FUNCTIONAL CHANGES IN THE HUMAN CORTEX OVER THE COURSE OF VISUAL PERCEPTUAL LEARNING

A THESIS SUBMITTED TO

THE GRADUATE SCHOOL OF ENGINEERING AND SCIENCE

OF BILKENT UNIVERSITY

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR

THE DEGREE OF

MASTER OF SCIENCE

IN

NEUROSCIENCE

By

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March 2020

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Perceptual Learning
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We certify that we have read this thesis and that in our opinion it is fully adequate,
in scope and in quality, as a thesis for the degree of Master of Science.

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ABSTRACT

FUNCTIONAL CHANGES IN THE HUMAN CORTEX OVER THE COURSE OF VISUAL PERCEPTUAL LEARNING

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M.S. in Neuroscience

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March 2020

In this study we assessed functional changes through visual perceptual learning with bisection discrimination task. Before learning, after third session of learning and after learning ended, behavioral threshold and fMRI data has been collected. Our results showed that while participants showed threshold decrease in the mid-learning session, the post-learning thresholds are turned to pre-learning levels. These results might be due to fatigue which caused by our experiment. Besides to training condition, we also tested location and task specificity. The results showed that only 150°polar angle location showed significant change between sessions. Along with the behavioral data, we collected task-based fMRI data while participants performing training and control conditions in the scanner. The analysis showed task-based BOLD response changed with session. However, post-hoc tests did not reveal significant results. The resting-state functional connectivity analysis showed that the functional connectivity between V1 and V2 regions is significantly increased. The Post Hoc analysis showed significant change in the 210°and 150°polar angle conditions. The changes in the behavioral and functional connectivity measurements at 150°polar angle conditions, these results might indicate the effect of the inter-hemispheric connections. Moreover, our analysis on resting state data also revealed that, while there is no change between pre-learning and mid-learning sessions, connectivity changes significantly in the post-learning session compared to other sessions. This finding supports the idea that functional connectivity changes related to perceptual learning might be occurring at the late phases of the learning. Overall, to rule out the confounds in the behavioral measurements and to link the behavioral data with the neural data, additional measurements should be taken in the future.

Keywords: visual perceptual learning, bisection discrimination task, functional

magnetic resonance imaging, resting state functional connectivity.

ÖZET

GÖRSEL ALGISAL ÖĞRENME SÜRECİNDE İNSAN KORTEKSİNDEKİ FONKSİYONEL DEĞİŞİMLER

Beyza Akkoyunlu
Nörobilimler, Yüksek Lisans
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Mart 2020

Bu çalışmada görsel algısal öğrenme sürecinde beyinde gerçekleşen fonksiyonel değişiklikler incelenmiştir. Bu amaçla, öğrenme öncesinde, üçüncü öğrenme seansından sonra ve öğrenme tamamlandıktan sonra davranışsal eşik ölçümleri ve işlevsel manyetik rezonans görüntüleme(iMRG) ölçümleri alınmıştır. Sonuçlar, katılımcıların öğrenme-öncesi ve öğrenme-sürecinde alınan ölçümlerde algısal eşiğin düştüğünü gösterirken, öğrenme-sonrası alınan ölçümlerde algısal eşik değerleri öğrenme öncesi değerlere dönmüştür. Görev ve yer spesifikliğini incelemek adına alınan kontrol ölçümleri yalnızca ayna pozisyonu olan 210°kutupsal açıda öğrenme bölgesine benzer değişiklik gözlemlenmiştir. Bu değişiklik öğrenme koşuluna benzer olarak, öğrenme öcesine kıyasla öğrenme sürecinde iyileşme göstermiş, ancak algısal eşik öğrenme sonrası ölçümlerde yeniden öğrenme öncesi seviyeesine dönmüştür. Bu sonuçların uzun deney sürecindeki yorgunluktan kaynaklanmış olabileceği düşünülmektedir. Davranışsal verilerle birlikte, görev-temelli ve dinlenme hali işlevsel çekimleri de toplanmıştır. Görev temelli işlevsel çekimlerin sonucunda gruplar arasında oturumlar arasında farklılaşmıştır. Ancak post-hoc testi istatistiksel olarak anlamlı bir sonuç vermemiştir. Dinlenme hali işlevsel bağlantısallık sonuçları ise, öğrenme koşulu ve 150°kutupsal açının V1 ve V2 bölgeleri arasındaki işlevsel bağlantısallığın öğrenme-sonrasında, öğrenme öncesi ve öğrenme sürecinde alınan ölçümlere göre arttığını göstermektedir. Kontrol bölgesindeki değişme, davranışsal veri ile değerlendirildiğinde hemisferler arası bağlantısallığın bir sonucu olarak değerlendirilebilir. Bununla birlikte, bu sonuçlar algısal öğrenme ile gözlemlenen işlevsel bağlantısallık değişimlerinin öğrenmenin geç dönemlerinde olabileceğini destekler niteliktedir. Genel olarak, davranışsal verilerdeki karıştırıcı değişkenlerin etkisini azaltmak ve davranışsal ve nöral verilerin ilişkisini incelemek adına ek ölçümler alınmalıdır.

Anahtar sözcükler: görsel algısal öğrenme, iki parça ayırma görevi, işlevsel

manyetik rezonans görüntüleme, dinlenme hali işselsel bağlantısallık.

Acknowledgement

First of all, I would like to thank to Assoc. Prof. Dr. Hüseyin Boyacı, for his guidance through my Master's. In these years, I learned much more than just neuroscience. I am thankful that I have the chance to start my academic journey with him.

I would also like to thank my jury committee, Dr. Burcu Ayşen Ürgen and Dr. Dicle Dövencioğlu, for their time and invaluable feedback. Even these catastrophic days, they gave such insight to me which helped me to develop myself beyond the scope of this thesis.

I am grateful for the valuable feedback, help and support offered by Dilara Erişen and Batuhan Erkat. Their intellectual contributions and companionship made this thesis possible. I would also like to thank all members of Computational and Biological Vision Lab, especially Buse Merve Ürgen, Ecem Altan, Cem Benar and Cemre Yılmaz. It was a great experience for me to share my achievements and failures in a such supporting environment.

I am also thankful to my parents, Davut and Selma, who tried their best to support me in every way. I am also grateful for the friendship offered by Rabia Şen. She and her loving dog Safari brought great joy to my life and my home in the last three years.

I'm also thankful to İmran Samancı and my cat Mestan, even though they came into my life so late, they were there in the hardest phases of this thesis. Their endless moral support helped me to get through these hard times.

Lastly, I would like to thank the people who has devoted their time to this thesis.

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Chapter 1

Introduction

The world that surrounds us constantly changes, to adapt to these changes visual system stays plastic even in adulthood. Perceptual learning is considered as a manifestation of adult neuroplasticity in the visual system. Perceptual learning term refers to increased performance in a perceptual domain with experience and/or practice. Improved performance can be seen in basic sensory discrimination e.g. contrast discrimination, or more complex tasks such as detecting abnormalities from a noisy ultrasound picture. The variety of tasks creates several real-world applications for perceptual training. Professions that require intense performance at visual tasks, for instance, radiology, benefit from visual perceptual learning. Moreover, perceptual learning can be used for therapeutic aims, e.g. people with visual deficits receive perceptual learning-based therapies and show improvement with affected visual tasks[1].

Neuroplasticity can be defined as the reorganization of the brain structure and/or function as a result of changing environment and/or physiology. A milestone study by Wiesel and Hubel (1963) with cats showed that the visual system, particularly ocular dominance can be affected by life experience in a limited time period, which is named as critical period [2]. The critical period refers to a term in which neurons are more sensitive to experience. It has been believed that experience-dependent changes are limited to the critical period and the brain is

stabilized after development. However, growing evidence shows that neuroplasticity can occur in adulthood. Adult neuroplasticity is shown in many different cortical regions such as the motor cortex [3], auditory [4, 5], and visual cortex [6] Visual cortex plasticity can be induced with experience. Pathology is one such situation. After retina is lesioned, the cortical region which is responsible for processing corresponding retinal area becomes silenced. In the recovery phase, the silenced cortical region starts to process visual input from areas which was not affected by the lesion. This phenomenon is seen in primates [7] and humans through fMRI. In one study, scientists are worked with patients with macular degeneration. Macular degeneration refers to a disorder that causes vision loss in the fovea and usually develops with age. The analysis showed that the cortical area which processes foveal input in healthy humans, reorganized to process stimuli that are in the periphery [8]. In the absence of pathology, the visual cortex also shows plasticity through perceptual learning [9]. Perceptual learning induced visual cortex plasticity helps participants to improve their visual abilities.

Perceptual learning is defined more than one century ago by William James [10], and since then numerous research has been conducted to understand its behavioral basis. On the other hand, the research on neural substrates of perceptual learning is limited due to constraints on neuroimaging techniques in the past. Nevertheless, relatively more recent neuroimaging studies enabled understanding its neural basis. Given the practical and theoretical influence of perceptual learning, it is important to unravel its neural underpinnings.

This thesis aimed to determine the functional changes in the human cortex at different phases of perceptual learning. To give a holistic view first, I will review the previous experimental and theoretical work on perceptual learning. Then, I will present our experimental setting and findings.

1.1 Behavioral Effects of Perceptual Learning

Perceptual learning has been reported in the visual system [11], taste [12], in the auditory system [4], olfactory learning [13], somatosensory learning [14]. In the scope of this thesis, I will review the hallmarks of visual perceptual learning. In vision, perceptual learning has been shown in the most basic tasks such as orientation discrimination [15, 16], spatial frequency discrimination[17], contrast discrimination [18], and hyper-acuity [19, 20]. Moreover, perceptual learning is also evident in higher-level tasks such as motion discrimination [21], texture discrimination [22, 23], as well as in more higher-level tasks such as face discrimination [24].

Perceptual learning results in improved performance with relatively limited training. It has been shown that even 200 trials show the learning effect [25]. Beyond that, the improved performance gained from perceptual learning was preserved over years [26, 27, 28]. The long-lasting performance improvements are accepted as a manifestation of permanent changes in the sensory information processing.

Another hallmark of perceptual learning is that improvement on a particular task is lost even with slight changes in the task characteristics. When the stimulus appeared in a different retinal position, or at different angle participants perform poorly in these tasks. This hallmark of perceptual learning is called specificity. It has been shown that improved performance is specific to trained retinal location [19] and angle [19, 29, 25], orientation [25] and trained eye [15].

Nonetheless, it has been shown that specificity is affected by numerous factors. It has been shown that with orientation discrimination when the training stimuli had a wide range, the performance improvement transferred to untrained orientations[30]. It also has been shown that prolonged training results in the reduced transfer of learning[31]. Moreover, novel training paradigms resulted in the complete transfer to new tasks and new spatial locations [32, 33]. This freshly developed results challenged the perceptual learning theories which will

be discussed in the next section.

The extensive behavioral research on perceptual learning revealed well-established results that answer when and how performance increases, how long its effects have lasted.

However, its neural basis is still undetermined. Even though the compelling findings from behavioral studies, such as specificity, guide the neural theories of perceptual learning, literature shows conflicting results. To understand which mechanisms mediate the increase in the perceptual performance more research is needed.

1.2 Neural Substrates of Perceptual Learning

In the course of perceptual learning research, diverse theories have been developed for understanding its neural basis. Two fundamental questions are being asked in regards to this issue. First,which neural mechanisms are used for perceptual learning?And where does perceptual learning originate? And in this section, I will review the previous research which might be the potential answer for these questions.

1.2.1 Functional Correlates of Perceptual Learning in the Human Brain

Regarding underlying physiological mechanisms of functional plasticity, Karmarkar and Dan [34] offered three possible scenarios: a possible explanation is that the response amplitude will increase to the trained stimulus. Another view is that learning might increase the cortical representation of the trained stimulus by allocating more neurons to process it. Furthermore, a distinct possibility is that learning would change the tuning curve's shape. These three different mechanisms are investigated by using different neuroimaging techniques and analysis

techniques. For answering where perceptual learning take place, copious experimental and theoretical work resulted with discrete answers. The relatively early theories focused on single brain regions to explain the neural basis. While some theories argues that perceptual learning based changes takes place in the different processing levels of visual cortex, other theories suggest temporal and/or frontal brain regions assist the learning process.

One of the early period views argues that perceptual learning is related to changes in the early visual cortex [22]. This view takes ground from the specificity of perceptual learning. Since neurons in early visual regions have location and orientation specificity, early visual areas have been considered the base of plasticity in the visual perceptual learning.

Supporting this theory, Schoups et. al (2001) trained two rhesus monkeys with an orientation discrimination task. The recordings from monkeys' V1 regions showed that the tuning curves are changed. The trained neurons became more responsive to the training stimulus. In humans, fMRI studies showed that blood oxygenation level-dependent (BOLD) signal increased with training in the V1 region. In Furmanski and colleagues research, participants trained on contrast discrimination task. After the learning, fMRI results showed response increase to trained stimuli, in the V1 region. [35]. Moreover, they did not detect any changes in the V2 and V3 region. The authors argued that, the converged receptive fields in the higher level might create a smaller region, and due to its size fMRI might not capture the changes in this region. Similarly, an electroencephalography (EEG) from Bao and colleagues [36] found that amplitude of responses in the primary visual cortex (V1) differed with learning.

Yotsumoto [37] and colleagues trained participants with texture-discrimination task in a series of experiment. In the first experiment, they collected fMRI data before training, after the first day of the training and when training is ended, in another saying 13 days later after experiment started and final measurements are taken 25 days later after experiment started. The fMRI results showed that, the BOLD amplitude is increased after first session of training, nonetheless, the amplitude turned into the baseline level in the 25th day of experiment, which means

after training ended. To investigate if the decrease in the BOLD amplitude is originated by ending training, they conducted second experiment. In this experiment, they carried out the same experiment procedure from first experiment, in addition, the participants continued to receiving training between 13th day and 25th day. The fMRI experiment from second experiment showed a similar pattern to first experiment. Therefore, authors claimed that, the signal increase at the early phases of learning is caused by synaptic strengthening which is triggered with training. Moreover, the signal is reduced at the late phases of the learning, since the learning is saturated, the synaptic strengthening is stopped.

