INVESTIGATION OF LINE BISECTION ACTIVITY IN THE BRAIN BY A SENSORY-MOTOR TASK: AN FMRI STUDY

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INVESTIGATION OF LINE BISECTION ACTIVITY IN THE BRAIN BY A SENSORY-MOTOR TASK: AN FMRI STUDY

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ABSTRACT

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Strongly right handed healthy people bias the selection of the midpoint leftward by neglecting right side of a line in line bisection task which is used for clinical assessment of neglect syndrome. The line bisection task relies mostly on visual judgements; involving a fronto-parietal visual loop. How does line bisection manifest itself in the realm of other senses is less addressed. In this study, we developed a tactile line bisection task compatible with MR device and implemented line bisection under both tactile and visual conditions in order not only to reveal neural substrates of line bisection when somatosensory cortex is recruited, but also to investigate whether there are different attentional mechanisms underlying line bisection in different sensory modalities. After administering ta ctile and visual line bisection task through fMRI experiments to a group of strongly right handed people, we observed additional brain activity in contralateral medial frontal gyrus and contralateral inferior parietal lobule when the task is performed with right hand in tactile sense instead of visual sense. Furthermore, the activity maps changed drastically when left hand is used instead of right hand, causing recruitment of large areas in ipsilateral temporal cortex probably due to dominating proprioceptive processes. The results provide a contribution to the idea that there are different cognitive processes underlying line bisection under tactile and visual senses.

Keywords: Line bisection, neglect syndrome, tactile sense, fMRI

ÖZ

SOMATOSENSÖR ÇİZGİ BÖLME TESTİNİN BEYİNDEKİ AKTİVİTESİNİN ARAŞTIRILMASI: BİR FMR ÇALIŞMASI

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İhmal Sendromunun klinik teşhisinde kullanılan çizgi bölme testinde, sağlıklı sağlak bireylerin bir çizginin orta noktasını işaretlemeleri istendiğinde genellikle çizginin sağ tarafını ihmal ederek orta noktanın solunu işaretledikleri görülmüştür. Çizgi bölme testi daha çok ön pariyetal görsel döngüde yer alan görsel muhakemelere dayanır. Çizgi bölme testinin kendini diğer duyuların hakimiyetinde nasıl gösterdiğine yönelik çalışmalar daha azdır. Bu çalışmada, somatosensör korteks aktif olduğu zaman, çizgi bölme testinin beyindeki nöral substratlarının ortaya çıkarılabilmesi, ayrıca farklı duyu modalitelerinde çizgi bölme testinin altında yatan dikkat mekanizmalarında bir farklılık olup olmadığını görebilmek için, MR ile uyumlu dokunma duyusu ile algılanabilen bir çizgi bölme test düzeneği geliştirilmiştir. MR içerisinde, dokunsal çizgi bölme test düzeneğinin baskın olarak sağlak olan popülasyona hem dokunsal hem görsel olarak uygulanmasıyla, görsel duyu yerine dokunma duyusu ile gerçekleştirildiğinde, beyinde kontralateral medial frontal korteks ve inferior pariyetal lobülde aktivasyonlar gözlemlenmiştir. Ayrıca, katılımcılar deneyi deneyimsiz olan sol elleriyle gerçekleştirdiklerinde beyindeki aktivasyon haritaları değişerek, ipsilateral temporal kortekste çok yaygın aktivasyon dağılımı gözlemlenmiştir. Bu sonuçlar çizgi bölme testinin dokunma duyusu ve görsel duyu altında farklı kognitif proseslere yol açtığı görüşüne katkıda bulunmaktadır.

Anahtar Sözcükler: Çizgi bölme, ihmal Sendromu, dokunma duyusu, fMRI

To My Precious Family,

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CHAPTER 1

INTRODUCTION

Line bisection is a clinical test used for determining attentional and motor biases in both healthy and brain damaged participants. The line bisection task has been used by neuropsychologists to investigate visuospatial and attentional deficits after brain damage (Fischer, 2001). Particularly, it is used as a metric for the clinical assessment of neglect syndrome which is a neurologic disorder that leads to attention failures, deficits in reporting and responding to visual stimuli in contralesional space. Often, after a right hemisphere damage (Lee et al, 2004), patients fail to be aware of objects to their left extrapersonal space.

Even though line bisection is used as a clinical assessment in neglect syndrome, it is also studied in healthy people in several studies (Fink et al., 2000; Jewell and Mccourt, 2000; Çiçek, et al., 2009) to reveal complex processes that underlie line bisection such as voluntary attention to focus to the middle point, target selection and detection simultaneously. Different factors and parameters that modulate the results of task performance, activated regions in the brain and connectivities of networks in the brain underlying this task are questions that still need to be answered.

Bowers and Heilman (1980) were the leading researchers who applied line bisection to healthy individuals. They revealed that right-handed healthy individuals detected the space asymmetrically, they neglected right visual space but not left visual space. Due to this, in line bisection test it has been seen that there is a left bias in heathy people (Jewell and Mccourt, 2000). Jewell and Mccourt (2000) stated that healthy individuals deviated slightly to the left side which is called pseudoneglect in healthy people. On the contrary, in patients with neglect syndome, mostly the bias is towards the right side, and they are shown to neglect the left visual space (Shulman et al., 2002).

The line bisection task is mostly based on visual judgements; involving a fronto-parietal visual loop. The fronto-parietal network is responsible from attention and composed of two separate networks. While ventral fronto-parietal network consisting of ventral prefrontal cortex, the inferior frontal junction (IFJ), and the temporo-parietal junction (TPJ) is responsible from stimulus-driven (bottom-up) attention, dorsal frontoparietal network including frontal eye field (FEF), the intra-parietal sulcus (IPS), and the neighboring superior parietal lobule (SPL) supports goal-directed (top-down) attention and is involved in the cognitive selection of sensory information and responses (Corbetta and Schulman, 2002).

There are many studies investigating visual line bisection in healthy people and patient groups (Vallar, 2008, Rorden et al, 2006, Verdon et al., 2010, Jewell and McCourt, 2000, Chokron et al., 1998, Fink and Marshall, 2001, Çiçek et al., 2009). In lesion studies, it is proposed that patients who have problems in the line bisection task have more posterior lesions around temporo-occipital junction and inferior parietal lobule (Vallar, 2008, Rorden et al, 2006, Verdon et al., 2010). Rorden et al. (2006) presented that patients suffering from neglect who exhibit irregularity on the line bisection task have more posterior lesions, especially located in Temporo-occipital areas. Verdon et al. (2010) proposed that line bisection task is more correlated with lesions in the right inferior parietal lobule (IPL).

In visual line bisection fMRI studies, Çiçek et al. (2009), found right lateralized intra-parietal sulcus (IPS), FEF and lateral peristriate cortex (LPC) activity in response to line bisection task. These activated regions highlight the importance of a right frontoparietal region in attentional network. Weiss et al. (2000) used PET in their line bisect study. They found a distinction of line bisection activity depending on near space versus far space stimulus. Near space line bisection activity was found at the left dorsal occipital cortex, left intraparietal cortex, left ventral premotor cortex and left thalamus, while task performed at far space involved the ventral occipital cortex bilaterally and the right medial cortex (Weiss et al., 2000). Fink et al. (2001) also showed that line bisection judgements activated the right parietal and prefrontal cortex in their earlier fMRI study. However, in a more recent study (Fink et al., 2002), same authors presented that a bilateral inferior parietal lobule activation. They extracted a wide functional activation network: right temporo-occipital cortex activation concerned with visual processing, as well as bilateral precentral gyrus and bilateral supplemetary motor area (SMA) activation correlated with motor response during their tasks. In addition to bilateral inferior parietal lobule activation, they found an attentional activation set including right anterior cingulate, right dorsolateral prefrontal cortex, right putamen and right thalamus. Saj et al. (2009) investigated a line bisection judgement task in which lines are transected previously and patients need to decide whether its bias is rightward or leftward or it is transacted by middle point. They found posterior parietal cortex activation which was right lateralized similar to results of studies in healthy people. They also observed anterior cingulate and bilateral IPS activation resulted from rightward and leftward biases of the bisection (Saj et al. 2009).

When it is taken into account that the line bisection task is mostly based on visual judgements; involving a fronto-parietal visual loop, how does line bisection task manifest itself in the realm of other senses is less addressed. Clinical tactile behavioural line bisection studies generally examine how tactile line bisection is modulated by different conditions and factors such as hand used, scanning direction, line length for particularly different type of subject groups (Laeng et al, 1996, Coudereau et al, 2006, Brooks et al, 2011, Chokron et al, 2002). For example, Laeng et al. (1996) found that there was a rightward bias when right hand was used whereas leftward bias when left hand was used. In contrast, Coudereau et al.(2006) stated reverse situation. Published results on tactile behavioural bisection by control subjects are remarkably variable and inconsistent since all studies not only explained results according to different factors, but also implemented different tactile line bisection task presentations.

The purpose of this study is to develop a tactile line bisection task which is applicable in the MR device to be performed exclusively by the touching sense. We aimed to reveal neural substrates and attentional aspects of tactile line bisection in the brain by implementing tactile line bisection design in fMR. We implemented the experiment with two different sensory modalities: Tactile line bisection and visual line bisection. Thus, the difference in attentional networks between the line bisection done visually and tactile was examined. To the best of our knowledge, a similar study on somatosensory line bisection with the use of fMR does not exist.

Thus, our study is an innovative study and it holds a significant importance for revelation of the neural substructures of line bisection. The design of the stimulus board mechanism is another element which adds innovation to our study with its compatibility with the fMRI device.

We hypothesize that there are differences between functional networks recruited by bisection decision under different sensory modalities, especially tactile and visual line bisection. On the other hand, since neural substrates of tactile line bisection is not studied in neuroimaging, except from clinical and lesion studies, we could not make an exact forecast about specific regions activated by tactile line bisection. However, we clearly expected activations around somatosensory cortex associated with both tactile sense and visual sense due to the motor response involved.

This thesis consists of six chapters including introduction. In chapter two, theoretical background focused on clinical and fMRI studies about visual line bisection as well as frontoparietal attention network, somatosensory pathway and neglect syndrome which are milestones for line bisection studies. In chapter three, design of our experiment and methodology are presented. Experimental set-up that was designed in order to implement the fMRI block design is illustrated in detail. In addition, processing of the data collected from fMRI is explained. In chapter four, our results from data analysis are presented. In chapter five, discussion of findings and results are explained and future works which will help enhancing our study and help it making significant contribution to the line bisection literature are discussed. Lastly in chapter six, conclusions are drawn.

CHAPTER 2

BACKGROUND AND LITERATURE

2.1 Line Bisection

Line bisection is a clinical test based on attentional and motor functions in both healthy and brain damaged participants. The line bisection task has been used by neuropsychologists to investigate visuospatial and attentional deficits after brain damage (Fischer, 2001). Particularly, it is used as a metric for the clinical assessment of neglect syndrome, a condition that results from brain lesions mostly located in the right hemisphere (Fox et al, 2006). In order to understand attentional mechanism of line bisection task and how it correlates with the brain regions, first, we need to know about processes and anatomical structures playing role in attentional networks in the brain.

2.1.1 Visuospatial Attention and Frontoparietal Network

As far as the distribution of spatial attentional network is concerned, posterior parietal cortex has an important role for linking the channels carrying out spatially relevant attentional information. Besides, it functions in linking these channels with multiple channels of motor outputs which are related to searching, orientating, reaching, and scaning. When the parietal component of the attentional network is damaged, independent input and output channels may still conserve their functionality, but they can not be communicate with each other.

The frontal component of the attentional network including FEF, premotor and prefrontal cortex plays a key role by converting attentional shifts into particular motor behaviour. In conclusion, we can think that while the posterior parietal cortex constitutes a template for attentional space, the FEF located in the frontal cortex chooses and arranges each activity which is needed for navigation related to the given attentional task (Mesulam, 1999). Frontal and parietal components of the attentional network are engaged and coordinated with each other. These components are involved in a wide attentional network called Frontoparietal network.

There are two forms of attention: one captured by an unexpected event, second under voluntary control. Corbetta et al. (2002) proposed that these two forms of visuospatial attention are correlated with two distinct brain networks;

Ventral frontoparietal network consisting of ventral prefrontal cortex, the inferior frontal gyrus (IFG), and the temporo-parietal junction (TPJ) is responsible for stimulus-driven attention and target detection. Corbetta and Shulman's (2002) model puts forward that ventral frontoparietal network is mostly lateralized to the right hemisphere and when relevant sensory events are unattended, independent from their location or presented in which sensory modality, this network is recruited during detection of unexpected events (Corbetta and Shulman, 2002).

Especially TPJ attends to stimulus-driven attention mediated by corresponding stimulus. For instance, TPJ activation of the right parietal lobe was observed during experiments in which subjects are presented a change in either a visual, tactile or auditory stimulus simultanously. However, this activation was only observed when the stimulus in the sense that is related to the actual behaviour changes (Behrmann et al., 2004).

On the other hand, dorsal frontoparietal network including frontal eye field (FEF), the intra-parietal sulcus (IPS), and the superior parietal lobule (SPL) supports goal-directed attention and is involved in the cognitive selection of sensory information (Asplund, 2010). Dorsal frontal and parietal regions, including areas in the superior parietal lobule, the IPS, and the frontal eye field have consistently been activated in various tasks involving spatially directed attention (Naghavi, 2005). These tasks generally concern the selection of information coming from sensory input. The activation of dorsal attentional network is usually bilateral. However, activations in ventral IPS and FEF regions are more noticable when attentional task is performed in the contralateral visual side (Corbetta et al., 2002). In Figure 1, red areas are involved in searching for the target, while blue areas recruited during detection.

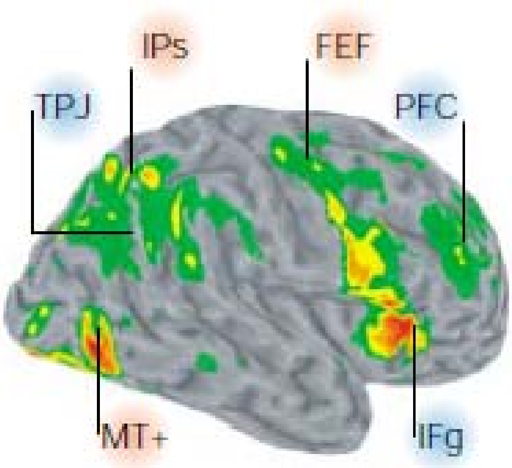

Figure 1 Brain activations in the dorsal and ventral frontoparietal network during search and detection (taken from Corbetta et al., 2002).

Interactions between ventral and dorsal frontoparietal network is a very debated issue assuming separate dorsal and ventral attentional networks form distinct anatomical and functional systems. Corbetta and Shulman (2002) proposed that there is a link between IPS and TPJ supporting that the goal directed stimulus excites ventral attentional network via IPS. Fox et al. (2006) suggested that middle frontal gyrus (MFG) activity correlates with both networks when a spontanous activity occurs. This suggestion implies that although ventral and dorsal networks do not interact directly, they are principally linked through prefrontal cortex (Fox et al., 2006).

Particularly, prefrontal cortex (PFC) plays an important role in attention. It can be divided functionally and anatomically into a number of distinct regions. Posterior PFC is related with attentional selection of behaviorally relevant perceptions and actions. It allows selecting items in our environment visually. Even though a lot of brain regions are related to attention and selection, particularly a specific part of posterior PFC called inferior frontal junction (IFJ) controls these functions and is assigned for human information processing (Asplund, 2010).

The IFJ is located at the junction of the inferior frontal sulcus and the precentral sulcus. This location is a transition region between premotor cortex and the prefrontal cortex. The IFJ has been found to take part in many different control and coordination processes consistent with its anatomical place and connectivities with neighbouring brain regions. The IFJ may not only to the ventral attention network, but it also appears to connect to the dorsal attention network since ventral to the IFJ is the inferior frontal gyrus (IFG) while dorsal to the IFJ is the FEF (Asplund, 2010).

What will occur if functional connectivity in ventral and dorsal attentional networks breaks down? Neglect syndrome which is an attentional deficit in perceiving and responding to stimuli in the contralesional side of the brain, is a severe consequence of the dysfunction of two networks. He et al. (2007) proposed that strokes causing neglect especially damage the ventral attentional network structurally. By using a visuospatial attention task, they revealed that neglect may result from a functional irregularity between left and right dorsal parietal cortex although they remain intact structurally. Interestingly, structural damage of ventral attentional network correlates with functional deficits of the posterior parietal regions of the dorsal attentional network (He et al., 2007). A detailed overview of neglect syndrome as well as more detailed anatomic background is presented in Appendix A.

2.1.2 Visual Line bisection

The line bisection task is mostly based on visual judgements; involving a visual fronto-parietal loop which involves the attention network mentioned above. In this context, there are many lesion studies, behavioural studies and fMRI studies (Vallar, 2008, Rorden et al, 2006, Verdon et al., 2010, Jewell and McCourt, 2000, Chokron et al., 1998, Fink and

Marshall, 2001, Çiçek et al., 2009) investigating line bisection in healthy people and patient groups under visual sense.

While, lesion and fMRI studies mostly search correlation between line bisection task and neural substrates or specific regions in the brain, clinical behavioural studies try to reveal cognitive aspects underlying line bisection task by applying different conditions and factors since this task has complicated and multidimensional attentional attributes.

2.1.2.1 Behavioral Findings in Visual Line bisection

In neglect patients, it is observed that there is a characteristic shift towards the ipsilesional hemispace. In other words, patients with right hemisphere lesions and unilateral spatial neglect usually place the midpoint to the right of the true center (Bonato et al. 2008). This rightward bias from the middle point is explained commonly as an attentional bias toward the right hemispace neglecting the left hemispace (Ishiai et al., 1998). This means that a leftward deviation of the spatial medium underlies the rightward neglect in patients with right brain damage (Vallar et al., 2008).

On the other hand, healthy individuals perform a leftward bias from the midpoint of the line. This leftward bias in healthy people is called pseudoneglect (Bowers & Heilman, 1980). Pseudoneglect corresponding to the leftward bias in linebisection task is explained with dominance of the right hemisphere due to visuospatial feature of the line biseciton task. This relation manifests itself densely when right handed people perform the task with their left hand which is represented contralaterally in the right hemisphere (Hausmann, et al., 2002). Even though leftward bias is commonly observed in healthy people in response to line bisection task, the direction and amount of bias is thought to be effected by different factors. Therefore, many researches examine visual and non-visual line bisection under different independent variables such as gender, age, line length, hemispace, hand used, scanning direction etc.

Jewell and Mccourt (2000) conducted a review comparing results of studies in literature and examining effects of different factors on line bisection errors in aspect of visual and non-visual line bisection in healthy population. According to the review, most authors concluded that there is leftward error with each hand. Indeed, when participants use their left hand, biases are more leftward than when the right hand is used (Jewell and Mccourt, 2000). Earlier studies contradict with this: There were rightward biases when the right hand were used while leftward biases when the left hand was used (Halligan, 1989). Yet reverse is reported by Chokron et al. (1993).

Similarly, Hausmann et al. (2003) proposed that the left bias in line bisection that is commonly observed in neurologically healthy people was found, particularly when the left hand was used. In addition, they investigated developmental changes in line bisection. In their study, they observed pseudoneglect effect in four age groups with left hand use. However, with right hand use, the youngest group exhibited deviation towards right, while the other groups exhibited a deviation towards left side (Hausmann, et al., 2003). According to Hausmann et al., pseudoneglect can be explained with an opinion that the two hemispheres in the brain differ regarding the distribution of spatial attention. The left hemisphere is related to attention directed towards right hemispace, whereas the right hemisphere is important in attention directed towards both left and right hemispaces (Hausmann, et al., 2003).

Clinical studies are consistent with Haussmann's (2003) proposal which support that the right hemisphere plays a special role in spatial attention and in line bisection. It is expected that pseudoneglect manifests itself especially with the left hand since the left hand is controlled by the right hemisphere (Hausmann et al. 2002, Jewell & McCourt, 2000). On the other hand, Mattingley et al. suggests that pseudoneglect is not only related to motor activation, but rather results from hemispheric control. When the right hand is used, leftward bias (pseudoneglect) reduced but still manifests itself. Lasting this leftward bias when the right hand is used reveals that the right hemisphere sends informations about perceptual attentional biases to the motor cortex of the left hemisphere (Mattingley et al. 2001).

2.1.2.2 Neural Substrates of Visual Line bisection

Lesion matching studies are still very controversial in line bisection. As mentioned before, in several lesion studies, it is proposed that patients who have problems on the line bisection task have more posterior lesions around temporo-occipital junction and inferior parietal lobule (Vallar, 2008, Rorden et al, 2006, Verdon et al., 2010). Rorden et al. (2006) presented that patients suffering from neglect who exhibit irregularity on the line bisection task have more posterior lesions such as Temporo-occipital. Verdon et al.(2010) proposed that line bisection task is more correlated with lesions in the right inferior parietal lobule (IPL)

Apart from lesion studies, more recent studies using brain imaging techniques such as functional magnetic resonance imaging (fMRI), positron emission tomoghraphy (PET), magnetoencephalography (MEG) in healthy individuals are carried out to reveal cognitive aspects of line bisection task by extracting functional activation maps of brain images. Brain imaging studies have confirmed a central role for particularly right parietal cortices in performance of line-bisection tasks (Weiss et al., 2000; Fink et al., 2001, 2002; Galati et al., 2000, Çiçek et al., 2009). In a recent fMRI study, Çiçek et al. (2009) implemented a line bisection task in which subjects moved a cursor and indicated middle point when it reached the center of the line with a tachistoscopic test in healthy people. Their results showed right lateralized intra-parietal sulcus (IPS), FEF and lateral peristriate cortex (LPC) activity in response to line bisection task (Figure 2). These activated regions highlight the importance of a right frontoparietal region in attentional network. According to Çiçek et al.(2009), IPS activation may have resulted from direction of spatial attention to the visual field which is used during perception of line length and decision of midpoint.

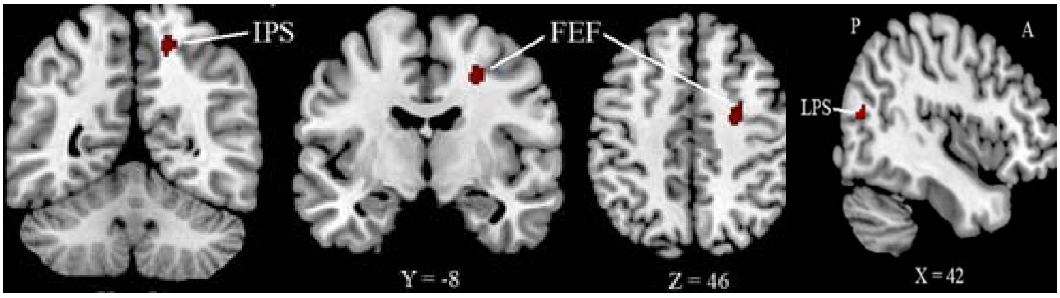

Figure 2 Results of visual line bisection task (taken from Çiçek et al. 2009).

In contrast with attentional network theory, the activations showed right hemisphere lateralization instead of bilateral activation generally observed in dorsal frontoparietal attentional network. providing evidence that the processes in which dominantly right hemisphere lateralization occurs, fail in neglect patients. The authors assume that the reason for right lateralization is that their task included allocentric (object-based) measures instead of egocentric measures (Çiçek et al. 2009).

Weiss et al. (2000) used PET to determine which brain regions are implicated when normal volunteers bisect horizontal lines at near and far space. They found line bisection at near space activated the left dorsal occipital cortex (1), left intraparietal cortex (2 and 3), left ventral premotor cortex (4) and left thalamus (5), while task performed at far space involved the ventral occipital cortex bilaterally (6 and 7) and the right medial temporal cortex (8) (Figure 3). Their results supported that activities in near space involved in visuomotor processing, while ones in far space take part in ventral visuoperceptual processing although the motor components of their task are same for task performed in two space. (Weiss et al., 2000).

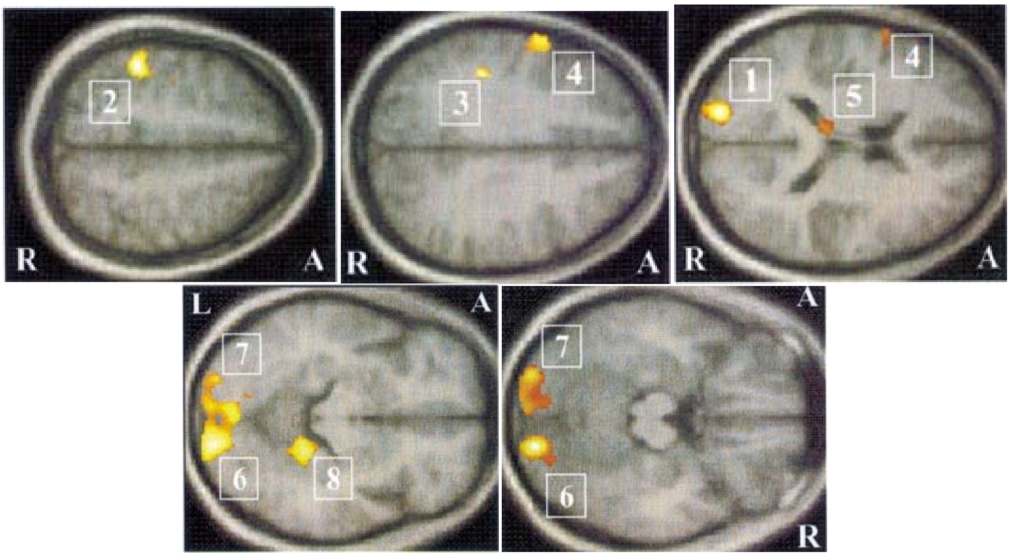

Figure 3 Activated Regions in Weiss et al.'s PET study. R: right, L: left, P:posterior, A: Anterior (taken from Weiss et al., 2000).

Further research investigating line bisection judgements is presented in Fink et al (2001). They showed that line bisection judgements activated the right parietal and prefrontal cortex in their earlier fMRI study. They observed right inferior parietal cortex activation during their line bisection tasks with different line orientation as vertical and horizontal (Fink et al. 2001). However, in a more recent study, same authors presented a bilateral inferior parietal lobule activation. They extracted a wide functional activation network: right temporo-occipital cortex activation concerned with visual processing, bilateral precentral gyrus and bilateral supplemetary motor area (SMA) activation correlated with motor response as well as an attentional activation set including right anterior cingulate , right dorsolateral prefrontal cortex , right putamen and right thalamus activations. They correlated their results with visuo-spatial neglect and highlighted that the activations of right putamen, thalamus and temporo-occipital cortex is consistent with the lesions in these regions augmenting left visuospatial neglect. Particularly, their right inferior parietal cortex activation was paired with its attentional mission in line bisection since this region is one of the main areas damaged in chronic left neglect that includes significant errors on line bisection task. Their bilateral activation results were interpretented as they resulted from the author's conjuction analysis between two different line bisection judgement tasks (Fink et al., 2002).

Another fMRI study performed in neglect patients by Saj et al. (2009) investigated a line bisection judgement task in which lines are transacted previously and patient need to decide whether its bias is rightward or leftward or it is transacted by middle point. They founded posterior parietal cortex activation which was right lateralized similar with results of studies in healthy people. They concluded that these findings showed that the left and right biases in attention which were triggered by bisection deviations, recruited the processes playing role in spatial attention. They also observed anterior cingulate and bilateral IPS activation resulting from rightward and leftward biases of the bisection (Figure 4) (Saj et al. 2009).

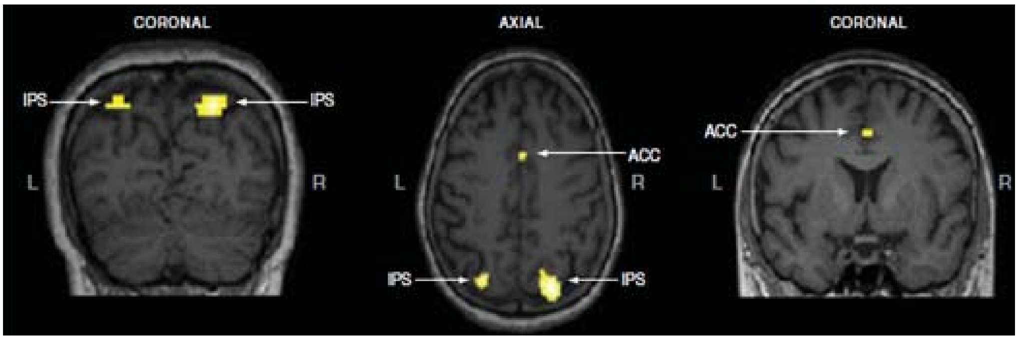

Figure 4 fMRI activations of Saj et al. study in different planes (taken from Saj et al. 2009).

2.1.3 Tactile Line bisection

As mentioned before, when it is taken into account that the line bisection task is mostly based on visual judgements involving a fronto-parietal visual loop, how line bisection task manifests itself in the realm of other senses is less addressed. Furthermore, tactile exploration of line bisection is a debated phenomenon in clinical behavioural studies Therefore motivation for our study is to develop a tactile line bisection task mechanism which is compatible with the MR device to interpret the cognitive basis of tactile line bisection by investigating brain activities in fMRI data.

2.1.3.1 Somatosensory Pathway

Touching sense includes touch, perception of vibration and pressure, which are all componenets within discriminative touching (Blakemore & Wolpert, 1999). Sensory information initiated from somatic parts of the body is transformed into action potential in the neurons with assistance of specific sensory receptors and then head through to the spinal cord from the back roots of the spinal nerves. Spinal neuron includes root ganglion neurons at the back of its roots. All sensor information coming from the body and the extremities are carried to the central nervous system with the axon branches of these back root ganglion neurons independent of modality. These axon branches connect the touch receptors into the spinal cord. From spinal cord, sensory information is transferred to the thalamus of the brain via medulla oblongata with the nerves which are crossed in the mid line so that the right side of the body is represented in the left hemisphere and left side in the right hemisphere.The information coming from the thalamic nucleus is distributed to the information association areas which reach the sensory cortex, where evaluation occurs (Figure 5) (Markus Bauer et al., 2006).

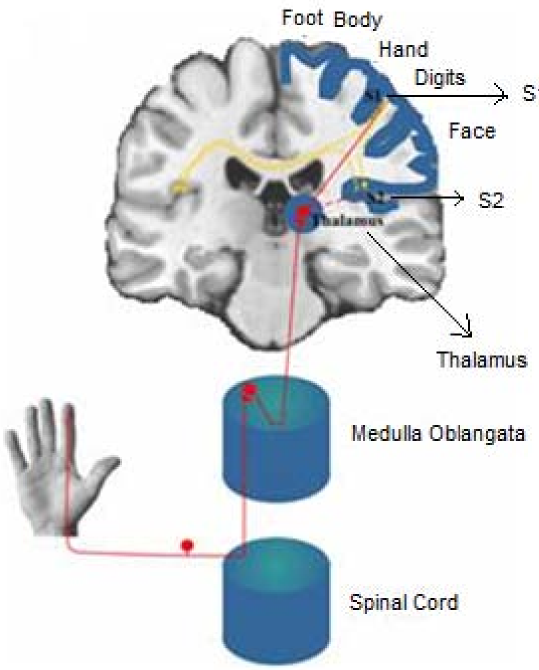

Figure 5 Somatosensory Pathway

The primary sensory area which represents touching sense in the cerebral cortex is named as the somatosensor cortex. Somatosensory cortex is topographically organized according to the information coming from all around the body surface (Haines, 1981).

