and storage duration. STM has less storage capacity and shorter storage duration compared to LTM (Miller, 1956; Peterson & Peterson, 1959).
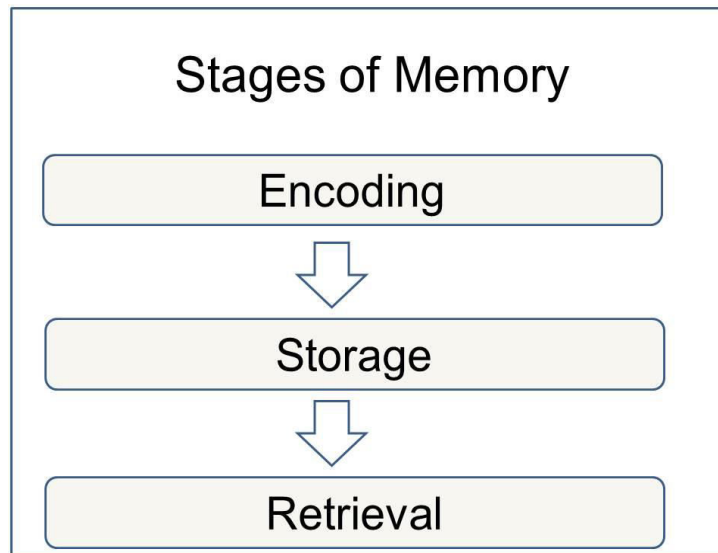
Figure 1. Three stages of memory adapted from Melton (1963).

2.1.1. Types of Memory

<u>Long Term Memory</u>

As mentioned in the previous section, there is no one type of memory. LTM differs from STM or working memory with its temporal characteristics. While STM or working memory had a very limited storage duration, LTM had theoretically unlimited duration time. The first and most prominent neurophysiological evidence of STM and LTM are separate systems coming from the H.M. case in the 1950s. In that clinical case, the patient abbreviated as H.M., underwent a temporal lobectomy operation which included removing his medial temporal lobe to treat his epileptic symptoms. As a result of that operation, H.M. experienced a long-term memory deficit (amnesia) with both retrograde and anterograde forms (Scoville & Milner, 1957). Although he was unable to form new memories in LTM, his ability to retrieve information in a short period of time (STM or working memory) was still intact. Although this distinction is quite useful for classifying memory, it was understood that there are also subsystems of the LTM system. In Figure 2, different long-term memory types are shown.

<div align="center">Declarative Memory</div>

LTM and STM distinction was based on temporal properties. However, LTM is not a monolithic construct, and it consists of several subcomponent systems. According to Squire and Zola Morgan (1991), the very first main distinction between LTM subsystems is the declarative (explicit) and non-declarative (implicit) distinction. This distinction is based on whether the memory information process is accompanied by conscious awareness or not. Nondeclarative memory is a memory subsystem that refers to the collection of learned information and outcomes that is not accessible for conscious awareness. Priming, classical conditioning, habits/skills (e.g., how to play basketball), and priming is the examples of non-declarative memory. By contrast, in declarative memory, learned and encoded information is accessible to conscious awareness. It consists of knowledge about facts or abstract concepts (semantic memory, the sum of the interior angles of a triangle) and personal experiences or events (episodic memory, remembering what you eat in the morning).

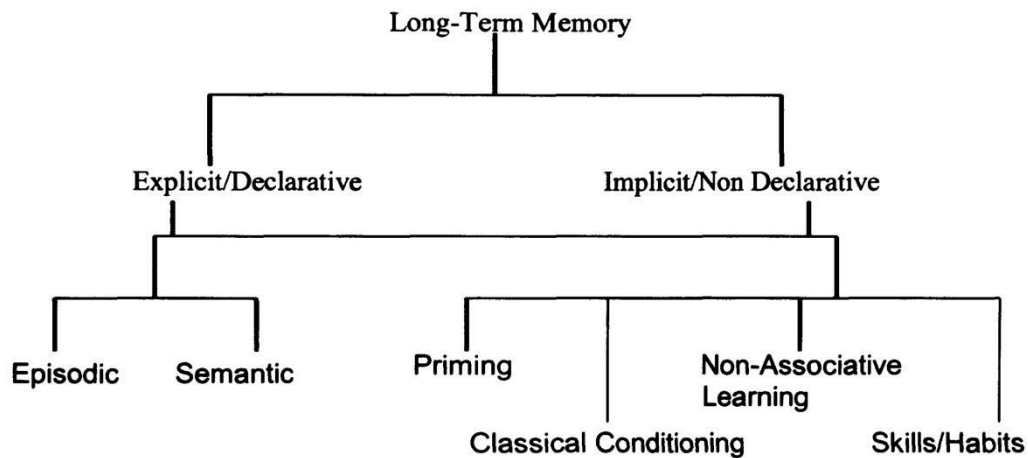
Figure 2. Different LTM types. Adapted from Squire and Zola Morgan (1991)

2.1.2. Models of Information Process

Contemporary models in memory information processes can be divided into the multistore model of Atkinson and Shiffrin (1968); the multi-component working model of memory of Baddeley and Hitch (1974); sleep-depending learning and memory consolidation models (Stickgold, 2004).

Atkinson and Shifrin's multi-store memory model (also called the modal memory model) had three components: sensory memory, short-term memory, and long-term memory (Figure 3). All perceptual input is captured by sensory memory stores in a very brief time. When a person pays her/his attention to any of these sensory store subsystems, then the sensory stimulus can be transferred into STM. Moreover, If the information in STM wasn't lost due to displacement or decay, it can be delivered to LTM.
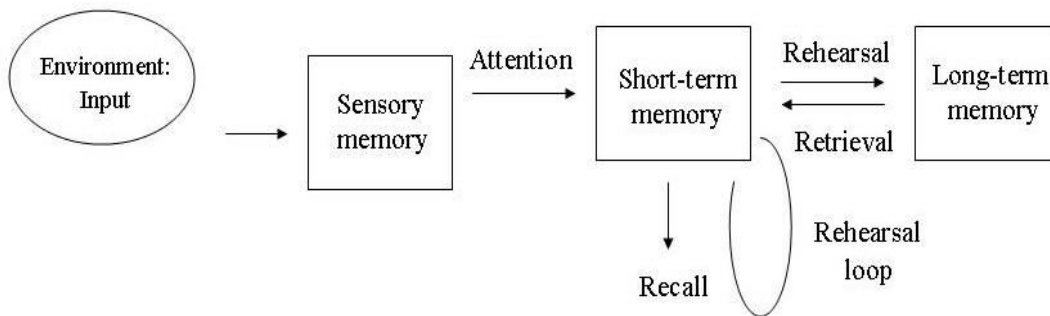
Figure 3. The modal memory model adapted by Atkinson and Shiffrin (1968)

Baddeley's conception of working memory is indeed a short-term memory. However, unlike Atkinson's modal memory model's single stored STM modeling, he suggested that STM comprises different subsystems for different types of information. According to the working memory model, there is their distinct memory storage: the central executive, phonological loop, and visuospatial sketchpad (Figure 3). The central executive is responsible for controlling and monitoring other subsystems in working memory and contributing to transferring the content of other subsystems into LTM. The central executive specified attention to controlling system properties rather than its storage capabilities (Baddeley, 1986).
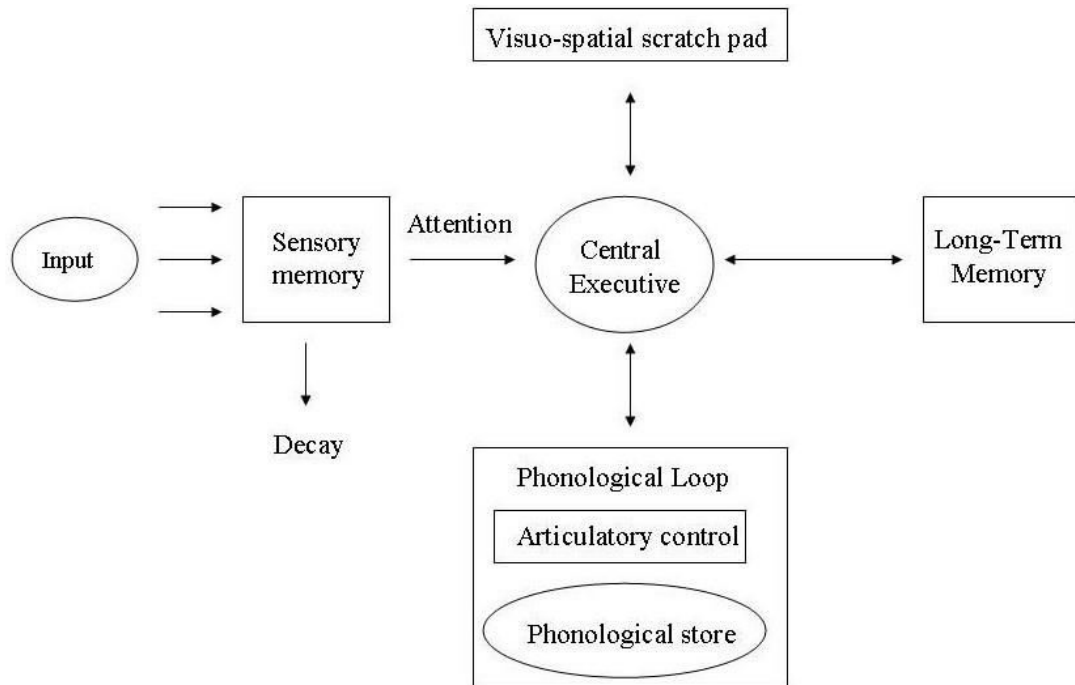
Figure 4. Working Memory Model adapted by Baddeley (1974)

2.1.3. Signal Detection Model of Recognition Memory

Recognition memory is a part of declarative memory that allows us to identify an object, people, and sounds previously encountered. In the laboratory setting, recognition memory is investigated by using the study and test paradigm. Although the experimental paradigm for evaluating the recognition memory could change according to research questions, it consists mainly of the following steps; first, subjects are asked to memorize the list of stimuli presented in the studying phase. In the second phase, participants are presented with 'old' stimuli that are presented in the studying phase and additionally 'new' stimuli (lures) that are not studied in the study phase. Then participants are asked to decide whether the presented stimuli are old (previously seen) or new. In the recognition memory experiment, there are four possible outcomes. The first outcome is 'hit', which is the correct identification of the previously studied item as 'old' in the test phase; the second is the false alarm, which is the wrong identification of the new (unstudied) item as 'old' item; third is the correct rejection that is the correct identification of unstudied 'new' item as 'new' item, and the fourth possible outcome is 'miss' that is the wrong identification of the old (studied) item as (new) item (Figure 5).

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Figure 5. Decision Matrix

One way of characterizing the recognition memory processes is by using Signal Detection Theory (Snodgrass & Corwin, 1988). According to the Signal Detection Theory account of recognition memory, recognition memory is characterized in terms of memory strength. In this framework, previously studied items and unstudied new items have their own probability distributions as a function of memory strength. While some stimuli have greater strength, others have less. When participants were asked to make a decision in the recognition memory task, they made their decision according to their decision criterion; subjects made an 'old' decision when their memory strengths were above their decision criterion, a 'new' decision when memory strength was below the criterion. Accordingly, four possible outcomes (hit, miss, false alarm, correct rejection) in the experiment occur through a combination of decision criterion and memory strength about stimuli which is depicted in Figure 6. If the side of decision criterion and memory strength of each stimuli type (studied and unstudied) are the same, hit and correct rejection occurs; if not, misses and false alarms occur.
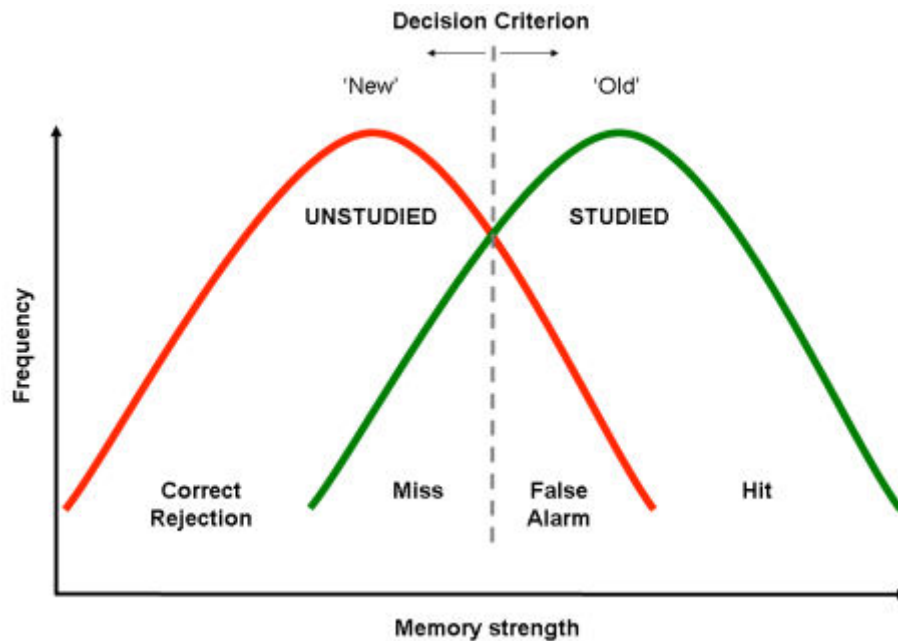
Figure 6. Signal Detection Model of Recognition Memory

Response bias and sensitivity are two measures that are used in many recognition memory studies. While sensitivity measures the subjects' ability to distinguish previously studied old items from the unstudied new items, response bias measures the subjects' tendency to respond 'old' in the case of uncertainty. In other words, response bias is a measure of where the decision criterion is placed in the memory strength distribution. If this decision criterion is high, it is called 'conservative response bias', which indicates subjects respond 'old' when they are only certain about the decision they made, and it reduces the false alarm rate. It also requires more attention because it demands extra cognitive comparison between studied and unstudied items. If the decision criterion is low, it is called 'liberal response bias'. In that case, subjects have a greater tendency to respond to items as' old' even when they are uncertain about it (low memory strength). The classification of response biases is depicted in Figure 7.

