# VISUAL INFORMATION PROCESSING IN THE PARIETAL LOBE

Thesis submitted for the degree of Doctor of Philosophy

**School of Psychology and Clinical Language Sciences**
**Centre for Integrative Neuroscience and Neurodynamics**

Nicolò Biagi

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## Declaration

I confirm that this is my own work and the use of all material from other sources has been properly and fully acknowledged. In paper two, students assisted with data collection (Karen Leeves and Kate Leslie).

The research presented in chapters 2-4 is in preparation for submission.

Biagi, N., Goodwin, C.  & Field, D. T. (submitted). The role of the Superior Parietal Lobule in the perception of the visual separation between stimuli: a rTMS study.

Biagi, N. & Field, D. T. (in preparation). The role of the Superior Parietal Lobule in the Müller-Lyer illusion: a TMS study.

Biagi, N. & Field, D. T. (in preparation). Using TMS to investigate the role of the Superior Parietal Lobule and the Front Eye Field in the perception of spatial separation

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# Abstract

The Superior Parietal Lobule is a region of the brain that has been implicated in a number of high-level cognitive functions, including shifting spatial attention between locations, the perception of heading direction and path of travel during locomotion, and motion tracking under attentional load. The wide range of cognitive functions linked to this region does not align with the high specificity normally seen in the brain, and therefore it might be possible that the SPL supports a lower-level function that is engaged in a wide range of cognitive tasks. Here we investigate the proposal that the lower-level function involves the perception of the 2D visual distances between objects. To test this hypothesis, we targeted the SPL with both high-frequency online repetitive Transcranial Magnetic Stimulation (rTMS) and offline continuous theta burst stimulation (cTBS) in order to explore the role played by this region in the perception of 2D visual space. We achieved this over three studies. In the first, we delivered online rTMS over the left SPL while participants performed a psychophysical task measuring the precision of their ability to judge the distance between objects. In the second, we explored the effect of delivering offline cTBS over the left SPL in relation to the effect of the Muller-Lyer illusion on the perception of the length of a line, as well as its effect on saccade amplitudes. In the final study, we broadened the investigation to also explore a possible role of the frontal eye field (FEF) in the perception of 2D visual distances. We explored the effect of delivering offline cTBS over the right SPL or the right Frontal Eye Field (FEF) on a range of tasks thought to rely on processing of visual distance including interception of a moving target, the magnitude of the Muller-Lyer illusion, amplitudes for reflexive, voluntary, and memory-guided saccades made to Muller-Lyer and control stimuli, and a reaction time control task. Overall, we observed no effect of rTMS and cTBS on the experimental tasks in Study 1 and Study 2, respectively, although rTMS did unexpectedly have a significant effect on the control task in Study 1. In Study 3, while we observed an effect of cTBS over the SPL for a subset of the experimental tasks, the same effect was observed when cTBS was delivered over the right FEF, which left us unable to rule out the possibility that the effects were a result of testing order rather than cTBS. Overall, the results obtained in this thesis do not fully elucidate the roles of the SPL or the FEF in the perception of 2D visual space, and therefore further research is suggested.

# Chapter 1. Introduction

## 1.1 Introduction

In every second of our waking existence, we perform 3 to 4 eye movements, i.e., saccades. These are necessary for us to be aware of the visual environment that surround us. These eye movements are so quick that their trajectories need to be programmed before they are executed. This means that the eye movements are a ballistic type of action, as opposed to closed -loop actions such as reach to grasp. The oculomotor system predicts where a saccade would land, and it can check the accuracy only after it has been executed. The cerebellum is involved in this mechanism of accuracy-checking of saccades (Panouillères, Neggers, Gutteling, Salemme, van der Stigchel, van der Geest, Frens, & Pélisson, 2012). But how do we know how big an amplitude of a given saccade needs to be in order to move our eyes from point A on the visual field to point B? How do we know the visual angle between point A and point B? In the three experiments presented in this thesis we will try to understand where the perception of visual angle arises in the brain.

A potential answer could be that the visual angle between objects in the visual field is a direct product of the retinotopic maps present in V1 and V2 in the occipital cortex (Figure 1.1), but this is not the case. The neurons in V1 encode stimulus positions (i.e., the retinotopic maps) but they are not responsible for computing the visual angle between different stimuli in the visual field (Schwarzkopf, 2015).

Another possible idea is that information about positions of objects and other salient features of the visual scene such as edges contained in retinotopic maps is sent to another area of the brain (Superior Parietal Lobule in Figure 1.1), that does higher-level visual processing (Biagi, Goodwin, & Field, 2021 submitted; Harvey, Fracasso, Petridou, & Dumoulin, 2015; Schwarzkopf, 2015). Alternatively, it could be that the visual sensory input is initially used to generate motor plans, which are inherently spatial, and then those spatial motor plans are used to generate spatial perception.

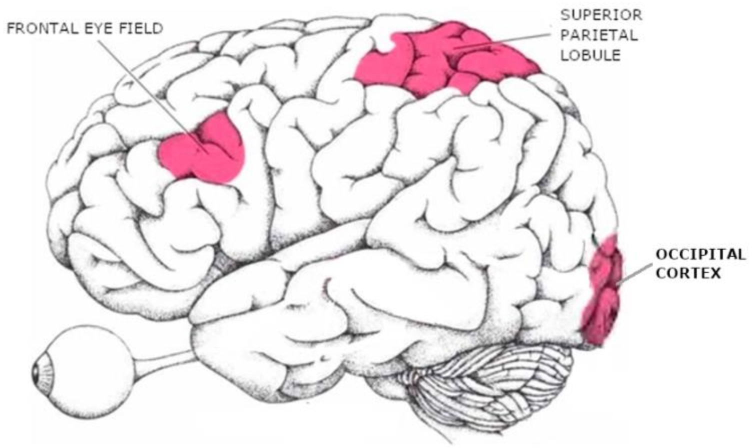

*Figure 1.1 - Location of Frontal Eye Field, Superior Parietal Lobule, and Occipital Cortex in the brain*

A recent theory proposed by Musseler and Van der Heijden (2004) suggested that our perception arises from two sources: a non-visual motor map and a visual sensory map. The visual sensory map provides the identity of what is present in the visual field, while the non-visual motor map incudes the motor movements needed to bring currently viewed objects into foveal vision. Our final perception is a product of the combination of these two maps.

Evidence for this theory comes from studies like the one conducted by Zimmermann and Lappe (2010), where using the double-step paradigm (McLaughlin, 1967) they were capable of inducing saccade adaptation on the motor map which induced an effect on the visual sensory map. The saccade adaptation was induced by asking participant to move their eyes from a starting fixation point to the location of a target, and consistently moving the location of a specific target while the participants were mid-saccade. Participants did not notice the misplacement of the target because visual sensitivity is less accurate during saccade execution (McLaughin, 1967), but had to deploy a corrective saccade once their visual system noticed the error between the landing of the saccade and the final location of the target. It was noticed that if the misplacement was constant and repeated several time, it was possible to induce the visual system to land the saccade directly on the final location of the target, instead of the original one, generating an adaptation. If the target was consistently moved towards the initial fixation point, we can talk of inward adaptation, while if the target was consistently moved further away from the initial fixation point, we can talk of outward adaptation.

After successfully obtaining saccade adaptation, participants were asked to fixate a point on the screen and then judge the location of a stimulus (i.e., probe) that was briefly flashed on the screen. It was found that the probe was mislocated in a direction consistent with the saccade adaptation (Zimmermann & Lappe, 2010). The fact that the probe was mislocated is clear evidence that the non-visual motor map and the visual map are highly interconnected.

In the study mentioned above (i.e., Zimmermann & Lappe, 2010), it was not possible to distinguish whether the error in probe location was due to the saccade adaptation or due to the incongruency between the landing point of the saccade and the final location of the stimulus, which was presented before identifying the location of the probe. A study conducted by Garaas and Pomplun (2011) addressed this problem, by presenting a large persistent cross on the screen and ask participants to compare the lengths of the vertical and horizontal component of the cross before and after saccade adaptation. They were able to show that after vertical inward adaptation the vertical component of the cross was perceived shorter and after vertical outwards adaptation it was perceived as longer. A similar effect was also found for horizontal outward adaptation. These findings clearly explain that the change that occurs in the non-visual motor map after saccade adaptation has also a clear effect on the visual motor map, proving that the two maps are highly connected.

Another example of how the visual map can be affected by the non-visual motor map is represent by the Müller-Lyer illusion (Figure 1.2). In the first stimulus, Figure 1.1A, two outwardly turned wings are attached to each end of the horizontal line, while the second stimulus, Figure 1.1B, two inwardly turned wings are attached to each end of the horizontal line. The horizontal shaft composing the stimulus presented on the top is perceived as longer than the horizontal shaft presented in the stimulus below it, even if they have the same physical length (Müller-Lyer, 1889).

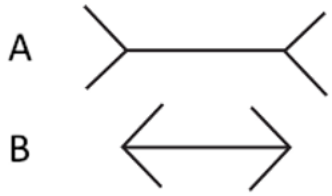

*Figure 1.2 – Müller-Lyer figures.*

One possible explanation for the fact that the shaft presented on top is perceived as longer, was given by Coren (1986). He suggested that the presence of the wings attached to the end of the horizontal shaft affects the amplitude of the eye movement plans made to move the eye from one end of the shaft to the other, and these eye movement plans in turn determines the perceived length of the horizontal shaft. This proposal is based on the fact that when a nontarget stimulus is placed in the proximity of a target stimulus, eye movements are affected by it: instead of landing directly on target (which happens in the absence of the nontarget stimulus), the eye movements tend to land in between the location of the target and the one of the nontarget (Bruell, & Albee, 1955, Findlay, 1981).

It is proposed that the visual system does that because its aim is to put the relevant information on the visual field directly in the area of the fovea (where the visual acuity is optimal), and by placing the end point of the eye movement between the target and the nontarget it assures the best visual acuity for both stimuli (Coren, 1986). This phenomenon is known as 'centre of gravity effect' (Findlay, 1982, He & Kowler, 1989) and is a plausible explanation for the biased eye movements that the Müller-Lyer illusion evokes. The outwardly turned wings (Figure 1.2A) drag the end point of the saccade away from the horizontal shaft increasing the amplitude of the eye movements, while the inwardly turned wings (Figure 1.2B) make the end point of the saccade end within the horizontal shaft, reducing the amplitude of the eye movement. Thus, the final eye movements elicited from the two stimuli are different in amplitude.

To relate these findings to the theory proposed by Musseler and Van der Heijden (2004) we can say that the centre of gravity effect has an effect on the non-visual motor map, which in turn influences the visual map and therefore the illusion in the perception of visual extent arises.

However, an unanswered empirical question is whether the saccade plans produce the perceptual illusion or the other way around, i.e. that the biased perception creates the biased saccade plans? The fact that a correlation between saccade amplitude and the perceived length of the stimulus was found is not enough to answer this question. In order to attempt to break this correlational-loop, Coren (1986) proposed the Theory of Efferent Readiness and designed several experiments to test it.

### 1.1.1 Alterative explanations of the Müller-Lyer illusion

Although the Müller-Lyer illusion has a simple configuration, and the effect is known to be produced by the two arrowheads, there is not an agreed upon theory that explains this effect.

Depth theories have explained the Müller-Lyer illusion as the result of a misinterpretation of certain depth cues, which make us perceive the configuration in Figure 1.2A as more distant from us and therefore longer (Gregory, 1963; Fisher, 1967; Dragoi, & Lockhead, 1999).

Assimilation theory (or averaging theory) has suggested that the wings attached to the horizontal shaft interfere with measuring the span of the horizontals and therefore the observer confuses or averages the distance between the tips of the wings, and as a result the illusion arises (Earlebacher, & Sekuler, 1969). Pressley (1970) suggested that our visual system cannot successfully isolate the parts from the whole, and in the Müller-Lyer case it cannot isolate the horizontal shaft from the wings. This causes the configuration in Figure 1.2A to be perceived as longer because in total the stimulus is longer than the other configuration.

The confusion theory suggested that the illusion is due to the fact that the perceptual system miscalculates the locations of the vertex of the wings, and it displaces them in the direction of the acute angle formed by the wings, and so away from the obtuse angle (Chiang, 1968). In the configuration in Figure 1.2B this causes the apparent end points of the wings to move inwards and as a result the configuration is perceived as shorter.

Howe & Purves (2005) suggested that the illusion produced by the Müller-Lyer stimuli is the result of a fundamentally probabilistic strategy of visual perception. They suggested that the two configurations are geometrical stimuli which are generated from real-word sources, and the illusory effect is due to the fact that the real-word sources have different probability distributions. They sampled a database composed of natural scenes for set of pixels whose configurations matched the Müller-Lyer figure and they found that the two probability distributions were different.

## 1.2 The Efferent Readiness Theory

In his quest to explain how visual perception arises Coren suggested that an afferent theory of perception cannot work, since it was empirically proved that our final perception could not arise just from the feedback from emitted eye movements. This was shown especially using optical illusions such as the Müller-Lyer figure, where our visual system puts the fovea on the end point of the horizontal shaft of the figure (using a second corrective saccade), but this adjustment is not enough to avoid the illusion of visual extent, while if the afferent theory of perception was valid this should not happen. Moreover, Coren pointed out that when subjects were given a dose of d-tubocurarine (a muscular relaxation substance) and could not move their eyes, they were still able to report the visual stimuli that were presented; therefore Coren proposed a theory where the final percept for simple forms of spatial perception such as the 2D separation between points (visual angle, or visual distance) is derived from eye movements held in readiness (1981). He suggested that a set of eye movements are computed but most of these are not carried out, they are held in readiness (i.e., held in preparation). From this set of eye movements held in readiness the final percept is synthesized. He named this theory the Efferent Readiness Theory (1986). In order to test his theory and attempt to break the correlational loop between eye movements amplitude and perceived length of the stimulus, he designed an experiment where he parametrically manipulated the amplitude of eye movements held in readiness; experiment that is presented in Figure 1.3 (1986).

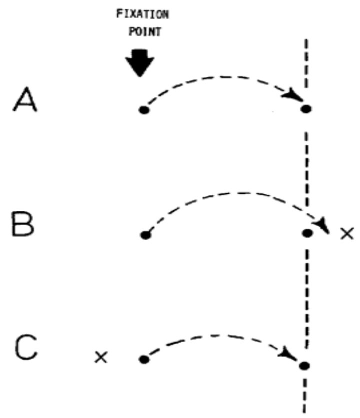

*Figure 1.3 - Coren's experiment.*

He presented a fixation point and a target and asked the participant to make a perceptual judgment about the distance between the fixation point and the target. He also placed an extraneous stimulus, which was different in shape from the target stimuli, either in vicinity of the fixation cross (Figure 1.3C) or beyond the location of the target (Figure 1.3B). Although it is not shown in Figure 1.3B, the distance of the extraneous stimulus from the target was parametrically manipulated.  His reasoning was that if the perceptual distortion arose from the global configuration properties (and was not related to eye movement planning), then just the presence of the extraneous stimulus should have generated a distortion, regardless of its location, meaning that the perceptual judgment made from the participants should have been the same regardless of the location of the extraneous stimulus. Otherwise, if the efferent theory was correct, the perceptual distortion should have been contingent on the location of the extraneous stimulus meaning that when the extraneous stimulus was placed beyond the target (Figure 1.3B) the centre of gravity effect would occur, dragging the end point of the saccades held in readiness beyond the location of the target and therefore generating a biased perceptual judgment, while when the extraneous stimulus was placed in the vicinity of the fixation point (Figure 1.3C) the amplitude of the saccade should have not affected therefore producing a non-biased perceptual judgment.

In order to test this prediction, he asked 12 subjects to use their finger (out of view) to make a perceptual judgment about the distance between the fixation point and the target. The results he obtained are presented in Figure 1.4.

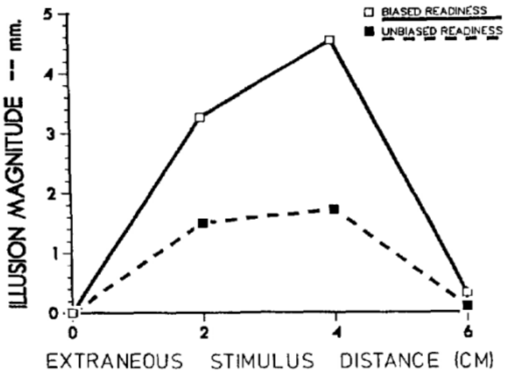

*Figure 1.4 - Results of Coren's experiment.*

He discovered that when the extraneous stimulus was placed beyond the target (Figure 1.3B), participants overestimated the physical length of the distance (solid line in Figure 1.4), compared to when the extraneous stimulus was absent (Figure 1.3A). He claimed that the presence of the extraneous stimulus after the location of the target affected the amplitude of the saccade held in readiness due to the Centre of Gravity (COG) effect, which gave rise to the biased perceptual judgment. Also, he discovered that in the condition where the extraneous stimulus was placed in the vicinity of the fixation point (Figure 1.3C), the distortion was not totally absent, but it was reduced (dotted line in Figure 1.4). He explains this unpredicted effect by speculating that the eyes tended to drift off from the fixation point towards the extraneous stimulus. He claimed that these results broke the correlation loop between eye movements and perceptual distortion and confirmed his Theory of Efferent Readiness.

## 1.3 Theory of Efferent Readiness and the brain

One thing that was not included in Coren’s theory (1986) was the neural basis of the COG effect on saccades and how that is integrated with spatial perception, including the regions of the brain where the relevant processing takes place. It is known that perception of individual visual locations is achieved thanks to retinotopic mapping within the brain (Schwarzkopf, 2015; Sereno, & Huang, 2014). These retinotopic maps are located in the occipital cortex (Figure 1.1), V1 being the largest and most detailed, and they mirror the organization of visual input from the retina. However, these retinotopic maps do not give any explicit information about distances or extent, they are just explicit position code only (Schwarzkopf, 2015). Neurons in V1 are tuned to a specific feature in the visual field (such as orientation, direction of motion, spatial and temporal frequency), and they fire only if that specific feature is presented within their receptive field.

There is no evidence that the visual cortex contains individual neurons whose activation is linked to visual separation of two points, therefore the perception of visual distances must be supported somewhere else in the brain. A good candidate is the Superior Parietal Lobule (SPL). This region receives input from the occipital lobe, and is heavily connected to the frontal eye field, which is known to be involved in eye movement planning and execution. The SPL is located in the Parietal lobe, behind the postcentral sulcus (PCS) and above the intraparietal sulcus (IPS), as shown in Figure 1.5 (Purves, Augustine, Fitzpatrick, Hall, LaMantia, McNamara, & White, 2008).

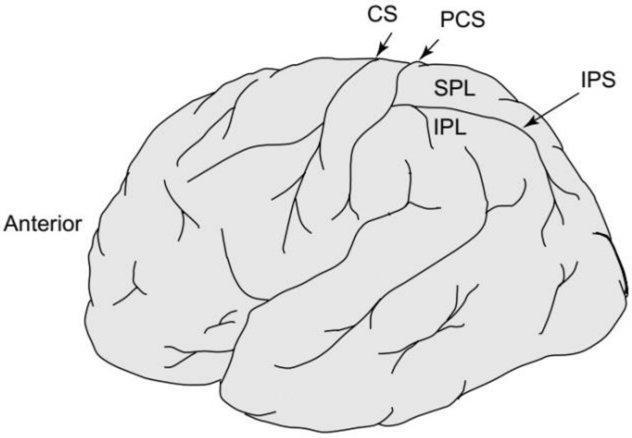

*Figure 1.5 - Location in the brain of the SPL.*

Many functions have been associated with this region, including eye movement planning, working memory, language and attention. The fact that multiple different functions have been attributed to this region has led to the idea that it could be composed of different sub-regions, each of which is involved in a different function (Culham, & Kanwisher, 2001). This idea was supported by a recent multimodal parcellation study (Wang, Yang, Fan, Xu, Li, Liu, Fox, Eickhoff, Yu, & Jiang, 2015), in which the SPL was found to be composed of five different sub-regions (each subregion was bilaterally present, with some difference depending on the hemisphere), based on relating a fine-grained analysis of its anatomy to the results of cognitive function localization studies (Figure 1.6). Particularly, the fifth sub-region, which was the most posterior and was cytoarchitectonically similar to the Brodmann area 7P, was associated with visual spatial attention and seems to be the perfect candidate for Coren’s theory.

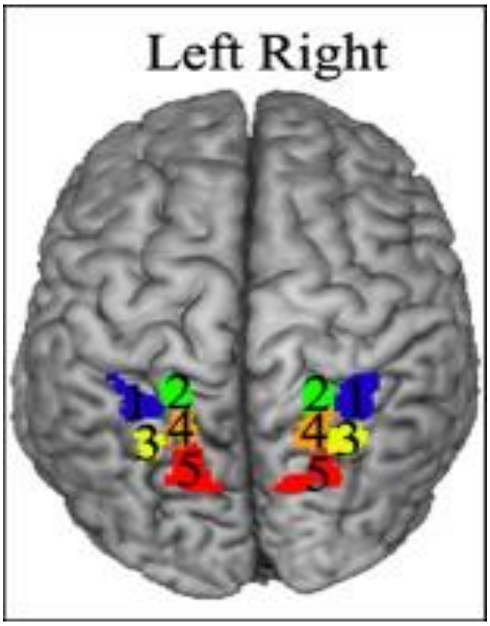

*Figure 1.6 - Parcellation of SPL by Wang et al., 2015*

A different possibility was put forward by Vandenberghe and colleagues (2001), when he claimed that the SPL might be involved in spatial attention shifting. In his fMRI experiment he presented a static fixation cross and a target square that would shift to 1 of ten predetermined locations. In the covert attention condition, the participants were asked to fixate the fixation cross but still track and attend the target square, while in the overt condition the participants were asked to fixate and attend the target. In addition to the overt/covert condition, participants were asked to attend the target when it was not moving and detect a dimming event and then press a button (maintaining attention). When the authors looked at the fMRI contrast for shifting of attention minus maintaining attention a bilateral activation of SPL was found (x= -24, y=-61, z=63; x=26, y= -62, z=68). The authors claimed that the activation in the SPL was due to the fact that the participants was shifting attention between different location.

However, an alternative hypothesis might be that the activation seen by Vandenberghe and colleagues is due to the design of the stimuli used in the experiment. During attention shifting in both overt and covert condition there was a change in visual separation between the static fixation cross and the target square, while in the maintaining attention it was not present. Therefore, in our lab we carried out several fMRI studies aimed at investigating whether the activation in SPL was driven by spatial attention shifting or by changes in the perceived visual separation, and the results seem to suggest that SPL is involved in visual separation (Field, & Goodwin, 2016, Goodwin, 2021).

When Wang and colleagues looked at whole brain connectivity, they noticed that the 2 subregions 5 (respectively L5 in the left hemisphere and R5 in the right hemisphere presented in Figure 1.6) were connected with the superior temporal gyrus (STG), the inferior frontal gyrus (IFG), the insula, the posterior hippocampus and the controlateral posterior parietal cortex (PPC) via the extreme capsule (EmC) and corpus callosum (CC). Moreover, they noticed that during the resting state L5 and R5 were connected to the frontal eye field (FEF), the middle frontal gyrus (mFG), the anterior IFG and the posterior inferior temporal gyrus (ITG), while the brain regions that coactivated with the two subregions of SPL5 were FEF, mFG, IFG, supplementary motor area (SMA), the posterior ITG and the visual cortex. They noticed that out of all the tasks they presented, the L5 was associated with vision motion, vision shape, space, attention, working memory and R5 was associated with vision motion, space, vision shape, working memory, motion learning, execution and attention. In the three studies reported in this thesis, we will target the whole Superior Parietal Lobule rather than the specific subregion 5 using Transcranial Magnetic Stimulation, in order to test our hypothesis that SPL is involved in perception of 2D visual separation.

## 1.4 The Superior Parietal Lobule and the perception of visual extent

According to Wang's study a subregion of the SPL is involved in attentional shifting, but a more recent study conducted by Field and Goodwin (2016) and Goodwin (2021) called this into question. In their study they presented fMRI-based evidence that the spatial attention shifting hypothesis of SPL function could not explain and linked the SPL with the perception of 2D visual separation. They found that when a single target square is presented in an otherwise featureless environment and participants are asked to make eye movement to track its movements, a very low activation in SPL is detectable; but when a task irrelevant central cross is added to the display and participants are asked to perform the same task, then a strong activation in SPL is found. This result does not align with the spatial attention shifting hypothesis, but is consistent with the idea that SPL is involved in the perception of 2D visual separation.

Moreover, a study conducted by Weidner and Fink (2007), suggested that the SPL is involved in the perception of 2D extent by showing that it plays a crucial role in the strength of the illusion generated by the Müller-Lyer configuration. In their fMRI study they presented the Brentano version of the Müller-Lyer illusion (Figure 1.5) and manipulated the strength of illusion by varying the angle of the fins and then asked participants to perform either a landmark task, where they had to indicate whether the bisection fin was shifted to the right or the left of the perceived centre of the horizontal shaft, or a control luminance task, where they had to indicate whether the upper or lower part of the bisection fin had a higher luminance.

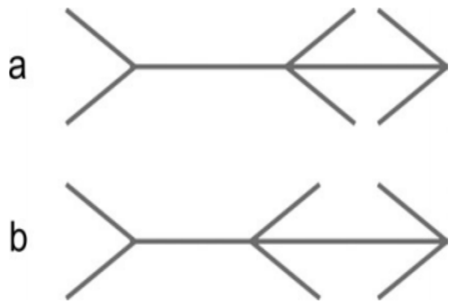

*Figure 1.7 - Brentano version of the Müller-Lyer illusion.*

When they looked at the brain regions that were more active for the landmark task, they found activations in the right inferior temporal cortex and in the right superior parietal cortex (Figure 1.6A), while when they looked for regions that covaried with the strength of the Müller-Lyer illusion they found activations in the right superior parietal lobule and bilaterally in the lateral occipital cortex (Figure 1.6B).

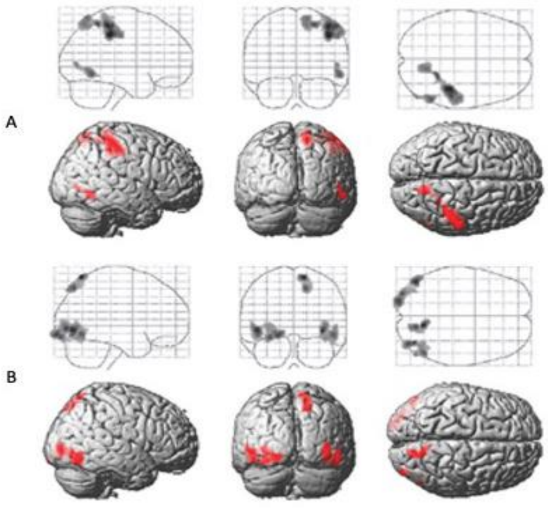

*Figure 1.8 - Results obtained by Weidner and Fink, 2007. Section A presents the activations specific to the landmark task, while section B presents the activations linked to the magnitude of the Müller-Lyer illusion.*

Another experiment that involved both the SPL and the Müller-Lyer illusion is the one conducted by Mancini and colleagues (2011). They delivered repetitive TMS stimulation (rTMS) over the regions identified by Weidner and Fink (i.e., the occipital-temporal cortex and the superior parietal lobule) and then ask the participant to use their index finger to divide in half the Judd variant of the Müller-Lyer illusion (Figure 1.7).

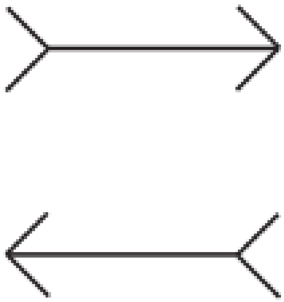

*Figure 1.9 - Judd variant of the Müller-Lyer illusion.*

They presented the illusion in 3 different modalities: visual, where subjects had to make a bisection task relying just on the visual presentation of the stimulus; haptic, where subjects were blindfolded and had to do the bisection task just by touching the stimulus and visuo-haptic where participants could rely on both sensor modalities in order to perform the bisection task. The experiment took place on 3 different days and in each day, before the presentation of the tasks, the subjects underwent a 20 minutes 1Hz rTMS delivered either to the occipital-temporal cortex or the superior parietal lobule (in the first day of the experiment no rTMS stimulation was administered). The 1Hz stimulation was used because, according to the literature, it has a long-lasting inhibitory effect (Chen, Classen, Gerloff, Celnik, Wassermann, Hallett, & Cohen, 1997). Coordinates for the regions targeted with the rTMS were converted into Talairach from the original stereotaxic coordinates obtained from Weidner's study. They found that overall, the rTMS over the SPL produced a trend for an effect on illusion strength, making the illusion weaker, while the rTMS over the occipital-temporal cortex significantly reduced the strength of the Judd variant illusion. However, it should be noted that in this study the Judd variant of the Müller-Lyer illusion was presented, which alters the perceived position of a segment, rather than perceived linear extent (Mack, Heuer, Villardi, & Chambers, 1985). This makes interpretation of the study results less certain.

# 1.5 Transcranial Magnetic Stimulation (TMS)

In the three studies reported in this thesis we will use Transcranial Magnetic Stimulation to further investigate the role played by the Superior Parietal Lobule in the perception of visual extent.

TMS is widely used in research because it is a non-invasive technique which can create a reversable impairment (i.e., virtual lesion) of a specific brain region in healthy subjects, thus leading to a better comprehension of the brain through the exploration of typical connectivity. The use of TMS in psychology experiments has gained popularity over recent years. This is the case because TMS allows researchers to non-invasively stimulate and study the cortex in healthy and diseased states (Fitzgerald, & Daskalakis, 2013). TMS relies on a simple physical principle: in the electric circuit within the coil an alternating current is flowing; its time-changing flows induces a time-varying magnetic field which induces an alternating current in the cerebral tissue underneath the coil (Rotenberg, Horvath, & Pascual-Leone, 2014). The electric field generated by the coil produces a current in the extracellular and intracellular space, which causes the membrane to become depolarised, and if the membrane is sufficiently depolarised then an action potential is fired.

The pulse used in TMS stimulation can have 2 different shapes: monophasic and biphasic (Rotenberg et al., 2104), as presented in Figure 1.8. Monophasic pulses have just unidirectional voltage and because of their nature they can only be delivered one at the time, while biphasic pulses have both negative and positive voltage oscillations. This latter shape of pulse can be delivered individually (i.e., just a single pulse, biphasic presented in blue in the figure) or can be delivered continuously (polyphasic pulses, presented in green in the figure).

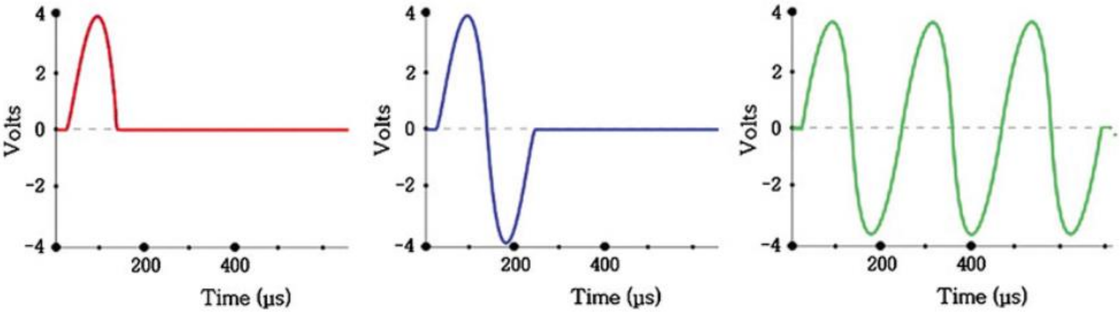

*Figure 1.10 – Monophasic pulse in red, biphasic pulse in blue, and polyphasic pulse in green.*

TMS stimulation can be composed of just a single pulse, paired pulses, or repetitive pulses. Single pulse paradigms are mainly used for diagnostic and exploratory measurements of cortical reaction to each pulse (Chen, Cros, Curra, Di Lazzaro, Lefaucheur, Magistris, Mills, Rösler, Triggs, Ugawa, & Ziemann, U., 2008). An example of single pulse TMS is when it is applied to the primary visual cortex, this stimulation generates phosphenes (the impression of flashes of light not due to the light entering the eyes) which can be used to determine the threshold for cortical activation by TMS. Paired-pulse paradigms are used to examine cortical excitability/inhibition in patients and in healthy subjects (Currà, Modugno, Inghilleri, Manfredi, Hallett, & Berardelli, 2002). Repetitive TMS, or rTMS, are composed of trains of pulses delivered over the same brain region. Depending on the frequency of stimulation (low vs high), the intensity of stimulation (sub-threshold vs supra-threshold) and the overall duration of the train and their pattern (continuous vs intermittent) different patterns of rTMS can be defined.

If the frequency of stimulation is between 1 to 5 Hz (i.e., 1 to 5 pulses delivered per second), then this is defined as low frequency TMS. Low frequency is generally applied continuously with no interval for 15-20 minutes and is thought to have a suppressive effect on cortical activity (Chen et al., 1997). On the other hand, if the frequency of stimulation is above 5Hz this is defined as high frequency TMS. High frequency TMS consists of several pulses delivered each second, usually the range is from 5 to 50 per second (i.e., 5-50 Hz) and normally it consists of a short period of stimulation (2-3 seconds) followed by a relatively long intertrain interval (20-30 s) in which no stimulation is delivered. This specific pattern of stimulation is thought to produce a facilitatory effect on cortical activity (Guse, Falkai, & Wobrock, 2010).