The area corresponding to the primary somatosensory cortex is located in the postcentral gyrus of the parietal lobe, while inferior and posterior parietal cortex contains areas associated with the secondary somatosensory cortex (Burton et al., 1997). The primary somatosensory cortex (SI) is essential for perceptual feature identification. On the other hand, secondary somatosensory cortex (SII) areas located primarily in the upper bank of the Sylvian fissure,immediately posterior to the central sulcus are high level tactile o bject processing areas (Burton, 1984). Maldijan et al. (1999) proposed that secondary somatosensory cortex (SII) is involved in complex tactile functions such as textural discrimination. As shown in Figure 5, the location of SII is thought to be in the parietal lobe, lateral and posterior to the face representation in primary sensory cortex SI, and anterior and medial to the primary auditory areas (Maldijan et al., 1999).

Penfield and Rasmussen (1950) proposed a schematic representation of anatomical divisions of the primary motor cortex and the primary somatosensory cortex which is called homunculus at 1950 (Figure 6). In Figure 6, it is seen that each specific cortical area in the somatosensory cortex represents sensation of a different body part, just as each specific cortical region in motor cortex controls movement of different body parts.

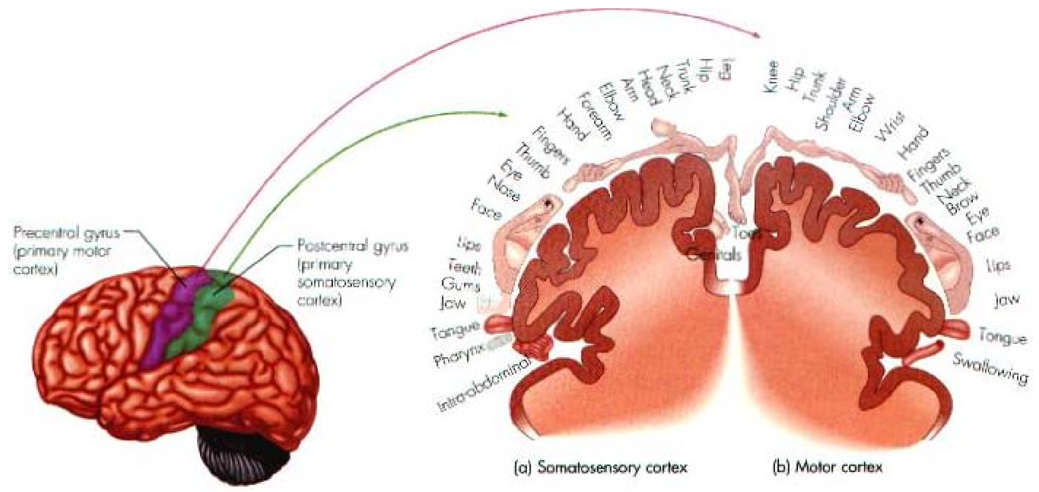

Figure 6 Representation of Motor and Somatosensory information in the primary and motor and somatosensroy cortex (https://medimages.hostzi.com).

2.1.3.2 Voluntary Tactile Attention Network

Activation maps occurring when tactile sense is recruited by several tactile stimuli with varying shapes or features have been a major interest (Burton et al., 1999, Reed et al., 2005, Rizzolatti et al., 2002, Roland et al., 1998, Binkofski et al., 1999). Burton et al. (1999) examined whether tactile attentional network correlates with non-somatosensory cortical areas.

The parietal lobe is composed of two major regions, the somatosensory cortex and the posterior parietal cortex. Posterior parietal cortex is located at the junction of multiple sensory regions and has four major components: The superior and inferior parietal lobules, the intraparietal sulcus (IPS) and the medial parietal cortex. It is located at the junction of visual, auditory and somatosensory regions and include an expansive model which supports multimodel integration (Mesulam, 1990).

An important question is whether the same or different nonsensory areas are active during tactile attention task with the visual attention network. In tactile attentional network, one main region is the right posterior parietal cortex since lesions here are associated with neglect of both visual and somatosensory stimuli present at the contralateral side to the lesion (Burton, 1999).

Effects of tactile attention can be predicted in primary (S1) and secondary (S2) somatosensory cortex. Larger responses resulting from tactile stimuli were usually observed in higher order somatosensory areas that are located along the parietal operculum and inferior lateral parietal cortex (Burton et al., 2008). On the other hand, in many visual attention studies, a task related activation of a dorsal parietal–frontal network including premotor and IPS is observed (Corbetta and Shulman, 2002). These regions support goal-directed attention as mentioned in the previous part. Goal-directed attention is indispensable in both visual and somatomotor tasks involving actions such as hand and arm movements (Binkofski et al., 1999), detecting differences in the lengths of rectangles (Roland et al., 1998), inspecting objects with touch (Reed et al., 2005).

Binkofski et al. (1999) focused to localize brain areas that are activated during perception of complex objects. In their experiment, subjects were asked to perceive geometric features of complex objects as compared to a simple object such as a sphere. Manipulation of complex objects resulted in an activation of ventral premotor cortex, intraparietal sulcus, and a region of the superior parietal lobule (Binkofski, 1999). Roland et al. (1998) studied activation of somatosensory association areas under tactile discrimination of geometric properties of objects. They observed activations of lateral parietal opercular cortex, IPS under voluntary tactile discrimination of length, shape and roughness of objects. Reed et al. (2005) investigated the neural pathway of tactile recognition of the objects with complex shapes by using fMRI. They proposed activation of parietal and insular somatosensory association cortices, as well as occipitotemporal visual areas, prefrontal, and middle temporal areas, medial and lateral secondary motor cortices. They observed contralateral activation of prefrontal cortex, premotor cortex, FEF while bilateral secondary somatosensory region activation (Reed et al., 2005).

All these studies investigated neural activations under voluntary and goal directed sensorymotor cognitive tasks even though they investigated neural substrates of different aspects of tactile stimuli. As it is seen in results, similar to visual attention network, IPS, ventral premotor cortex and superior prietal lobule activations occur.

2.1.3.3 Behavioral Findings in Tactile Line bisection

Clinical behavioural studies concerning line bisection task in tactile sense, generally examine how tactile line bisection is modulated by different conditions and factors such as hand used, scanning direction, line length and particularly different type of subject groups (Laeng et al, 1996, Coudereau et al, 2006, Brooks et al, 2011, Chokron et al, 2002).

Laeng et al. (1996) investigated relative contribution of perceptual, attentional and scanning factors in a tactile bisection task performed in left and right hemispace in 16 healthy blind-folded and right handed people. They observed gender effect as well as rod length, hemispace bias in line bisection by applying a line bisection task in left and right hemispace where each hand was used. Their set-up consist of 6 wooden rods with 20, 24, 28, 30, 35, 40 cm of lengths. Subjects scanned the rods from one end to the other to understand total length of lines until they decide that the pointer is at the centre of the line. They concluded that subjects bisected to the left of the true center when the rods were in left hemispace, to the right of the true center when rods were in right hemispace when using either right or left hands. According to study, hemispace and hand influenced the estimation in a consistent way: Left hand or left hemispace shifted the bias in leftward while right hand or right hemispace shifted the bias rightward. The two hands were biased equally in left hemispace but their biases were different in right hemispace (Laeng et al, 1996).

In a similar way, Coudereau et al. (2006) studied perception of space in visually deprived 20 right handed neurologically healthy people to see how pseudoneglect is manifested in a tactile bisection task administered in the centre of the visual space. Participants used both right and left hand again. There were 10 rods with 14, 16, 18, 20, 22, 24, 28, 30, 32, 34 cm of lengths in their set up. Participants scanned the rods from one end to the other three times. As a result, participants deviated significantly to the left of the midpoint when using their right hand, whereas they deviated to the right of the midpoint when using their left hand. This is contradiction with Laeng et al.'s (1996) results (Coudereau et al, 2006).

Another tactile line bisection task was conducted to observe difference about visual and tactile performance of neglect patients along with healthy adults. Chokron et al. (2002) tested whether the ipsilateral shift of the egocentric frame of reference is responsible for a spatial bias in neglect. The task was applied in central space and only right hand was used. Two wooden rods in 10 and 22 cm lengths were used in experiment. After scanning rod from one end to the other, the subjects was asked to stop at a point which they estimated to be the middle of the rod. The bisection was made from the same direction with the starting end. The healthy participants, while bisecting the rods with their right hand, showed a nonsignificant leftward bias which known as pseudoneglect effect. Interestingly, neglect patients also faulted to the left of the objective middle instead of rightward bias. When visual and tactile bisection results were compared, visual line-bisection protocol showed a significant rightward bias in neglect patients whereas tactile rod bisection performance did not differ in normal and neglect patients. It was found that there was no significant effect of the starting position or scanning direction prior to bisection (Chokron et al., 2002).

As we see in the results above, published results on bisection by control subjects are remarkably variable and inconsistent. In their extensive review about factors affecting line bisection in visual and non-visual tasks, Jewell and Mccourt (2000) presented that bias is very controversial according to different factors. Particularly, with respect to the hand-used, across tactile bisection studies investigating the hand used to perform bisection, several studies found no significant effect of hand used. Many studies found that using the right hand resulted in rightward error while using the left hand caused leftward error. Other studies found that there were leftward errors when subjects pointed using their right hand, and rightward errors when pointing with the left hand. There are also few studies reporting that both hands erred to the leftward and the left hand erring farther to the left than the right hand (Jewell and McCourt, 2000). More importantly, most of the studies about tactile line bisection investigated effects of different parameters in bias instead of revealing neural substrates of tactile line bisection in the brain.

2.2. Motivation

In line bisection task, patients with neglect syndrome mark middle point of a line with a bias toward a specific side of the line. Researches in normal subjects as well as neglect presented adequate evidence that clinical tasks using to assess neglect may involve different neural substrates (Gazzinga, 2004). We hypothesize that there are differences between functional networks recruited by bisection decision under different sensory modalities, especially tactile and visual line bisection.

Results of the studies in literature is important for our study to form a hypothesis about activation maps of tactile line bisection task since our task includes voluntary tactile attention while anticipating rod lengths. For this purpose, we implemented a new, unattempted line bisection task design, surveying the task types and results of these studies in the literature in detail. It is expected that by reaching at several conclusions about how line bisection test r ecruits the attentional network when visual space is taken away, the underlying representation of the dysfunction in neglect syndrome can be clarified.

In our experiment, participants did not only perform the task separately using visual and tactile senses, but also performed the task with each hand respectively. Hence, hand used and handedness may present a cue about our results' significancy. In addition to tactile line bisection task, in even visual line bisection, participants use their upper limbs to perform a paper and pencil line bisection, or proceeding bisection via a mouse or button. Since unilateral limb manifests itself by crossing cerebral activation on the contralateral hemisphere, understanding of h ow this interaction affect line bisection performance is an important matter.

During implementation, mechanical design to create an optimum tactile line bisection set-up for use in MR device, with respect to rod lengths, rod numbers, rod positions became extremely important. Behavioral literature survey included here in guided us about hand used effects and gave an idea to design an optimum mechanical tactile line bisection set-up compatible with the MR device.

Our study have two different aspects from the studies in the literature:

1. Our line bisection task was performed while the somatosensory cortex was active regardless of the visual sense.

2. We investigated the neural substrates of tactile and visual line bisection with support of fMR brain images.

To the best of our knowledge, a similar study on tactile line bisection with the use of fMR does not exist. The design of the tactile line bisection board compatible with MR device is an innovation of our study since it is difficult to implement a tactile line bisection task in MR device where space is constricted for arm movements, particularly in a line bisection set-up.

Since neural substrates of tactile line bisection has not yet been studied in neuroimaging, we could not make an exact forecast about localization of brain activations. However, we clearly expected activations around somatosensory cortex associated with both tactile sense and visual sense due to the motor response involved. In Table 1, differences in two line bisection tasks that we administered with our wooden tactile setup are summarized.

Table 1 Activations that are expected in each condition

	Activity	
Condition	Tactile	Visual
Motor vs off	Motor, Somatosensory	Motor, Somatosensory, Visual cortex
Linebisect vs off	Line bisection, Motor, Somatosensory	Line bisection, Motor, Somatosensory, Visual cortex
Linebisect vs motor	Line bisection Decision	Line Bisection Decision

CHAPTER 3

METHOD

As mentioned in the previous chapter, it is important for us to observe how somatosensory cortex is recruited during line bisection. With regard to this, our research question is how line bisection activity manifests itself in the tactile versus visual sense within the fronto-parietal visual loop. Therefore we designed a novel fMRI task in which line bisection activity is performed first with closed eyes and secondly opened eyes.

In the experiment, at first, subjects tried to find middle points of a wooden rod by moving a sponge cursor through the rod with closed eyes (tactile). Secondly, the subjects performed same experiment with opened eyes (visually). Line bisection decisions are performed repetitively in both of these cases for twelve different rods with variable lengths.

In order to differentiate tactile line bisection from visual line bisection as well as standard motor activity, we used block design paradigm. Block design paradigm consists of presenting stimuli sequentially within a condition and then introducing another condition for the same amount of time. Conditions are referred as blocks. Block design technique is preferable, since results of it are robust and BOLD signal change related to baseline is relatively large in this technique (Amaro and Barker, 2006). Usually, two conditions are used repetitively back to back: the first condition is the actual task under the research question, the second one is a baseline task. In this study, there are several conditions to consider: tactile line bisection, visual line bisection, and motor sweep as actual tasks; and idle resting as baseline task.

It is hard for a subject to find middle point of a rod he has never seen before directly. At first, the subject scans the length of the rod by moving the cursor from one end to the other end of the rod for several times and when he anticipates the middle point, he leaves the cursor on the point where he thinks is the middle point. So motor sweep is an inherent part of the line-bisection activity. Therefore, we need to categorize the motor sweep activity that was done before middle point decision which is involved in the line bisection block separately. This way we can obtain activity related to line bisection decision exclusively.

After several pilot studies, we set up motor sweep within a separate block design experiment in which motor activity condition is one block and a rest occurs as baseline. We have two other block design experiments in this study: the first one is composed of the eyes closed tactile line bisection activity as one block and a rest activity as baseline; while the second one is composed of the visual line bisection activity as one block and a rest activity as baseline.

The reason why we did not set up motor sweep and line bisection activity in the same experiment design is twofold: 1. For preventing the subject to keep thinking middle point while performing just motor sweep activity, 2. For avoiding large arm movements in between active task conditions (See in Appendix-B). Therefore we separated motor sweep and line bisection tasks as different fMRI experiments.

In Figure 7 these are illustrated such that OFF comprises rest condition and T comprises active task condition. T corresponds to motor sweep in experiment 1, tactile line bisection in experiment 2, and visual line bisection in experiment 3.

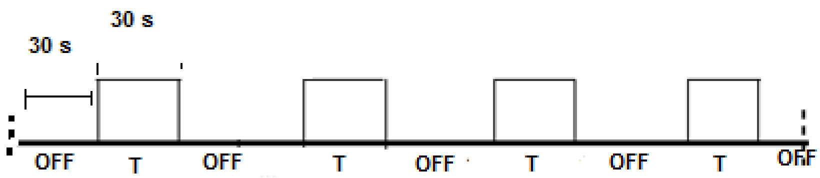

Figure 7 Block design experiments

There are four repetitions of each cycle to collect enough samples for analysis in all tasks. fMR image sample number is calculated in the formula given below, where time of repetition (TR), 2000 msec, is the time between each sample. Sample numbers for the entire experimental run are given in Table 2.

$$S = \frac{\text{Duration (msec)}}{\text{TR}} \qquad (1)$$

Table 2 Durations and sample numbers of blocks in each block design.

	Duration(s)	Number of Samples
OFF Condition	30	15
Motor / Line Bisection Condition	30	15
One Cycle	60	30
Total Experimental Run (4 Cycles + OFF condition at end)	270	135

3.1. Sensorymotor Apparatus

We designed a simple portable MR compatible wooden tactile line bisection set-up with dimensions of 25 cm x 25 cm. A rectangular wooden board is positioned on the subject's body fixed via a retro belt as seen in Figure 8-a. There are three thinner wooden plates which can be mounted to main board one by one. One of the thinner plates (Figure 9-a) is spared for experiment 1, which is used for the motor sweep task. There is one wooden rod with length of 16 cm on the middle of the control plate.

In order to conduct line bisection experiments, twelve wooden rods with different lengths and positions are used. Six of them are placed on one plate while the other six rods are placed on another plate due to space limitations within the gantry. As shown in Figure 9-b, these two plates are mountable to the board fixed on the subject's body and are replaceable during experimental runs. The rods are located on the plates horizontally. Since it is reported that subjects consistently made errors during vertical line bisection tasks (Fink, 2001), horizontal line bisection task is preferred. Compared with other studies (Laeng et al, 1996, Coudereau et al, 2006, Brooks et al, 2011, Chokron et al, 2002), we can say that the rod number is sufficient. In addition, the size of the board is optimized for minimizing the motion of the arm in order to prevent motor artifact during line bisection decision. The length of the rods are chosen accordingly, restricted between 10-18 cm. The rods are assigned randomly to the four active task blocks, such that the subject is expected to perform three line bisections within each active block, which is 30 sec. To ensure similar performance between subjects, the rods are fixed on the boards randomly as follows: In active task period 1, part A of the board is attempted, in active task period 2, part B of the board is attempted, in active task periods 3 and 4, parts C and D of the board are attempted. Table 3 shows the rod lengths for each part, A,B,C,D.

Table 3 Arrangement of the rods on sections.

Section	Rod Lengths (cm)
A	18, 17, 10
B	15, 12, 13
C	16, 14, 11
D	17, 16, 12

The four parts encoded with letters A,B,C,D are distributed to the two wooden boards such that two parts (A and B) are in one board while other two (C and D) are in the second board. There are transparent separators between each part so that the subject could differentiate the sections both by touch and visually (Figure 9-b). Line bisection is achieved by positioning the moveable sponge cursors on the rods. Sponge material was used due to the fact that it must be MR compatible and provide sufficient friction to stay in place after the boards are retrieved. At initial condition all cursors are at the side of the rods in the same side of used hand in experiment.

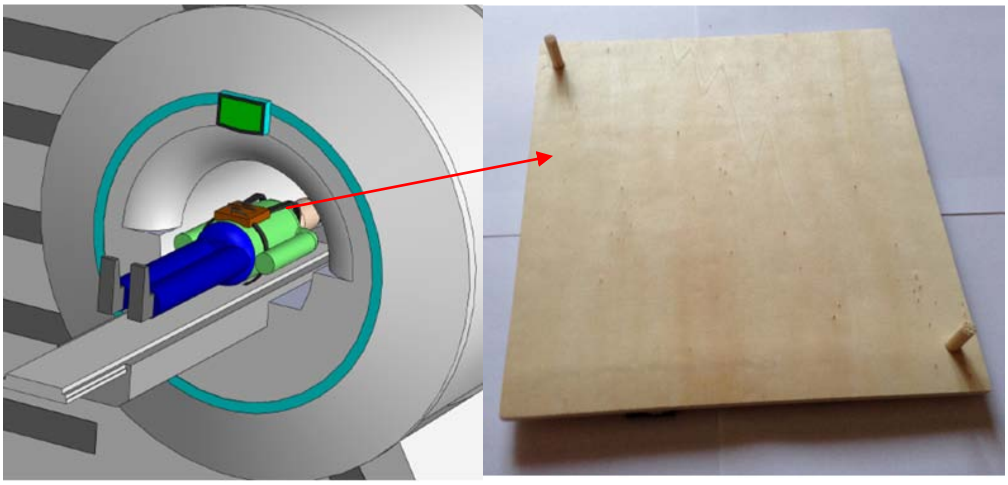

Figure 8 (a) Representation of position of participant in MR Device with experimental set up, (b) Main board fixed on participant.

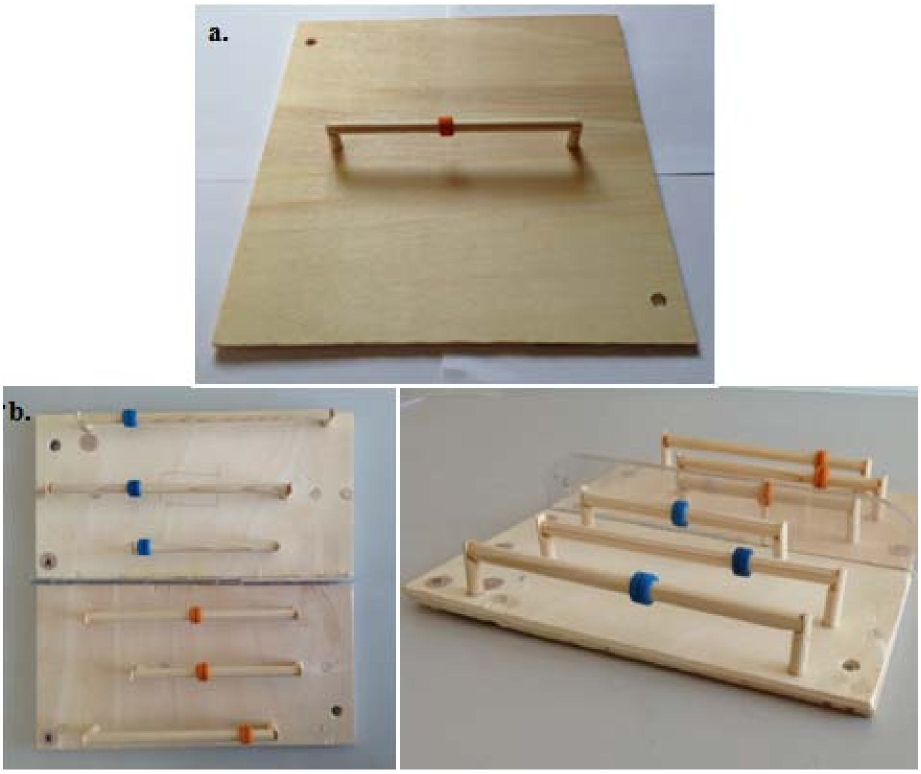

Figure 9 (a) Wooden board for motor-sweep task, (b) View of boards in different planes used for line bisection task.

The initial board design contained the rod for the motor-sweep condition at the very bottom of the two boards, not on a separate board. Pilot behavioral experiments are run on a set of ten subjects to finalize board design and guarantee its suitability for the duration of fMR image collection session. We found that having the motor-sweep rod at the bottom part created a lot of arm movement and unexpected motion artifacts in between experimental conditions. Therefore, we redesigned the boards by separating the control condition – which is the motor sweep task- on another board as shown in Figure 9-a. The entire tactile behavioral line bisection data collected using the initial board design is presented in appendix B.

3.2 Administration of fMRI Experiments

As mentioned earlier, we are concerned if there are different implications of this task under tactile and visual senses in clinical applications. In order to guarantee that the subjects stay naive to the requirements of the task, we applied line bisection activity first with closed eyes and secondly with opened eyes. There are three experiments as mentioned before and six runs, for performing each of these experiments with different hands[1]:

1. Control run (motor sweep activity) with their right hand and closed eyes
2. Control run (motor sweep activity) with their left hand and closed eyes
3. Line bisection activity with their right hand and closed eyes
4. Line bisection activity with their left hand and closed eyes
5. Line bisection activity with their right hand and opened eyes
6. Line bisection activity with their left hand and opened eyes

During experiment, while subject performs the activity in MR, one person gives the instructions to the subject via a headphone. One observer waits in the MR scan room to replace the wooden boards as each experiment proceeds. Parts of the wooden boards are counterbalanced across experiments as seen in Table 4 to avoid learning.

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[1]Motor activity and line bisection activity in sensorymotor task are separated as two different runs in fMRI experiment to isolate motor activity entirely from line bisection percept. Also, when motor and line bisect blocks were presented within the same run, extensive arm movements cause motion artifacts in the fMR scans. Results from our pilot fMRI runs are presented in Appendix B.

Table 4 Combinations of sections and plates for each run and condition.

	Motor (Closed Eye)		Tactile (Closed Eye)		Visual (Open Eye)	
	Right Hand	Left Hand	Right Hand	Left Hand	Right Hand	Left Hand
	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6
Cycle 1	Motor Sweep (Single rod)	Motor Sweep (Single rod)	A	B	A	B
Cycle 2			B	A	B	A
Cycle 3			C	D	C	D
Cycle 4			D	C	D	C

For example, in the third run which subject performs line bisection with his right hand and closed eyes, first plate which includes parts A and B are placed initially. Later, at the start of cycle 3, the observer replaces the plates and puts the second plate including parts C and D. Anatomical and functional images were acquired on a Siemens Magnetom 3T whole-body scanner with Echo planar imaging (EPI) capability using standard radiofrequency head coil for transmit and receive. At the beginning of the experiment, a T1 weighted mprage anatomical scan with high resolution is utilized. Duration of each functional run is 4.5 minutes. Since, there was 6 runs in experiment, total duration of experiment is 27 minutes. Parameters of the EPI functional acquisition is as follows:

TE= 30 msec, TR=2000msec., flip angle= 90°, slice thickness= 4mm, slice number=34, interslice gap= 3mm, Matrix Size= 64x64, Field of view (FOV)=192mm x192mm, with FOV including whole brain from vertex to lower cerebellum.

3.3 fMRI Data Collection and Analysis

The study was approved by the local ethics committee of the Ankara University Medicine School, Ankara, Türkiye. (Approve of ethical committe is given in Appendix J). 12 healthy, right handed volunteers (4F, 8 M) with no history of neurological or psychiatric illness were admitted to fMRI experiment. All volunteers were in 24-32 age range and mean age was 26.60. Before the experiments, Edinburgh-Handedness Inventory given in Appendix E was applied to determine whether dominant hand of the participant is right or not. Informed Constent was also obtained prior to participation (see in Appendix F). After individual data analysis, 3 subjects were discarded due to the following reasons: 1. Abnormal ventricle anatomy (extremely large ventricles, 1 subject) 2. No activation for the baseline motor-sweep task (2 subjects).

AFNI (Analysis of Functional Brain Imaging) tool was used for all fMRI data analysis. The flowchart given below (Figure 10 Flow chart of fMRI Data Analysis Steps) summarizes the data analysis steps. At first, data of each subject was analyzed individually: DICOM format data from scanner is converted into a format that AFNI can use. After preprocessing steps, general linear modal (GLM) analysis was used to extract statistical functional activation maps related to line bisect and motor activities for each subject. Talairach transformation was applied for each subject's anatomical and functional images respectively in order to transform each brain into a standart space because anatomical and functional brain coordinates differ in spaces from one subject to another. Then, group level analysis was done with 2x2 (visual,tactile x right hand, left hand) repeated measure ANOVA in AFNI to extract functional group mean and contrast maps. Finally clustering was performed to determine the clusters that survived an activation threshold of $p<0.001$ as well as their coordinates.

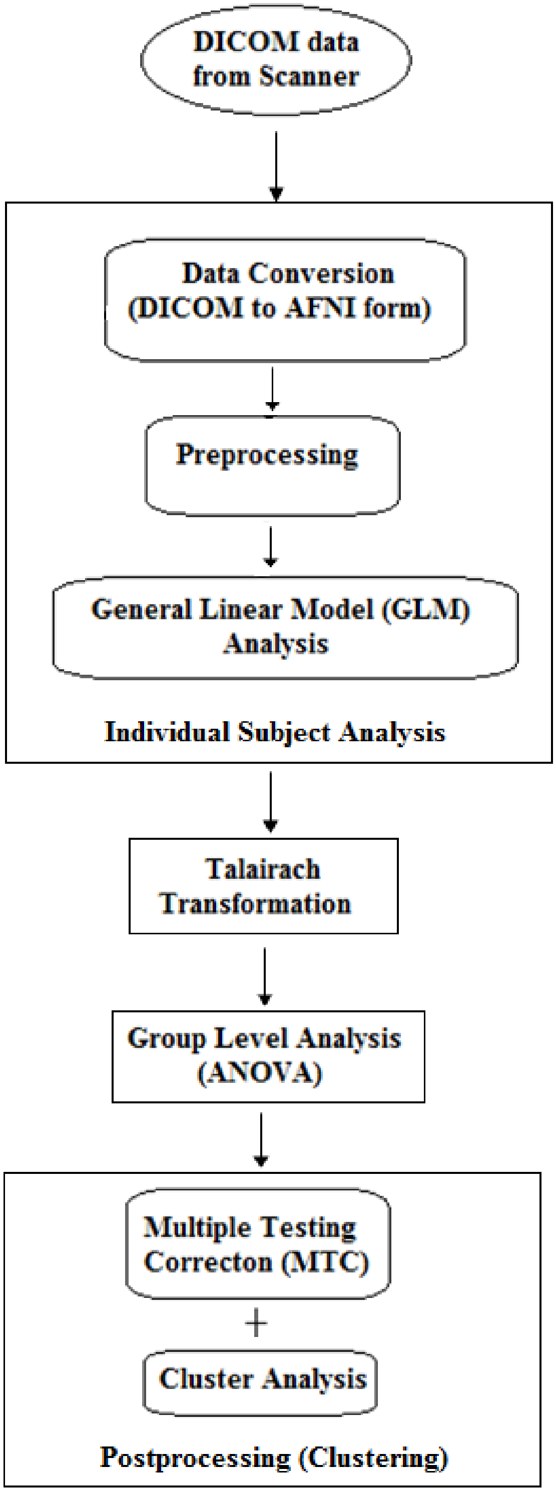


Figure 10 Flow chart of fMRI Data Analysis Steps

3.3.1 Individual Subject Analysis of FMRI data

3.3.1.1 Pre-processing

To obtain a clean, noiseless fMRI data for GLM analysis, first, pre-processing is done. Main goal of pre-processing is to reduce non-task-related variability in the data. Preprocessing steps for each individual are given in the following flowchart (Figure 11):

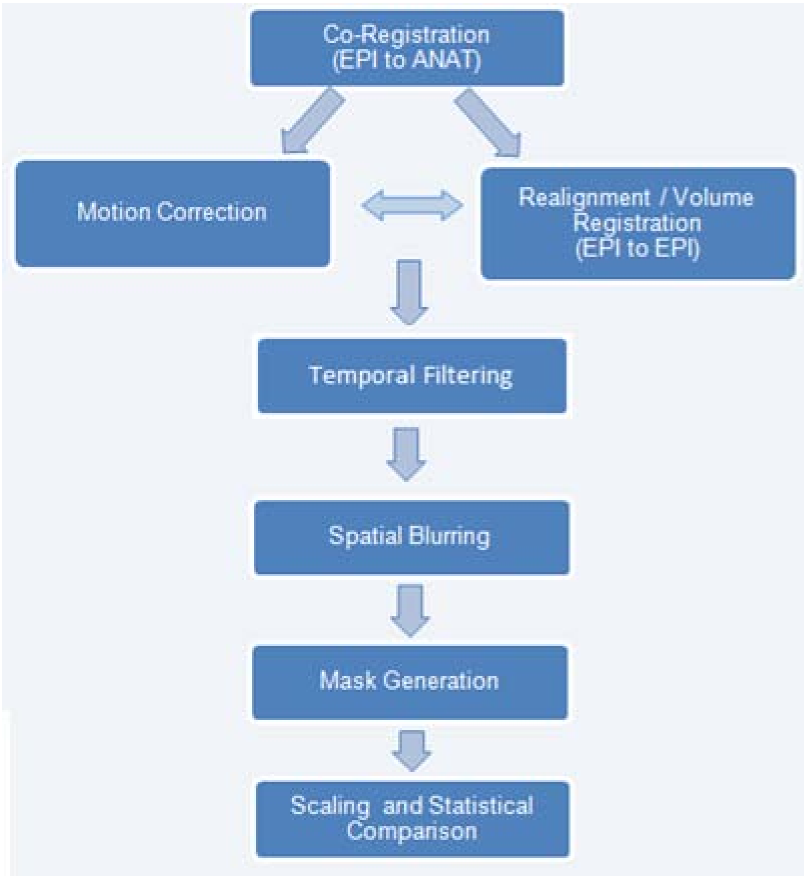


Figure 11 Block Diagram of Preprocessing Steps of individual Subject Data Analysis

During data acquisition, we acquired oblique fMR images in order to adjust FOV efficiently For these oblique datasets to correspond to a cardinal orientation, warping and interpolation are done with **3dwarp**.