Figure 7. Response Bias Conditions

2.2. Saccade-Induced Retrieval Enhancement (SIRE)

After the effectiveness of EMDR therapy in diminishing various psychological symptoms gained a respectable amount of evidence in both the laboratory and therapeutic settings, some researchers speculated that if the exposure of saccadic eye movements 30 seconds before the therapeutic actions facilitated to cure of some impaired cognitive abilities, such as retrieving the traumatic memory, reducing its emotional effect, then maybe bilate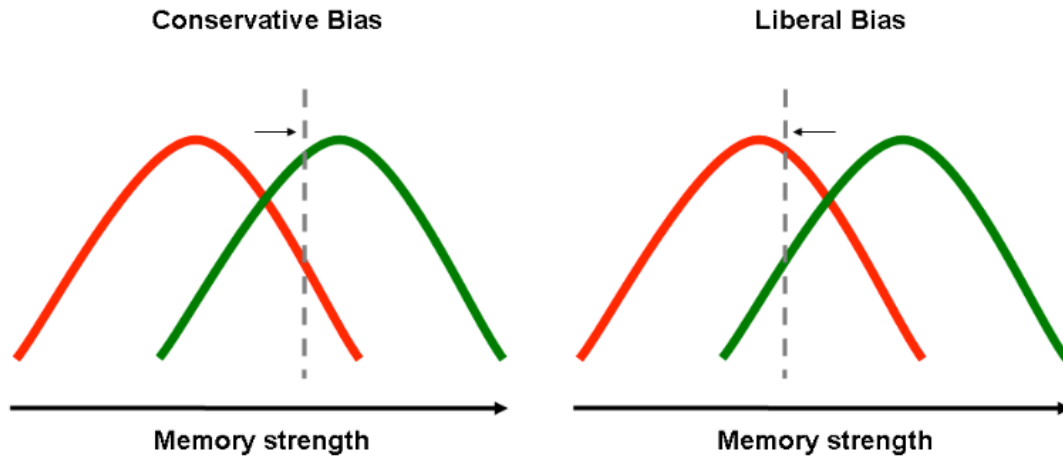ral stimulation that is used in EMDR therapy could also enhance cognitive abilities in a non-traumatic and neutral setting for healthy subjects. In 2003, Christman conducted pioneering research investigating the effects of bilateral saccadic eye movements on episodic memory retrieval with healthy participants. To test whether the bilateral horizontal saccadic eye movement enhances retrieval performance, he conducted a memory experiment that mimics EMDR therapy procedures. In that experiment, subjects studied 30 words in the study session, and then they were tested in both free recall and recognition tests. The experiment showed that subjects who engaged in bilateral saccadic eye movements had better results in both tests than subjects assigned to the control condition. After the promising results of this experiment, memory boost after the alternating bilateral stimulation (mainly bilateral visual alternated stimulus, but other kinds of modalities such as auditory and tactile had also promising results, see Nieuwenhuis, 2013) was termed as Saccade-Induced Retrieval Enhancement (SIRE). Moreover, the results of this memory boost were repeated in many different cognitive experiments (Christman et al., 2004; Lyle et al.,

2010; Lyle et al., 2008; Parker & Dagnall, 2012). In the following subsections, respectively:

1. Behavioral evidence of the SIRE phenomenon
2. Two proposed theories for explaining that phenomenon
3. Neuroimaging evidence for testing these two theories will be examined.

2.2.1. Behavioral Evidence of SIRE

The first study that the SIRE phenomenon is pronounced was Christman's experiment. In his experiment, participants are divided into (1) horizontal saccadic eye movement condition, (2) vertical saccadic eye movement condition, (3) smooth eye movement condition; one is horizontal, the other is vertical and lastly, (4) central fixation, which means no movement in the stimulus. Stimulus presentation for each was designed to mimic the therapeutic EMSR practices. Saccadic movements mimicked alternating dots in 500 ms intervals on the left and right side of the eye field. In the smooth eye movement condition (3), there was no saccadic movement; instead, smooth movement is presented for understanding the effects of saccadic vs. smooth movement. In the first experiment, he used a standard memory test. In that experiment, subjects are presented with 36 words in the study phase. Then after the study phase, subjects are informed to write as many remembered words as possible in the study phase. The experiment resulted in subjects assigned to horizontal saccadic eye condition (1) getting higher episodic memory retrieval performance compared to other conditions, and memory performance of other conditions was not significantly differentiated in the statistical sense. In the second experiment in that study, Christman investigated the effect of horizontal saccadic eye movements on autobiographical memory retrieval. Subjects were asked to make a diary and write the distinctive events for one week. After one week, subjects who performed saccadic eye movements got a greater recall rate compared to subjects who didn't perform saccadic eye movements.

Christman (2004) conducted a new study investigating the effects of saccadic eye movements on a false memory test. In false memory tests, subjects were presented with a list of words in the form of sounds that are closely related in the semantical sense. After listening to those words, subjects were asked to recall as many words as possible in the list. Because words are semantically related, lure words that are not in the list are falsely recalled, and memory performance was evaluated by the number of falsely recalled lure words that are not a member of the lists. According to the study's results (Christman, 2004), false recall rates in subjects who performed saccadic eye movement were lower than in subjects who did not perform.

In 2006, Christman designed a new experiment to explore horizontal saccadic eye movements' effects on early childhood memories. In that study, subjects are asked to remember the earliest memories after subjects are assigned to either horizontal saccadic eye movement condition or other conditions. The study resulted that the average age of remembering the earliest memory of subjects who were assigned to eye movement condition have significantly lower age than subjects who were assigned other conditions.

In 2007, Parker and Dagnall repeated the false memory experiment (Christman, 2004). They replicated the results of previous research by observing that reducing false memory rate in horizontal saccadic eye movement condition compared to vertical and other conditions. They also reported that subjects in horizontal saccadic eye movement increased their recognition rates compared to other conditions.

In 2008, Parker designed a two-phased study to look at the effects of horizontal saccadic eye movements on episodic memory using a recognition memory paradigm called to remember–know procedure. In that memory paradigm, after subjects are presented with the words or different kinds of stimuli during the retrieval phase, they respond with their retrieval judgment as either 'know' or 'remember' in the test phase. In that way, the 'know' answer represents the semantic aspect of the memory, and the 'remember' answer indicates its episodic aspect. They found that subjects who were assigned to the horizontal saccadic eye movement condition had a superior performance than subjects with no eye movement condition, with higher hit responses and lowered false alarm responses. In the second experiment, they also found that the horizontal saccadic eye movement condition has superior to retrieving the object location and color of the presented stimulus compared to other conditions.

Lyle (2008) conducted two experiments to see the effect of eye movement on memory tasks by elaborating research with handedness conditions (left-handers, right-handers, and mix-handers. Hand issue is essential for explaining the underlying mechanism of SIRE. Because corpus callosum volumes are greater in left-handers than right-handers, right-handed individuals should benefit more from the SIRE effect than left-handed individuals. (Chirsitman, 2008)). In the first experiment, he found that horizontal saccadic eye movement performance-enhancing effects of memory retrieval occurred in right-handed individuals compared to other conditions. In the second experiment, contrary to other experiments, he found memory performance boosts not only in subjects who assigned 'horizontal' saccadic eye movement condition but also in subjects who assigned 'vertical' saccadic eye conditions.

In 2013, Nieuweunhuis designed memory experiments that investigated how the bilateral stimuli type effect the outcomes of memory performance. In his experiment, he used bilateral visual stimuli, bilateral auditory tone, and bilateral tactile stimuli. The

study resulted that memory enhancement occurred in visual bilateral saccades and bilateral tactile stimulation.

Samara (2011) investigated the effect of SIRE in the context of whether there is a difference in recall performance depending on the recalled world's emotional content. In the experiment, subjects are given to recall both emotional and neutral words in the study session. It is observed that the increase in memory performance happened just in emotional words, not in neutral words.

2.2.2. Explanations of SIRE effect

Although the retrieval enhancement after bilateral saccadic movement has been investigated and replicated in a great deal of different research, the underlying mechanism of such an enhancement still needs to be discovered. There are two main hypotheses: the interhemispheric interaction hypothesis (Christman, 2003) and the top-down attentional control hypothesis (Lyle & Edlin, 2015).

Interhemispheric Interaction Hypothesis

The interhemispheric Interaction hypothesis was first proposed by Christman (2003) after he discovered the first episodic memory enhancement phenomenon after horizontal saccadic eye movements. According to the interhemispheric interaction hypothesis, the neuromodulatory mechanism behind boosting the effect of episodic memory retrieval performance after left-right alternating saccadic eye movements is that alternating saccades enhance the inter-hemispheric activity between hemispheres that have not interacted that much before saccadic eye movements. More straightforwardly, bilateral stimulation creates activity in contra-lateral brain areas, and increased activity in contra-lateral hemispheres facilitates the retrieval processes in responsible regions by increasing communication with other hemispheres. Indeed, the main reason he focuses on increasing communication between hemispheres is the functional asymmetries in the brain regions responsible for memory encoding and retrieval processes. That functional asymmetry issue is vital. Because the interhemispheric interaction hypothesis on saccade-induced retrieval enhancement was grounded on the hemispheric encoding–retrieval asymmetry model (HERA) (Tulving, 1994) and cortical asymmetry of reflective activity (CARA) model (Nolde, 1998). According to the HERA model, while 'encoding of episodic memories' is executed mainly through the activity on the 'left' prefrontal areas, the 'right' prefrontal areas increase their activity in the 'retrieval' process of episodic memory. However, although the main literature on lateralization on episodic memory is based on the relationship between memory retrieval and the right prefrontal cortex, in 1998, Nolde suggested that left prefrontal cortex activity could also increase in the retrieval process when the memory retrieval tasks demand reflective thinking due to

complexity of it. In brief, horizontal saccadic eye movements (or other stimulation techniques that induce contralateral brain activity) give rise to an increase in the communication between both hemispheres (or equalize the brain activity) by stimulating contra-lateral brain regions (prefrontal areas), then this increased communication between brain regions support episodic memory retrieval process in memory tasks that require reflective and effortful cognitive processes.

Although the inter-hemispheric interaction hypothesis promises a very consistent explanation of the SIRE phenomenon by building its foundation based on empirically reliable hemispheric encoding retrieval asymmetry (HERA) and cortical asymmetry of reflective activity (CARA) models, this explanation wouldn't be adequate, it would be indeed unsuccessful, if horizontal saccadic eye movement didn't induce a contralateral increased activation as Christman (2003, 2008) have argued for it. His argumentation of inducing increased interhemispheric activity by engaging horizontal eye movements has been based on mainly three clusters of empirical evidence:

(1) The first cluster of evidence comes from studies examining the relationship between lateral eye movements and contralateral brain activities. According to that studies, lateral eye movements equalize the alpha band activity on contralateral hemispheres (Bakan & Svorad, 1969). Moreover, Christman (2001) showed that hemispheric asymmetries were reduced when subjects performed left-right saccadic eye movements.

(2) The second cluster of evidence is coming from the studies that support the increasing interhemispheric activation after the contralateral stimulation and which correlates between hemispheric activation and corpus callosum, which is the interaction pathway of the different hemispheres. Some studies show that one hemisphere has a greater activation level than the other hemisphere (Klein & Armitage, 1979). Furthermore, mixed-handed individuals (people who use both hands efficiently) have larger corpus callosum (Luders, 2010). Moreover, studies showed that mixed (inconsistent) handed individuals have outperformed in various memory tasks compared to consistent handers (people who consistently use one specific hand).

(3) The last cluster of evidence comes from the REM sleep physiology and REM sleep and memory relations (Stickgold, 2002). According to research, movements of the eye during REM sleep are mainly horizontal (Hansotia, 1990), and interhemispheric coherence level also increases in the REM sleep cycle (Nielsen, 1990). Moreover, Stickgold explains the EMDR effectiveness in episodic traumatic memory retrieval enhancement in PTSD by making a connection with bilateral stimulation of EMDR mimicking eye movements of REM sleep. He connects this idea by considering the memory consolidation effect of REM sleep. Sleep-dependent memory consolidation theory states that in the nonREM stage of sleep, activations are mainly from the

hippocampus to the neocortex, which functions for transferring episodic memory to semantic memory; in REM sleep neocortex to the hippocampus, which functions for integrating episodic memories to semantic memories. According to Stickgold (2002), the main reason why EMDR has a positive effect on remembering traumatic memories is that it alleviates the negative aspect of traumatic episodic memory by turning it into more semantic content by mimicking REM sleep through the activation of similar areas.

Consistent with the hypothesis and its assumptions, the main independent variables in the SIRE research program are handedness (inconsistent-consistent, or in another terminology strongly right/left-handed – weekly right/left-handed) and the visual stimuli type (horizontal saccadic, vertical saccadic, and smooth). According to the hypothesis, firstly, only horizontal saccadic eye movements should increase memory performance compared to vertical or smooth movements (not saccadic) because only horizontal saccadic ones cause interhemispheric interaction. Secondly, consistent handers (left or right) should benefit more from the left-right horizontal movements on memory performance compared to inconsistent handers who have larger corpus callosum because inconsistent handers already have a maximum limit of their interhemispheric interaction limits due to their larger corpus callosum.

Top-Down Attentional Control Hypothesis

After the lack of neuroimaging evidence of any horizontal or bilateral stimulation failed the show any interhemispheric interaction indexed by EEG coherence and inconsistencies of the effect of vertical and horizontal eye movement manipulations in SIRE researchers, which interhemispheric interaction hypothesis assumed that there is just memory retrieval enhancement occur in horizontal saccadic eye movements, not vertical ones, Lyle (2008, 2015) have tried to explain SIRE phenomenon based on attentional components by abandoning the interhemispheric interaction theory. According to this theory, SIRE effects occur not because of interhemispheric interaction but because of the effect on frontal eye fields and parietal sulcus, part of the frontoparietal attention network that is responsible for top-down attentional control (Corbetta,2002). Furthermore, its effect is not limited to memory tasks but also other cognitive tasks such as attention. These activations facilitate the cognitive performance of subjects when tasks are required more cognitively demanding. In that context, saccadic eye movements should increase the more challenging task like free recall but should not affect less cognitively demanding tasks such as recognition.

According to this view, there should be no importance on the direction of the eye movement (vertical or horizontal). Moreover, some studies showed that vertical eye movements also enhanced memory performance (Edlin, 2008; Lyle, 2008). In 2013, Lyre directly tested his hypothesis with an attention test, and the study showed that eye

movements also enhance attention processes. In another study, he tested whether eye movement enhances memory performance depending on the test difficulty. According to his theory, eye movements should increase performance when the task is difficult that demands more cognitive control. Results showed that SIRE effects occurred only in the more challenging task (Lyle,2015).

2.2.3. Neuroimaging Evidence

Starting with Christman's (2003) study and its interhemispheric interaction hypothesis, the memory-enhancing effect of bilateral eye movements was replicated by many researchers in different experimental settings and paradigms. However, the neuroimaging studies haven't had the same success in showing evidence for the hypothesis of the interhemispheric interaction model. Indeed, all of the neuroimaging studies failed to find any cue for supporting bilateral stimulation to increase interhemispheric communication. Moreover, some studies showed that there is a decrease in EEG interhemispheric coherence instead of an increase.

The neuroimaging studies on the effect of Bilateral stimulation could be classified into two areas. While the first group focuses on directly Saccade-Induced Retrieval Enhancement research program (Propper,2007; Samara, 2011; Fleck, 2018) other group investigated neuroimaging data in the context of EMDR (Keller, 2014; Yaggie, 2015).

The first neuroimaging study in the SIRE research program was done by Propper (2007) to test the interhemispheric interaction hypothesis to find a piece of evidence for interhemispheric interaction in an EEG coherence form. In that experiment, they take EEG recording in eyes open and closed baseline without any eye movement, and then, eyes open condition subjects are asked to follow the saccadic stimuli in the computer. Also, the experiment was performed between-subject design. However, they found a decrease in EEG coherence between Fp1 and Fp2 channels in the gamma frequency band (35 – 54 Hz) instead of any increase in coherence.

In the second study, Samara (2011) designed an experiment in a within-subject fashion. In that study, the EEGs of participants are recorded before and after the emotional and neutral recall task. Only the SIRE effect was observed in the emotional memory recall task. EEG analyses are done using homologous electrodes. However, the results of EEG coherence, like previous research by Propper (2007), failed to show any increase in interhemispheric coherence. Instead, the only change in EEG coherence occurred in FT7 and FT8 in alpha frequency, but like other studies, there was a decrease in horizontal eye movement condition.