The distinct signature of both low and high frequency rTMS is the ability to induce an effect that lasts after the end of the stimulation. The duration of the effect on cortical activity following a low-frequency stimulation can last up to 60 minutes (Iyer, Schleper, & Wassermann, 2003), while for high-frequency stimulation it depends on stimulation intensity, pulse number and frequency, but it usually last for about half the duration of the stimulation train (Guse et al., 2010). The long-lasting effect that can be obtained with low and high frequency rTMS cannot be obtained with a single pulse/paired-pulse stimulation (Klomjai, Katz, & Lackmy-Vallée, 2015; Rotenberg et al., 2014). The effect that rTMS produces in the cortex is known because researchers have measured motor evoked potentials (MEPs) over the primary motor cortex before and after a stimulation session. It was found that MEPs measured at a peripheral muscle were suppressed for a period of time following low frequency rTMS and were enhanced after a session of high frequency rTMS. Therefore, it is thought that low frequency rTMS has an inhibitory effect on cortical activity and the high frequency rTMS leads to an increase in cortical activity (Klomjai et al., 2015; Rotenberg et al., 2104).

Two specific patterns of stimulation known to have a long-lasting effect on the MEPs are continuous theta burst stimulation (cTBS) and interval theta burst stimulation (iTBS).

### 1.5.1 Continuous Theta Burst Stimulation (cTBS)

The cTBS consists of 3 pulses of 50 Hz (i.e., 20 ms interval between each pulse) which is repeated at interval of 200 ms (i.e., 5Hz), while the iTBS consists of 10 bursts of 50 Hz triplets delivered over 200 ms (5 Hz) which are separated by an 8 second interval where no stimulation is delivered, for a total of 190 second. The cTBS can be administered for either 20 seconds (for a total of 300 pulses) or 40 seconds (for a total of 600 pulses). When researchers measured MEPs following a cTBS stimulation, they noticed that in the case of a 20 second cTBS they were suppressed for 20 minutes, while in the case of a 40 second stimulation they were suppressed for 60 minutes (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). While when the MEPs were measured following an iTBS stimulation it was found a facilitatory effect on MEPs size that lasted for 15 minutes. These durations can be used as guidelines when designing experimental paradigms and have been used in the experiments reported in this thesis.

### 1.5.2 Online vs Offline TMS protocol

In research when TMS is involved in an experiment, researchers can either use an online or an offline protocol (Rotenberg et al., 2014). Both approaches are used in this thesis, online in Chapter 2 and offline in Chapters 3 and 4. In the offline protocol the TMS stimulation is administered before the presentation of a task. This is possible because rTMS can induce an effect that can persist for many minutes after the end of the stimulation.

On the other hand, in an online protocol the subject undergoes a given task while the rTMS is administered. In this protocol the short trains administered at carefully chosen points in time during the behavioural task are intended to create ‘noise’ in the neural activity, which should affect the performance of the subject in the task. This specific protocol allows researchers to investigate both the role played by a given cortical region in a specific task and also the stage of elaboration at which the cortical region is involved. This is not the case for the offline protocol, where just the role played by a specific region in a given task can be investigated.

### 1.5.3 TMS studies of other cognitive functions in the SPL

Many studies have used TMS/cTBS paradigms to investigate the role played by the Superior Parietal Lobule in a wide variety of tasks such as lexical processing in sign language (Banaszkiewicz, Bola, Matuszewski, Szczepanik, Kossowski, Mostowski, Rutkowski, Śliwińska, Jednoróg, Emmorey, & Marchewka, 2021), visuospatial attention (Wu, Wang, Zhang, Zheng, Zhang, Rong, Wu, Wang, Zhou, & Jiang, 2016), deductive reasoning (Tsujii, Sakatani, Masuda, Akiyama, & Watanabe, 2011), and gestural imitation (Vanbellingen, Bertschi, Nyffeler, Cazzoli, Wiest, Bassetti, Kaelin-Lang, Müri, & Bohlhalter, 2014).

In their study on lexical processing in sign language Banaszkiewicz and colleagues (2021) investigated the role played by the SPL in sign language comprehension in both deaf signers and hearing learners. They presented sign language video clips and ask participants to perform a Lexical Decision Task where participants had to discriminate between signs and pseudo signs. TMS was delivered 400, 600, 800, 1000 and 1200 ms after stimulus onset, to three different locations (i.e., left and right SPL, and the occipital pole was used as control site). It was found that stimulation of right and left SPL in both groups decreased performance compared to stimulation of the control site. Moreover, it was found that TMS over the right SPL resulted in decreased accuracy for both late learners and deaf signer, while TMS over the left SPL resulted in a reduction of accuracy only in hearing learners. The authors claimed that the reduction in accuracy in both groups during stimulation of the right SPL indicates that the region is involved in visuospatial attention and this finding is in line with previous literature;

while the decrease in accuracy following the TMS of the left SPL in hearing learners indicates that the region is linguistically relevant in visuospatial linguistic processing only in novice signers.

In a study conducted by Wu and colleagues the role played by SPL in visuospatial attention was investigated (2016). They delivered online rTMS to either the left or right SPL (or sham TMS as a control) while a spatial attention task was presented. The TMS was delivered for 300 seconds before the behavioural task started and continued until the end of the task. It was found that while accuracy was not affected by the location of TMS, the stimulation of the right SPL resulted in significant higher reaction times compared to both left SPL and sham TMS. The authors claimed that the result indicates that the right SPL is more dominant that left SPL in visuospatial attention.

Tsujii and colleagues (2011) investigated the role played by the SPL in deductive reasoning. Participants received either a stimulation over the SPL (left and right plus a control site) or over the Inferior Frontal Gyrus (left and right plus a control site) for 10 minutes at 1 Hz and then were presented with a categorical syllogistic reasoning task, which involved congruent, incongruent, and abstract trials. It was observed that both left and right TMS of the SPL resulted in a reduction in the performance on abstract and incongruent trials compared to control TMS; while left IFG resulted in impaired congruent reasoning and facilitated incongruent reasoning performance; right IFG impaired incongruent reasoning. The authors claimed that these funding are in line with the dual-process theory which suggests that humans have two different reasoning system: a belief-based system and a logic-based analytic system. The findings suggest that the left IFG is involved in the heuristic system, while the bilateral SPL is involved in the analytic system.

In a study conducted by Vanbellingen and colleagues (2013) the role played by SPL in gestural imitation was investigated. They delivered either cTBS (801 pulses delivered in 267 bursts, with each burst composed of 3 pulses at 30 Hz with and an interburst interval of 100ms for a total of 44 seconds) over the SPL or the Inferior Parietal Lobule, or sham TMS over the vertex. After the stimulation they presented an imitation task where participants had to imitate both meaningful and meaningless gestures. It was found that cTBS over SPL and IPL impaired with gestural imitation, however there was no difference in performance between meaningful versus meaningless gesture imitation, therefore the hypothesis suggesting a different role for SPL and IPL depending on meaningful or meaningless gestures could not be confirmed.

While the studies reviewed above suggest that the SPL is involved in a range of cognitive functions, in the three studies reported in this thesis we will use both online high frequency rTMS and offline cTBS over the SPL to understand the role played by the superior parietal lobule in the perception of 2D visual space, and in the final experiment we will also investigate the role of the frontal eye field (FEF) in this, which is a brain region that is heavily connected to the SPL and works together with it in the planning of eye movements.

To reiterate the background that has been covered here, we have explored the link between perceptual processing of visual extent and separation in the SPL and the Muller-Lyer illusion in its various forms. An existing theory that makes a potentially important link between the two, Efferent Readiness Theory, was described in some detail. We considered how a number of findings about the role of the SPL in cognitive functions might alternatively be explained by the proposal that the SPL supports the perception of visual separation. Because TMS is a promising methodology to test these ideas further, we explored the different TMS methodologies that might be used as well as previous TMS studies of the cognitive functions of the SPL.

The literature review summarised above has suggested the following aims for this thesis:

- To use TMS to investigate whether the Superior parietal Lobule plays a role in the processing and perception of visual separation;
- To use TMS to investigate the role played by the Superior Parietal Lobule in the processing of eye movements and perception of visual extent in the context of the Müller-Lyer illusion;
- To use TMS to investigate the processing of eye movements and perception of extent and visual separation in the parietal lobule, compared to the frontal eye field.

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# Chapter 2. The role of the Superior Parietal Lobule in the perception of the visual separation between stimuli: an rTMS study

## 2.1 Abstract

The Superior Parietal Lobule (SPL) is a region of the brain that has been associated with a diverse range of high-level visual and cognitive functions. This suggests the possibility that it supports a lower-level function that is engaged in a wide range of experimental tasks. Analysis of tasks used in previous studies suggests that one such lower-level function might be the perception of the distance between stimuli in the image plane. In this study we applied online high frequency repetitive Transcranial Magnetic Stimulation (rTMS) over the left Superior Parietal Lobule in order to further investigate the role played by this region in the perceived visual separation between points. The results failed to support the hypothesis, but due to methodological problems the hypothesis remains open. We unexpectedly found that rTMS to left SPL improved performance in a contrast sensitivity control task, and we suggest that this result should be confirmed and investigated in further studies.

# 2.2 Introduction

The brain areas in the occipital lobe that are relevant for the visual system mostly contains neurons whose visual receptive fields are tuned to specific retinal locations and at the population level these neurons are organized into retinotopic maps. This system is well suited to encode the positions of stimuli in a retinal coordinate frame. However, it does not provide in any direct way information about the separations (retinal distance) between individual stimuli. Specifically, neurons have not been found in visual cortex whose firing rate depends on the separation or distance between two stimuli. Nonetheless, humans are good at perceiving the separation between two points in visual space when it defines such properties such as the width of a circle (Morgan, 2005) or the height of a rectangle (Nachmias, 2008).

One suggested explanation of this perceptual ability is that a higher visual area reads out position information about edges or corners of salient and attended stimuli from early visual areas and computes separations between positions (Harvey, Fracasso, Petridou, & Dumoulin, 2015; Schwarzkopf, 2015). Consistent with this proposal, the precision of psychophysical judgements of higher order properties of shape such as geometrical angle and aspect ratio is good and cannot be accounted for by sensitivity to properties of the components of the shapes (Chen, & Levi, 1996; Heeley, & Buchanan-Smith, 1996; Nachmias, 2008). The computational mechanism by which this is done is unknown but is likely to be different from the kind of formal trigonometry that a computer vision algorithm might use to solve this problem. Here, rather than focusing on the computational mechanism we aim to determine which brain area performs the read-out and the computation. Note that our investigation focuses on the perceived visual separation between points in the coordinate frame of the retinal image, not the perceived distance or separation in depth between objects in the world.

The Superior Parietal Lobule (SPL) is a part of the parietal lobe, located in the posterior part of the brain, close to the midline. Brain imaging studies have associated many different functions with this region and report similar activation coordinates in SPL for different functions, e.g., shifting spatial attention between locations (Vandenberghe, Gitelman, Parrish, & Mesulam, 2001); the perception of heading direction (Peuskens, Sunaert, Dupont, Van Hecke, & Orban, 2001); the perception and planning of the path of travel during locomotion (Field, Wilkie, & Wann, 2007; Billington, Field, Wilkie & Wann, 2010); and motion tracking under attentional load (Jovicich, Peters, Koch, Braun, Chang, & Ernst, 2001). One study set out to study activation produced in SPL by making smooth pursuit eye movements, but instead found that activation in the region appeared to be driven by the presence of perceived relative motion between display elements (Ohlendorf, Sprenger, Speck, Glauche, Haller, & Kimmig, 2010).

Whilst the authors of these studies reported contrasting explanations for SPL activation that reflected their particular sets of stimuli and tasks it is possible that a single underlying function could provide a unifying explanation of the activation in these apparently diverse studies. The experimental tasks used in in all but one of the aforementioned studies would require participants to shift their attention between elements of the visual display, which suggests that shifting spatial attention may be the underlying function explaining these results, as proposed by Vandenberghe et al., (2001). On the other hand, all these studies – including Vandenberghe's – also used stimuli in which the visual percept is that of changing visual separations between stimulus elements. Therefore, an alternative possibility is that SPL supports the perception of visual separation, which is why it was selectively activated in all the studies reviewed here. One exception is the study of Ohlendorf et al. (2010), in which the pattern of results considered in relation to the stimuli used does not appear to implicate SPL in attention shifting but is consistent with a role in the perception of visual separation.

As a step towards determining whether either of the two basic functions described above might explain the selective activation of SPL by a range of experimental tasks, Filed and Goodwin directly tested the attention shifting hypothesis of SPL in an fMRI experiment and found that it was unable to account for the results (Field, & Goodwin, 2016, Goodwin, 2021). Specifically, when a single target square displaces in an otherwise featureless environment and the displacement is tracked by saccadic eye movements SPL activation is very low, despite the mandatory shift of spatial attention to the new target location that occurs before each saccadic eye movement (Deubel, & Schneider, 1996). Yet when a task irrelevant central cross was added to the display and the participant continued, as before, to make saccadic eye movements to track the displacing square strong activation occurred in SPL; adding the task irrelevant cross changed nothing in terms of saccade related spatial attention shifting, but it did introduce the percept of time varying visual separation to the display which we propose drives activation in the SPL subregion. This result is problematic for the attention shifting hypothesis of SPL activation, which would have to make the implausible claim that saccades to targets can be made without shifting spatial attention in order to explain the results, but consistent with the proposal that a subregion of SPL processes visual separations.

The present study aimed to test the proposal that a subregion of SPL was critical for the processing and perception of visual separation using a non-invasive brain stimulation technique known as transcranial magnetic stimulation (TMS). TMS can disrupt targeted brain regions to reveal their causal role in task performance. The behavioural task performed while TMS was applied to SPL was a psychophysical visual separation judgment task, in which two different pairs of dots were presented on a computer screen and the participant indicated in which pair the distance between the dots was larger. We predicted that TMS to the SPL would result in less precise performance on this task but did not expect accuracy to be affected by TMS to SPL. In the experiment the stimuli were confined to the right visual field and the TMS was applied to SPL in the contralateral hemisphere. This arrangement followed from the fact that SPL is found bilaterally in the brain and shows a bias to process the contralateral side of visual space, i.e. the left visual field was processed mainly in the right hemisphere of SPL (Silver, & Kastner, 2009). To increase methodological rigor, we also applied TMS to a control region (i.e., the vertex) that was not thought to play a role in processing visual separation. For the same reason, we included a control psychophysical task that did not require judgment of visual spatial separation but shared many of the generic task features, such as deciding between two alternatives and pressing a button, with the main task of interest. Our first prediction was that the slopes of the psychometric functions obtained during the visual separation task would be shallower when TMS stimulation was delivered over SPL compared to when it was delivered over the vertex. But for the hypothesis that the SPL subregion we targeted is the specific part of the brain that supported the perception of visual separation to be supported by this study an additional prediction must be fulfilled: that TMS delivered over SPL does not influence slopes of psychometric functions obtained from the control task. We had no specific reason to predict that TMS would differentially affect the point of subjective equality (PSE) in either the experimental or control task, and so performed an exploratory analysis of this.

# 2.3 Method

## 2.3.1 Participants

For this study 20 healthy participants (16 females, 4 males) were recruited for a 2 non-consecutive days TMS study at the University of Reading. This sample size was sufficient to detect an effect size of d = 0.57 for our one tailed prediction (power 0.8, alpha 0.05, paired samples t-test). Participants were recruited via the University of Reading Student Volunteer Panel (SONA), where the study was advertised. The age range of the participants varied from 19 to 28 years old (Median 21, range 19-28). All participants were informed that their participation in this study was voluntary and that they could withdraw at any time without providing a reason.

## 2.3.2 Ethical Approval

This study was granted ethical approval by the University of Reading Ethics Committee (UREC) 17/24, expiration 1/10/2020. Due to the seizure potential that TMS stimulation carries (Wassermann, & Lisanby, 2001), participants were asked to complete a TMS screening form before each TMS stimulation. The TMS screening form was approved by UREC and was composed of 24 questions aimed to investigate if the participant had previous psychiatric, neurological or other medical condition and therefore was not eligible for the TMS stimulation (Rossi, Hallett, Rossini, & Pascual-Leone, 2009). Moreover, the experimental design took into account the TMS safety parameter specified by Wassermann & Lisanby (2001) and Rossi (2009) that was computed from the combined duration, intensity and frequency of stimulation. Before the start of the TMS stimulation participants were reminded that they could withdraw at any time from the study without providing a reason.

### 2.3.3 Apparatus and Materials

All the experiments presented in this study were programmed using Psychtoolbox (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007; Pelli, 1997), a freely available package toolbox for MATLAB. All the stimuli were displayed on a 24-inch ViewPixx monitor (1920 (H) x 1080 (V) pixels), placed 90 centimetres away from the participant. In order to reduce the head movements, participants were asked to rest their chin on a chinrest for the entire duration of the experiment (the chinrest was placed 90 centimetres away from the ViewPixx monitor).

### 2.3.4 Design and Procedure

The design of this study was fully repeated measures, with every participant undergoing online TMS stimulation in each experimental condition over 2 different regions: the Superior Parietal Lobule (SPL) and the Vertex (control region). Each region was stimulated on a different day and there was at least a 48-hour interval between the 2 sessions. For half of the participants, on Day 1 the stimulation was delivered over the SPL, and on Day 2 it was delivered over the vertex, while for the other half of the participants the order was reversed. In each session, both the control task and then experimental task were performed. For half of the participants the experimental task was presented first on both days, while for the other half the order of presentation was reversed.

In the experimental task the effect of TMS on the perceptual judgment of visual distances was investigated. In order to do so, the point of subjective equality (PSE) between 2 simultaneously presented visual separations was measured. This was done by presenting a 2 alternative forced choice task.

On each trial the participant was briefly presented with 2 pairs of white dots, and judged which pair defined the larger visual distance (see Figure 2.1). The TMS stimulation was paired with the brief presentation of the two set of dots.

In the control experiment the effect of TMS on the PSE between the contrast of two Gabor patches was determined (see Figure 2.2). The cognitive and motor aspects of this task were identical to those in the experimental task, but the perceptual comparison required did not involve spatial extent.

#### *2.3.4.1 Stimuli*

In the experimental task 2 pairs of white dots and a fixation cross were presented against a black background (Figure 2.1a).

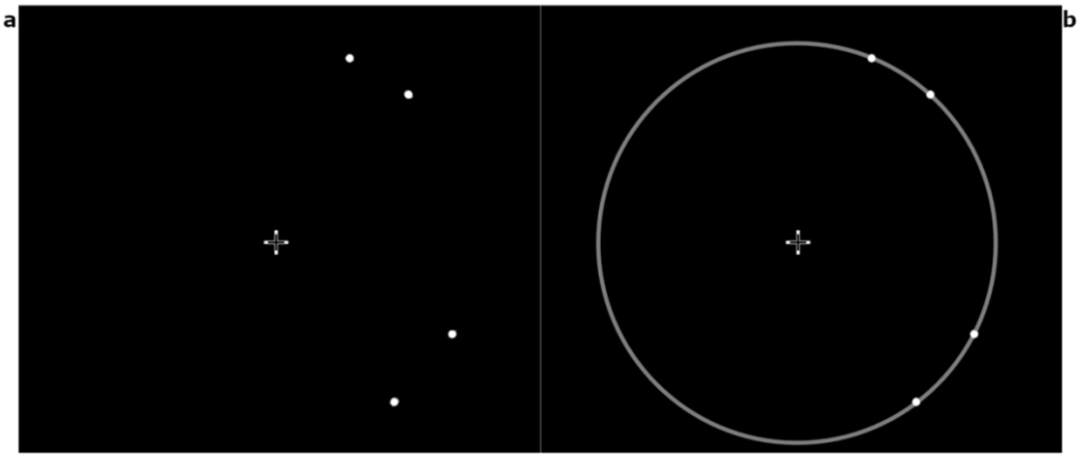

*Figure 2.1 -Stimuli used in the Experimental task: (a) stimuli presented to the participants were a pair of dots presented above the fixation cross (2nd quadrant) and a pair presented below the fixation (4th quadrant); (b) dots making up the stimuli lay on an imaginary circle of radius 5 degrees of visual angle.*

One set of dots was presented below the fixation cross (4th quadrant of the screen, using the fixation/centre of the imaginary circle as the origin), while the other set was presented above the fixation cross (2nd quadrant of the screen). All the individual dots lay on an imaginary circle with a radius of 5 degrees of visual angle that was centred on the fixation cross (Figure 2.1b). All the dots presented subtended 0.2

degrees of visual angle. From trial to trial, the visual distance between the two dots making up each pair was manipulated. The pair of dots presented below the fixation cross was defined as the ‘Standard’ and the distance between the two dots ranged from 2.59 to 5 DOVA. The locations of the two dots making up the ‘Standard’ was randomly jittered within the quadrant by MATLAB on each trial.

The pair of dots presented above the fixation cross was defined as the ‘Comparison’ and the distance between these two dots in each trial was a percentage of the Standard. These percentages were 70%, 79%, 88%, 97%, 102%, 112%, 121%, & 130%, and each percentage was presented 30 times during the experiment. On each trial, the participant indicated whether the visual separation defined by the Standard, or the Comparison appeared larger using the up and down arrow keys on the keyboard.

The 2 pairs of dots were presented on the screen for only 200 ms to prevent saccadic eye movements during the trial, and participants were not allowed to look directly at them, they had to fixate at the centre of the screen (where a fixation cross was presented) and use their peripheral vision to detect them and complete the task. The fixation cross was composed of a black cross placed on top of a white one.

Each arm of the white fixation cross was set to 0.3 degrees of visual angle, while each arm of the black fixation cross was set to 0.2 degrees of visual angle. The line width of the white fixation cross was set to 0.2 degrees of visual angle, while the line width of the black cross was set to 0.1 degrees of visual angle.

In the control task a fixation cross and two Gabor patches were presented against a grey background (Figure 2.2).

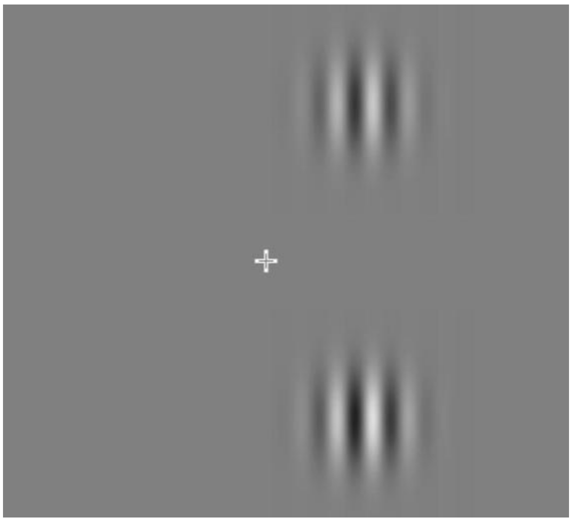

*Figure 2.2 - Stimuli used in the control task.*

Both Gabor patches were presented to the right of the fixation cross, one above and the other one below it. The centre of both Gabor patches lay on the same imaginary circle that was used in the experimental task, which was centred on the fixation cross with a radius of 5 degrees of visual angle.

The fixation cross was composed of a grey cross placed on top of a white one. Each arm of the white fixation cross was set to 0.3 degrees of visual angle, while each arm of the grey fixation cross was set to 0.2 degrees of visual angle. The line width of the white fixation cross was set to 0.2 degrees of visual angle, while the line width of the grey cross was set to 0.1 degrees of visual angle.

On each trial the contrast of the Standard Gabor patch presented below the fixation cross was randomly selected between a range varying from 0.4 to 0.7 in steps of 0.1. The contrast of the Comparison Gabor patch presented above the fixation cross was a percentage of the contrast used of the Gabor below the fixation cross. During the entire experiment 8 different values were used as percentages (70%, 79%, 88%, 97%, 103%, 112%, 121% 130%), and each of them was presented 30 times. Both the Standard Gabor patch and the Comparison Gabor patch had a spatial frequency of 1 cycle per degree, were oriented vertically, had radius of 3 degrees, and the sigma of the gaussian envelope was 0.43 degrees. The two Gabor patches were displayed on the screen for 200 milliseconds.

### *2.3.4.2 Resting Motor Threshold*

After the participant successfully completed the screening form and after obtaining written consent form, the resting motor threshold (RMT) was acquired on each day of the experiment for all the participants.

The RMT is the lowest intensity of stimulation needed to be delivered to the primary motor hand area (M1-HAND) in order to evoke a peak-to-peak Motor Evoked Potential (MEP) of 50 µV in at least five out of ten consecutive trials in the contralateral relaxed first dorsal interosseus (FDI) muscle (Quartarone, Bagnato, Rizzo, Morgante, Sant'Angelo, Battaglia, Messina, Siebner, & Girlanda, 2005).

In order to define the starting position for the search for the M1-HAND area, the TMS coil was firstly placed on top of the vertex (defined as the mid-distance between the nasion-inion, and the left-right auricular bones) and then moved 1 centimetre to the left, away from the vertex and 4-5 centimetres forward (Groppa, Oliviero, Eisen, Quartarone, Cohen, Mall, Kaelin-Lang, Mima, Rossi, Thickbroom, Rossini, Ziemann, Valls-Solé, & Siebner, 2012).

During the entire RMT assessment, the handle of the coil was pointed backwards at a 45° angle away from the midline, approximately perpendicular to the line of the central sulcus. For each subject, the RMT was determined as the intensity at which single pulses applied over the hand area of right M1 produced a visible muscle twitch in 5 of 10 consecutive trials, which is a standard procedure in the field Feredoes, Tononi, & Postle, 2006; Schutter, & van Honk, 2006).

Once the RTM for the day was defined, we set the intensity of stimulation for the experimental tasks to 110% of that value. Mean ± SE RMT was 59.85 ± 1.5%

maximum stimulator output (MSO) for the SPL and 59.65 ± 1.9 MSO for the Vertex. Mean ± SE experimental stimulation intensity was 65.8 ± 1.7% MSO for the SPL and 66 ± 2.1% MSO for the Vertex. Note that if T1 MRI scans had been available for all participants then more sophisticated procedures for setting stimulation intensity would have been available to us, such as adapting the RMT of each participant on the basis of the distance between the motor cortex where it is measured and the SPL and the distance between the brain and the skull, as recommended by Stokes et al. (2005) and Davis (2021).

#### *2.3.4.3 Location of the TMS target*

After defining the RMT and the intensity of TMS stimulation for the day, we located the target for the stimulation on that day. On the day in which the vertex was the target of the stimulation, the target was located in each participant as the mid-distance between the nasion-inion, and the left-right auricular bones.  On the day in which the SPL was the target, the location was found using the Brainsight software (Brainsight TMS, Rogue Resolutions Ltd) and MNI coordinates. The targeted MNI coordinates in the SPL were selected on the basis of a series of fMRI studies running concurrently in the lab (Field & Goodwin, 2016; Goodwin 2021), and were also consistent with the activation peaks reported in the studies reviewed in the Introduction here. The coordinates used for the SPL were x = -20, y = -60, z = 60. Unfortunately, due to a major upgrade causing the MRI scanner to become unavailable, only 9 participants had a T1w image that we could use to locate the SPL, so for the remaining participants we used a standardised 2 mmT1w that comes with the Brainsight software. The procedure for locating the SPL was the same in all the participants: after loading either the participant's T1w image or the standardised 2mm T1w included in Brainsight, the participant was asked to sit in front of the Polaris camera and wear a subject tracker, which was strapped to their forehead. Then the researcher used a pointer to point at the nasion, auricular bone on both the left and the right, in order to register the participant's head within the Brainsight Software and recreate a skull based on the participant's landmarks. After that the above MNI coordinate for the SPL subregion were entered, or for the vertex the landmark defined during the RMT procedure was used. After the TMS target for the day was located, participants were asked to place their chin on a chinrest, placed 90 centimetres away from a ViewPixx monitor, and then the TMS coil was placed over the target, and it was hold in place using a mechanical arm.

### *2.3.4.4 TMS Stimulation*

The experimental and control tasks were both composed of 240 trials and during each trial a pattern of TMS pulses was delivered. During the experimental task the TMS stimulation was synchronised with the 200 ms presentation of the two sets of dots, while in the control task the TMS stimulation was synchronised with the presentation of the two Gabor patches. For both tasks the end of the TMS stimulation was paired with the removal of the stimuli from the screen.

Four pulses were delivered during a 200 ms time window (20 Hz) and the intensity of stimulation was set to 110% of the Resting Motor Threshold acquired earlier that day; the pulses were delivered using a figure-of-8 coil, which was attached to a PowerMag machine (Mag & More GmbH, München, Germany). A 5 seconds ITI was inserted between each experimental trial, in order to avoid any add-up effects of the TMS (Hamidi, Johson, Feredoes, & Postle, 2011). These timings are illustrated in Figure 2.3 for the experimental task and Figure 2.4 for the control task. Overall, in both the experimental and control conditions 960 pulses were delivered to each participant, 1920 in total on each day.

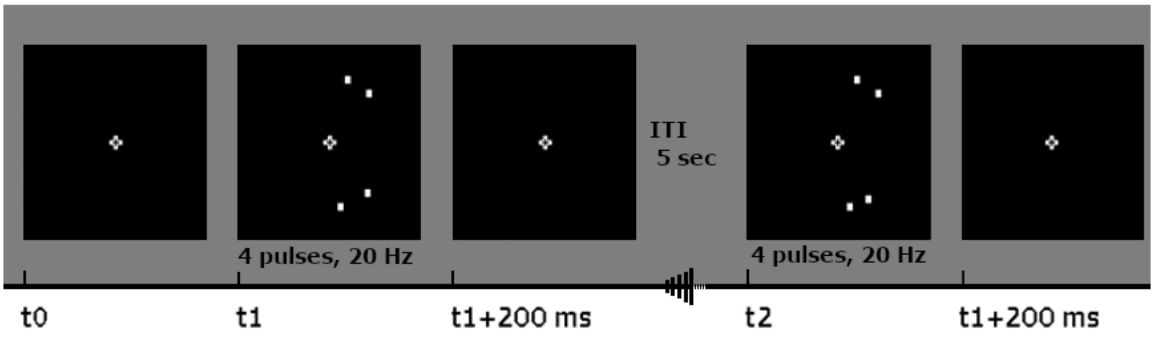

*Figure 2.3 - Timeline of the Experimental Task. At t0 just the fixation cross is present on the screen; at t1 the two pairs of dots are presented on the screen, one pair above and the other one below the fixation cross, the presentation of the stimuli is paired with the TMS pulses; after 200 ms the TMS stimulation stops and also the stimuli are removed from the screen.*

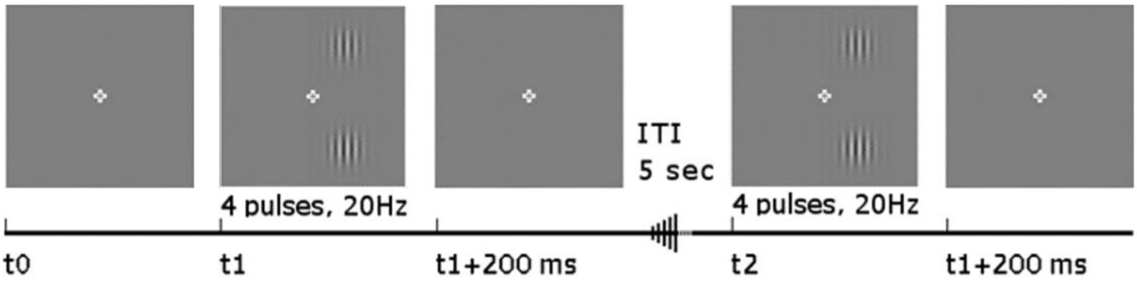

*Figure 2.4 - Timeline of the Control Task. At t0 just the fixation cross is present on the screen; at t1 the two Gabor patches are presented on the screen, one above and the other one below the fixation cross, the presentation of the stimuli is paired with the TMS pulses; after 200 ms the TMS stimulation stops and the stimuli are removed from the screen.*

## 2.4 Results

All the participants successfully completed both sessions of this study, and no data was discarded or excluded.

By using the Palamedes toolbox for MATLAB (Prins, & Kingdom, 2018), we fitted a Cumulative normal function to the data acquired for each task on both days, resulting in 4 cumulative normal functions for each participant (Figure 2.5).

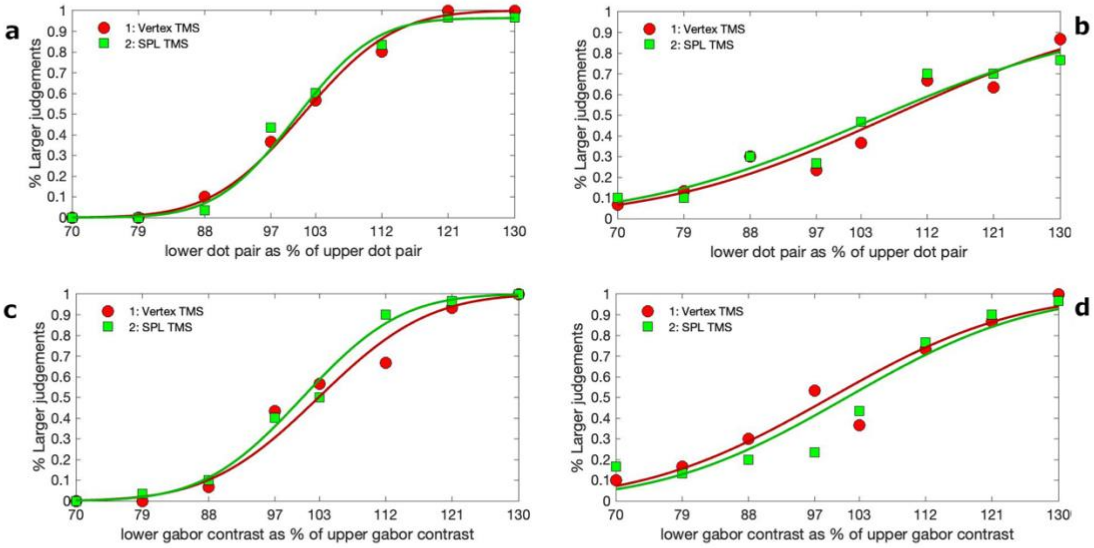

*Figure 2.5 Four example cumulative normal functions from individual participants. (a) An example from a participant with good relatively good performance in the experimental task, reflected in a steep slope; (b) an example of a participant with relatively poor performance in the experimental task; (c) and (d) provide similar examples of good and poor performance in the control task.*

From each fitted psychometric function, we extracted and statistically analysed the PSE (i.e., the Comparison stimulus as a percentage of the Standard for the point where the two visual extents were judged to be equal) and the slope. The descriptive statistics of these 2 parameters are included in Table 1

*Table 1 - Descriptive statistics for the Visual Separation Task and the Control Task.*

| **Parameter** | **Statistic** | **VisSep-SPL** | **VisSep-Vertex** | **Control-SPL** | **Control-Vertex** |
|---|---|---|---|---|---|
| PSE | mean | 102.3 | 101.4 | 102.9 | 104.6 |
| | median | 102.6 | 102.2 | 101.5 | 104.5 |
| | SD | 6.8 | 8.1 | 6.1 | 5.2 |
| | SE | 1.5 | 1.8 | 1.4 | 1.2 |
| | min | 89.9 | 86.01 | 91.7 | 95.2 |
| | max | 116.4 | 115.1 | 115.6 | 114.3 |

|  |  |  |  |  |  |
|---|---|---|---|---|---|
| SLOPE | mean | 0.058 | 0.070 | 0.060 | 0.059 |
|  | median | 0.057 | 0.071 | 0.055 | 0.059 |
|  | SD | 0.018 | 0.018 | 0.020 | 0.015 |
|  | SE | 0.004 | 0.004 | 0.004 | 0.003 |
|  | min | 0.032 | 0.046 | 0.040 | 0.032 |
|  | max | 0.103 | 0.114 | 0.118 | 0.085 |

Pirate plots showing the mean, SD and distribution of the PSE and the slope in the four experimental conditions are presented in Figure 2.6 and Figure 2.7.