Co-registration is a fundamental step for functional localization in the space of the high-resolution anatomy. However, fMRI scans are collected in low-resolution space, to collect data faster.

We need to bring anatomical and functional images into the same space so that location within one image corresponds to the same location in the other. We applied **3dwarp** and **3dAllineate** to register echoplanar data (fMRI) to structural data (MRI) in order to eliminate misalignment between anatomic and functional images. First, we checked for outliers with **3dToutcount**, to determine a subbrick without head-motion. Then this sub-brick is registered to anatomic data.

Motion correction is a common step in preprocessing functional magnetic resonance imaging (fMRI) data in which slice-to-slice head movement is estimated and removed, provided that motion is limited to 1-2 mm. It has been shown that even small head motion can create artifacts in activation maps when analyzing fMRI data, particularly when the motion is correlated with the activation paradigm (Field et al.,2000; Hajnal et al.,1994). The purpose of motion correction in fMRI data analysis is to maximize sensitivity to true activations while minimizing false activations related to motion (Johnstone et al., 2006). In co-registration or volume registration, each volume are aligned in a time series to a representative reference brain volume, preferably the same subbrick aligned with the high resolution MRI (Steger and Jackson, 2004). Since misalignments of image sequences is mostly due to movements, we used **3dvolreg** to correct misalignments between slices by aligning a sequence of images to this representative reference brain image. Since the size and shape of the registered images are the same, an iterative linear least squares rigid-body motion correction is adequate (Oakes et al., 2005).

We used the same sub-brick used in registration with the anatomic data for as the reference brain image for motion correction. In 3dvolreg, motion parameters that are calculated are saved can then be used to censor timepoints that contain too much motion. We applied 3dToutcount again to observe changes in outliers after motion correction. We expected a decrease in amplitudes instead of eliminating motions in total.

Temporal Filtering was applied after motion correction. High pass filter provides removing low temporal frequency variations, while low pass filtering smoothes changes with frequencies higher than hemodynamic response function (Sabuncu et al., 2010). We used low pass filtering to remove high frequency noises. Temporal variations with higher frequencies than 0.2 Hz. We used **3dFourier** for temporal filtering.

Volume registered data was needed to be smoothed to average out high frequency noise. Spatial smoothing improves signal to noise ratio (SNR) and allows for bleeding the collected activity profiles to nearby voxels, which in turn blurs the localization with respect to regular anatomical variability. Although it spoils the data, this type of averaging helps us attain greater sensitivity in statistical analysis later. We applied a 6 mm Full Width Half Max

(FWHM) Gaussian kernel to the dataset for blurring by using **3dmerge** AFNI command which performs convolution with Gaussian kernel. After noise reduction with spatial blurring, we eliminated non-brain areas by using **3dAutomask** AFNI command. It masked the spatial blurred data by keeping only the largest connected component of the threshold voxels. It writes result as a functional dataset which will be 1 inside the brain mask and 0 outside the mask.

Another problem lies in the difference of DC parts of the fMRI time series. The baseline signal values differ from voxel to voxel and subject to subject. To eliminate this variability, it is useful to convert each subject's fMRI time series to a common scale before combining the results for statistical analysis. By using scaling, differences between subjects in the overall scaling of fMRI data were removed. To scale each subject's data, we calculated mean values per voxel and percent signal change by using **3dTstat** and **3dcalc** AFNI commands. First, we calculated the mean value of every voxel's time course in each run with **3dTstat** and we applied scaling to functional volumes and calculated the percent signal change voxel by voxel with 3dcalc AFNI command. We used equation 2 to compute percent signal change,

$$Percent\ Signal\ Change = \left(\frac{(a-b)}{b} \times 100\right) \times c \qquad (2)$$

where,

'a' is the smoothed data, 'b' is the mean intensity value and 'c' is the masked brain.

3.3.1.2 GLM Analysis

After preprocessing steps, we obtained suitable data for the statistical analysis. We used general linear model analysis to extract statistical functional maps for individual subjects. GLM uses a sum of scaled and time-delayed versions of the stimulus time series (Douglas, 2006). For this purpose, a stimulus file which reflects the ideal expected impulse response function should be prepared.

A stimulus file contains the representation of the timing of the cognitive paradigm. An ideal task file is a .txt file composed of zeros and ones in one column, zeros corresponds to samples belongs to 'off' state (baseline) while ones corresponds to samples belongs to 'on' states (active conditions) which are motor-sweep and line bisection for our experiment. As mentioned in the block design part, in our experiment since both 'off' and 'on' states include 15 samples, there are fifteen zeros and fifteen ones sequenced in our ideal wave text file. Because there are 135 samples in one run, including 4 cycles of off and on blocks, ending with an extra off cycle, 75 zeros and 60 ones take part in the ideal text file in an alternating fashion. We created only one ideal wave text for motor-sweep and line bisection runs as given in Figure 12;

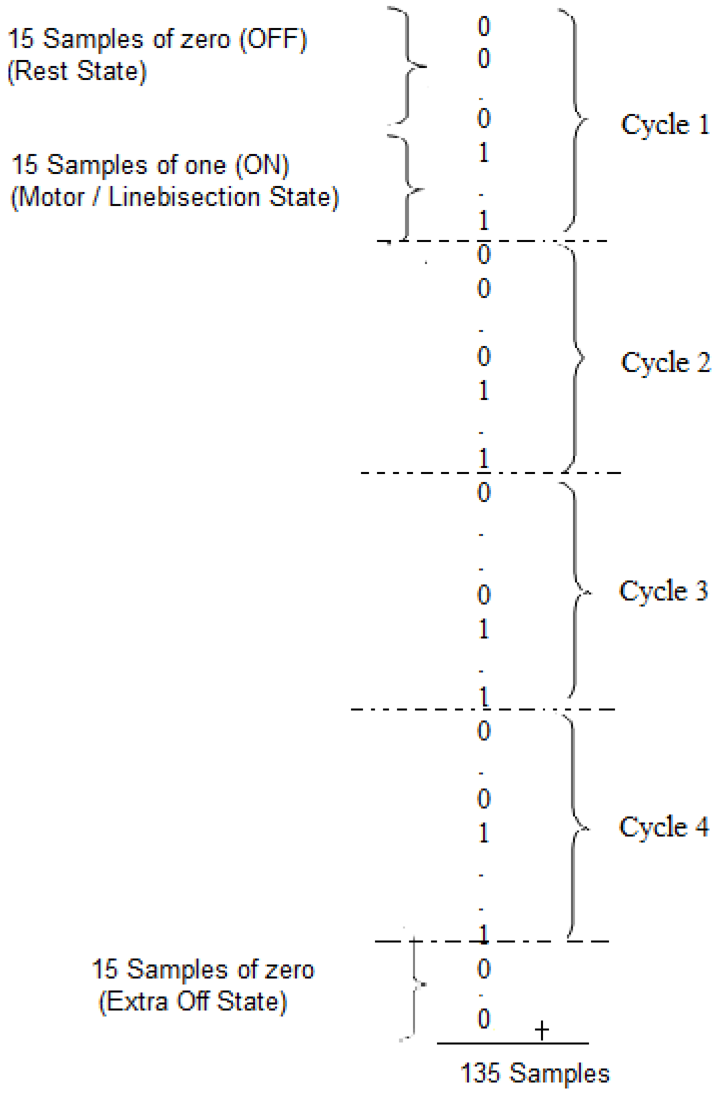


Figure 12 Content of ideal task file.

After generating ideal task file, we generated an ideal hemodynamic response function from the ideal task representative by using waver AFNI command. Wavercreates an ideal waveform time series file by convolving ideal task wave with theoretical hemodynamic response function in the shape of a gamma density, which is a commonly used default in AFNI software (Meltzer et al., 2008).

Visual representation of estimated hemodynamic response function is given in the following Figure 13:

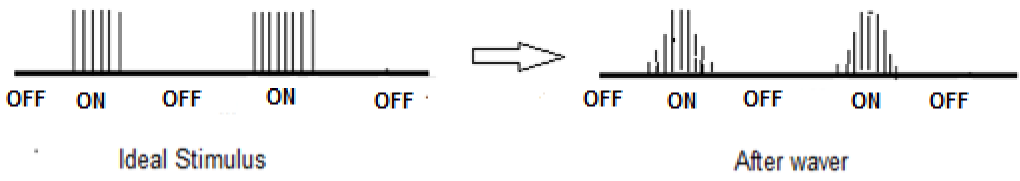


Figure 13 Visual representation of estimated hemodynamic response function

We used Gamma variety function as a model of the shape of the hemodynamic response in waver command. Our Gamma degree was 2 due to TR=2000 msec (sampling rate).

In general linear model analysis, we applied multiple linear regression in which we already assumed the hemodynamic response produced by the AFNI waver program. Theorically, a general linear model equation is similar in the following way:

$$Signal = \beta_1 \times F_1 + \beta_2 \times F_2 + \beta_3 \times F_3 + C + Err \quad (3)$$

where, F_1, F_2 and F_3 are the predictor functions or ideal hemodynamic response functions as presented in Figure 13 and β_1, β_2, β_3 are regressor coefficients. C is the constant and Err is the error (Friston et al., 1995).

We applied GLM analysis using **3dDeconvolve** AFNI command. 3dDeconvolve was used to create a statistical map of voxels with signal patterns related to the task by filtering the relevant voxels which have β coefficients that pass the null hypothesis. At the end of GLM analysis, each voxel contains statistics: t-values, p -values (Douglas, 2006). In our analysis, there was a single regressor since we had one estimated HRF which can be used in all runs. We can compare each calculated beta weight to zero. If the beta weight differs significantly from zero for a given voxel, we may say that the voxel is activated under the experimental condition that corresponds to that beta weight (Wang et al., 2011). In our experiment, there was one calculated beta for each run. We observed motor activity by comparing 'motor sweep' to 'off' in first and second runs, line bisection activity (including motor-sweep activity) by comparing 'line bisect' to 'off'. A separate 'censor' file was used to indicate which points are to be excluded from the analysis, in case there are large motion spikes in the time series.

3.3.2 Talairach Transformation

Functional localization involves the application of a sequence of statistical image processing operations in order to identify the location of brain activity or to produce functional / parametric maps with respect to the brain structure. After individual subject analysis is completed for data of each participant, we need to to control for variability in brain shape and size so that we can perform across-subject comparisons of datas easily. Since anatomical and functional brain coordinates differ in spaces from one subject to another, brain of each subject is required to be transformed into a standart space. When we use a standart template space, it will allow us to know where a voxel is located in an atlas. For this purpose, coordinates are stardardized by mapping the images to Talairach (stereotaxic) format. During group level analysis, statistical functional activation maps must be overlaid on a mean anatomical image.

We transformed T1-weighted structural MRI volumes of all subjects into Talairach space manually by demarkating anterior commissure, posterior commissure and 6 extrme points of the brain in all 3 planes. Following it, we averaged these anatomical brain images among subjects by calculating the mean of Talairached images in order to obtain one template anatomic brain image which is used as underlay in group level analysis. Similarly, we performed Talairach transformation for functional brain images with 'adwarp' in AFNI by resampling the mean IRF datasets for each subject to the same grid.

3.3.3 Group Level Analysis of fMRI Data

In order to make a correct interpretation about results of our fMRI study, we need to be sure about validity and reliability of functional statistical activation maps that we extracted from GLM analysis. More specifically, one needs to aggregate the activations of more than one subject, to a 'group', to see significant results about conditions of the task. After alignment of each subject's data into a stereotaxic space, we applied group level analysis by using ANOVA which is a type of parametric statistical analysis program.

We designed our statistical model according to factors and conditions in our experiment. Our design model is 2 by 2 within-subject repeated measure ANOVA, since we had two factors as one of them is sensory modality, other one is the Hand-Used factor. Each factor had two levels since there was two conditions in each factor (Sensory modality: Tactile, Visual and Hand-Used: Right Hand, Left Hand). Our design models of repeated measure ANOVA are represented in the following Table 5;

Table 5 Design Models of 2x2 within-subject ANOVA analysis

	Factor	Level
ANOVA Model-1	Factor 1: Task	Level 1: Motor
		Level 2: Tactile
	Factor 2: Hand-Used	Level 1: Right Hand
		Level 2: Left Hand
ANOVA Model-2	Factor 1: Task	Level 1: Motor
		Level 2: Visual
	Factor 2: Hand-Used	Level 1: Right Hand
		Level 2: Left Hand
ANOVA Model-3	Factor 1: Sensory Modality	Level 1: Tactile
		Level 2: Visual
	Factor 2: Hand-Used	Level 1: Right Hand
		Level 2: Left Hand

We obtained 6 mean and 3 contrast of mean images resulting from the above three 2x2 ANOVAs:

<u>Means:</u>

1. Motor-sweep with Right Hand Mean
2. Motor-sweep with Left Hand Mean
3. Tactile Line bisection with Right Hand Mean image
4. Tactile Linebiseciton with Left Hand Mean image
5. Visual Line bisection with Right Hand Mean image
6. Visual Line bisection with Left Hand Mean image

<u>Contrasts (for each hand):</u>

1. Tactile line bisection versus Motor-sweep
2. Visual line bisection versus Motor-sweep
3. Tactile line bisection versus Visual line bisection

Our examination is within subjects, because we had only one subject group with same properties. We used 3dANOVA3 command for 2 by 2 within subject ANOVA in AFNI.

3.3.4 Post-Processing

After group level analysis, for each experiment, we obtained mean functional statistical activation maps resulting from multiple subjects. In order to realize whether the activation maps form significant clusters or not, we applied clustering in two steps: multiple comparison correction and clustering.

We used **AlphaSim** in AFNI which is based on Monte Carlo simulations (also known as family-wise error method) to correct for multiple comparisons. Accordingly, a meaningful combination of probability thresholding (pthr) and cluster size thresholding (minimum cluster size corresponding to corrected p value) is chosen to prevent false positives. It is important to determine a meaningful uncorrected p value due to the fact that if we choose too high p level, there will be probably false positives in clusters which act as a true activation, on the other hand if we choose too small p level, the power of calculation decrease which means that we may lose significant task-related activations. We took account of several criteria to obtain a desired p value and minimum cluster size combination at a high significance level (alpha = 0.001). Connectivity radius (rmm) between voxels that form a cluster is an important factor. It is a number that enforces the voxels within the cluster to touch each other at least by their corners, as given in equation 4. Since our voxel dimensions are 3mmx3mmx4mm, we chose rmm=5.5.

$$\text{r mm} > \sqrt{\mathbf{3^2 + 3^2 + 4^2}}\ ;\ \text{r mm} > 5.2 \qquad (4)$$

After determining optimum combination of uncorrected p (pthr) and minimum cluster size, we used **3dclust** in AFNI to find clusters of task-related active voxels that refers to nonzero voxels surviving above the threshold we specified. Our uncorrected p value is 0.001 which is mostly used in fMRI studies. Our minimum cluster size is 24 according to Monte Carlo simulation (AlphaSim). Therefore our minimum cluster volume (vmul) is voxel dimensions multiplied with minimum cluster size which is equal to 3x3x4x24 = 864 mm^3. It means that if the clusters survive above the threshold value (threshold value of the t-test is 4,527 corresponding to p=0,001) and their voxel size are larger than 24 voxels (or 864 mm^3), they are classified as task-related significant activation.

3.4 Statistical Analysis of Line bisection Performances

In addition to fMRI brain image analysis, line bisection performances in terms of bias amount and direction are evaluated. A tactile behavioural experiment which is presented in appendix B was applied to ten volunteers at out of MR device by using pilot sensorymotor apparatus.

An additional visual behavioural task which is presented in appendix C was also introduced to ten healthy volunteers at out of MR device. The purpose of visual behavioural experiment is to clarify whether deviations from middle points differ in amount or direction when the experiment is performed by subject's himself eyes at out of MR device insted of performing with help of a mirror in MR device.

Apparently, behavioural data of actual fMR experiments was also investigated. In all behavioural experiments, we measured the deviations from the middle points of the rods and noted deviation amounts and directions. Each behavioural experiment was performed by the subject with both right-hand and left-hand separately.

Bias Amounts and bias directions were analyzed with separate two ANOVAs in SPSS. The directional bias from midpoint was measured to the nearest centimeter by determining the distance between the subjective middle and the objective middle of the rod and calculated as a percentage of the rod length in a simple way given in Equation 5. The resulting score is negative or positive: negative scores indicate a leftward bias while positive values indicate a rightward bias (relative to the true centre). A score of zero reflects no bias.

$$Bias = \frac{Subjective\ Middle - Objective\ Middle}{Rod\ Length} \times 100 \qquad (5)$$

We took absolute values of percentage bias values for bias amount analysis. On the other hand, asymmetry index was calculated for analysis of bias directions in the way given equation 6 since it clues us in directions of the deviations;

$$Asymmetry = 2 \times \frac{(R-L)}{(R+L)} \qquad (6)$$

Where, L is the leftward bias and R is the rightward bias in absolute values.

Since participants performed the experiment 4 times (two times with their right hand and two times with their left hand) in tactile behavioural experiment, first, mean values of bias and directions (asymmetry) were calculated for each subject individually. Secondly, mean values of bias and directions were calculated for ten participants. In other experiments (visual behavioural and fmri behavioural) there is not repetitions, each condition is performed for one time.

In fMRI experiment, we have 4 variables, two of them were dependent variables (bias amount and bias direction), while two of them were independent variables (sensory modality and hand-used in total. Since we examined the main effects of hand-used and two sensory modalities to bias amounts and bias direction separately, we have two independet variables (sensory modality and hand-used) with two levels and one independent variable (bias amount or bias direction). Therefore, we used 2 x 2 ANOVAs (left hand, right hand x tactile,visual). It is undisputed that there will be further deviations under tactile sense with eye closed than the visual condition.

CHAPTER 4

RESULTS

4.1 Individual Subject Analysis

As it was explained in chapter three in detail, general linear model (GLM) analysis was applied after each individual's functional image was preprocessed. With respect to GLM analysis, we examined linear regression analysis for six runs;

1. Motor-sweep with Right Hand
2. Motor-sweep with Left Hand
3. Tactile Line bisection with Right Hand
4. Tactile Line bisection with Left Hand
5. Visual Line bisection with Right Hand
6. Visual Line bisection with Left Hand

4.1.1 Hemodynamic Response Functions

As told in chapter three, we generated an ideal hemodynamic response function from ideal task representative to give as regressor into GLM by using waver AFNI command (Figure 14).

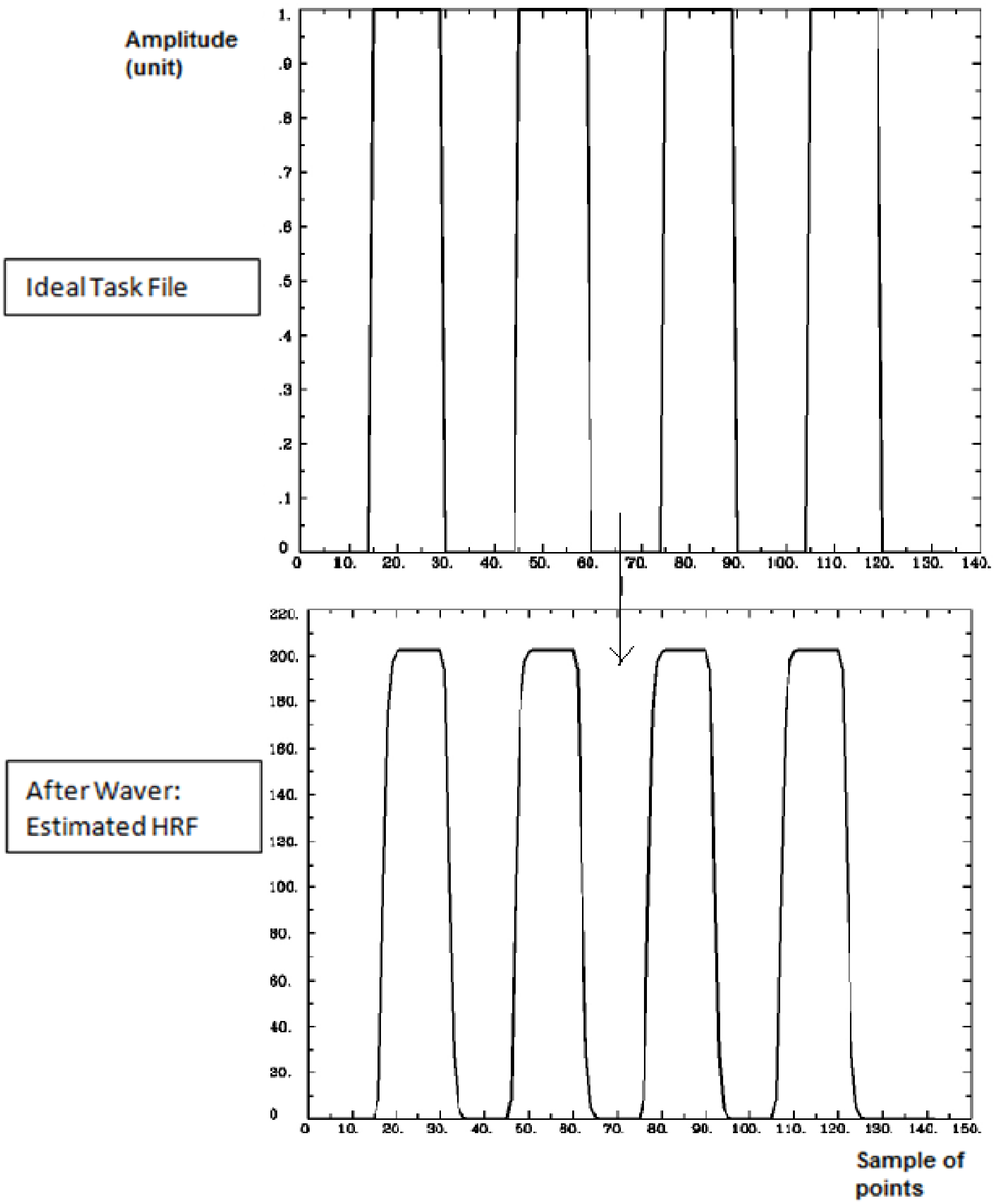
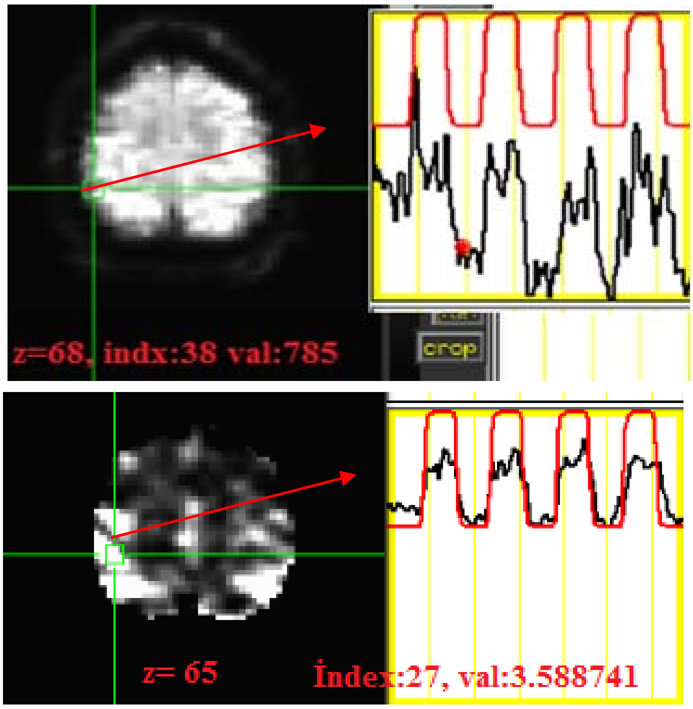


Figure 14 Graphs of ideal task file which we generated as a text file and its waver output



a.
b.

Figure 15 Hemodynamic Response Function and ideal pick (a. Before preprocessing, b. After preprocessing)

In Figure 15, fMRI time series data is given before and after preprocessing along with ideal estimated HRF for one participant. After preprocessing steps, a clean and rescaled data was obtained for GLM analysis. Data is motion corrected, smoothed, masked and scaled respectively. Separating motor and line bisection tasks enhanced fMRI signal, it is seen that baselines are more proper and signal is fitting with ideal HRF better.

4.1.2 GLM Analysis Results

We applied general linear model analysis with linear regression. In GLM analysis, we examined 6 c onditions in total for each participant, where each regressor reflected exclusively the active condition in one of the 6 runs. Activity maps for a specific individual participant (Subject-4), is presented in the following results.

4.1.2.1 Motor-Sweep Condition with Right Hand

In Figure 16, Comparison of motor-sweep activity with rest is presented for right hand in three different planes: axial, coronal and sagittal respectively. Motor activation is our basic control activation in order to obtain pure line bisection decision later.

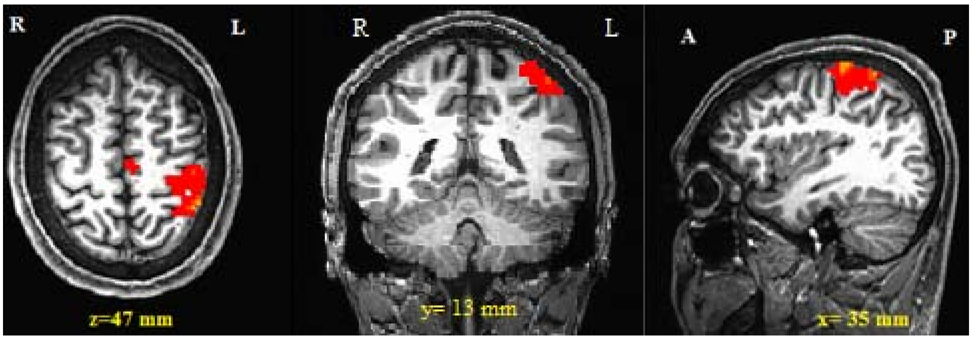


Figure 16 Result of motor task with right hand (R: Right, L: Left, A: Anterior, P: Posterior, p=0.001, Thr=3.360).

As it is seen from Figure 16, contralateral left motor cortex activation is observed very clearly as it is expected. Since somatomotor pathway is contralateral, motor cortexes in each hemisphere of brain controls the motor activations at the opposite (contralateral) side.

4.1.2.2 Motor-Sweep Condition with Left Hand

In Figure 17, Comparison of motor-sweep activity with rest is presented for left hand in three different planes again.

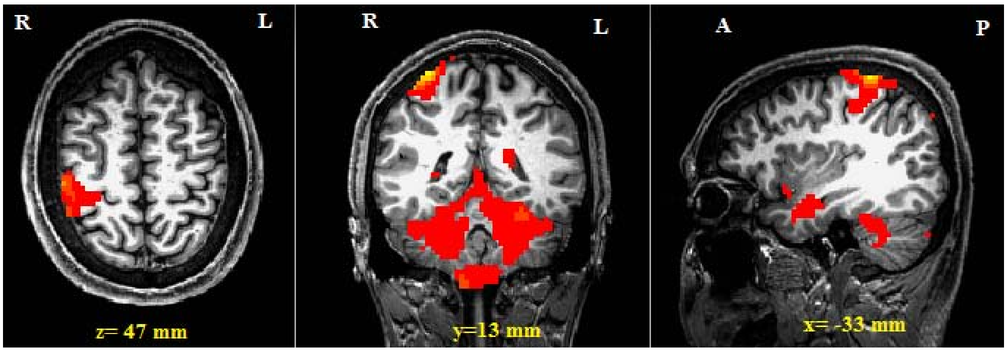


Figure 17 Result of motor task with left hand (R: Right, L: Left, A: Anterior, P: Posterior, p=0.001, Thr=3.360).

As it is seen from Figure 17, contralateral right motor cortex activation is observed very clearly as it is expected again. However, other than the expected contralateral motor cortex activity, there exists a wide contralateral activation region including temporal cortex, as well as bilateral cerebellum, and subcortical areas such as putamen and caudate as it is seen in Figure 17. This pattern is consistently observed in all subjects when the experiment performed with left hand. Since all our participants were dominantly right-handed according to Edinburgh Handedness Inventory, and our experiments include proprioceptive action (motor activity to perform desired activity), participants made an extra effort to perform with their left hand which has reduced dexterity with respect to their dominant hand. Probably this leads to complicated processes in the brain which involve both proprioceptive and somatomotor activity with their non-dominant hand.

4.1.2.3 Tactile Line Bisection Condition with Right Hand

Figure 18 presents comparison of tactile line bisection with rest for right hand in different brain slices. We expected to see both motor-sweep and line bisection activations since line bisection activity includes repetitive motor scanning through rod length in order to estimate total rod length.

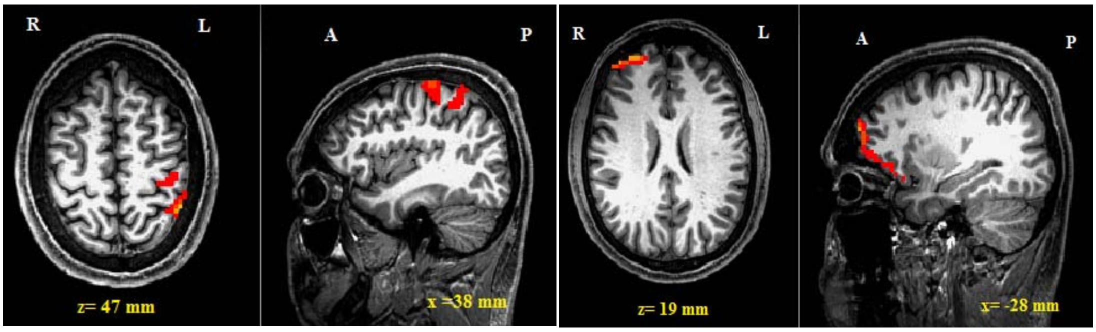


Figure 18 Results of tactile line bisection task with right hand (R: Right, L: Left, A: Anterior, P: Posterior, p=0.001, Thr=3.360).