Some scientists considered the middle-level visual processing areas such as V4 and MT as the locus of perceptual learning. This view raised from the behavioral findings showing learning transfers to untrained directions when participants are trained with larger direction intervals. Scientists argued that these results indicate contribution of mid-level visual processing, where neurons responsive to a wide range of orientations and locations. In a study, which collected fMRI data along with learning data, participants were trained with motion discrimination task. The fMRI results showed that BOLD response in the MST region, which is responsible from motion detection, is increased after learning and this increase is correlated with behavioral performance [21]. BOLD response is also increased in the V2 and V3A areas, however, those changes did not correlate with the behavioral improvement.

A research by Chen and colleagues, trained participants with motion direction discrimination task[38]. This research used univariate analysis to investigate changes in the response amplitude. Besides, they also analyzed data with multivariate analyzing techniques to decode orientation information. The results showed significant BOLD amplitude and decoding accuracy change for the V3A region. These changes were also present one month after learning ended.

Furthermore, it has been also suggested that visual perceptual learning is associated with changes in beyond the visual cortex. This view claims that decision making and/or attention-related brain regions underlay visual perceptual learning. A study with monkeys, using motion direction discrimination task, found

that neural firing rate to trained stimulus in the LIP which is known to be related to perceptual decision making is changed with training while they did not find any changes in the MT [39]. The scientists interpreted these results as an indicator of performance improvement's dependency on higher level processes rather than sensory. In an fMRI study with humans, researchers trained participants on an orientation discrimination task with reinforcement. To identify which brain regions contain information related to learning, the scientists run a voxel-wise comparison analysis, the results showed that only the ACC region had a significant relationship with learning [40]. More recent research with face view discrimination task revealed that with learning, the left fusiform area, a region in the inferior temporal cortex which is responsible for processing faces increased its response[24]. MRI data collected, also, one month after training ended and, the change in the BOLD amplitude is vanished. Nevertheless, decoding accuracy of the left fusiform area increased after the learning, and this increase was persistent after one month.

Taken together, previous literature presents evidence for changes in the discrete neural regions. Unlike the before-mentioned views, a lately revived perspective suggests that perceptual learning takes ground from various brain regions [41, 42, 43, 44]. These multi-region theories takes ground from different mechanisms. For instance two stage model [41] claims that two different plasticity mechanisms occurs in relation to perceptual learning, on the other hand, reverse-hierarchy theory [43] claims that at the early phases of perceptual learning, higher-level brain regions assist learning and at the late phases, the early-perceptual regions takes over. In a recent study [45], participants are trained with motion discrimination task, and neural changes in whole-brain are assessed with fMRI. The neuroimaging results showed that, while the BOLD signal in the training direction in the V3A and MT+ is changed with learning, activity in the intraparietal sulcus (IPS) changed for trained and untrained directions[45]. Moreover, scientists have found additional areas such as frontal eye field (FEF), ventral premotor cortex (PMv) which are related to perceptual decision making[46, 47],

also showed signal expansion for training direction. Unlike this study, the majority of the studies which reviewed above, mostly focused on limited brain regions. Nonetheless, previous research with investigated resting-state functional connectivity gives us an opportunity to understand how the functional properties changes with learning in whole-brain. Lewis and colleagues trained participants with shape identification task showed changes in resting-state functional connectivity in the dorsal attention network which contains spatially distributed brain regions between different lobes [48]. Similarly, after participants trained on a motion discrimination task, the MT region's connectivity with widespread brain regions are changed [49].

In sum, studies that investigated functional modification which is related to perceptual learning, provide supporting evidence for Karmarkar and Dan's three hypotheses [34]. However, which mechanism is vital for the behavioral performance increase is still an open question. Regarding to the locus of perceptual learning, individual studies give different answers. To resolve these inconsistencies in the literature, studies which investigate whole-brain regions are needed. Also, unraveling the time-course of these changes would help us to understand how perceptual learning established.

1.2.2 Structural Correlates of Perceptual Learning in the Human Brain

The functional plasticity is often accompanied by structural plasticity. The structural plasticity is implemented by various physiological mechanisms such as building or detaching synapses, changing place of axonal branches [50]. In humans, the structural changes related to perceptual learning assessed with anatomical MRI imaging. The analysis of the cortical thickness showed that cortical thickness changes in the perceptual learning-related areas are correlated with learning. An MRI study conducted on humans with motion-color conjunction search task showed that the cortical thickness in the right posterior superior temporal sulcus (pSTS), which is an area that responsive to coherently moving

stimuli, increased with the training [51]. Moreover, the functional runs showed that the pSTS area's BOLD response is increased with the learning as well. Along the same line, Bi and colleagues are trained their participants on face view discrimination task [24]. The learning modulation index which quantifies the neural processing changes related to learning, showed a significant correlation with behavioral learning.

Regarding cellular mechanisms of perceptual learning-induced plasticity, it has been claimed that perceptual learning and long term potentiation (LTP) has similar traits [52]. LTP is one of the models of activity-dependent plasticity. The term refers to strengthened synaptic connections as a result of long-lasting stimulation. LTP is first shown in the hippocampus [53] and later research also showed in the amygdala [54], primary motor cortex [3] and sensory cortices [5, 55]. According to Aberg and Herzog's view, repetitive stimulus presentation, in other terms perceptual training, directly or through visual perceptual learning causes visually evoked potentials (VEP) which in turn results in LTP. In terms of spatial precision, the most sensitive measurements are taken from animals. In a study, rats are trained with spatial frequency discrimination tasks. After the last training session, the animals' life immediately terminated and electrical stimulation applied to the slices taken from V1. The amplitude of field excitatory postsynaptic potentials was higher in the training group compared to control group rats [56] which indicated LTP-like activity.

Aberg and Herzog's view based on perceptual learning-related plasticity is shared by other scientists like Gilbert and Li [57, 9]. Furthermore, Gilbert and Li claim that LTP changes the long-range horizontal connections in the V1. The view claims that the long-range horizontal connections undergo axonal sprouting and axonal pruning during reorganization of V1. Supporting this view, recent research with primates using two-photon imaging showed that new long-range horizontal connections are established with visual perceptual learning [58]. In the study, two adult monkeys are trained with contour detection task. The V1 region was imaged in three different time points: before training, in the sixth week and eighth week of training. The results showed that at different time points new axonal branches are formed and some of the preexisting axonal branches are

sprouted.

1.3 Scope and Motivation of the Present Study

In neuroscience, the locus of plasticity has the importance to understand adult visual plasticity in depth. Despite the long-standing interest in neural mechanisms of perceptual learning, the literature still contains conflicting results. Therefore, "which brain region or regions assist perceptual learning?" is a still an open question. To answer this question we conducted behavioral and MR imaging experiments. Our participants are trained with bisection discrimination task which is a frequently used task in the perceptual learning literature [52, 59, 60, 19, 61, 29]. For detecting how brain regions change their function as a result of this learning process, we collected task-based and resting-state fMRI data. While task-based fMRI show us how BOLD signal changes performing training task, resting-state fMRI inform us about the changes in the functional connectivity between brain regions.

As outlined in the previous sections, the literature showed that the BOLD signal showed different characteristics at different time points of the training [37, 38], therefore to get a full picture of the learning-related changes we also collected neural data at different time points. These time points were as follows before-learning, mid-learning, after-learning. Since a big portion of the learning occurs at the early phases, to capture changes which occur in the early phase of learning, we collected MRI data after third training session. Then, participants received five additional session of training to assure saturation of learning.

In our study, we used multimodal imaging by collecting task-based fMRI, resting state fMRI, population receptive fields (pRF), Neurite Orientation Dispersion and Density Imaging (NODDI) and tractography. We believe that by virtue of high-resolution fMRI we will be able to capture the neuronal changes in the human cortex. In the extent of this thesis only, task-based and resting-state functional connectivity changes are assessed. Nonetheless, the output from pRFs will be

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used to delineate sub-regions of the visual cortex. Together with the functional localizer and pRF delineation maps, we analyzed the perceptual learning-based functional changes in depth.

Chapter 2

Behavioral Experiment

2.1   Background

To train participants on perceptual learning, we have used line bisection discrimination task, which is used widely in the visual perceptual learning literature [19, 61, 29, 62, 60, 63]. A research by Crist and colleagues [19] investigated specificity of bisection discrimination task. Bisection discrimination task consists three lines, participants' task determine the middle line's displacement direction. In this study, participants are trained with vertical bisection discrimination task in lower-left visual field. The practiced trial number in a day varied between 450 to 900 and participants completed three to five sessions in each week. However, authors did not specify how long the training lasted on average. As a result of training, all participants showed reduction in thresholds, the amount of reduction is varied between 22% to 71% with 51% mean. When participants thresholds are compared for horizontal bisection discrimination task in the trained visual region, the mean improvement decreased to 20% . Similarly, when authors compared the before-after thresholds in the untrained spatial locations with trained task, the reduction in the thresholds started to disappear as the distance from trained location got bigger. The researchers concluded improved performance with that bisection discrimination task is specific to trained task's charactheristics.

Four years after Crist et al.'s study, another study assessed the specificity of the bisection discrimination task. In this experiment, participants trained with 450 trial in each day, for ten sessions. They tested how change in the configuration of the bisection discrimination task effects transfer. For this purpose, they tested transfer for the dot bisection discrimination task, tilted bisection discrimination task. The results showed that, even when orientation of the trained task changes for 10°increased performance with training diminishes. Moreover, they also showed that changing the color or length of the stimulus also dissolve the learning effect [29].

One of the main purposes of choosing this stimuli is that we wanted to asses if there is a neural change in the conditions which shows specificity. As reviewed above previous research shows that bisection discrimination task is specific to trained location, to replicate previous research we also collected data from different polar angles in the same eccentricity. Moreover, we also collected that from the trained spatial location and 90 °rotated task to test task specificity. Another purpose of choosing this stimuli is t have a stimulus which shares the receptive field properties of V1. As known for a long time, simple cells in V1 has elongated receptive fields, each V1 cell is responsive to certain orientations [64].

In behavioral experiment sessions, we collected participants threshold for training and control conditions. Number of days/sessions for training varies across studies, and there is not an exact conventional procedure for training in the literature. However, a very common interval for training is 5 to 10 days in general. Accordingly, we determined 8 sessions and 12 days, which include 11 psychophsysics sessions which includes 8 training and 3 threshold measurement session and 6 fMRI sessions. The outline of the experiment is given in Figure 2.1
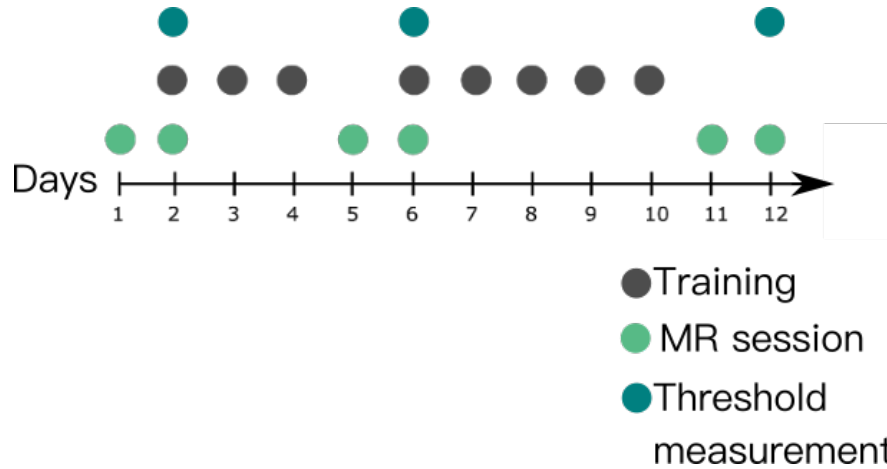
Figure 2.1: Outline of experiment. The data collected over 12 days. Baseline, in other saying pre-training MR measurements were taken when participants were naive. After second MR session, threshold measurements were assessed and then participants received their first training. After 3rd training session, the mid MR measurements and thresholds were taken. After 8th, last, training session MR and threshold measurements were collected again.

2.2 Method

2.2.1 Participants

Six participants participated in this study (5 female, 1 male, age range: *18-30, M=23,5, SD=4,46*). Five participants were right handed. All participants had normal or corrected vision and, no history of neurological disorders. The study is approved by Bilkent University Human Ethics Committee. Before the experiment, all participants gave consent by signing informed consent forms. For each one hour, participants were promised to receive 15TL worth gift card. The gifts were promised to be given at very end of the experiment (after one month the training is completed).

2.2.2　Stimuli and Apparatus

The experiment is programmed in MATLAB2017 with using Psychtoolbox-3 [65, 66] Stimuli presented in NEC MultiSync LCD 2190UXp (21-inch, 1600x1200, 60Hz) monitor. Participants seated 95cm away from monitor, their heads immobilized with chin-rest.

Bisection stimuli contained three vertical lines, the outer elements placed with 1.5°distance. The length of lines was also 1.5°. The central line of the bisection stimulus placed slightly closer to one of the outer lines. The displacement direction of central line determined randomly in each trial. For determining the amount of the displacement, adaptive staircase method had been used [67].

The vertical bisection discrimination stimulus is presented with a gray background and a fixation point on the center of the screen. The fixation point and task stimulus are presented as black. In the training condition, participants trained at 210°polar angle, vertically. Additionally, the experiment had five control conditions in the behavioral sessions. The control conditions are as follow: 210°polar angle horizontal stimulus, 150°polar angle vertical, 150°polar angle horizontal, 45°polar angle vertical, 45°polar angle horizontal.