After Lyle (2008, 2015) proposed the top-down attentional control theory, evidenced by the research that showed the bilateral eye movements enhancing effect on a test that measures executive attention (ANT-R, attention network test), Fleck (2019) designed an event-related potential study in EEG. In this study, they showed that alongside bilateral eye movements' positive effect on cognitive performance, they have also observed N100 and P200 ERP component modulation due to bilateral eye movements. Lastly, Fleck (2019) found a delta band power reduction in subjects in bilateral eye movement condition compared to the control condition.

There are two other studies that the interhemispheric interaction hypothesis tested in similar to the EMDR setting that simulates the therapeutic procedures. In 2014, Keller investigated the interhemispheric coherence difference in an experiment in which subjects were asked to retrieve positive childhood memory. In this study, researchers again failed to find evidence for the assumption of the interhemispheric interaction hypothesis. In 2015, this experiment was repeated by Yaggie in a setting where subjects were asked to retrieve negative memories instead of positive memories. Researchers again failed to show any increase in coherence that indicates the existence of interhemispheric interaction.

2.3. ERP Components

2.3.1. N100 Components

The N100 component is a negative-going waveform that peaks at about 100 ms. Previous studies revealed that it is modulated by attention-related cognitive processes. One of the characteristics of this ERP component is that its amplitude covaries with the increased attention (Luck, 1993; Rugg, 1987). In addition, the N100 component is modulated when subjects increase their attention to visual stimuli (Hackley, 1990). This component also has decreased by vigilance and arousal-related factors such as sleep deprivation (Morgas, 2009) and sleep onset (Weitzman & Kremenn, 1965).

2.3.2. P200 Components

P200 is an early ERP component that reaches its peak latency from 100 ms to 200 ms and is maximal over parietocentral brain areas. Like the N100 ERP component, P200 is also a component that is indexed by attentional and top-down modulatory functions. Unlike the N100 component, the attentiveness level of subjects reveals a decrease in its amplitude (Crowley, 2004). In parallel with this modulatory behavior of the P200 component, its amplitude increases with age because the capacity to use attentional resources decreases depending on age (Pfefferbaumet, 1998).

2.3.3. LPC (Late Positive Component)

The late positive component is a positive-going waveform in the time interval between 500 ms and 1000. LPC is one of the well-studied event-related components in the studies related to episodic memories. Especially in study phase design recognition memory experiments, LPC is thought of as a neural marker of the process of recollection (Allan,1998).

2.4. Research Questions

(1) Studies indicate that exposure to left-right saccadic eye movement before retrieval induces memory retrieval enhancement or with an area-specific name, SIRE, which manifests itself by increasing recall, and recognition rates and decreasing the false recall and miss rates. Although most studies focused on vertical eye movements as a bilateral stimulus, some studies showed bilateral tactile stimuli also have a memory-boosting effect (Nieuwenhuis, 2013). Accordingly, the first research question is whether the SIRE will be replicated in bilateral tactile stimulation manifesting itself by increasing hit and correct rejection rates and reducing miss and false alarm rates.

(2) According to Christman, this memory boost is induced by the temporary increase of the interaction (indexed by interhemispheric EEG coherence) between hemispheres through bilateral stimulation. Although most of the SIRE studies are applied based on that theory, there was no evidence for increasing EEG coherence (rather, studies showed there is a decrease) (Propper et al., 2007; Samara et al., 2011; Keller, 2014; Yaggie, 2015; Fleck, 2018). But all neuroimaging studies in SIRE studies recorded the EEG independent of the task (just eyes open and closed, not Event-Related). In that study, EEG was recorded during the episodic memory task, which is a greater opportunity to test the interhemispheric interaction hypothesis compared to other studies that test this hypothesis. Hence, the second research question is whether bilateral tactile stimuli increase interhemispheric EEG coherence during retrieval.

(3) After the lack of neuroimaging evidence for the interhemispheric interaction hypothesis, Lyle (2008, 2015) introduced the Top-Down Attentional Control hypothesis, which indicates that this memory boost occurs because the bilateral stimulus activates the brain areas that control the top-down attention (frontoparietal attention network). Fleck (2019) showed that vertical eye movements have a neuromodulatory effect on N100 and P200 ERP components in an attention task. Moreover, Ciaramelli (2008) proposed a theory about the role of top-down attention on episodic memory retrieval, which asserts that brain regions that are responsible for top-down processes allocate required attention to brain regions that are responsible for memory retrieval. If so, bilateral stimuli should increase the capacity of top-down attention, which is indexed by

the N100 and P200 ERP components. Finally, the last research question is whether bilateral tactile stimulation modulates the top-down attention-related N100 and P200 ERP components.

CHAPTER 3

MATERIALS AND METHODS

3.1.Data and Participants

The EEG data that is used and analyzed in this study was acquired previously by the staff of the METU Neurosignal Lab (Göktepe, 2017; Göktepe et al., 2017; Göktepe and Özkurt, 2020). Besides the EEG data acquisition, the experimental paradigm design and the experimental stimuli implementation were realized by the same staff. Additionally, the design and procedures of the experiment were authorized by the METU ethical committee.

In the conducted experiment, 21 (male = 10, female = 11) volunteer university students were recruited for the experiment. Participants had no psychopathological background or visual disturbances. The range of the participants' age was between 18 and 30 (mean and standard deviation of age = 23.45 ± 1.39). Each participant signed the consent form before the experiment. Each participant was carefully informed not to take drinks that can contain alcohol, drugs, and caffeine substance. Only one participant was included in the experiment at a time, and it was ensured that the participants did not interact with each other during the experiment.

There are 336 randomly selected neutral human faces used as visual stimuli to create visual episodic memory representation for participants in the experiment. Human face images were presented to the participants for each experimental session (encoding and recognition sessions). These human face images were taken from the Chicago face database (Ma, Correll, & Wittenbrink, 2015) and stratified according to ethnicities and genders. In stimuli presentation, the white background is used for all images that are centered on the screen, as shown in Figure 8.

Figure 8. Examples of Stimulus

3.2. Experimental Setup and Paradigm

In the designed experiment, there are two conditions: bilateral tactile stimulation (BLS) and control conditions. These conditions were applied to the participants within subject design. No stimuli or inhibitors were applied to the subjects in the control condition. The NeuroTek Tac/AudioScan device was used to create a bilateral tactile stimulus for BLS conditions that is also widely practiced in Eye Movement Desensitization and Reprocessing (EMDR) therapies.

There were two stages of the experimental paradigm as encoding and recognition (Göktepe, 2017) using ready-to-use libraries in Matlab R2014a Psychophysics Toolbox Version 3. All of the responses were obtained using human faces as visual stimuli displayed on a 21-inch computer screen standing 90 centimeters away from the participants. Responses were collected via using the Logitech Wireless Gamepad F710 gamepad.

In the encoding session, 240 human face images randomly selected from different races were shown to the participants by stating that they would be asked to remember these images later. Each trial begins with 1 second of the fixation cross and continues with the face image presentation in 4 seconds. In the third phase, the question was asked as to which race the human faces showed belonged to. Lastly, 4 seconds of math quiz were asked to participants in order to decrease the recency effect and to rectify the cognitive load. Subjects were supposed to respond as "correct" or "wrong" according to the result

of the generated simple math questions. The response time of subjects was limited to 4 seconds. They did not need to answer all the questions.
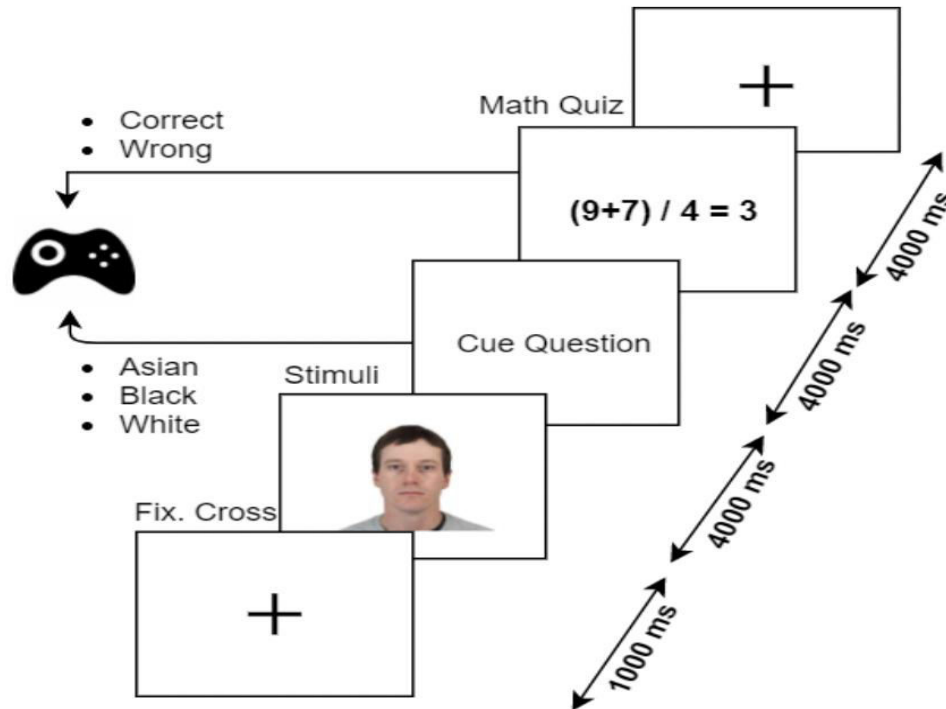

Figure 9: Demonstration of an encoding part.

The one-minute EEG data were recorded to generate a baseline after one hour break after the encoding session. The aim of creating a baseline is to detect subject-specific biased data like physiological noises and specify background activity for each subject separately to prevent group data from being impacted by bias. The BLS condition was applied in this session using NeuroTek Tac/AudioScan device, which produces a bilateral tactile stimulus. In addition to the 240 old human face images used in the encoding session, 96 new human face images were shown to the participants.

In the recognition session, participants had to respond whether the presented human faces on screen, had -been previously encountered while the bilateral tactile stimulus was applied to their hands for the BLS condition. The control condition was free of any stimulus in this session. The recognition session begins with stabilization and presentation like the encoding session. The next step, unlike the encoding session, continues by asking the participants the question "Have you seen this person before?". The trials took 9 seconds, and like the encoding session, the response time of subjects was limited to 4 seconds.
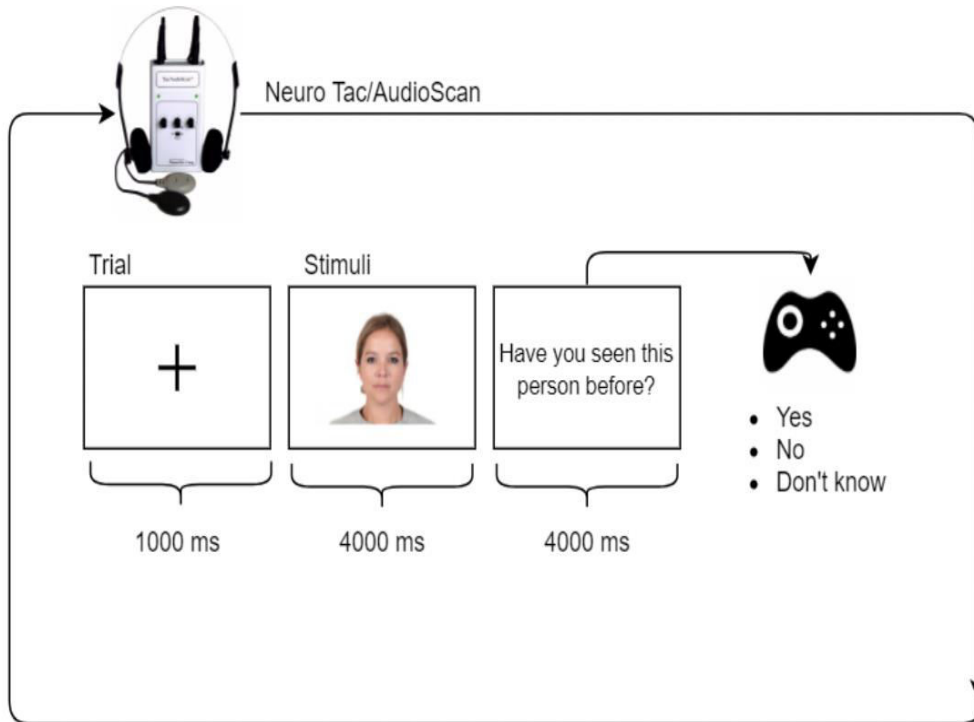
Figure 10: Demonstration of recognition part.

3.3. EEG Measurement and Procedure

Easy cap 32 Channel Standard EEG Recording Cap, which helps to control electrode replacement efficiently, was used in the experimental setup and the "Easy Cap Installation" manual was followed to place electrodes properly. According to this manual, caps should be fitted to the subject so that the electrodes are located properly, and the impedance level should be minimized. The central electrode was placed in the middle of the head and settled during the mounting process. The electrodes were cleansed with alcohol and placed as stated in the 10/20 universal placement system.
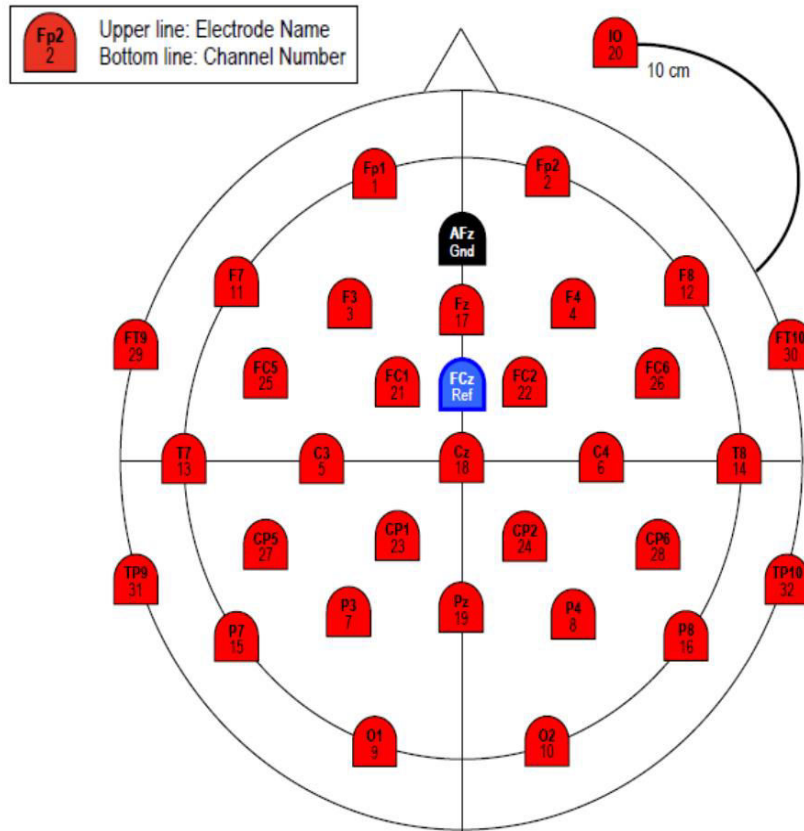
Figure 11: Standard EEG Recording Cap

Faraday cage was used to block electromagnetic and acoustic fields during EEG recording. A 32-channel Brain Amp System (10/20 universal system) was used for converting AC signals to DC signals. The sampling frequency was 1000 Hz. The impedance level was reduced to under 10k with the methods specified in the "Easy Cap Installation" guide. For detecting eye movements both vertical and horizontal, Electrooculogram (EOG) was utilized.