In Figure 18, left hemisphere (contralateral) handbump activation is observed as expected in precentral gyrus as well as postcentral gyrus. As we proceeded to lower slices in axial plane, we observed right lateralized prefrontal activation (middle frontal gyrus) on ipsilateral side of the brain. Although this prefrontal activity seems to indicate processes involved in line bisection decision, group analysis results must be investigated to generalize for all subjects.

4.1.2.4 Tactile Line bisection Condition with Left Hand

Figure 19 presents comparison of tactile line bisection with rest for left hand in different brain slices. We expected to observe both motor-sweep and line bisection activations.

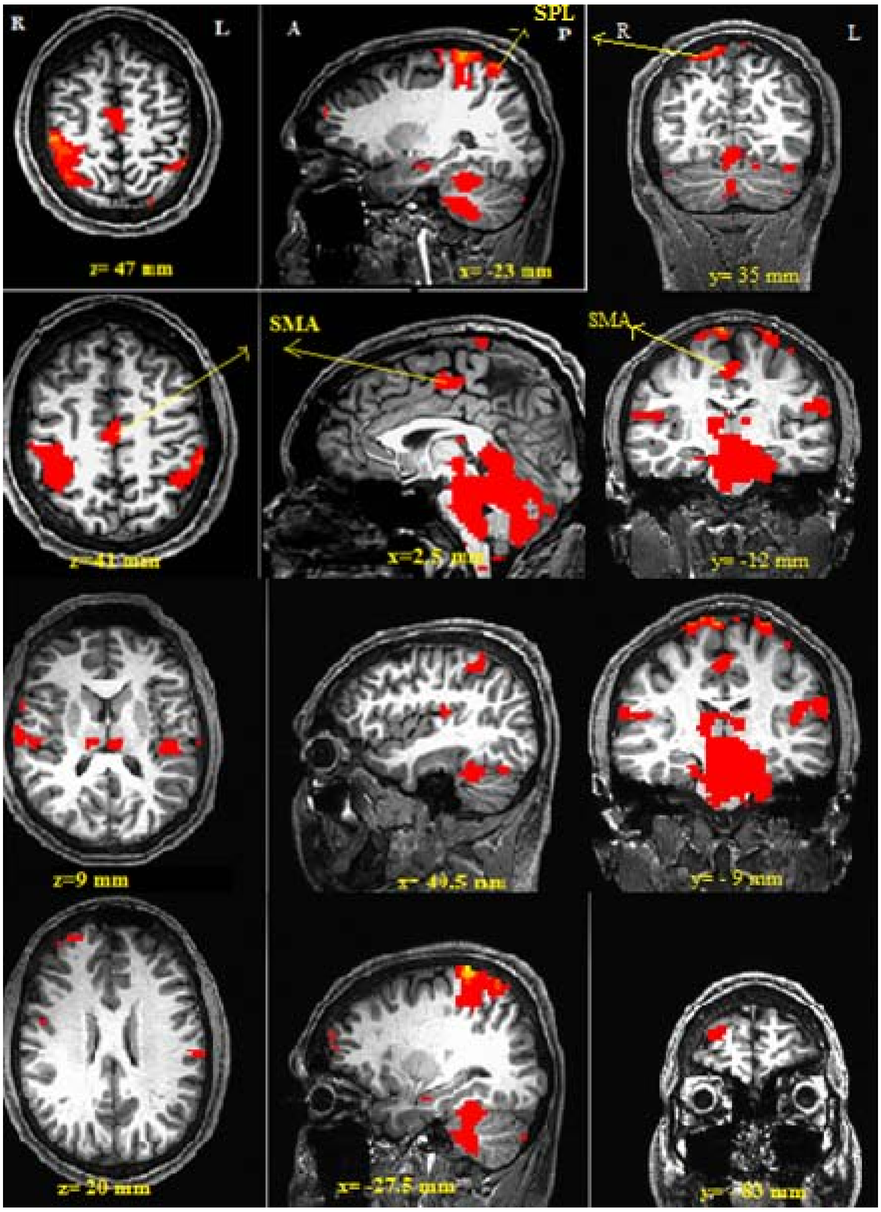


Figure 19 Results of tactile line bisection task with left hand.(R: Right, L: Left, A: Anterior, P: Posterior, p=0.001, Thr=3.360).

According to Figure 19, expected right hemisphere (contralateral) motor cortex activation was observed. Interestingly, there also exists bilateral somatosensory cortex (postcentral gyrus), superior temporal cortex, SMA, limbic and cerebellar activation. Contralateral superior parietal lobule activation was also observed. As we proceeded to lower slices in axial plane, we observed right lateralized contralateral prefrontal activity. Since experiment is performed with non-dominant left hand, it was observed that there are activities in a wide range of brain areas.

4.1.2.5 Visual Line bisection Condition with Right Hand

Figure 20 indicates comparison of visual line bisection by using right hand with rest in different brain slices. We intended to see both motor and linebisect activations again.

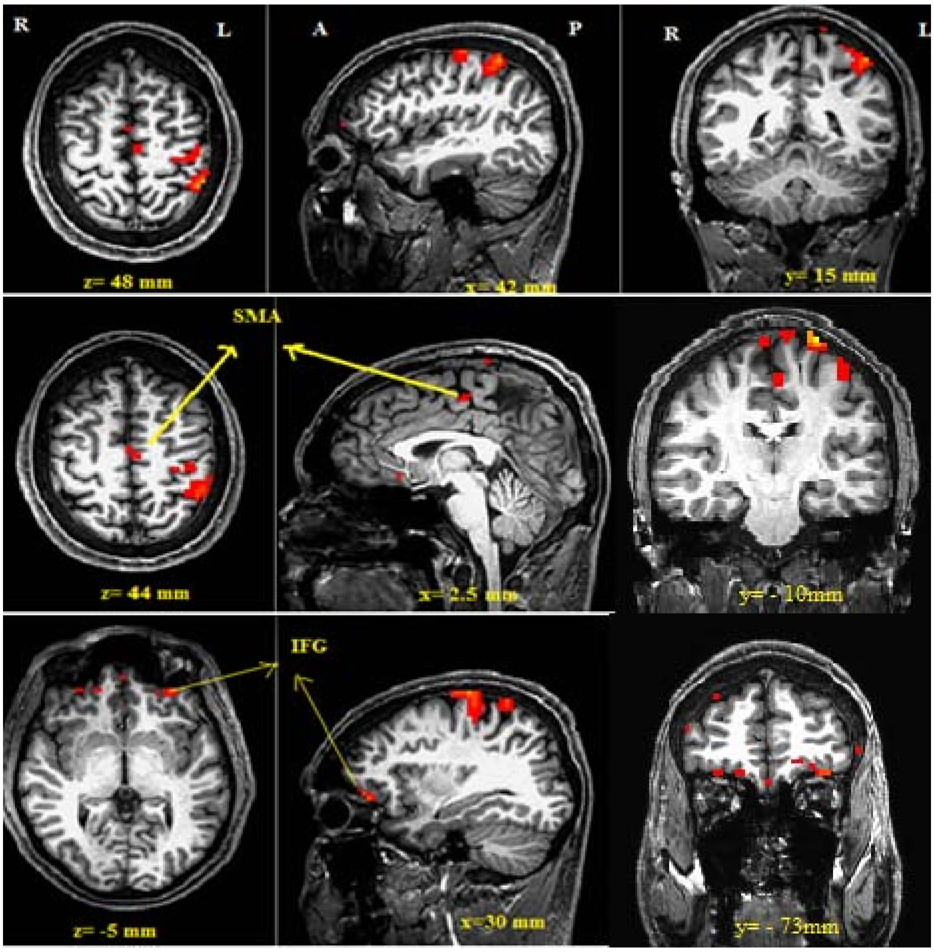


Figure 20 Results of visual line bisection task with right hand (R: Right, L: Left, A: Anterior, P: Posterior, p=0.001, Thr=3.360).

In Figure 20, left hemisphere handbump activation is observed as it is expected, but also activity is observed in the contralateral postcentral gyrus as well as SMA. As we proceeded to lower slices inferiorly in axial plane, we observed bilateral prefrontal cortex activation.

4.1.2.6 Visual Line bisection Condition with Left Hand

Figure 21 presents comparison of visual line bisection with rest performed with left hand.

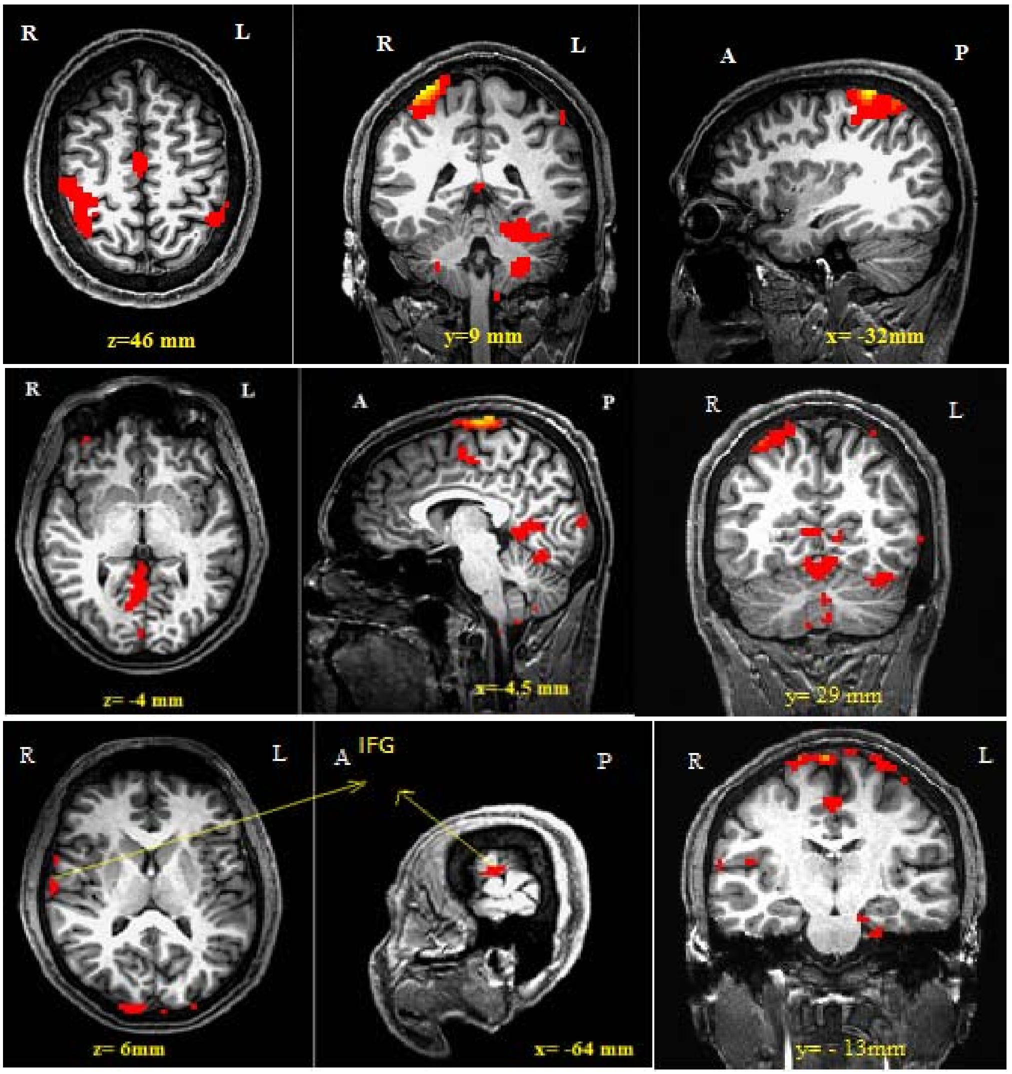


Figure 21 Results of visual line bisection task with left hand (R: Right, L: Left, A: Anterior, P: Posterior, p=0.001, Thr=3.360).

According to Figure 21, right hemisphere motor cortex activation is observed as expected. Bilateral somatosensory cortex (postcentral gyrus), supplementary motor cortex activation and occipital lobe activation associated with visual processing was seen as well. Contralateral inferior frontal gyrus activation was detected similar to the results performed with right hand.

4.2. Talairach Transformation Results

As it is explained in chapter three, after individual subject analysis, structural and functional maps were standardized coordinates into Talairach (stereotaxic) coordinates before group level analysis. Figure 22 represents a T1 weighted structural image in cardinal space and in stereotaxic space after Talairach transformation.

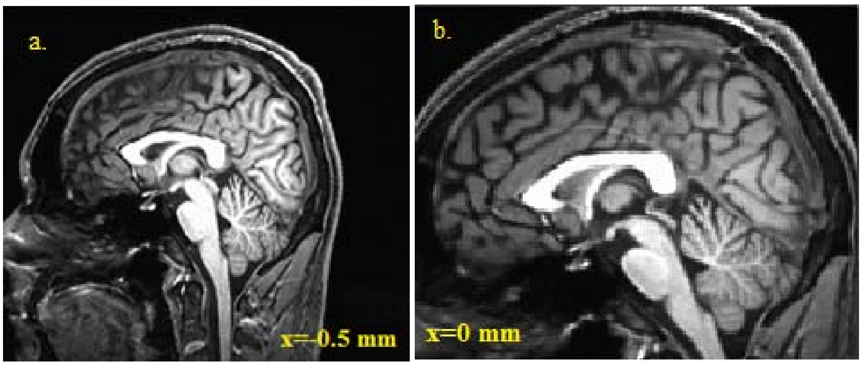


Figure 22 Result of Talairach Transformation.(a). original image, (b) Talairach transformed image)

After we transformed T1-weighted structural MRI volumes of all nine subjects into Talairach space one by one, we obtained mean brain image by averaging these anatomical brain images among subjects. Mean structural brain image is used as underlay in our group level analysis. Figure 23 shows representation of mean brain image. Due to the fact that we averaged individual brains with structural variation, resolution of mean brain image decreased.

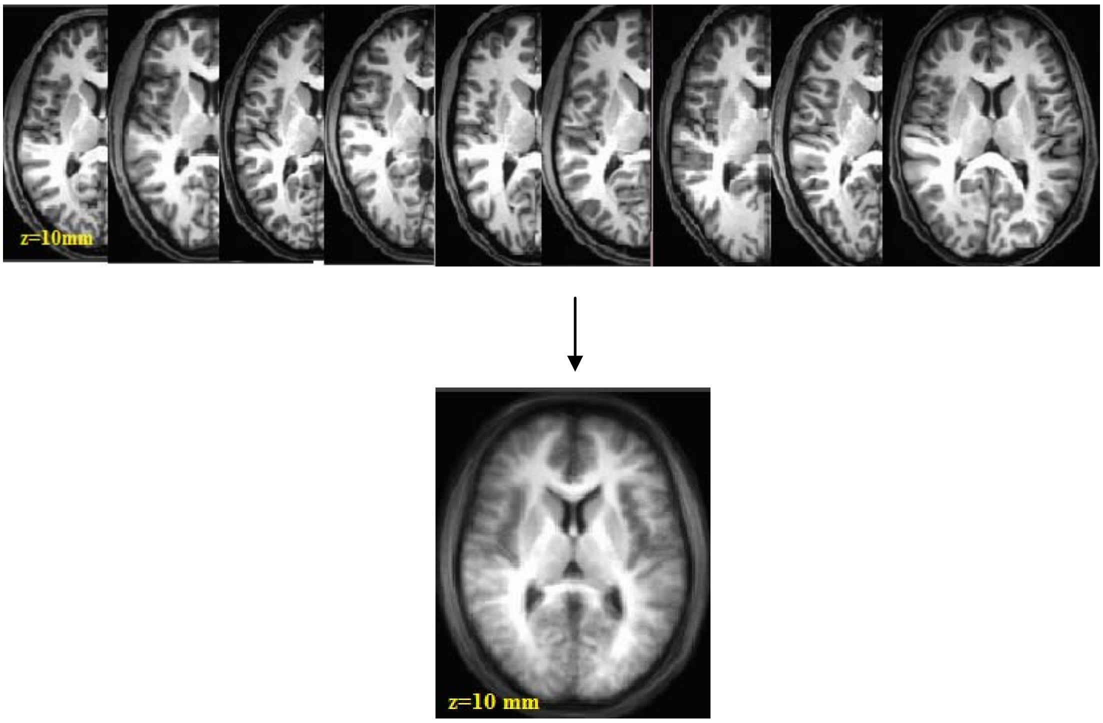


Figure 23 Structural Brain images averaged for 9 subjects

4.3 Group Level Analysis Results

We obtained 3 means, one for each experimental run (motor-sweep; tactile line bisection; visual line bisection) and 3 contrasts, one between each experimental condition (Tactile line bisection vs Motor-sweep ; Visual line bisection vs Motor-sweep; Tactile line bisection vs Visual line bisection) for each hand.

4.3.1 Mean Results

The results of mean activations from functional statistical maps of nine subjects for each condition are presented in the following.

4.3.1.1 Motor-Sweep Mean with Right Hand

We obtained fundamental mean motor activity in order to substract from line bisection task so that we can observe the activations exclusively for line bisect decision without motor activity. Figure 24 shows nine subjects' motor activations with right hand in same slice for each participant and mean motor activation after averaging and statistical filtering. With right hand, there is only contralateral left handbump (motor and somatosensory cortex) activation as it is expected.

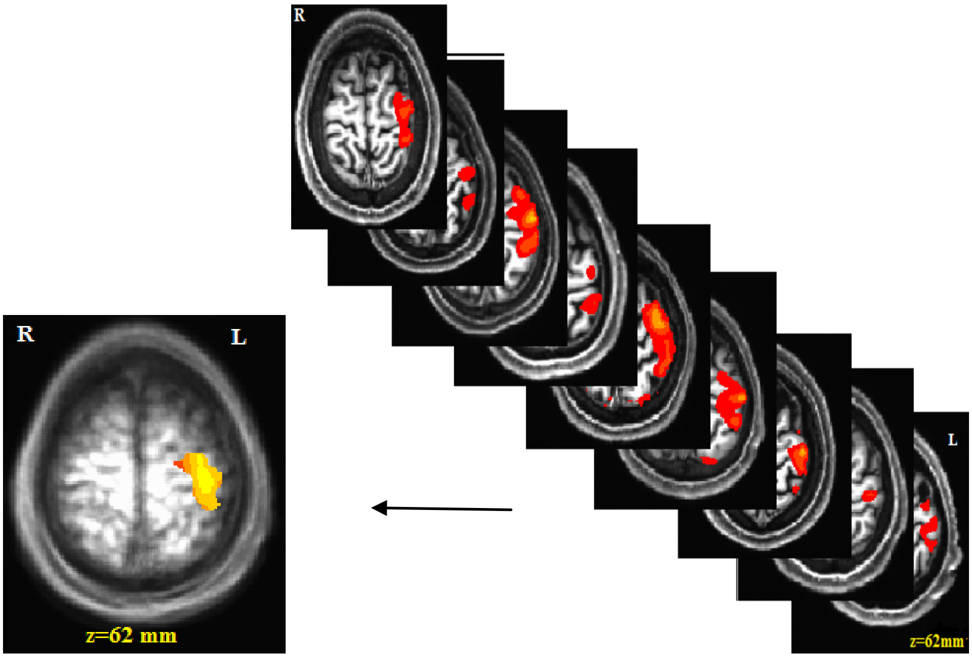


Figure 24 Mean functional map under motor condition with right hand (R: right, L: left, p=0.001, Thr: 4.526, minimum cluster size=24).

4.3.1.2 Motor Sweep Mean with Left Hand

Figure 25 presents mean motor activity with left hand in three different planes. It is very different from activations of motor-sweep with right hand not only in terms of laterality, but also in terms of their spread. Even though motor task includes only motor and to some extent somatosensory activity, there are also limbic, cerebellar, frontal and temporal activations. Bilateral handbump and SMA activation associated with motor response is seen although we expected exclusively contralateral handbump activation. Wide ipsilateral temporal cortex activation was noticable. Lastly, ipsilateral middle frontal gyrus activation was observed.

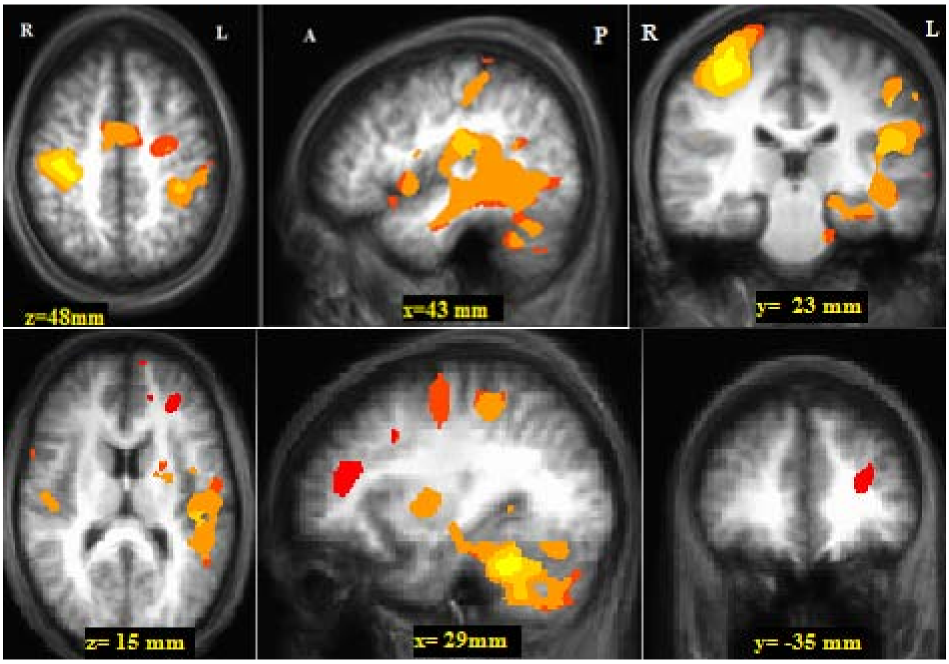


Figure 25 Results of mean motor activation with left hand. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

As mentioned before, this vast activity may be explained with manual dexterity which is a skill evaluated with several tests to examine hand function. All our participants were dominantly right-handed according to Edinburgh Handedness Inventory and all of them seems to have complicated processes running while using their left hand since they have lack of dexterity causing increased proprioceptive demands.

4.3.1.3 Tactile Line Bisection Mean with Right Hand

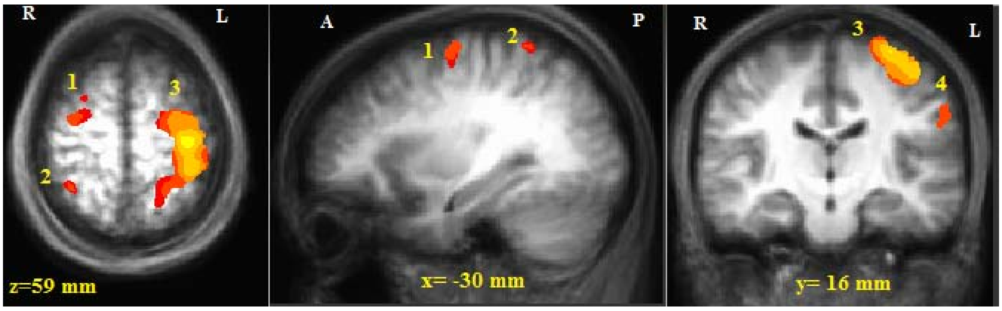


Figure 26 Results of mean tactile line bisection activation with right hand. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

In Figure 26, a dense contralateral left handbump (precentral gyrus and postcentral gyrus) activation (3) was observed as expected. In the same way, ipsilateral postcentral gyrus activation (4) occured. Secondly, we observed bilateral superior frontal gyrus activation (1 and 3). Finally, bilateral superior parietal lobule activation (2) was also observed.

Result of frontal cortex activation is consistent with Corbetta and Shulman's (2002) attention theory. SPL activation is also consistent with Asplund (2010) and Corbetta et al.'s (2002) proposals stating that IPL and SPL are the regions involved in dorsal attentional network that is responsible for goal-directed attention. Since line bisection has goal-directed attribute, we can claim that SPL activation is caused by attentional demands.

4.3.1.4 Tactile Line Bisection Mean with Left Hand

Figure 27 presents mean tactile line bisection activity with left hand in three different planes. Differences between activations in line bisections with right hand and left hand under tactile sense are noticable.

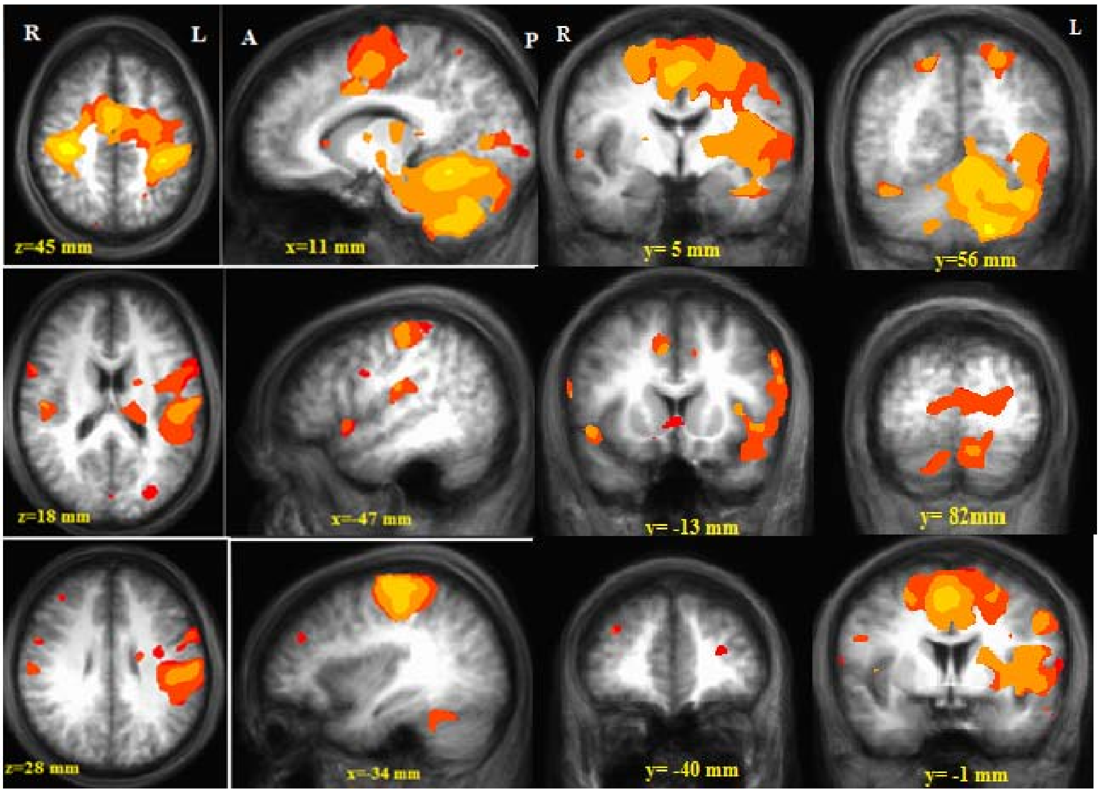


Figure 27 Results of mean tactile line bisection activation with left hand. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

According to Figure 27, there is extended acitivity bilaterally around cerebellar region, handbump area including SMA and ipsilaterally around temporal cortex. As proceeding lower sides on axial plane, bilateral insula, ipsilateral caudate, contralateral middle frontal gyrus (MFG), ipsilateral superior frontal gyrus (SFG), bilateral middle occipital gyrus activations were observed. Particularly Middle frontal gyrus activation is consistent with suggestion of Fox et al. (2006). They suggested that middle frontal gyrus (MFG) correlates with dorsal and ventral attentional networks, these networks are principally linked through prefrontal cortex (Fox et al., 2006).

Furthermore, bilateral middle occipital gyrus and precuneus activity was seen, although the eyes were closed. Generally, middle occipital gyrus is associated with visual processing. When participants use their non-dominant hand, they may have imaginary support even though their eyes were closed.

4.3.1.5 Visual Line Bisection Mean with Right Hand

Figure 28 presented mean result of visual line bisection with right hand in different brain slices.

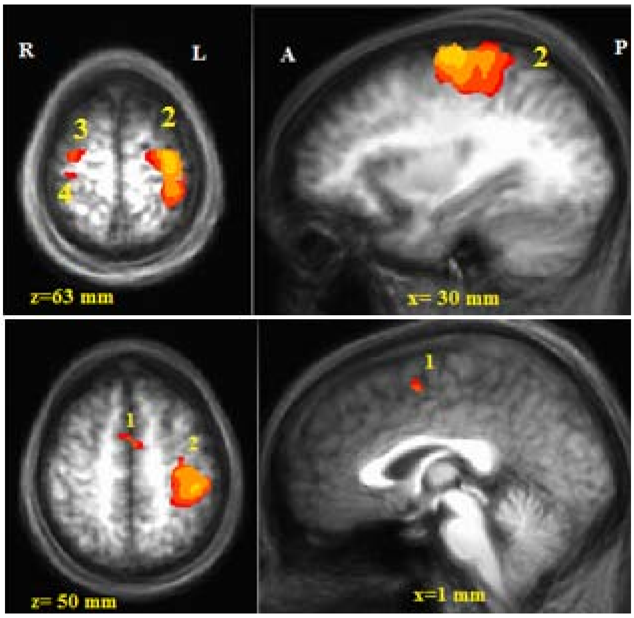


Figure 28 Results of mean visual line bisection activation with right hand. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

In Figure 28, a dense left handbump (precentral gyrus and postcentral gyrus) activation (2) was observed as expected. Bilateral SMA activation (1) was also observed associated with motor response. We observed bilateral superior frontal gyrus activation (2, 3). Interestingly, ipsilateral precentral activation (4) was also observed which was not so profound compared with the left handbump activation.

4.3.1.6 Visual Line Bisection Mean with Left Hand

Figure 29 and Figure 30indicate mean results of visual line bisection with left hand in different brain slices.

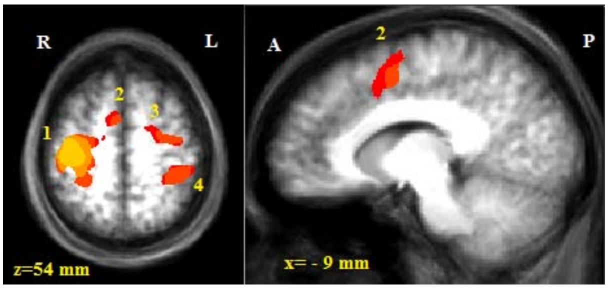


Figure 29 Results of mean visual line bisection activation with left hand. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

According to Figure 29, right motor cortex activation (1) were observed contralaterally as expected in somatosensory pathway. Bilateral primary somatosensory cortex (SI) (postcentral gyrus) activation (1 and 4) was also observed. Result of supplementary motor area (SMA) activation (2) associated with motor response was also clearly supportive with our task required motor response. In visual line bisection with left hand, bilateral SFG activation (1, 3) was also observed.