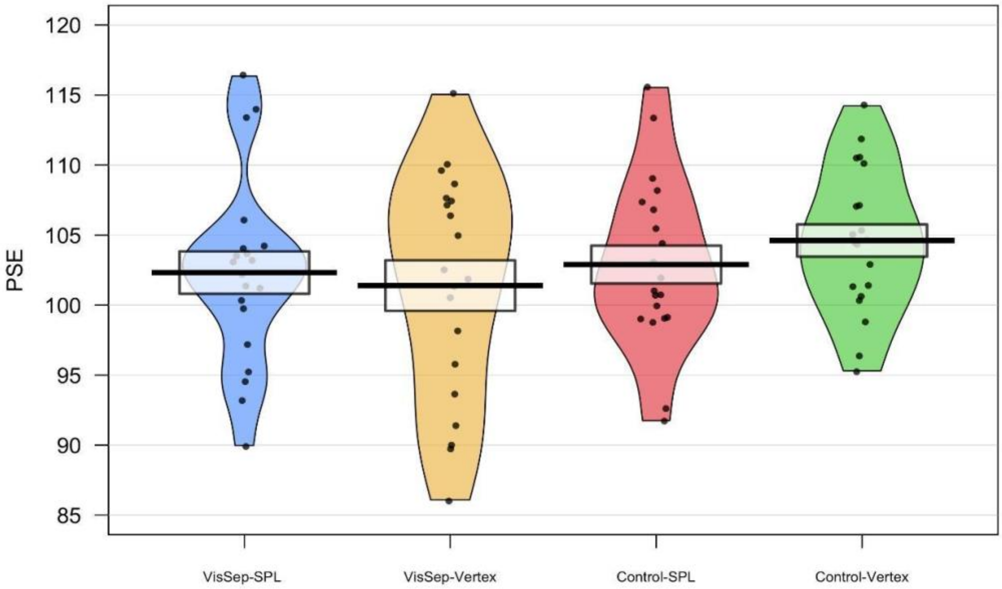

*Figure 2.6 - Pirate plots showing the mean, SD and distribution of the PSE for both the visual separation judgment and the control contrast judgment task, with TMS applied to either the SPL or the vertex.*

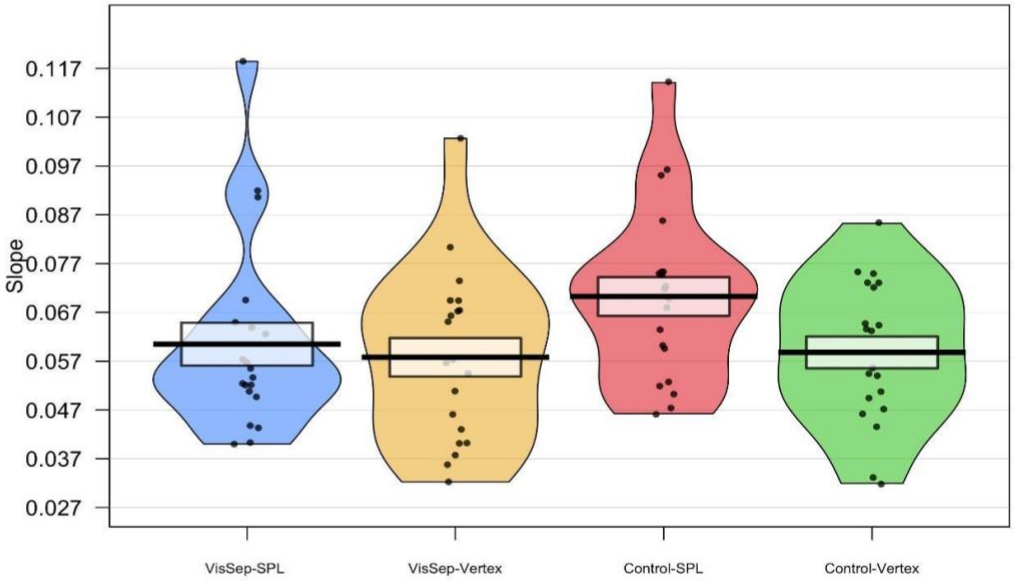

*Figure 2.7 – Pirate plots showing the mean, SD and distribution of the slope of the fitted psychometric functions for both the visual judgment and the control task, with TMS applied to either the SPL or the vertex.*

### 2.4.1 Influence of SPL TMS compared to vertex TMS on precision of visual separation judgments

Our prediction was that the TMS stimulation of the SPL should have affected the precision of the visual separation task. Moreover, we predicted that the disruptive effect of the TMS stimulation of the SPL should have resulted in a shallower slope for the psychometric function, compared to the slope obtained in the psychometric function for the same task when the stimulation was delivered over the Vertex.

In order to test our prediction a paired sample t-test was run for the slopes of psychometric function obtained from the visual separation tasks. There was not a significant difference between the slope obtained for the SPL stimulation (M = 0.061, SD = 0.020) and the slope obtained for the Vertex stimulation (M = 0.058, SD = 0.018); t(19) = -1.046, p = 0.309; d = -0.23

### 2.4.2 Influence of SPL TMS compared to vertex TMS on precision of visual separation judgments in the control contrast judgment task

Our hypothesis suggested that the TMS stimulation would have no effect on the slope obtained in the control task.

A paired-sample t-test was run for the slopes of psychometric function obtained from the control task. Unexpectedly, the SPL stimulation resulted in steeper psychometric functions (more precise judgment) than the vertex stimulation, and this difference was significant; (SPL M= 0.07, SD= 0.018) (Vertex: M= 0.059, SD= 0.015), t(19)= -3.322, p = 0.004; d = -0.74

### 2.4.3 Exploratory analysis of the effect of TMS on the PSE (bias)

We had no specific reason to predict that TMS would differentially affect the point of subjective equality (PSE) in either the experimental or control task, and so performed an exploratory analysis of this. A paired sample t-test was run on the PSEs of the psychometric functions obtained from the visual separation task. There was not a significant difference between the PSEs obtained for the SPL stimulation (M= 102.3211, SD= 6.7698) and the PSEs obtained for the Vertex stimulation (M= 101.3948, SD= 8.0682), t(19)= -0.893, p= 0.383; d = -0.2. The mean and standard deviation for the PSEs obtained for the visual separation task are presented in Figure 2.7, in the columns labelled VisSep-SPL and VisSep-Vertex.

Another paired sample t-test was run for the PSEs of psychometric function obtained from the control task. There was not a significant difference between the PSEs of the psychometric function obtained for the control task when the TMS was delivered over the SPL (M= 102.892, SD= 6.047) and the PSEs obtained for the control task when the TMS was delivered over the Vertex (M= 104.612, SD= 5.168), t(19)= 1.372, p=0.186; d = 0.31.

# 2.5 Discussion

The main purpose of this experiment was to test the hypothesis that part of the SPL is involved in supporting the perception of the 2D visual separation between two points. In order to achieve this goal a 2-day TMS experiment was carried out. On the first day of the experiment the TMS stimulation was delivered over the left SPL while two different tasks were presented: the experimental task was aimed to measure the just noticeable difference in visual separation between two points. On the second day of the experiment the TMS was delivered over the Vertex (a control site for TMS stimulation), while the same two tasks were presented. We predicted that TMS over SPL would reduce the precision of judgments of visual separation compared to TMS over the vertex, but not in a control task. The data failed to support this prediction. However, we unexpectedly found that TMS over SPL compared to vertex increased the precision of performance in the control task, which measured the ability to detect differences in luminance contrast.

The results of this study do not support the hypothesis that a subregion of SPL is critical for the perception of two-dimensional visual separation or extent, but because the study had a number of limitations neither do they refute it. The design made the assumption that TMS delivered to the control location, which was the vertex of the skull, would not influence neural activity in the SPL or behavioural task performance. However, Davis & van Koningsbruggen (2013) highlight that unplanned stimulation of non-target areas may result from TMS. This was demonstrated in the case of the vertex by Jung, Bungert, Bowtell, & Jackson (2016) who delivered TMS stimulation (120% of RMT) to the Vertex concurrently with functional BOLD MRI and found that Vertex TMS produced a significant deactivation in a number of brain regions including the right SPL and the precuneus. The general effect was deactivation in the ‘default mode network’, which may have had the knock-on effect of an increase in excitability in the ‘salience’ network. Previous studies (Goulden, Khusnulina, Davis, Bracewell, Bokde, McNulty, & Mullins, 2014; Sridharan, Levitin, & Menon, 2008) have shown that the salience network is responsible for switching between the default mode network and the central executive network, and therefore stimulating the Vertex might have inadvertently activated regions of the brain involved in the task. While the TMS we delivered to SPL would be expected to produce BOLD activation rather than the deactivation likely caused by the Vertex stimulation, given the highly interconnected nature of the brain we suspect that the control condition was not inert. An improved design would have incorporated an additional no-TMS control condition, which would have allowed us to establish whether Vertex TMS had any effect on our behavioural task. Without a no-TMS condition, it cannot be ruled out that Vertex and SPL TMS both had similar effects on the visual separation judgement task.

Another consequence of methodological limitations is that we are not confident of having delivered TMS to the same subregion of SPL in all participants, or to have consistently delivered it to the same location within individual TMS sessions. The former concern arises because we were unable to use MRI based functional localisers, which are the gold standard for TMS (Sack, Cohen Kadosh, Schuhmann, Moerel, Walsh, & Goebel, 2009; Sparing, Buelte, Meister, Paus, & Fink, 2008) and were able to make use of anatomical scans in only half of our participants. The latter concern arises because in our online TMS paradigm using a robotic arm to keep the TMS coil in place does not take into account the slight head movements that the participant makes over the course of the long session. Given that the figure of 8 coil is known to deliver a very focal stimulation (Wasserman, Epstein, & Ziemann, 2008), slight head movements might result in a stimulation of a region different from the target of this study. Under our hypothesis that a subregion of SPL centred on the MNI coordinates x = -20, y = -60, z = 60 is responsible for the perception of visual separation, the combined consequence of these two problems would be an increase in error variance and a reduction of effect size. To address the latter problem, we are switching our efforts to offline TMS paradigms such as continuous theta burst, in which the stimulation is administered in a short period before the experiment begins, as during this short period the participant can successfully remain still. The former problem can be addressed by the introducing MRI based functional localisers to future studies.

We did unexpectedly find that precision of judgement in the control contrast sensitivity task was better following SPL TMS than following Vertex TMS. As well as being unpredicted, the result is unusual in that delivering HF-rTMS usually results in reduced rather than improved task performance (Rotenberg, Horvath, & Pascual-Leone, 2014). If the effect is genuine rather than a Type 1 error, then we are not currently able to explain it. The same pattern of results did not occur in the experimental task and the two tasks were well matched in terms of cognitive and motor requirements, so we may speculate that TMS to SPL improves the ability to compare stimulus features across two spatial locations. However, before seeking to test such explanations the result should be confirmed by a replication study, which could also introduce related measurements such as contrast sensitivity. Furthermore, we can conclude that future studies testing the primary hypothesis investigated here should not use a control task to demonstrate functional specificity of TMS effects, because our assumption that it would be unaffected by TMS to the SPL proved unfounded.

In conclusion, further studies with greater statistical power and methodological improvements discussed above should be conducted to test the hypothesis that a subregion of SPL supports the perception of visual separation, as well as to further investigate the unexpected finding that TMS to the SPL improved the ability to compare visual contrast levels at nearby spatial locations.

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# Chapter 3. The role of the Superior Parietal Lobule in the Müller-Lyer illusion: a TMS study

## 3.1 Abstract

Previous studies have implicated the Superior Parietal Lobule (SPL) in the Müller-Lyer illusion as well as eye movement planning. In this study we investigated the role played by the Superior Parietal Lobule (SPL) in both the effect of the illusion on eye movements generated by the Müller-Lyer illusion, and on the well-known perceptual illusion of extent. The perceptual illusion of extent was measured using the bisection bias generated by both the Judd and Brentano variants of the Müller-Lyer illusion. We delivered offline continuous theta burst stimulation (cTBS) for 40 seconds to either the SPL (identified as the electrode CP1 in the 10-20 EEG system) or a control region (i.e., the vertex) before presenting the tasks. We found that cTBS stimulation over the SPL did not significantly affect saccade amplitudes recorded during the presentation of the Müller-Lyer or reduce the bisection bias generated by the Judd variant or the Brentano version of the Müller-Lyer stimuli compared to cTBS over the vertex.

# 3.2 Introduction

How do we perceive the visual distances (visual angles) between stimuli or points in the image plane? No direct information about visual angles between stimuli arises from the firing rates of the individual neurons organised into retinotopic maps that are present in V1 and V2. Individual neuron firing rates in V1 encode stimulus position, while information about visual angles is preserved in the pattern of firing across neurons. One possibility is that higher level visual processing takes the position signals from V1/V2 as its input and uses them to compute visual angles (e.g., Biagi, Goodwin, & Field, 2021 submitted; Harvey, Fracasso, Petridou, & Dumoulin, S. 2015; Schwarzkopf, 2015). A radically different possibility is that efference copies of sensorimotor plans that are inherently spatial are used to fill this gap. In this chapter, we focus on the latter possibility. Note that we use the terms visual distance and visual separation refer to the simple 2D visual separation in degrees of visual angle between two points in the image plane, not to higher level perception of distance between objects in the world.

In Chapter 2 we carried out experiments in order to test the hypothesis that the SPL plays a role in the perception of visual separation using an online TMS stimulation during a psychophysical visual separation judgment task, but found no evidence to support our hypothesis. It may be that the decision to use online TMS stimulation in conjunction with a psychophysical methodology failed to capture the role played by the SPL in the perception of visual separation. As such, in this chapter we decided to further investigate the role played by the SPL in the perception of visual separation using a different approach.

Efferent theories of perception have a long history and are grounded in the idea that the visual system evolved to guide movement in response to stimuli rather than to produce perception of the world. Being closely coupled to sensory input, eye movements have provided a testbed for this theory. Many experiments have confirmed the prediction that stimulus configurations that produce biased spatial perception also produce biased patterns of eye movements. For example, in the Müller-Lyer figures, the amplitude of saccadic eye movements made along the shaft is altered by the illusion (Binsted, & Elliott, 1999; Delabarre, 1898; Festinger, White, & Allyn, 1968; Stratton, 1906; Yarbus, 1967). However, as Coren (1986) points out, it is hard to determine whether the perceptual illusion drives the eye movement biases or vice versa. Because experimental conditions that prevent overt eye movements do not abolish illusions such as the Müller-Lyer, a role for proprioceptive information about eye position after saccades have been made in perception has been ruled out. However, Coren (1986) proposes that what influences perception of angular extent is not proprioceptive feedback but planned eye movements, which may or may not go on to be executed. Coren’s 6th experiment attempts to show that eye movement plans are prior to perception in the causal chain rather than the other way around by demonstrating that illusory biases in perception are influenced by the presence of an eye movement plan, independently of low-level stimulus configurations. While this is a useful demonstration, the findings could potentially also be explained in terms of the distribution of spatial attention across the stimulus, and so further lines of evidence are needed. To address this, here we will use the Müller-Lyer illusion to induce a bias in both perception and eye movements and use TMS to try and disrupt these effects.

Consistent with an efferent explanation for the ability to perceive visual extent, Zimmermann & Lappe (2010) showed that there is a shared map for motor and visual space. They showed that using an adaptation paradigm (McLaughlin, 1967) it was possible to change the map of motor representation, and in turn affected the perceptual visual space. In the method of saccade adaptation, participants are asked to move their eyes from a fixation point to a target on the screen and, once they have initiated the saccade and their eyes are moving the target position changes (either towards the fixation point, i.e., inward adaptation, or further away from the fixation point, i.e., outward adaptation). Because visual sensitivity is reduced during saccade execution, participants remain unaware of the displacement of the target (McLaughlin, 1967), but after the saccade has landed, the oculomotor system detects the error between the end position of the saccade and the location of the target, and a second corrective saccade is deployed to reduce the gap. If the misplacement of the target remains constant for several trials, then the oculomotor system adapts to it and the saccade triggered by the target stimulus lands closer to the misplaced position instead of the original position of the target (Zimmermann & Lappe, 2010).

After saccade adaptation was achieved, participants were asked to judge the perceptual location of a probe that was flashed briefly on the screen before an adapted saccade. It was found that the probes were mislocated in the direction of the adaptation. However, it was not clear whether this was caused by the saccade adaptation or by the mismatch between the expected and actual landing position of the saccade.

An answer to this question had been previously suggested by Garaas & Pomplun (2011), where they presented a large persistent cross and asked participants to compare the lengths of the horizontal and vertical component of it before and after saccade adaptation. They discovered that after vertical outward adaptation, the vertical lines were perceived as longer, while after vertical inward adaptation were perceived shorter. They found a similar effect for horizontal adaptation, where after horizontal inward adaptation horizontal lines were perceived as shorter. This suggests that the saccade adaptation not only changes the motor map, but also the visual space. This is in line with the two-factor theory proposed by Müsseler & Van der Heijden (2004), where it was suggested that the perception of visual space is established by a visual sensory map, which gives information of what composes the visual field, and a non-visual motor map, which contains all the possible eye movements necessary to bring various locations under foveal inspection. These two maps are highly connected and together they establish the locations and identities of objects in the visual field. This theory would explain why saccadic adaptation, which affects the non-visual motor map has also an effect on the visual sensory map.

A number of lines of evidence suggest that the parietal lobe, which we target with TMS, plays an important role in generating the linked motor and visual maps. Panouillères, Habchi, Gerardin, Salemme, Urquizar, Farne, & Pélisson (2014) showed that the parietal lobe is involved in the process of saccade adaptation. They delivered single pulse TMS (spTMS) over the right posterior intra-parietal sulcus (pIPS) at different timings after saccade onset (30, 60 and 90 ms). They discovered an impairment of saccade adaption for voluntary saccades when the spTMS was delivered 60 ms after saccade onset, and a facilitation of saccade adaptation for reflexive saccades when the spTMS was delivered 90 ms after saccade onset. These results show that there are two different system for the saccade adaptation, one for voluntary and another one for reflexive saccade, and the Parietal Lobe is important for both of them.

As well as being implicated in saccadic adaptation and the concurrent distortion of visual space, the parietal lobe has been shown to play a role in producing the distortion of perceived extent in the Müller-Lyer illusion and as noted above this illusion also affects eye movement amplitudes. Specifically, in an fMRI study Wiedner & Fink (2007) varied the magnitude of the illusion by varying the angle formed between the main shaft and the wings that induce the illusion. Activation in the right superior parietal cortex and the lateral occipital cortex covaried with illusion magnitude.

In a follow up study, Mancini, Bolognini, Bricolo & Vallar (2011) delivered repetitive TMS stimulation (rTMS) over the regions identified by Weidner and Fink (2007) (i.e., the occipital-temporal cortex and the superior parietal cortex) and then ask the participant to perform a bisection task using the Judd variant of the Müller-Lyer illusion. They found that rTMS over the SPL produced a trend for an effect on illusion strength. However, as the Judd variant of the Müller-Lyer illusion, has been shown to produce an illusion of position rather than extent (Mack, Heuer, Villardi, & Chambers, 1985), this cannot be taken to confirm a role for right superior parietal cortex in biases of extent perception. Finally, fMRI studies carried out recently in our lab using minimal stimulus configurations made up of dots to test whether superior parietal lobule activation is driven by spatial attention shifts or alternatively by changes in perceived visual separation between stimuli concluded that changes in visual separation were the key factor (Field & Goodwin, 2016; Goodwin, 2021).

Turning to the current study, our purpose is to address the question Zimmerman & Lappe (2016) highlighted: *"To understand how saccade adaptation modifies space perception we need to ask how and where in the brain the common metric for saccades and spatial perception may reside."*. Again, we chose to target the SPL with TMS because the studies reviewed here suggest it has a role in the perception of extent and visual separation, and it has also been implicated in eye movement planning (Koyama, Hasegawa, Osada, Adachi, Nakahara, & Miyashita, 2004). As a stimulus we selected the Müller-Lyer illusion because in its standard form it produces biased perception of the separation between two points in space (Mack et al., 1985), as well as a corresponding bias in landing positions of saccadic eye movements. Furthermore, studies reviewed above show that the superior parietal region plays a role in producing the illusion.

The present study aimed to test the proposal that SPL was critical for the processing and perception of eye movements and visual extent in the Müller-Lyer illusion. Instead of using TMS to try and induce a reduction in the precision of judging visual separation (psychophysical slopes) as we did in Chapter 2, we designed the current study so that TMS might induce biases in the perception of visual extent. In order to do so, 2 main changes were made: we decided to deliver offline continuous theta burst stimulation (cTBS) instead of online TMS, and we abandoned the psychophysical approach to the tasks. We decided to deliver offline cTBS instead of online TMS for practical reasons: an online TMS might result in a less precise stimulation given that the artificial arm holding the TMS coil does not adjust for small movements that participants might make during the task. Moreover, offline stimulation has a well-known effect of inhibiting the target region for up to 60 minutes after the stimulation, which allowed us to present various tasks in which the perception of a horizontal line was measured. cTBS is a specific pattern of TMS stimulation and it is composed of a burst of 3 stimuli at 50 Hz (i.e., 20 ms between each stimulus), repeated at intervals of 200 ms. It lasts for 40 seconds and a total of 600 pulses are delivered (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). This specific pattern of TMS stimulation is known to generate a long-lasting depolarisation effect which affects Motor Evoked Potentials (MEPs) up to 60 minutes after stimulation (Huang et al., 2005).

The tasks used in this study are very different from the ones used in Chapter 1. One reason for moving away from the psychophysical approach was to have shorter tasks which might have allowed participants to concentrate better. The behavioural tasks performed after the cTBS was applied to SPL were an eye-movements task, where participants had to move their eyes from one end to the other of the horizontal shaft of a standard Müller-Lyer stimulus (Figure 3.1a); a perceptual bisection task, where participants had to correctly bisect a Judd variant of the Müller-Lyer stimuli (Figure 3.1b); and another bisection task where participants had to bisect a Brentano version of the Müller-Lyer stimuli (Figure 3.1c). To increase methodological rigor, we also applied cTBS to a control region (i.e., the vertex) that was not thought to play a role in processing visual extent. In line with the proposal that eye movement planning and perception of space are closely coupled processes, we predicted that cTBS to the SPL would result in significantly different performance in all three tasks compared to the performance recorded after the cTBS was applied to the control region (vertex).

We measured both the perceptual Müller-Lyer illusion as well as the eye movement bias as targeting the SPL with TMS could produce a number of potential changes in these outcomes relevant to our underlying theoretical question concerning the relationship between perception and eye movement plans. If TMS to SPL is found to disrupt only the effect of the illusion on eye movements, or only the effect of the illusion on perception, then this would count as evidence against the proposal that motor plans and perception are closely linked, suggesting instead independent processing pathways. However, if TMS to SPL disrupts both perceptual and eye movement aspects of the illusion then this would support the idea that eye movement plans, and perception are closely linked.

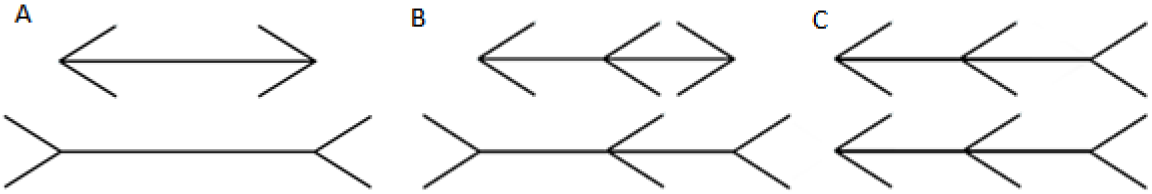

*Figure 3.1- Stimuli used in this study. (a) the standard Müller-Lyer figure. (b) the Judd variant of the Müller-Lyer figure, (c) the Brentano version of the Müller-Lyer figure.*

# 3.3 Method

## 3.3.1 Participants

For this study 21 healthy participants (5 males, 16 females) were recruited for a 2 non-consecutive day TMS study at the University of Reading. This sample size was sufficient to detect an effect size of d = 0.56 for our one tailed prediction (power 0.8, alpha 0.05, paired sample t-test). Participants were recruited via the University of Reading Student Volunteer Panel (SONA), where the study was advertised. The age range of the participants recruited was between 18 and 41 years old (Median = 20, range= 18-41). All participants were informed that they participation to this study was voluntary and that they could withdrawal at any time without providing a reason.

## 3.3.2 Ethical approval

This study was granted ethical approval by the University of Reading Ethics Committee (UREC), with an UREC code 17/49, expiration date 1/10/2020. Due to the seizure-potential that the TMS stimulation has (Wassermann, & Lisanby, 2001), participants were asked to complete a TMS screening form before each cTBS stimulation. The TMS screening form was approved by the UREC and was composed of 24 questions aimed to investigate if the participant had previous psychiatric, neurological or other medical conditions and therefore was not eligible for the cTBS stimulation (Rossi, Hallett, Rossini, & Pascual-Leone, 2009). Moreover, the experimental design conformed to the TMS safety parameters specified by Wasserman & Lisanby (2001) and Rossi (2009) regarding duration, intensity and frequency of stimulation. In order to ensure the safety of the participants, after each stimulation the participant was asked to stay with one of the experimenters for approximately one hour, until the effect of cTBS had fully disappeared. Before the start of the cTBS stimulation participants were reminded that they could withdraw at any time from the study without providing a reason.

### 3.3.3 Apparatus and Materials

All the experiments presented in this study were programmed using Psychtoolbox (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007; Pelli, 1997), a freely available toolbox for MATLAB. All the stimuli were displayed on a 24-inch ViewPixx monitor (1920(H) x 1080(V) pixels), placed 90 centimetres away from the participant. In order to reduce head movements, participants were asked to rest their chin on a chinrest for the entire duration of the experiment (the chinrest was placed 90 centimetres away from the ViewPixx monitor). Placed under the monitor there was an Eyelink 1000 eye tracker (sampling frequency of 1000 Hz) for the purpose of recording the eye movements.

## 3.4 Design and Procedure

The design was fully repeated measures, with every participant undergoing offline cTBS stimulation over 2 different regions in two different days: the Superior Parietal Lobule (SPL) and the Vertex (control region). Each stimulation took place on a different day and there was at least a 48-hour interval between the 2 sessions. For half of the participants, on Day 1 the stimulation was delivered over the EEG electrode C1 (used as a proxy for the SPL, as suggested by Koessler, Maillard, Benhadid, Vignal, Felblinger, Vespignani, & Braun, 2009), and on Day2 it was delivered over the Vertex, while for the other half of the participants the order of stimulation was reversed. In each session, three short experiments were completed after the cTBS stimulation. The order of presentation of the experiments was the same for all the participants.

In experiment 1 the effect of cTBS on eye movements was investigated. In order to do so, saccades amplitudes were recorded while three different variations of the Müller-Lyer figure, one of which was a control figure with vertical fins, were presented in white on a black screen (Figure 3.2). On each trial the participant was presented with one configuration of the Müller-Lyer figure and was asked to saccade back and forth rapidly between one end of the horizontal shaft and the other end for 10 seconds. Each configuration was presented 3 times, for a grand total of 9 trials.

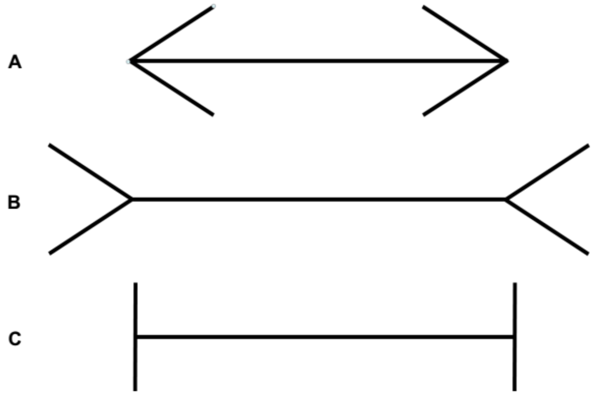

*Figure 3.2 - Stimuli used in Experiment 1.*

In experiment 2 the effect of the cTBS on the perceptual bisection point bias induced by the Judd variant of the Müller-Lyer illusion was investigated. In order to do so, bisection judgments were recorded for 3 different configurations of the Judd variant of the Müller-Lyer illusion were used (Figure 3.3). On each trial the participant was presented with one configuration of the Judd variant of the Müller-Lyer stimuli, with a middle fin displayed randomly at a randomly decided starting point along the horizontal shaft and was asked to bisect the main shaft of the stimuli by adjusting the position of the middle fin using the left and right arrow keys on the keyboard. The participants had 10 seconds in each trial to bisect the stimulus and press the spacebar to confirm their adjustment. A total of 24 trials were presented.

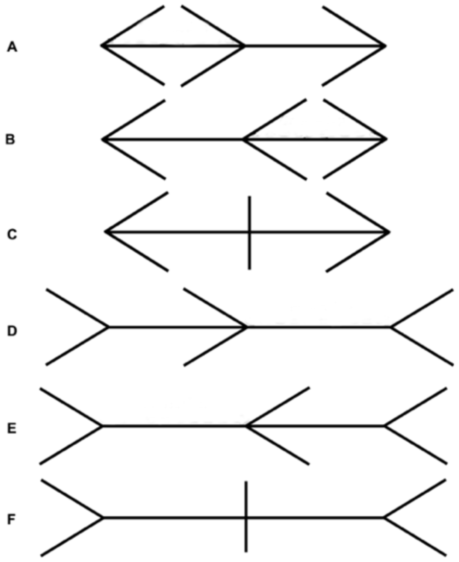

*Figure 3.3 - Stimuli used in Experiment 2. Stimuli A and B are the same configuration and therefore we referred to them as Group 1; Stimuli D and E are the same configuration and therefore we referred to them as Group 2; Stimuli C and F are the same configuration and therefore we referred to them as Group 3.*

In experiment 3 the effect of cTBS on the bisection bias induced by the Brentano version of the Müller-Lyer illusion was also investigated. In order to do so, 3 different configurations of the Brentano version of the Müller-Lyer illusion were used (Figure 3.4). On each trial the participant was asked to adjust the location of the middle fin so that it bisected the horizontal shaft by using the left and right arrow keys on the keyboard. In each trial the middle fin was presented at a randomly decided starting point along the horizontal shaft. The participants had 10 seconds in each trial to bisect the stimulus and press the spacebar to confirm their adjustment. A total of 24 trials were presented.

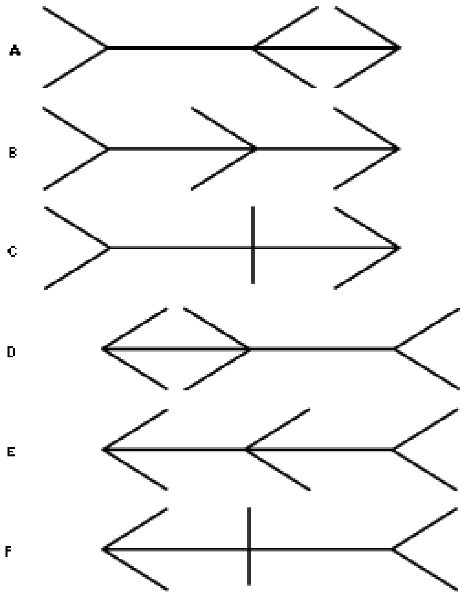

*Figure 3.4 - Stimuli used in Experiment 3. Stimuli A and D are the same configuration and therefore we referred to them as Group 1; Stimuli B and E are the same configuration and therefore we referred to them as Group 2; Stimuli C and F are the same configuration and therefore we referred to them as Group 3.*

### *3.4.1 Stimuli*

All the configurations of the stimuli used in the 3 experiments were composed of a horizontal shaft and two wings, each of which was attached to one of the end points of the main shaft.

In all the configurations the length of the main shaft was 10°, and the length of the wings was 1/3 of the length of the main shaft, while the angle between the two parts of the wing was set to be equal to 65° (or 295º if you consider the wing pointing outward). This has been suggested to be the shaft/wing configuration that can induce the strongest illusion (Weidner & Fink, 2007).