The control conditions are used to evaluate task and location specificity of the learning. The participants did not receive training for these conditions but underwent threshold measurements at three different time points during the experimental time course as described in Figure 2.1.

2.2.3　Task and Experimental Design

In each trial, a black fixation point presented continuously. Participants are asked to fixate on the fixation point. The bisection stimulus presented for 300ms. After stimulus presentation, participants' response obtained without time limit. In the vertical bisection task, the middle line placed closer to left or right line; in the horizontal bisection task, the middle line placed closer to upper or
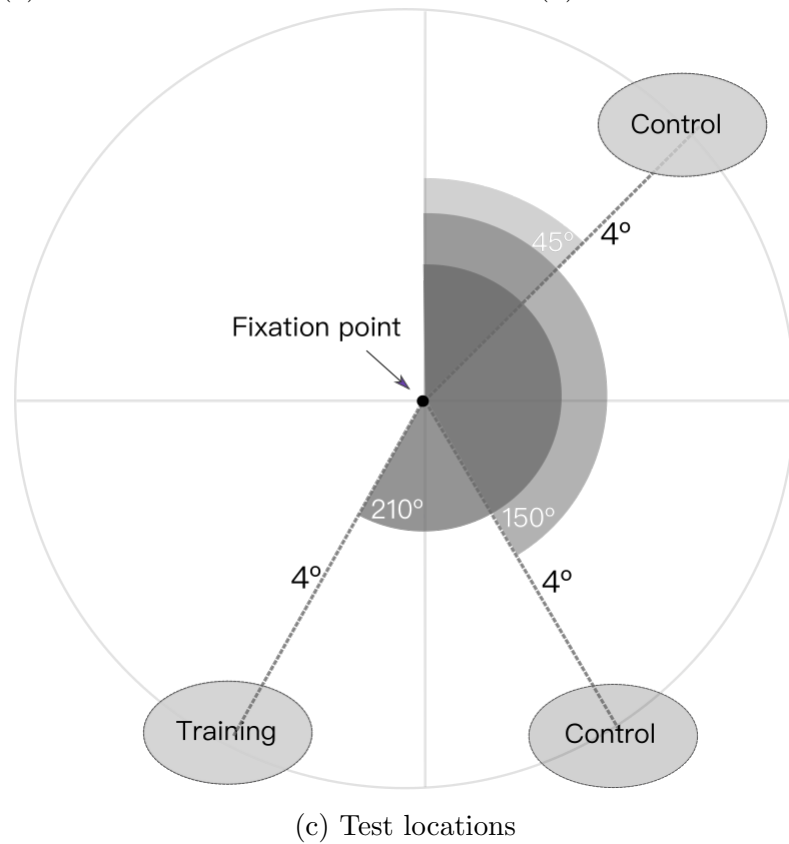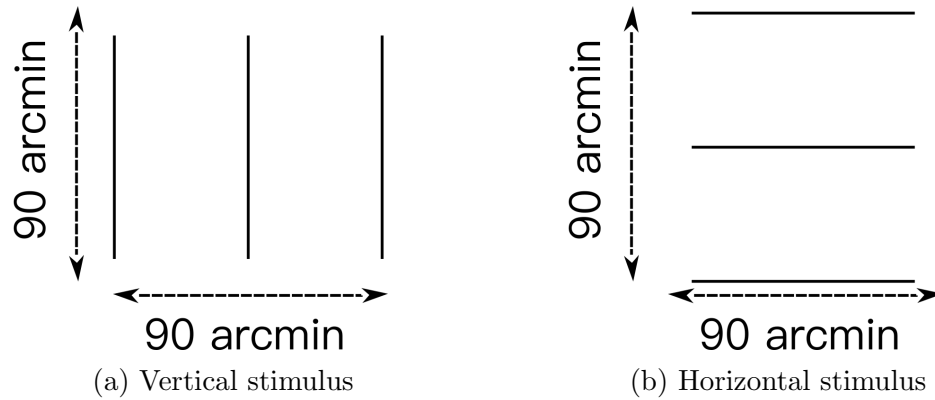
(a) Vertical stimulus

(b) Horizontal stimulus

(c) Test locations

Figure 2.2: Stimulus specifics: The height and width of the stimulus was 90',
which corresponds to 1.5 degree. The stimulus contained three lines. According
to conditions, the lines appeared vertically (a) or horizontally (b). The middle
point of stimulus was 4°away from the fixation point. While polar angle of training
location is 210°, the 45°and 150°polar angles are used as control locations. For
behavioral experiments, the threshold measurements are taken with vertical and
horizontal stimulus at all of the three spatial locations. However, training was
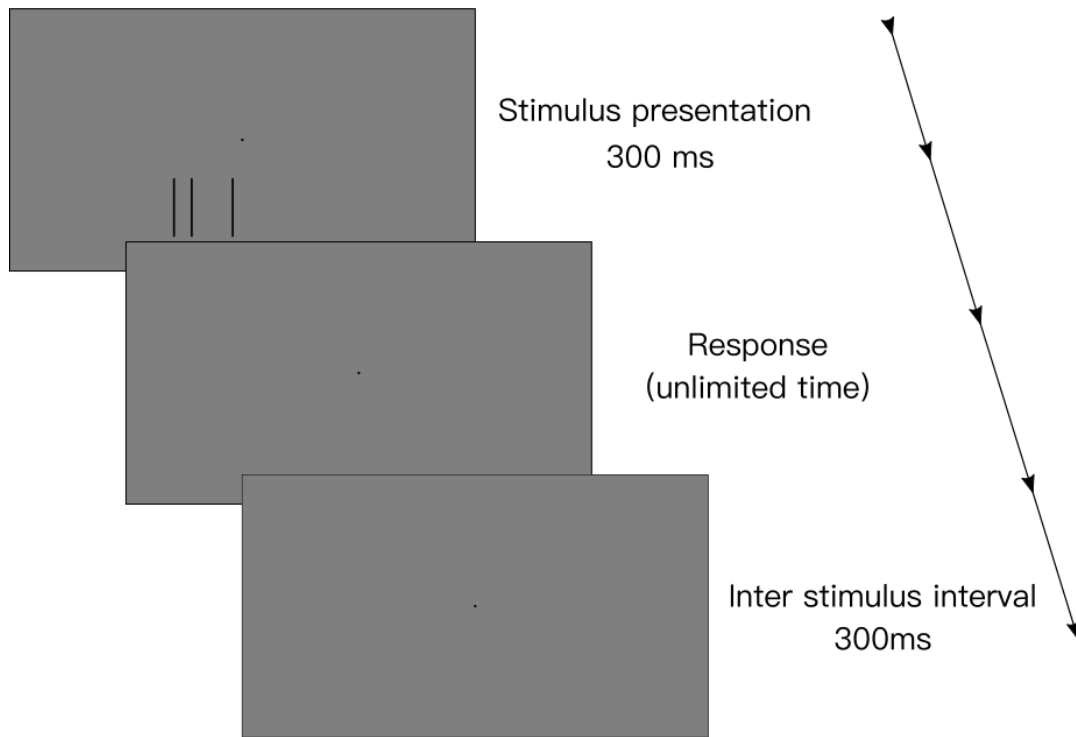only done at 210°polar angle with vertical stimulus.

Figure 2.3: Time course of single trial in behavioral experiment: The stimulus presented for 300 ms. After stimulus presentation, a blank screen with only fixation point appeared to wait participants response. Participants responded using the direction keys on the keyboard. After response is collected 300ms break was given before presenting the next trial. The visualized trial is belongs to the training condition.

lower line. In a two- forced alternative choice (2AFC) task, participants asked to indicate the central line's displacement by pressing direction keys on the keyboard. The next trial initiated 300ms after the participant responded. Test line displacements are determined according to participant's response history with two 3-up 1-down staircases. Figure 2.3 shows the temporal configuration of the stimulus.

Threshold measurement: Threshold measurements were acquired before training (1st measurement), after third session of training (2nd measurement), after training completed (3rd measurement). In each measurement session, participants completed 150 trials for each condition. The threshold measurements were obtained from three different polar angle with both vertical and horizontal

bisection task. The sorting of the conditions was randomized for each participant.

The staircase method comprised two staircases: easy and hard. Each staircase consisted of 75 trials, which results in 150 trials in one threshold measurement block. The easy staircase started with 0.5°and the hard started with 0.08 degree, step size was 0.05°for both of the staircases .

Training session: In each training session, participants completed 10 blocks, each of them containing 120 trials. There were 8 training sessions in the experiment which results in 9600 trial for each participant. In the training blocks, the stimulus presented at 210 polar angle, vertically. The test intensities are determined with 3up-1down staircases. The starting values of staircases and the step size was identical to threshold measurement staircase values, as stated above.

Training sessions conducted on a daily basis except the one day break between third and fourth session of training. The break is given in order to collect MRI data.

2.2.4   Data Analysis

Behavioral analyses are conducted on MATLAB2017b, using Psignifit4 [68] toolbox. Psychometric function are fitted with Weibull function. To compare the thresholds, repeated measures ANOVA performed. Statistical analysis is performed using JASP software [69].

2.3 Results

2.3.1 Training condition

The pre-training measurements showed that the mean thresholds for vertical bisection discrimination task presented at 210°polar angle was 4.35 arcmin *(SD=1.01)*. The mid-training threshold which were taken after third session of training, measurements showed that the mean threshold decreased to 2.90 arcmin *(SD=0.83)*. One day after training ended, post-training measurements were taken. The results showed that the mean threshold increased to 4.56 arcmin *(SD=1.83)*. For descriptive figure for training condition please see Figure 2.4.

The 3x1 repeated measures ANOVA test, independent variable was session (with 3 levels: pre-learning, mid-learning and post-learning) revealed effect of session in the training condition (210°polar angle, training stimuli) *(F(2,10)=4.35, p=0.04)*, please see table 2.4. The post-hoc analysis on session, did not reveal any effect between sessions (please see Table 3.1).

Table 2.1: Within Subjects Effects

	Sum of Squares	df	Mean Square	F	p
Session	9.750	2	4.875	4.348	0.044
Residual	11.212	10	1.121		

Table 2.2: Post Hoc Comparisons - Session

		Mean Difference	SE	t	p_{holm}
Mid	Post	-1.655	0.643	-2.574	0.100
	Pre	-1.446	0.458	-3.155	0.076
Post	Pre	0.210	0.705	0.297	0.778

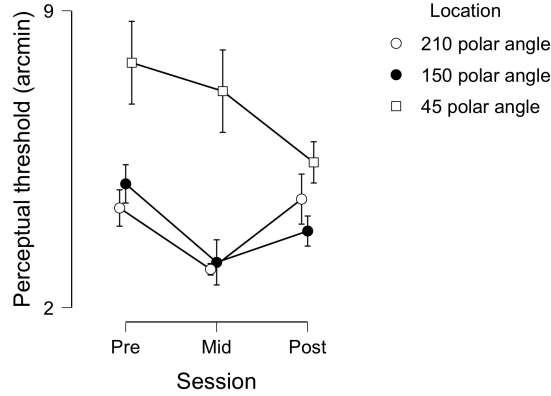*Note.* Bonferroni adjusted confidence intervals.

Figure 2.4: Threshold changes across visual locations with horizontal task.

2.3.2 Control Conditions

2.3.2.1 Location Specificity

The location specificity was evaluated by comparing threshold changes in the control locations (150°and 45°polar angle), with vertical discrimination task. The descriptive information regarding to vertical conditions are given in Table2.4 and Figure 2.4.

Table 2.3: Descriptives for vertical bisection discrimination thresholds

Session	Location	Mean	SD	N
Pre	210 polar angle	4.350	1.011	6
	150 polar angle	4.919	1.479	6
	45 polar angle	7.775	2.098	6
Mid	210 polar angle	2.904	0.831	6
	150 polar angle	3.068	1.398	6
	45 polar angle	7.104	2.449	6
Post	210 polar angle	4.559	1.816	6
	150 polar angle	3.806	1.020	6
	45 polar angle	5.425	1.506	6

To assess location specificity, repeated measures of ANOVA performed . The ANOVA test had a factorial design with two independent variables, session(with 3 levels: pre-learning, mid-learning and post-learning) and location(with 3 levels: 210°, 150°and 45°polar angle). The results of ANOVA showed
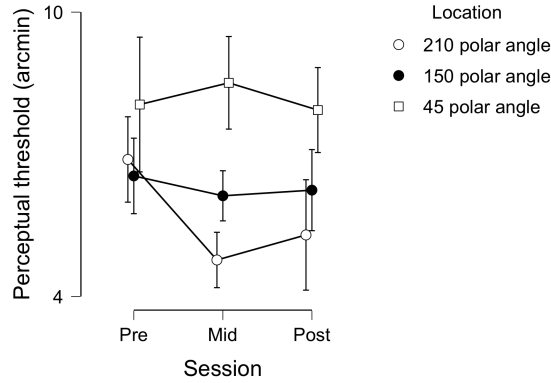
Figure 2.5: Threshold changes across visual locations with horizontal task.

effect of location (F(2,10)=46.50, p= 0.0000270). There was no effect of session (F(2,10)=2.76, p=0.11). Interaction of session and location was also insignificant (F(2,10)=2.20, p=0.11) The simple main effects analysis showed session's effect on 210°and 150°polar angle locations was significant (F(2,10)=4.35 ,p=0.04 and F(2,10)=4.42, p=0.04). For the 45°polar angle condition, the simple effect of session was insignificant (F(2,10)=1.61, p=0.25).