The experimental procedure was operated as follows:

Subjects were trained in 1-minute sessions in Faraday cage. Subjects answered questions by looking at 240 human face images on the screen using the gamepad. At the end of this part, a 1-hour break was given. The EEG preparation continued during the break.

After the break, the process began with a one-minute EEG recording to extract the baseline. Then in the recording session, all answers were collected via a gamepad during EEG recording. At the end of this session, the experimental process was finalized, and EEG devices were removed from the subjects.

3.4. Data Analysis

3.4.1. Behavioral Analysis

For behavioral data analysis, all participants' probability rates were calculated for all cases, i.e., hit rate, miss rate, correct rejection rate, and false alarm rate. Probability rates were calculated with the following formulae:

P(hit) = number of hits/number of signal (old) trials

P(miss) = 1 - P(hit)

P(false alarm) = number of false alarms/number of noise (new) trials

P(correct rejection) = 1 – p(false alarms)

Then sensitivity analyses were realized to see how successful the subjects were to discriminate the old (studied) item from the new (unstudied) item. To extract sensitivity values, previously calculated hit rates and false alarm rates were normalized and transformed into a z-score for each one. Then z transformed hit rate was subtracted from the z-transformed false rate. Greater values indicate higher discrimination for each task:

sensitivity = z[P(hit)] – z[P(false alarm)]

Response biases were calculated following the formula (z stands for z-score);

response bias = -1/2 * [z(P(hit)) + z(P(false alarm))]

3.4.2. EEG Analysis

15 subjects out of 21 subjects were selected for subsequent analysis. One of them was excluded because the bilateral tactile stimulation device did not work properly (only one side of the device worked), and the other five subjects were excluded due to the large noise observed within their data.

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EEG Preprocessing

MATLAB with Fieldtrip package was used for analysis. Raw EEG recordings were bandpass filtered for the range of 0.2 -100 Hz 4th order Butterworth filter. Then, the filtered data were segmented according to conditions. In the next step, ICA was applied to remove the eye artifacts and muscle artifacts. Because episodic memory retrieval was the main focus of this thesis, only hit trials were selected for further analysis. The range of trial numbers of hits for the BLS condition was between 35 and 96 (mean and standard deviation of hits trial numbers = 58.86 ± 21.17) and for the control condition, it was between 34 and 99 (mean and standard deviation of the number of hit trials = 58.86 ± 19.89).

ERP Analysis

ERP analysis focused on the temporal and spatial aspects of mean amplitudes assumed to be induced by attention and memory-related cognitive processes. Time windows for ERPs were decided through visual inspection. The time windows used in the following analysis paralleled with the previous attention studies. Peaks for N100, P200, and LPC corresponded to time windows of 60–124ms, 124–190 ms, and 750–1000 ms, respectively. Mean ERP amplitudes were created by taking averages of ERP waveforms for both BLS and control conditions during episodic memory retrieval. The time interval of [-200-0 ms] was used for baseline correction for each time window. Mean amplitudes for both N100 and P200 components were obtained for frontal regions (F3, Fz, F4), central regions (C3, Cz, C4), and parietal regions (P3, Pz, P4) along with their lateralization aspects. For repeated measures ANOVA analysis, mean amplitude values for each ERP window were analyzed 2 conditions (BLS and Control) X 3 region (frontal, central, and parietal) X 3 lateralization (left, midline, right) with Greenhouse-Geisser corrected for violation of sphericity assumption if it is necessary.

EEG Coherence Analysis

The main hypothesis of the interhemispheric interaction hypothesis is that after the bilateral stimulation, communication between hemispheres increases, and then this increased communication facilitates episodic memory retrieval. To test that hypothesis, both amplitude and imaginary coherency values were calculated between the control condition and BLS condition during the successful retrieval (hit and correct rejections) (4 seconds). Channels were selected based on their opposite pairs. Selected channels were Fp1 – Fp2, F3 – F4, FC3 – FC4, C3 – C4, CP3 – CP4, P3 – P4, O1 – O2, F7 – F8, FT7 – FT8, TP7 – TP8 and P7 – P8. Seven frequency bands were selected for analyses: delta (1 – 3 Hz), theta (4 – 7 Hz), alpha (8 – 13 Hz), beta (14 – 28 Hz), lower gamma (29 – 44 Hz), and upper gamma (45 – 90 Hz).

Both amplitude and imaginary coherency were calculated. Imaginary coherence is practical, especially for analyzing the functional connection without affecting the volume conduction problem (Nolte, 2004). It is calculated as the imaginary part of the normalized cross spectrum as shown in the formula:

$$icoh_{xy}(f) = \text{imag}(\frac{\langle s_{xy}(f)\rangle_n}{\sqrt{\langle s_{xx}(f)\rangle_n \langle s_{yy}(f)\rangle_n}}),$$

where S_{xx} and S_{yy} denote the autospectra, while S_{xy} denotes the cross spectra.

In order to see the effect of BLS, coherence values in BLS and control condition were compared, and paired t-test was used. False discovery rate was used for hypothesis testing to deal with the multiple comparison problem by applying the Benjamini and Hochberg procedure (Benjamini and Hochberg, 1995). It was calculated as shown in the formula:

FDR = FP / (FP + TP)

where FP is false positive, and TP is true positive.

CHAPTER 4

RESULTS

4.1. Behavioral Results

Mean probability values for memory performances, sensitivity, and response bias values for both the BLS condition and control condition are shown In Table 1. At the first glance, there is almost no difference in the hit rate between the BLS condition and the control condition, but the false alarm rate of the BLS condition is lower than the control condition. Extended analyses for both memory performance and reaction time are in the next sections. In performance metrics, the sensitivity of the BLS condition is higher than the control condition, which indicates BLS manipulation increases the subject's discrimination of 'studied' face pictures from 'unstudied' face pictures. The response biases of the BLS condition are also higher than the control condition indicating that the BLS condition is more conservative than the control condition.

Table 1. Mean and Standard Deviations Performance Metrics

Probability	BLS	Control
Hits	0.55 (±0.18)	0.54 (±0.19)
False Alarms	0.76 (±0.1)	0.81 (±0.15)
Correct Rejections	0.24 (±0.1)	0.19 (±0.15)
Misses	0.45 (±0.18)	0.46 (±0.18)
Performance Metrics		
Sensitivity (d')	- 0.620 (±0.691)	- 0.843 (±0.991)
Response Bias (c')	- 0.431 (±0.232)	- 0.596 (±0.232)

4.1.1. Performance Results

Mean probabilities and standard errors of responding as 'old' for studied faces (hit rate) and unstudied face stimuli are shown in Figure 12. Similarity of hit rates shows that there is no SIRE effect. Although there is a very high false alarm rate for both conditions, there is a slightly reduced false alarm rate in the BLS condition than the control condition.
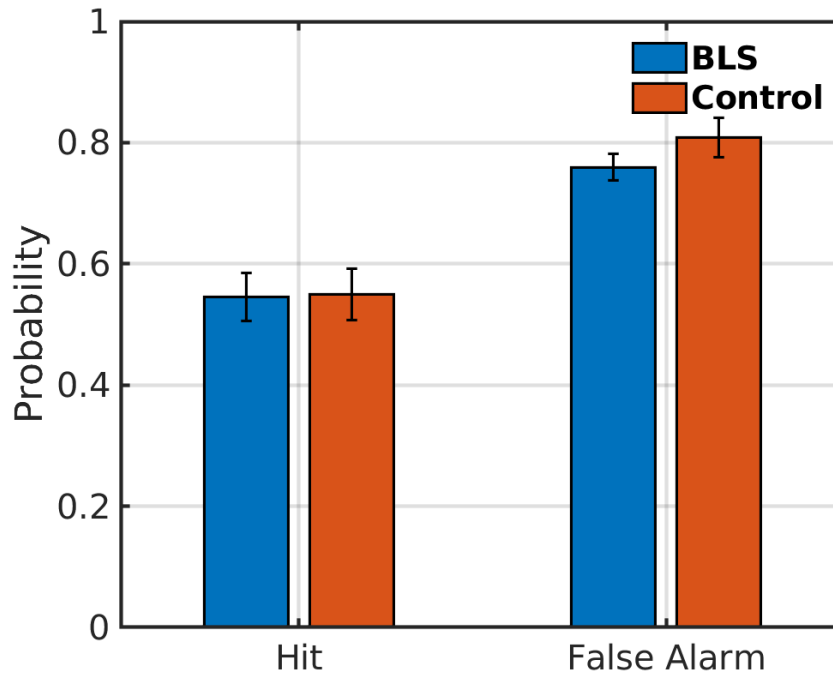
Figure 12. Mean Probability Values with standard errors

Considering the memory retrieval aspect of the SIRE, the hit rates of subjects in the BLS condition should be greater than the control condition, and the false alarm rates of subjects in the BLS should be fewer than the control group. To see whether there is a difference between conditions, two-way repeated ANOVA was done using factors condition (BLS/ control) and status (hit / false alarm).

The repeated measures ANOVA revealed that there is no main effect of the condition [$F(1,19) = 2.124$ p = 0.161]; there is a main effect of status [$F(1,19) = 18.232$ p < 0.001] and no interaction effect [$F(1,19) = 0.810$ p = 0.379]. Results reflect that there is no SIRE effect on hit rates and false alarm rates.

Statistical analysis shows that the probability rates were not modified by experimental manipulation. However, just an analysis of the probability values may not be adequate to show the whole picture of the memory performance by BLS. Regarding that, we analyzed the Signal Detection Theory (SDT) metrics. As explained in the method and literature review sections, 'discriminability' (sensitivity) measures the ability to discriminate previously 'studied' face pictures from the 'unstudied' face pictures, and 'response bias' measures how likely subjects respond 'old' when they aren't sure about the decision they will make. To see the true effect of the BLS manipulation according to SDT, sensitivity metrics were computed. Mean sensitivity values for each condition are

shown in Figure 13. To analyze the BLS effect in sensitivity, the paired t-test was computed. Results showed that there was no difference in sensitivity between the BLS condition and the control condition [t(19)= 1.32; p=0.202].
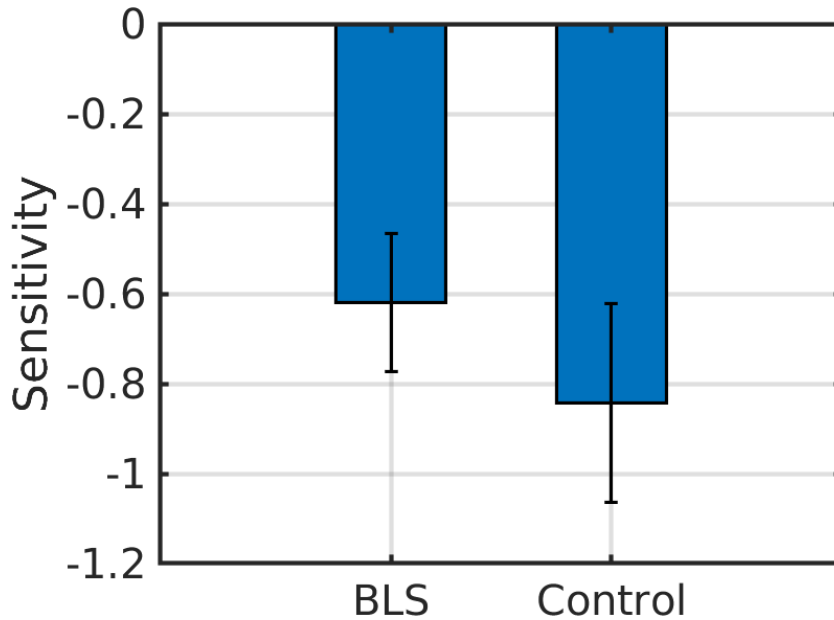

Figure 13. Mean Sensitivity Values with standard errors

Figure 14. shows the mean response bias values for BLS and Control conditions. Although the response bias values of each condition look negative which indicates both conditions have a liberal bias, the response bias value of the BLS condition is less negative than the control condition. It indicates that the response bias of the BLS condition is more conservative than the Control Condition. For investigating whether the BLS condition modulated response biases, paired t-test was conducted. Results showed that subjects exposed to BLS have statistically significantly more conservative response biases than those exposed to no BLS [t(19)=2.25; p <0.05, Cohen's d = 0.503].
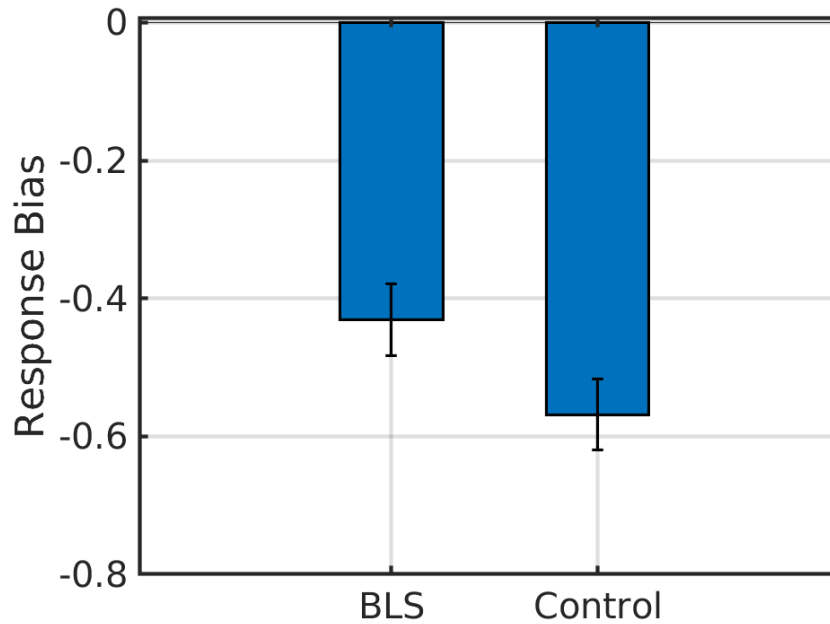
Figure 14. Mean Response Bias Values with standard errors (p <0.05, the response bias of the BLS condition is higher than the response bias of the control condition.)

4.1.2. Reaction Times

Reaction times of BLS manipulation and control condition in each memory performance metric are plotted in Figure 15. The mean and standard deviations of each condition are shown in Table 2.