The configurations of the stimulus where the fins are vertical does not induce an illusion (Weidner & Fink, 2007), and therefore this stimulus was used as a baseline against which the illusion magnitude of the other two stimuli was quantified.

### *3.4.2 Resting Motor Threshold*

After a participant successfully completed the screening form and after obtaining written consent, the resting motor threshold (RMT) was acquired on each day of the experiment.

The RMT is the lowest intensity of stimulation the primary motor hand area (M1-HAND) that evokes a peak-to-peak Motor Evoked Potential (MEP) of 50 µV in at least five out of ten consecutive trials in the contralateral relaxed first dorsal interosseus (FDI) muscle (Quartarone, Bagnato, Rizzo, Morgante, Sant’Angelo, Battaglia, Messina, Siebner, & Girlanda, 2005).

In order to define the starting position for the search for the M1-HAND area, the TMS coil was firstly placed on top of the vertex (defined as the mid-distance between the nasion-inion, and the left-right auricular bones) and then moved 1 centimetre to the left, away from the vertex and 4-5 centimetres forward (Groppa, Oliviero, Eisen, Quartarone, Cohen, Mall, Kaelin-Lang, Mima, Rossi, Thickbroom, Rossini, Ziemann, Valls-Solé, & Siebner, 2012). The best position to produce the FDI muscle activation was located by moving the TMS coil in 0.5 centimetres steps from the starting position.

During the entire RMT assessment, the handle of the coil was pointed backwards at a 45° angle away from the midline, approximately perpendicular to the line of the central sulcus. For each subject, the RMT was determined as the intensity at which single pulses applied over the hand area of right M1 produced a visible muscle twitch in 5 of 10 consecutive trials, a procedure that has been used previously in the field (Feredoes, Tononi, & Postle, 2006, Schutter, & van Honk, 2006).

Once the RMT for the day was defined, we set the intensity of stimulation to 80% of that value. This is common practice for cTBS stimulation (Huang et al.,2005). Mean ± SE RMT was 59.2 ± 1.2% maximum stimulator output (MSO) for the session where the SPL was the target of stimulation, and 59.5 ± 1.3 MSO for the Vertex. Mean ± SE experimental stimulation intensity was 47.4 ± 0.9% MSO for the SPL and 45.2 ± 2.6% MSO for the Vertex.

### *3.4.3 Location of the TMS target*

After defining the RMT and the intensity of TMS stimulation for the day, we located the target for the stimulation on that day. In one of the two days of the experiment, the cTBS was delivered over the vertex, while in the other day the cTBS was delivered over the left Superior Parietal Lobule. The vertex (Cz) was located as the half-point distance between the nasion-inion and the two auricular bones, while the left Superior Parietal Lobule was determined according the international 10-20 system of electrode placement: participants were asked to wear an EEG cap and the position of the electrode CP1 was marked on the skull (Figure 3.5). According to Koessler and colleagues (2009) the electrode CP1 is the one closest to the left Superior Parietal Lobule.

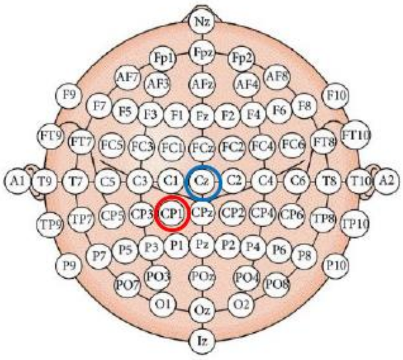

*Figure 3.5 - Location of electrode CP1 and Cz (vertex) on the 10-20 EEG system.*

In half of the participants the vertex was the target of cTBS in Day 1 while the electrode CP1 was the target in Day 2. For the other half of the participants the order of TMS stimulation was inverted. Immediately after the TMS session, in each day of the experiment, the three tasks were presented. After the TMS target for the day was located, participants were asked to place their chin on a chinrest, placed 90 centimetres away from a ViewPixx monitor, and then the TMS coil was placed over the target, and it was hold in place by the researcher.

### *3.4.4 TMS Stimulation*

Once the RMT was acquired, the participants underwent a single session of cTBS. The cTBS consisted of three pulses of stimulation given at 50 Hz, repeated every 200 ms for a total of 600 pulses. The stimulus intensity was set at 80% of RMT (Huang et al., 2005). The cTBS was delivered with a figure of 8 coil (7 centimetres diameter), attached to a PowerMag 1000 stimulator (Mag & More GmbH, München, Germany) and the pattern of stimulation was programmed in MATLAB.

# 3.5 Results

Two participants did not undergo both sessions of the experiment, reducing the sample from 21 to 19 participants.

## 3.5.1 Experiment 1

### *3.5.1.1 Pre-processing and descriptive statistics*

Due to technical issues the eyetracker data for one participant was not saved, further reducing the sample size to 18 participants. The continuous stream of eyetracker data for all the participants acquired during experiment 1, in which participants saccaded back and forth between the two ends of the shaft of the Müller-Lyer figure, was loaded into RStudio and out of all the saccades recorded during this task, just the saccades made when the stimuli were on the screen were selected, for a total of 9407 saccades. After that, the saccade amplitudes were converted into a percentage of shaft length and just the saccades either bigger than 50% or smaller than 150% of the shaft length were furthered analysed, reducing the number of saccades to 5490. Then, all the saccades that deviated more than 1.5º from a straight line between the two end of the stimulus were removed, further reducing the sample to 4081 saccade. These two filtering steps were taken from de Brouwer and colleagues (de Brouwer, Brenner, Medendorp, & Smeets, 2014). After the filtering procedure the average saccade amplitude for each configuration of the stimulus was obtained for each participant. Pirate plots showing the effects of TMS on the mean, 95 % CI and distribution of the saccade amplitudes in the 3 experimental conditions are presented in Figure 3.6.

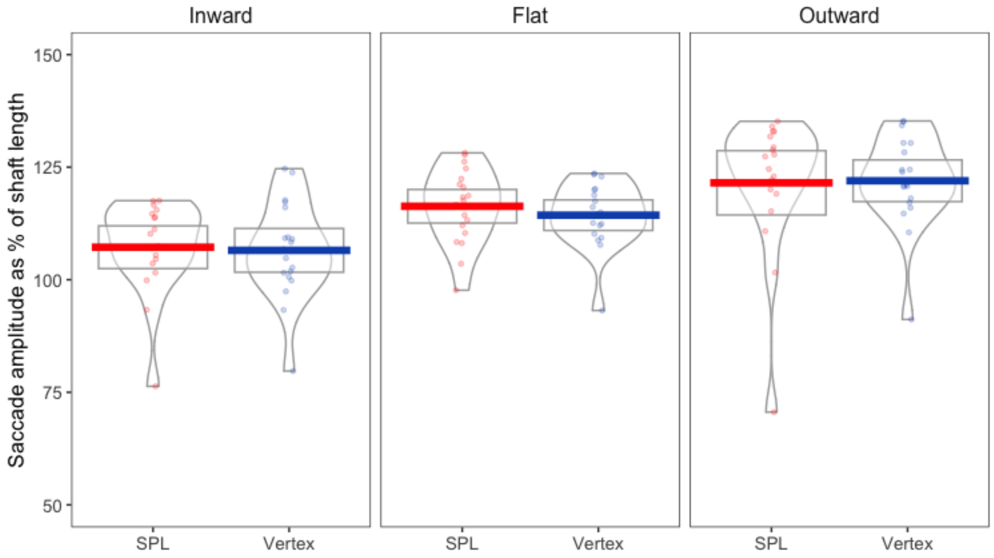

*Figure 3.6 - Pirate plots with mean and 95 %CI for the 3 configurations of the stimulus used in Experiment 1.*

### *3.5.1.2 Statistical Analysis*

Our prediction was that the cTBS stimulation of the SPL should have affected the saccade amplitudes elicited by the Müller-Lyer stimuli. Moreover, we predicted an overall reduction of the strength of the Müller-Lyer illusion’s effect on saccade amplitudes; we predicted that the cTBS should have reduced the saccade amplitudes elicited by the version of stimulus with the wings pointing outwards, and we predicted an increase in saccade amplitudes for the ones elicited by the inwards configuration of the stimulus. Means and SE for the 3 configurations of the Müller-Lyer used in Experiment 1 are presented in Figure 3.7.

In order to test our prediction, we carried out a 2 (Stimulation type: SPL vs Vertex) x 3 (Stimulus type: Outward/Flat/Inward) Repeated Measure ANOVA. The Mauchly's test for Sphericity for the 2-way interaction violated the assumption (sig. = 0.039), therefore we used the Greenhouse-Gassier correction.

The main effect for stimulation ($F(1,15) = .35$, $p = .563$, $\eta2= .023$) was not significant, while the main effect for stimulus type was significant ($F(22, 30)= 20.197$, $p < .001$, $\eta2=.574$). The interaction between the two main effect was also not significant ($F(1.459, 21.878) = .402$, $p=.673$, $\eta2=.026$). Regarding the main effect for stimulus type, pairwise comparisons with a Bonferroni adjustment revealed that saccade amplitudes were significantly increased from Inward to Flat (8.86.95 (95% CI, 5.45 to 12.28) %, $p < .001$), and from Inward to Outward (13.71 (95% CI, 8.58 to 18.84) %, $p < .001$), and trending towards significance from Outward to Flat (4.84 (95% CI, -.37, 10.06) %, $p =.066$).

This indicates that we replicated the previously found effects of the Müller-Lyer illusion on saccade amplitude, but cTBS failed to influence that.

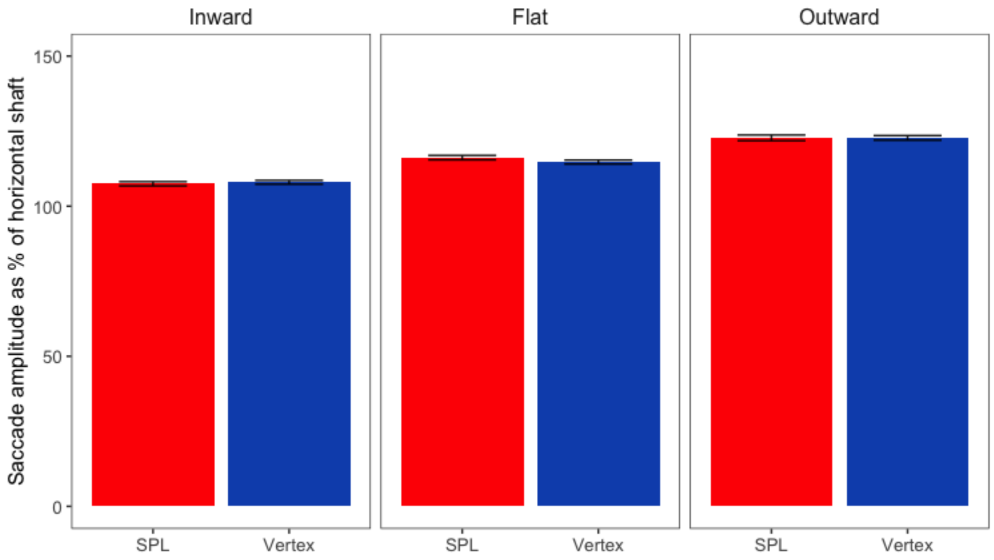

*Figure 3.7 - Bar plot with mean and SE for the stimuli used in Experiment 1.*

## 3.5.2 Experiment 2

### *3.5.2.1 Pre-processing and descriptive statistics*

The behavioural data from experiment 2 was loaded into RStudio, and before computing the bisection bias for the Judd version of the Müller-Lyer illusion, all the trials in which the participants failed to confirm their bisection before the 10 second response limit ran out were removed. This reduced the total number of trials from 984 to 975 trials. The bisection point was calculated as the distance between the final location of the middle fin and the true midpoint of the stimulus. For Stimulus A and Stimulus E in Figure 3.3 the bisection point was multiplied by -1 so that biases produced by the inward facing fins would be represented by a negative number and biases produced by the outward facing fins would be represented by a positive number. Group 3, in which no bias due to the fins was expected, the absolute value of the bisection point was used. After that, for each trial we computed the bisection bias as a percentage of shaft length. Pirate plots showing the effects of TMS on the mean, 95%

CI and distribution of the bisection bias in the 6 Judd variants of the Müller-Lyer illusion are presented in Figure 3.8.

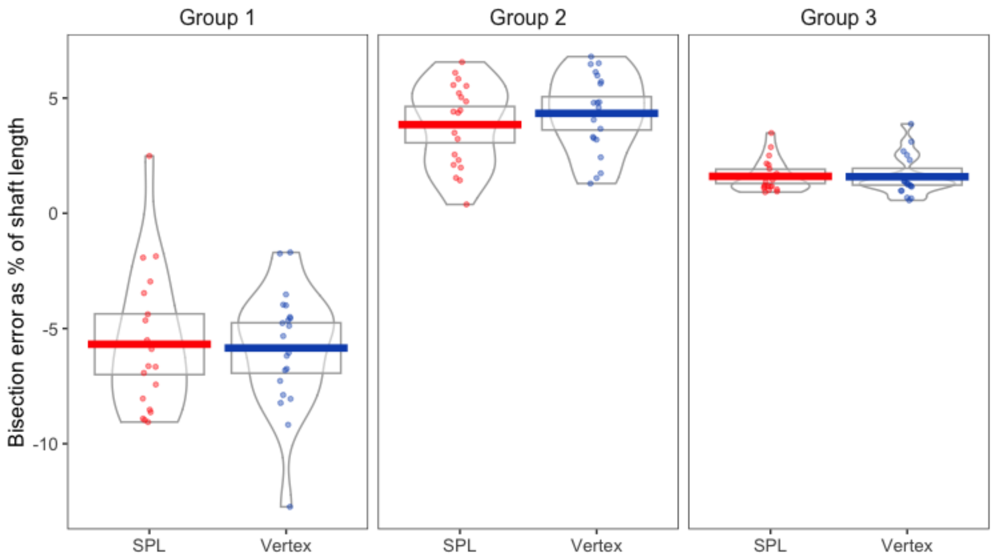

*Figure 3.8 - Pirate plots with mean and 95% CI for the 3 configurations of the stimulus used in Experiment 2*

### *3.5.2.2 Statistical Analysis*

Our prediction was that the cTBS stimulation of the SPL should have reduced the bisection bias elicited by the Judd variant of the Müller-Lyer illusion. Means and SE for the 3 configurations of the Judd variant of the Müller-Lyer used in Experiment 2 are presented in Figure 3.9.

In order to test our prediction, we carried out a 2 (Stimulation type: SPL vs Vertex) x 3 (Stimulus type: Group 1/ Group 2/ Group 3) Repeated Measure ANOVA. The Mauchly’s test for Sphericity for the stimulus factor (sig <.001) and for the 2-way interaction violated the assumption (sig. < .001), therefore we used the Greenhouse-Gassier correction.

The main effect for stimulation (F(1, 19) = .184, p = .673, η2= .01) was not significant, while the main effect for stimulus type was significant (F(1.264, 24.008)= 138.134, p < .001, η2=.879 ). The interaction between the two main effects was also not significant (F(1.245, 23.65) = 1.041, p=.363, η2=.052). Regarding the main effect for stimulus type, pairwise comparisons with a Bonferroni adjustment revealed that illusion strength was significantly decreased from Group 1 to Group 2 (-10 (95% CI, -12.15 to -7.85) %, p < .001), and from Group 1 to Group 3 (-7.49 (95% CI, -9.05 to -5.93) %, p < .001), and statistically increased from Group 2 to Group 3 (2.52 (95% CI, 1.49, 3.55) %, p < 0.001).

Inspection of Figure 3.10 suggests a possible reduction of the strength of the Müller-Lyer illusion caused by outward facing fins (Group 2) due to cTBS. This was tested with a paired samples t-test, which trended towards significance, t(19)=-1.932, p=.068, d = .043. This indicates that we replicated the previously found effects of the Judd variant of the Müller-Lyer illusion on bisection, but overall cTBS failed to influence that.

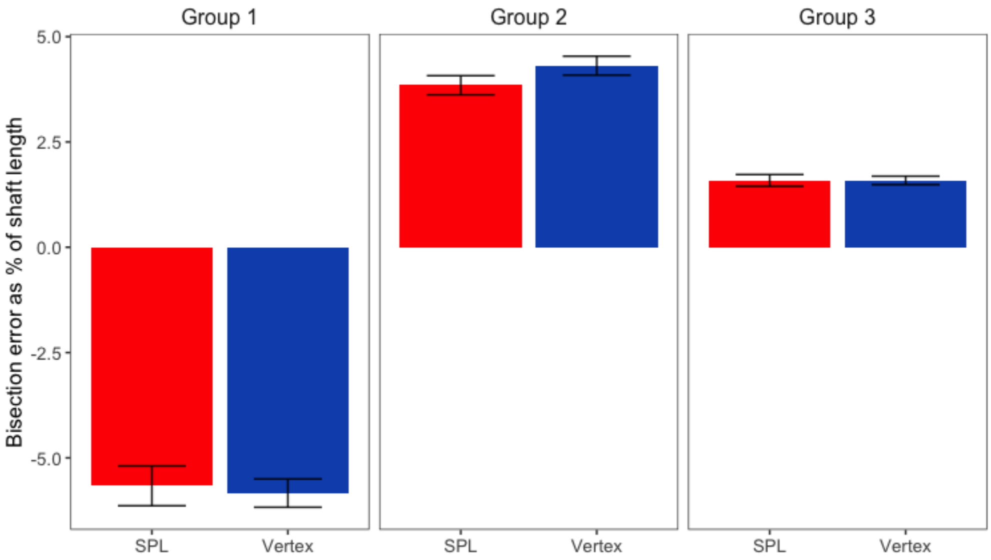

*Figure 3.9 - Bar plot with mean and SE for the stimuli used in Experiment 2.*

### 3.5.3 Experiment 3

#### *3.5.3.1 Pre-processing and descriptive statistics*

The behavioural data from experiment 3 was loaded into RStudio, and before computing the bisection bias for the Brentano version of the Müller-Lyer illusion, all the trials in which the participants failed to confirm their bisection before the 10 seconds response limit ran out were removed. This reduced the total number of trials from 984 to 977 trials. The bisection bias was calculated as the absolute value of the distance between the final location of the middle fin and the true midpoint of the horizontal shaft of the stimulus. After that, for each trial we computed the bisection bias as a percentage of shaft length. Then we computed the average bias per participant for each configuration of the stimulus, where a negative number meant a compression of one half of the shaft, and a positive number meant a bisection point consistent with the perceptual expansion of one half of the shaft. Pirate plots showing the mean, 95% CI and distribution of the bisection bias in the Brentano version of the illusion and its altered version are presented in Figure 3.10.

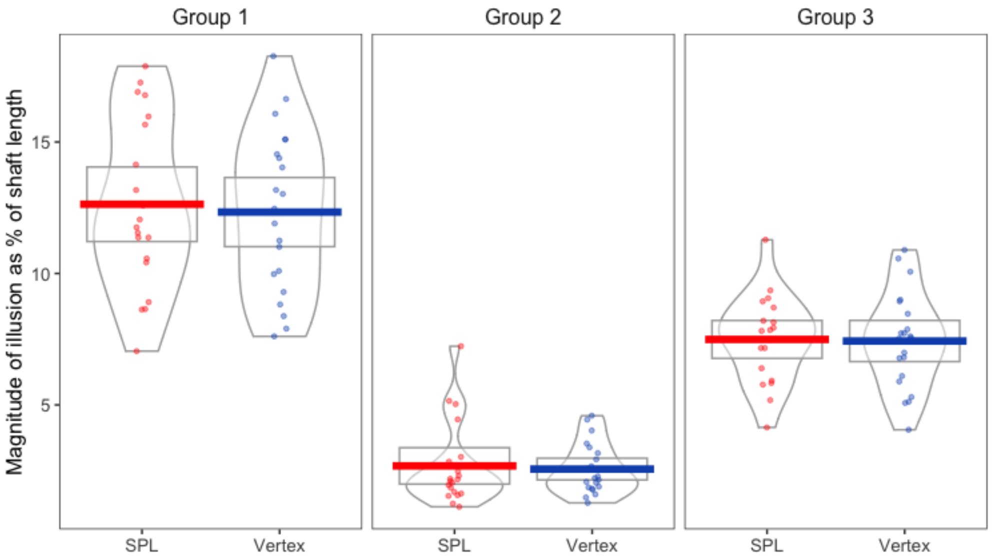

*Figure 3.10 - Pirate plots with mean and 95% CI for the 3 configurations of the stimulus used in Experiment 3.*

### *3.5.3.2 Statistical Analysis*

Our prediction was that the cTBS stimulation of the SPL would reduce the bisection bias elicited by two of the three configurations of the ML stimuli used in this experiment (see Methods Figure 3.4). Means and SE for the 3 configurations of the Brentano version of the Müller-Lyer used in Experiment 3 are presented in Figure 3.11.

In order to test our prediction, we carried out a 2 (Stimulation type: SPL vs Vertex) x 3 (Stimulus type: Group 1/ Group 2/ Group 3) Repeated Measure ANOVA. The Mauchly's test for Sphericity for the stimulus factor violated the assumption (sig. = 0.001), therefore we used the Greenhouse-Gassier correction.

The main effect for stimulation ($F(1, 19) = .389$, $p = .54$, $\eta2= .02$) was not significant, while the main effect for stimulus type was significant ($F(1.261, 23.951)= 167.914$, $p < .001$, $\eta2=.898$ ). The interaction between the two main effect was also not significant ($F(2, 38) = .059$, $p=.943$, $\eta2=.003$). Regarding the main effect for stimulus type, pairwise comparisons with a Bonferroni adjustment revealed that illusion strength was significantly increased from Group 1 to Group 2 (9.95 (95% CI, 8.44 to 11.45) %, $p < .001$), and from Group 1 to Group 3 (5.04 (95% CI, 4.1 to 5.99) %, $p < .001$), and statistically decreased from Group 2 to Group 3 (-4.9 (95% CI, -5.74, -4.06) %, $p < 0.001$).

This indicates that we replicated the previously found effects of the Brentano version of the Müller-Lyer illusion on bisection, but cTBS failed to influence that.

Group 2 stimuli (see Figure 3.4) were not expected to produce a line bisection bias due to the expansion or contraction of apparent shaft length because the inducing arrows all faced in the same direction. However, although smaller than the biases found for the other stimuli, a small but consistent line bisection bias was found. We ran a one-sample t-test to test if a bisection error occurred for Group 2 after both cTBS stimulation. The performance recorded after the cTBS stimulation of the SPL (M=3.85, SD=1.80) indicated a significant bisection error t(19)=9.551, p<.001; and also the performance recorded after the stimulation of the Vertex (M=4.34, SD=1.69) was significant t(20)=11.758, p<.001. This result will be considered in the Discussion and is consistent with the previous literature.

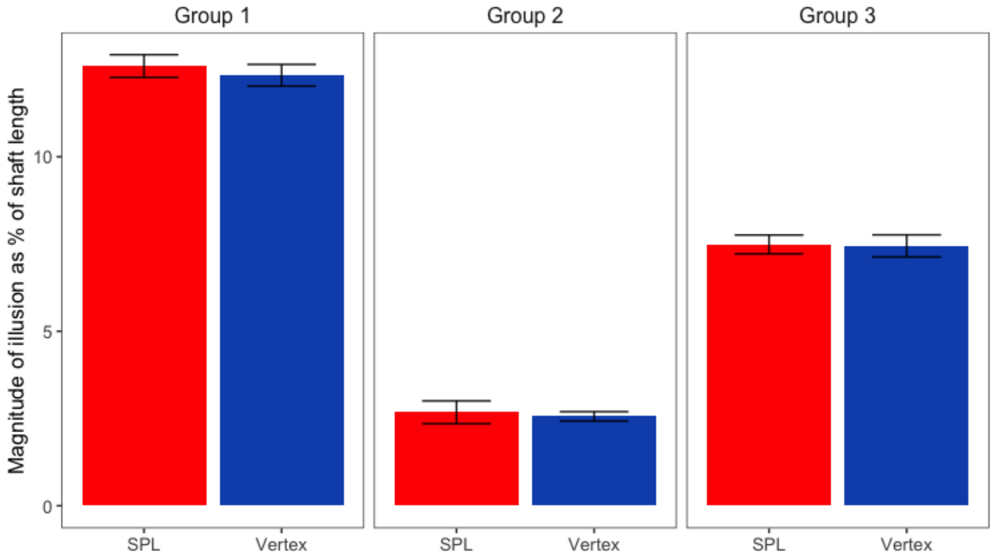

*Figure 3.11 - Bar plot with mean and SE for the stimuli used in Experiment 3.*

## 3.6 Discussion

The main purpose of this study was to test the hypothesis that the SPL is involved in the processing of visual extent. In order to achieve this aim, a 2-day cTBS study was carried out. On one day of the experiment the cTBS stimulation was delivered over the EEG electrode CP1 (used as a proxy for the left SPL region) while three different experiments were presented: an eye-movement task where the three different configurations of the Müller-Lyer illusion were presented, a bisection task where six different configurations of the Judd variant of the Müller-Lyer illusion were presented, and finally a bisection task where the two configurations of the Brentano version of the Müller-Lyer illusion and 4 more configurations were presented. On the other day of the experiment cTBS was delivered over the Vertex (a control site for the cTBS stimulation), while the same three tasks were presented. We predicted that the cTBS over the SPL would reduce the effect of the illusion on saccade amplitudes and would reduce the bisection bias generated by the Judd variant and the Brentano variant of the Müller-Lyer stimuli compared the cTBS over the vertex. The data failed to support our predictions.

We found a significant difference in saccade amplitudes depending on the stimulus type, which meant that the illusion of extent was present in the data. This replicates previous findings (Binsted & Elliott, 1999; Delabarre, 1898; Festinger et al., 1968; Stratton, 1906; Yarbus, 1967) however, we found that the cTBS stimulation over the SPL did not significantly affect the saccade amplitudes recorded during the presentation of the ML. In our task the Müller-Lyer stimulus remained visible while saccades and fixations were made, which may have allowed the visual system to compensate and correct for TMS effects. In a future study we are planning to investigate eye movement tasks in which the Müller-Lyer stimulus is occluded before the saccade is made.

In addition to this, we found that the cTBS over the left SPL reduced the perceptual bisection bias induced by the Judd version of the ML just for one configuration of the stimuli (stimulus E in figure 3.5), but this effect only trended towards significance; moreover, cTBS over the SPL did not affect the bisection bias generated by the Brentano version of the ML stimuli compared to cTBS over the vertex.

The results of this study do not support the hypothesis that the SPL is critical for the perception of visual extent, but because the study had several limitations is not possible to rule out the hypothesis either. The design made the assumption that cTBS delivered to the control location, which was the vertex of the skull, would not influence neural activity in the SPL or behavioural task performance. This assumption is called into question by the findings of Jung, Bungert, Bowtell, & Jackson (2016) who delivered TMS stimulation (120% of RMT) to the Vertex concurrently with functional BOLD MRI. They found that Vertex TMS produced a significant deactivation in a number of brain regions including the right SPL and the precuneus. The general effect was deactivation in the 'default mode network', which may have had the knock-on effect of an increase in excitability in the 'salience' network. While the cTBS we delivered to SPL would be expected to produce BOLD activation (as seen in Agnew, Banissy, McGettigan, Walsh, & Scott, 2018) rather than the deactivation likely caused by the Vertex stimulation, given the highly interconnected nature of the brain we suspect that the control condition was not inert. An improved design would have incorporated an additional no-TMS control condition, which would have allowed us to establish whether Vertex cTBS had any effect on our behavioural tasks. Without a no-cTBS condition, it cannot be ruled out that Vertex and SPL cTBS both had similar effects on the tasks we presented in this study.

Another methodological limitation is that in this study we asked participants to wear an EEG cap and then we located the SPL by selecting the electrode CP1 (on the left hemisphere) on the 10-20 EEG system as the target for the cTBS stimulation. According to a previous study this a legitimate method of localisation of cortical areas (Herwig, Satrapi, & Schönfeldt-Lecuona, 2003), and the CP1 is the electrode that has the closest proximity to the SPL (Koessler et al., 2009). However, a study conducted by Sparing, Buelte, Meister, Paus, & Fink (2008) has showed that the EEG method of location of cortical regions is not very reliable. In their study they compared 5 different modalities of localisation of the left motor cortex: the 10-20 EEG system, the standardized function-guided procedure, the structural MR image, the individual functional MRI data and the group functional MRI data (Sparing et al., 2008) and they measured both MEP amplitudes and spatial accuracy of cortical regions. They discovered that out of the 5 modalities, the 10-20 EEG gave the lowest MEP amplitudes and spatial accuracy of cortical regions, while the best results were found after the localisation guided by individual functional MRI data. Therefore, the results we obtained need to be considered with caution, because we cannot be totally convinced that the cTBS stimulation was exactly delivered over the Superior Parietal Lobule.

Another consideration is the fact that the cTBS stimulation was delivered just over the left Superior Parietal Lobule. Corbetta, Shulman, Miezin, & Petersen (1995) found that a bilateral activation of the Superior Parietal Lobule occurs during the early spatial shift of attention, which is a covert form of eye movement “readiness”. So, a possible explanation for the lack of significant result is that targeting just the left Superior Parietal Lobule is not enough to reduce the centre of gravity effect that may underly the ML illusion. A possible solution for this problem would be using the cTBS bilaterally on the Superior Parietal Lobule. Such bilateral cTBS studies have been done in the past, for example, for treating tinnitus and auditory hallucinations (Schraven, Plontke, Rahne, Wasserka, B., & Plewnia, 2013), to study how learning new vocabulary happens (Sliwinska, Elson, & Pitcher, 2021), or to study the attentional network (Vesia Niemeier, Black, & Staines, 2015).

We did not predict the significant line bisection biases found in Group 2 stimuli (see Figure 3.4) because the inducing arrows all faced in the same direction. However, these findings are consistent with existing literature on line bisection biases (Dellatolas, Vanluchene, & Coutin, 1996 ; Varnava, McCarthy, & Beaumont, 2002). We found no effects of cTBS on these line bisection biases.

Finally, the statistical power of the study for detecting cTBS effects was relatively low (power = 0.8 to detect an effect size of d = 0.56 for our one tailed prediction). In conclusion, further studies with greater statistical power and methodological improvements discussed above should be conducted to test the hypothesis that a subregion of SPL supports the perception of visual extent.

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# Chapter 4. Using TMS to investigate the role of the Superior Parietal Lobule and the Front Eye Field in the perception of spatial separation

## 4.1 Abstract

Previous studies have implicated the Superior Parietal Lobule (SPL) in the Müller-Lyer illusion as well as eye movement planning, which suggests it may also have a role in perception of spatial separation. In this study we investigated the role played by the SPL and the frontal eye field (FEF) in a series of visual tasks that depend on processing of spatial separation, including intercepting a moving target, the magnitude of the Müller-Lyer illusion, amplitudes for reflexive, voluntary, and memory-guided saccades made to Müller-Lyer and control stimuli, and a reaction time task. We delivered offline continuous theta burst stimulation (cTBS) for 40 seconds to either the SPL or the FEF before and after presenting the range of tasks. We found that cTBS stimulation over either SPL or FEF made responses for the interception task less accurate for faster velocities. Moreover, stimulation of either FEF or SPL significantly increased reaction times and reduced the final length of the comparison line in the Müller-Lyer line adjustment task, including for the control stimuli in which the illusion was not present. However, methodological issues mean that these findings cannot confidently be attributed to the neural effects of TMS. Amplitudes of reflexive, voluntary, and memory

guided saccades were not affected by TMS to either SPL or FEF compared to baseline. An incidental finding was that latencies for reflexive saccades were significantly increased after TMS to either SPL or FEF, while latencies for memory-guided saccades were decreased. Latencies of voluntary saccades were unaffected by the stimulation.

# 4.2 Introduction

In Chapter 3 we carried out an experiment which examined the role played by the SPL in perception of visual extent by using offline TMS before presenting an eye movement task and 2 line bisection tasks using variants of the Muller Lyer illusion. We found, contrary to our hypothesis, that the TMS stimulation of the SPL had no effect on the saccade amplitudes, nor on the bisection tasks. However, this could have been due to the fact that the method of SPL localisation was sub-optimal, using the CP1 position on an EEG cap. We also used the vertex as a control region for TMS, with the assumption that the stimulation of this region would not influence neural activity in the SPL. However, due to the highly interconnected nature of the brain we suspect that the Vertex was not a good control region, and a stimulation of the Vertex might have had an effect on the neural activity of the SPL.

To further examine the hypothesis that the SPL plays a role in the perception of visual extent, the experiments in this chapter build upon those in Chapter 3, with some improvements to the methodology previously used. We decided to still use the Muller Lyer illusion as stimuli for our experiments, and we continued to perform cTBS stimulation of our chosen target regions. However, compared to the study presented in Chapter 3, a few adjustments were made. Firstly, we decided to abandon the Vertex as a control region of the cTBS stimulation as it was problematic in the previous experiments because we could not rule out the possibility that the Vertex was involved in the tasks we presented, and instead we target the Frontal Eye Field (FEF). We decided to target the FEF with TMS because there are a number of reasons to suggest possible involvement of the FEF in the kind of ‘planned but not executed’ eye movements that Coren (1986) proposed as the basis of spatial perception. Firstly, FEF is heavily connected to the superior parietal lobe (Stanton, Bruce, & Goldberg, 1995), and both are part of the network that programs eye movements although the FEF is primarily involved in programming voluntary saccades and posterior parietal areas in reflexive saccades (Vernet, Quentin, Chanes, Mitsumasu,, & Valero-Cabré, 2014). Reflecting this, delivering TMS to the FEF has generally been found to increase the latency of voluntary saccades (Thickbroom, Stell, & Mastaglia, 1996) and memory guided saccades (Wipfli, Felblinger, Mosimann, Hess, Schlaepfer, & Müri, 2001), but not reflexive saccades (Müri, Hess, & Meienberg, 1991; van Donkelaar, Lin, & Hewlett 2009). The second reason we decided to target the FEF is because of it is involved in programming the amplitude of all types of eye movements (Vernet et al., 2014) and amplitude is the key efferent parameter that could be used to provide a perceptual representation of 2D visual separation. Furthermore, the FEF plays a more general role in visual cognition and has been closely linked to the saliency map (Walker, Techawachirakul, & Haggard, 2009), which is itself closely linked to spatial attention. One perspective on spatial attention is that it reflects premotor activity in eye movement planning areas such as the FEF (Rizzolatti, Riggio, Dascola, & Umiltá, 1987). While this theory proposes that prepared but not overtly executed saccades underly covert attention effect, we are investigating the closely related proposal that such saccades plans support spatial perception.