Table 2.4: Within subjects effects for vertical bisection discrimination thresholds

	Sum of Squares	df	Mean Square	F	p
Session	17.882	2	8.941	2.758	0.111
Residual	32.413	10	3.241		
Location	96.362	2	48.181	46.499	< .001
Residual	10.362	10	1.036		
Session * Location	19.859	4	4.965	2.204	0.105
Residual	45.041	20	2.252		

2.3.2.2 Task Specificity

To test task specificity, threshold measurements with horizontal bisection discrimination task evaluated. The horizontal bisection discrimination thresholds were taken in 210 °, 150 °and 45 °polar angles. Descriptive information regarding to this threshold measurements are given in Table 2.5 and Figure 2.5.

Table 2.5: Descriptives for horizontal bisection discrimination thresholds

Session	Location	Mean	SD	N
Pre	210 polar angle	6.891	3.613	6
	150 polar angle	6.544	3.452	6
	45 polar angle	8.050	3.408	6
Mid	210 polar angle	4.770	1.633	6
	150 polar angle	6.124	2.593	6
	45 polar angle	8.508	1.952	6
Post	210 polar angle	5.298	1.636	6
	150 polar angle	6.244	1.850	6
	45 polar angle	7.933	3.272	6

Task specificity assessed with repeated measures of ANOVA test using horizontal bisection discrimination task thresholds. The ANOVA test had a factorial design with two independent variables, session(with 3 levels: pre-learning, mid-learning and post-learning) and location(with 3 levels: 210°, 150°and 45°polar angle). The ANOVA results showed that there were no effect of location$(F(2,10)=3.86, p=0.06)$ and session

Chapter 3

Task Related Functional Magnetic Resonance Imaging

3.1 Background

The functional MR imaging developed three decades ago and has been used extensively in neuroscience research thanks to its non-invasive nature. In visual perceptual learning, task-based fMRI has been used widely to examine which brain regions are related to the learning process. Moreover, scientists assessed how the functional properties are changed in the perceptual-learning related regions.

As reviewed earlier, previous research showed that with learning, the functional properties of various brain regions had changed [40, 70, 71, 28, 72, 73, 21, 74, 24, 35]. To investigate changes in the BOLD signal, we collected fMRI data while participants performing a bisection discrimination task in the scanner. The task-related fMRI data collected at trained (210 polar angle) and untrained locations (45 and 150 polar angle) with trained task (vertical stimulus) to examine how location specificity is represented in the BOLD signal. Moreover, we also collected data with rotated stimulus(horizontal bisection discrimination task) at

trained (210 polar angle) and untrained (45 polar angle) locations, to test the task specificity. For a more sensitive analysis, we collected functional localizer and pRF data. From the intersection of these two analysis, we obtained stimulus processing functional ROIs for each visual subregion. After that, the BOLD amplitude and the shape of hemodynamic response function have assessed.

3.2 Methods

3.2.1 Participants

Participants who attended the behavioral sessions, also attended to all MRI sessions. However, one of the subject's data did not analyzed, because functional localizer runs did not show significant activation for progress further steps of analysis. By excluding this subject, the mean of subjects' (5 female) age became *22,75* and the standard deviation became *4,60*. Before every MR session, participants were given informed consent form. For each hour spent in the MR sessions, participants are promised of 25TL worth gift card. The gift card given at the very end of experiment (after the final session).

3.2.2 MRI Data Acquisition

3.2.2.1 Apparatus

The data collected at the National Magnetic Resonance Research Center (UMRAM), Bilkent University. MRI data collected on a Siemens Tim Trio 3T scanner with a 32-channel phase array head coil. The stimuli was displayed on a MR compatible LCD monitor (TELEMED, 1920 X 1080 pixel, 32 inch). Participants looked the monitor through a mirror placed above their eyes. The viewing distance from the scanner was 168cm. Participants' response is transmitted by a MR compatible response pad (Current Design, fORP 904 fMRI trigger and

response system).

3.2.2.2 MRI Acqusition Parameters

Anatomical images are collected with an T1-weighted 3D MPRAGE squence (1x1x1 mm^3 resolution, TE: 3.02 ms, TR: 2600 ms, FOV read: 256, FOV phase: 87.5, flip angle: 8 degrees). For functional scans, T2*-weighted sequence is used (1.6x1.6x1.6 mm^3 isotropic voxel, TR:2000ms, TE:42.8ms, Flip Angle: 80 degrees, Slice thickness: 1.6mm, Number of Slices: 76, FOV:192mm, Multiband factor: 4, EPI factor: 120).

For distortion correction, two images which have opposite phase encoding direction, in other saying blip-up blip-down data, has collected in the anterior-posterior and posterior-anterior direction. The blip-up blip-down data is collected with a gradient echo EPI sequence (1.6x1.6x1.6 isotropic voxel, TR:10484, TE:76.6, Flip Angle:80, FoV:192mm, Slice number:76, Multiband factor: 1, EPI factor: 120).

3.2.2.3 Functional Localizer Scan

To determine region of interest, for each stimulus location (45, 150, 210 polar angles) that are used in the task-based fMRI, a functional localizer scan obtained. The functional localizer runs are conducted in separate runs for each location, the order of runs are randomized. A circle flickering (at 10 Hz) checkerboard stimulus which has 90' size was used. For each test location a separate run has carried out. The localizer scan had 10 repetition of 12TR length blocks. At the beginning of the scan, 5TR dummy scans collected to ensure signal is saturated and 6TR rest collected. In each block, 6TR checkerboard stimulus presented, then 6TR of rest period initiated, meaning no stimulus is presented. After 10 blocks, 5TR of overrun images are collected. Each run lasted 136TR, equals to 4minutes 32 seconds. During whole functional localizer scan, participants fixated on the fixation point in the middle of the screen. While the functional localizer
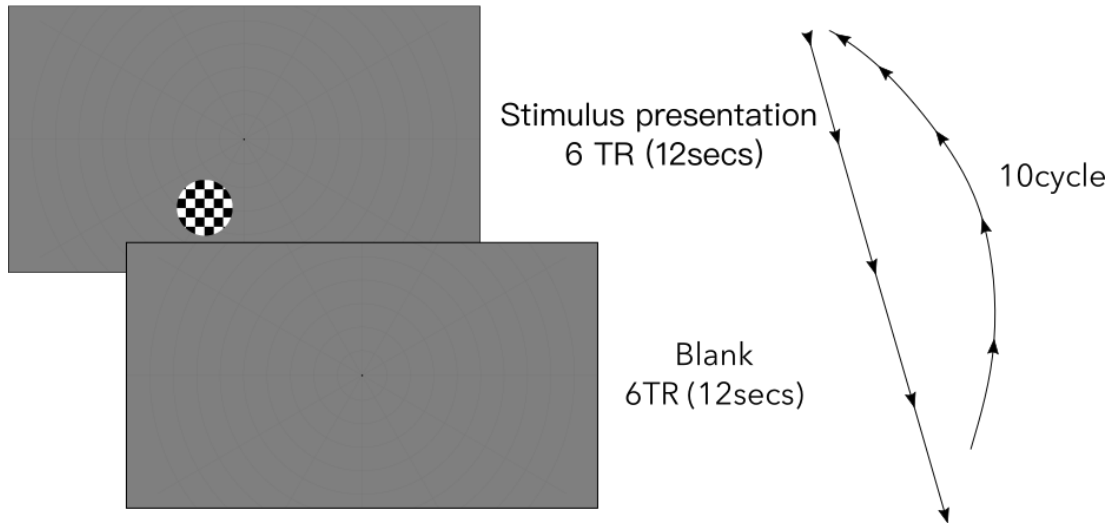
Figure 3.1: Experimental design of functional localizer scan. The scan had block design. In each block, 6TR (12 seconds) a checkerboard stimulus flickering at 10Hz presented. After stimulus presentation 6TR (12seconds) break were given. This cycle is repeated for 10 times.

scans were carried out, to ensure participants are looking to the fixation point, a fixation task has been performed. Participants indicated the color of the fixation point by pressing the assigned button on the response box. A visual representation of localizer run is given in Figure 3.1.

3.2.2.4 Task Based fMRI Stimuli and Task

For the behavioral task which was performed in the scanner, the parameters of the behavioral task are revised. The stimulus size was 90' and eccentricity was 4°, as in the behavioral experiments. The task based scan contained 5 runs, each of the runs containing one condition. The scanned conditions were training condition(vertical-210 polar angle stimulus), control 1 (vertical-45 polar angle stimulus), control 2(vertical-150 polar angle stimulus), control 3 (horizontal-210 polar angle stimulus), control 4 (horizontal-45 polar angle stimulus) conditions. The order of task based fMRI scans is counterbalanced between participants.

Method of constant stimuli was used, the middle line presented at 6,12 and, 18 arcmin away from the middle of the outer lines. The direction and amount of displacement was randomized for each run. Each run consisted of 48 trials, 8 trials for test line displacement. At the beginning of each run, 5TR dummy runs were collected to ensure signal is saturated. Then for 6TR rest data obtained. Rapid event related design is used in the fMRI experiment. Each event lasted one TR, at the beginning of the trial the fixation point turned red for 500ms to indicate test stimulus will be presented soon. Then test stimulus presented for 300ms, response duration is limited with 1200ms. Participants indicated the direction of displacement by pressing the assigned button on response boxes. After each event, jittered inter-stimulus interval is given which varied between 1 and 4 TR. A visual representation of time course of a trial is given in the Figure 3.2. After all trials completed, 5TR overrun collected in order to capture signal fully. Each run lasted 185TRs which equals to 6minute 22seconds.

3.2.3 MRI Data Analysis

3.2.3.1 Preprocessing

Anatomical Surface Reconstruction: The high-resolution anatomical images are skull stripped, segmented to white and gray matter, normalized for intensity and smoothed, surface reconstructed by using FreeSurfer's recon-all command [75].

Functional Scan Preprocessing: Before starting preprocessing, five volumes are deleted in order to assure signal quality. For distortion correction, FSL's TopUp has been used to unwarp each functional run. After distortion correction FSL's FMRI Expert Analysis Tool (FEAT) version 6.00 has been used. FMRI data registrated to each subject's own anatomical images and standard MNI152 spaces using FSL's FLIRT. Motion correction applied to functional images using FSL's MCFLIRT and spatial smoothing (Gaussian kernel, FWHM 5mm) and high pass filtering applied. The intensity normalisation applied by using a single
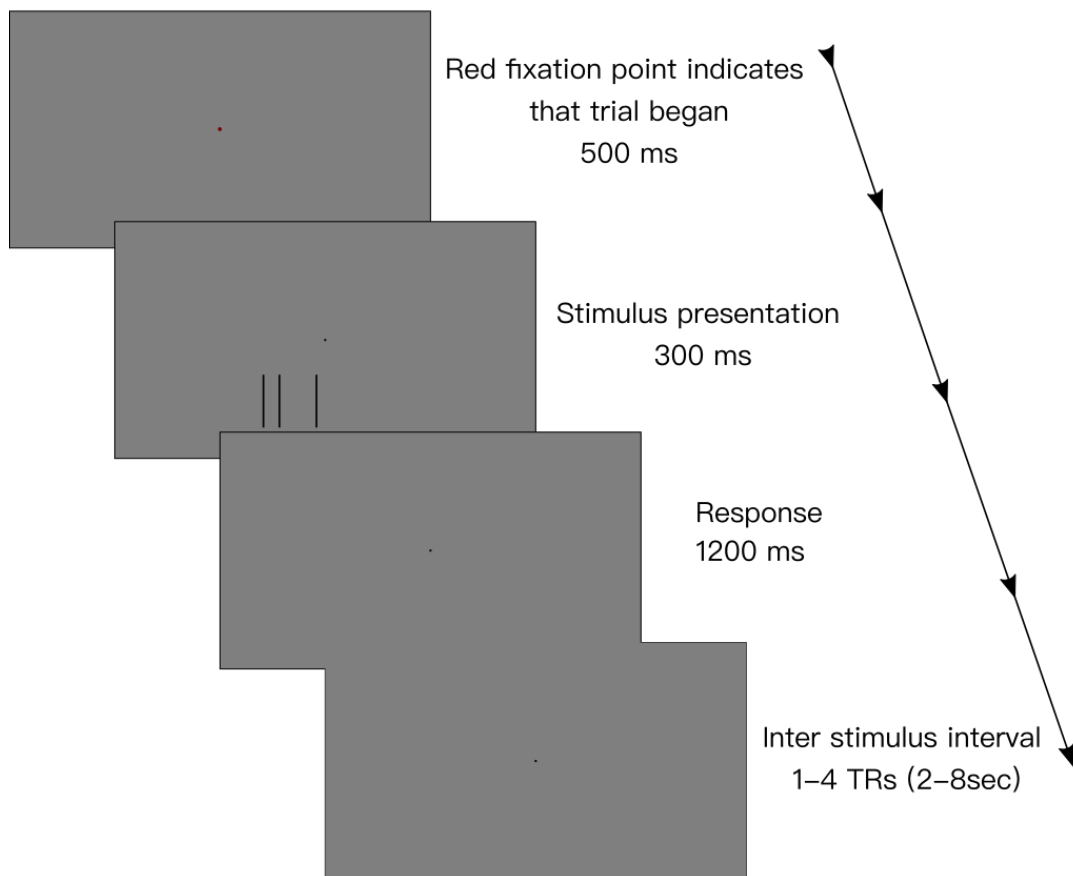
Figure 3.2: Time course of single trial in task based fMRI scan. Before stimulus presentation, the fixation point turned red for 500ms to indicate that the stimulus will be presented soon. Then, the stimulus presented for 300ms. Participants were given 1200ms for response. After trial ended, blank screen with only fixation point presented until the inter stimulus interval has ended. The inter stimulus interval is jittered between 1-4TR (2-8 seconds)

multiplicative factor. The brain is extracted from functional scans using brain extraction tool (BET).