Table 2. Mean and Standard Deviations of Reaction Times (s)

Reaction Time	BLS	Control
Hits	0.487 (±0.138)	0.489 (±0.228)
False Alarms	0.559 (±0.225)	0.526 (±0.285)
Correct Rejections	0.549 (±0.166)	0.578 (±0.330)
Misses	0.599 (±0.234)	0.525 (±0.234)

To investigate whether the BLS condition has any effect on reaction times, two-way repeated ANOVA was done using factors condition (BLS/ Control) and status (hit / false alarm/correct rejection/ misses). The repeated measures ANOVA revealed that there is no main effect of the condition $[F(1,19) = 2.249\ p = 0.624]$, there is a main effect of status $[F(3,57) = 3.9222\ p < 0.05]$ and no interaction effect $[F(3,57) = 0.0199\ p = 0.241]$. Post hoc analysis for status revealed that reaction times of hit responses (M=0.488) are significantly faster than miss responses (M = 0.562) (t = -3.6575, p<0.05) reflecting that subjects have faster reaction times when correctly retrieved than when they failed to retrieve. No effect of BLS condition on reaction times could be found.
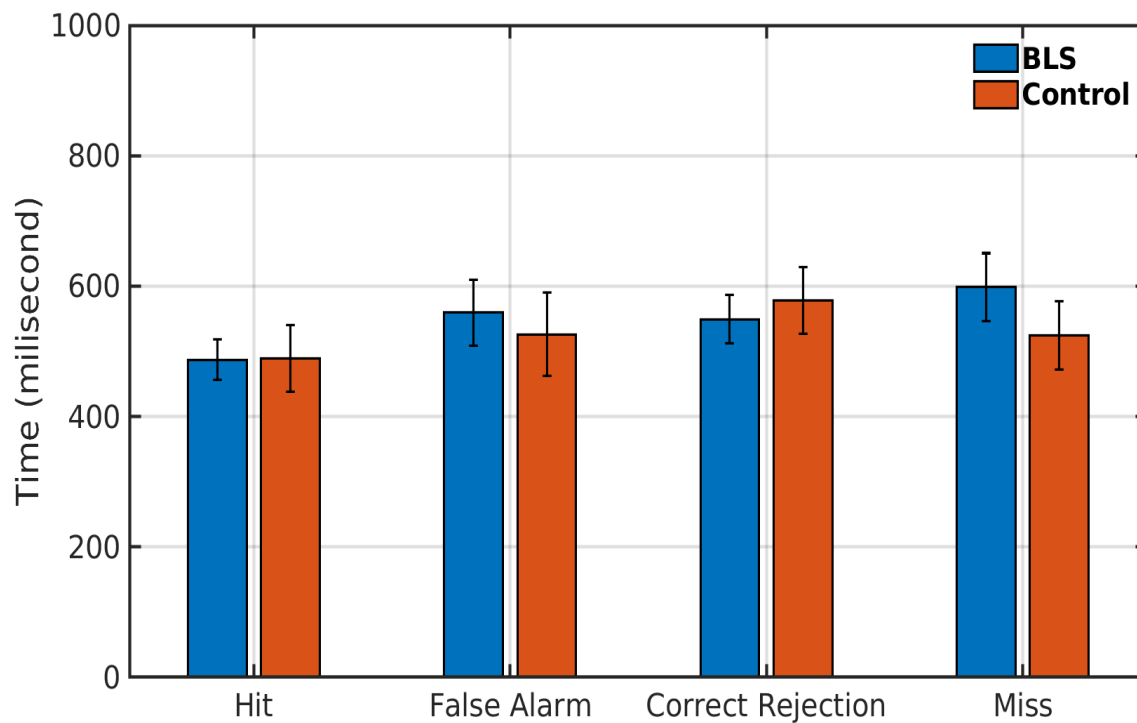
Figure 15. Mean Reaction Times with standard errors for BLS and Control condition

4.2. ERP Component Results

Each electrode, used in analyses for computing grand averages of ERP components, is shown in Figure 16 for -200 and 1000 ms time periods both for BLS and Control conditions.

Figure 16. Channels and Grand averages of ERPs used in analyses with standard errors

4.2.1. N100 Component (60–124 ms)

According to attention-related explanations of the BLS effect on episodic retrieval, the mean amplitude of the N100 ERP component in hit responses should be more negative in the BLS condition than in the control condition. Moreover, to understand the effect of

the contralateral hemispheres, three channels (F3 / F4 and Fz) are selected. ERP data were analyzed at mentioned channels using three-way repe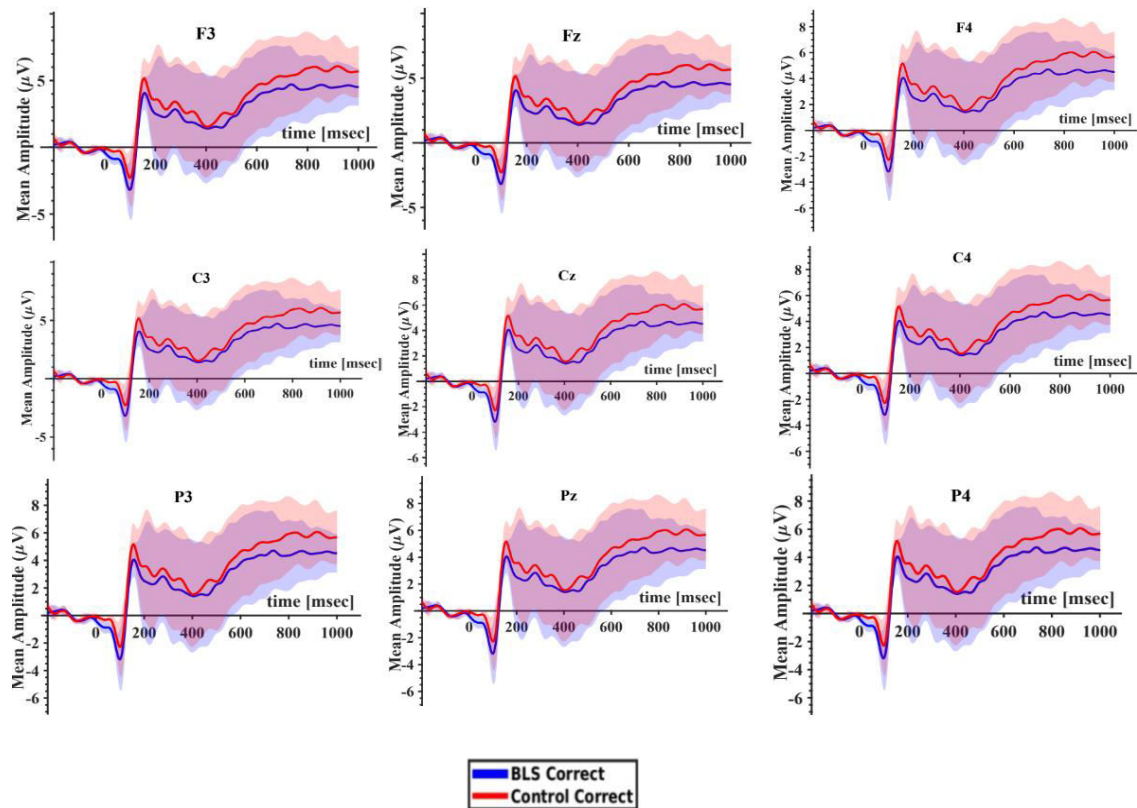ated measures ANOVA. The model consists of 2 'BLS condition' (BLS – control) X 3 regions (frontal, central, and parietal) X 3 lateralization (left, midline, right).

Repeated measures ANOVA applied for the N100 time window revealed the main effect of the BLS condition [$F(1,14) = 7.345$; $p < 0.01$, $\varepsilon = 0.066$]; the main effect of the region [$F(2,28) = 7.102$; $p < 0.01$, $\varepsilon = 0.080$]; main effect of laterality [$F(1.53, 21.45) = 11.280$; $p < 0.001$, $\varepsilon = 0.030$] and the significant region and lateralization interaction effect [$F(4,56) = 16.803$; $p < 0.001$, $\varepsilon = 0.015$].

The first follow-up analysis was done to investigate the BLS effect for each region separately (Figure 17). For that, each electrode site was averaged all over the frontal (F3, Fz, F4), central (C3, Cz, C4), and parietal regions (P3, Pz, P4). ANOVA results revealed that there was a main effect of BLS condition [$F(1,14) = 7.345$; $p < 0.05$, $\varepsilon = 0.080$] and a main effect of the region [$F(2,28) = 7.102$; $p < 0.01$, $\varepsilon = 0.090$]. Subsequent analyses showed that the BLS condition (M = -2.90) has a lower amplitude than the control condition (M = -1.82) (t = - 2.71, p<0.05). For region analysis, the central region (M =-2.81) had a lower amplitude than the parietal region (M =-1.52) (t = - 3.262, p<0.05). There is also a trend (almost significant) for frontal (M =-2.74) and parietal regions (M =-1.52).
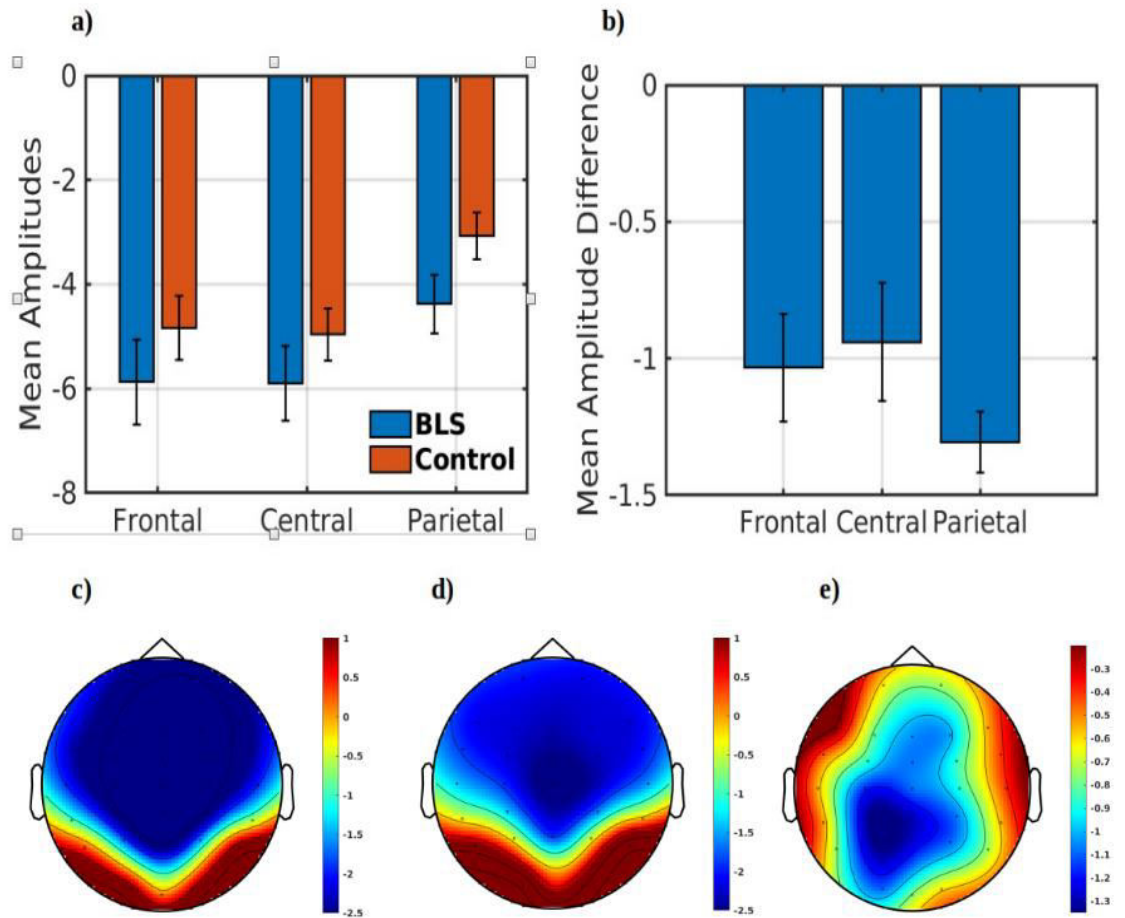
Figure 17. (a) Mean Amplitudes of N100 component in both BLS and Control Conditions with Standard Errors, (b) Mean amplitude differences between BLS and Control conditions in different regions (Frontal, Central, and Parietal). Mean amplitudes are calculated by collapsing (averaging) three lateralization components into one computational unit (For each region, averaging the left, midline, and right electrode in a given time window), (c) Topographical representation of BLS condition, (d) Topographical representation of Control condition, (e) Topographical representation of the difference between BLS condition and Control condition.

The second follow-up analysis was done to see the laterality effect for each region separately (Table 3). Repeated measure ANOVA results showed that at frontal region BLS condition ($M = -3.32$) has a lower amplitude than the control condition ($M = -2.26$) ($t = -2.52$, $p<0.05$). There was no significant effect of laterality in the frontal region. For

the central region, the BLS condition (M = -3.34) has a lower amplitude than the control condition (M = -2.29) (t = - 2.50, p<0.05); for laterality mean amplitude of middle electrode Cz (M= -3.22) is lower than left electrode C3 (M = -2.51) (t = - 4.739, p<0.001). For the parietal region, the BLS condition (M = --2.138) has a lower amplitude than the control condition (M = -0.903) (t = - 2.51, p<0.05). In terms of laterality mean amplitude of the middle electrode Pz (M = -2.507) was lower than both left electrode P3 (M = -1.070) (t = - 6.238, p<0.001) and right electrode P4 (M = -0.985) (t = - 6.065, p<0.001).

Table 3. Follow-up ANOVA N100 results for each region
Follow up 2 (BLS Condition) x 3 (Laterality) repeated measures ANOVA results

Region	BLS Condition		Laterality		Interaction	
	F	η²	F	η²	F	η²
Anterior	6.354*	0.055	1.696	0.003	0.77	0.001
Central	4.04*	0.076	6.013**	0.025	0.926	0.001
Posterior	6.307*	0.087	19.387***	0.111	0.849	0.001

*p <.05; **p <.01; ***p <.001

To sum up, the main and the follow-up analyses indicate that BLS has an overall neuromodulatory effect on the N100 ERP component. We also observed the main effect of lateralization and region. Although interaction effects were not significant, N100 modulation is greater in parietal regions when compared to frontal and central regions.

4.2.2. P200 Component

Regarding the top-down attention explanation of the BLS effect on memory performance during episodic memory retrieval, the P200 ERP component is expected to be lower in the BLS condition than in the control condition. To check that effect, P200 ERP data were analyzed using three-way repeated ANOVA. The model consists of 2 'BLS condition' (BLS – control) X 3 regions (frontal, central, and parietal) X 3 lateralization (left, midline, right) like the previous analysis in the N100 component.

The repeated measures ANOVA in P200 time window revealed main effect of BLS condition [F(1,14) = 5.094; p < 0.05, ε = 0.030] and main effect of region [F(2,28) =

5.031; p < 0.05, ε = 0.057]. There was no significant main effect of laterality [F(1.73, 24.19) = 1.494; p = 0.244, ε = 0.002].