Moreover, we decided to present the stimuli before and after cTBS stimulation. In Chapter 3 outcome variables were measured only after TMS, and this cause a problem in that it was not possible to determine the effect of TMS without a baseline comparison. Therefore, here we decided to present stimuli before and after the TMS stimulation so that a pre-post comparison could be made. Regarding the tasks used in this study, they differ from the one presented in Chapter 3: we decided to not use bisection task, as they are relevant for perception of position and not perception of extent, and instead we included an interception task and 2 line adjustment tasks. We did include 3 eyetracker tasks, but they differ from the one included in Chapter 3: this time we had a task for voluntary saccades, a task for reflexive saccades, and a task for memory-guided saccades because we wanted to see the effect of the cTBS stimulation on these type of saccades. In addition to that, the Muller Lyer stimuli used in these tasks were left on the screen for just enough time that one saccade was carried out by the participants, while in the eyetracker task presented in Chapter 3 the Muller Lyer stimuli were left on the screen for 10 seconds. We decided to do so because previous studies have shown that prolonged exposure to the Muller Lyer illusion weakens its effect.

Therefore, by incorporating the changes mentioned above, the aim of the present study was to more thoroughly investigate the role played by the SPL and the FEF in the perception of visual extent. In order to do so, 6 different experiments were presented before and after a cTBS stimulation of either the SPL or the FEF.

## 4.3 Method

Six different experiments were performed. In Experiment 1, subjects performed an interception task, where they had to press a spacebar when they thought that a moving square was exactly on top of a white dot. In Experiment 2 and Experiment 3 participants had to adjust the length of a straight line to match the length of the horizontal shaft of a Müller-Lyer figure. In Experiment 4, subjects performed a reflexive saccade task, where they had to move their eyes from one and to the other of the horizontal shaft of the Müller-Lyer figure. In Experiment 5, subject performed a voluntary saccade task, where they were asked to look at a cue and then decide whether to move their eyes from one end to the other of the horizontal shaft of the Müller-Lyer illusion, or to move their eyes in the hemifield where the stimulus was not presented. Finally, in Experiment 6 participants had to do a memory-guided saccade task, where they were asked to move their eyes to the end point of the horizontal shaft of a Müller-Lyer figure that was previously presented.

### 4.3.1 Participants

For this study 16 participants (6 males, 10 females) were recruited for a 2 non-consecutive days TMS study at the University of Reading. This sample size was sufficient to detect an effect size of d=0.75 for two tailed prediction (power 0.8, alpha 0.05, paired sample t-test). Participant were recruited via the University of Reading Research Panel website (SONA), where the study was advertised. The age range of the participants varied from 19 to 39 years old (Median= 25.5). All participants were informed that they participation in this study was voluntary and that they could withdraw at any time without providing a reason.

### 4.3.2 Ethical approval

This study was granted ethical approval by the University of Reading Ethics Committee (UREC), with an UREC code 17/49, expiration date 01/12/2021. Due to the seizure-potential that the cTBS stimulation has (Wassermann, & Lisanby, 2001), participants were asked to complete a TMS screening form before each cTBS stimulation. The TMS screening form was approved by the UREC and was composed of 24 questions aimed to investigate if the participant had previous psychiatric, neurological or other medical condition and therefore was not eligible for the cTBS stimulation (Rossi, Hallet, Rossini, & Pascual-Leone, 2009). Moreover, the experimental design took into account the TMS safety parameter specified by Wasserman & Lisanby (2001) and Rossi (2009) regarding duration, intensity and frequency of stimulation. In order to ensure the safety of the participants, after each stimulation the participant was asked to stay with one of the experimenters for approximately one hour, until the effect of cTBS had fully disappeared. Before the start of the cTBS stimulation participants were reminded that they could withdraw at any time from the study without providing reason.

### 4.3.3 Apparatus and Materials

All the experiments presented in this study were programmed using Psychtoolbox (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007; Pelli, 1997), a freely available package toolbox for MATLAB. All the stimuli were displayed on a 24-inch ViewPixx monitor (1920(H) x 1080(V) pixels), refresh rate 120 Hz, placed 90 centimetres away from the participant. In order to reduce the head movements, participants were asked to rest their chin on a chinrest for the entire duration of the experiment (the chinrest was placed 90 centimetres away from the ViewPixx monitor). Placed under the monitor there was an Eyelink 1000 eye tracker (sampling frequency of 1000 Hz) that was used to record eye movements.

### 4.3.4 Design and Procedure

The design of this study was fully repeated measures, with every participant undergoing offline cTBS stimulation over 2 different regions: the Superior Parietal Lobule (SPL) and the Frontal Eye-Field (FEF). Each stimulation took place on a different day and there was at least a 48-hours interval between the 2 sessions. Half of the participants received cTBS stimulation over the FEF on Day 1 and a cTBS stimulation over the SPL on Day 2, while for the other half of the participants the order of stimulation was reversed. In both days of the study, 6 different experimental tasks were presented before the cTBS stimulation, and then presented again after the cTBS stimulation

### 4.3.5 TMS and experimental procedures

After the participant successfully completed the screening form, they were presented with all 6 experiments in the following order: reaction time task (control task for

Experiment 1), practice trials for Experiment 1 with feedback (8 trials), Experiment 2, Experiment 3, Experiment 4, Experiment 5, Experiment 1, and then Experiment 6. After that the resting motor threshold (RMT) was acquired on each day of the experiment for all the participants. The Brainsight software (Brainsight TMS, Rogue Resolutions Ltd) was used in order to locate the target of the cTBS stimulation for the day (either the right Frontal Eye Field, or the right Superior Parietal Lobule). After the stimulation target for the day was located, a 40 second cTBS was delivered. After that the participant waited 5 minutes before being presented again with all the experiments. For all the participants the order of presentation of the experiments was the following: Experiment 2, Experiment 3, Experiment 4, Experiment 5, Experiment 1, Experiment 6, and finally the reaction time task (control task for Experiment 1).

The RMT is the lowest intensity of stimulation that must be delivered to the primary motor hand area (M1-HAND) in order to evoke a peak-to-peak Motor Evoked Potential (MEP) of 50 μV in at least five out of ten consecutive trials in the contralateral relaxed first dorsal interosseus (FDI) muscle (Quartarone, Bagnato, Rizzo, Morgante, Sant'Angelo, Battaglia, Messina, Siebner, & Girlanda, 2005). In order to define the starting position for the search for the M1-HAND area, the TMS coil was firstly placed on top of the vertex (defined as the mid-distance between the nasion-inion, and the left-right auricular bones) and then moved 1 centimetre to the left, away from the vertex and 4-5 centimetres forward (Groppa, Oliviero, Eisen, Quartarone, Cohen, Mall, Kaelin-Lang, Mima, Rossi, Thickbroom, Rossini, Ziemann, Valls-Solé, & Siebner, 2012). The best position to produce the FDI muscle activation was located by moving the TMS coil in 0.5 centimetres steps from the starting position.

During the entire RMT assessment, the handle of the coil was pointed backwards at a 45° angle away from the midline, approximately perpendicular to the line of the central sulcus. For each subject, the RMT was determined as the intensity at which single pulses applied over the hand area of right M1 produced a visible muscle twitch in 5 of 10 consecutive trials, which is a standard procedure in the field (Feredoes, Tononi, & Postle, 2006; Schutter, & van Honk, 2006).

Once the RMT for the day was defined, we set the intensity of stimulation to 80% of that value, which is common practice for cTBS stimulation (Huang et al., 2005). Mean ± SE of the RMT in the sample was 60.33 ± 6.7% maximum stimulator output (MSO) for the SPL and 61.94 ± 5.9 MSO for the FEF. Therefore, the mean ± SE intensity for the cTBS stimulation was set to 48.27 ± 5.3% MSO for the SPL and 49.55 ± 4.7% MSO for the FEF, i.e., 80% of the RMT acquired earlier in the same day.

### 4.3.6 Location of the TMS target

Once the MRT was detected, the participant was asked to undergo the location of the region of interest for the cTBS session. This was performed with the Brainsight Software (Brainsight TMS, Rogue Resolutions Ltd). Because of restrictions caused by COVID-19 we decided to use the anatomical T1 image (2mm resolution) that comes with the Brainsight software, instead of asking participants to undergo an fMRI functional localiser session. After loading the T1 image, participants were asked to sit in front of the Polaris camera and to wear a subject tracker, which was strapped to their forehead. For the SPL the following right hemisphere coordinates were used x= 54, y=-58, z=60; while for the FEF the right hemisphere coordinates were x = 31, y = -2, z = 4.

### 4.3.7 cTBS Stimulation

After locating the target for the cTBS session, the TMS coil was placed on top of the target and the cTBS stimulation was delivered. The cTBS was delivered using a figure of 8 coil, attached to a PowerMag machine (Mag & More GmbH, München, Germany). The cTBS consisted of 3 pulses of stimulation given at 50Hz repeated at intervals of 0.2

seconds (i.e., 5Hz) as presented in Figure 4.1. The intensity of stimulation was set to 80% of the RMT acquired previously on the day (Huang et al., 2005). After the stimulation a period of 5 minutes was waited before the post-TMS behavioural experimental measures were performed Because of the nature of the cTBS stimulation, participants stayed with one of the experimenters for one hour after the stimulation.

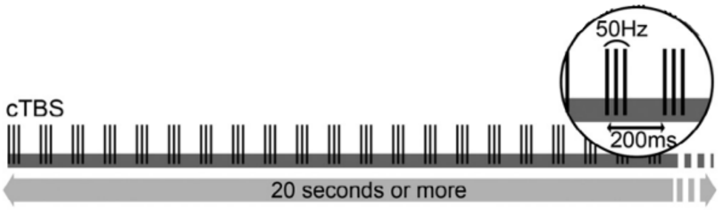

*Figure 4.1 - The pattern of cTBS stimulation.*

# 4.4 Experiment 1: interception task

## 4.4.1 Introduction

In the first experiment the effect of cTBS on an interception task was investigated. This was a time to contact (TTC) interception task that required monitoring and internally extrapolating the changing 2D visual angle between a moving stimulus and a stationary one in order to time a button press to coincide with the moment when the moving stimulus would collide with the stationary one.  Previous behavioural research on TTC tasks strongly suggests that their performance relies on direct use of visual angular information, even in more complex cases than the one we used in which objects move in depth (Lee, 1976, Tresilian, 1995; Field & Wann 2005; Lopez-Moliner, Field, & Wann,2007).

## 4.4.2 Methods

In each trial of this task a white dot appeared on the far-left side on the screen and a white square was presented on the far-right side of the screen (Figure 4.2a). After the initial presentation, the white square moved towards the left side of the screen while the dot on the right side of the screen remained stationary (Figure 4.2b). The moving square was occluded before it reached the stationary circle, requiring participants to internally extrapolate the motion (Figure 4.2c). Participants had to fixate on the stationary dot on the left-hand side of the screen at all times and press the spacebar to stop the moving square. The aim of this task was to stop the square exactly on top of the white dot (Figure 4.2d).

Prior to baseline performance of this task, participants were calibrated by performing a small number of trials with feedback. This consisted of the reappearance of the moving square after they had pressed the spacebar, at the position it would have reached if not occluded. This informed them whether they'd responded too early or too late, and by how much. In the main task, no such feedback was provided because our purpose was to measure the spatial/temporal error.

To allow us to verify that participants responded on the basis of their internal estimate of TTC rather than simply pressing the spacebar as soon as the moving target was occluded, we also measured performance in a modified reaction time control condition, which was performed prior to the interception task. In this version of the task the stimuli were as before, but after the square appeared it remained stationary and participants had to react as quickly as possible by pressing the spacebar.

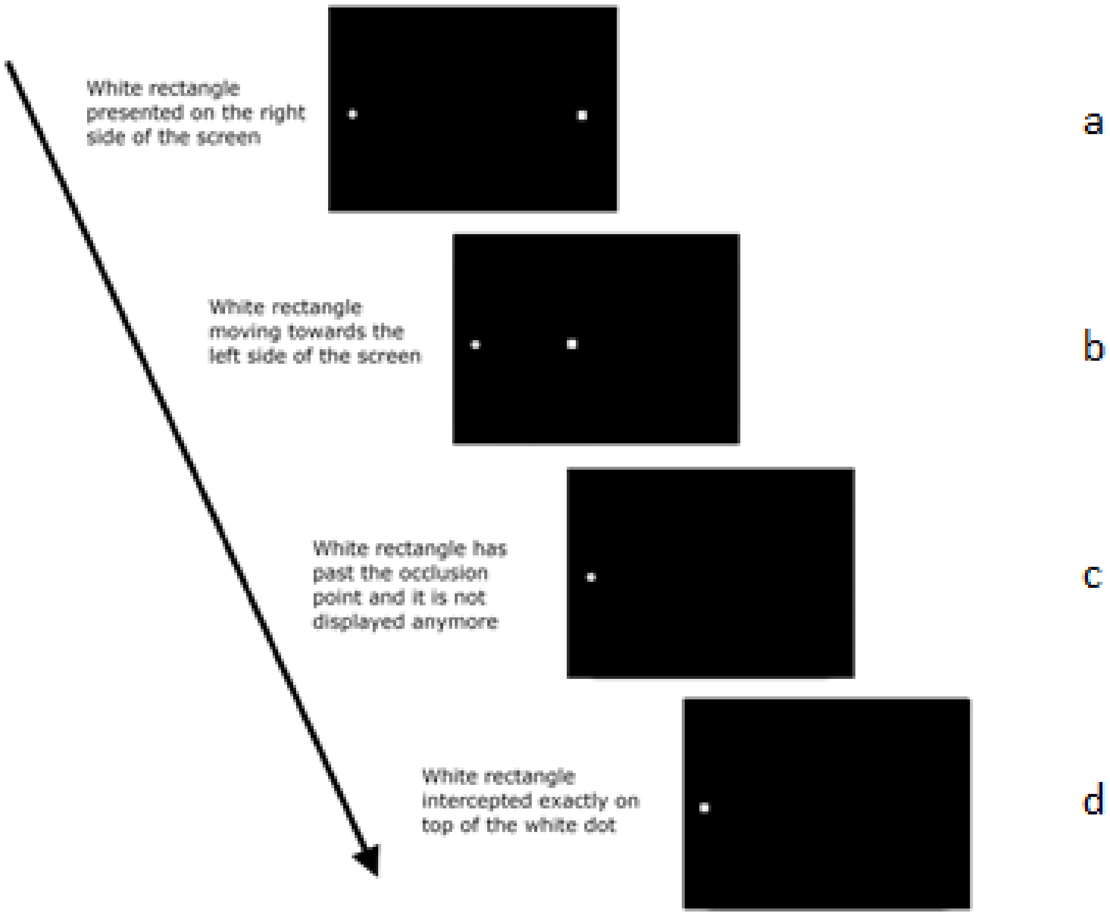

*Figure 4.2 - Procedure for Experiment 1 interception task*

At the beginning of each trial the white dot was presented on the left side of the screen, with the y-coordinates set as half of the screen height and the x-coordinate offset from the screen edge  set as 1/10 of the screen length; while the square was presented on the right side of the screen, with the same y-coordinates as the dot, and the x-coordinates was calculated by subtracting an offset from the whole length of the screen. 5 different offsets were used in this experiment (60, 70, 80, 90 & 100 pixels away from the right end of the screen), each presented 20 times, for a total of 100 trials. As soon as the square was presented on the screen it started traveling at a constant velocity towards the other side of the screen. Five different velocities were used in this experiment (14, 19, 24, 30 & 35 centimetres per second), which were converted into pixels per frame of the 120Hz display; each velocity was presented 20 times.

Given the offset and the velocity used in each trial, it was possible to calculate the time required for the square to travel from its' starting point on the right side of the to be exactly on top of the white dot; this time distance was called "time of contact". On each trial at one specific point the dot was not presented on the screen anymore, although it continued its journey towards the left side of the screen. The point in time in which the dot was no longer presented on the screen was called "occlusion time" and it referred to a distance in time before the dot would be exactly on top of the square. Four different occlusion times were used in this task (0.200, 0.350, 0.500, 0.650 sec) each of which was repeated 25 times. The occlusion times defined how much time should elapse after occlusion before the spacebar press occurred in the case of perfect task performance.

In the reaction time control condition, the white dot was presented in the same location, with the y-coordinates set to half of the screen height and the x-coordinates set to 1/10 of screen length. During this task participants were asked to visually fixate the white dot and press the spacebar as soon as they noticed a white square displayed on the screen. The square had the same y-coordinates as the dot but had different x-coordinates which was pseudo-randomised in MATLAB in each trial. 50 trials were performed.

### 4.4.3 Results

#### *4.4.3.1 Pre-processing and descriptive statistics*

In this experiment the distance in space (i.e., spatial error) and in time (i.e., temporal error) between the position of the moving stimulus and the static target when the keypress was made was calculated for each trial, relative to a perfectly timed response.

All the trials in which the participant pressed the spacebar before the white square was occluded were removed, reducing the number of valid trials from 6000 to 5963. We then calculated for each trial the temporal error as the duration in milliseconds between the timepoint when the white square would have been exactly on top of the white dot and the timepoint when the participant pressed the spacebar, where negative values indicated an early press of the spacebar, and positive values indicated a late press of the spacebar. Then we produced a histogram of the temporal error on the remaining 5963 trials, in order to look for any outliers (Figure 4.3).

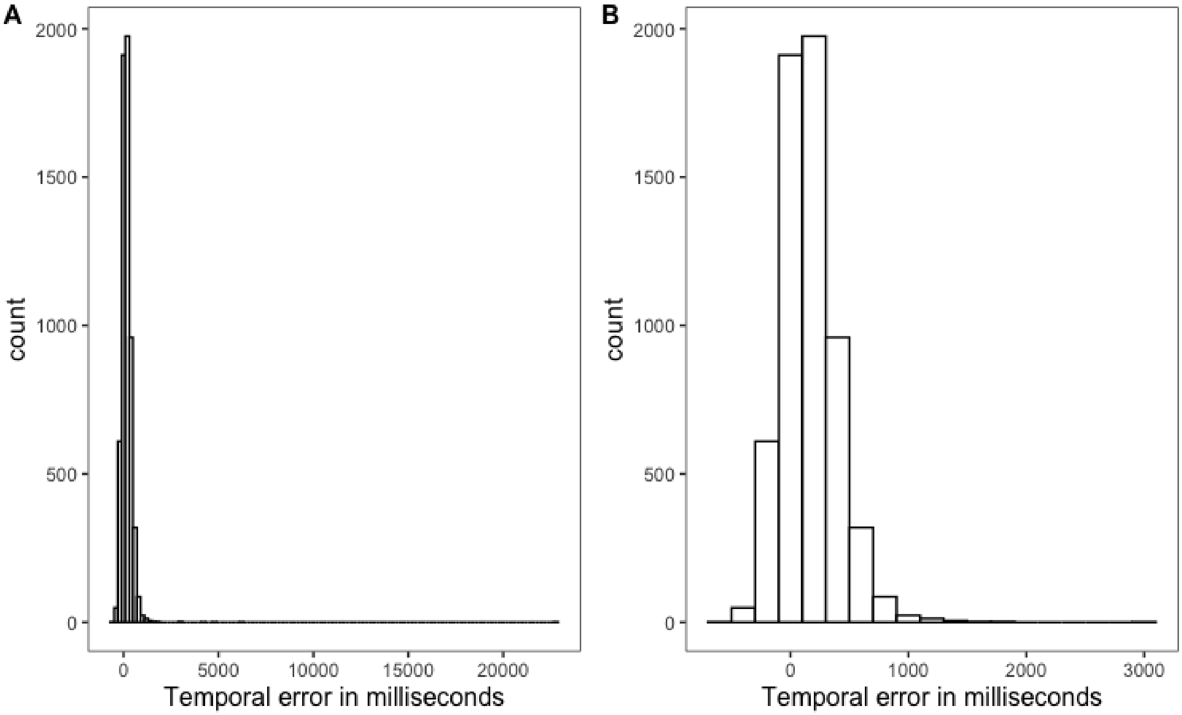

*Figure 4.3 - Histograms for the temporal error in the interception task. Panel A includes some very extreme values. These were removed and the data re-plotted to produce the histogram in Panel B.*

Based on Figure 4.3, panel B, we decided to remove all the values smaller than -0.5 second and bigger than 1 second, this reduced the number of valid trials to 5923.

After that, the spatial error was calculated as the distance in pixels between the landing point of the moving white square and the location of the white dot, where negative values indicated that the white square was stopped before the actual location of the white dot, and positive values indicated that the white square was stopped after the white dot. Then we produced a histogram of the spatial error, in order to look for any outliers (Figure 4.4).

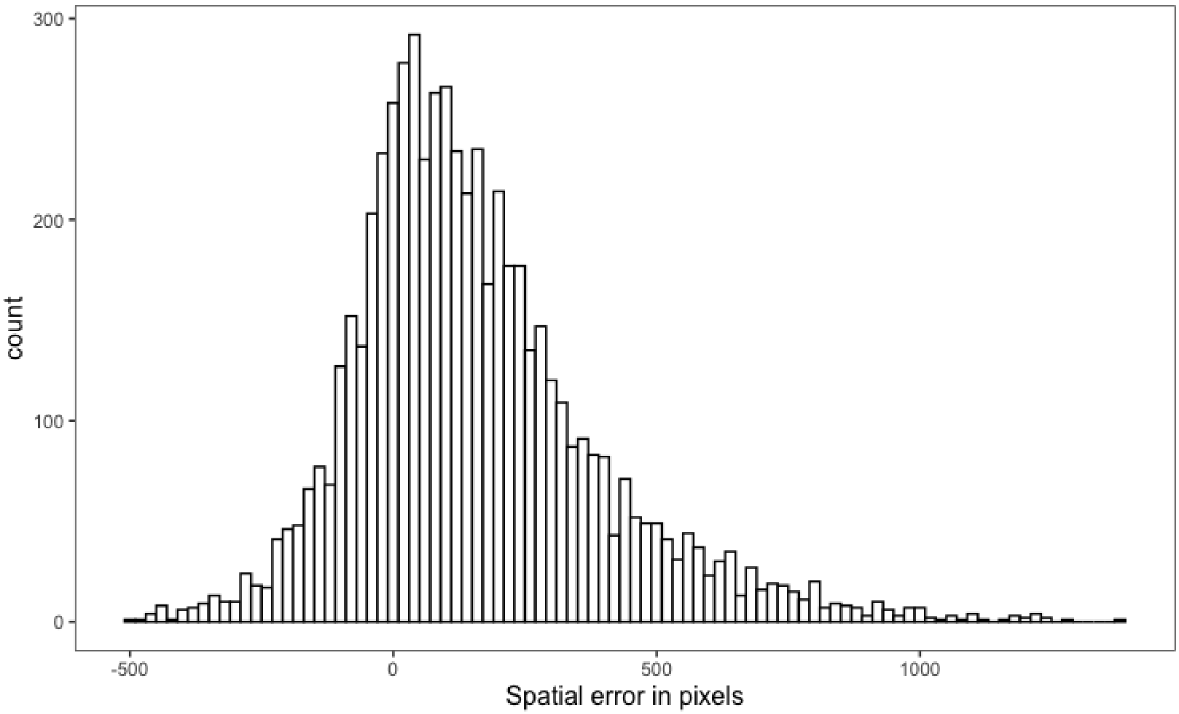

*Figure 4.4 - Histogram for the spatial error in the interception task.*

We decided to remove all values smaller than -500 pixels and bigger than 1000 pixels, this further reduced the number of valid trials to 5894. We then calculated the average spatial error and temporal error for each of the 5 velocities used in this task.

Pirate plots showing the mean, 95% CI and distribution for both the spatial error and the temporal error are presented in Figure 4.5 and Figure 4.6.

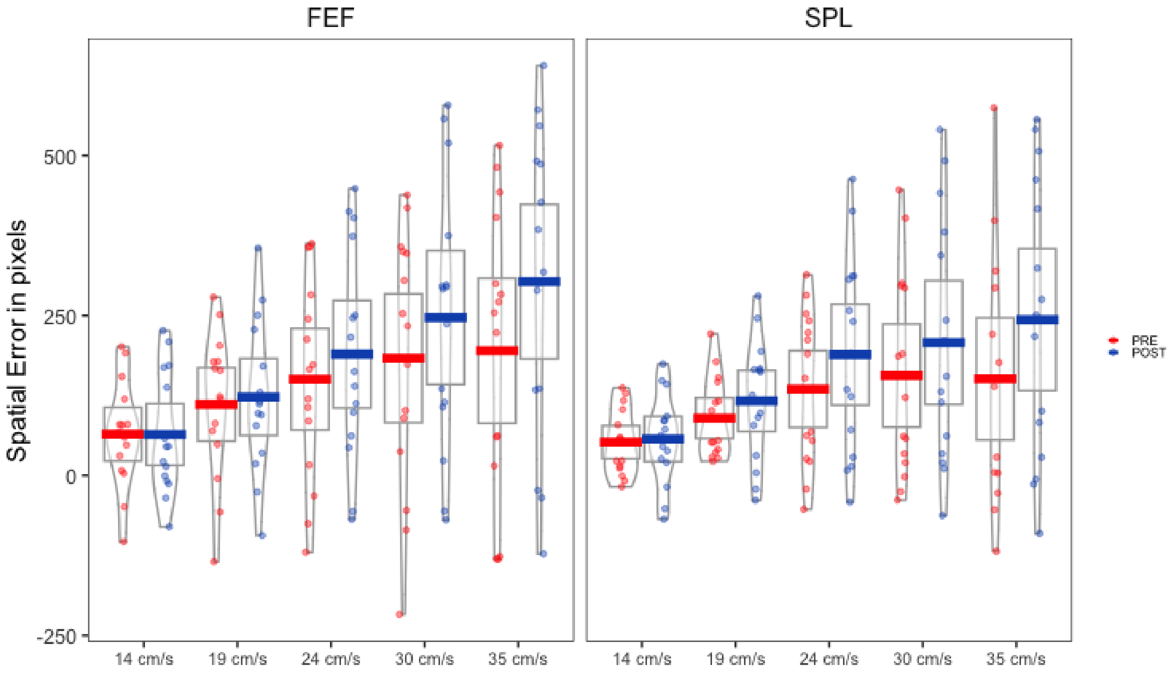

*Figure 4.5 - Pirateplots with means and 95% CIs for the Spatial error in Experiment 1.*

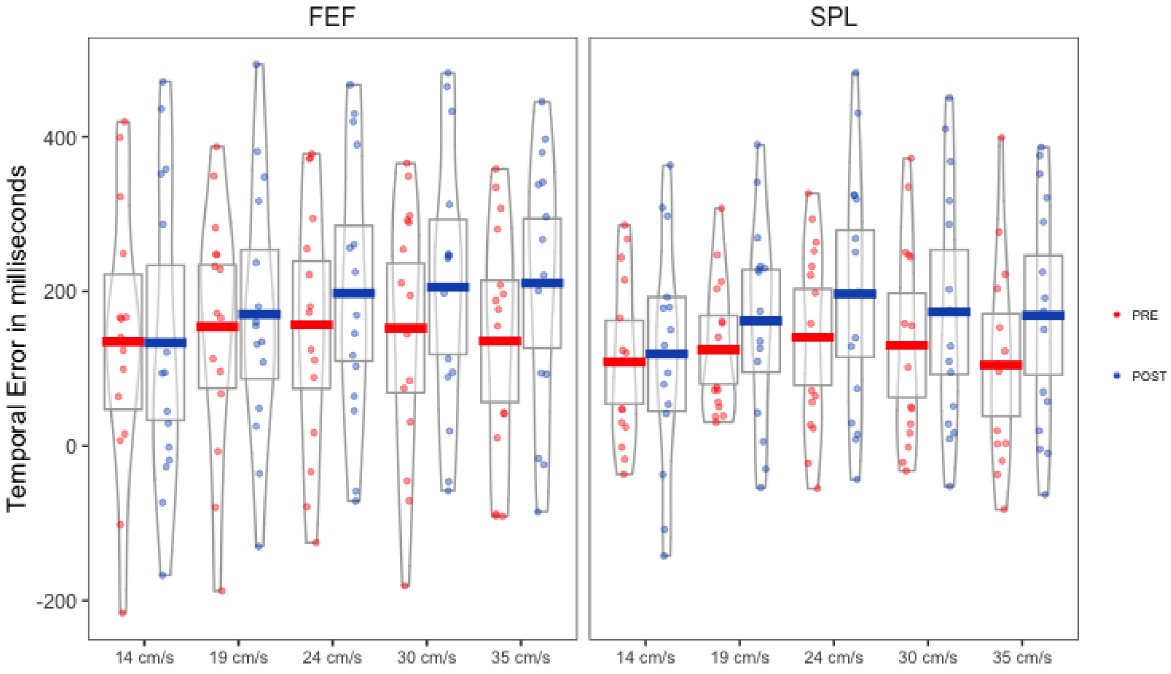

*Figure 4.6 - Pirateplots with means and 95% CIs for the Temporal error in Experiment 1.*

As a control condition in the first experiment the reaction times elicited by the presentation of a white square were recorded for each participant. Before computing the average reaction time for each participant, we removed the trials in which the participants pressed the spacebar before the white square was displayed, this reduced the number of valid trials from 3000 to 2958. We then plotted a histogram of the RTs in order to detect any outliers (Figure 4.7).

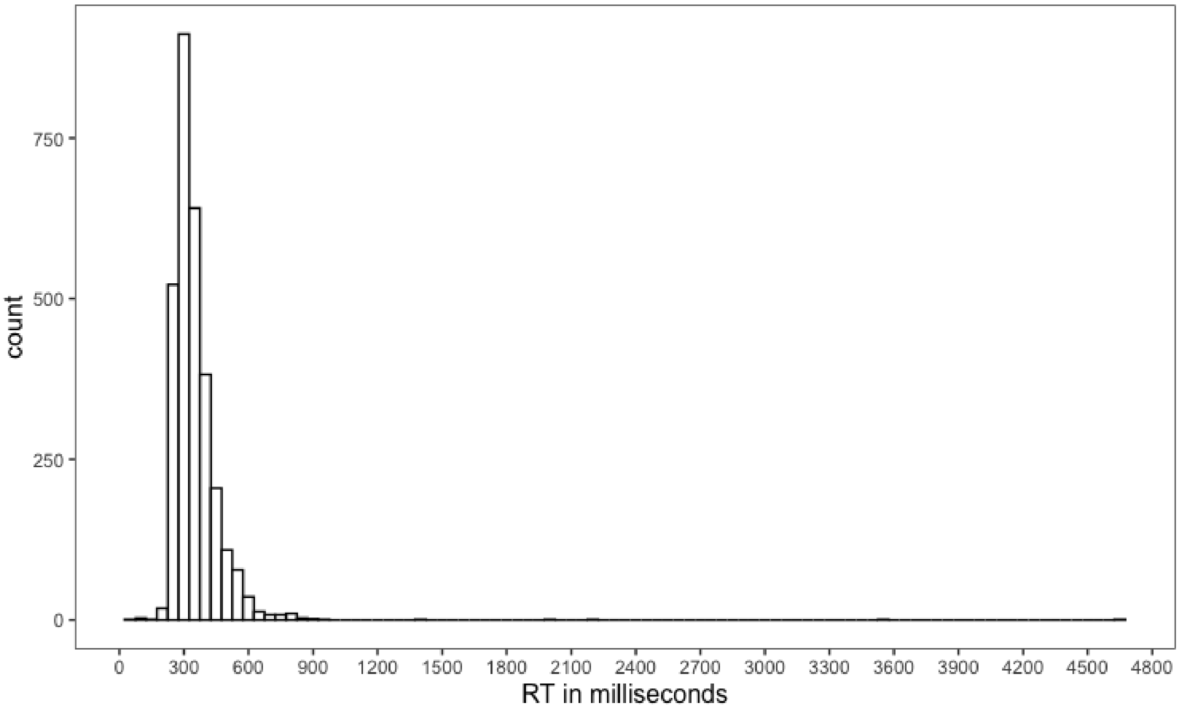

*Figure 4.7 - Histogram for the RT in the control task of Experiment 1.*

Based on Figure 4.7, we decided to remove all the values smaller than 150 milliseconds and all the value bigger than 1000 milliseconds. This reduced the number of valid trials to 2949.

The main purpose of including the reaction time trials in the study was to allow us to verify that performance in the interception task was based on an attempt to process TTC, rather than just responding with a button press immediately after the moving stimulus was occluded. To check for this, we used individual participant mean reaction times in each session to model what the grand mean interception task temporal errors would have looked like if performance was governed purely by reacting to the occlusion event. Figure 4.8 compares the results of this modelling to the actual temporal errors in the interception task as a function of velocity. This clearly indicates that performance in the interception task is not based on a reaction time strategy.