3.2.3.2 First Level Analysis

Functional Localizer Scans: The General Linear Model (GLM) applied with using FSL's FEAT. For removing the temporal autocorrelations, FILM prewhitening applied. For thresholding data, P=0.05 (corrected) threshold set as cut point.

Task Based fMRI scans: The analysis is conducted at MATLAB using custom code. From the preprocessed task based run raw signal timecourse extracted. Then, the mean of each ROI, z-scored and detrended. For estimating BOLD amplitude, Pernet's percent signal change formula is adapted to our experiment [76]. To determining signal change due to task, the baseline signal which corresponds to 12 second rest measurement, extracted from the mean of the signal after 2 seconds of stimulus onset.

3.2.3.3 Second Level Analysis

For comparing the diffeerent time-points, repeated measures of ANOVA had performed using JASP software.

3.3 Results

To asses the changes occur during the task we used functional ROI's derived from pre-training functional localizer runs. To separate functional regions to visual regions, we planned to use visual region borders which derived from pRF analysis. However, the pRF analysis did not yield sufficient measurements for delineation of visual areas for all subjects. Therefore, to be consistent FreeSurfer's
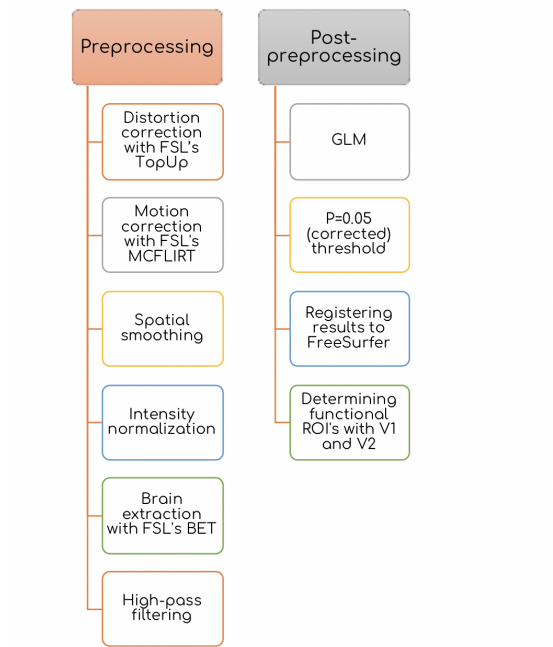
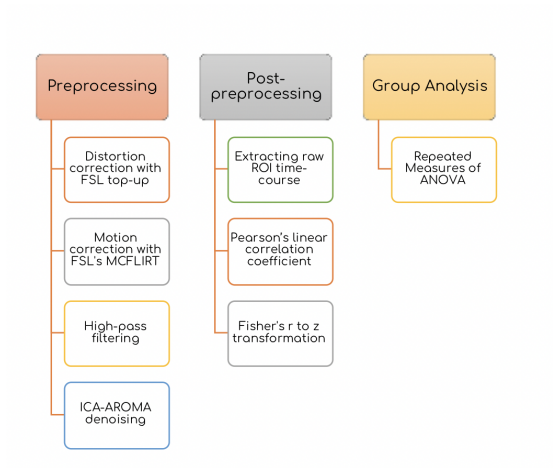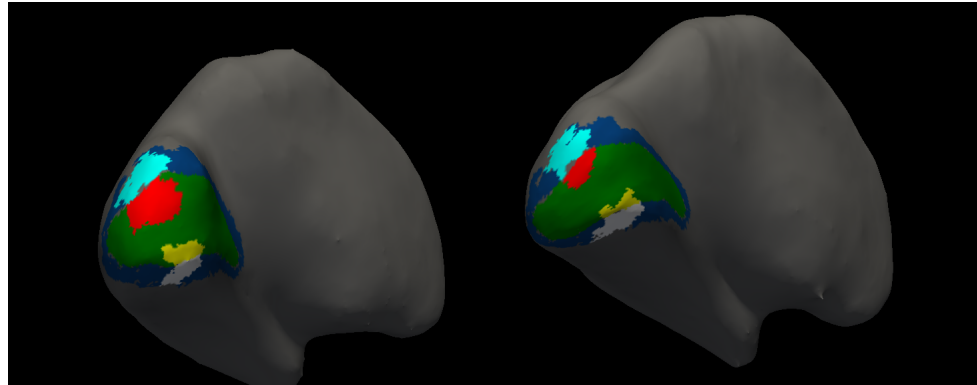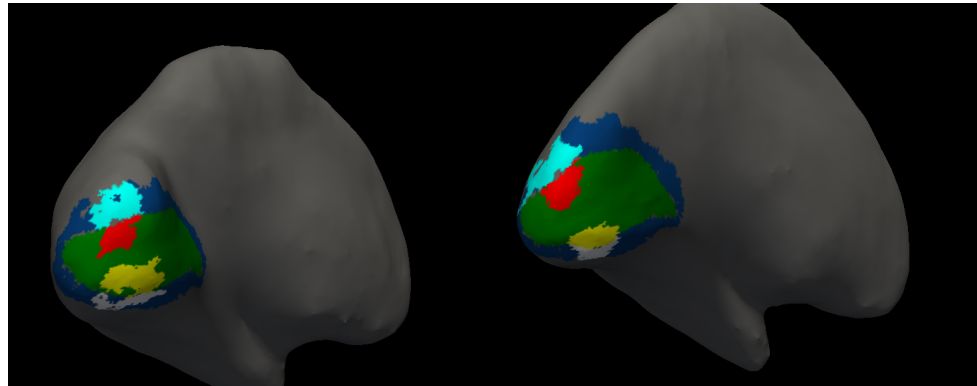Figure 3.3: Functional localizer scan analysis pipeline

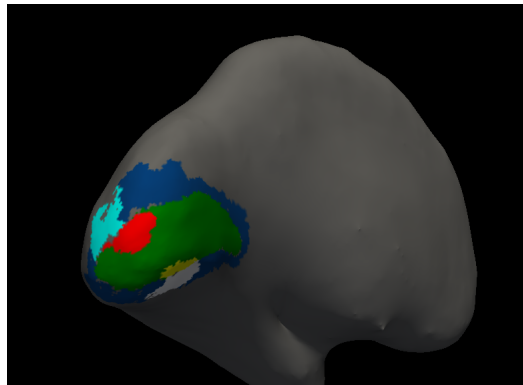Figure 3.4: Task-based fMRI scan analysis pipeline

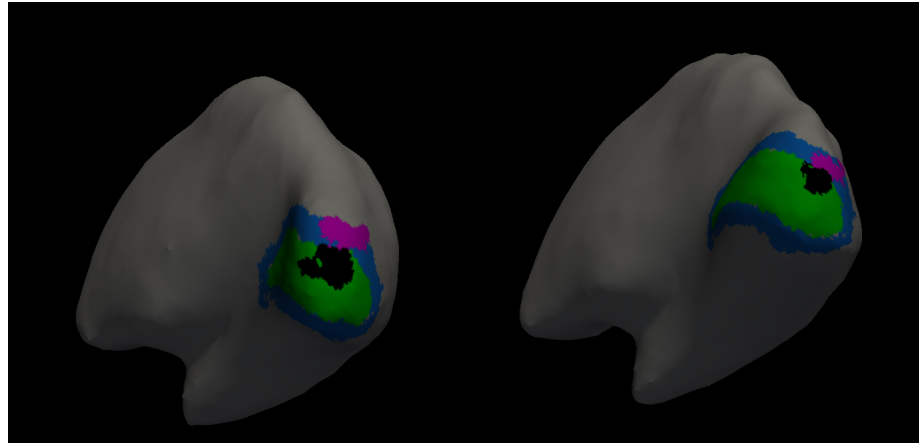(a) sub-01 left hemisphere

(b) sub-02 left hemisphere

(c) sub-04 left hemisphere
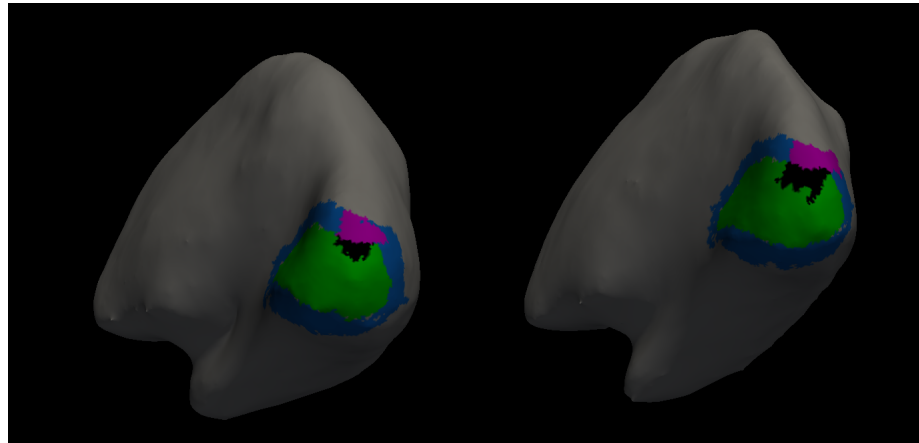

(d) sub-05 left hemisphere

(e) sub-07 left hemisphere

Figure 3.5: Left-hemisphere functional ROIs.The green region represents V1 border, the ocean-blue represents V2 border. V1 and V2 borders are drawn by Freesurfer in subject's native anatomical space. 150 °polar angle functional localizer activation's intersection with visual regions are represented with Turkish-blue in the V2 region and red in the V1 region. 45 °polar angle functional localizer activation's intersection with visual regions are represented with white in the V2 region and yellow in the V1 region. All the functional localizer scans are derived from pre-learning scans except sub-04. In sub-04's pre-session localizer scans did not yield reliable results, therefore, post-session localizer runs are used to identify functional ROIs.

(a) sub-01 right hemisphere (b) sub-02 right hemisphere

(c) sub-04 right hemisphere (d) sub-05 right hemisphere
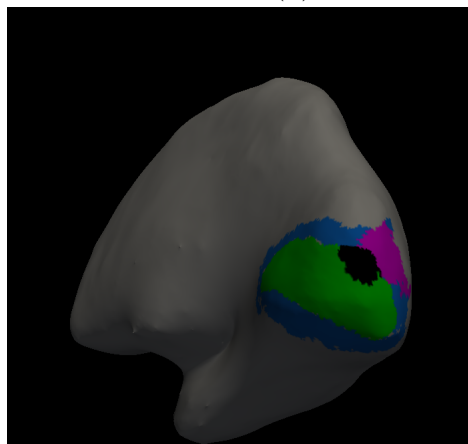
(e) sub-07 right hemisphere

Figure 3.6: Right-hemisphere functional ROIs.The green region represents V1 border, the ocean-blue represents V2 border. V1 and V2 borders are drawn by Freesurfer in subject's native anatomical space. 210 °polar angle functional localizer activation's intersection with visual regions are represented with dark-magenta in the V2 region and black in the V1 region.

Figure 3.7: BOLD amplitude change for the training condition

anatomic delineations of V1 and V2 regions are used to divide functional localizer to visual regions.

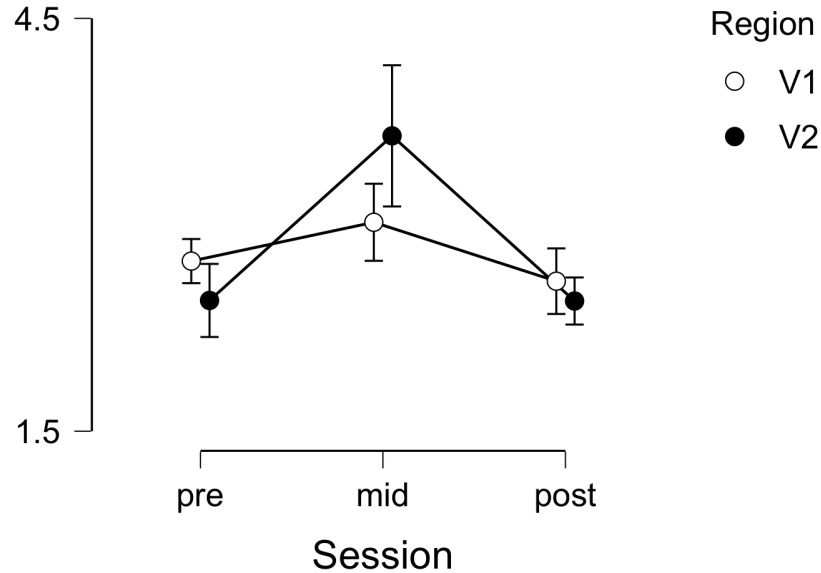### 3.3.1 Training condition

A 2x3 repeated measures ANOVA was conducted to investigate the effect of brain region (with 2 levels: V1 and V2) and the scanning session(with three levels: pre-learning, mid-learning, and post-learning). Session ($F(2,8)=$ 6.62, $p=0.02$) had effect. On the other hand, there is no effect of region($F(1,4)=0.14$, $p=0.73$). Post-hoc test on session, did not show any effect,too (please see Table 3.1)

Table 3.1: Post Hoc Comparisons - Session

		Mean Difference	SE	t	p_{holm}
Mid	Post	0.814	0.275	2.960	0.083
	Pre	0.739	0.193	3.835	0.056
Post	Pre	-0.075	0.266	-0.282	0.792

33

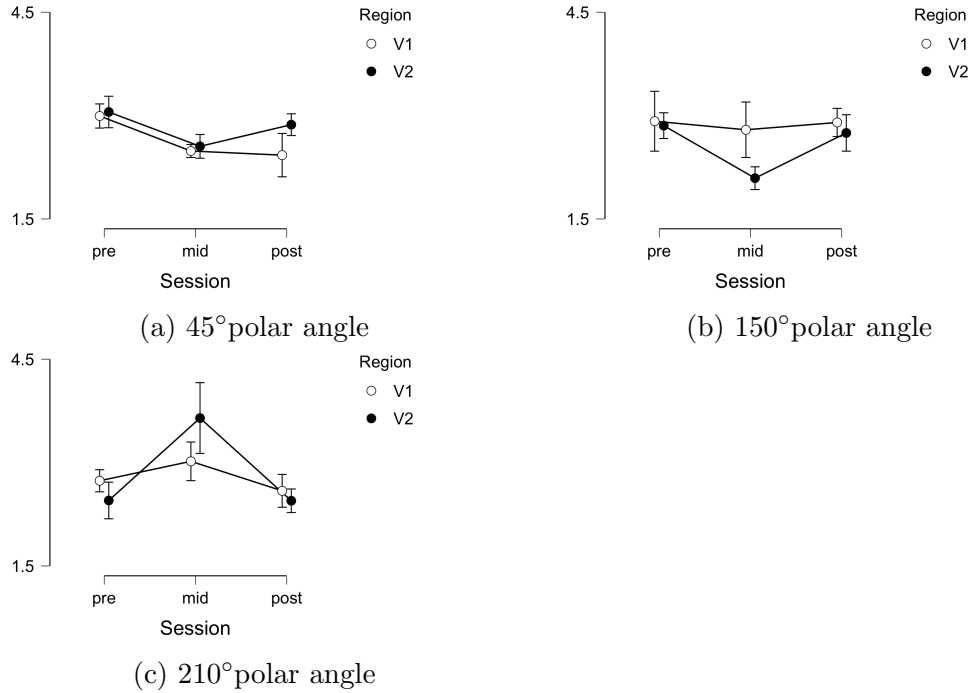(a) 45°polar angle

(b) 150°polar angle

(c) 210°polar angle

Figure 3.8: BOLD amplitudes for vertical bisection discrimination tasks. Each plot shows one of the test locations. 45°polar angle presented at the a, 150°polar angle presented at the b and 210°polar angle presented at the c.