The follow-up analyses were done to see the BLS effect for each region separately (Figure 18). For that, each electrode site is averaged all over the frontal (F3, Fz, F4), central (C3, Cz, C4), and parietal (P3, Pz, P4) regions. According to ANOVA results, there was no main effect of the BLS condition [F(1,14) = 3.309; p = 0.9, ε = 0.080]. However, there was a main effect of the region [F(2,28) = 3.389; p < 0.05, ε = 0.040].
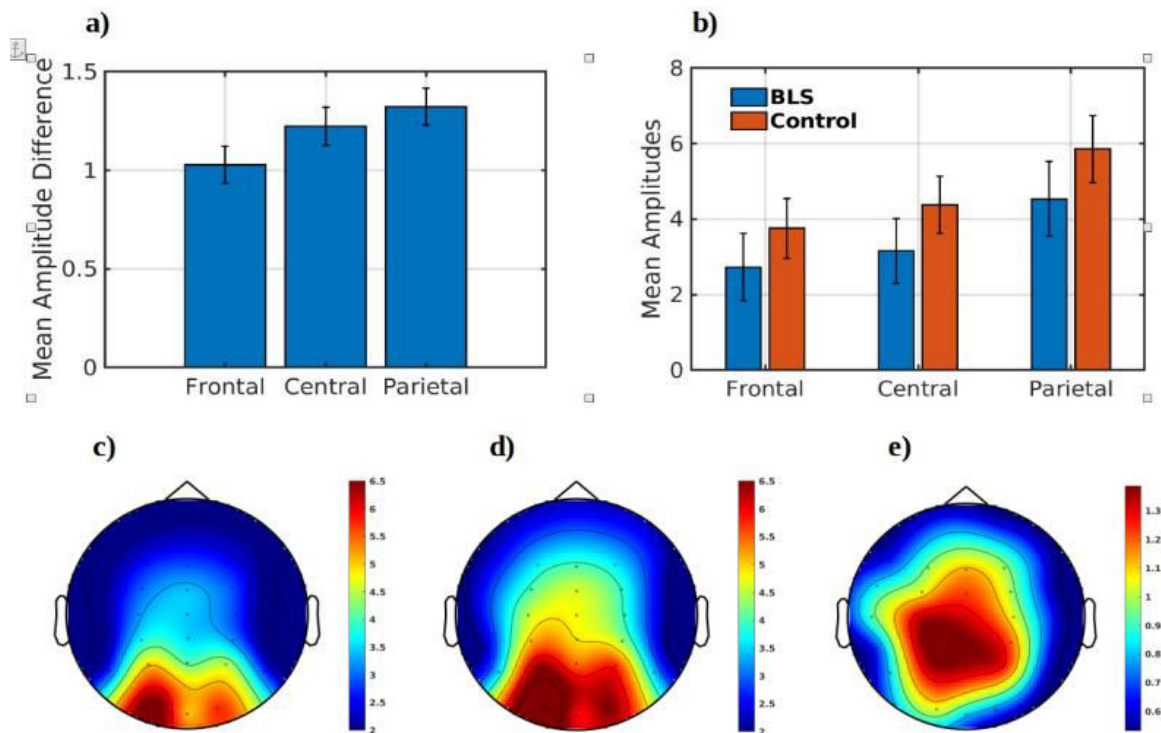
Figure 18. (a) Mean Amplitudes of P200 component in both BLS and Control Conditions with Standard Errors, (b) Mean amplitude differences between BLS and Control conditions in different regions (Frontal, Central, and Parietal). Mean amplitudes are calculated by collapsing (averaging) three lateralization components into one computational unit (For each region, averaging the left, midline, and right electrode in each time window), (c) Topographical representation of BLS condition, (d) Topographical representation of Control condition, (e) Topographical representation of the difference between BLS condition and Control condition.

The second follow-up analysis was done to see the effect of laterality for each region separately (Table 4). Repeated measure ANOVA results showed there is no main effect of BLS condition and laterality for the frontal region. For the central region, the control condition (M = 4.38) has a higher amplitude than the control condition (M = 4.38) (t = -2.28, p<0.05); for laterality, there was no significant difference. For the parietal region, differences between conditions and regions were also not significant.

Table 4. Follow up ANOVA P200 results for Each Region
Follow up 2 (BLS Condition) x 3 (Laterality) repeated measures ANOVA results

Region	BLS Condition		Laterality		Interaction	
	F	η^2	F	η^2	F	η^2
Frontal	4.367	0.025	1.696	0.003	0.325	0.000
Central	4.04*	0.038	6.013*	0.010	0.181	0.000
Parietal	3.801	0.032	2.870	0.010	0.128	0.000

*p <.05; **p <.01; ***p <.001

In conclusion, the mean amplitude of the P200 component is higher in the BLS condition than in the control condition. ANOVA 2 (BLS – control) X 3 (frontal, central and parietal) X 3 (left, midline, right)) results showed that BLS has an overall effect on P200 amplitude decrease. However, follow-up analyses for the region didn't show the P200 amplitude decrease effect. Only the third analysis that is done in three regions separately showed a significant effect, however, the significant effect doesn't survive in t-tests. In general, despite the mean P200 component looking different in visual inspections, the difference is not significant, thus there is no BLS modulation on the P200 component.

4.2.3. LPC Component

To test the BLS neuromodulatory effect on LPC, 2-way repeated ANOVA was applied. Because LPC in recognition memory task is expected parietal area factors are selected as left inferior (P7), left superior (P5), central (Pz), right superior(P4), and right inferior (P8). 2 (BLS, Control) X 5 (left inferior, left superior, central, right superior and right

inferior) repeated measures ANOVA showed that there was a main effect of the condition [$F(1,14) = 5.22$; $p < 0.05$, $\varepsilon = 0.029$]; main effect of the area [$F(1,14) = 15,71$; $p < 0.01$, $\varepsilon = 0.162$]. Interaction effect was not significant [$F(2,28) = 7.102$; $p < 0.01$, $\varepsilon = 0.090$] . Follow-up t-test results showed that the mean amplitude of LPC in the control condition (8.04) is higher than in the BLS condition (6.54) (t = 2.28, p<0.05) (Figure 19).
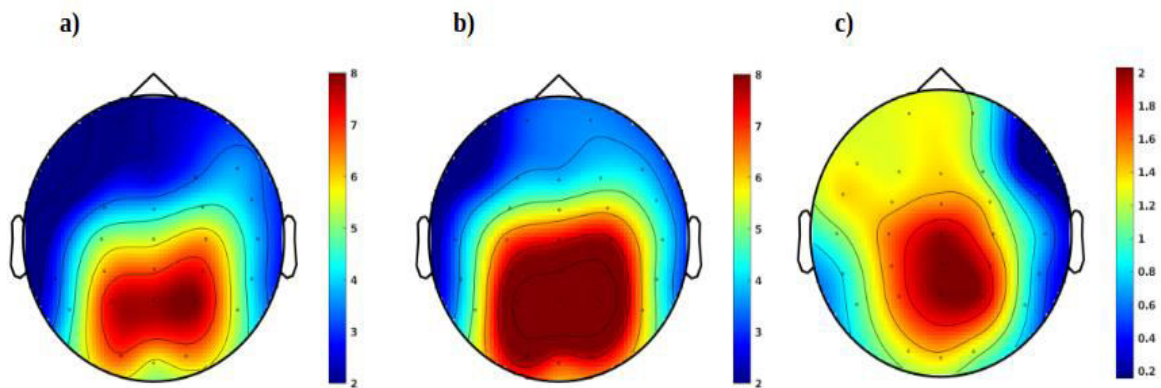

Figure 19. **(a) Topographical representation of the BLS condition, (b) Topographical representation of the Control condition, (c) Topographical representation of the difference between BLS and Control conditions**

4.3. Interhemispheric Connectivity Analysis

According to the interhemispheric interaction hypothesis, memory boost after horizontal saccadic eye movements is a result of the increased communication between hemispheres. Consistently, engaging any kind of bilateral stimulus induces an interaction between contralateral hemispheres and this contralateral activation equalizes the brain activity in the right brain regions responsible for memory retrieval with the left brain regions. In order to test that hypothesis, both amplitude coherence and imaginary coherency (to get rid of volume conduction issues) analyses were computed. To test the interhemispheric interaction hypothesis, subjects performed two recognition tasks in two conditions within the subject design for control and BLS conditions. If the assumptions of the interhemispheric interaction model were right, EEG interhemispheric coherency values of subjects in the BLS condition would be greater than in the control condition. In

Figure 20, grand average inter-hemispheric amplitude, and imaginary coherency value differences between BLS and Control (BLS minus Control) are shown.
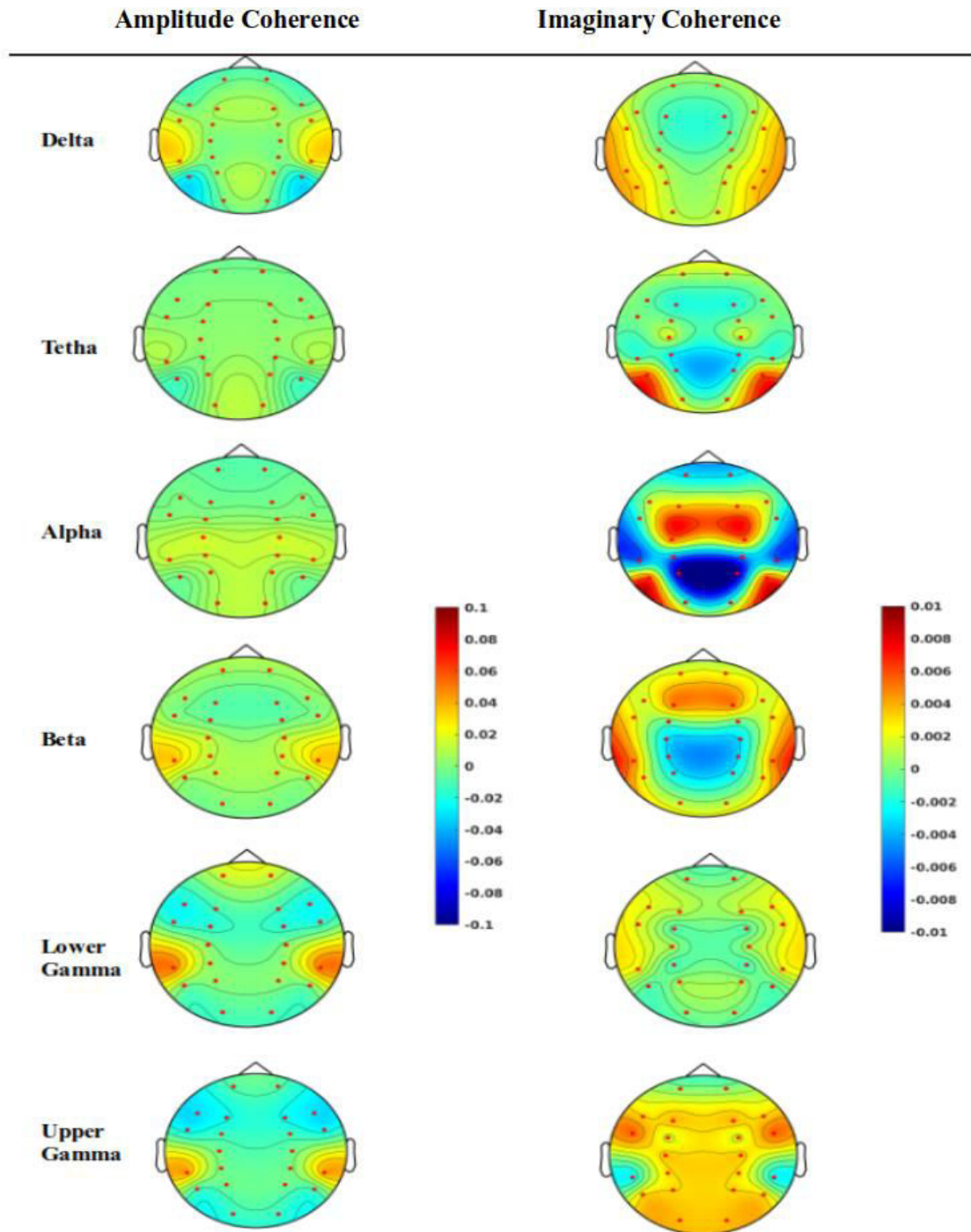
Figure 20. Grand averages of amplitude coherence and imaginary coherency value differences between BLS and Control conditions for each frequency band.

When topographic plots are visually inspected in amplitude coherence, an increase in interhemispheric coherence in temporal regions and a decrease in inferior parietal regions in the delta frequency band are seen. There is a slight increase in beta band parietotemporal regions and finally, there is an increase in parietotemporal regions in both upper and lower gamma frequency bands. Imaginary coherence in delta band increase in frontotemporal and frontocentral regions was observed. A slight decrease in superior parietal regions and an increase in inferior parietal regions in the theta frequency band, an increase in the frontocentral and inferior parietal regions and a decrease in central regions in the alpha band, an increase in frontotemporal regions in the upper gamma band was also observed.

However, none of them survived after the post hoc paired t-test (p values adjusted p < 0.0045 for multiple comparison issues). Noteworthy analyses are shown in Table 5. Although the increase in interhemispheric coherence values is expected according to the interhemispheric interaction hypothesis, there was not a general increase. Amplitude coherence analysis showed that there was no significant difference between conditions. However, when it comes to imaginary coherence analysis, frontal regions showed an increase in the delta frequency band and parietal regions showed a decrease in the beta band.

Although none of the comparisons show statistically significant results with corrections, among all noteworthy comparisons, FT7 – FT8 showed more significant results (t = 3.224, uncorrected p = 0.006, corrected p = 0.066) that indicate an inter-hemispheric interaction increase due to BLS. There is also a difference due to BLS manipulation in a week significant level (t = 1.773, p = 0.098). However, in parietal and central regions in the delta band, there is a general trend that indicates that BLS manipulation causes a decrease in inter-hemispheric coherence; in C3 – C4 channels (t = -2.891, uncorrected p = 0.012, corrected p = 0.11); CP3 – CP4 channels (t = -2.973, uncorrected p = 0.010, corrected p = 0.066); P3 – P4 channels (t = -2.296, uncorrected p = 0.038, corrected p = 0.14).

Table 5. Means and Standard Deviations Interhemispheric imaginary coherency values and comparisons

Electrodes and Frequency Band	BLS mean	Control mean	t value	Uncorrected p value	Corrected p value
FT7 – FT8 (Delta)	0.01106 (0.00575)	0.00727 (0.00369)	3.225	0.006	0.066
F3 – F4 (Delta)	0.00513 (0.00300)	0.00725 (0.00588)	1.773	0.098	0.539
C3 – C4 (Beta)	0.0135 (0.00683)	0.0181 (0.00735)	-2.891	0.012	0.11
CP3 – CP4 (Beta)	0.0149 (0.00994)	0.0207 (0.01059)	-2.973	0.010	0.066
P3 – P4 (Beta)	0.0165 (0.01134)	0.0211 (0.01390)	-2.296	0.038	0.14

CHAPTER 5

DISCUSSION

5.1. Discussion

After Christman's (2003) pioneering work, the saccadic horizontal eye movements effect started to become a research topic, not only for PTSD patients but also for healthy populations to investigate memory processes in general. Many researchers reported that after execution of 30-second left and right bilateral saccadic eye movements or any other activity induces a contralateral activation in the brain and it leads to memory performance enhancement compared to control groups (Christman, 2003, 2004, 2006; Parker, 2007; Lyle, 2008, 2011, 2015; Nieuwenhuis, 2013). Although these enhancing effects were repeated in many different experimental settings, there is no consensus about the underlying neurobiological or neuromodulatory mechanisms. Two types of explanation were offered yet: interhemispheric interaction theory (Christman, 2003) and top-down attentional control theory (Lyle, 2008, 2011). While the interhemispheric interaction hypothesis explanation of memory enhancement asserts that bilateral saccadic eye movements increase the interhemispheric activity between the contralateral brain regions, which in turn increases activation to facilitate memory retrieval and memory performance, top-down attentional control theory assumes that bilateral stimulation increases activity in top-down attention brain regions (frontoparietal attention network) and when the task requires top-down attention due to complexity and required cognitive effort, memory performance improves.

In this thesis, my primary purpose, firstly, was to see whether bilateral tactile stimulation has any enhancing effect on memory performance metrics like previous SIRE research. Evaluation of memory was realized by analyzing hit rates, false alarm rates, sensitivity, and response bias, as well as response times. Secondly, according to the top-down attentional control theory of SIRE, bilateral stimulus should modulate attention-related functioning. In this study, we compared the neuromodulatory effect of bilateral tactile stimuli on N100 and P200 ERP components that are well-known as top-down attention-related components (Luck & Kappenman, 2011; Luck, 1990). Moreover, lastly, inter-

hemispheric coherence values were analyzed during the memory retrieval for testing the inter-hemispheric interaction hypothesis.