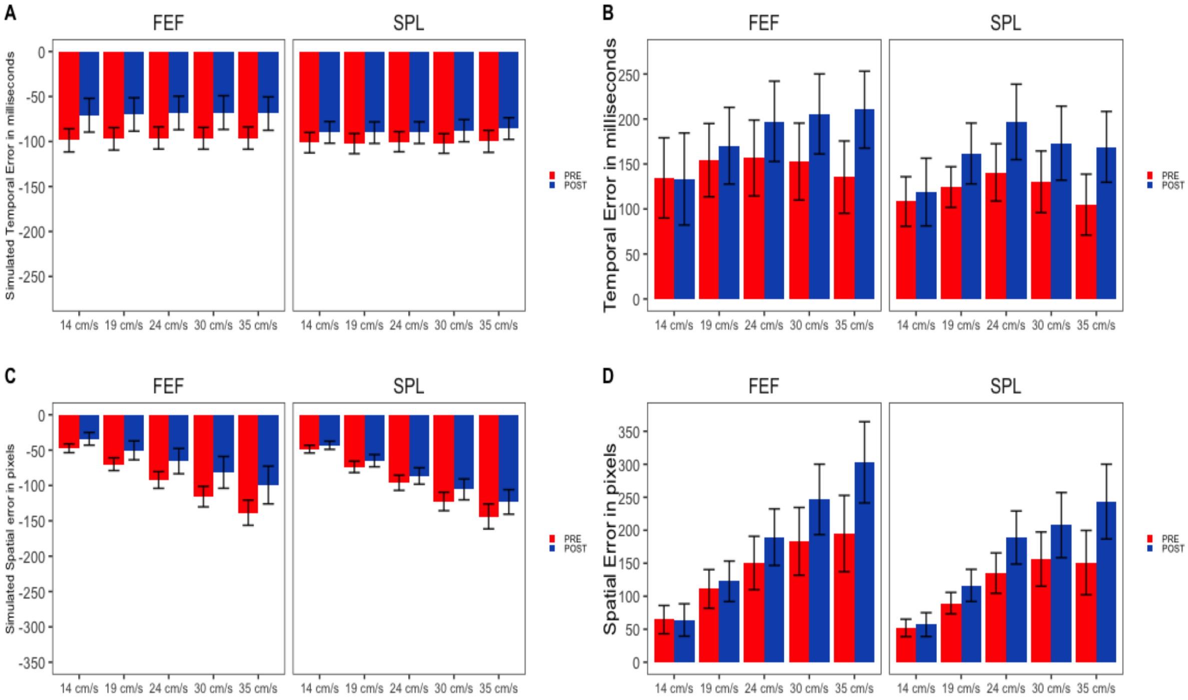

*Figure 4.8 - Predicted Temporal Error and Spatial Error for Experiment.*

The inclusion of the reaction time task in the study also allowed us to check if cTBS to SPL or FEF had an effect on reaction time. Pirate plots showing the grand mean, 95% CI and distribution of the reaction time data are presented in Figure 4.9.

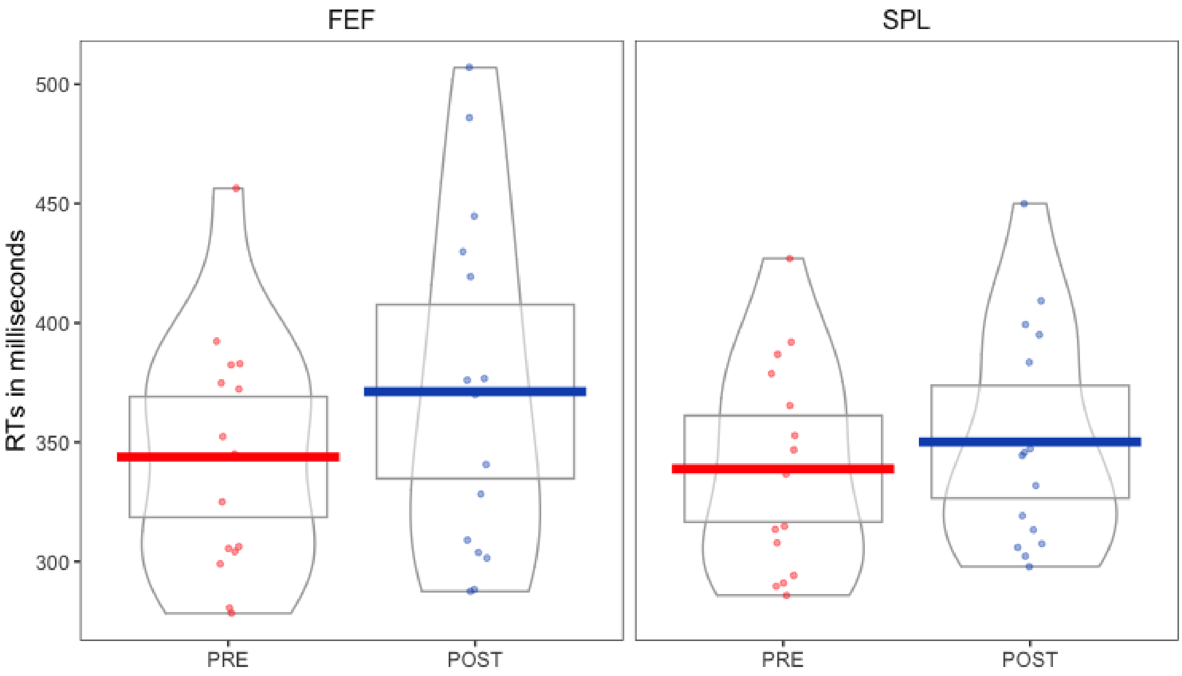

*Figure 4.9 - Pirate plots with means and 95% CIs for the RT in Experiment 1.*

### *4.4.3.2 Statistical analysis*

If TMS to either SPL or FEF influences the accuracy of performance on the interception task this would suggest a role for that region in the visual control of interception. Means and SE for the Spatial error and for the Temporal error recorded in Experiment 1 are presented in Figure 4.10 and in Figure 4.11, where negative numbers represent early responses and positive numbers late ones.

In order to analyse the data, a 2 (cTBS: FEF vs SPL) x 2 (Session: Pre vs Post) x 5 (Velocity: 14, 19, 24, 30 & 35 centimetres per second) repeated measures ANOVA was run for both the spatial error (i.e., distance in pixels between the location of the target and the final location of the moving square) and also for the temporal error (i.e., the duration between the point when participants pressed the spacebar and the moment when they should have pressed it).

The Mauchly’s test of Sphericity for the Spatial error showed that the Velocity factor (sig < 0.001), the 2-way interaction between the cTBS and the Velocity factors (sig < 0.001), the 2-way interaction between the Session and the Velocity factors (sig=0.001), and the 3-way interaction (sig =0.022) violated the assumption of Sphericity, therefore we used the Greenhouse corrections.

The main effect for the cTBS stimulation location was not significant (F(1, 14) = .323, p=.579, η2=.023), while the main effects for Session (F(1,14)=10.159, p=.007, η2 = .421) and for Velocity (F(1.153, 16.137)=16.892, p<.001, η2=.547) were significant. The 2-way interaction between cTBS location and Session (F(1,14)=.002, p=.961, η2=0.001) and the 2-way interaction between cTBS location and Velocity (F(1.528, 21.392)=1.28, p=.29, η2=.084) were not significant, while the 2-way interaction between Session and Velocity (F(2.059, 28.824)=14.695, p<.001, η2=.512) was significant. The 3-way interaction was also not significant (F(2.591,36.277)=.332, p=.773, η2=.213). Overall, the results suggest that cTBS to either SPL or FEF may have caused participants to respond less accurately (later) for the faster velocity stimuli only.

However, there are some possible alternative explanations of this finding that will be considered in the Discussion.

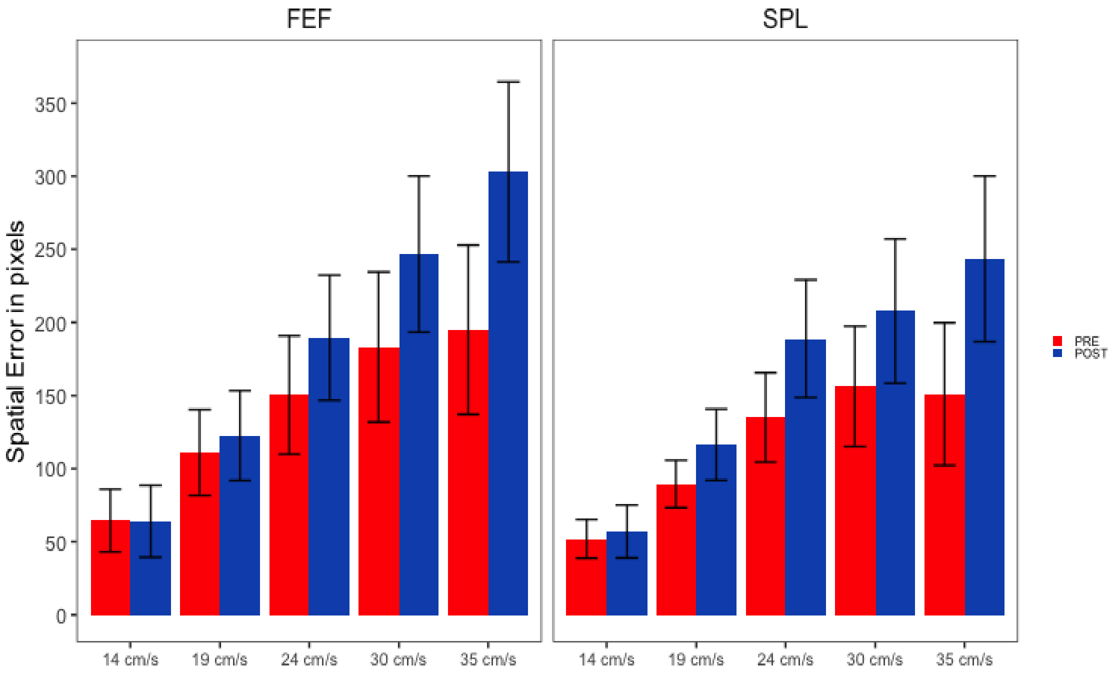

*Figure 4.10 - Bar plot with mean and SE for the Spatial error in Experiment 1.*

The Mauchly's test of Sphericity for the Temporal error showed that the Velocity factor (sig < 0.001) violated the assumption of Sphericity therefore we used the Greenhouse correction.

The repeated measure ANOVA for the temporal error showed that the main effect for Session (F(1,14)=7.197, p=.018, η2 = .34) ,while the main effect for Velocity showed a trend toward significance (F(1.409, 19.727)=3.069, p=0.084, η2=0.18), and the main effect for the cTBS location was not significant (F(1,14)=0.259, p=.619, η2= .018). The 2 way interaction between Session and Velocity was significant (F(4,56)=8.853, p< .001, η2=.387), while all the other interactions were not significant.

Overall, the temporal error results confirm the pattern shown in the spatial error results, although this is unsurprising because the two measures are highly correlated.

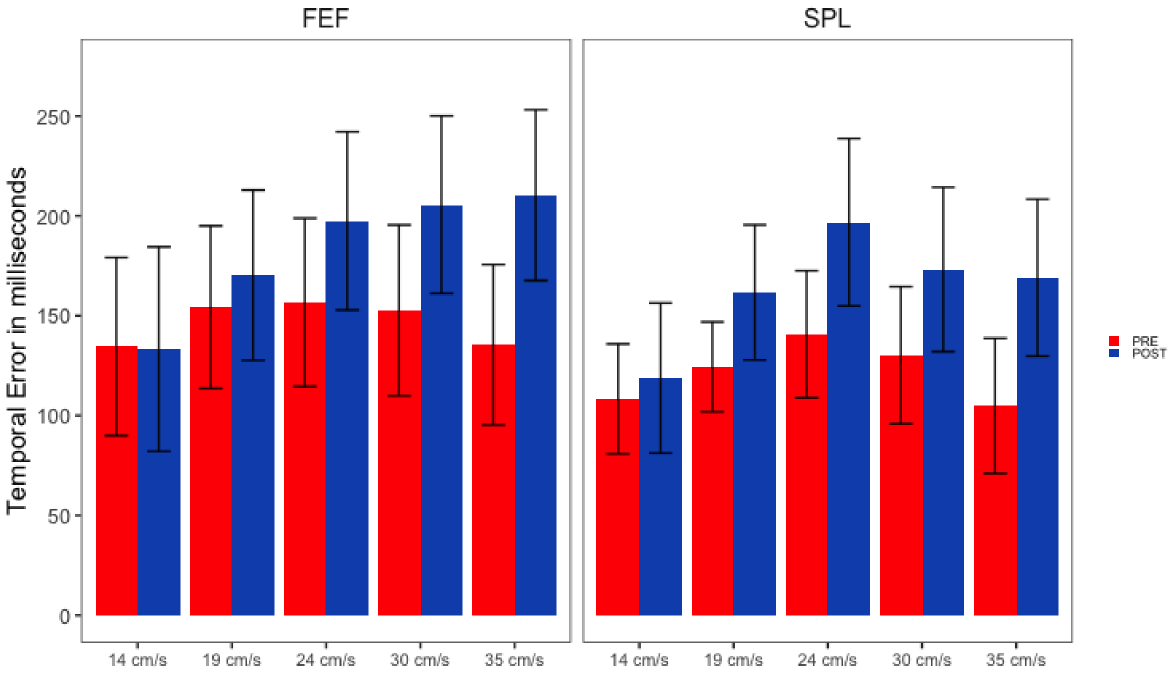

*Figure 4.11 - Bar plot with mean and SE for the Temporal error in Experiment 1.*

Turning to the reaction time control condition, we took the opportunity to test whether cTBS to either FEF or SPL had any effect on reaction times.  Means and SE for the RT recorded in Experiment 1 are presented in Figure 4.12.

We ran a 2 (cTBS: SPL vs FEF) x 2(Session: Pre vs Post cTBS) repeated measures ANOVA. The main effect of cTBS was not significant (F(1,14)=1.862, p=0.194, η2= 0.117), while the main effect of session was significant (F(1,14)=8.107, p=0.013, η2=0.367). The 2-way interaction was also not significant (F(1,14)=0.823, p=0.38, η2=0.056 It is possible that these results reflect an unpredicted effect of TMS to increase reaction times, but alternative explanations will be considered in the Discussion.

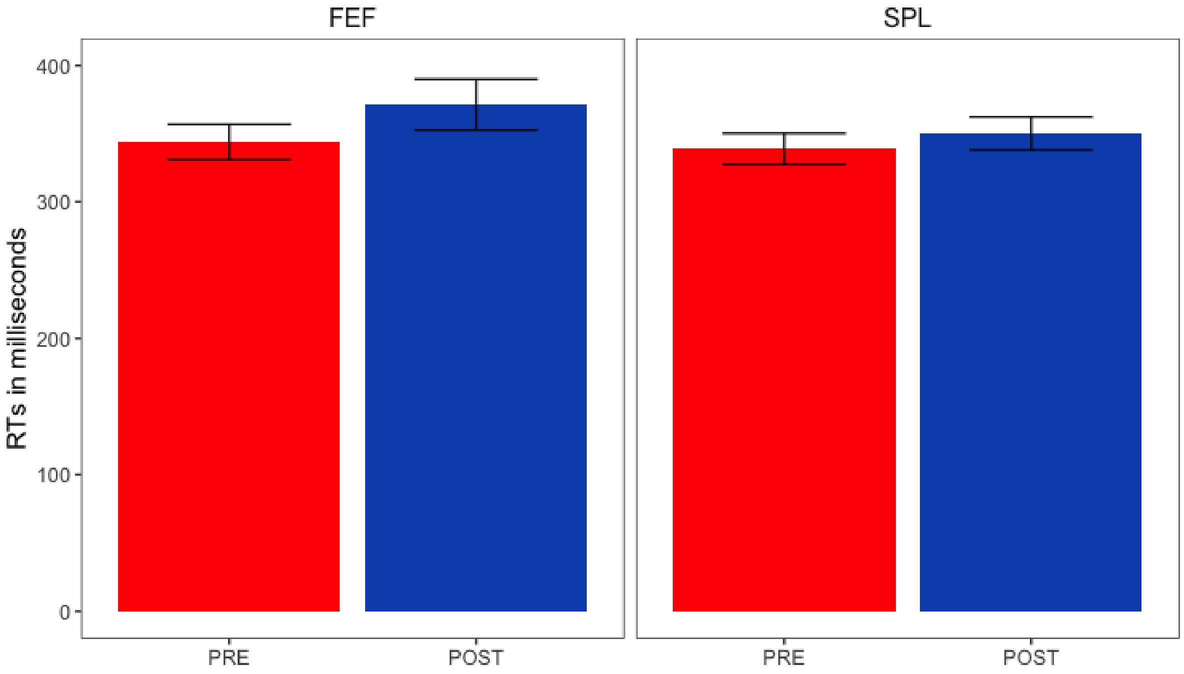

*Figure 4.12 - Bar plot with mean and SE for the reaction time control condition in Experiment 1.*

### 4.4.4 Discussion

In Experiment 1 we found that after cTBS to either SPL or FEF caused participants to respond less accurately (i.e., they produced later interception responses) for the faster velocities in the stimulus set. There are theoretical reasons to expect this pattern of results because task performance relied on attending to the 2D visual separation, and SPL and FEF are heavily connected brain regions (Heinen, Feredoes, Ruff, & Driver, 2017; Paus, Jech, Thompson, Comeau, Peters, & Evans, 1997) where TMS to either might be expected to produce similar effects. But unfortunately, the design of this study cannot allow us to rule out an alternative explanation other than TMS of the later interception responses we observed, which means that they might occur even in the absence of TMS. Specifically, we calibrated participants performance in the interception task using 8 feedback trials that took place at the start of the baseline tests on each day (the interception trials without feedback took place at the end of the baseline testing session, after the other tasks). But the calibration session was not included in the post-TMS measurements because we reasoned that if TMS effects on interception were present then feedback trials might act to abolish them. This decision made the design vulnerable to potential effects of a drift of task performance away from calibration. If such a drift occurred at higher velocities only, then that would produce the pattern of data we observed. We subsequently made some pilot observations without TMS to check if such performance drifts after initial calibration do happen and the results, although inconclusive, showed that it can happen under some circumstances. Further studies should add a control condition (i.e., sham TMS) on a third testing day. This would tell us if the effect we observed here is due to TMS to SPL/FEF or only due to a performance drift as more trials without feedback build up following the end of the feedback training session.

In the control task we used for Experiment 1 we found that cTBS stimulation to either SPL or FEF increased the reaction times. Because this result is not specific for just the stimulation of the right SPL or the right FEF, we cannot confidently claim that it represents an effect of TMS on the processes producing the reaction times. Further studies should present this experiment before and after sham TMS stimulation of the brain, in order to investigate if this finding is an order of testing effect or if it is an effect of cTBS to the SPL and FEF.

## 4.5 Experiment 2: Müller-Lyer illusion perceptual magnitude

### 4.5.1 Introduction

In the second experiment the effect of cTBS on the perceptual magnitude of the Müller-Lyer illusion was measured.

## 4.5.2 Method

A Müller-Lyer illusion was presented to the left of a fixation cross centred in the middle of the screen, and a comparison line was presented to the right of said fixation cross. Participants had to adjust the length of the comparison line to match the length of the horizontal shaft of the Müller-Lyer stimulus. They were asked to complete this task while starting at the fixation cross (Figure 4.13). Three configurations of the Müller-Lyer stimulus were presented: fins-out, which produced perceptual expansion of the shaft length, fins pointing inwards, which compresses the shaft, and a control version with vertical fins.

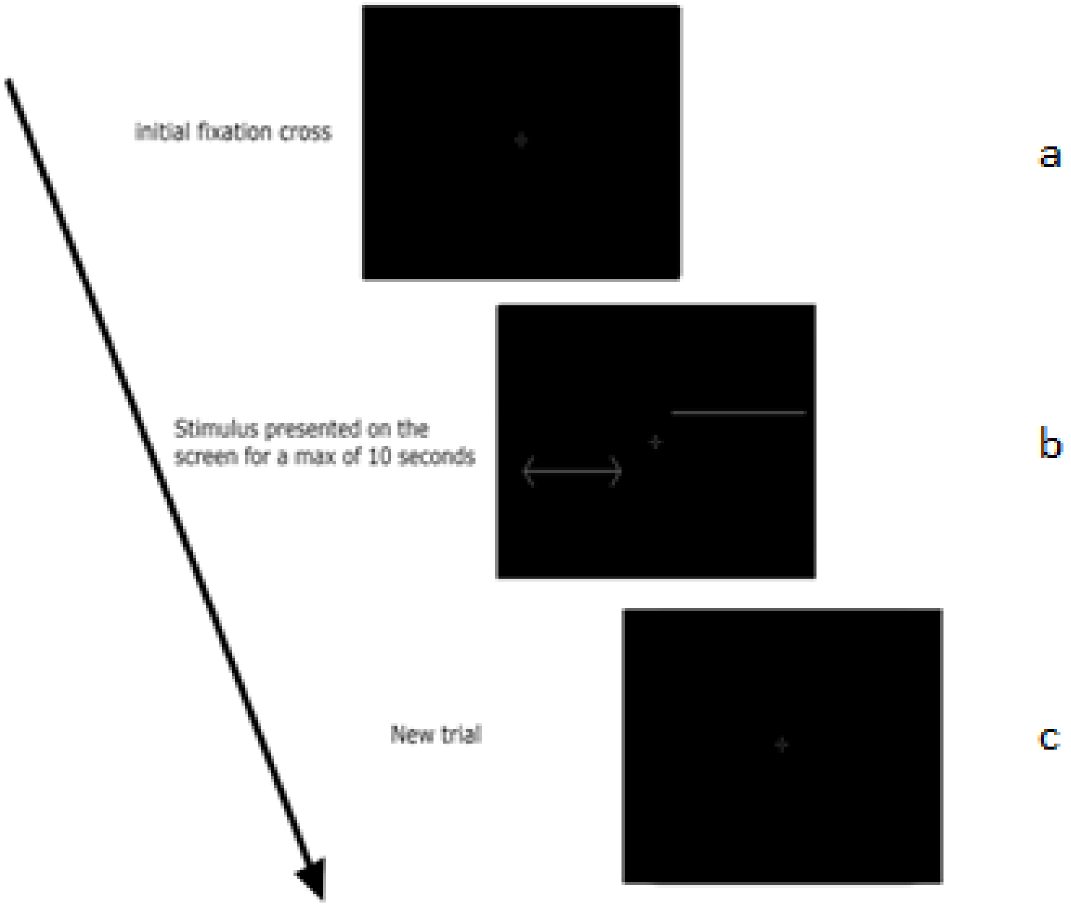

*Figure 4.13 - Procedure for Experiment 2.*

In this experiment a double fixation cross was presented in the centre of the screen, with a configuration of Müller-Lyer figure presented to its left and a comparison line to its right (Figure 4.14).

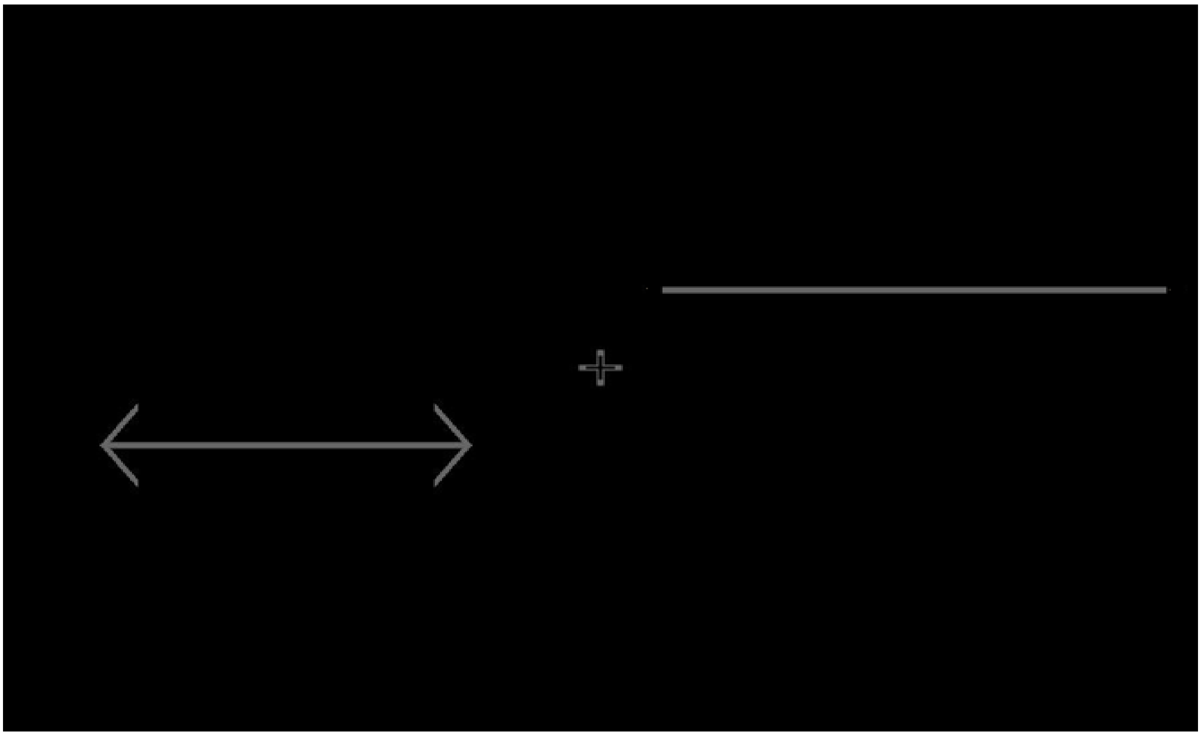

*Figure 4.14 - Example of stimuli used in Experiment 2.*

Participants were asked to use the left and right arrow keys to adjust the size of the comparison line to match the length of the horizontal shaft of the Müller-Lyer figure and then press the spacebar when they were happy with the adjustment. They were told that they had a maximum of 10 seconds in each trial to make the adjustments and press the spacebar, and if they failed to press the spacebar within the time limit no response for that trial would be saved. They were also told to perform this task while fixating on the fixation cross presented in the centre of the screen.

Three different configurations of the Müller-Lyer figure were used in this experiment as presented in Figure 4.15. The Müller-Lyer configurations are known to produce an illusion of extent (Mack et al., 1985). The configuration with the ingoing fins (stimulus A in Figure 4.15) is perceived as shorter than the configuration with the outgoing fins (stimulus B in Figure 4.15). The configuration with the perpendicular fins (stimulus C in Figure 4.15) does not induce any visual illusion, therefore it was used as the control stimulus.

Each stimulus was presented in 2 different sizes: with the length of the main shaft set to 3º and with the length set to 5º and the other of presentation was randomised. In both sizes the length of each arm of the outer wings was set to 1/3 of the length of the main shaft. The angle formed between the two arms of the wings was set to 45º for the ingoing fin (stimulus A in Figure 4.15) and to 315º for the outgoing fin (stimulus B in Figure 4.15). Each configuration of the stimulus (i.e., each wing type in both sizes) was presented 8 times, for a grand total of 48 trials. In each trial the starting length of the comparison line was set to either 50%, 80%, 120% or 150% of the horizontal shaft of the Müller-Lyer figure presented in the same trial.

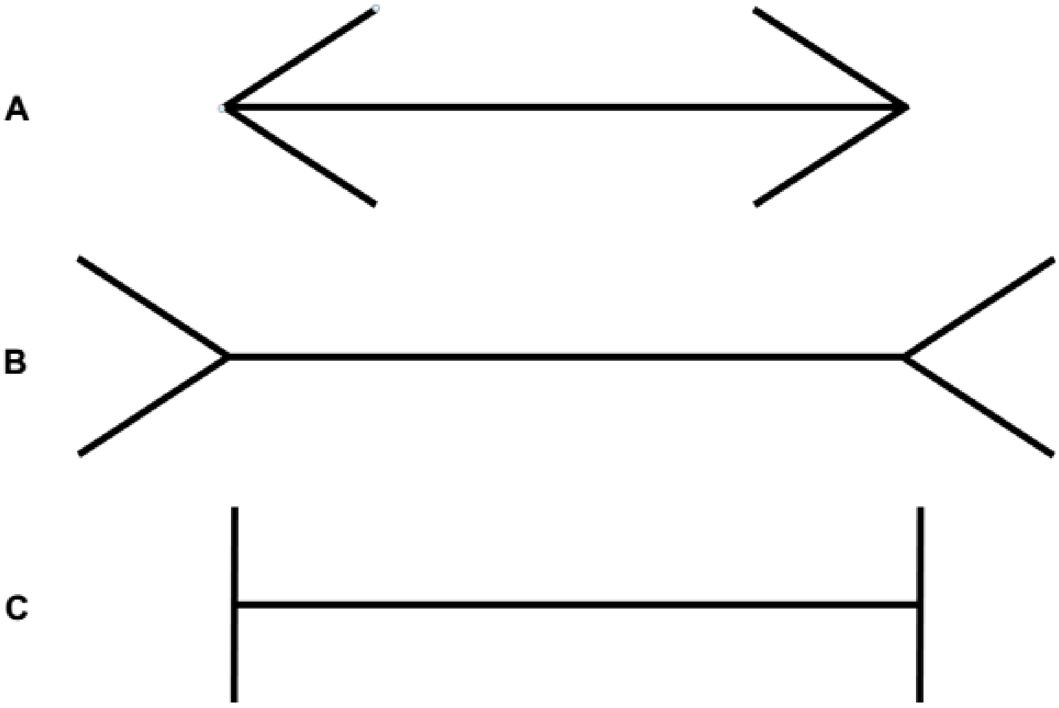

*Figure 4.15 - Stimuli used in experiment 2,3,4,5 & 6.*

## 4.5.3 Results

### *4.5.3.1 Pre-processing and descriptive statistics*

The behavioural data from this experiment was loaded into RStudio, and before computing the adjustment for the comparison line, all the trials in which the participants failed to confirm their adjustment before the 10 seconds response limit ran out were removed. This reduced the total number of trials from 2880 to 2868 trials. After that, for each trial we computed the final adjustment of the comparison line as a percentage of the horizontal shaft length of the Müller-Lyer stimulus, where a value below 100% meant an adjustment shorter the actual length of the ML stimulus, and a value above 100% meant an adjustment longer than the actual length of the ML stimulus. The histogram in Figure 4.16 shows the distribution of final adjustment of the comparison line for this experiment. On the basis of Figure 4.16, we excluded all values smaller than 50% or bigger than 150% of the actual shaft length. This reduced the total number of trials from 2868 to 2866.

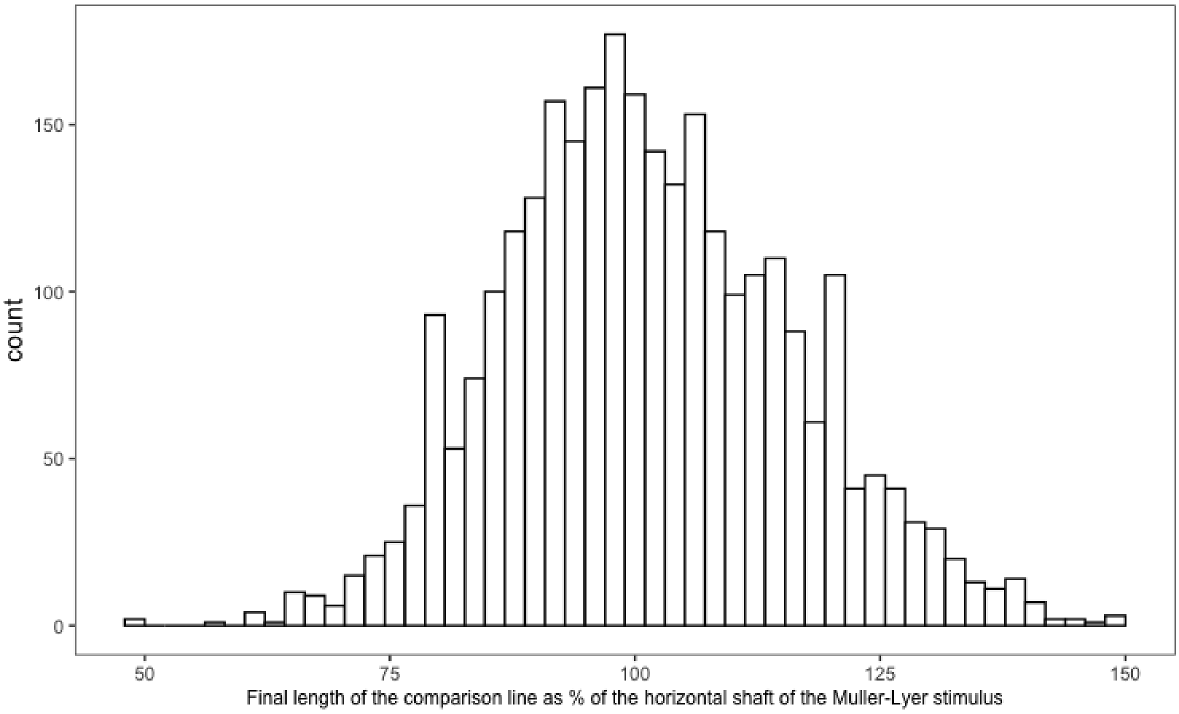

*Figure 4.16 - Histogram for the final length of the comparison line in Experiment 2.*

Pirate plots showing the effects of TMS on the mean, 95% CI and distribution of the adjustments of the comparison line are presented in Figure 4.17.