3.3.2 Control Conditions

3.3.2.1 Location Specificity

A 3x3x2 repeated measures ANOVA was conducted to investigate the effect of session (with 3 levels: pre-learning, mid-learning and, post-learning), location (with 3 levels: 210°, 150°, and 45°polar angle), region(with 2 levels: V1 and V2). There was no effect of session ($F(2,8)=0.54$, $p=0.60$), location ($F(2,8)=0.19$, $p=0.83$), and region($F(1,4)=0.06$, $p=0.82$). The descriptive plots of conditions are given in Figure 3.8.
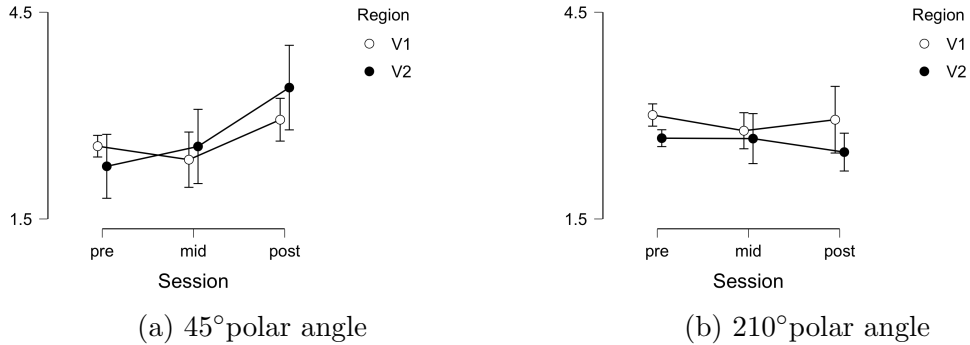
(a) 45°polar angle　　　　　　　　(b) 210°polar angle

Figure 3.9: BOLD amplitudes for horizontal bisection discrimination tasks. The plot on the left (a) shows BOLD amplitude while participants performing horizontal bisection discrimination task at 45°polar angle, 210°polar angle shown on the right(b).

3.3.2.2　Task Specificity

A 3x3x2 repeated measuresANOVA analysis performed with the same design as 3.3.2.1 section, except in this analysis, location had two sub-levels as 210°and 45°polar angle. There was no effect of session ($F(2,8)=0.64$, $p=0.55$), location ($F(1,4)=0.36$, $p=0.58$), and region($F(1,4)=0.38$, $p=0.57$). The descriptive plots of BOLD amplitude in the horizontal conditions given in the Figure 3.9.

3.4　Intermediate Discussion

In this part of the thesis, we obtained task-based fMRI data before-training, mid-training and post-training. The BOLD amplitude while participants performing training task changed between sessions. However, post-hoc tests did not reveal any effect.

For the control conditions, the analysis which examines neural effects of location specificity showed that neither 150°polar angle vertical discrimination task nor 45°polar angle task did not show any significant change between sessions. Furthermore, task specificity control conditions that participants are performed horizontal bisection discrimination task, did not yield any significant changes

between sessions.

Overall, the analysis of task-based fMRI data did not showed any significant evidence across perceptual training in terms of BOLD amplitude in the V1 and V2 regions. However, given that our sample size is very small, this might introduced noise into the data. Increasing sample size would clarify the results.

Chapter 4

Resting State Functional Magnetic Resonance Imaging

4.1 Background

Almost three decade ago, Biswal and colleagues instructed participants to rest in the scanner and collected functional MRI images [77]. The correlation analysis of this data showed that timecourse of a seed region selected from left motor cortex, had correlated with other brain regions' timecourses in the motor system. The findings of this research has been replicated with numerous studies [78].It has been believed that, the correlations in the timecourses represented the functional communications in the anatomically distant brain regions.

In terms of plasticity, previous researches has shown functional connectivity changes with training. Guerra-Carrillo and other researchers reviewed and evaluated over ten studies which focused on changes in the resting state functional connectivity in time-course of learning. They concluded that, resting-state

functional connectivity can capture the experience-dependent changes in the functional arthitecture. [79]. Moreover, as reviewed in the Introduction chapler (Section 1.2.1.), visual perceptual learning studies also showed change in the functional connectivity in resting state networks [48, 45] and connectivity between visual areas [48, 49].

4.2 Method

4.2.1 Participants and MRI Acqusition Parameters

The information related to participants were given in 2.2.1 and 3.2.1 Participants sections and information regarding to MR sessions were given in the 3.2.2.2 MRI Acqusition Parameters section.

4.2.2 Resting State fMRI Protocol

In resting state scan, 305 volumes (approximately 10minutes) are obtained. Participants instructed to fixate gray fixation point on the black background and asked to think nothing specific and remain passive. Resting state scans were obtained first in each MR session to avoid confounds.

4.3 Analysis

4.3.1 Preprocessing

Before starting preprocessing, five volumes are deleted in order to assure signal quality. For distortion correction, FSL's TopUp has been used to unwarp each run. After distortion correction, motion correction applied using FSL's
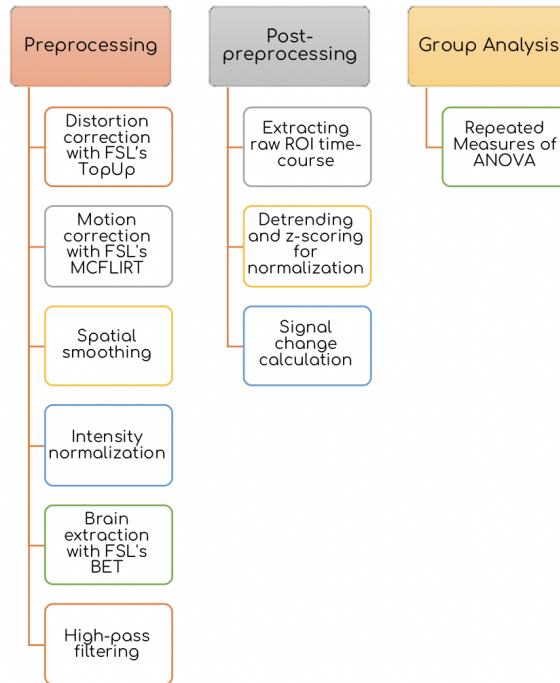
Figure 4.1: Resting-state functional connectivity analysis pipeline

MCFLIRT. Then, high-pass filtering (0.005 Hz) applied to the data. Then by using ICA-AROMA the data denoised.

4.3.2 Functional Connectivity Analysis

For analyzing functional connectivity, Pearson's linear correlation coefficient is calculated between each functional ROI. The process of determining ROI's are explained in the Section 3.3. Correlation coefficients are converted using Fischer's r-to-z transformation.

4.3.3 Second-level Analysis

For comparing different timepoints, 3x3 repeated measures of ANOVA carried out tested location (with 3 levels: 210°, 150°, 45°polar angles) and session
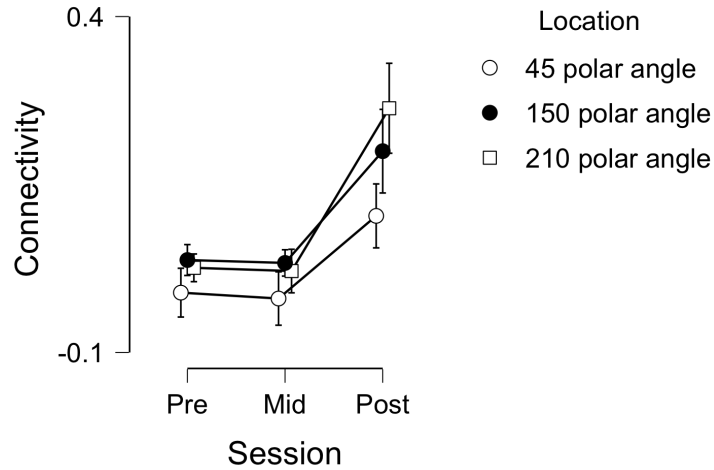
Figure 4.2: Connectivity changes across sessions.

(with 3 levels: pre-learning, mid-learning, post-learning). The results showed significant main effect of session ($F_{(2,8)}$=28.72, p=0.000223). The main effect of location was insignificant ($F_{(2,8)}$=0.64, p=0.64). Post Hoc comparison showed that post session was significantly different from pre session (p= 0.000939, Holm corrected) and from mid session (p= 0.00396, Holm corrected). Moreover, simple main effect analysis showed that 210°(p <0.05) and 150°(p <0.005) polar angle are significantly changed between sessions. Descriptive plot visualizing group means are given in Figure 4.2.

4.4 Intermediate Discussion

The analysis of the resting-state functional-connectivity between V1-V2 regions which process 4°eccentricity conducted. The results showed statistically significant changes in 210°which is the training condition. Previous research also supports this findings [48, 49]. Furthermore, 150°polar angle in the post-training session also showed significant change between sessions. Besides, there was no significant change between pre-training and mid-training conditions at these locations.

This change in the 150°polar angle condition can be interpreted change in

the opposite hemisphere because of inter-hemispheric connections. The simple main effect analysis revealed that, there is no significant effect of session on 45°polar angle. Since 45°polar angle is free from inter-hemispheric connections, it also supports the our previous interpretation.

The most notable finding from this analysis that, while functional connectivity changes did not show any significant change between pre-training and mid-training sessions, strong changewas seen at the late phases of the perceptual training.

Chapter 5

General Discussion

The main purpose of this study was to examine the functional changes through the visual perceptual learning process. For this purpose, we investigated the effect of learning, task specificity, location specificity in V1 and V2 regions. Our results showed that learning changed thee task-based fMRI response and resting-state functional connectivity. Previous research on this matter reports inconsistent results. While some researchers report change in the responsiveness to the trained stimuli [15, 73, 21], there are also reports which did not find such a change [38, 24]. Therefore, the contribution of early visual areas for the accommodation of visual perceptual learning and its mechanisms are still in question. In order to reveal the early visual areas' role in visual perceptual learning, participants received perceptual training and in the course of learning, we collected task-based and resting-state fMRI data.

Participants are trained with a bisection discrimination task at 210°polar angle, 4°eccentricity with vertical stimulus. The threshold measurements with the training stimulus settings showed that the discrimination threshold scaled-down, the post-learning threshold results turned back to pre-learning levels. This finding is contradicting with the literature, usually, perceptual learning's effect shown to be long-lasting, persistent over the years [26, 80]. Unlearning a visual skill which is learned, did not reported before. To have a deeper understanding

about the training, we represented our whole training data in the Appendix, Figure A.2. As we can see from that figure, the thresholds from each training block shows great fluctuations, the fluctuations got bigger after mid-learning measurements. One exceptional characteristic of our experiment is the long-lasting and time-consuming nature of it with the additional MR sessions. Our psychophysics measurements show similarity with other studies which reported achievement of perceptual learning[19, 29]. Previous researches which trained participants with the bisection discrimination task had varying daily trial numbers from 450[29, 19] to 1600[81], and the total trial numbers are varied between 1200[63] to 10000∼ (authors did not specify the exact number)[19]. Our training regime included 800 trials per day and eight training sessions. Yet, each MR session in our experiment took around 1.5 hours and there were totally 6 MR sessions. This might caused decreased motivation and hence attention. The effect of attention on threshold measurements is shown before[82, 83]. Given that our experiment occupied participants for almost two weeks, contained six exhaustive MR sessions, at the very end of the experiment our participants might had fatigue, hence as the experiment proceeded, their performance might got affected by lack of motivation and attention.