Before discussing the results of the analysis of the study, I would like to mention why this study is designed and conducted in METU Neurosignal Lab (Göktepe et.al, 2017) has desirable qualities compared to previous SIRE literature. First, the number of stimuli that are tested in the recognition memory task is considerably large, especially when we compare it with previously conducted SIRE studies. Most of the studies used at most 90 stimuli in the task. However, in this study, there are 240 old and 94 new stimuli in the recognition task. The second desirable quality is that EEG data is recorded during the memory retrieval, while the other neuroimaging studies recorded EEG either without any memory task or before and after the memory task. It allowed us to analyze both ERP components and EEG coherence components at the same time. Previous research was interested in either ERP (Fleck, 2018) or just in EEG coherence (Propper,2017; Samara, 2011). It is the first study in which subjects' EEG data are recorded "during" the task, which can elucidate a more detailed picture of the effect of bilateral stimuli on the exact moment the brain functions its task. Lastly, the procedure in the experiment was designed in a within-subject design fashion. It allowed testing the neuromodulatory premises and arguments of the most prominent theories in SIRE literature, which are interhemispheric interaction theory and top-down attentional control theory.

Behavioral results we obtained don't show any positive effect on subjects' stimulus discrimination measured as sensitivity contrary to other SIRE studies. A possible reason for this could be related to the number of stimuli. As we mentioned before, the number of stimuli that are used in our case is greater than the others. Another plausible reason could be the emotional status of the stimulus that is presented to participants. Although there is a great deal of evidence that BLS enhances memory retrieval performance in neutral stimuli, there are also studies that the BLS effect could differ according to the emotional status of the stimulus. In a recognition memory study (Samara, 2011), while the SIRE effect was observed for emotional stimuli, there was no effect for neutral stimuli. However, it is observed that bilateral tactile stimuli affected the subjects' response bias. Subjects showed more conservative response biases in the bilateral tactile stimulation condition compared to the control condition. Conservative response biases are more cognitively demanding and require more attention control because subjects with more conservative bias tend to give "old" responses only when there is enough memory strength (Kantner & Lindsay, 2012). Regarding that, our results support the idea of the top-down attentional control hypothesis. Although top-down attentional control theory assumes that bilateral stimulation increases performance only for cognitively demanding tasks like free recall rather than easier tasks of recognition (Lyle, 2015). Since the number of stimuli used in the recognition task is greater than in other studies in SIRE literature, it can be accepted as a cognitively demanding task due to the

subjects' possible number of comparisons during the retrieval process. Thus, our behavioral analysis supports the top-down attentional control theory.

To test the main assumptions of the top-down attentional control theory, N100 and P200 ERP components were analyzed. Analyses revealed that bilateral tactile stimuli have a statistically significant overall neuromodulatory effect on the N100 ERP component. However, although P200 was modulated by bilateral sensory stimulation, this modulation effect was not statistically significant. While increased attention manifests itself as the increased amplitude of the N100 ERP component, the effect of reduced attention causes a reduction of N100 amplitude (Mogras, 2009; Luck, 2011; Noldy, 1996). Modulation of the N100 component by horizontal saccadic eye movement was observed in Attention Network Task (Fleck, 2019). In addition, there are implications that the mean amplitude of the N100 ERP component also showed a decrease when subjects were sleep deprived, which is characterized by decreased vigilance and selective attention during memory retrieval (Mogras, 2009). The ERP pattern we observed is very similar to the one that Mogras (2009) obtained. Especially when we consider the top-down attentional control theory, the similarity between the ERP results of our analysis and Mogras's study is becoming more important. Because in his study, sleep deprivation not only decreases the top-down attention (vigilance) performance but also diminishes the N100 ERP component amplitude. In our study, we observed that the subjects showed more conservative response bias for the BLS condition. This reflects more top-down regulation and higher N100 ERP component amplitude. The correspondence between behavioral and ERP results of the two studies strongly supports top-down attentional control theory. Moreover, Ciaremelli (2008) proposed a model that brain regions responsible for top-down attention contribute to episodic memory retrieval when tasks are cognitively demanding. Regarding the experiments and models, the N100 component we observed in our study reflects a top-down attentional process rather than any other cognitive process. As a result, the N100 ERP component modulated by bilateral stimulation in this study supported the top-down attentional control hypothesis proposed by Lyle (2010).

Additionally, the interhemispheric interaction hypothesis was tested in our study. According to that hypothesis, bilateral horizontal saccadic eye movements or any stimulation that activates brain areas contralaterally should equalize activation between hemispheres, and this equalization facilitates memory retrieval. Although this hypothesis was supported by behavioral experiments considering horizontal eye movements and handedness issues, there was no neuroimaging evidence supporting it. In our analyses, although results are not statistically significant after correction (false discovery rate was applied to eliminate the multiple comparison effect), there were noteworthy delta band interhemispheric coherence in frontal areas (uncorrected $p = 0.006$, corrected $p = 0.066$) and a decrease in the beta frequency band (uncorrected $p = 0.010$, corrected $p = 0.066$)) in parietal areas. The aforementioned result is worth mentioning because of two reasons.

First, the possible reason why the previous researchers failed to reveal any interhemispheric coherence could be that all studies record EEG data before and after the bilateral stimulation, not the moment when retrieval occurs. This effect may be revealed only during the retrieval, which could be a reason why other researchers failed to show any interhemispheric coherence. Considering EMDR therapy settings, memory retrieval should start during the saccadic eye movement session, although patients report what they remember after the eye movement procedure. Second, when researchers conduct their experiment, they bet on either the interhemispheric interaction hypothesis or the top-down attentional control hypothesis. It implies that researchers accepted these two hypotheses as mutually exclusive. Perhaps, interhemispheric interaction and the top-down attentional control hypothesis could explain the SIRE effect together. To put it more explicitly, it is also possible that while bilateral stimuli equalize the brain activity in frontal areas as the interhemispheric interaction hypothesis postulates (according to CARA theory, when the task requires top-down attention, the left side of the brain could also be active during retrieval), parietal areas could also be activated for the demand of top-down attentional control 'simultaneously' due to bilateral stimulus. However, although our connectivity analysis pointed out the existence of possible interhemispheric interaction, those results were statistically insignificant even though there was a noteworthy increase for some of the subjects. Regarding the outcomes of this thesis, it could be said that the neuromodulatory explanation of top-down attentional control theory is a better candidate than the interhemispheric interaction hypothesis based on behavioral (conservative response bias) and neuroimaging results (N100 ERP modulation).

Additionally, while not being investigated by the previous SIRE literature, in our study, LPC ERP component modulation was observed between the BLS condition and the control condition. The mean amplitude of LPC in the BLS condition was lower than in the control condition. This difference could be meaningful by working memory taxing hypothesis in EMDR literature (van den Hout et al., 2011). According to this theory, BLS has a therapeutic effect because it makes traumatic memories less vivid by taxing the working memory. Moreover, the LPC is a well-known component associated with recollection in the episodic memory retrieval process, and its amplitude was associated with the power of recollection. Considering the role of LPC in recollection, we observed lower LPC mean amplitude in the BLS condition, which may be explained by BLS's taxing effect on working memory.

5.2. Limitations

The first limitation of our study is the number of samples that were analyzed. Although the total number of subjects in the original experiment was 21, it was reduced to 15 due to signal quality and the number of hits for conditions. This lack of trials could potentially affect the robustness of the results.

Another limitation was that nearly none of the subjects had enough numbers of correctly rejected trials. This was the most significant limitation because correct rejections are one of the essential baseline factors in ERP research in typical recognition memory paradigms, which are commonly called the old-new effect. In this ERP research paradigm, different subprocesses in episodic retrieval that are familiarity, and recollection were indexed by the differences between the ERP components of the hit trials and the correctly rejected trials at the frontal and parietal regions. Accordingly, to conduct analysis, the minimum number of correctly rejected trials recommended by the recognition memory research literature is 15. Unfortunately, most of the subjects' correctly rejected trial numbers in the experiment were under the recommended trial size. Because of these reasons, well-known episodic memory components and their ERP components, the frontal FN400 component for familiarity and parietal LPC for recollection, could not be analyzed on the basis of the old-new effect research paradigm.

5.3. Future Studies

In this study, BLS's behavioral and neuromodulatory effects on healthy subjects were investigated based on the SIRE research paradigm. Moreover, the results indicate that the neuromodulatory effect of BLS was consistent with the postulates of the top-down attentional control theory based on both behavioral and ERP results. However, interhemispheric coherency analysis revealed some clues that support the interhemispheric interaction hypothesis, even though the results are not statistically significant. For future studies, visual and auditory stimuli could be used to understand the effect of the modality on the top-down processes. Another potential modification could be using bilateral tactile stimuli in a unilateral fashion instead of bilateral. In that way, the top-down attention hypothesis could be tested directly without confounding the experimental design with the interhemispheric interaction hypothesis that requires contralateral stimulation. This modification could especially be beneficial because vertical eye movements caused SIRE effects in behavioral experiments. Eventually, using emotional faces in the dataset for the recognition memory task could reveal the neuromodulatory effect of BLS not only based on the SIRE literature but also the EMDR literature. Because the SIRE effect was observed only in emotional words in some studies (Samara, 2011).

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Nielsen, T., Abel, A., Lorrain, D., & Montplaisir, J. (1990). Interhemispheric EEG coherence during   sleep and wakefulness in left-and right-handed subjects. Brain and cognition, 14(1), 113-125.

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APPENDICES

APPENDIX A

HIT AND FALSE ALARM RATES

Subject Number	Control Condition			BLS Condition	
	Sensitivity	Response Bias		Sensitivity	Response Bias
1	0.9	0.45		0.78	0.79
2	0.74	0.8		0.72	0.83
3	0.52	0.65		0.51	0.8
4	0.78	0.83		0.79	0.66
5	0.75	0.85		0.63	0.75
6	0.40	0.86		0.43	0.94
7	0.21	0.86		0.57	0.67
8	0.30	0.97		0.41	0.87
9	0.5	0.83		0.57	0.83
10	0.55	0.81		0.71	0.78
11	0.3	0.89		0.19	0.84
12	0.47	0.91		0.25	0.85
13	0.56	0.91		0.4	0.78
14	0.62	0.65		0.58	0.68
15	0.6	0.75		0.7	0.73
16	0.43	0.82		0.35	0.63
17	0.82	0.46		0.81	0.54
18	0.67	0.91		0.54	0.83
19	0.44	0.97		0.56	0.73
20	0.35	0.88		0.41	0.64

APPENDIX B

SENSITIVITY AND RESPONSE BIAS

Subject Number	Control Condition			BLS Condition	
	Sensitivity	Response Bias		Sensitivity	Response Bias
1	1.402	- 0.596		- 0.053	- 0.786
2	- 0.144	- 0.732		- 0.385	- 0.775
3	- 0.33	- 0.235		- 0.824	- 0.43
4	- 0.167	- 0.884		0.401	- 0.612
5	- 0.362	- 0.855		- 0.356	- 0.497
6	- 1.347	- 0.445		- 1.734	- 0.683
7	- 1.929	- 0.16		- 0.244	- 0.309
8	- 2.547	- 0.764		- 1.342	- 0.44
9	- 0.967	- 0.484		- 0.773	- 0.567
10	- 0.763	- 0.527		- 0.234	- 0.657
11	- 1.763	- 0.364		- 1.904	- 0.061
12	- 1.446	- 0.66		- 1.722	- 0.193
13	- 1.22	- 0.762		- 1.034	- 0.264
14	- 0.099	- 0.359		- 0.26	- 0.343
15	- 0.421	- 0.464		- 0.086	- 0.567
16	- 1.112	- 0.397		- 0.717	0.016
17	1.015	- 0.427		0.761	- 0.485
18	- 0.936	- 0.915		- 0.849	- 0.529
19	- 2.118	- 0.922		- 0.438	- 0.379
20	- 1.595	- 0.423		- 0.599	- 0.066

APPENDIX C

RESPONSE TIMES (MILLISECOND)

| Subject Number	Control Condition			BLS Condition	
	Hit Rate	False Alarm		Hit Rate	False Alarm
1	398	364		403	504
2	632	545		611	583
3	384	379		442	490
4	530	455		463	600
5	277	251		395	416
6	1105	1151		753	1079
7	352	491		381	380
8	395	511		471	474
9	278	231		297	350
10	318	294		521	553
11	339	361		544	520
12	560	584		610	604
13	980	1281		551	867
14	709	676		526	489
15	491	723		529	609
16	346	327		430	367
17	270	223		304	373
18	331	365		320	279
19	511	529		377	517
20	584	781		815	1126