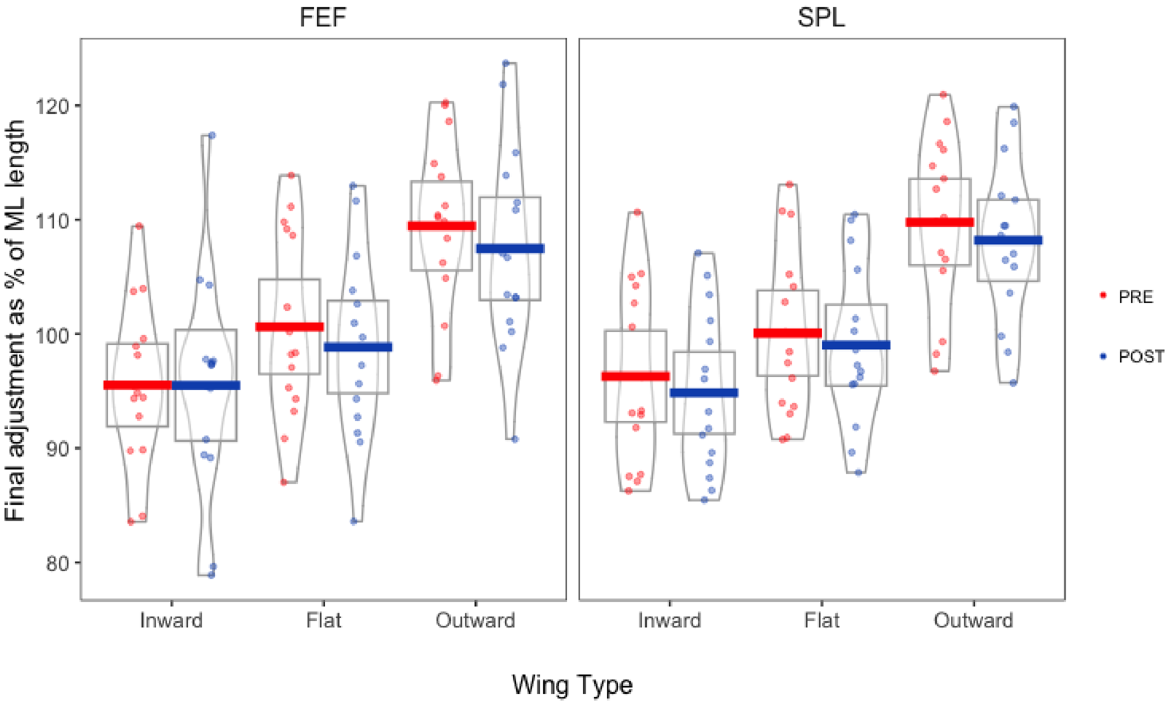

*Figure 4.17 - Pirateplots with means and 95% CIs for the line adjustments in Experiment 2.*

### *4.5.3.2 Statistical analysis*

Means and SE for the adjustments recorded in Experiment 2 are presented in Figure 4.18. We ran a2 (cTBS location: FEF vs SPL) x 2 (Session: Pre vs Post) x 3 (Wing type: Inward vs Flat vs Outward) repeated measure ANOVA.

The simple main effect of both the Session (F(1, 14)=8.081, p=.013, η2=.366) and Wing type (F(2,28)=190.225, p<.001, η2=.931) were significant, while the simple main effect of cTBS was not (F(1,14)=.019, p=.892, η2=.001). None of the 2-way interactions, nor the 3-way interaction were significant. The main effect of session, which was a general tendency to report line length as shorter after TMS in the second session, could either be a genuine effect of TMS to either SPL or FEF, or alternatively could be accounted for by an order of testing effect. Because it also occurred in the condition with flat fins, it does not represent an interaction of TMS with the processes producing the illusion.

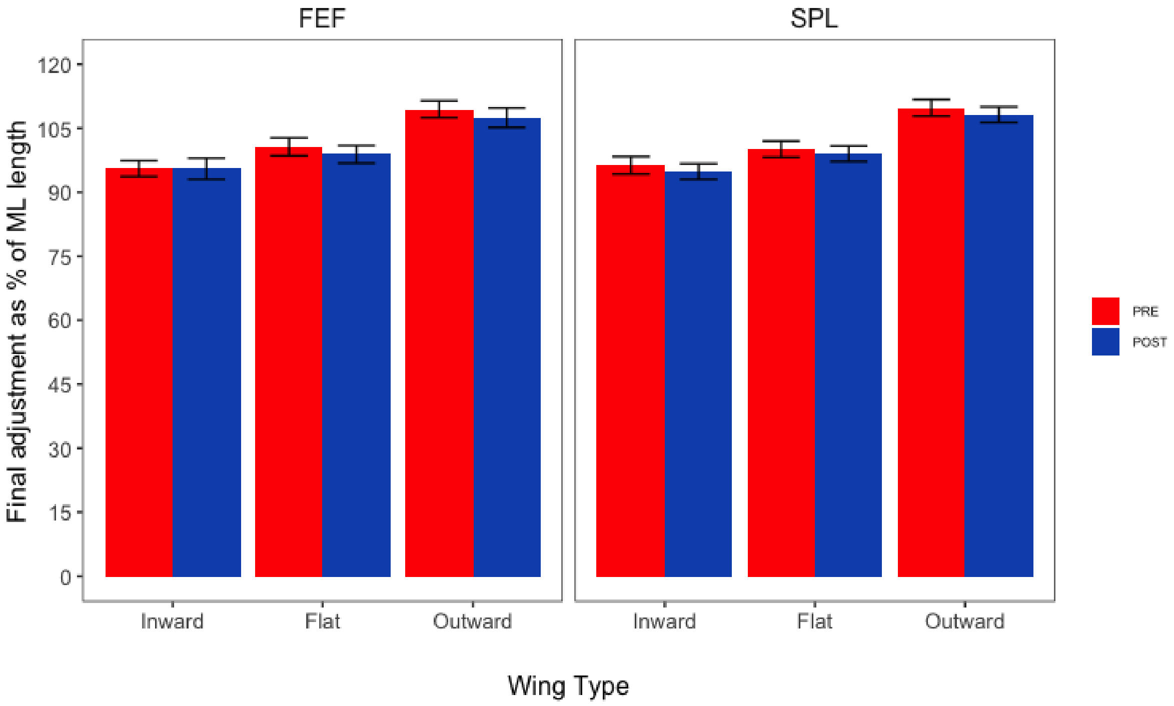

*Figure 4.18 - Bar plot with mean and SE for the stimuli used in Experiment 2.*

### 4.4.4 Discussion

In Experiment 2 we found a significant difference in apparent length of the horizontal shaft of the Müller-Lyer figure depending on the stimulus type, which meant that the illusion of extent was present in the data. This replicates previous findings (de Brouwer et al., 2014; Mack et al., 1985; Mancini et al., 2010). We also found that after TMS stimulation of either the FEF or the SPL there was a reduction in the final length of the comparison line for all the type of stimuli. Because this result is not specific for just the stimulation of the right SPL, and also because it occurred for the configuration of the stimulus with flat fin (i.e., the control configuration of the Müller-Lyer stimulus), we cannot claim that it represents an interaction of TMS with the processes producing the illusion. Further studies should present this experiment before and after a sham TMS stimulation of the brain, in order to investigate if this finding is an order of testing effect or if it is an effect of the cTBS of the SPL and FEF.

# 4.6 Experiment 3: Müller-Lyer illusion perceptual magnitude (memory version)

## 4.6.1 Introduction

In the third experiment the effect of cTBS on the perceptual magnitude of the Müller-Lyer illusion was again investigated. We speculated that effects of cTBS on neural processing were more likely to manifest if the Müller-Lyer stimuli were presented only briefly, requiring the participant to use short term memory of the stimuli.

## 4.6.2 Methods

The cognitive and motor aspects of this task were identical to those in the third experiment, but this time while the participants were making the adjustments to the comparison line, both the central fixation cross and the Müller-Lyer stimulus were removed from the screen (Figure 4.19).

a

b

c

Figure 4.19 - Procedure for Experiment 3.

In the third experiment the same stimuli as Experiment 2 were presented. This time both the double fixation cross and the Müller-Lyer figure were just briefly flashed on the screen for 100 ms and then removed, so the participant was asked to adjust the length of the comparison line with nothing else displayed on the screen. The participants were asked to adjust the length of the comparison line to match the length of the horizontal shaft of the Müller-Lyer figure and press the spacebar once they were happy with the adjustments. They were told they had a maximum of 10 seconds in each trial to press the spacebar and confirm the adjustments, if they failed to do so within the time limit no response would be saved for that trial and they would be moved to the next one. During this experiment participants were allowed to look directly at the comparison line while performing the task. This experiment was composed of 48 trials.

## 4.6.3 Results

### *4.6.3.1 Pre-processing and descriptive statistics*

The behavioural data from this experiment was loaded into RStudio, and before computing the adjustment for the comparison line, all the trials in which the participants failed to confirm their adjustment before the 10 seconds response limit ran out were removed. This reduced the total number of trials from 2880 to 2879 trials. After that, for each trial we computed the final adjustment for the comparison line as a percentage of the horizontal shaft of the Müller-Lyer stimulus, where a value below 100% meant an adjustment shorter the actual length of the ML stimulus, and a value above 100% meant an adjustment longer than the actual length of the ML stimulus. The histogram in Figure 4.20 shows the distribution of final adjustment for the comparison line for this experiment. We removed all values smaller than 50% or bigger than 150% of the actual shaft length, further reducing the total number of trials to 2874.

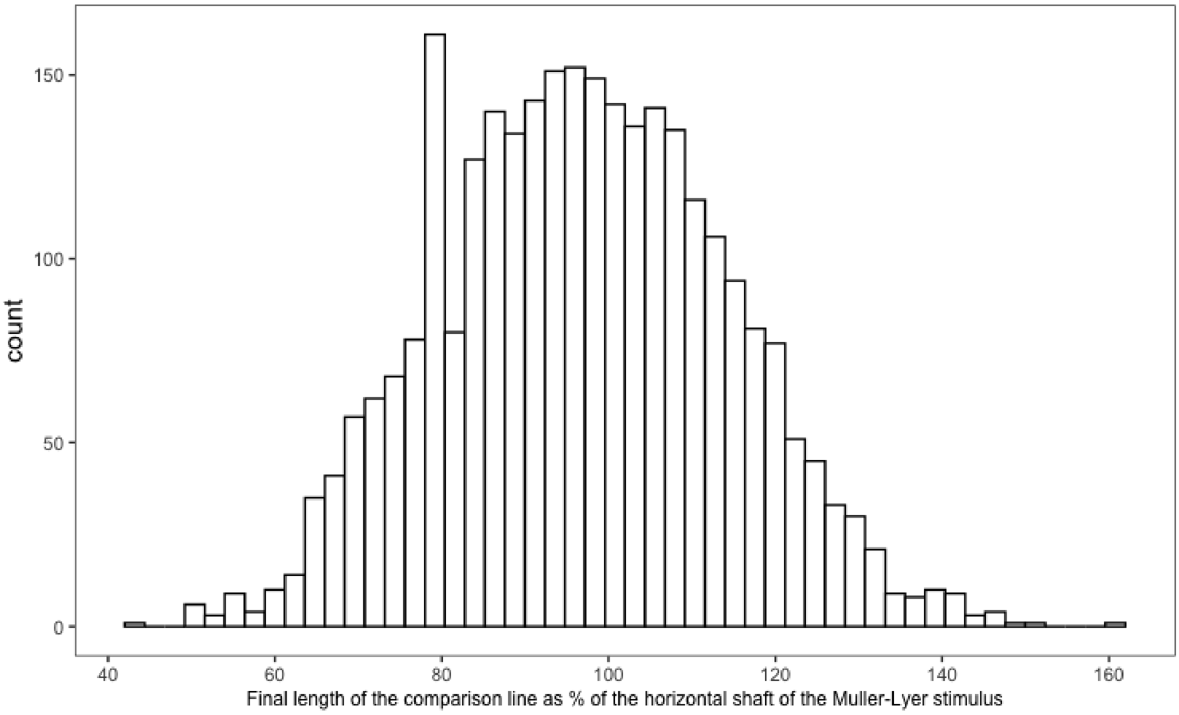

*Figure 4.20 - Histogram for the final length of the comparison line in Experiment 3.*

Pirate plots showing the effects of TMS on the mean, 95% CI and distribution of the adjustments of the comparison line are presented in Figure 4.21.

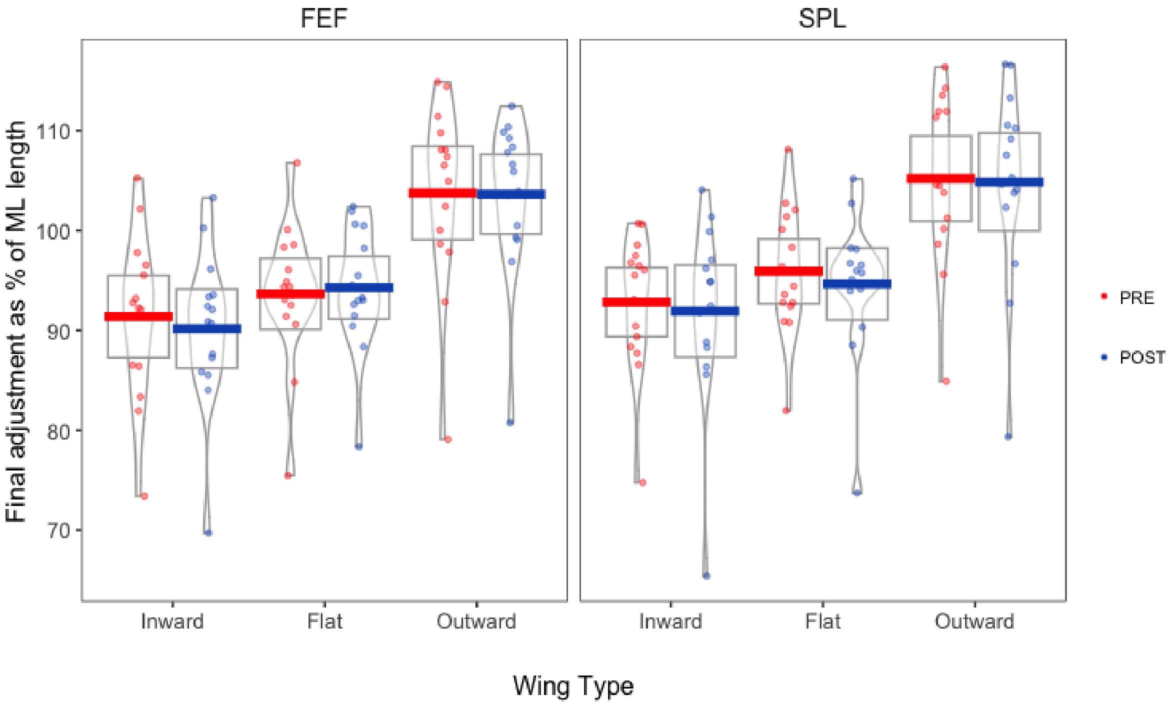

*Figure 4.21 - Pirateplots with means and 95% CIs for the line adjustments in Experiment 3.*

### *4.6.3.2 Statistical analysis*

Means and SE for the adjustments recorded in Experiment 3 are presented in Figure 4.22. We ran a 2 (cTBS location: FEF vs SPL) x 2 (Session: Pre vs Post) x 3 (Wing Type: Inward vs Flat vs Outward) repeated measure ANOVA.

The simple main effect for Wing Type was significant (F(2, 28)=97.745, p<.001, η2=.875), while the simple main effect of cTBS (F(1,14)=3.024, p=.104, η2=.178), and the simple main effect of Session were not significant (F(1,14)=.354, p=.561, η2=.025). None of the 2-way interactions, nor the 3-way interaction were significant. This indicates that we replicated the previously found effects of the Müller-Lyer illusion on line adjustments, but cTBS failed to influence that.

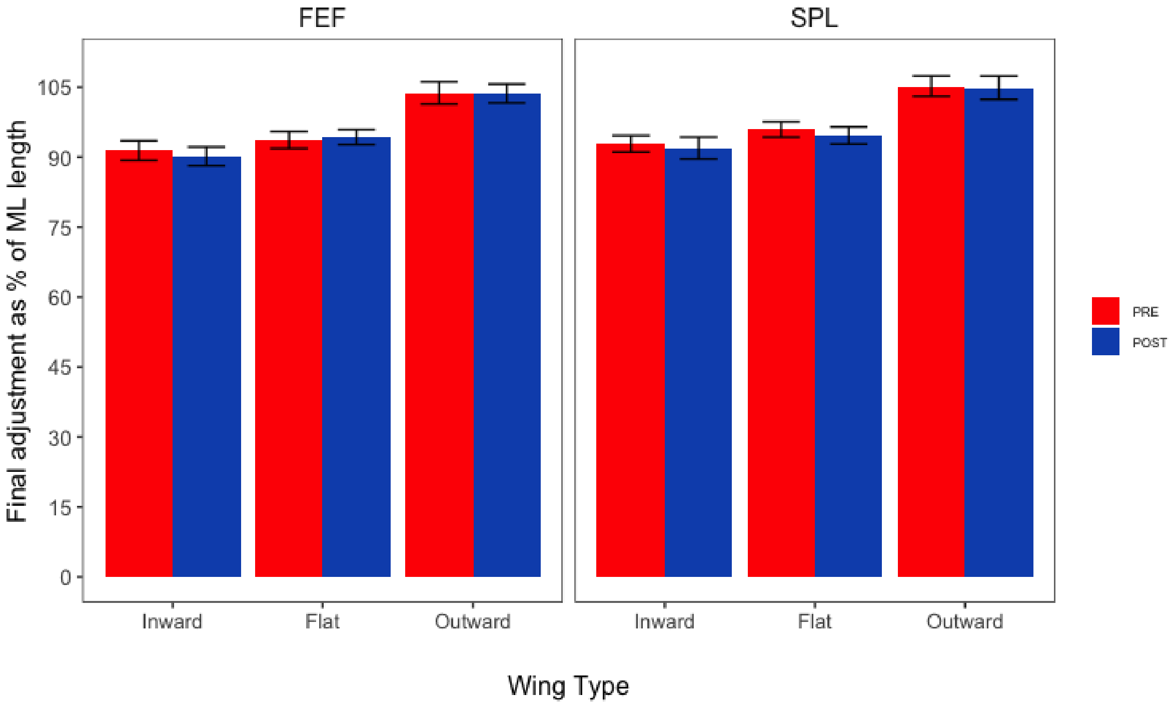

*Figure 4.22 - Bar plot with mean and SE for the stimuli used in Experiment 3.*

### 4.6.4 Discussion

In Experiment 3 we found a significant difference in adjustment length depending on the stimulus type, which meant that the illusion of extent was present in the short-term memory of the Müller-Lyer figure. This replicates previous findings (de Brouwer et al., 2014; Mack et al., 1985; Mancini et al., 2010), however, we found that the cTBS stimulation did not significantly affect the length of the comparison line recorded after the presentation of the Müller-Lyer stimulus.

## 4.7 Experiment 4: Müller-Lyer illusion reflexive saccades

### 4.7.1 Introduction

In the fourth experiment the effect cTBS on reflexive saccades elicited by the Müller-Lyer stimuli was investigated.

### 4.7.2 Method

In each trial a Müller-Lyer stimulus was presented either to the left or to the right of a central fixation cross, which disappeared as the Müller-Lyer stimulus appeared, for 100 ms, and the participants were asked to move their eyes to the end of the horizontal shaft of the Müller-Lyer stimulus (Figure 4.23).

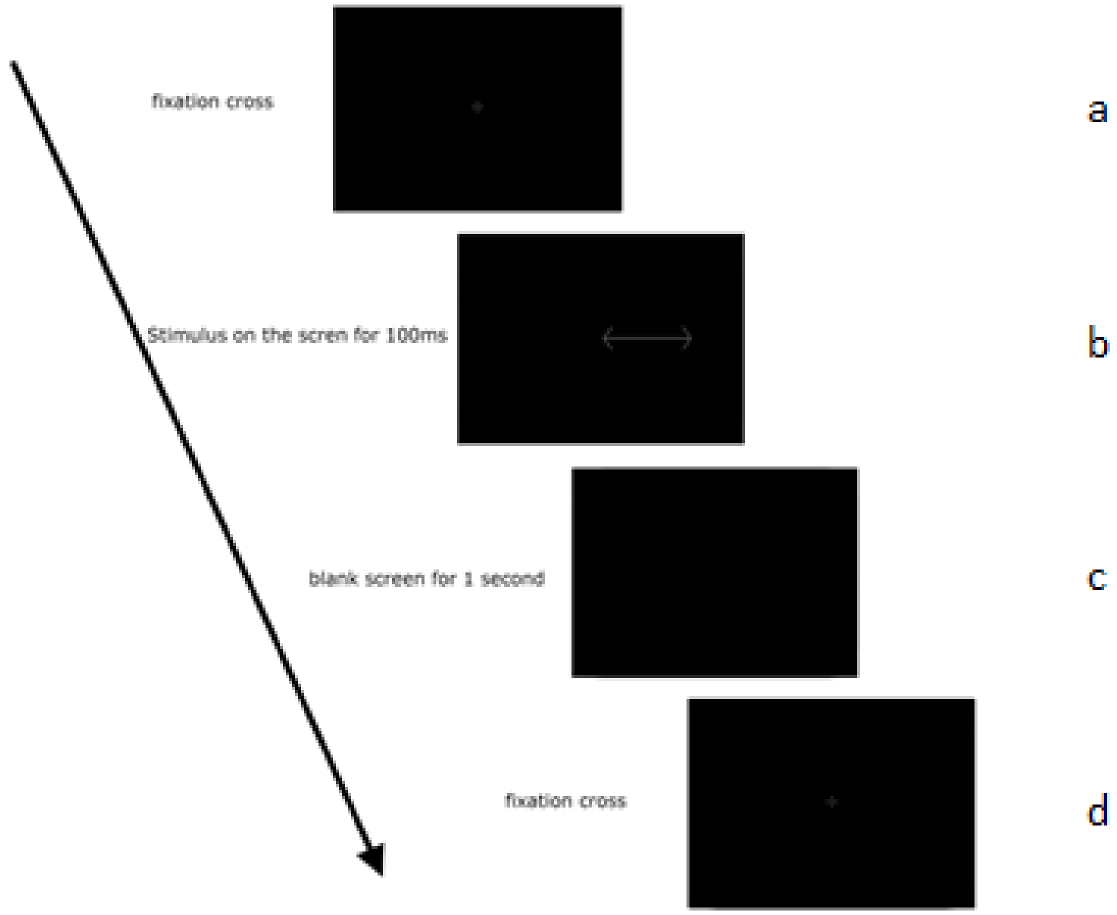

*Figure 4.23 - Procedure for Experiment 4.*

In the fourth experiment a fixation cross and a configuration of the Müller-Lyer figure were presented in succession on the screen.

*Figure 4.24 - Example of stimuli used in Experiment 4.*

Participants were asked to move their eyes to the end of the Müller-Lyer stimulus furthest from the fixation cross. The stimuli used in this experiment are presented in Figure 4.15. At the beginning of each trial a double fixation cross (each arm was set to 0.3º) was presented for 1 second against a black background (Figure 4.24a). After 1 second the fixation cross was removed from the screen and a Müller-Lyer stimulus was presented on the screen, with one end of the main horizontal shaft placed in the centre of the screen with the other end of the horizontal shaft placed either to the left or right of the centre (Figure 4.24b). The stimulus was in white, and it was presented on the screen for 100 ms and then removed from the screen. Participants were left with a blank black screen for 1 second before the fixation cross was presented again, which indicates the start of a new trial.

So that saccades of varying amplitudes had to be performed, and to ensure participants fully attended to the shaft length on each trial, each configuration of the stimuli was presented in 3 different sizes: either the length of the main shaft of the Müller-Lyer was set to 2º,4º or 8º. A total of 120 trials were presented for this task, in a randomised order.

### 4.7.3 Results

#### *4.7.3.1 Pre-processing and descriptive statistics*

The eyetracker data for all the participants acquired during Experiment 4, in which participants saccaded towards the end point of the horizontal shaft of the Müller-Lyer figure, was loaded into RStudio and out of all the saccades recorded during this task, just the saccades made when the stimuli were on the screen were selected, for a total of 29243 saccades across all four sessions of the experiment and all participants. There were 7200 individual trials, and the aim of pre-processing was to identify one saccade per trial. To begin, for each trial just the saccades made in the correct direction (i.e., towards the end point of the horizontal shaft of the Müller-Lyer figure and not the returning saccades) were filtered, reducing the total number of saccades to 13585. The histogram in Figure 4.25 shows the distribution of latency for the saccades that survived the filter.

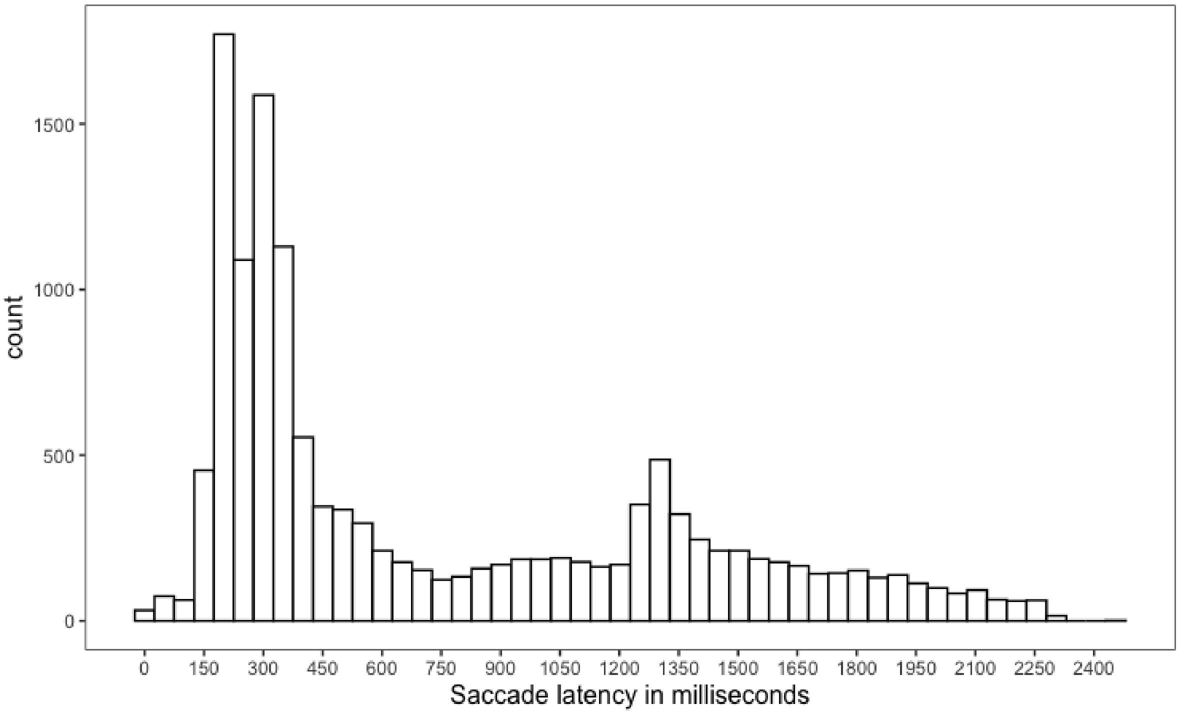

*Figure 4.25 - Histogram for the saccade latency in Experiment 4.*

We decided to remove all the saccades with a latency smaller than 100ms and also the ones with a latency bigger than 500ms, many of which may have been secondary saccades made after the initial saccade along the shaft of the Müller-Lyer stimulus. This further reduced the number of saccades to 7139. We then converted the saccade amplitudes into percentage of shaft length. A histogram of the distribution of the saccade amplitudes is presented in Figure 4.26.

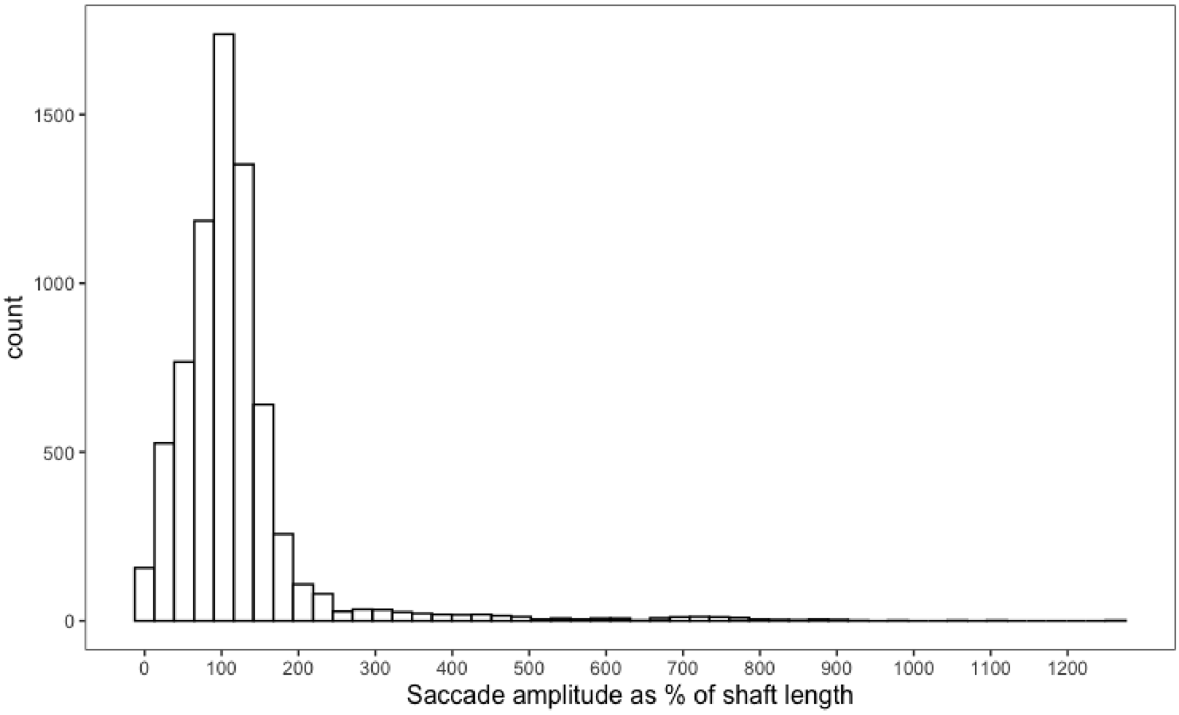

*Figure 4.26 - Histogram for the saccade amplitude in Experiment 4.*

On the basis of Figure 4.26, we decided to keep the saccades either bigger than 50% or smaller than 200% of the shaft length, and this reduced the number of saccades to 6062. We then calculated for each saccade the angle at which it was produced relative to horizontal (we calculated it by using the arctangent function of the ratio between the horizontal component and the vertical component of the saccade). Histogram in Figure 4.27 shows the distribution of the saccade angle.

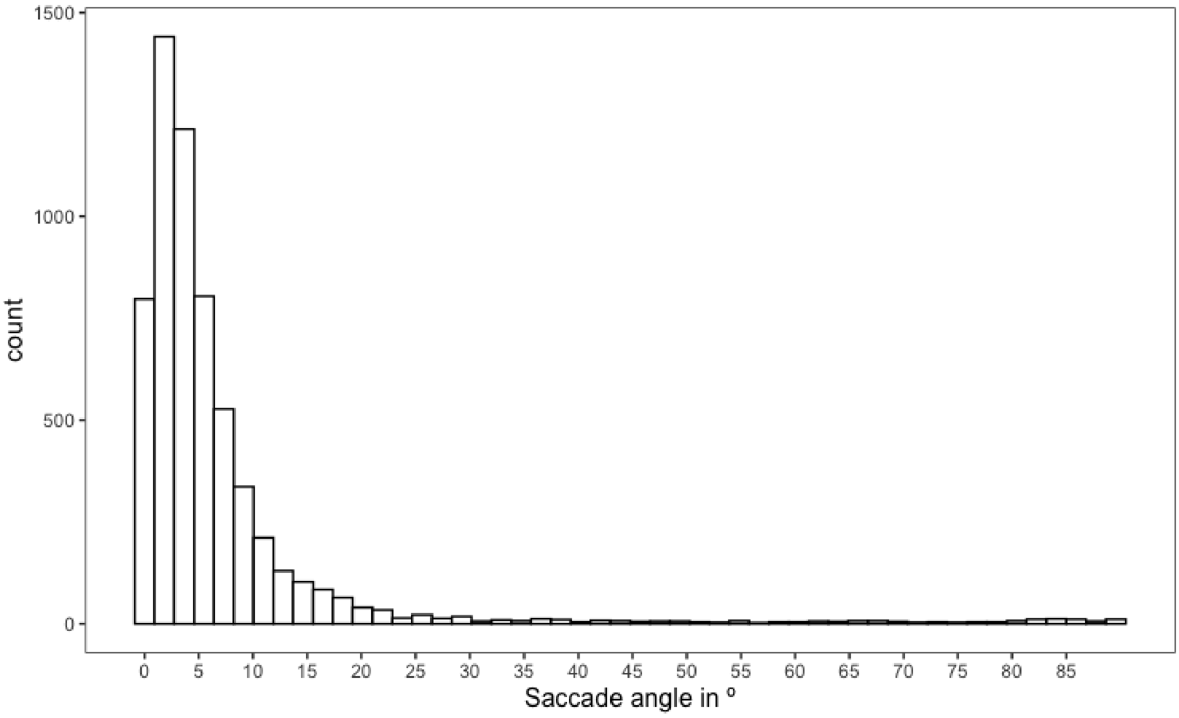

*Figure 4.27 - Histogram for the saccade angle in Experiment 4.*

On the basis of Figure 4.27, we decided to remove all the saccade with an angle bigger than 15º, which reduced the number saccades to 5532. Inspection of the remaining raw data revealed that some saccades remained that had starting points distant from the fixation point. For this reason, we decided to remove all the saccades that were initiated more than 100 pixels away from the centre of the screen in any direction. The exception to this was when inspection of plots of saccades for some individual participants in some sessions strongly suggested that the eye tracker calibration had drifted in either the X or Y dimension. Where this happened, we adjusted the 100 pixel window. This reduced the sample to 4629 saccades. We also checked that the end point of all the saccades was within 200 pixels vertically from the centre of the screen, and all the saccades satisfied this criterion. These filtering steps were based on those used by de Brouwer and colleagues (2014). After the filtering procedure the first saccade recorded in each trial was obtained for each participant. One participant (ID-12) was further removed from the data set because less than 5% of the initial number of trials survived the filtering procedure (Figure 4.28). Pirate plots showing the effects of TMS on the mean, 95% CI and distribution of the saccade amplitudes in the 3 experimental conditions are presented in Figure 4.29.