Another behavioral aspect of our study was assessing classical perceptual learning's specificity, for this purpose we had five behavioral control conditions. The control conditions were contained two additional polar angles which are 210°and 45°, and horizontal bisection discrimination task. While control locations are used to assess location specificity, the horizontal task used to evaluate task specificity. We observed a threshold decrease at vertical 150°polar angle condition, which is the mirror location, at mid-learning sessions, like the training condition, threshold decrease effect is diminished at the post-learning session. As discussed earlier the post-learning measurements might not reflect the actual performance of the participants and fatigue might create a confound. Regarding the threshold decrease between pre-learning and mid-learning sessions at 150°polar angle with the vertical task, inter-hemispheric connections might be a possible explanation for it. It is known that, mirror positions in the visual cortex share callosal connections [84]. Neurons at the vertical 150°polar angle, 4°eccentricity

might exposed to the training stimuli with perceptual training, therefore, threshold decrease in the mid-learning. The control condition at the vertical 45°polar angle condition is free from these callosal inter-hemispheric connections and no learning effect is observed at this condition. This result also supports our interpretation for the vertical 150°polar angle condition. Moreover, this decrease also in line with Crist et al.'s study [19], even though the mirror position of the training did not measured, they've found that as we go further from the training location, the learning effect diminishes. Similarly, in our study, participants are trained at 210°polar angle, and at the 150°polar angle, the learning effect is observable, however, at the 45°polar angle there is no effect. Additionally, there were no change in the thresholds for horizontal bisection discrimination tasks at all of the thre control conditions. These results are in line with previous research which examines task specificity of bisection discrimination task [19, 29].

Supporting inter-hemispheric connections, our resting state analysis functional connectivity analysis on the test locations yielded significant connectivity increase between V1 and V2 in 210°and 150°polar angle conditions. Functional connectivity change at the end of the visual perceptual learning has been previously shown [48, 49]. However, in this study, besides pre-learning and post-learning measurement, we also collected resting-state data after third session of learning. While functional connectivity between V1 and V2 regions did not change between pre-learning and mid-learning sessions, our post-learning measurements were significantly different than mid-learning and pre-learning measurements. Our results suggest that functional connectivity does not change at the early stages of the learning, the change on the functional connectivity might be arising at the late stages of the learning. A recently published study [85] reports results that are in line with our connectivity results. In this study, they trained participants with texture discrimination task over 14 days. They've collected resting-state fMRI data before-learning, after first session of learning, mid-learning and after perceptual learning procedure has ended. Their results showed that, functional connectivity between V1 and region covering inferior longitudinal fasciculus(ILF), ILF is a track and regions surround it is associated with the mid-level visual skills, had changed after learning has ended.

In addition to resting-state fMRI data, we also gathered task-based fMRI data. The analysis of task-based fMRI data showed session's effect for the training task. Moreover, other conditions did not reveal any effect of session. Since the behavioral performance analysis on the task-based fMRI scans (please see Section A.1), and the fMRI scans are collected a separate day, the confound of fatigue might not be affected our fMRI measurements considerably, therefore our fMRI results stand valid.

The task-based fMRI with perceptual learning shows results with the change in the activity at early visual regions [86, 28, 21]. On the other hand, there is also research that reports no-change[87, 37, 72]. Yet, it should be noted that, all these researches investigated learning with comparing before and after learning measurements. A more detailed research that reviewed above [37] investigated the learning effect with taking measurements pre-learning, mid-learning and post-learning. Their results showed increased BOLD response in the mid-learning fMRI assessments. Our analysis showed that BOLD amplitudes are changed between the sessions, however the post-hoc test did not reveal any significant effect. It should be emphasized that, the descriptive figures indicate trend to increase in the mid-learning measurement (please see Figure 3.7).

Unlike the behavioral and resting-state functional connectivity, task-based fMRI data did not result with change at 150°polar angle for vertical task. While we argue that, exposure to the stimuli might cause behavioral learning effect and connectivity change with inter-hemispheric connections, these connections might not create large changes in the BOLD signal that can significantly alter the task-based characteristic. Since resting-state functional connectivity is directed by smaller fluctuations in the BOLD signal [78], it can be captured easily, compared to task-based BOLD.

The main limitation of our study is that, our behavioral data present too much noise to deduce clear results for both behavioral and neural data. Therefore, future research should be aware of this potential pitfall of multi-modal imaging. Unfortunately, we did not benefit from the tools which ease the learning process. These tools are feedback and reward for learning. Even though learning occurs in

the absence of feedback, it is known that, feedback has an accelerating effect on learning [88]. Also, reward has been shown to increase and accelerate perceptual learning process [89]. Zhang and colleagues [90] examined effect of different types of reward on perceptual learning using various tasks. The results showed that, high and instant reward was the most effective for increasing performance on the trained task. Besides, in an additional experiment, they tested how internal and external noise is effected by the high reward. The researchers found that, high reward increases learning through reducing the internal noise. On the contrary, we did not provide feedback for our participants. While we did not reward the high performance, the base experiment reward was not given until the experiment is completed which might add up to lack of motivation.

Participants dedicated themselves to long research without any instant outcome, which resulted in unexpected and doubtful results. In the case of the experiments which consume many hours, giving the instant gift might be beneficial in order to assure participants' motivation. Another strategy which might improve the power our analysis is increasing the subject size, this would minimize the effect of inter-subject variability in statistical analysis.

Our task-based fMRI data revealed limited knowledge about functional change while performing the training task. We analyzed task-based fMRI data using univariate tecnique. Multivariate analysis techniques gives more insight about the source of the change. However, due to limited time, we couldn't gather enough data for examining multivariate changes. Previous research conducted both univariate and multivariate analysis showed that V3A region increased BOLD response, moreover, decoding accuracy for the orientation is increased. [38]. This increase in the decoding accuracy informs us about the orientation tuning of the neurons in the V3A region. Therefore, collecting more data and conducting multivariate analysis can improve our understanding about the BOLD changes.

Moreover, as reviewed in Section 1.2.1, it has been proposed that [34] neural changes underlying behavioral changes might be seen in the amplitude of response, the increase of neuron allocation, or refining tuning curves. In this

study, we only tested the first possibility. Therefore, the following two neuroplasticity strategies are still an open question for this study.

Our findings showed an only significant increase in the resting-state functional connectivity between early visual areas. As reviewed in the Introduction chapter, it has been proposed that experience-dependent neuroplasticity might accommodate different strategies at different time-points of learning [91, 92]. Therefore, the changes in the functional connectivity might be occurring at the late-phases of the learning.

Since our pRF analysis did not reveal usable maps for delineating the visual regions, we conducted our analysis with the anatomically delineated labels, which only gives us V1 and V2 regions. These regions represents very limited portion of visual processing. Therefore, changes in regions that are beyond V2 remain untested for our study.

In sum, this study provides insights of behavioral and neural mechanisms of visual perceptual learning. The unexpected results show that combining perceptual training with neuroimaging might introduce a confound to behavioral measurements. Moreover, our resting-state data supports the idea that functional connectivity might be gained in the late phases of the learning. However, to have a more concrete conclusion more subjects should be tested while supporting learning with feedback and reward.

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Appendix A

Appendix

A.1 Individual threshold data for training and task based fMRI, and behavioral performance on task-based fMRI scans
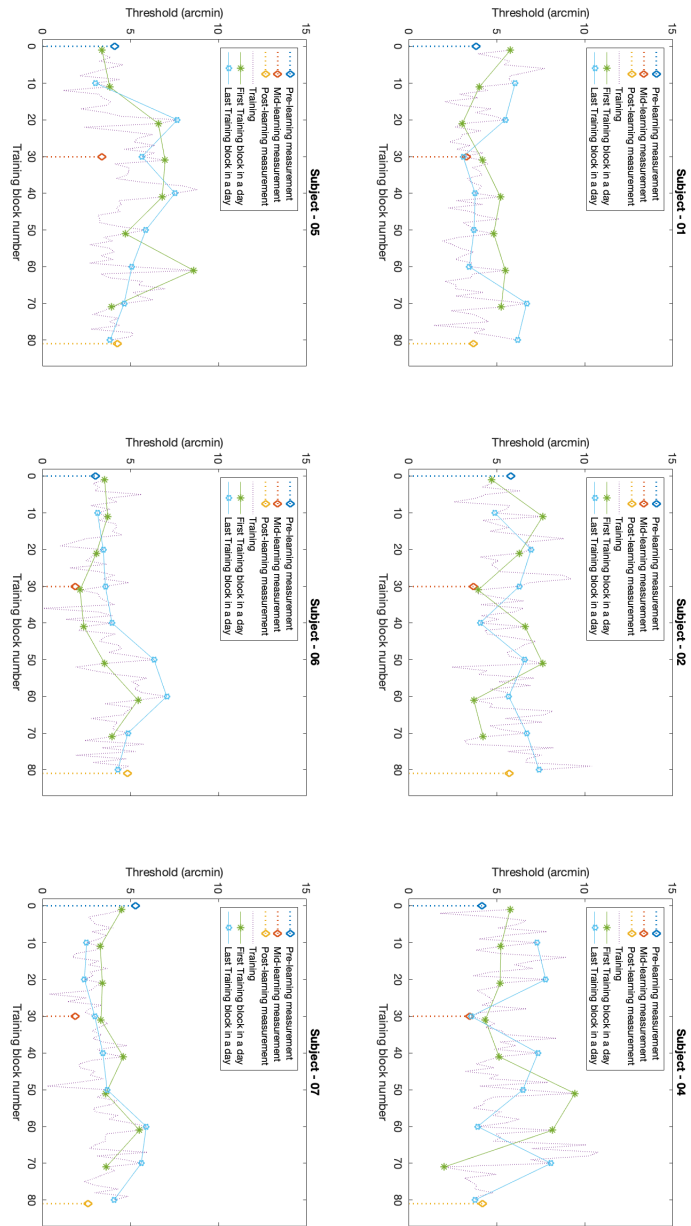
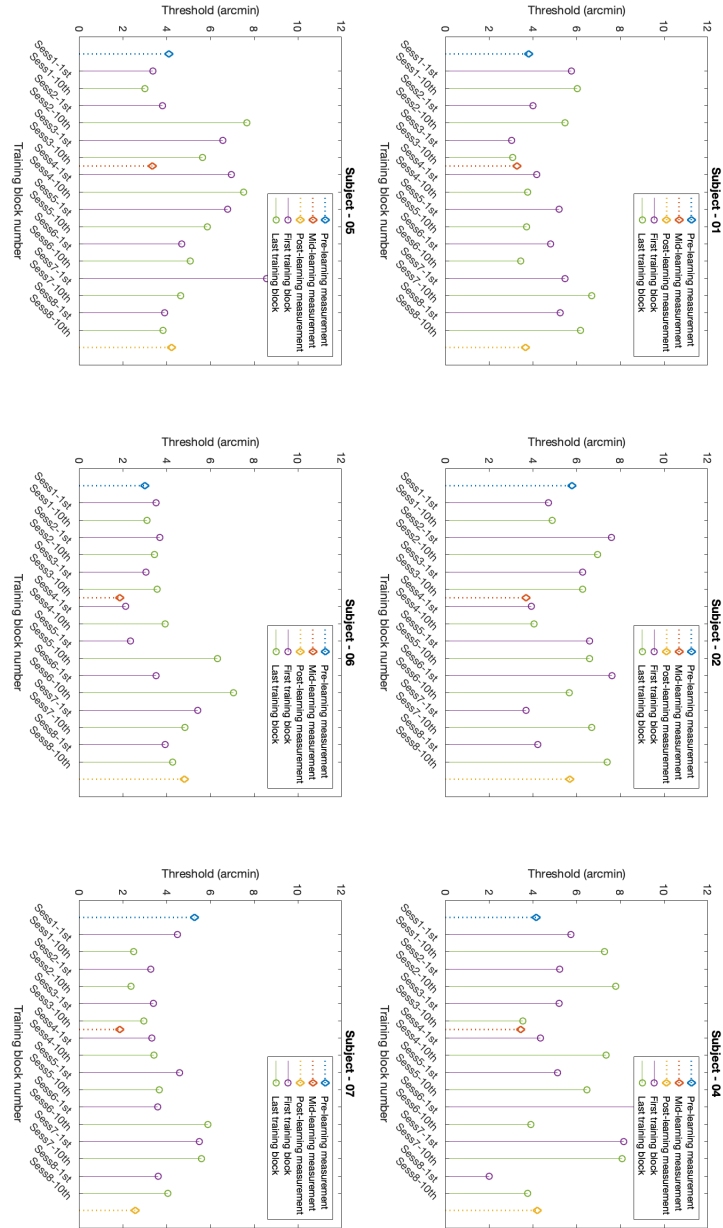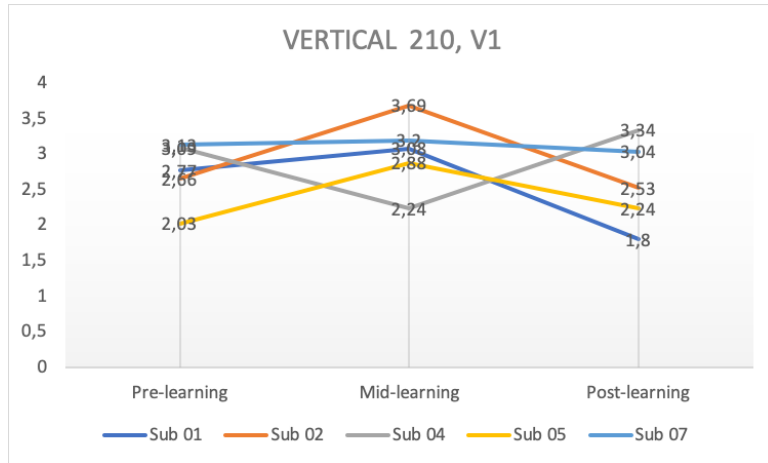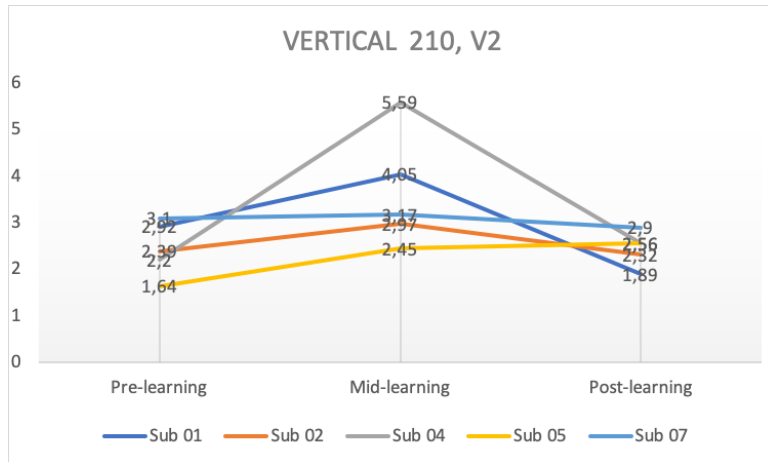Figure A.1: Individual data representing thresholds of all blocks