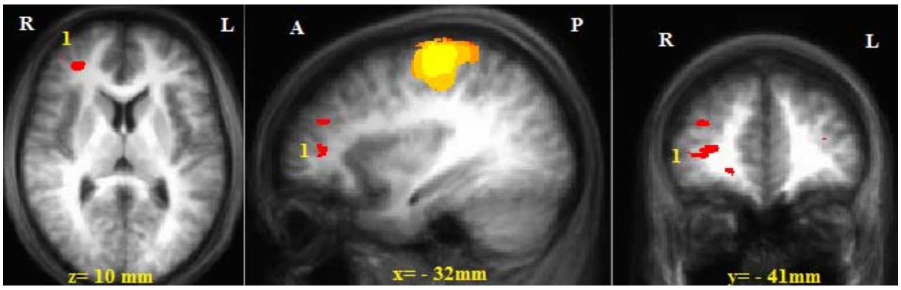


Figure 30 Results of mean visual line bisection activation with left hand (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

In Figure 30, A dense prefrontal cortex activity was observed. Specifically, contralateral middle frontal gyrus (1) was activated. To summarize mean results, results of clustering analysis are shown for each condition in Table 6 Cluster Report of Mean Activations (Bilateral activations are marked with *).Clusters (actual active voxels forming a connected cluster), Cluster size, anatomical names of activated regions corresponding to CA_N27_ML_Macro Labels Brain ATLAS, lateralization of activations (side) and coordinates of clusters in x,y,z planes are presented in Table 6.

Table 6 Cluster Report of Mean Activations (Bilateral activations are marked with *).

Activated Region	Side	Cluster Size	x	y	z
1.Right Motor Mean					
Handbump Region	L	7558	32.0	21.0	61.0
2.Left Motor Mean					
HandBump	R	13070	-33	26,0	57,0
Middle Frontal Gyrus *	R	9643	-8,0	9,0	49,0
Superior Temporal Gyrus	R	1339	-42,0	-5,0	7,0
Insula	R	540	-48,0	18,0	19,0
Inferior Frontal Gyrus	R	239	-26,0	-15,0	-14,0
Caudate	R	142	51,0	-4,0	-18,0
Putamen	L	2251	27,0	3,0	6,0
Insula	L	1030	41,0	-2,0	4,0
Middle Frontal Gyrus *	L	673	28,0	-29,0	23,0
Parahippocampal Gyrus	L	451	25,0	42,0	8,0
Middle Temporal Gyrus	L	163	47,0	-10,0	-7,0
3.Right Tactile Line bisection Mean					
Hand Bump, SPL*, SFG*	L	10989	30.0	20.0	63.0
Postcentral Gyrus	L	90	55.0	20.0	40.0
Superior Frontal Gyrus*	R	296	-29.0	9.0	62.0
Superior Parietal Lobule*	R	50	-31.0	46.0	59.0
4.Left Tactile Line bisection Mean					
Hand Bump Region *	R,L	262784	-39	22.0	54.0
Inferior Frontal Gyrus	R	1153	-57.0	10.0	12.0
Precuneus/SPL	R	941	-16.0	57.0	52.0
Superior Temporal Gyrus	R	544	-48.0	-13.0	-2.0
Middle Frontal Gyrus	R	135	-35.0	-38.0	24.0
Caudate	L	375	9.0	-19.0	8.0
Superior Frontal Gyrus	L	108	27.0	-30.0	22.0
5. Right Visual Line bisection Mean					
Hand Bump, SFG*	L	8959	30.0	18.0	63.0
SMA*	R,L	31	4.0	1.0	49.0
Superior Frontal Gyrus*	R	409	-29.0	10.0	62.0
Precentral Gyrus	R	150	-31.0	21.0	63.0
6.Left Visual Line bisection Mean					
Hand Bump, SFG*	R	13964	-31.0	22.0	61.0
Middle Frontal Gyrus	R	84	-35.0	-39.0	23.0
Insula	R	37	-45.0	18.0	19.0
Post Central Gyrus *	L	4640	36.0	31.0	44.0
Superior Frontal Gyrus *	L	3209	6.0	0.0	47.0
Post Central Gyrus *	L	541	44.0	20.0	28.0

4.3.2 Contrasts of Means (Right Hand)

Since mean line bisection results contain also motor activity, we need to know whether activations resulted from motor activation or line bisection decision. Therefore, we needed to compare contrasts of line bisection and motor tasks by subtracting motor result from line bisection result in order to reveal activity related to attention and decision making.

4.3.2.1 Tactile Line Bisection vs Motor Sweep

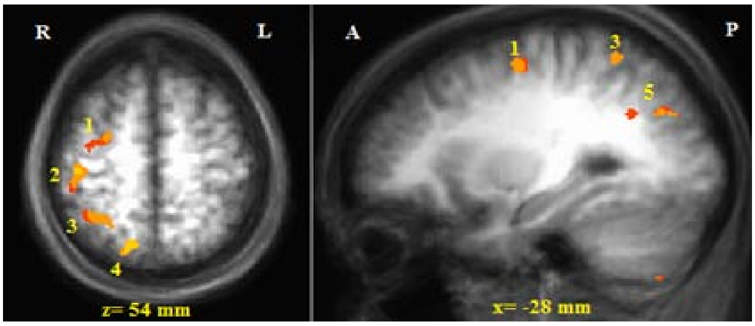


Figure 31 Results of subtraction of motor task from tactile line bisection with right hand, (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

In Figure 31 Results of subtraction of motor task from tactile line bisection with right hand, (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24)., when we subtract motor task from tactile line bisection, we observed highly right lateralized (ipsilateral) activations. Ipsilateral superior frontal gyrus (1), postcentral gyrus (2), superior parietal lobule (SPL) (3), precuneus (4) and cuneous (5) activations were observed. This result is one of the important results of our study to understand neural correlates of tactile line bisection. SPL activity under tactile sense is highly consistent with several line bisection studies with fMRI under visual sense (Çiçek et al., 2009; Weiss et al., 2000).

Our tactile line bisection results are all right lateralized in right hand. However, Corbetta's (2002) attention network model proposed that dorsal attentional network responsible for goal-directed (voluntary) attention is generally observed bilaterally. Ipsilateral postcentral gyrus activation corresponding to primary somatosensroy cortex (S1) may reveal tactile exploration in the brain except activations resulted from motor task. In addition to studies in literature, we observed ipsilateral precuneus activity.

4.3.2.2 Visual Line Bisection vs Motor Sweep

We investigated subtraction of motor task from visual task performed with right hand. Figure 32 Results of subtraction of motor task from visual line bisection with right hand. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24). presents right precuneus (3), right postcentral gyrus (2), right SFG (1) and right cuneus (4), right middle frontal gyrus (5), right fusiform gyrus (6). Consistency of SFG activation is explained in the previus parts. Figure 33 shows bilateral middle occipital gyrus (MOG) (1 and 2) associated with visual processing as it is expected. Differently from tactile line bisection, we observed bilateral MOG activation and ipsilateral fusiform gyrus activation, which are areas related to visual processing.

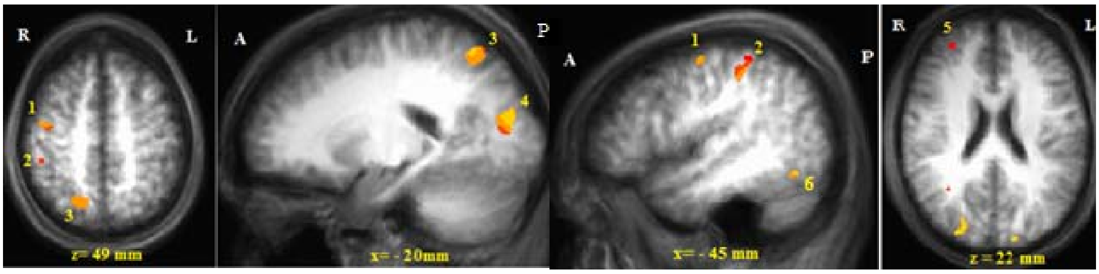


Figure 32 Results of subtraction of motor task from visual line bisection with right hand. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

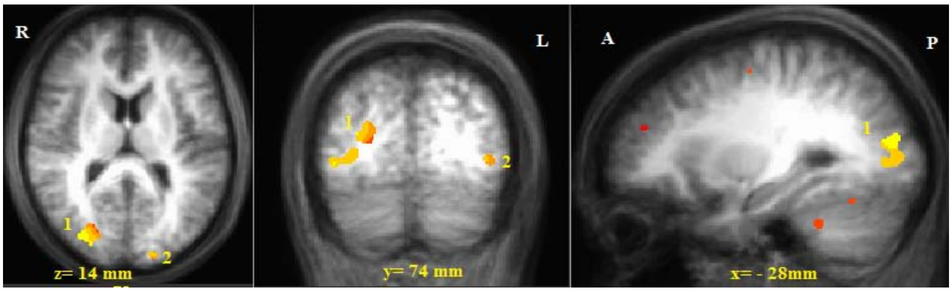


Figure 33 Results of subtraction of motor task from visual line bisection with right hand, (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

4.3.2.3 Tactile Line Bisection vs Visual Line Bisection

This contrast is the most important result of our study. Our hypothesis suggests that there is a difference in line bisection decision under different sensory modalities. Figure 34 and Figure 35 presents results of tactile versus visual line bisection with right hand. Activation patterns for which tactile line bisection is greater than visual are shown by hot colors (red, orange, yellow) while activation patterns for which visual line bisection is greater than tactile are shown by cold colors (dark blue, light blue).

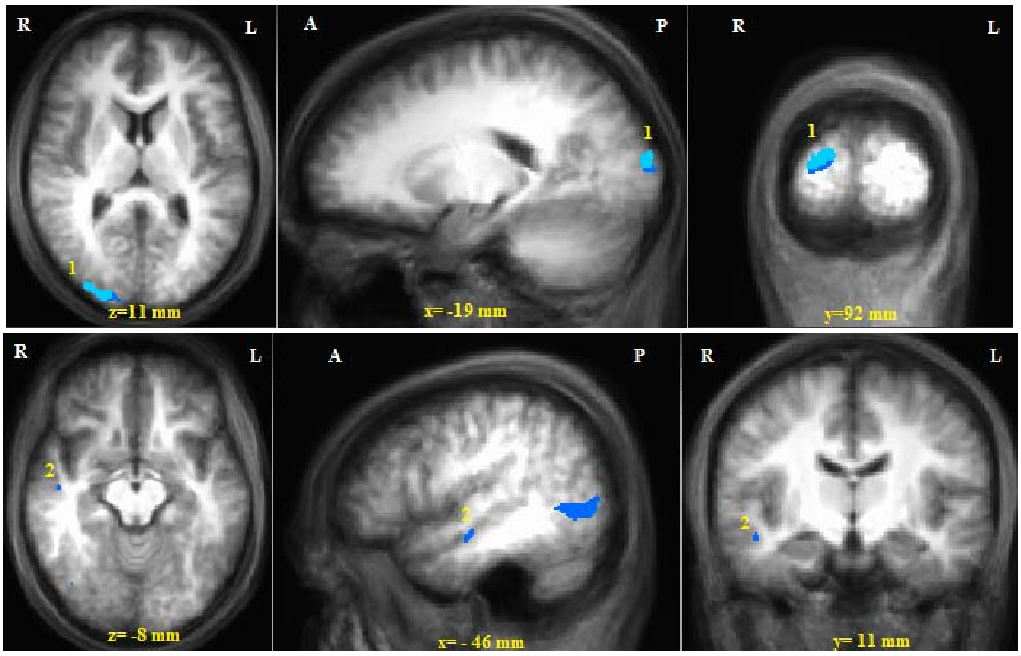


Figure 34 Results of contrasts between tactile and visual line bisection with right hand, (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

In Figure 34, right middle occipital gyrus activation (1) obtained from visual processing was observed. Ipsilateral right middle temporal gyrus activation (2) was also observed from visual line bisection's effect. Right MTG activation is consistent with its role in attentional network model of Corbetta (2002): Ventral attentional network generally appears right lateralized and responsible from target detection beside stimulus-driven attention. More consistently, right middle temporal cortex activation was also reported in Weiss et al.'s (2000) fMRI study. Furthermore, Karnath et al. (2011) found that there is a link between middle temporal cortex and frontal cortex as a result of their lesion study in neglect patients.

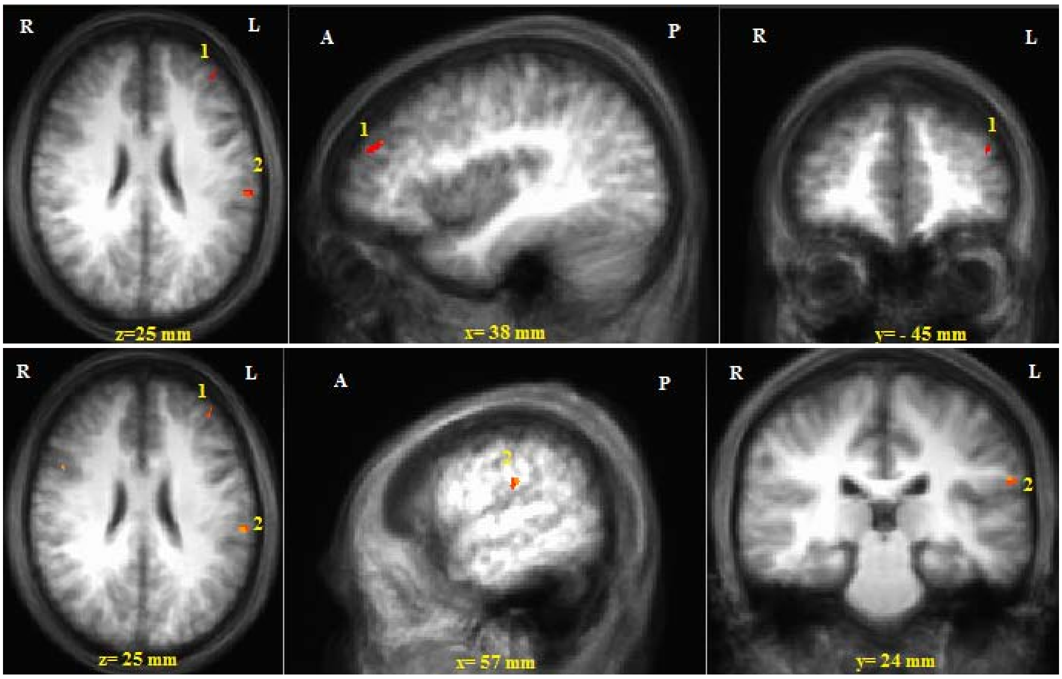


Figure 35 Results of contrasts between tactile and visual line bisection with right hand, (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

In Figure 35 contralateral left middle frontal gyrus activation (1) coming from tactile line bisection effect was observed as well as left IPL activation (2) for which functional roles are as explained in tactile versus motor comparison. Middle frontal gyrus activation is consistent with suggestion of Fox et al. (2006) which states that middle frontal gyrus (MFG) correlates with dorsal and ventral attentional networks, these networks are principally linked through prefrontal cortex. IPL activity is consistent with Fink et al.'s (2001) findings which include activity in bilateral inferior parietal lobule in their fMRI study. Saj et al. (2009) also found IPL activity as a result of rightward and leftward biases in their line bisection task applied to neglect patients.

To summarize contrast results, cluster report is shown for each contrast with right hand in Table 7 Cluster Report of Contrast Results with Right Hand (Bilateral activations are marked with *).Clusters (actual active voxels forming a connected cluster), Cluster size, anatomical names of activated regions corresponding to CA_N27_ML Brain ATLAS, lateralization of activations (side) and coordinates of clusters in x,y,z planes are presented in Table 7. For tactile versus visual line bisection results, negatives represent activated regions caused by visual line bisection, while positives represent those caused by tactile line bisection.

Table 7 Cluster Report of Contrast Results with Right Hand (Bilateral activations are marked with *).

Activated Region	Side	Cluster Size	x	y	z
Right Tactile Line bisection vs Motor					
SPL	R	354	-27.0	47.0	56.0
PostCentral Gyrus	R	190	-40.0	23.0	56.0
Cuneus	R	118	-27.0	69.0	29.0
Precuneus	R	140	-13.0	64.0	54.0
Superior Frontal Gyrus	R	52	-25.0	6.0	50.0
Right Visual Line bisection vs Motor					
Middle Occipital Gyrus *	R	2306	-32.0	78.0	13.0
Precuneus	R	697	-22.0	57.0	54.0
Superior Frontal Gyrus	R	296	-40.0	60.0	-9.0
Fusiform	R	153	-37.0	44.0	-16.0
Cuneus	R	209	-13.0	89.0	19.0
Middle Occipital Gyrus *	L	125	39.0	73.0	2.0
Right Tactile vs Visual Line bisection					
Middle Occipital Gyrus (-)	R	4377	-34.0	82.0	8.0
Middle Temporal Gyrus (-)	R	34	-46.0	13.0	-7.0
IPL (+)	L	40	57.0	26.0	25.0
Middle Frontal Gyrus (+)	L	26	38.0	-40.0	26.0

4.3.3 Contrasts of Means (Left Hand)

For non-dominant left hand, it is difficult to distinguish bisection decision's activation since the dominant activity profile is due to widespread proprioceptive processing.

4.3.3.1 Tactile Line Bisection vs Motor Sweep

Figure 36 shows negative correlations between tactile line bisection and motor sweep. Negative correlations correspond to activity that is greater in motor than line bisection. We could not observe any positive correlation activity for which line bisection is larger than motor. This shows us that widespread activation is more dominant in motor sweep rather than line bisection.

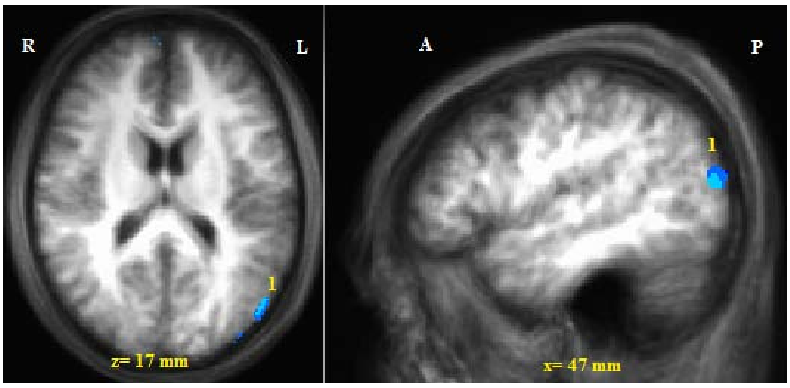


Figure 36 Results of substraction of motor task from tactile line bisection with left hand, (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

In Figure 36, ipsilateral middle temporal gyrus (1) activity is indicated. In addition to this activity, contralateral middle frontal gyrus and left superior occipital gyrus activations (Table 7) were also observed. So far, fMRI studies of line bisection task were implemented to right-handed people and by using right hand. Because of this, we could not make any significant comparison of the results we obtained with left hand with another study in literature.

4.3.3.2 Visual Line Bisection vs Motor Sweep

Similarly, we could not observe any positive correlation between visual line bisection and motor sweep due to more dominant activation in motor sweep. When we subtract motor task activity from line bisection activity, as it is seen in Figure 37, contralaterally inferior frontal gyrus (3) and ipsilaterally superior occipital gyrus (2) and middle frontal gyrus (1), activations are observed. However, these are due to negative correlations, indicating that these regions are more dominant in motor sweep than visual line bisection.

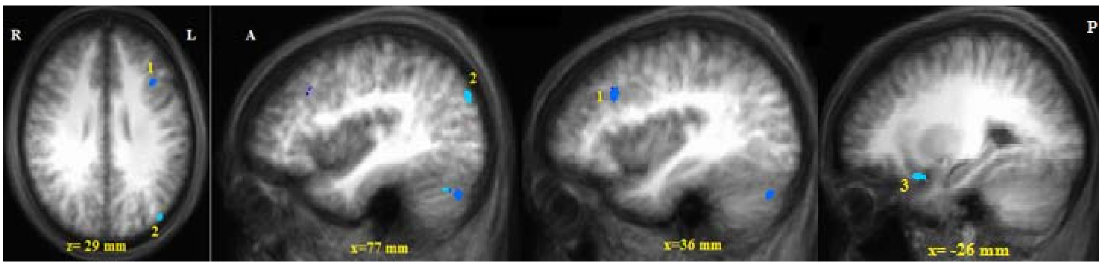


Figure 37 Results of substraction of motor task from visual line bisection with left hand, (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24)

4.3.3.3 Tactile Line Bisection vs Visual Line Bisection

It is interesting that only results with positive correlations were observed when we compared tactile line bisection with visual line bisection with left hand. This means that tactile line bisection activity was larger compared to visual line bisection. In Figure 38, ipsilateral middle frontal gyrus (1), ipsilateral cuneus activation (2), contralateral superior parietal lobule (SPL) activations was shown. In addition, contralateral inferior frontal gyrus activation (Table 8) was observed. SPL activity is highly consistent with several line bisection studies with fMRI under visual sense. Prefrontal cortex activity was expected again.

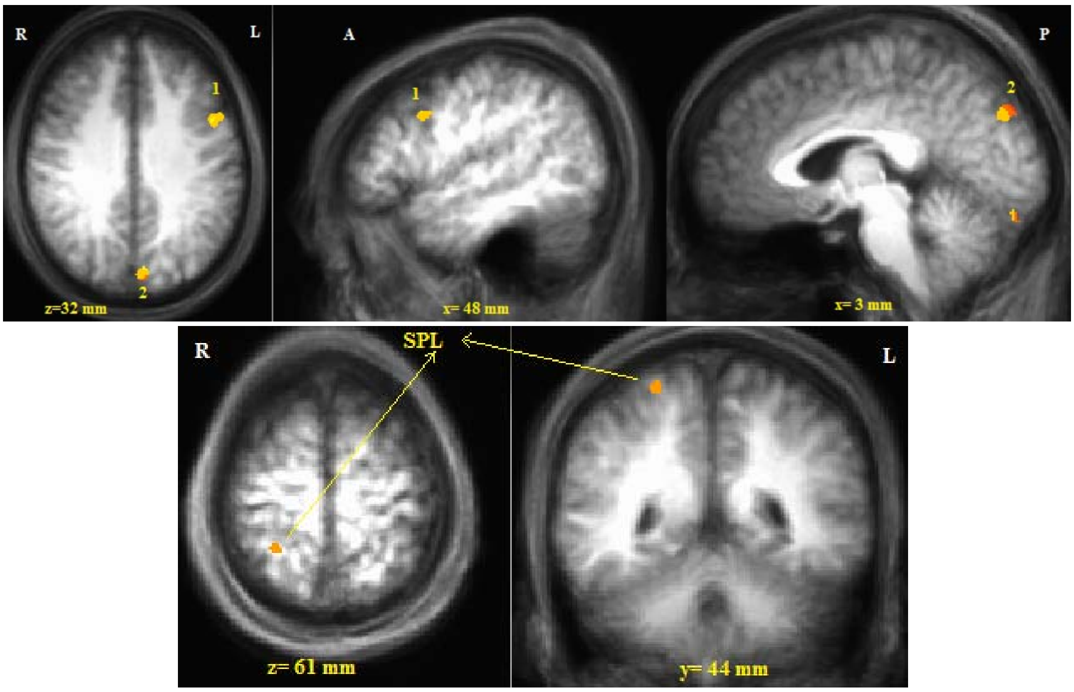


Figure 38 Results of contrasts between tactile and visual line bisection with left hand, orange regions represents tactile effect. (R: Right, L: left, A: anterior, P: posterior, p=0.001, Thr: 4.526, min.cluster size=24).

Cluster report is shown for each contrast with left hand in Table 8. Clusters (actual active voxels forming a connected cluster), Cluster size, anatomical names of activated regions corresponding to CA_N27_ML Brain ATLAS, lateralization of activations (side) and coordinates of clusters in x,y,z planes are presented.

Table 8 Cluster Report of Contrast Results with Left Hand (Bilateral activations are marked with *).

Activated Region	Side	Cluster Size	x	y	z
Left Tactile Line bisection vs Motor					
Middle Temporal Gyrus (-)	L	147	49.0	68.0	19.0
Superior Occipital Gyrus (-)	L	33	37.0	78.0	32.0
Middle Frontal Gyrus(-)	R	24	-3.0	-58.0	17.0
Left Visual Line bisection vs Motor					
Middle Frontal Gyrus (-)*	R	270	-4.0	-58.0	18.0
Inferior Frontal Gyrus (-)	R	174	-24.0	-12.0	-13.0
Superior Occipital Gyrus (-)	L	137	41.0	75.0	31.0
Middle Frontal Gyrus(-)*	L	25	8.0	-61.0	17.0
Left Tactile vs Visual Line bisection					
Middle Frontal Gyrus (+)	L	84	51.0	-11.0	34.0
Inferior Frontal Gyrus (+)	L	48	38.0	-27.0	9.0
Cuneus (+)	L	43	6.0	75.0	31.0
SPL (+)	R	6	-25.0	43.0	60.0

4.4 fMRI Behavioural Results

The calculations indicated in chapter three are performed to analyse line bisection behavioural data of the fMRI experiments. As it was explained, 2 b y 2 ANOVA was performed, which one factor is hand used with levels of right hand and left hands, while the other is sensory modaliy with levels of visual and tactile sense. Figure 39 indicate relationship between mean asymmetry directions for nine subjects when right hand and left hand used for two different sensory modalities which are tactile and visual.

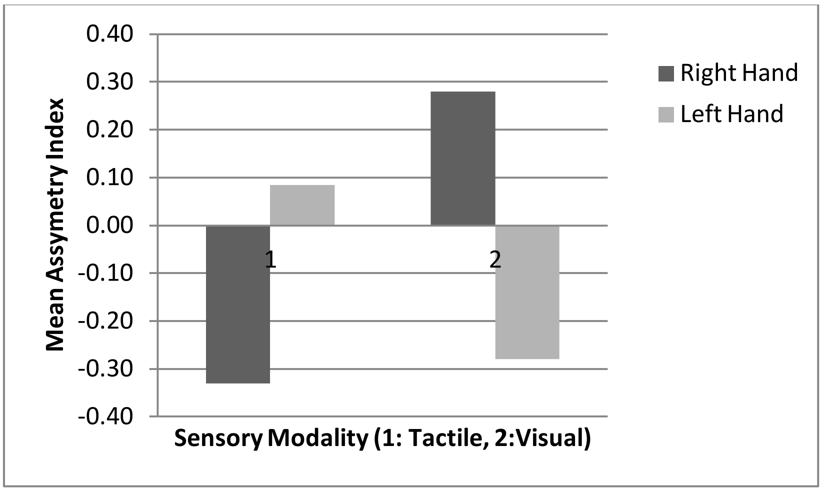


Figure 39 Effect of Hand used on Bias directions for two sensory modalities (1: Tactile, 2: Visual).

According to Figure 39, in tactile line bisection (1), a leftward bias was observed when right hand is used,while a rightward bias was observed when left hand is used. Interestingly, bias is different in visual line bisection (2): A rightward bias was observed when right hand is used, while leftward bias was observed when left hand is used. The interaction between hand used and sensory modality was significant: p=0.025.

Another 2 by 2 ANOVA with same factors and levels was applied for bias amounts instead of directions. Hand used had not a significant affect on deviation amounts (p=0,691), whereas apparently bias amounts are more larger in tactile sense than in visual sense (p=0,000).

CHAPTER 5

DISCUSSION

We designed a tactile line bisection set-up compatible with the MR scanner to observe how somatosensory cortex is recruited during line bisection. The question that we tried to answer is how line bisection activity manifests itself in the tactile versus visual sense within the fronto-parietal visual loop.

Behaviorally, during the fMR experiment, in tactile line bisection, a leftward bias was observed when right hand is used, while a rightward bias was observed when left hand is used. On the other hand, in visual line bisection, a rightward bias was observed when right hand is used, while leftward bias was observed when left hand is used. Pseudoneglect effect is not observed in fMRI behavioural task. Results in tactile condition are consistent with Coudereau et al.'s (2006) line bisection results. They concluded that participants deviated to the left when using their right hand, whereas they deviated to the right when using their left hand. For visual line bisection in MR, our findings are consistent with Halligan and Marshall's results (1989). They found that there were rightward biases when the right hand were used while leftward biases when the left hand was used. In Jewell and Mccourt's review (2000) about factors affecting line bisection in visual and non-visual tasks, it is presented that biases are very controversial according to different factors. Interestingly, for bias amounts, after analysing hand used, sensory modality and MR condition factors' effects in SPSS separately, it was observed that hand used and MR condition had not a significant affect on deviation amounts, although bias amounts are more larger in tactile sense than in visual sense.

When fMR activities are considered, in our motor sweep results, contralateral motor cortex activations are very clear for each hand used. More precisely, left motor cortex activation was observed when the activity was performed with right hand compared to the use of the non-dominant left hand. This is obviously undisputed and consistent with theory of somatomotor pathway, since pathway of somatomotor acts contralaterally, motor cortexes in each hemisphere of brain controls the motor activations in their contralateral side by a cross transmission of motor information. However, there was an overwhelming difference in overall brain activity patterns when the non-dominant left hand was used compared to the use of the dominant right hand. Abundant activations in line bisection are obtained with use of left hand probably because all our participants were dominantly right-handed according to Edinburgh Handedness Inventory. These results reveals that our experiment includes both proprioceptive and somatosensory action.

Due to manual dexterity phenomena, participants made an extra effort to perform experiment with their left hand for which they have lack of dexterity. It leads to complicated processes in the brain since they struggle for both proprioceptive and somatosensory activity with their non-dominant hand. Probably, proprioceptive effect interferes with attentional activity and line bisection decision in results of left hand condition. More specifically, activity around temporal cortex, cerebellum, bilateral somatosensory cortex (postcentral gyrus), bilateral supplementary motor area (SMA) associated with motor response are observed as well as insula and STG. In addition, there are several additional bilateral activations such as limbic, subcortical activations (putamen, caudate, thalamus). These activations apparently serve supplementary mechanisms caused by usage of non-dominant hand. Proprioceptive effect in right hand is minimum due to the fact that participants are used to perform daily activities with their right hand. So, the processes in the brain while using right hand are more silent compared to when left hand is used.

We observed several spots when tactile line bisection activity is contrasted with motor sweep, or when visual line bisection activity is contrasted with motor sweep or when tactile and visual line bisection activities are contrasted. However, due to prominent proprioceptive response, results of contrasts may not give us a significant response about differences. We could not know whether the neural substrates result from somatosensory response or from proprioceptive response. Accordingly, it is not so significant to investigate contrast results in left hand. Since even motor task performed with left hand included abundant activation, all significance activations are eliminated when we compared contrast of motor and linebisect tasks in left hand.

In right hand, for tactile line bisection we observed bilateral prefrontal activation (superior frontal gyrus) and ipsilateral superior parietal lobule activation beside contralateral handbump area activity (precentral and post central gyrus activations). Prefrontal cortex activation is consistent with Corbetta's explanation (2002) that prefrontal cortex is recruited after attentional detection. Since our experiment required a high level attention and detection, prefrontal activation was included in our hypothesis. SPL activation is another consistent finding with other studies. Asplund (2010) and Corbetta et al. (2002) proposed that IPL and SPL are the regions involved in dorsal attentional network that is responsible for goal-directed attention. Since line bisection task has goal-directed attribute, this finding may confirm relation between line bisection and focus based voluntary attention.