APPENDIX D

ERP Figures For Each Subject
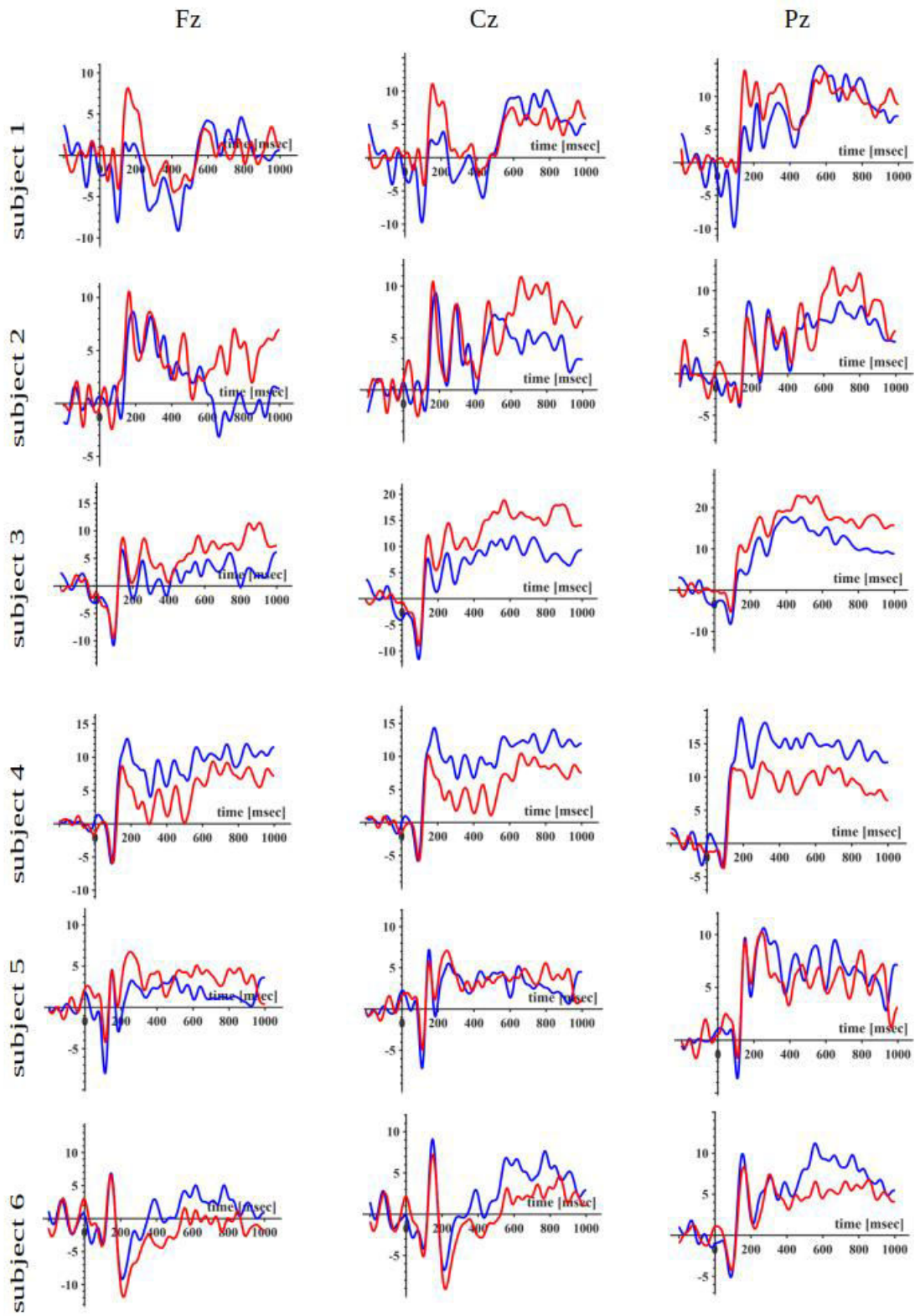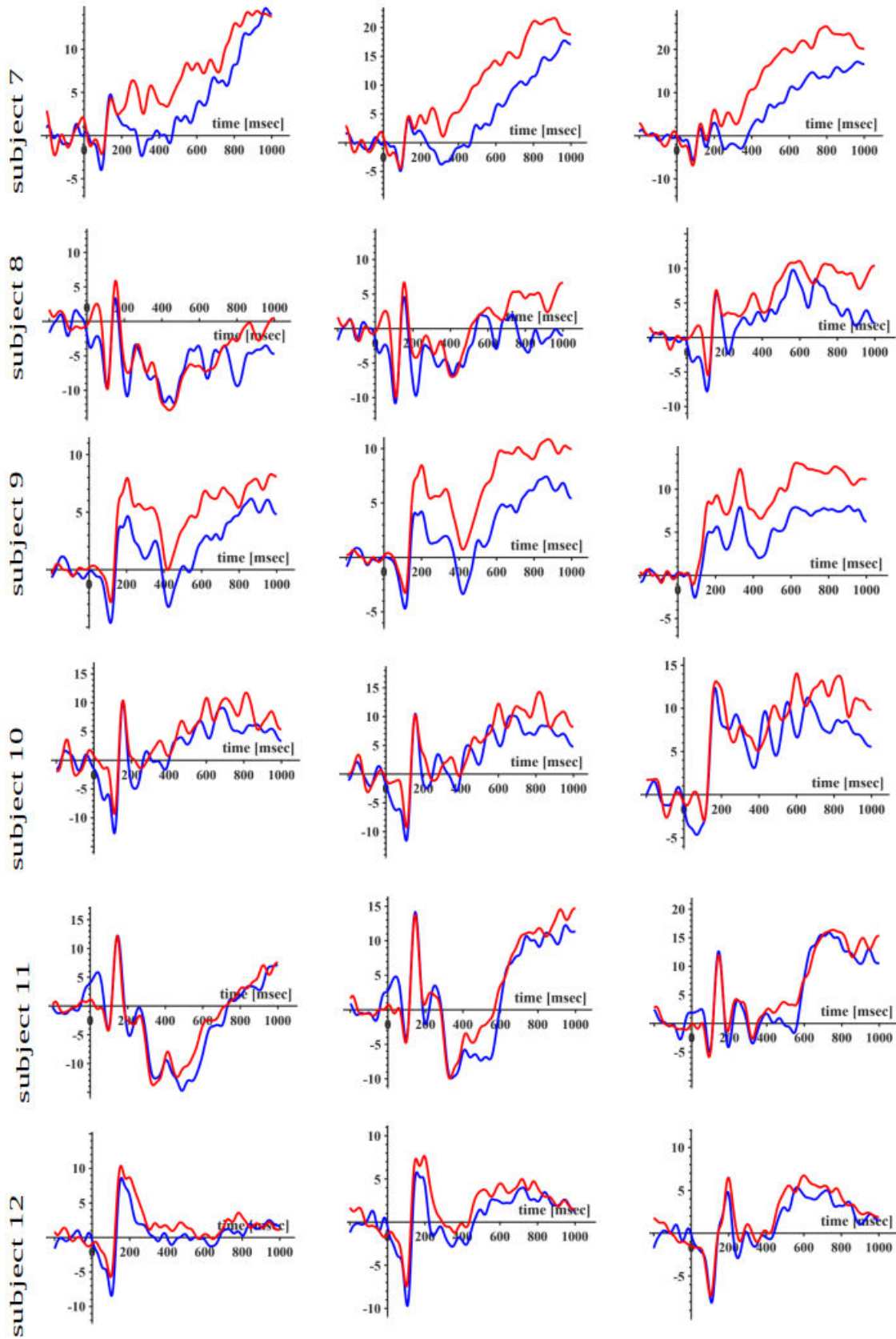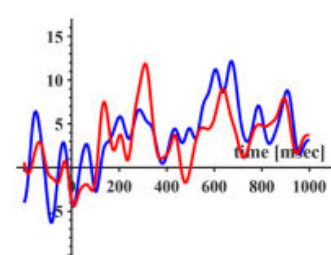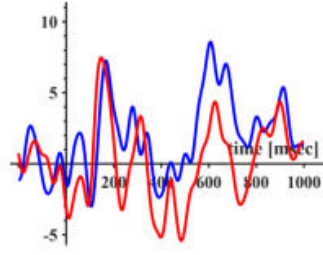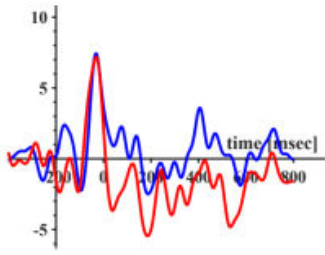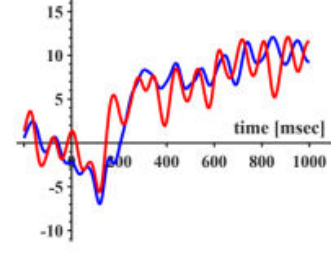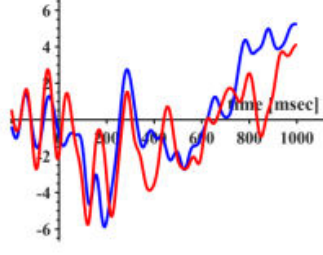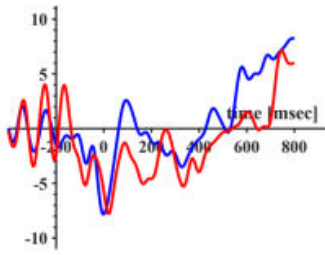
APPENDIX E
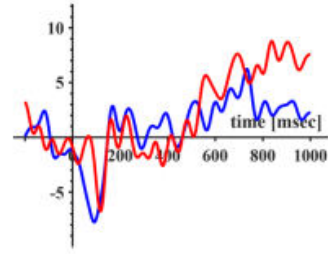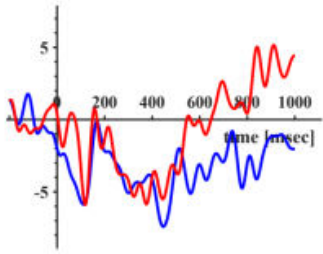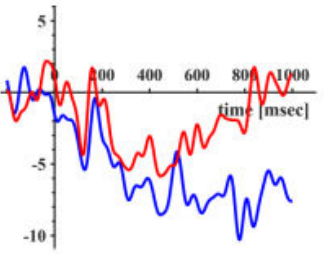
Source Codes for ERP Extraction

```
%% defining the paths of the EEG and behavioral data-------------------------------------

path_trials  = '/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/Clean_trials';

subjects = {'sbj1' 'sbj2' 'sbj3' 'sbj4' 'sbj5'...
    'sbj6' 'sbj7' 'sbj8' 'sbj9' ...
    'sbj11' 'sbj12' 'sbj13' 'sbj14' 'sbj15'...
    'sbj16' 'sbj17' 'sbj18' 'sbj19' 'sbj20'...
    'sbj21' };
nsubj = numel(subjects);
%% initialization of cell arrays for further analysis
erp_FT_C_old = cell(1, nsubj);
erp_FT_C_new = cell(1, nsubj);
erp_FT_W_old = cell(1, nsubj);
erp_FT_W_new = cell(1, nsubj);
erp_CC_C_old = cell(1, nsubj);
erp_CC_C_new = cell(1, nsubj);
erp_CC_W_old = cell(1, nsubj);
erp_CC_W_new = cell(1, nsubj);
%%
```

```matlab
for i=1:length(subjects)

    datafile = strcat(path_trials, '/', subjects{i}, '.mat');

     % load the ERP data of subject i from disk

    data_out = load(datafile);

    cfg=[];

    cfg.demean        = 'yes';

    cfg.baselinewindow  = [-0.2 0];

    data_out = ft_preprocessing(cfg, data_out);

    % Bilateral Stimulation and Control Condition data selection

    % for correct-wrong and old-new trials

    cfg=[];
 cfg.trials = data_out.trialinfo(:,1) ==19 & data_out.trialinfo(:,2) ==1 &       data_out.trialinfo(:,3)
==150;

    FT_C_old= ft_selectdata(cfg, data_out);

    cfg=[];
 cfg.trials = data_out.trialinfo(:,1) ==19 & data_out.trialinfo(:,2) ==1 &    data_out.trialinfo(:,3)==111;

    FT_C_new= ft_selectdata(cfg, data_out);

    cfg=[];

    cfg.trials = data_out.trialinfo(:,1) ==19 & data_out.trialinfo(:,2) ==0 & data_out.trialinfo(:,3)==150;

    FT_W_old= ft_selectdata(cfg, data_out);

    cfg=[];

    cfg.trials = data_out.trialinfo(:,1) ==19 & data_out.trialinfo(:,2) == 0 & data_out.trialinfo(:,3)==111;

    FT_W_new= ft_selectdata(cfg, data_out);

    cfg=[];

    cfg.trials = data_out.trialinfo(:,1) ==7 & data_out.trialinfo(:,2) ==1 & data_out.trialinfo(:,3)==150;
```

```
CC_C_old= ft_selectdata(cfg, data_out);

cfg=[];

cfg.trials = data_out.trialinfo(:,1) ==7 & data_out.trialinfo(:,2) ==1 & data_out.trialinfo(:,3)==111;

CC_C_new= ft_selectdata(cfg, data_out);

cfg=[];

cfg.trials = data_out.trialinfo(:,1) ==7 & data_out.trialinfo(:,2) ==0 & data_out.trialinfo(:,3)==150;

CC_W_old= ft_selectdata(cfg, data_out);

cfg=[];

cfg.trials = data_out.trialinfo(:,1) ==7 & data_out.trialinfo(:,2) ==0 & data_out.trialinfo(:,3)==111;

CC_W_new= ft_selectdata(cfg, data_out);


    erp_FT_C_old{i}  = ft_timelockanalysis(cfg, FT_C_old);

    erp_FT_C_new{i}  = ft_timelockanalysis(cfg, FT_C_new);

    erp_FT_W_old{i}  = ft_timelockanalysis(cfg, FT_W_old);

    erp_FT_W_new{i}  = ft_timelockanalysis(cfg, FT_W_new);

    erp_CC_C_old{i}  = ft_timelockanalysis(cfg, CC_C_old);

    erp_CC_C_new{i}  = ft_timelockanalysis(cfg, CC_C_new);

    erp_CC_W_old{i}  = ft_timelockanalysis(cfg, CC_W_old);

    erp_CC_W_new{i}  = ft_timelockanalysis(cfg, CC_W_new);


end
%% saving the extracted ERPs
save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_FT_C_old.mat','erp_FT_C_old')
```

```matlab
save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_FT_C_new.mat','erp_FT_C_new')

save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_FT_W_old.mat','erp_FT_W_old')

save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_FT_W_new.mat','erp_FT_W_new')

save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_CC_C_old.mat','erp_CC_C_old')

save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_CC_C_new.mat','erp_CC_C_new')

save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_CC_W_old.mat','erp_CC_W_old')

save('/home/user/Desktop/THESIS_ANALYSIS/Tez_Analizi/ERP/erp_CC_W_new.mat','erp_CC_W_new')

%%--------------------------------------------------------------------------------------------------

function erps = extract_erp2(time,channel)

% takes channels and time inteval as input, and gives

% mean amplitude of ERPs' in given time interval for

% both conditions (BLS and Control)

    path1 ='/home/user/Desktop/THESIS_ANALYSIS/Son_Analiz2/erp_CC_C_old';

    path2 ='/home/user/Desktop/THESIS_ANALYSIS/Son_Analiz2/erp_FT_C_old';


    erp1= load(path1);

    name = fieldnames(erp1);erp1 = erp1.(name{1});

    erp2= load(path2);

    name = fieldnames(erp2);erp2 = erp2.(name{1});


    erp1 = erp1(:,[1 2 3 4 5 6 10 13 14 15 16 17 18 19 20]);
```

```matlab
    erp2 = erp2(:,[1 2 3 4 5 6 10 13 14 15 16 17 18 19 20]);


    cfg      = [];

    cfg.latency = [-0.2 1];

    gerp1  = ft_timelockgrandaverage(cfg, erp1{:});

    gerp2  = ft_timelockgrandaverage(cfg, erp2{:});

    idx = find(ismember(string(erp1{1}.label), channel))';

    timesel_cor_FT = find(gerp1.time >= time(1) & gerp1.time <= time(2));

    mean_erp1 = [];mean_erp2 = [];

    for i=1:15

        mean_erp1(i,:) =mean((erp1{1,i}.avg(:,timesel_cor_FT)),2)';

        mean_erp2(i,:) =mean((erp2{1,i}.avg(:,timesel_cor_FT)),2)';

    end

    erps = [mean_erp1 mean_erp2 ];

end
```

TEZ FOTOKOPİ İZİN FORMU

ENSTİTÜ

Fen Bilimleri Enstitüsü ☐

Sosyal Bilimler Enstitüsü ☐

Uygulamalı Matematik Enstitüsü ☐

Enformatik Enstitüsü ☑

Deniz Bilimleri Enstitüsü ☐

YAZARIN

Soyadı : Delikaya
Adı : Anıl Berk
Bölümü : Sağlık Bilişimi

TEZİN ADI (İngilizce):

NEUROMODULATORY EFFECT OF BILATERAL RHYTHMIC TACTILE STIMULATION ON RECOGNITION MEMORY

TEZİN TÜRÜ: **Yüksek Lisans** ☑   **Doktora** ☐

1. Tezimin tamamı dünya çapında erişime açılsın ve kaynak gösterilmek şartıyla tezimin bir kısmı veya tamamının fotokopisi alınsın. ☑

2. Tezimin tamamı yalnızca Orta Doğu Teknik Üniversitesi kullanıcılarının erişimine açılsın. (Bu seçenekle tezinizin fotokopisi ya da elektronik kopyası Kütüphane aracılığı ile ODTÜ dışına dağıtılmayacaktır.) ☐

3. Tezim bir (1) yıl süreyle erişime kapalı olsun. (Bu seçenekle tezinizin fotokopisi ya da elektronik kopyası Kütüphane aracılığı ile ODTÜ dışına dağıtılmayacaktır.) ☐

Yazarın imzası ....   Tarih ....