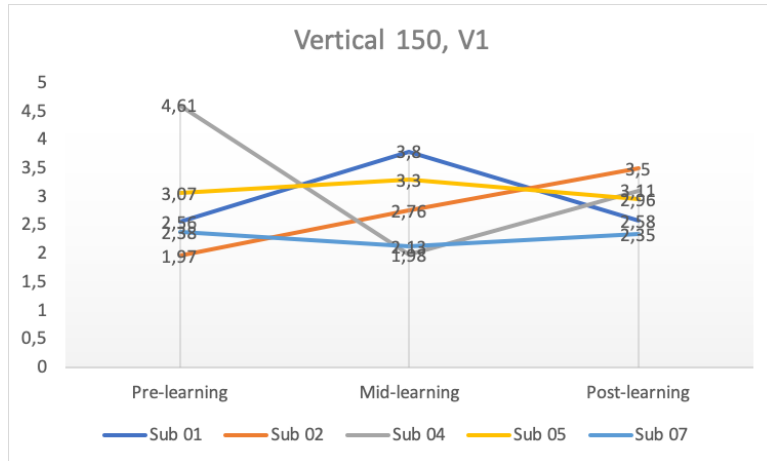Figure A.2: Individual data representing thresholds of first and last training blocks for each session
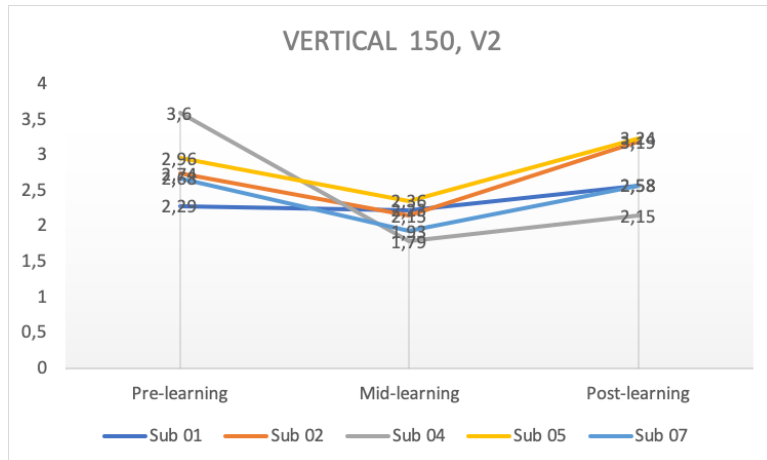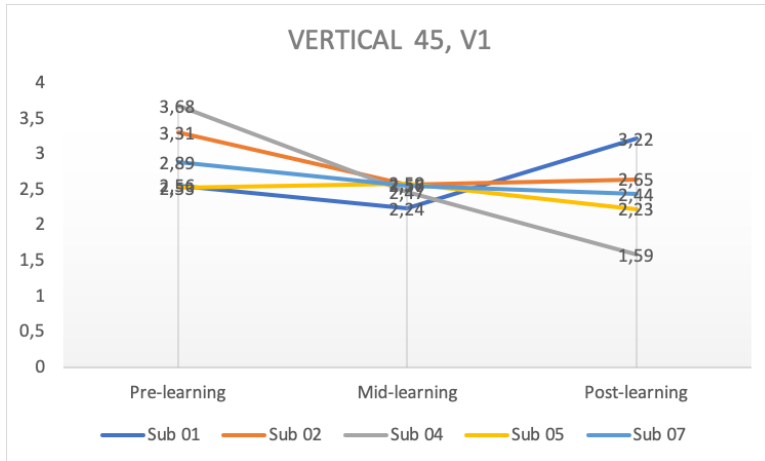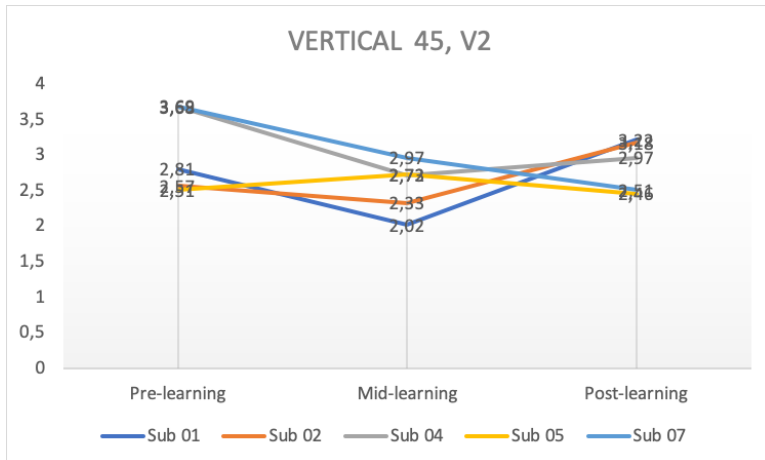
(a) Vertical 210°polar angle V1 region

(b) Vertical 210°polar angle V2 region

Figure A.3: Individual task-based fMRI data for Vertical 210°polar angle condition. The figure above presents data from V1 region, the figure in the below presents data from V2 region
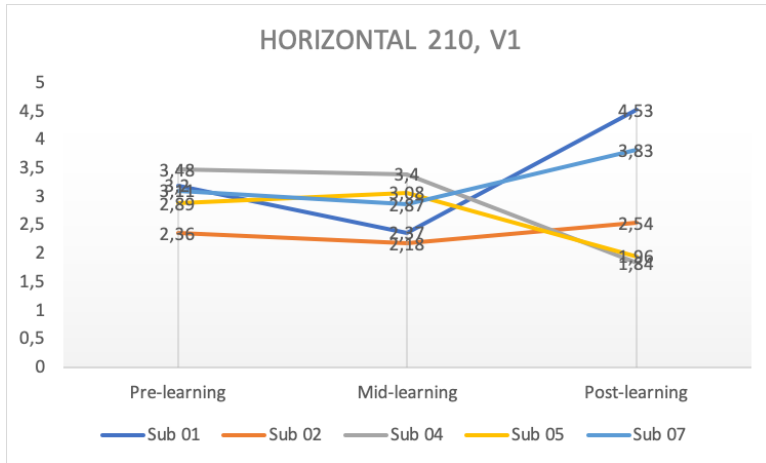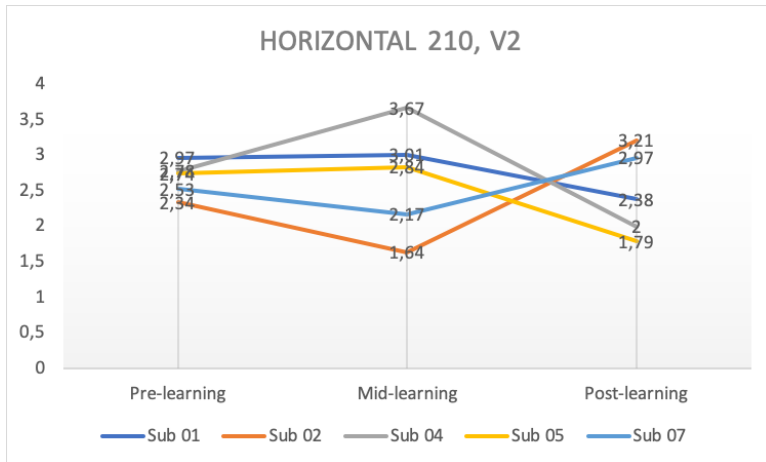
(a) Vertical 150°polar angle V1 region

(b) Vertical 150°polar angle V2 region

Figure A.4: Individual task-based fMRI data for Vertical 150°polar angle condition. The figure above presents data from V1 region, the figure in the below presents data from V2 region

(a) Vertical 45°polar angle V1 region

(b) Vertical 45°polar angle V2 region

Figure A.5: Individual task-based fMRI data for Vertical 45°polar angle condition. The figure above presents data from V1 region, the figure in the below presents data from V2 region
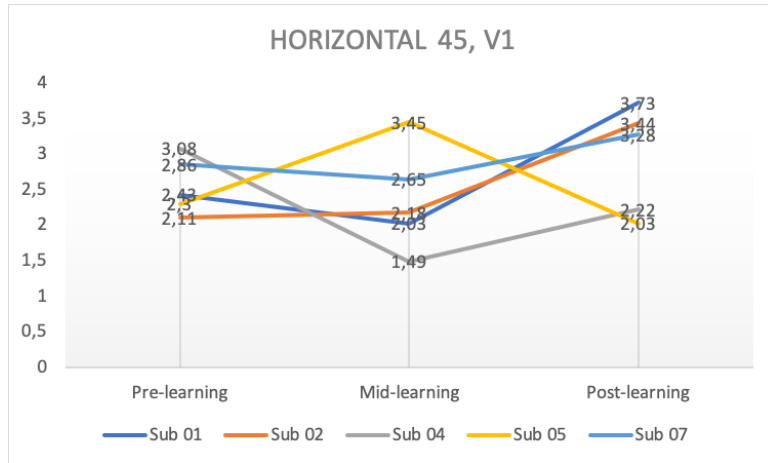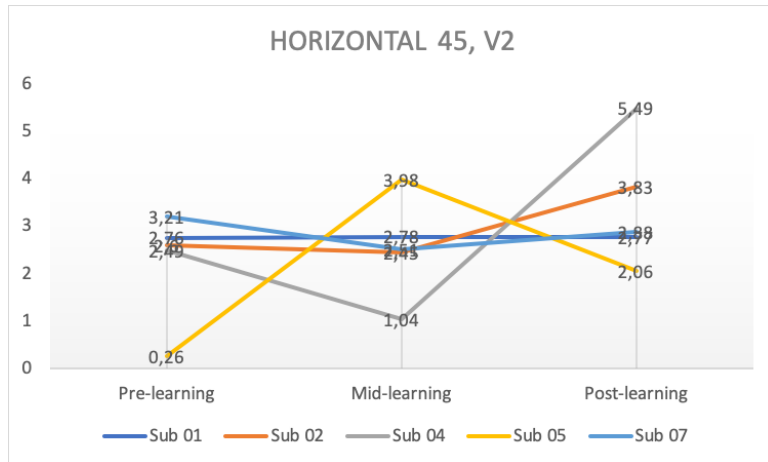
(a) Horizontal 210°polar angle V1 region

(b) Horizontal 210°polar angle V2 region

Figure A.6: Individual task-based fMRI data for Horizontal 210°polar angle condition. The figure above presents data from V1 region, the figure in the below presents data from V2 region

(a) Horizontal 45°polar angle V1 region

(b) Horizontal 45°polar angle V2 region

Figure A.7: Individual task-based fMRI data for Horizontal 45°polar angle condition. The figure above presents data from V1 region, the figure in the below presents data from V2 region

(a) 210°polar angle conditions

(b) 150°polar angle conditions
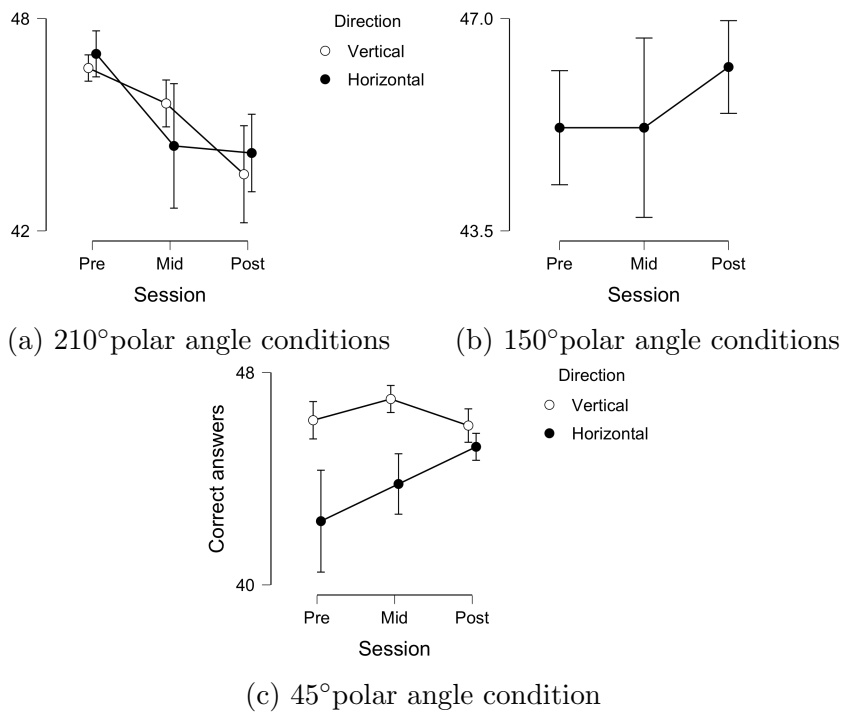
(c) 45°polar angle condition

Figure A.8: Behavioral performance on task-based fMRI experiments. All conditions and all subjects the maximum number of correct answer was 48 which corresponds to 100 percent correct, the minimum number of correct answer was 39 which corresponds to >80 percent correct.