When we substracted motor task from tactile line bisection, we observed highly right lateralized activations. Ipsilateral superior frontal gyrus, postcentral gyrus, SPL (superior parietal lobule) and precunous activations were observed. Actually, these results are very impressive and satisfy our main goals in understanding neural correlates of tactile line bisection decision. Importantly, this time there is not motor activity in this condition. Ipsilateral postcentral gyrus activation corresponding to primary somatosensroy cortex (S1) may reveal tactile exploration in the brain except activations resulted from motor task. SPL activation is consistent with Çiçek et al's (2009) fMRI line bisection study, eventhough they implemented line bisection under visual sense modality. They found specifically right lateralized IPS activation. Weiss et al. (2000) also found parietal cortex activation as a consequence of their visual fMRI study. Fink et al. also (2001) presented bilateral parietal cortex in their fMRI study. Saj et al. (2009) found IPS activity in their visual line bisection with fMRI study in neglect patients as a result of rightward and leftward biases in line bisection task.

It is also significant that all activities are right lateralized in tactile line bisection decision with right hand. This aspect also consistent with Cicek et al.'s study (2009) visual fmri study about line bisection. Although two studies were implemented under different sensory modalities, they also found all right lateralized results. However, Corbetta's attention network model (2002) proposed that dorsal attentional network responsible for goal-directed (voluntary) attention generally observed bilateral. In contrast with Corbetta's model, our results are right lateralized instead of bilateral although line bisection decision requires voluntary attention. But right lateralization was explained with the idea that the right hemisphere is very dominant in controlling spatial attention as Cicek et al. (2009) proposed.

In addition to studies in literature, it is expected that we observed ipsilateral precunous activity since it is a part of SPL and is involved in executive functions, motor planning. SPL activation is an important observation since SPL is involved in dorsal attentional network which is responsible for volunteer attention and take part in cognitive selection of sensory information as presented by Asplund, 2000.

In visual line bisection with right hand, the results again matched up with Corbetta's attentional model that suggest prefrontal cortex involves in attentional detection (Corbetta et al., 2002). When we substracted motor motor task from visual line bisection, similarly with tactile line bisection decision, right SPL, right SFG and right precuneus activation was observed. Differently from tactile line bisection decision right fusiform gyrus and bilateral middle occipital gyrus activations were also observed. Since middle occipital gyrus activation is associated with the visual processing it is obviously expected. Ipsilateral fusiform gyrus activation may be correlated with task requirements since it is involved in visual discrimination activities such as color processing, face or word recognition.

In result of contrast between visual and tactile line bisection, right middle occipital gyrus activation came from visual line bisection effect is an expected hypothesis since it is associated with the visual processing. **Right middle temporal gyrus activation coming from visual line bisection effect was a crucial finding to validate our hypothesis that there is an attentional difference between visual and tactile line bisection.** Right MTG activation is consistent with its role in attentional network model of Corbetta (2002). They proposed that middle temporal region involved in ventral attentional network generally appears right lateralized and responsible from target detection beside stimulus-driven attention (Corbetta et al, 2002). More consistently, Weiss et al.(2000) found right middle temporal cortex activation in their visual line bisection study with fMRI. This result is directly consistent with Weiss et al.'s (2000) fMRI study. **Another important result confirming our hypothesis is the left middle frontal gyrus and IPL acitivations coming**

from tactile line bisection effect. Middle frontal gyrus activation is consistent with suggestion of Fox et al. (2006). They suggested that middle frontal gyrus (MFG) correlates with dorsal and ventral attentional networks, these networks are principally linked through prefrontal cortex.**These findings may reveal that line bisectiontask is more related with prefrontal regions under tactile sense, while more related with temporal regions under visual sensein the manner of attentional regions rather than sensory regions.**

Beside all of these findings, some activations in our results are also correlated with lesion regions in neglect patients. MTG activation in tactile line bisection with left hand was supported by Karnath et al's (2011) findings that there is a link between middle temporal cortex and frontal cortex as a result of their lesion study in neglect patients. IPL activation in tactile line bisection with right and left hand is consistent with Verdon et al's (2010) proposal that line bisection task is more correlated with lesions in the right inferior parietal lobule (IPL) in neglect patients. Background underlying neglect syndrome is a problematic issue. For example, Mesulam (1999) defended that neglect represents a dysfunction of the dorsal IPS–FEF network for spatial attention, while Corbetta et al. (2002) proposed that the anatomy of neglect matches the ventral TPJ–VFC system. According to Corbetta et al. (2002), neglect patients can voluntarily pay attention to the contralesional side, consistent with sparing of the IPS–FEF network. The dysfunction in neglect corresponds to more closely the dysfunction of a target detection than an orienting network, particularly when the stimuli are unexpected. Some of our results which are consistent with some neglect studies (Karnath et al, 2011, Verdon et al. 2010) are more closer to Mesulam's defense due to IPL activation.

In addition, since our prefrontal and SPL activations are right lateralized independent from hand used, they confirm that right hemisphere is dominant in controlling voluntary attention. Due to spatial neglect being is commonly caused by lesions or strokes in right hemisphere, our right lateralized results may support the right hemisphere lesions' dominance in neglect syndrome.

<u>Limitations of the Study:</u>

There were several limitations that might affect the results of this study. As it is mentioned before, it was very difficult to implement the tactile line bisection task inside the MR scanner. Participants had a constricted space in the gantry to move their arms for performing the task. Even though the experiment set up was designed taking these limitations into account, there were difficulties in the arm movements since our experiment require much proprioceptive action. Because we needed to measure deviations, an observer was present in MR scan room during entire data acquisition, while another person were giving the comment to switch from active blocks to rest with 30 s econds intervals. In order to obtain enough sample points for the BOLD activation and due to the need to investigate four conditions (right hand-tactile, left hand-tactile, right hand-visual, left hand visual) the time of experiment was long and it was difficult to stay in MR device for participants for approximately 40-45 minutes. Administration of experiment was very difficult to provide optimum conditions for obtaining better results.

A different tactile line bisection apparatus design such as a cylindirical one is considered. In order to decrease arm movements and motion artifacts, a cylindirical design may be populated with twelve rods placed with equal distances. Participant would only spin the cylindirical board with one hand, and performs line bisection with other hand. With this design, we may prevent arm movement in z-axis, but there are several limitations of this design to perform experiment. On a spinning cylindirical board, possibility of skipping a rod is very high since participants eyes are closed and can not anticipate where to stop. Another limitation is that while participant spins the board, the sponge cursors may move from the mid-point that the participant had set. Most importantly, to place all twelve rods with minimum 3 cm distance between them, minimum 45 cm of circumference is required for the cylinder. This translates into a diameter with 14 cm along with at least 4-5 cm height from participant's body. This requires nearly 20 cm height between participant and ceiling of gantry, but there is no sufficient space in the MR gantry. When all these limitations are taken into account, we believe that we designed optimum tactile line bisection apparatus compatible with MR to implement line bisection task.

Among several analyses that we perfomed, fmri behavioural data has not been correlated with brain image results. Since six conditions are presented in separate sequences during fMR experiment, there are 6 GLM analysis for each individual subject. In each condition, line bisection performances (bias amounts) for each rod may also be provided to GLM analysis as each of them represent one regressor. Furthermore, the behavioral tactile line bisection performance could have been compared inside and outside MR device.

Finally, the results we obtained are only generalizable to strongly right handed people. Our experiment can be conducted on left-handed people in order to investigate dexterity effects of non-dominant hand in the results in the future.

CHAPTER 6

CONCLUSION

In this study, we investigated neural substrates of line bisection task while somatosensory cortex is recruited. Our main aim was to implement a tactile line bisection fMRI task by designing a plain somatosensory line bisection apparatus compatible with MR device. Difference of our study is that the participants performed the line bisection task by using both tactile and visual sense in the MR and the results obtained under different sensory modalities are compared. Studies investigating tactile line bisection conducted without fMR, was only able to examine how different factors modulate tactile line bisection performances, while we investigated the neural substrates of tactile line bisection in the somatosensory modality and attentional network with support of fMR brain images. This made our study innovative and important for revelation of the difference between attentional substructures of line bisection under different sensory modalities.

In order to implement tactile line bisection, we created a new set-up utilizing a wooden board. We conducted behavioral tests outside the scanner environment as well as pilot experiments inside the MR scanner. After a few experimental changes, our tactile line bisection set-up worked for revealing neural substrates of tactile line bisection by using fMR.

According to our results, we observed right lateralized activations in tactile line bisection decision with right hand. Ipsilateral superior frontal gyrus, postcentral gyrus, SPL (superior parietal lobule) and precuneus activations were observed. In visual line bisection with right hand, when we substracted motor task, similarly with tactile line bisection decision, right SPL, right SFG and right precuneus activation was observed. Differently from tactile line bisection decision right fusiform gyrus and bilateral middle occipital gyrus activations were observed.

When we compare tactile line bisection with visual line bisection under right hand use, right middle temporal gyrus activation coming from visual line bisection is detected which is an important finding to validate our hypothesis Another important result confirming our hypothesis is the left middle frontal gyrus and left IPL activations coming from tactile line bisection effect. So it seems that tactile line bisection differs from visual line bisection in the contralateral ventral fronto parietal loop.

When we evaluated the results of line bisection when using left hand, we observed an over activity in a widespread brain areas in each condition. Activations around temporal cortex, cerebellum, subcortical areas such as putamen and caudate, bilateral somatosensory cortex (postcentral gyrus), bilateral supplementary motor area (SMA) associated with motor response, bilateral thalamic activation, insula, particularly, in tactile line bisection, superior parietal lobule activation was observed. In tactile line bisection performed with the non-dominant hand, differently from right hand, subcortical areas and middle occipital gyrus activations was seen. In visual line bisection with left hand, MFG activation was observed beside right premotor cortex, bilateral somatosensory cortex activations and supplementary motor area activation associated with motor response.

When we compare visual line bisections with tactile line bisection with left hand, ipsilateral middle frontal gyrus, ipsilateral cuneus, contralateral superior parietal lobule (SPL), contralateral inferior frontal gyrus activations were observed. All these activations were positive correlations which means that tactile line bisection supressed visual line bisection. Any activation with negative correlation was not observed.

Overall, our results confirmed our hypothesis that there are different cortical elements underlying line bisection under different sensory modalities. Furthermore, differences of neural networks between the dominant and non-dominanant hands was striking, which calls in for future studies. To sum up, the task implemented in this study was innovative in revealing left versus right hemispheric activity differences when line bisection is perfomed by dominant versus non-dominant hand, as well as revealing frontal, parietal and sub-cortical differences in tactile versus visual performances.

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APPENDIX A

OVERVIEW OF NEGLECT SYNDROME

1.Neglect Syndrome

Origin of the studies related to the line bisection test are based on studies which reveal neglect syndrome. Patients with neglect syndrome has a neurologic disorder causing failure to attend, report and respond to visual stimuli in contralesional space (Wang et al., 2004). Generally right parietal lobe damage of the brain causes unilateral neglect. Patients who suffer from unilateral neglect exhibit behaivours like failing to be aware of objects to their left in extrapersonal space (Asplund, 2010). Similarly, a spontaneous and sustained bias of eyes and head toward ipsilesional side is observed in individuals with right hemisphere damage When a patient with neglect is asked to look ahead and remain in his position, it is also seen that there is a bias gaze direction on the clinical scans. (Karnath, 2011).

Patients with neglect may behave as if only one half of the universe exist in a meaningful form. Males may shave only right side of their face, patients may groom only the right side of their body , may fail to eat food on the left side of the plate. They may omit to read left side of the sentences, may fail to copy detail on a left side of a drawing and so on (Mesulam, 1981). Dramatically, they are not even aware of this neglection. Several examples about performance of patients with neglect in some clinical paper-pencil tasks such as copying, cancellation, line bisection etc. are seen in Figure 40. In Figure 40-a, some copying test examples performed by neglect patients are shown. (top: template, bottom: patient's copy) (Chokron, 2007). Patients had neglected the left side of the template pictures. Figure 40-b, shows an example of clinical cancellation test in which a neglect patient crossed out only targets on the right of the page. In Figure 40-c, in a line bisection test, patient with neglect performed linebisect along several lines with different lengths. It is seen that as the length of the lines increase, a bias to the right of the middle point occured.

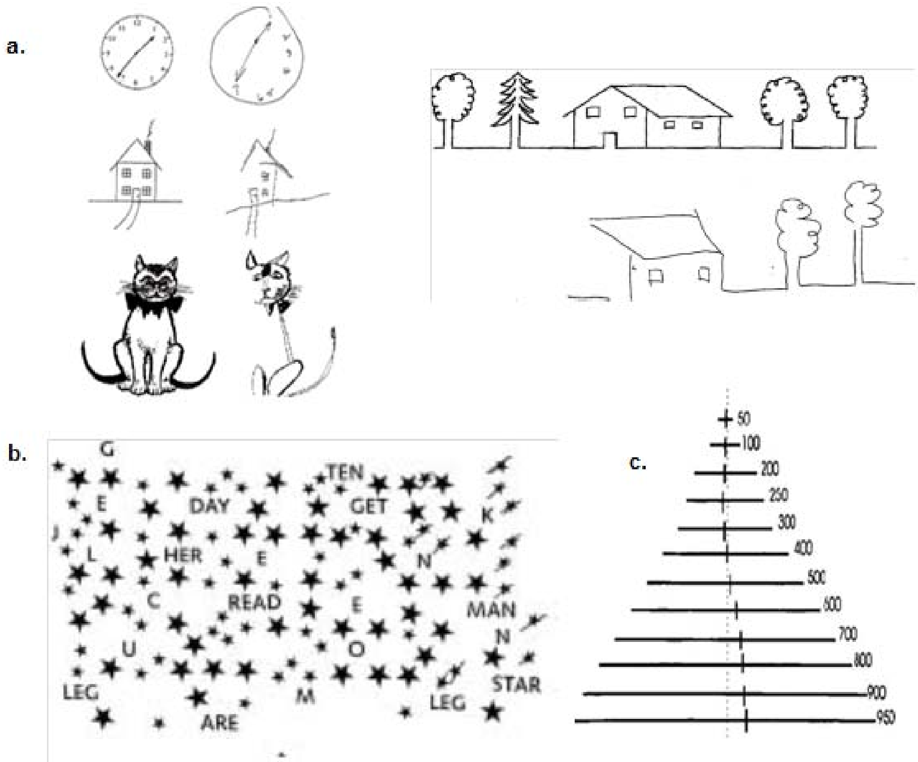

Figure 40 Clinical paper - pencil tasks which are used in neglect syndrome: (a) Copying, (b) Cancellation, (c) line bisection (taken from Chokron, 2007).

1.1 Anatomy of the Neglect

Spatial neglect often corresponds to versatile and heterogenious symptoms correlating with abnormality in anatomical structures. Brain regions associated with neglect are controversial. Studies based on brain imaging of neglect usually suggest three major cortical areas:

The temporo-parietal junction (TPJ) and inferior parietal lobule (IPL),
The superior/middle temporal cortex (STC/MTC) and insula,
The ventrolateral prefrontal cortex (VPC) (Karnath, 2011, Mesulam, 1999, Corbetta, 2002).

Mesulam has proposed that neglect represents a dysfunction of the dorsal IPS–FEF network for spatial attention (Mesulam, 1999). However, Corbetta et al. (2002) proposed that the problems in neglect matches the functions associated with ventral TPJ–VFC system better.

They defended that lesions causing neglect are located in more ventral regions in the brain, particularly the right TPJ. According to same authors, neglect patients can voluntarily pay attention to the contralesional side, consistent with sparing of the IPS–FEF network. The dysfunction in neglect corresponds to more closely the dysfunction of a target detection than an orienting network, particularly when the stimuli are unexpected. This functional matching gets along with impairment of the ventral frontoparietal attention network under stimulus-driven attention. Since network of Temporoparietal junction (TPJ) cortex and the ventral frontal cortex is strongly lateralized to the right hemisphere, ventral attentional network has significant clinical implications for the pathophysiology of unilateral spatial neglect (Corbetta, 2002). Besides, lesions that cause neglect are frequently localized in right ventral prefrontal and opercular cortex, rather than in the dorsal FEF region in the frontal cortex. Accordingly, Corbetta et al. (2002) claim that neglect manifests itself structurally in the ventral TPJ-VFC attention network than the dorsal IPS-FEF attention network (Corbetta, 2002).

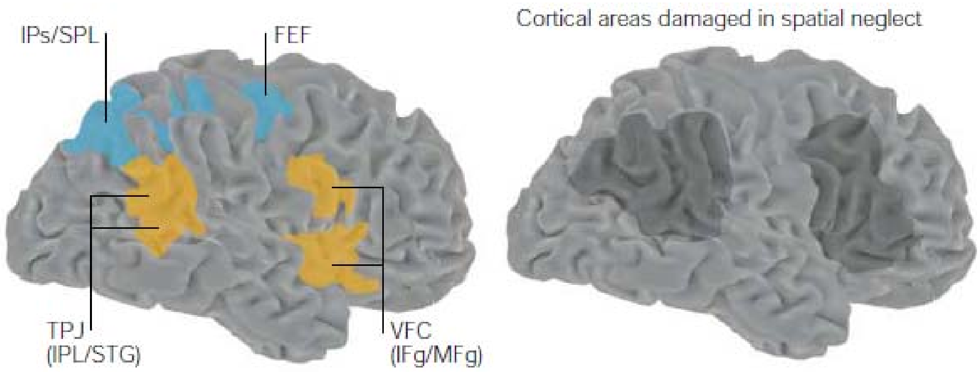

Figure 41 Dorsal and ventral frontoparietal networks and their anatomical relationship with regions of damage in patients with unilateral neglect (taken from Corbetta, 2002).

As seen in Figure 41, the dorsal frontoparietal network consists of FEF, frontal eye field; IPs/SPL, intraparietal sulcus/superior parietal lobule. The stimulus driven ventral frontoparietal network includes TPJ, temporoparietal junction (IPL/STG, inferior parietal lobule/superior temporal gyrus); VFC, ventral frontal cortex (IFG/MFG, inferior frontal gyrus/middle frontal gyrus).

Similarly, Golay et al. (2008) identified a region that matches with the TPJ and the superior temporal gyrus (STG), connecting the inferior parietal lobe with the prefrontal cortex, insula as a correlation of neglect in their lesion study. They observed these results in a group of neglect patients suffering from right-hemispheric vascular brain damage. These pateints exhibited large amount of bias in cancellation task and also small biases in line bisection. Their observations were correlated with while frontal structures may be related to spatial exploration, IPL may play a role in object-based attention,especially performed in line bisection (Golay et al., 2008).

Karnath et al. (2011) are another group of researchers investigating spatial neglect. In 2009, after applying diffusion tensor imaging and tract racing techniques, they found a profound interconnection between inferior parietal lobe and lateral prefrontal cortex, lateral prefrontal cortex with superior temporal cortex, and superior temporal cortex with the inferior parietal lobule. In Figure 42, links between inferior parietal lobule and ventrolateral frontal cortex (via subcomponents of superior longitudinal fasciculus (SLF II, SLF III) and superior occipitofrontal fasciculus (SOF)), ventrolateral frontal cortex with superior/middle temporal cortex and insula (via arcuate fasciculus (AF), extreme capsule (EmC)/inferior occipitofrontal fasciculus (IOF)), and superior temporal cortex with the inferior parietal lobule (via middle longitudinal fasciculus (MdLF), EmC/IOF) are shown. IPC is the inferior parietal cortex, TPJ is the temporo-parietal junction, S/MTC is superior/middle temporal cortex; and VPC is ventrolateral prefrontal cortex. These findings are important about the anatomical basis of spatial orienting (Karnath, 2011).

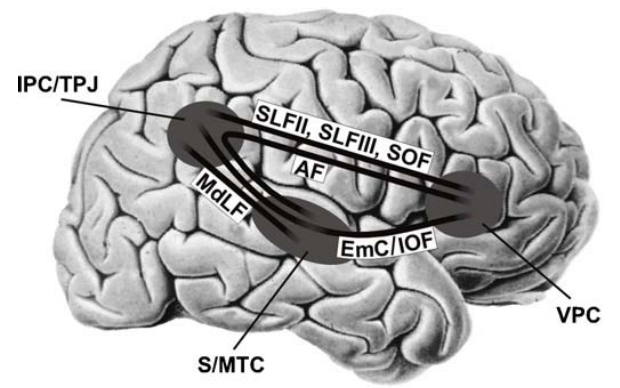

Figure 42 Links between inferior parietal lobule and ventrolateral frontal cortex (Taken from Karnath, 2011)

On the other hand, Mort et al. (2003) proposed that lesions in the angular gyrus on the lateral surface of the IPL and parahippocampal region on the medial surface of the temporal lobe are associated with neglect. In their lesion mapping study, they examined patients who had suffered from neglect and had brain lesion in the right-hemisphere. Eventhough STG was damaged in half of neglect patients, it remained intact in the rest of them. For neglect patients with posterior cerebral artery stroke, lesions in parahippocampal region were observed in all patients (Mort et al., 2003).

1.2 Line Bisection Studies in Neglect and Anatomic Correlates

It is known that various different kinds of tasks can be used to assess and understand neglect behavior. The most common clinical approach consists of visual and behavioural scanning by paper-and-pencil tasks such as line bisection, copying, cancellation (Morganti, 2007). Although neglect syndrome can be assessed with several paper-and-pencil tests, these tests may lead to correlations with different regions in the brain due to their different demands. Especially, cancellation and line bisection tests are mostly used to assess neglect syndrome. It is unclear if different cortical processess are activated with these two tests (Molenbergh et al., 2011). It is important for us to know which regions in the brain are activated underlying line bisection test in order to have an idea about attentional processes of line bisection test to forecast region specific deficits relating to neglect.

Rorden et al. (2006) presented that patients suffering from neglect that exhibit irregularity on the line bisection task have more posterior lesions such as Temporo-occipital junction compared to patients that show bad performance on the target cancellation task. In cancellation test, it was observed that patients have lesions in the STG (Rorden et al, 2006). More recently, Verdon et al. (2010) proposed that line bisection task is more correlated with lesions in the right inferior parietal lobule (IPL) while target cancellation is related to right dorsolateral prefrontal cortex. In their study (Verdon et al, 2010), cancellation task was associated with frontal and temporal damage while line bisection task was related to more posterior areas consistent with Rorden et al.'s (2006) researches. This dissociation between line bisection and cancellation task is explained with an idea that the line bisection task is related to object-based representation while other clinical tests are relative to the egocentric measures (i.e. position of body of the subjects). This means that egocentric measures related to body position of the subjects is associated with STG, in contrast the measures related to object-based presentation correlated with more posterior and inferior sites in the brain (Karnath, 2011).

In a recent study, Molenberg et al. (2011) observed that problems due to neglect are commonly associated with right parietal region of the angular gyrus They observed that the neglect patients with lesions in the angular gyrus failed in both cancellation and line bisection tests. In light of this informations, the correlation between lesion location and outputs of clinical tests used to assess neglect is a disputed issue (Molenberg et al. 2011).

APPENDIX B

PILOT STUDIES OF LINE BISECTION OUTSIDE AND INSIDE MR SCANNER

1. Tactile Behavioural Task outside the MR scanner

Experiment was applied as tactile (closed eyes) to ten volunteers by using a different sensorymotor apparatus which contained the motor-sweep rod at the very bottom of the boards with sections A/B and C/D. 10 healthy, right-handed volunteers with no history of neurological or psychiatric illness were studied in tactile behavioural experiment without fMRI. All volunteers were in 18-30 age range and mean age was 23.90.

There were four runs which was applied with only tactile sense, first two times of them were performed with right hand and other two of them were performed with left-hand. We calculated the measurements of the deviations from midpoints and performed statistical analysis of the results by using one way ANOVA in SPSS before fMRI experiments. Since we analyzed bias amount and bias direction separately (we analyzed bias direction by using Asymmetry indexes), we have only one independent variable (hand used) with two levels (right hand, left hand), and one dependent variable (bias amount). Therefore, we use one-way ANOVA. Since the important issue is the investigation of deviations from the middle points in behavioural task, we applied motor and line bisection activity in the same task. Thus, we shortened the experiment duration.

There are four runs in the experiment. It means that subjects perform the line bisection activity for four times as in the following way:

1. With their right hand and closed eyes,
2. With their right hand and closed eyes
3. With their left hand and closed eyes,
4. With their left hand and closed eyes.

Thinner wooden plates of sensorymotor apparatus was placed on the subject as in the given way in
Table **9** for each run. Combinations of runs were arranged so that subjects could not learn the order of the rods after a time.

Table 9 Combinations of sections for each run used in Behavioural Task

	Tactile (Closed Eye)			
	Right Hand		Left Hand	
	1.Run	2. Run	3. Run	4.Run
Section-1	A	B	B	A
Section-2	B	A	A	B
Section-3	C	C	D	D
Section-4	D	D	C	C

<u>Results of Tactile Behavioural Task:</u>

As mentioned in chapter three, we calculated asymmetry indexes in order to see effect of hand-used on bias direction. Figure 43 indicate relationship between mean asymmetry values when right hand and left hand are used for each rod independent from their length. Negative values represent leftward biases while positive values represent rightward biases.

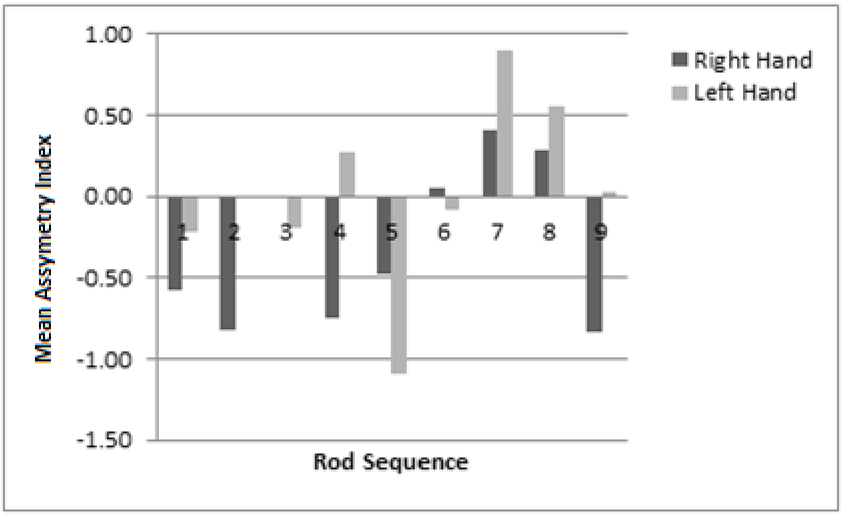

Figure 43 Hand-Used effect on Bias directions. p=0.016

According to Figure 43, for the first rod, when participants used their right hand, effect of leftward bias is larger. Same effect is seen in the second rod. In overall, it is observed that when participants use either their left hand or right hand, they have leftward bias tendency. More specifically, it is seen that leftward bias is more dense when right hand is used. This result is conflicted with Laeng et al's (1996) tactile behavioural line bisection study. According to their results, subjects biased leftward of true midpoint when they used thier left hand. On the contrary, they biased to the right of true midpoint when they use their right hand. Similarly, this results conflict with Coudereau et al.'s (2006) tactile line bisection study. They concluded that participants deviated to the left when using their right hand, whereas they deviated to the right when using their left hand. Interestingly, our results are consistent with Chokron et al's (1998) line bisection study conducted in both neglect and healthy people. According to their results, the healthy participants, while bisecting the rods with their right hand, showed a leftward bias. Even neglect patients also errored to the left of the objective middle instead of rightward bias. With regard to this, our tactile behavioural results support pseudoneglect phenomennon.

Affect of Hand used factor on Bias amounts were analysed in SPSS separately by using one way ANOVA. Hand used had not a significant affect on deviation amounts (p=0,699).

2. Tactile Task inside the MR scanner

Pilot fMRI study was implemented as tactile (closed eyes) and visual (opened eyes) to nine volunteers by using a different sensorymotor apparatus which contained the motor-sweep rod at the very bottom of the boards with sections A/B and C/D before. 9 healthy, right-handed volunteers (5 F, 4 M) with no history of neurological or psychiatric illness were studied with FMRI (ages were in 20-30 range, mean age was 26.44). These nine volunteers were different people from the participants in behavioural and actual fMRI experiments.

In pilot study, since motor and line bisect blocks were presented within the same run, each cycle was composed of 3 blocks as given in Figure 44.

1.OFF State (OFF)
2.Motor State (M)
3.Line bisection State (L)

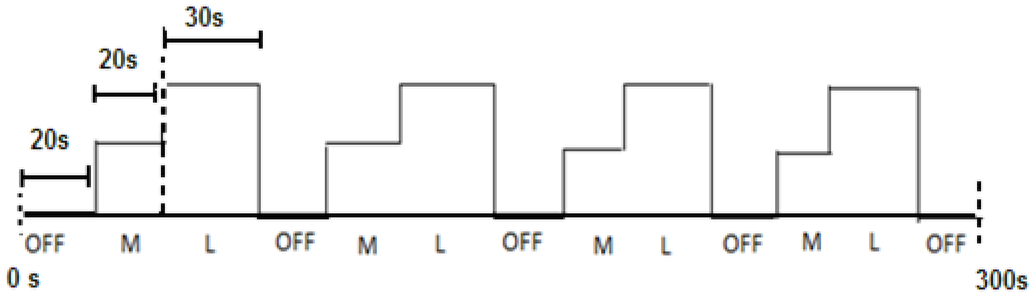

Figure 44 Block Design of Pilot Study

There were four repetitions of each cycle to take enough sample for analysis. Sample numbers are given in Table 10.

Table 10 Durations and sample numbers of blocks in block design.

	Duration(s)	Number of Sample
OFF State	20	10
Motor State	20	10
Line bisection State	30	15
One Cycle	70	35
Total Run (4xCycle + OFF)	300	150

Participants performed the experiment for six times, with their right hand and closed eyes for two times, with their left hand and closed eyes for two times, with their right hand and opened eyes for one time and with their left hand and opened eyes for one time respectively. Combination are provided by change the sides and arrangement of two plates. Combinations are given in Table 11 in details.

Table 11 Combinations of sections for each run and condition.

	Tactile (Closed Eye)				Visual (Opened Eye)	
	Right Hand		Left Hand		Right Hand	Left Hand
	1.Run	2. Run	3. Run	4.Run	5.Run	6.Run
1.Section	A	B	B	A	A	B
2.Section	B	A	A	B	B	A
3.Section	C	C	D	D	C	D
4.Section	D	D	C	C	D	C

Example Results of Pilot fMR study:

Few examples of HRF functions of different participants (a. Subject-7, b. Subject-4) with estimated ideal HRFs in the same figure are given in below Figure 45. We observed that transitions between motor and line bisection cycles were bad in fMRI signal when we applied them in one block design during pilot study.

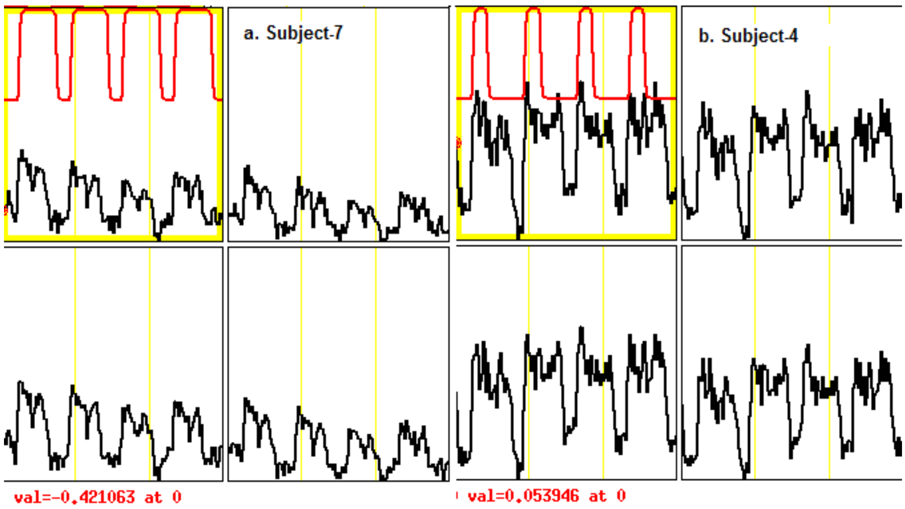

Figure 45 Hemodynamic Response functions of different participants: (a) Subject-7, (b) Subject-4.

Extensive arm movements causing motion artifacts in the fMR scans was also observed. One example of fMRI outlier file for one run was shown in Figure 46. Artifacts caused by arm and head movements are clearly seen between 20-30, at 80 , between 90-100 timepoints.

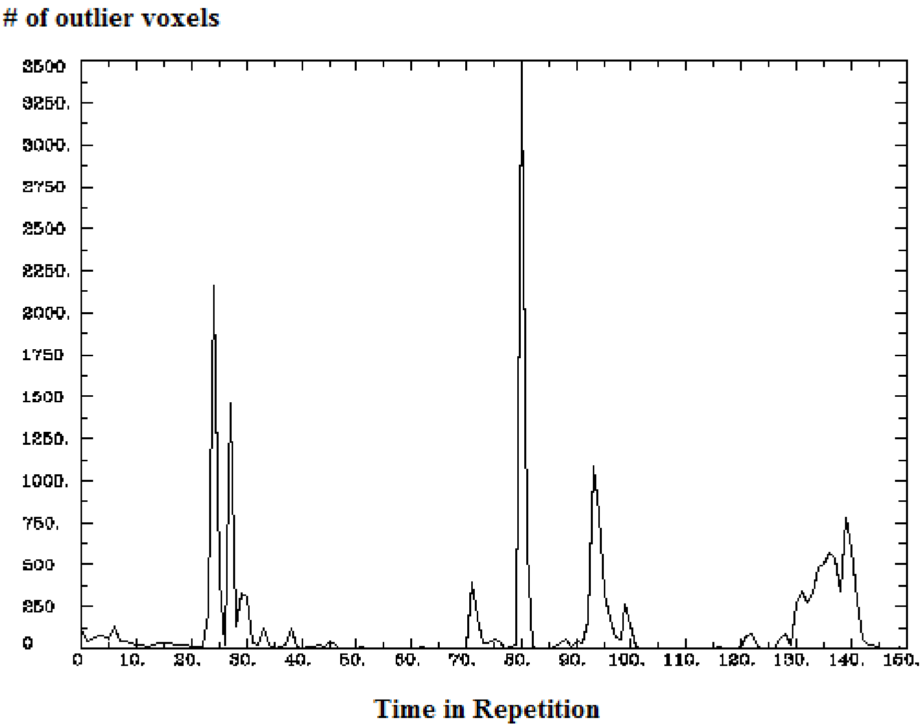

Figure 46 Outliers of fMR data for subject-1

In Figure 47, one example of GLM result of pilot study. It shows comparison of tactile line bisection with baseline when subject used his right hand. As it is seen, motor cortex activation was observed very clearly, but it was not observed any attentional activation in terms of line bisection.

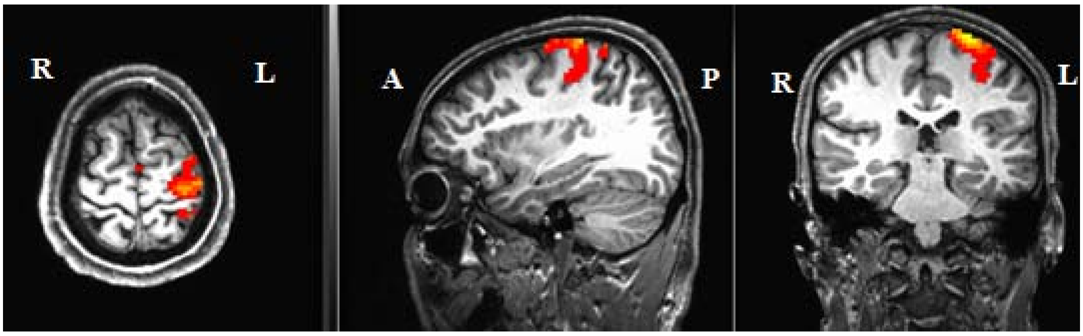

Figure 47 Result of Comparison of motor & line bisection activity with baseline for right hand,tactile condition.(Thr=9.627, p=0,0004)

APPENDIX C

COMPARISON OF VISUAL LINE BISECTION PERFORMANCE INSIDE AND OUTSIDE THE MR SCANNER

An additional behavioural task was introduced to ten healthy volunteers as they perform same experiment visually at out of MR device. The purpose of visual behavioural experiment is to clarify whether deviations from middle points differ in amount or direction when the experiment is performed by subject's himself eyes at out of MR device insted of performing with help of a mirror in MR device. Since a mirror symmetry will take place when the subject performs the visual line bisection by looking form the mirror in MR device, it is debated that there may be difference in deviation directions and amounts between two conditions.

10 healthy, right-handed volunteers with no history of neurological or psychiatric illness were studied in visual behavioural experiment without FMRI. All volunteers were in 18-30 age range and mean age was 26.00. These 10 volunteers are the same with ten of twelve people who participate to fMRI experiment in order to see whether there is a significant difference between line bisection performances applied with mirror symmetry and human eye.

Visual behavioural task was consists of two runs and the same with visual runs of fMRI experiment with respect to block design and rod combinations in order to make a meaningful comparison between results of behavioural and fMR experiments (Table 12). Control run was not applied since there is not any brain image data analysis. We calculated only deviations from middle points and performed statistical analysis of the behavioural data by using ANOVA in SPSS.

For visual behavioural task, similar statistical analysis techniques with tactile behavioural tasks was used. Differently from tactile behavioural task, we compared the bias amounts with the amounts performed by same subject group in MR device in order to see whether there is a significant difference between line bisection performances applied with mirror symmetry and human eye. Accordingly, we have two independent variables with two levels:

One variable (factor) is hand-used with right hand and left hand levels, the other one is condition with in MR and out of MR levels. Since we examined interactions with two factors on bias amounts, we applied 2 by 2 within subject ANOVA in SPSS for bias amounts. Similarly with tactile behaviour task, bias directions are analyzed by using assymetry indexes.

Table 12 Combinations of sections for each run and condition used in visual behavioural task.

	Visual (Opened Eye)	
	Right Hand	Left Hand
	1.Run	2. Run
Section-1	A	B
Section-2	B	A
Section-3	C	C
Section-4	D	D

<u>Results of Visual Behavioural Task:</u>

Figure 48 indicate relationship between mean asymmetry values when experiment performed out of MR and in MR for each hand used. Vertical axis indicate mean assymetry values for ten subjects.

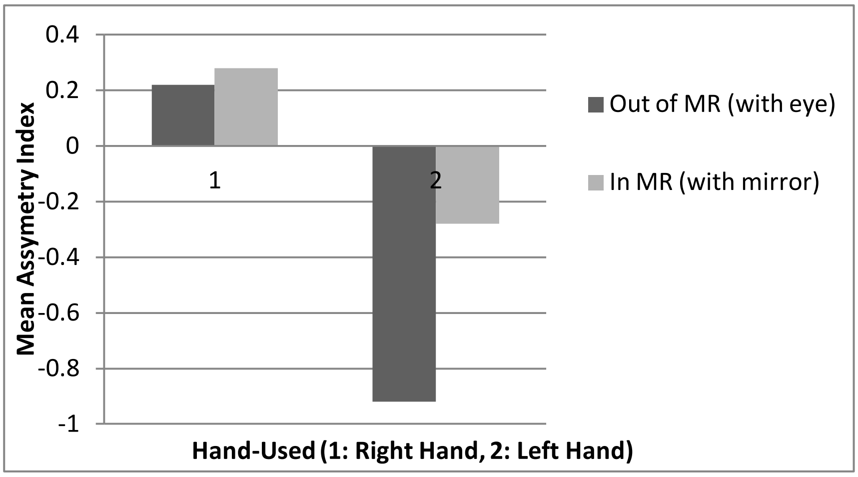

Figure 48 Effect of out MR or in MR conditions on Bias directions (1: right hand, 2: left hand). p=0.043 for hand used, p= 0.743 for MR condition.

According to Figure 48, when participants used their right hand (1), a rightward bias was observed in visual sense. It did not differ when participants performed the experiment directly with their eye out of MR device and with mirror syymetry in MR device. In each condition, subjects exhibit a rightward bias when they use their right hand. On the contrary, When they use their left hand, a leftward bias was observed for each condition again. We concluded from the results that there is not a difference between performing the experiment directly wity eye or looking from a mirror. However, these results differed from the results of tactile behavioural task. This time, pseudoneglect effect did not appear. A rightward bias was observed when right hand was used, whereas leftward bias was observed when left hand was used. This results may be differ because of different sensory modalities. Results for visual behavioural line bisection are consistent with Halligan and Marshall's results (1989). They also found that there were rightward biases when the right hand were used while leftward biases when the left hand was used. On the contrast, our results are conflicted with Chokron et al.'s (1993) suggestion from their another line bisection study. They suggested vice versa situation in their visual line bisection study.

Affect of Hand used and condition factor on Bias amounts were analysed in SPSS by using 2 by 2 ANOVA. Hand used had not a significant affect on deviation amounts (p=0,791). Condition also had not affect on bias amounts (p=0,8). This reveals us thet there is not a significance difference between visual tactile performance inside and outside the mr scanner in terms of bias amounts.

APPENDIX D

DEVIATON DATA TABLE

.... /......./.......

DEVIATION DATAS

Subject Name: ....

Age: ....

Hand-Used: ....

	TACTILE						VISUAL			
	Right Hand	Left Hand	Right Hand		Left Hand		Right Hand		Left Hand	
	1.Run	2.Run	3.Run		4.Run		5.Run		6.Run	
			Rod Length (cm)	Deviation (cm)	Rod Length (cm)	Deviation (cm)	Rod Length (cm)	Deviation (cm)	Rod Length (cm)	Deviation (cm)
1.Section	KONTROL	KONTROL	18		13		18		13	
			A 17		B 12		A 17		B 12	
			10		15		10		15	
2.Section			15		10		15		10	
			B 12		A 17		B 12		A 17	
			13		18		13		18	
3.Section			16		17		16		17	
			C 14		D 16		C 14		D 16	
			11		12		11		12	
4.Section			12		11		12		11	
			D 16		C 14		D 16		C 14	
			17		16		17		16	

Figure 49 Deviation Data Table

APPENDIX E

EDINBURGH-HANDEDNESS TEST

BASKIN EL TESTİ (EDINBURGH TEST)

Aşağıdaki listede günlük hayatta gerçekleştirdiğiniz bazı aktiviteler ve kullandığınız nesneler yer almaktadır. Bu aktiviteleri daha çok ve rahatlıkla hangi elinizi kulanarak gerçekleştirdiğinizi veya nesneleri hangi elinizle tutturğunuzu işaretleyiniz.

Sol	Sağ	
		Yazma
		Çizme
		Atma
		Makas
		Diş Fırçası
		Bıçak (çatal olmadan, tek başına kullanırken)
		Kaşık
		Süpürge (üstte duran el)
		Kibrit Yakmak
		Kutu Kapağı Açmak
		Tekmelemek için hangi ayağı kullanırsınız?
		Sadece bir gözünüzü kullanırken hangisini kullanırsınız?

Ad Soyad:

Tarih:

Figure 50 Edinburgh Handedness Test Form

APPENDIX F

INFORMED CONSTENT FORM

BİLGİLENDİRİLMİŞ GÖNÜLLÜ OLUR FORMU

Araştırmanın Adı: SOMATOSENSÖR ÇİZGİ BÖLME TESTİNİN BEYİNDEKİ AKTİVİTESİNİN ARAŞTIRILMASI: BİR FMRG ÇALIŞMASI

Sorumlu Araştırmacı: Yrd.Doç.Dr. Didem Gökçay

Araştırmanın Yapılacağı Yer: ODTÜ Enformatik Enstitüsü, Bilkent UMRAM MR Merkezi

Bu çalışma, Orta Doğu Teknik Üniversitesi Fen Bilimleri Enstitüsü, Biyomedikal Mühendisliği bölümü yüksek lisans öğrencisi Burçin Gümüş tarafından, yine Orta Doğu Teknik Üniversitesi Enformatik Enstitüsü öğretim üyelerinden Yrd.Doç.Dr. Didem Gökçay danışmanlığında yürütülen, yüksek lisans tezi kapsamında bir çalışmadır. Çalışmanın amacı, dokunma duyusu ile algılanabilen ve MR cihazı ile uyumlu bir çizgi bölme test düzeneği geliştirilmesi ve dokunma duyusu aktif iken, bu çizgi bölme testi ile gerçekleştirilen orta nokta bulma eylemi sonucunda beyin aktiviteleri ile ilgili bulgu toplanmasıdır. Calışmamız sadece sağlıklı yetişkinleri kapsamaktadır ve çalışmaya 20 gönüllü katılacaktır.

Çalışmaya katılım tamamiyle gönüllülük temelindedir. Katılacağınız deney MR cihazı içerisinde gerçekleşecektir ve herhangi bir potansiyel risk içermemektedir. MR cihazında bilindiği üzere, herhangi bir radyoaktif madde ya da X-ışını kullanılmaz, klinik olarak günlük hayatımızda pekçok uygulamaları vardır. MR çekimi uygun önlemler alındığı takdirde zararsız bir işlemdir; ancak aşağıda sıralanan niteliklere sahip kişilerin MR cihazına girmesi sakıncalıdır:

Vücudunda;
metal protez, metal implant veya metal stent,
kalp veya beyin pili,
metal diş teli,
ve benzeri metal maddeler bulunan kişiler MR cihazına girmemelidir.

Deneyde, MR cihazı içerisinde önünüze ahşap bir düzenek yerleştirilecektir. Bu ahşap düzenekte, üzerlerinde sünger bir boncuk bulunan on iki adet ahşap çubuk bulunmaktadır. Sizden, düzeneği görmeden, gözleriniz kapalı bir şekilde tamamiyle ellerinizi kullanarak ve size ileteceğimiz ses komutlarını dinleyerek, önünüzde bulunan ahşap çubukların orta noktalarını, üzerlerindeki sünger boncukları ilerleterek bulmanız istenecektir. Siz bu işlemi yaparken, bu esnada MR beyin görüntüleriniz çekilecektir. Deney yaklaşık 50 dakika sürecektir. MR çekimi başladığında ritmik sesler duyacaksınız. Personel bu sesi azaltmak için size kulak tıkacı temin edecektir. Cihazın içerisinde, iletişim yapabilmeniz için yerleştirilmiş bir ses sistemi bulunmaktadır. Bu vesile ile teknisyen ile konuşmanız mümkündür. Çekim süresince hiçbir kafa hareketi olmaması gerekmektedir. Öksürme, boğazı temizleyecek şekilde yutkunma gibi hareketler çekim kalitesini düşürdüğünden, bazı çekimlerin tekrarlanması gerekebilir. Bu nedenle mümkün olduğunca kafanızı kıpırdatmamanız gerekmektedir.

Elde edilen beyin görüntüleriniz tamamiyle gizli tutulacaktır. Sadece araştırmacılar veya etik kurul tarafından görüntülerinize gizli tutulmak kaydıyla erişilebilecektir. Tüm bilgiler sadece bilimsel yayınlarda kullanılacak, hiçbir şekilde kimlik bilgileriniz belirtilmeyecektir.

Deney, genel olarak kişisel rahatsızlık verecek unsurlar içermemektedir. Ancak, katılım sırasında herhangi bir nedenden ötürü kendinizi rahatsız hissederseniz yanınızda duracak diyafona sesli komut vererek deneyi yarıda bırakıp çıkmakta serbestsiniz. Araştırmaya katılımınız tamamiyle gönüllülük çerçevesinde olup, istediğiniz zaman, hiçbir yaptırım veya cezaya maruz kalmadan, hiçbir hak kaybetmeksizin araştırmaya katılmayı reddedebilir veya araştırmadan çekilebilirsiniz.

Deney sonunda, bu çalışmayla ilgili sorularınız cevaplanacaktır. Çalışmaya katıldığınız için şimdiden teşekkür ederiz. Çalışma hakkında daha fazla bilgi almak için veya herhangi bir sorunuz olduğunda, ODTÜ Biyomedikal Mühendisliği Bölümü yüksek lisans öğrencisi Burçin Gümüş (Tel: 3857799; Eposta: burcin.gumus@hotmail.com) ya da ODTÜ Enformatik Enstitüsü öğretim üyelerinden Yrd.Doç.Dr.Didem Gökçay (Oda:A-216 Tel: 210 3750 ; E-posta: didemgokcay@gmail.com) ile iletişim kurabilirsiniz.

Bilgilendirilmiş Gönüllü Olur Formu'ndaki tüm açıklamaları okudum. Yukarıda konusu ve amacı belirtilen araştırma ile ilgili tüm yazılı ve sözlü açıklama aşağıda adı belirtilen araştırmacı tarafından yapıldı. Bu çalışmaya tamamen gönüllü olarak katılıyorum ve istediğim zaman gerekçeli veya gerekçesiz olarak yarıda kesip çıkabileceğimi veya kendi isteğime bakılmaksızın araştırmacı tarafından araştırma dışı bırakılabileceğimi biliyorum. Verdiğim bilgilerin bilimsel amaçlı yayınlarda isim bilgilerim olmadan kullanılmasını,

görüntü kayıtlarıma sadece araştırmacı veya etik kurul tarafından gizli tutulmak kaydıyla erişilebilmesini kabul ediyorum. Kendi özgür iradem le, hiçbir baskı ve zorlama olmadan 'SOMATOSENSÖR ÇİZGİ BÖLME TESTİNİN BEYİNDEKİ AKTİVİTESİNİN ARAŞTIRILMASI: BİR FMRG ÇALIŞMASI' ***adlı çalışmaya katılmayı kabul ettiğimi ve bu formun bir kopyasının bana verildiğini aşağıdaki imzamla beyan ederim.***

Gönüllü :

İsim Soyad Tarih İmza
...../....../......

Tanıklık Eden Yardımcı Araştırmacı:

İsim Soyad Tarih İmza
....../...../......

APPENDIX G

INSTRUCTIONS OF THE EXPERIMENT

DENEY YÖNERGESİ

Bu deney tamamen gönüllülük üzerinedir. Deney sırasında herhangi bir rahatsızlık hissederseniz veya deneyi bırakmak isterseniz, sesli komut vererek deneyi bırakıp çıkabilirsiniz.

AÇIKLAMA:

- Deney başlangıcında, üzerinizde kemer yardımıyla sabitlenmiş ahşap bir platform yer alacaktır. Deney düzeneği, bu platforma sırasıyla yerleştirilmek üzere 3 adet ayrı ahsap plakalardan oluşmaktadır. İlk plakada, 1 adet kontrol çubuğu yer almaktadır. İkinci plakada, toplam 6 adet çubuk bulunmaktadır ve bu plaka 3 çubuk bir bölümde, diğer 3 çubuk bir bölümde olmak üzere saydam bir ayraç ile ayrılmış iki bölümden oluşmaktadır. Üçüncü plaka da ikinci plaka ile aynı düzendedir. Plakalardaki çubuklar üzerinde sünger boncuklar mevcuttur.

İŞLEM:

- Üzerinize kemer yardımıyla ahşap platformu sabitledikten sonra, kontrol çubuğunun bulunduğu ilk plakayı platforma yerleştireceğiz. Başınızın üzerine uygun bir açıyla bir ayna yerleştirdikten sonra MR cihazı içerisine alınacaksınız. Deneye başladığımızda, öncelikle MR çekimine başladığımız ilk 5 dakika kadar hiç hareket etmeden bekleyiniz. MR çalışıyor olacak ve cihazın seslerini duyacaksınız. Bu esnada anatomik çekimlerinizi gerçekleştiriyor olacağız ve hiçbir hareket yapmadan kollarınız yanlarda sabit ve gözleriniz kapalı bir şekilde bekleyiniz. Kulağınızdaki kulaklık yardımıyla dışarıdan size yöneltilecek komutlar doğrultusunda deneyi gerçekleştireceksiniz. Aynı şekilde siz de içeriden konuştuğunuzda dışarıdan sesiniz duyulabilecektir. Hareketsiz bir şekilde 5-6 dk'lık bir süre bekledikten sonra, '**Şimdi fonksyonel çekime başlıyoruz'** komutunu duyduğunuzda deneyimiz başlıyor olacak. Size bazı komutlar verilecek ve komutlara göre hareket etmeniz istenecektir.

- Deneyde yapılacak işlem 6 kez gerçekleştirilecektir, her bir işlem yaklaşık 5 dakika sürecek, deney toplam yaklaşık 30 dakika sürecektir.

1. **İşlem:** Birinci işlemde, **gözleriniz kapalı** bir şekilde, **sağ elinizi kullanarak** ilk plakanın tam ortasında bulunan 1 adet kontrol çubuğunu, size verilecek komutlar doğrultusunda, üzerinde bulunan sünger boncuğu, çubuğun bir ucundan diğer ucuna sürükleyerek, çubuğu taramanız istenecektir. Bu işlemde iki komut serisi duyacaksınız: '**Rahat'** ve '**Kontrol**' komutları.

-***‘Rahat’ Komutu:*** Deney başladığında, öncelikle ‘Rahat’ komutunu duyacaksınız ve ikinci komut gelene kadar hiç bir şey yapmadan bekleyeceksiniz. İşlem sırasında her rahat komutunu duyduğunuzda diğer komut gelene kadar hiç birşey yapmadan ve hareket etmeden kollarınız yanlarda sabit bir şekilde (Mümkünse parmaklarınızı dahi kıpırdatmayınız) bekleyiniz.(Rahat komutu 30 sn kadar sürecektir.)

-***‘Kontrol’ Komutu:*** ‘Rahat’ komutundan sonra ‘Kontrol’ komutunu duyduğunuz anda plakanın ortasında bulunan çubuğun üzerindeki süngeri hareket ettirerek bir uçtan bir uca tarayınız. İkinci bir rahat komutu gelene kadar durmayınız ve çubuğu sürekli taramaya devam ediniz. (Bu işlem 30 sn kadar sürecektir). **Kolunuzun yorulmaması için çubuğu tararken mümkün olduğunca yavaş tarayın.**

2. **İşlem:** Birinci işlemin aynısını **gözleriniz kapalı**, bu s efer **sol elinizle** yapacaksınız.

3. **İşlem:** İkinci işlemden sonra, üzerinize başka bir plaka yerleştirilecek, bu sefer yine **gözleriniz kapalı** , **sağ elinizle**, plakada bulunan 6 çubuğun, üzerlerindeki süngerleri ilerleterek orta noktasını tahmin edecek ve süngeri orta noktada bırakacaksınız. 3. işlem, **‘Rahat’** ve **‘Orta Nokta’** komutlarından oluşmaktadır. Her Rahat komutunda aynı şekilde orta nokta komutunu duyana kadar hiçbirşey yapmadan bekleyiniz.

- ***‘Orta Nokta’ Komutu:*** ‘Rahat‘ komutundan sonra ‘Orta Nokta’ komutunu duyduğunuz zaman plakada bulunan saydam ayraçla ayrılmış iki bölümden ilkini yani ilk 3 çubuğun orta noktasını bir sonraki ‘Rahat’ konutunu duyana kadar bulmalısınız. (ilk bölüm baş bölgenize uzak olan bölümdür). Acele etmeyiniz, sakin bir şekilde yapınız. Verilen süre yeterli gelecektir. Size en uzak çubuktan başlayarak, Çubuk boyunu üzerindeki sünger boncuğu çubuğun bir ucundan diğer ucuna hareket ettirerek birkaç kez tarayınız. (Süngerin takılmasını engellemek için bastırmadan ilerletiniz.) Çubuğu birkaç kez tarayıp boyunu tahmin edebildikten sonra orta nokta olduğunu düşündüğünüz yerde süngeri bırakınız.

- 1. Çubuk bittikten sonra aşağı doğru ilerleyerek 2. Çubuğu bulunuz ve aynı işlemi 2. Çubuk için yapınız. Aynı şekilde 3. Çubuğu bulunuz ve 3. Çubuk için orta nokta bulma işlemini gerçekleştiriniz.

Hata yaptığınızı veya orta noktayı bulamadığınızı düşünürseniz bir önceki çubuğa geri dönmeyiniz. Hatalı bile olsa bırakın o şekilde kalsın. Süngerleri bir kez bıraktıktan sonra yerlerini bozmamaya çalışınız. Mümkün olduğunca bir önceki çubuğa dokunmamaya çalışarak sırayla gidiniz. Bölüm bittikten sonra 3 çubuktan az yapmışsanız yani çubuklardan birini bulamamışsanız, geri dönüp çubuğu bulmaya çalışmayın. Yaptığınız çubukları bozma ihtimaliniz olabilir. (Çubukların düzenek üzerindeki pozisyonları farklıdır. Kimisi daha içerde başlayıp kimisi daha dışarıda yer almaktadır. Çubukları bulamama ihtimaliniz olabilir)

- ‘**Orta nokta’** komutundan sonra tekrar ‘**Rahat**’ komutunu duyacaksınız.

- İkinci ‘Orta nokta’ komutu geldiğinde bu sefer 2. Bölüme geçiniz (Ayracın altındaki başınıza yakın olan 3 çubuk). 2. Bölümü, elinizi düzeneğin kenarından ilerleterek saydam ayraç yardımıyla bulabilirsiniz. Ayıracı bulduktan sonra ayraça en yakın çubuktan başlayarak 2. Bölümdeki 3 Çubuk için orta nokta bulma işlemini tekrarlayınız. **Plakadaki İkinci bölümü bitirdikten sonra ‘Rahat’ komutu geldiğinde siz hareketsiz beklerken MR odasında bulunan gözlemci 3. Plakayı yerleştirecektir. İrkilmeyiniz ve rahat komutunda kalmaya devam ediniz.** Aynı şekilde her ‘Rahat’ ve ‘Orta Nokta’ komutlarını duyduğunuzda yapmanız gerekenleri yine size uzak olan bölümden başlamak üzere, 3. Plakadaki iki bölüm için de gerçekleştiriniz.

-

4. **İşlem:** Üçüncü işlemin aynısını **sol elinizi kullanarak ve gözleriniz kapalı olarak** gerçekleştireceksiniz.

5. **İşlem:** 4. işlemden sonra ‘Şimdi gözleriniz açabilirsiniz’ komutunu duyacaksınız. Üçüncü ve dördüncü bölümde yaptıklarınızın aynısını bu kez **gözleriniz açık, sağ elinizle** yapacaksınız.

6. **İşlem:** Üçüncü işlemde yaptıklarınızın aynısını **gözleriniz açık, sol elinizle** yapacaksınız. (Deneyi gözünüz kapalı veya açık mı ya da hangi elinizle gerçekleştireceğiniz deney sırasında size söylenecektir. Sizin sadece komutlarda ne yapmanız gerektiğini aklınızda tutmanız yeterlidir.)

- Toplamda deneyi 4 kez düzeneği görmeden ve 2 kez düzeneği görerek 6 kez gerçekleştirdikten sonra ‘Deney Bitmiştir’ komutunu duyacaksınız ve MR cihazından çıkarılacaksınız. Deney toplamda anatomik çekimle birlikte yaklaşık 35 dakika sürecektir. **Bütün bu işlemler sırasında kafanızı hiç hareket ettirmemeniz çok büyük önem taşımaktadır. Çekimler hareket sırasında bozulmaktadır.**

DİKKAT EDİLMESİ GEREKENLER:

1. Kol hareketinizin mümkün olduğunca stabil olması gerekmektedir. Mümkün olduğunca kollarınızı çok havaya kaldırmadan, bilek ve el hareketlerinizle orta noktayı bulmaya çalışınz ki , elde edilecek sonuçlar kol hareketinden fazlasıyla etkilenmektedir.

2. Çubukların düzenek üzerindeki pozisyonları farklıdır. Kimisi daha içerde başlayıp kimisi daha dışarıda yer almaktadır. Dolayısıyla bazı çubukları bulamayıp atlama ihtimaliniz olabilir. Çubukları bulmakta zorlanırsanız, çubuğu ararken mümkün olduğunca çubukların üzerlerine dokunmadan kenarlarından bulmaya çalışın ki bir önceki yaptığınız çubuk bozulmasın.

3. Gözlerinizi kapatınız. Tamamen dokunma duyunuzun aktif olması gerekir. **Bunun için gözlerinizi açabilirsiniz komutu gelene kadar, gözlerinizin kapalı olması son derece önemlidir.**

4. İlk iki işlemde sadece çubuğu tarayınız orta nokta ile ilgili birşey düşünmeyiniz. Sadece tarama işlemine konsantre olunuz. Sonraki 4 işlemde, başka bir şey düsünmeden sadece orta nokta tahminine konsantre olunuz. Deneyde yapacağınız şeylere konsantre olmanız sonuçlar için son derece önemlidir. (Özellikle kontrol bölümünde zihninizi boşaltarak orta nokta düşünmeyin.)

5. Çubuk boyu tarama ve Orta Noktayı bulma işlemleri sırasında süngerleri çok sıkmadan ve bastırmadan ilerletiniz. Yoksa sünger takılabilir ve çubuğun boyunu yanlış algılayabilirsiniz.

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APPENDIX H

DEBRIEFING FORM

Geri Bildirim Formu

Aşağıdaki Soruları cevaplamanız ,deney ve projenin gidişatı açısından önem taşımaktadır. Kısa bir şekilde bir iki cümle ile düşüncelerinizi belirtiniz.

1. Komutlar Yeterince açık mıydı?
   ....
2. Ayraçları /Ayraçlar ile ayrılan bölümleri rahat ayırt edebildiniz mi?
   ....
3. Sünger boncukları kolay ilerletebildiniz mi? Boncuklar takılıyor muydu?
   ....
4. Atladığınız veya bulamadığınız çubuk oldu mu?
   ....
5. İşlem süresi nasıldı? Erken ya da geç bitirdiğiniz durumlarla karşılaştınız mı?
   ....
6. Gözünüz kapalı olarak yaptığınız işlemlerde orta nokta bulabilmek için ortalama kaç kez çubuğun boyunu bir uçtan bir uca taradınız?
   ....
7. Gözünüz açık olarak yaptığınız işlemlerde orta nokta bulma işlemlerini ortalama ne kadar erken bitirdiniz ? (30 sn'lik periyot içerisinde)
   ....
8. Ayrıca bize iletmek istediğiniz bir durum ya da öneri var mı?
   ....

Not: 6. ve 7. Sorulara doğru bir şekilde cevap vermeniz deneyin doğruluğu açısından önemlidir!

Ad Soyad:
Tarih:

APPENDIX I

SCRIPT FOR DATA ANALYSIS

Individual Analysis (For subject-1):

DICOM Conversion:

> to3d *
> to3d -time:zt 34 135 2000 altplus -prefix anl_run1 *
> to3d -time:zt 34 135 2000 altplus -prefix anl_run2 *
> to3d -time:zt 34 135 2000 altplus -prefix anl_run3 *
> to3d -time:zt 34 135 2000 altplus -prefix anl_run4 *
> to3d -time:zt 34 135 2000 altplus -prefix anl_run5 *
> to3d -time:zt 34 135 2000 altplus -prefix anl_run6 *

<u>Noise Removal and Preprocessing:</u>

Run1:

>3dWarp -deoblique -prefix anl_anat_warped anl_anat+orig

>3dWarp -deoblique -prefix anl_run1_warped anl_run1+orig

>3dToutcount -automask anl_run1_warped+orig>outlier1.1D

>1dplot outlier1.1D

>3dAllineate -base anl_anat_warped+orig –source anl_run1_warped +orig'[40]'

>3dvolreg -verbose -base anl_run1_warped+orig'[40]' –prefix anl _run1_warped_volreg -heptic -zpad 4 -1Dfile motionfile1.1D -1Dmatrix_save matrix1.1D anl_run1_warped+orig'[0..134]'

>1dplot motionfile1.1D

>3dToutcount -automask anl_run1_warped_volreg+orig>aftermc1.1D

>1dplot aftermc1.1D

(Nudge plugin in GUI)

>3dFourier -prefix anl_run1_warped_volreg_fourier -lowpass 0.2 -retrend anl_run1_warped_volreg+orig

>3dmerge -1blur_fwhm 6 -doall -prefix anl_run1_warped_volreg _merged anl_run1_warped_volreg_fourier+orig

>3dAutomask -prefix mask_anl_run1_volreg_merged anl_run1_warped _volreg_merged+ orig

>3dTstat -prefix mean_anl_run1_volreg_merged anl_run1_warped _volreg_merged+orig

>3dcalc -a anl_run1_warped_volreg_merged+orig –b mean_anl_run1 _volreg_merged+orig -c mask_anl_run1_volreg_merged+orig -expr '((a-b)/b*100)*c' -prefix last_anl_run1_volreg _merged

Run 2:

>3dWarp -deoblique -prefix anl_run2_warped anl_run2+orig

> 3dToutcount -automask anl_run2_warped+orig>outlier2.1D

>1dplot outlier2.1D

>3dAllineate -base anl_anat_warped+orig -source anl_run2_warped +orig'[40]'

>3dvolreg -verbose -base anl_run2_warped+orig'[40]' -prefix anl _run2_warped_volreg -tshift -heptic -zpad 4 -1Dfile motionfile2 .1D -1Dmatrix_save matrix2.1D anl_run2_warped+orig'[0..134]'

>1dplot motionfile2.1D

>3dToutcount -automask anl_run2_warped_volreg+orig>aftermc2.1D

>1dplot aftermc2.1D

(Nudge plugin)

>3dFourier -prefix anl_run2_warped_volreg_fourier -lowpass 0.2 -retrend anl_run2_warped_volreg+orig

>3dmerge -1blur_fwhm 6 -doall -prefix anl_run2_warped_volreg _merged anl_run2_warped_volreg_fourier+orig

>3dAutomask -prefix mask_anl_run2_volreg_merged anl_run2_warped _volreg_merged+orig

>3dTstat -prefix mean_anl_run2_volreg_merged anl_run2_warped _volreg_merged+orig

>3dcalc -a anl_run2_warped_volreg_merged+orig -b mean_anl_run2_ volreg_merged+orig -c mask_anl_run2_volreg_merged+orig -expr '((a-b)/b*100)*c' –prefix last_anl_run2_volreg _merged

Run 3:

>3dWarp -deoblique -prefix anl_run1_warped anl_run3+orig

>3dToutcount -automask anl_run3_warped+orig>outlier3.1D

>1dplot outlier3.1D

>3dAllineate -base anl_anat_warped+orig –source anl_run3_warped +orig'[40]'

>3dvolreg -verbose -base anl_run3_warped+orig'[40]' –prefix anl _run3_warped_volreg -heptic -zpad 4 -1Dfile motionfile3.1D -1Dmatrix_save matrix3.1D anl_run3_warped+orig'[0..134]'

>1dplot motionfile3.1D

>3dToutcount -automask anl_run3_warped_volreg+orig>aftermc3.1D

>1dplot aftermc3.1D

(Nudge plugin in GUI)

>3dFourier -prefix anl_run3_warped_volreg_fourier -lowpass 0.2 -retrend anl_run3_warped_volreg+orig

>3dmerge -1blur_fwhm 6 -doall -prefix anl_run3_warped_volreg _merged anl_run3_warped_volreg_fourier+orig

>3dAutomask -prefix mask_anl_run3_volreg_merged anl_run3_warped _volreg_merged+ orig

>3dTstat -prefix mean_anl_run3_volreg_merged anl_run3_warped _volreg_merged+orig

>3dcalc -a anl_run3_warped_volreg_merged+orig -b mean_anl_run3_ volreg_merged+orig -c mask_anl_run3_volreg_merged+orig -expr '((a-b)/b*100)*c' –prefix last_anl_run3_volreg _merged

Run 4:

>3dWarp -deoblique -prefix anl_run4_warped anl_run4+orig

>3dToutcount -automask anl_run4_warped+orig>outlier4.1D

>1dplot outlier4.1D

```
>3dAllineate -base anl_anat_warped+orig –source anl_run4_warped +orig'[65]'

>3dvolreg -verbose -base anl_run4_warped+orig'[65]' –prefix anl _run4_warped_volreg -heptic -zpad 4 -1Dfile motionfile4.1D -1Dmatrix_save matrix4.1D anl_run4_warped+orig'[0..134]'

>1dplot motionfile4.1D

>3dToutcount -automask anl_run4_warped_volreg+orig>aftermc4.1D

>1dplot aftermc4.1D
```

(Nudge plugin in GUI)

```
>3dFourier -prefix anl_run4_warped_volreg_fourier -lowpass 0.2 -retrend anl_run4_warped_volreg+orig

>3dmerge -1blur_fwhm 6 -doall -prefix anl_run4_warped_volreg _merged anl_run4_warped_volreg_fourier+orig

>3dAutomask -prefix mask_anl_run4_volreg_merged anl_run4_warped _volreg_merged+orig

>3dTstat -prefix mean_anl_run4_volreg_merged anl_run4_warped _volreg_merged+orig

>3dcalc -a anl_run4_warped_volreg_merged+orig –b mean_anl_run4 _volreg_merged+orig -c mask_anl_run4_volreg_merged+orig -expr '((a-b)/b*100)*c' -prefix last_anl_run4_volreg _merged
```

Run 5:

```
>3dWarp -deoblique -prefix anl_run5_warped anl_run5+orig

>3dToutcount -automask anl_run5_warped+orig>outlier5.1D

>1dplot outlier5.1D

>3dAllineate -base anl_anat_warped+orig –source anl_run5_warped +orig'[60]'

>3dvolreg -verbose -base anl_run5_warped+orig'[60]' –prefix anl _run5_warped_volreg -heptic -zpad 4 -1Dfile motionfile5.1D -1Dmatrix_save matrix5.1D anl_run5_warped+orig'[0..134]'

>1dplot motionfile5.1D

>3dToutcount -automask anl_run5_warped_volreg+orig>aftermc5.1D

>1dplot aftermc5.1D
```

(Nudge plugin in GUI)

>3dFourier -prefix anl_run5_warped_volreg_fourier -lowpass 0.2 -retrend anl_run5_warped_volreg+orig

>3dmerge -1blur_fwhm 6 -doall -prefix anl_run5_warped_volreg _merged anl_run5_warped_volreg_fourier+orig

>3dAutomask -prefix mask_anl_run5_volreg_merged anl_run5_warped _volreg_merged+orig

>3dTstat -prefix mean_anl_run5_volreg_merged anl_run5_warped _volreg_merged+orig

>3dcalc -a anl_run5_warped_volreg_merged+orig –b mean_anl_run5 _volreg_merged+orig -c mask_anl_run5_volreg_merged+orig -expr '((a-b)/b*100)*c' -prefix last_anl_run5_volreg _merged

Run 6:

>3dWarp -deoblique -prefix anl_run6_warped anl_run6+orig

>3dToutcount -automask anl_run6_warped+orig>outlier6.1D

>1dplot outlier6.1D

>3dAllineate -base anl_anat_warped+orig –source anl_run6_warped +orig'[75]'

>3dvolreg -verbose -base anl_run6_warped+orig'[75]' –prefix anl _run6_warped_volreg -heptic -zpad 4 -1Dfile motionfile6.1D -1Dmatrix_save matrix6.1D anl_run6_warped+orig'[0..134]'

>1dplot motionfile6.1D

>3dToutcount -automask anl_run6_warped_volreg+orig>aftermc6.1D

>1dplot aftermc6.1D

(Nudge plugin in GUI)

>3dFourier -prefix anl_run6_warped_volreg_fourier -lowpass 0.2 -retrend anl_run6_warped_volreg+orig

>3dmerge -1blur_fwhm 6 -doall -prefix anl_run6_warped_volreg _merged anl_run6_warped_volreg_fourier+orig

>3dAutomask -prefix mask_anl_run6_volreg_merged anl_run6_warped _volreg_merged+orig

>3dTstat -prefix mean_anl_run6_volreg_merged anl_run6_warped _volreg_merged+orig

>3dcalc -a anl_run6_warped_volreg_merged+orig –b mean_anl_run6 _volreg_merged+orig -c mask_anl_run6_volreg_merged+orig -expr '((a-b)/b*100)*c' -prefix last_anl_run6_volreg _merged

Computation of Individual Activity Maps:

waver -GAM -dt 2 -input task.txt>task_waver.1D

3dDeconvolve -polort 3 -input last_anl_run1_volreg_merged+orig
-num_stimts 1 -stim_file 1 'task_waver.1D' -stim_label 1 control
-tout -fout -bucket f_stats_anl_right_control -fitts fitts_control_anl_right_control

3dDeconvolve -polort 3 -input last_anl_run2_volreg_merged+orig -num_stimts 1 -stim_file 1 'task_waver.1D' -stim_label 1 c ontrol -tout -fout -bucket f_stats_anl_left_control -fitts fitts_control_anl_left_control

3dDeconvolve -polort 3 -input last_anl_run3_volreg_merged+orig -num_stimts 1 -stim_file 1 'task_waver.1D' -stim_label 1 tactile_linebisect -tout -fout -bucket f_stats_anl_right_tactile -fitts fitts_control_anl_right_tactile

3dDeconvolve -polort 3 -input last_anl_run4_volreg_merged+orig -num_stimts 1 -stim_file 1 'task_waver.1D' -stim_label 1 tactile_linebisect -tout -fout -bucket f_stats_anl_left_tactile -fitts fitts_control_anl_left_tactile

3dDeconvolve -polort 3 -input last_anl_run5_volreg_merged+orig -num_stimts 1 -stim_file 1 'task_waver.1D' -stim_label 1 visual_linebisect -tout -fout -bucket f_stats_anl_right_visual -fitts fitts_control_anl_right_visual

3dDeconvolve -polort 3 -input last_anl_run6_volreg_merged+orig -num_stimts 1 -stim_file 1 'task_waver.1D' -stim_label 1 visual_linebisect -tout -fout -bucket f_stats_anl_left_visual -fitts fitts_control_anl_left_visual

Talairach Transformation:

3drefit -markers anl_anat_warped+orig

-adwarp -apar anl_anat_warped+tlrc –dpar f_stats_anl_right _control+orig

adwarp -apar anl_anat_warped+tlrc -dpar f_stats_anl_left_control +orig

adwarp -apar anl_anat_warped+tlrc -dpar f_stats_anl_right_tactile +orig

adwarp -apar anl_anat_warped+tlrc -dpar f_stats_anl_left_tactile
+orig

adwarp -apar anl_anat_warped+tlrc -dpar f_stats_anl_right_visual +orig

adwarp -apar anl_anat_warped+tlrc -dpar f_stats_anl_left_visual +orig

3dcalc -a anl_anat_warped+tlrc -b bll_anat_warped+tlrc -c ece _anat_warped+tlrc -d erdm_anat_warped+tlrc -e esn_anat_warped +tlrc -f frk_anat_warped+tlrc -g prl_anat_warped+tlrc -h srdr _anat_warped+tlrc -j zhr_anat_warped+tlrc -expr '((a+b+c+d+e+f+g +h+j)/9)' -prefix mean_anat_warped

Group Analysis:

3dANOVA:

Tactile Line bisection versus Motor Sweep:

```
#!/bin/tcsh
#-a motorVSlinebisect -b rightvsleft -c subjects

3dANOVA3 -type 4 -alevels 2 -blevels 2 -clevels 9
-dset 1 1 1 f_stats_anl_right_control+tlrc'[2]'
-dset 1 1 2 f_stats_esn_right_control+tlrc'[2]'
-dset 1 1 3 f_stats_srdr_right_control+tlrc'[2]'
-dset 1 1 4 f_stats_bll_right_control+tlrc'[2]'
-dset 1 1 5 f_stats_frk_right_control+tlrc'[2]'
-dset 1 1 6 f_stats_ece_right_control+tlrc'[2]'
-dset 1 1 7 f_stats_prl_right_control+tlrc'[2]'
-dset 1 1 8 f_stats_erdm_right_control+tlrc'[2]'
-dset 1 1 9 f_stats_zhr_right_control+tlrc'[2]'

-dset 1 2 1 f_stats_anl_left_control+tlrc'[2]'
-dset 1 2 2 f_stats_esn_left_control+tlrc'[2]'
-dset 1 2 3 f_stats_srdr_left_control+tlrc'[2]'
-dset 1 2 4 f_stats_bll_left_control+tlrc'[2]'
-dset 1 2 5 f_stats_frk_left_control+tlrc'[2]'
-dset 1 2 6 f_stats_ece_left_control+tlrc'[2]'
-dset 1 2 7 f_stats_prl_left_control+tlrc'[2]'
-dset 1 2 8 f_stats_erdm_left_control+tlrc'[2]'
-dset 1 2 9 f_stats_zhr_left_control+tlrc'[2]'

-dset 2 1 1 f_stats_anl_right_tactile+tlrc'[2]'
-dset 2 1 2 f_stats_esn_right_tactile+tlrc'[2]'
-dset 2 1 3 f_stats_srdr_right_tactile+tlrc'[2]'
-dset 2 1 4 f_stats_bll_right_tactile+tlrc'[2]'

-dset 2 1 5 f_stats_frk_right_tactile+tlrc'[2]'
-dset 2 1 6 f_stats_ece_right_tactile+tlrc'[2]'
-dset 2 1 7 f_stats_prl_right_tactile+tlrc'[2]'
-dset 2 1 8 f_stats_erdm_right_tactile+tlrc'[2]'
-dset 2 1 9 f_stats_zhr_right_tactile+tlrc'[2]'
```

```
-dset 2 2 1 f_stats_anl_left_tactile+tlrc'[2]'
-dset 2 2 2 f_stats_esn_left_tactile+tlrc'[2]'
-dset 2 2 3 f_stats_srdr_left_tactile+tlrc'[2]'
-dset 2 2 4 f_stats_bll_left_tactile+tlrc'[2]'
-dset 2 2 5 f_stats_frk_left_tactile+tlrc'[2]'
-dset 2 2 6 f_stats_ece_left_tactile+tlrc'[2]'
-dset 2 2 7 f_stats_prl_left_tactile+tlrc'[2]'
-dset 2 2 8 f_stats_erdm_left_tactile+tlrc'[2]'
-dset 2 2 9 f_stats_zhr_left_tactile+tlrc'[2]'
```

-fa motor_fstat -fb hand_fstat -fab motor_hand_interaction -aBcontr -1 1 : 1 Motor_RightvsLinebisect_Right -aBcontr -1 1 : 2 Motor_LeftvsLinebisect_Left -Abcontr 2 : 1 -1 Right_linebisect vsLeft_linebisect -Abcontr 1 : 1 -1 Right_motorvsLeft_motor -abmean 1 1 Rightmotor_mean -abmean 1 2 Leftmotor_mean -abmean 2 1 Rightlinebisect_mean -abmean 2 2 Leftlinebisect_mean -Abdiff 1 : 1 2 Right_motor-Left_motor -Abdiff 2 : 1 2 Right_linebisect-left_linebisect -aBdiff 2 1 : 1 Right_linebisect-Right_motor -aBdiff 2 1 : 2 Left_linebisect-Left_motor -bucket 2by2_anova _tactile_tstat

<u>Visual Line Bisection versus Motor Sweep:</u>

```
#!/bin/tcsh
#-a motorVSlinebisect -b rightvsleft -c subjects

3dANOVA3 -type 4 -alevels 2 -blevels 2 -clevels 9
-dset 1 1 1 f_stats_anl_right_control+tlrc'[2]'
-dset 1 1 2 f_stats_esn_right_control+tlrc'[2]'
-dset 1 1 3 f_stats_srdr_right_control+tlrc'[2]'
-dset 1 1 4 f_stats_bll_right_control+tlrc'[2]'
-dset 1 1 5 f_stats_frk_right_control+tlrc'[2]'
-dset 1 1 6 f_stats_ece_right_control+tlrc'[2]'
-dset 1 1 7 f_stats_prl_right_control+tlrc'[2]'
-dset 1 1 8 f_stats_erdm_right_control+tlrc'[2]'
-dset 1 1 9 f_stats_zhr_right_control+tlrc'[2]'

-dset 1 2 1 f_stats_anl_left_control+tlrc'[2]'
-dset 1 2 2 f_stats_esn_left_control+tlrc'[2]'
-dset 1 2 3 f_stats_srdr_left_control+tlrc'[2]'
-dset 1 2 4 f_stats_bll_left_control+tlrc'[2]'
-dset 1 2 5 f_stats_frk_left_control+tlrc'[2]'
-dset 1 2 6 f_stats_ece_left_control+tlrc'[2]'
-dset 1 2 7 f_stats_prl_left_control+tlrc'[2]'
-dset 1 2 8 f_stats_erdm_left_control+tlrc'[2]'
-dset 1 2 9 f_stats_zhr_left_control+tlrc'[2]'
-dset 2 1 1 f_stats_anl_right_visual+tlrc'[2]'
-dset 2 1 2 f_stats_esn_right_visual+tlrc'[2]'
-dset 2 1 3 f_stats_srdr_right_visual+tlrc'[2]'
-dset 2 1 4 f_stats_bll_right_visual+tlrc'[2]'
-dset 2 1 5 f_stats_frk_right_visual+tlrc'[2]'
-dset 2 1 6 f_stats_ece_right_visual+tlrc'[2]'
```

-dset 2 1 7 f_stats_prl_right_visual+tlrc'[2]'
-dset 2 1 8 f_stats_erdm_right_visual+tlrc'[2]'
-dset 2 1 9 f_stats_zhr_right_visual+tlrc'[2]'

-dset 2 2 1 f_stats_anl_left_visual+tlrc'[2]'
-dset 2 2 2 f_stats_esn_left_visual+tlrc'[2]'
-dset 2 2 3 f_stats_srdr_left_visual+tlrc'[2]'
-dset 2 2 4 f_stats_bll_left_visual+tlrc'[2]'
-dset 2 2 5 f_stats_frk_left_visual+tlrc'[2]'
-dset 2 2 6 f_stats_ece_left_visual+tlrc'[2]'
-dset 2 2 7 f_stats_prl_left_visual+tlrc'[2]'
-dset 2 2 8 f_stats_erdm_left_visual+tlrc'[2]'
-dset 2 2 9 f_stats_zhr_left_visual+tlrc'[2]'

-fa motor_fstat -fb hand_fstat -fab motor_hand_interaction -aBcontr -1 1 : 1 Motor_RightvsLinebisect_Right -aBcontr -1 1 : 2 Motor_LeftvsLinebisect_Left -Abcontr 2 : 1 -1 Right_linebisect vsLeft_linebisect -Abcontr 1 : 1 -1 Right_motorvsLeft_motor -abmean 1 1 R ightmotor_mean -abmean 1 2 Leftmotor_mean -abmean 2 1 Rightlinebisect_mean -abmean 2 2 L eftlinebisect_mean -Abdiff 1 : 1 2 R ight_motor-Left_motor -Abdiff 2 : 1 2 Right_linebisect-left_linebisect -aBdiff 2 1 : 1 Right_linebisect-Right_motor -aBdiff 2 1 : 2 Left_linebisect-Left_motor -bucket 2by2_anova _visual_tstat

<u>Tactile versus Visual Line Bisection:</u>

#!/bin/tcsh
#-a tactileVSvisual -b rightvsleft -c subjects

3dANOVA3 -type 4 -alevels 2 -blevels 2 -clevels 9
-dset 1 1 1 f_stats_anl_right_tactile+tlrc'[2]'
-dset 1 1 2 f_stats_esn_right_tactile+tlrc'[2]'
-dset 1 1 3 f_stats_srdr_right_tactile+tlrc'[2]'
-dset 1 1 4 f_stats_bll_right_tactile+tlrc'[2]'
-dset 1 1 5 f_stats_frk_right_tactile+tlrc'[2]'
-dset 1 1 6 f_stats_ece_right_tactile+tlrc'[2]'
-dset 1 1 7 f_stats_prl_right_tactile+tlrc'[2]'
-dset 1 1 8 f_stats_erdm_right_tactile+tlrc'[2]'
-dset 1 1 9 f_stats_zhr_right_tactile+tlrc'[2]'

-dset 1 2 1 f_stats_anl_left_tactile+tlrc'[2]'
-dset 1 2 2 f_stats_esn_left_tactile+tlrc'[2]'

-dset 1 2 3 f_stats_srdr_left_tactile+tlrc'[2]'
-dset 1 2 4 f_stats_bll_left_tactile+tlrc'[2]'
-dset 1 2 5 f_stats_frk_left_tactile+tlrc'[2]'
-dset 1 2 6 f_stats_ece_left_tactile+tlrc'[2]'
-dset 1 2 7 f_stats_prl_left_tactile+tlrc'[2]'
-dset 1 2 8 f_stats_erdm_left_tactile+tlrc'[2]'
-dset 1 2 9 f_stats_zhr_left_tactile+tlrc'[2]'

-dset 2 1 1 f_stats_anl_right_visual+tlrc'[2]'
-dset 2 1 2 f_stats_esn_right_visual+tlrc'[2]'
-dset 2 1 3 f_stats_srdr_right_visual+tlrc'[2]'
-dset 2 1 4 f_stats_bll_right_visual+tlrc'[2]'
-dset 2 1 5 f_stats_frk_right_visual+tlrc'[2]'
-dset 2 1 6 f_stats_ece_right_visual+tlrc'[2]'
-dset 2 1 7 f_stats_prl_right_visual+tlrc'[2]'
-dset 2 1 8 f_stats_erdm_right_visual+tlrc'[2]'
-dset 2 1 9 f_stats_zhr_right_visual+tlrc'[2]'

-dset 2 2 1 f_stats_anl_left_visual+tlrc'[2]'
-dset 2 2 2 f_stats_esn_left_visual+tlrc'[2]'
-dset 2 2 3 f_stats_srdr_left_visual+tlrc'[2]'
-dset 2 2 4 f_stats_bll_left_visual+tlrc'[2]'
-dset 2 2 5 f_stats_frk_left_visual+tlrc'[2]'
-dset 2 2 6 f_stats_ece_left_visual+tlrc'[2]'
-dset 2 2 7 f_stats_prl_left_visual+tlrc'[2]'
-dset 2 2 8 f_stats_erdm_left_visual+tlrc'[2]'
-dset 2 2 9 f_stats_zhr_left_visual+tlrc'[2]'

-fa sense_fstat -fb hand_fstat -fab sense_hand_interaction -aBcontr 1 -1 : 1 Tactile_RightvsVisual_Right -aBcontr 1 -1 : 2 Tactile_LeftvsVisual_Left -Abcontr 2 : 1 -1 Right_Visualvs Left_Visual -Abcontr 1 : 1 -1 Right_TactilevsLeft_Tactile -abmean 1 1 Right_Tactile_mean -abmean 1 2 Left_Tactile_mean -abmean 2 1 R ight_Visual_mean -abmean 2 2 Left_Visual_mean -Abdiff 1 : 1 2 R ight_Tactile-Left_Tactile -Abdiff 2 : 1 2 Right_Visual-left_Visual -aBdiff 1 2 : 1 Right_Tactile-Right_Visual -aBdiff 1 2 : 2 Left_Tactile-Left_Visual -bucket 2by2_anova_tactilevsvisual _tstat

Post Processing:

Alphasim:

AlphaSim -nxyz 64 64 34 -dxyz 3 3 4 -iter 10000 -pthr 0.001 -fwhm 6 -rmm 5.5 -quiet -fast -approx -out alpha_p0.001.out

Clustering:

#!/bin/tcsh
pthr=0.001, thr=4.526 , cls=24
mean values, tactilevsmotor, visualvsmotor, tactilevsvisual

3dclust -1Dformat -nosum -1dindex 34 -1tindex 35 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24 /home/burcin/linebisect/Group/2by2_anova_tactile_tstat+tlrc.HEAD>clust_right_motor_mean.out

3dclust -1Dformat -nosum -1dindex 36 -1tindex 37 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_tactile_tstat+tlrc.HEAD>clust_left_motor_mean
.out

3dclust -1Dformat -nosum -1dindex 40 -1tindex 41 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_tactile_tstat+tlrc.HEAD>clust_left_tactile_mea
n.out

3dclust -1Dformat -nosum -1dindex 38 -1tindex 39 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_tactile_tstat+tlrc.HEAD>clust_right_tactile_me
an.out

3dclust -1Dformat -nosum -1dindex 38 -1tindex 39 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_visual_tstat+tlrc.HEAD>clust_right_visual_mea
n.out

3dclust -1Dformat -nosum -1dindex 40 -1tindex 41 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_visual_tstat+tlrc.HEAD>clust_left_visual_mean
.out

3dclust -1Dformat -nosum -1dindex 20 -1tindex 21 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_tactile_tstat+tlrc.HEAD>clust_left_tactilevsmot
or.out

3dclust -1Dformat -nosum -1dindex 18 -1tindex 19 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_tactile_tstat+tlrc.HEAD>clust_right_tactilevsm
otor.out

3dclust -1Dformat -nosum -1dindex 18 -1tindex 19 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_tactilevsvisual_tstat+tlrc.HEAD>clust_right_tac
tilevsvisual.out

3dclust -1Dformat -nosum -1dindex 20 -1tindex 21 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_tactilevsvisual_tstat+tlrc.HEAD>clust_left_tacti
levsvisual.out

3dclust -1Dformat -nosum -1dindex 20 -1tindex 21 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24
/home/burcin/linebisect/Group/2by2_anova_visual_tstat+tlrc.HEAD>clust_left_motorvsvisu
al.out

3dclust -1Dformat -nosum -1dindex 18 -1tindex 19 -1noneg -1clip 4.526 -2thresh -4.526 4.526 -dxyz=1 1.75 24 /home/burcin/linebisect/Group/2by2_anova_visual_tstat+tlrc.HEAD>clust_right_motorvsvisual.out

APPENDIX J

APPROVE OF LOCAL ETHICAL COMMITEE

ANKARA ÜNİVERSİTESİ TIP FAKÜLTESİ KLİNİK ARAŞTIRMALAR ETİK KURUL KARARI

BAŞVURU BİLGİLERİ	ARAŞTIRMANIN AÇIK ADI	Somatosensör çizgi bölme testinin beyindeki aktiivitesinin araştırılması:Bir fMRG çalışması			
	ARAŞTIRMA PROTOKOL KODU				
	KOORDİNATÖR/SORUMLU ARAŞTIRMACI UNVANI/ADI/SOYADI	Yrd.Doç.Dr.Didem Gökçay			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ UZMANLIK ALANI	Nörobilim/Kognitif Nörobilim, Nörogörüntüleme			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ BULUNDUĞU MERKEZ	Ortadoğu Teknik Üniversitesi Enformatik Enstitüsü Sağlık Bilişimi Anabilim Dalı			
	DESTEKLEYİCİ				
	DESTEKLEYİCİNİN YASAL TEMSİLCİSİ				
	ARAŞTIRMANIN FAZI	FAZ 1	☐		
		FAZ 2	☐		
		FAZ 3	☐		
		FAZ 4	☐		
	ARAŞTIRMANIN TÜRÜ	Yeni Bir Endikasyon	☐		
		Yüksek Doz Araştırması	☐		
		Diğer ise belirtiniz: Laboratuar Çalışması			
	ARAŞTIRMAYA KATILAN MERKEZLER	TEK MERKEZ ☐	ÇOK MERKEZLİ ☒	ULUSAL ☒	ULUSLARARASI ☐

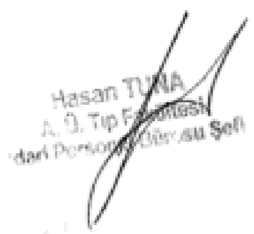

Figure 51 Etik Kurul Onayı 1. Sayfa

DEĞERLENDİRİLEN BELGELER	Belge Adı	Tarihi	Versiyon Numarası	Dili
	ARAŞTIRMA PROTOKOLÜ			Türkçe ☐ İngilizce ☐ Diğer ☐
	BİLGİLENDİRİLMİŞ GÖNÜLLÜ OLUR FORMU			Türkçe ☐ İngilizce ☐ Diğer ☐
	OLGU RAPOR FORMU			Türkçe ☐ İngilizce ☐ Diğer ☐
	ARAŞTIRMA BROŞÜRÜ			Türkçe ☐ İngilizce ☐ Diğer ☐

DEĞERLENDİRİLEN DİĞER BELGELER	Belge Adı		Açıklama
	TÜRKÇE ETİKET ÖRNEĞİ	☐	
	SİGORTA	☐	
	ARAŞTIRMA BÜTÇESİ	☐	
	BİYOLOJİK MATERYEL TRANSFER FORMU	☐	
	HASTA KARTI/GÜNLÜKLERİ	☐	
	İLAN	☐	
	YILLIK BİLDİRİM	☐	
	SONUÇ RAPORU	☐	
	GÜVENLİLİK BİLDİRİMLERİ	☐	
	DİĞER:	☐	

KARAR BİLGİLERİ		
	Karar No:10-302-12	**Tarih: 11 Haziran 2012**
	Yukarıda bilgileri verilen klinik araştırma başvuru dosyası ile ilgili belgeler araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri ile bilgilendirilmiş gönüllü olur formu incelenmiş, **ancak "Dışlama Kriterleri içinde MRI'nın kontraendike (yasak) olduğu durumların maddeler halinde hem yaklaşım ve yöntemlerde hem Bilgilendirilmiş Gönüllü Olur Formunda yazılması koşuluyla**, çalışmanın başvuru dosyasında belirtilen merkezlerde gerçekleştirilmesinde etik ve bilimsel sakınca bulunmadığına toplantıya katılan Etik Kurul üye tam sayısının salt çoğunluğu ile karar verilmiştir.	

Figure 52 Etik Kurul Onayı 2. Sayfa