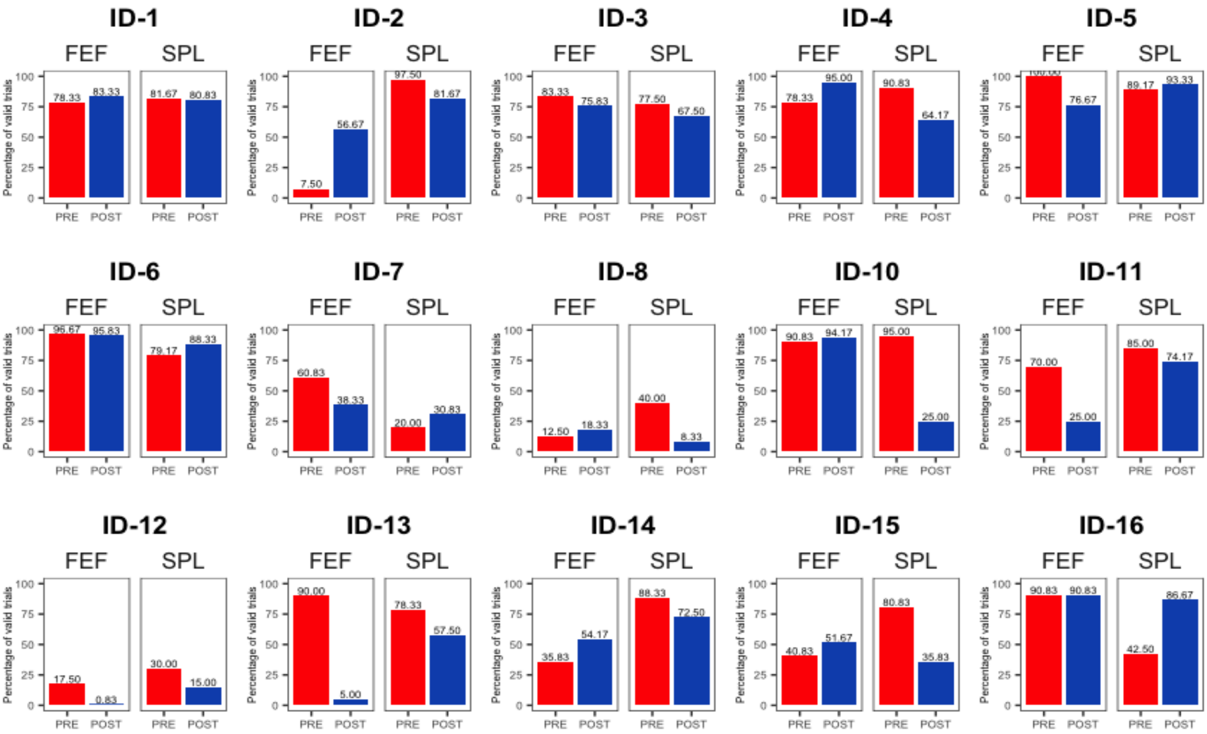

*Figure 4.28 - Number of valid trials for each participant in Experiment 4.*

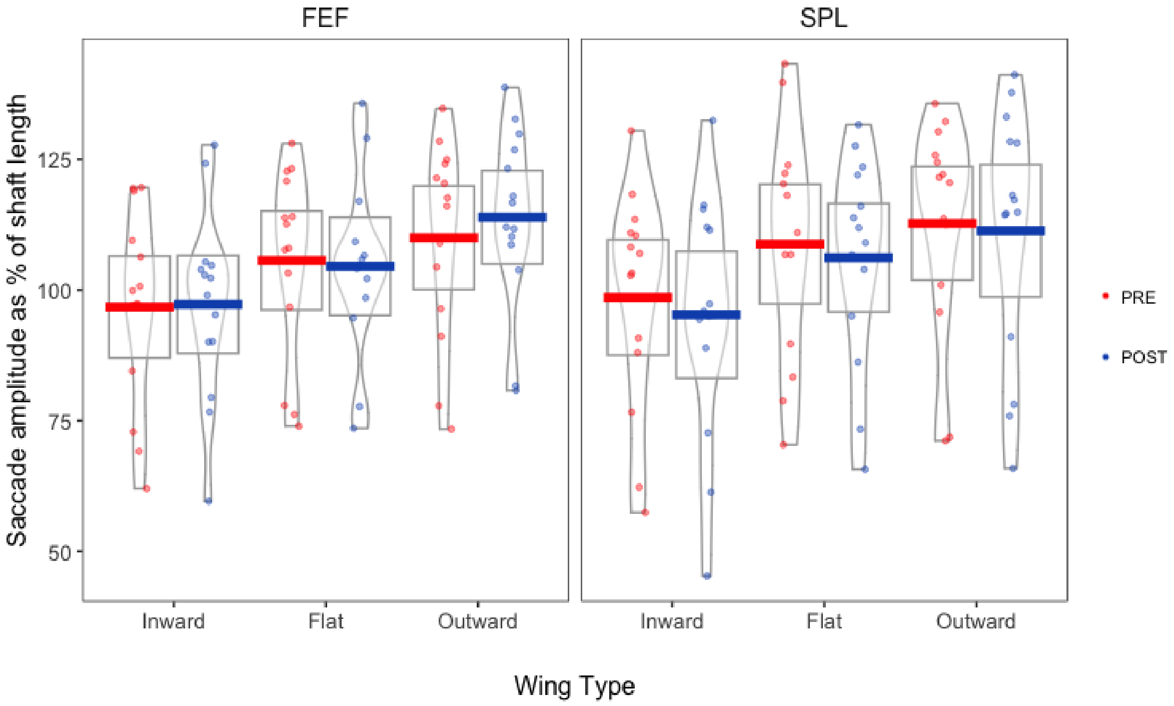

*Figure 4.29 - Pirateplots with means and 95% CIs for the line saccade amplitudes in Experiment 4.*

### *4.7.3.2 Statistical analysis*

We expected to find that cTBS would reduce the influence of the Müller-Lyer illusion on saccade amplitudes. Means and SE for the saccade amplitudes recorded in Experiment 4 are presented in Figure 4.30.

In order to test our prediction, a 2 (cTBS: FEF vs SPL) x 2 (Session: Pre vs Post) x 3 (Wing: Inward vs Flat vs Outward) repeated measure ANOVA was run.

The Mauchly's test of Sphericity showed that the 3-way interaction between cTBS, Session and Wing (sig = .037) violated the assumption of Sphericity therefore we used the Greenhouse correction.

The simple main effect for Wing Type was significant (F(2, 24)=45.695, p<.001, η2=.792), while the simple main effect of Session (F(1,12)=.001, p=.992, η2=.001), and the simple main effect of cTBS (F(1,12)=.273, p=.611, η2=.022) were not significant. None of the 2-way interactions, nor the 3-way interaction were significant. This indicates that we replicated the previously found effects of the Müller-Lyer illusion on amplitude of reflexive saccades, but cTBS failed to influence that.

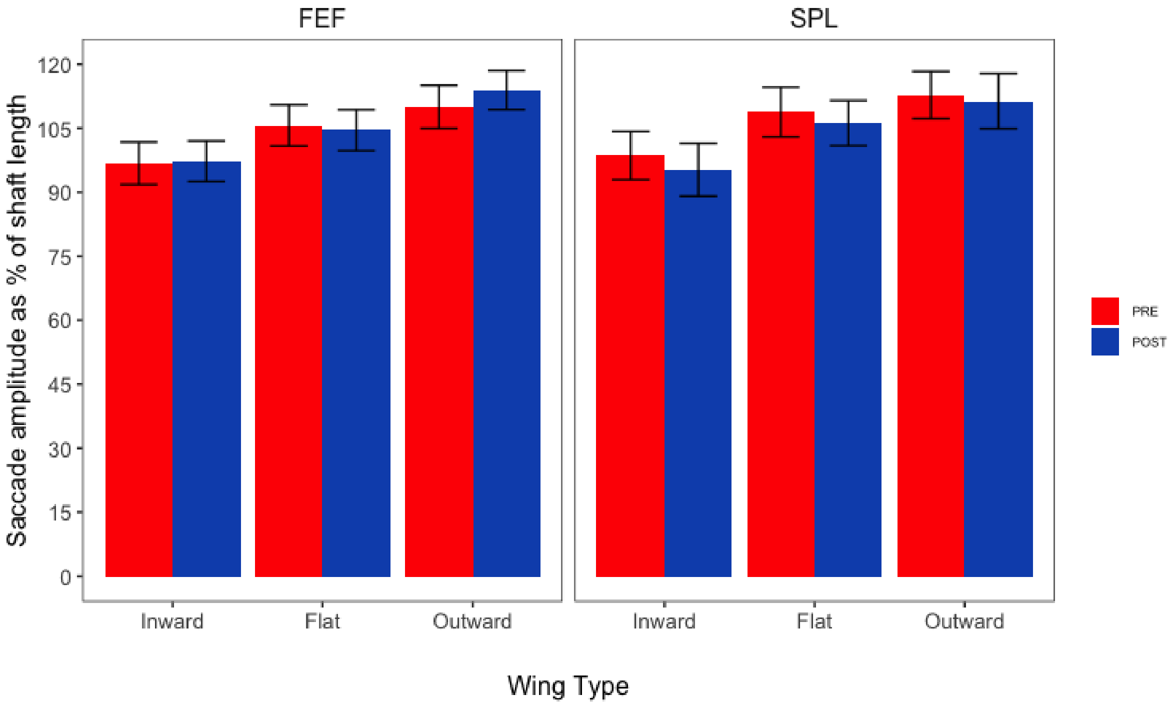

*Figure 4.30 - Bar plot with mean and SE for the stimuli used in Experiment 4.*

### 4.7.4 Discussion

In Experiment 4 we found a significant difference in amplitude of the reflexive saccades depending on the fin type, which meant that the illusion of extent was present in the data. This replicates previous findings (Binsted, & Elliott, 1999; Delabarre, 1898; Festinger, White, & Allyn, 1968; Stratton, 1906; Yarbus, 1967).  However, we found that the cTBS stimulation did not significantly affect the amplitudes of the reflexive saccades.

# 4.8 Experiment 5: Müller-Lyer illusion voluntary pro-saccades

## 4.8.1 Introduction

In the fifth experiment the effect of the cTBS on voluntary saccades made in response to Müller-Lyer stimuli was measured.

## 4.8.2 Method

In each trial a central white dot was initially presented, then the dot changed its colour to either red or blue. A blue dot indicated a prosaccade trial, while a red dot indicated an antisaccade trial. After the dot changed its colour a Müller-Lyer stimulus was presented either to the left or to the right of the centre of the screen. In the prosaccade trials the participants were asked to move their eyes towards the end point of the horizontal shaft of the Müller-Lyer stimulus, while in the antisaccade trials they were asked to move their eyes away from the Müller-Lyer stimulus (i.e., into the half of the screen where the stimulus was not displayed). The procedure for this experiment is presented in Figure 4.31.

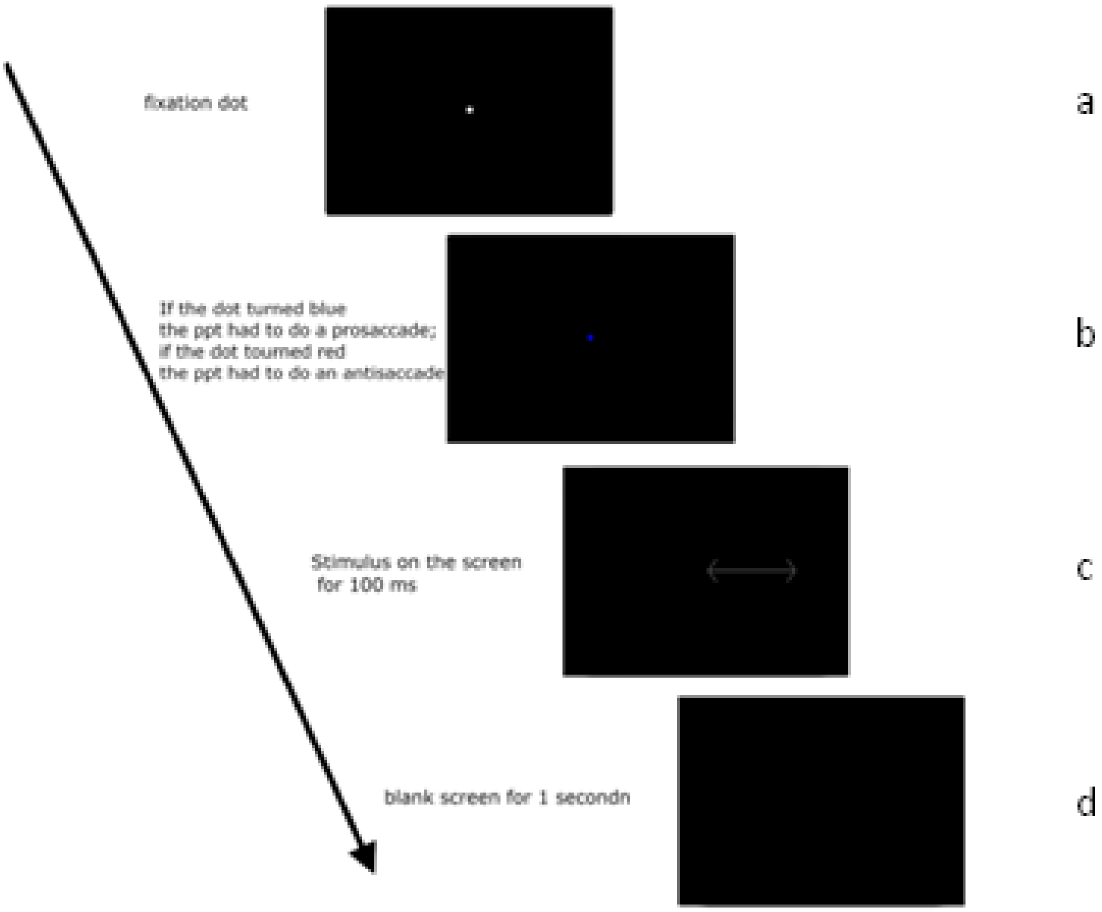

*Figure 4.31 - Procedure for Experiment 5.*

In the fifth experiment a dot and a configuration of the Müller-Lyer figure were presented on the screen.

*Figure 4.32 - Example of stimuli used in Experiment 5.*

At the beginning of each trial a white dot (0.5º in radius) was presented in the centre of the screen for 1 second (Figure 4.32a). After that, the dot changed its colour to either red or blue, and after 1 second a configuration of the Müller-Lyer figure was presented on the screen for 100ms (Figure 4.32b). If the white central dot had changed its colour to blue (which indicated a pro-saccade trial, as shown in Figure 4.33a), the participants were asked to move their eyes from the end of the horizontal shaft presented in the centre of the screen to the other end of the horizontal line (i.e., the end of the horizontal line further away from the centre of the screen); while if the white central dot changed its colour to red dot (which indicated an anti-saccade trial, as shown in Figure 4.33b) participants had to move their eyes into the half of the screen where the stimulus was not presented.

*Figure 4.33 - Example of coloured dots used in Experiment 5.*

The 3 configurations of the Müller-Lyer figure presented in Figure 4.15 were used for this experiment, and they all had just one size: the main shaft of the Müller-Lyer stimuli was set to 4.5º and each arm of the wing was set 1/3 of the main shaft length, and the angle formed between the two arms of the wings was set to 45º. A grand total of 144 trials were presented for this experiment in a randomised order.

## 4.8.3 Results

### *4.8.3.1 Pre-processing and descriptive statistics*

The eyetracker data for all the participants acquired during Experiment 5, in which participants saccaded towards the end point of the horizontal shaft of the Müller-Lyer figure, was loaded into RStudio and out of all the saccades recorded during this task, just the saccades made when the stimuli were on the screen were selected, for a total of 23810 saccades across all participants and all four testing sessions. The total number of pro-saccade trials was 4320, and the aim of pre-processing was to identify one saccade for each of these trials. To begin, all the saccades recorded in anti-saccade trials (i.e., when the dot changed its colour to red and participant was asked to move their eyes into the visual field where the stimulus was not presented) were removed, reducing the total to 11360 saccades. After that, for each trial just the saccades made in the correct direction (i.e., towards the end point of the horizontal shaft of the Müller-Lyer figure and not the returning saccades) were filtered, reducing the total number of saccades to 6173. We then produced a histogram of the saccade latency (Figure 4.34).

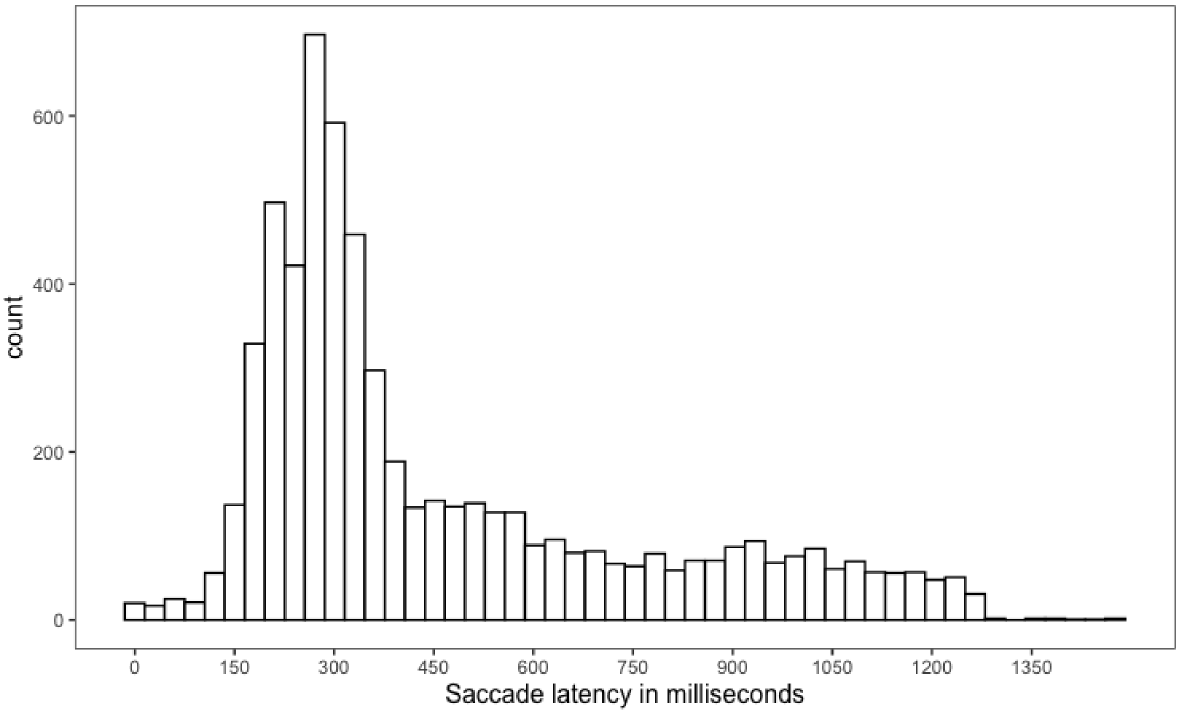

*Figure 4.34 - Histogram for the saccade latency in Experiment 5.*

On the basis of Figure 4.34, we decided to remove all the saccades with a latency shorter than 100 ms or bigger than 750 msec, many of which may have been secondary saccades made after the initial saccade along the shaft of the Müller-Lyer stimulus. This step reduced the number if saccades to 4932. The latency filter used the 750 msec value rather than 500 msec because latencies are expected to be longer in voluntary saccades than reflexive ones. Then we converted the saccade amplitudes into percentage of shaft length, and we produced a histogram (Figure 4.35).

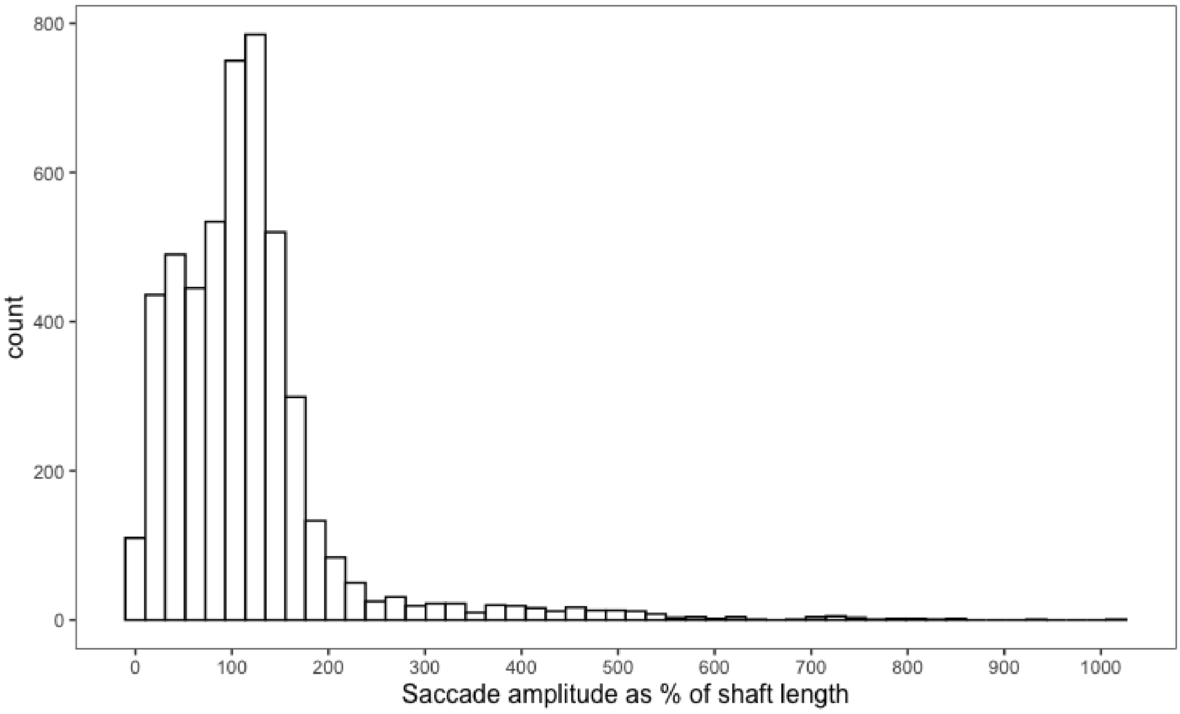

*Figure 4.35 - Histogram for the saccade amplitude in Experiment 5.*

On the basis of Figure 4.35, we removed all the saccades that were either smaller than 35% or bigger than 200% of the shaft length, and this lowered the number of saccades to 3876. We then calculated for each saccade the angle at which it was produced relative to horizontal (we calculated it by using the arctangent function of the ratio between the horizontal component and the vertical component of the saccade). Figure 4.36 shows the distribution of the saccade angle.

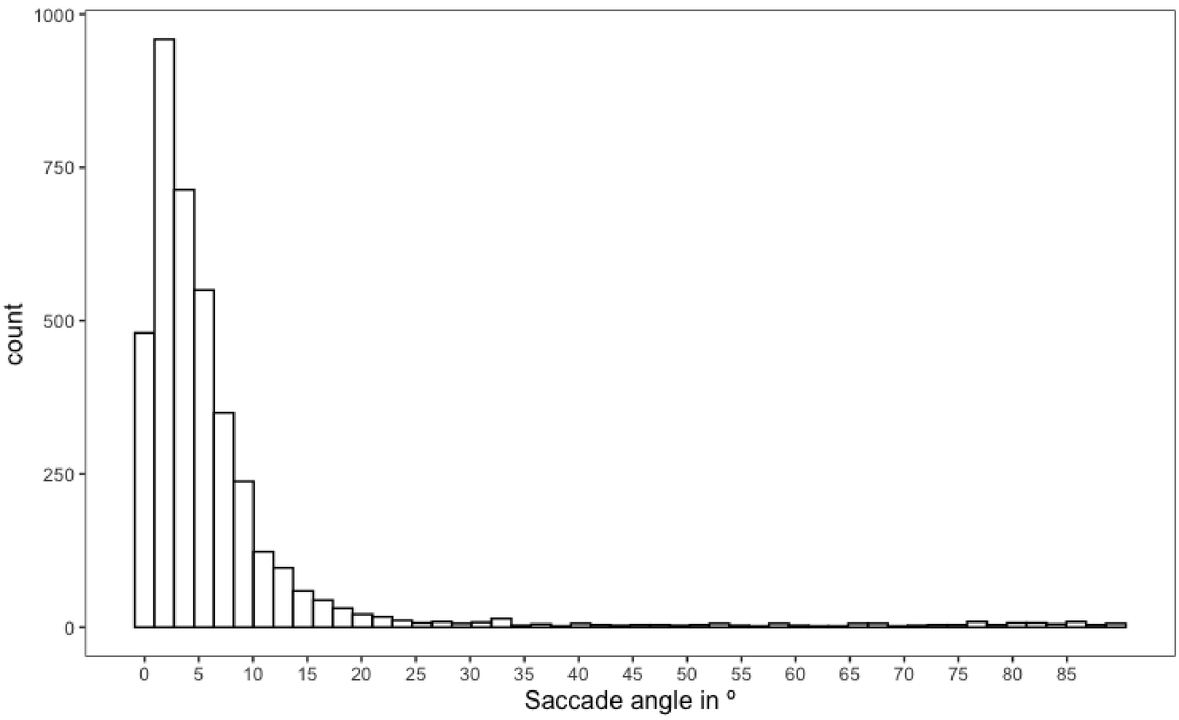

*Figure 4.36 - Histogram for the saccade angle in Experiment 5.*

On the basis of Figure 4.36, all saccades with an angle bigger than 15º were removed, and this reduced the sample to 3556 saccades. Inspection of the remaining raw data revealed that some saccades remained that had starting points distant from the fixation point. For this reason, all the saccades that were initiated more than 100 pixels away from the centre of the screen in any direction were removed. The exception to this was when inspection of plots of saccades for some individual participants in some sessions strongly suggested that the eye tracker calibration had drifted in either the X or Y dimension. Where this happened, we adjusted the 100 pixel window. This reduced the sample to 2668 saccades. We also checked that the end point of all the saccades was within 200 pixels vertically from the centre of the screen, and all the saccades satisfied this criterion. These filtering steps were based on those used by de Brouwer and colleagues (2014), and the one used by McCarley and colleagues (McCarley, Kramer, & DiGirolamo, 2003). After the filtering procedure the first saccade recorded in each trial was obtained for each participant. Two participants (ID-8 and ID-12) were removed from the data set because less than 5% of the initial number of trials survived the filtering procedure (Figure 4.37). Pirate plots showing the effects of TMS on the mean, 95% CI and distribution of the saccade amplitudes in the 3 experimental conditions are presented in Figure 4.38.

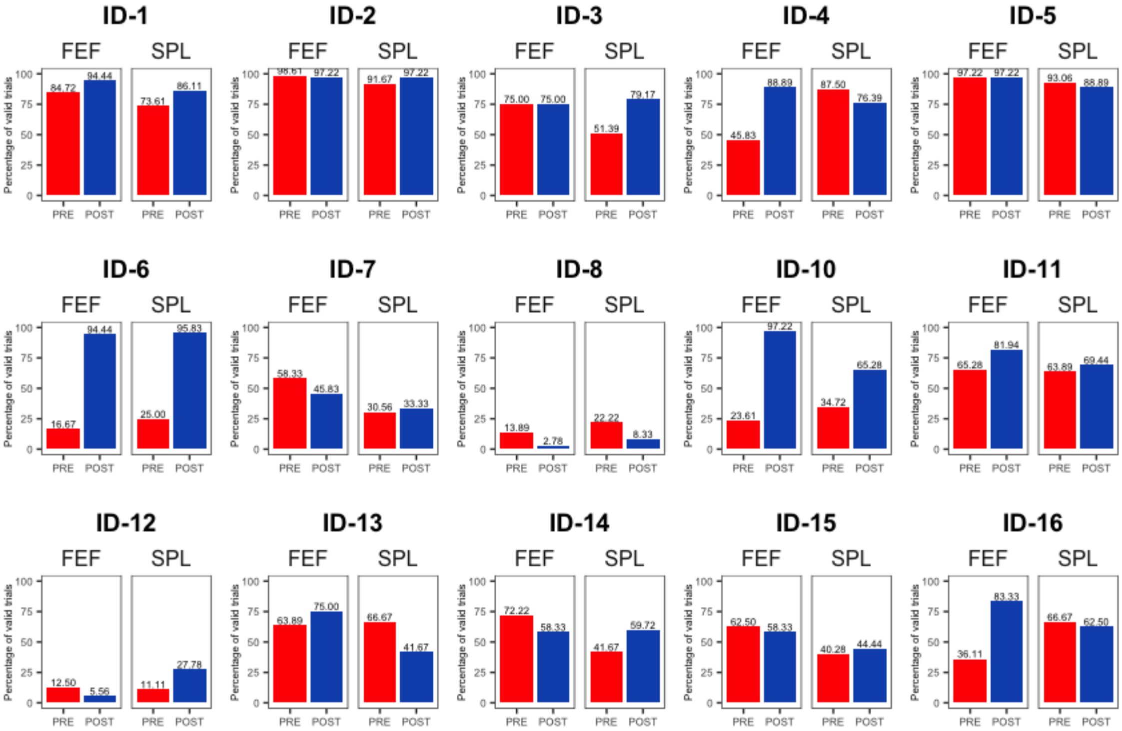

*Figure 4.37 - Number of valid trials for each participant in Experiment 5.*

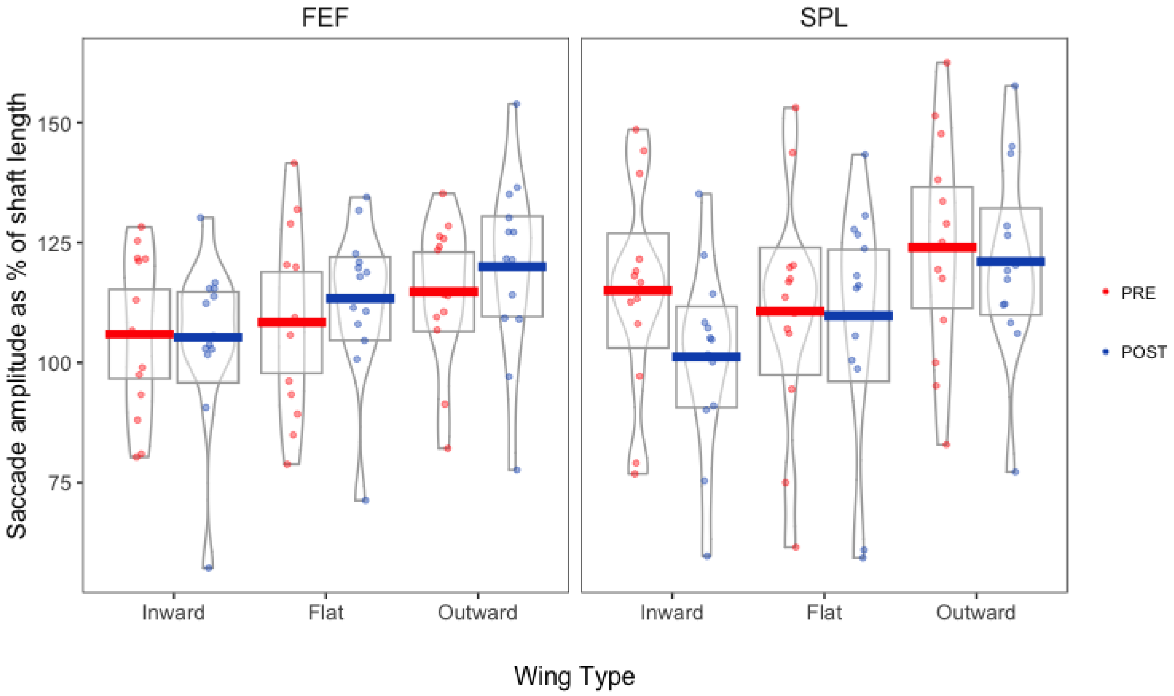

*Figure 4.38 - Pirateplots with means and 95% CIs for the line saccade amplitudes in Experiment 5.*

### *4.8.3.2 Statistical analysis*

We expected to find that cTBS would reduce the influence of the Müller-Lyer illusion on saccade amplitudes. Means and SE for the saccade amplitudes recorded in Experiment 5 are presented in Figure 4.39.

In order to test our prediction, a 2 (cTBS: FEF vs SPL) x 2 (Session: Pre vs Post) x 3 (Wing: Inward vs Flat vs Outward) repeated measure ANOVA was run.

The Mauchly's test of Sphericity showed that neither the factors nor the interaction violated the assumption of sphericity.

The simple main effect for Wing type was significant (F(2, 24)=21.088, p<.001, η2=.637), while the simple main effects of cTBS (F(1,12)=.828, p=.381, η2=.065), and of Session (F(1,12)=.287, p=.602, η2=.023) were not significant. The 2-way interaction between cTBS and Session (F(1,12)=4.751, p=.05, η2=.284) and the 2-way interaction between Session and Wing (F(2, 24)=5.292,p=.012, η2=.306) were significant, while the 2-way interaction between cTBS and Wing and the 3-way interaction were not significant. To further understand this pattern of results we looked at pairwise comparisons and found that in the SPL condition there was a significant difference for the Inward wing between the Pre and Post cTBS stimulation, with saccade amplitudes POST cTBS stimulation being smaller than the PRE stimulation (p=.007). However, inspection of Figure 4.39 suggests that this difference was driven mainly by an unusual result for the inward wing condition in the pre-test, rather than by an effect of TMS. The mean apparent shaft length for the inward wing condition is actually greater than the vertical wings control condition, which suggests a possible Type 1 error. Supporting this interpretation, the amplitudes registered for the Inward configuration of the stimulus before the cTBS stimulation of the SPL, were significantly bigger than the one recorded for the amplitude of the same configuration of the stimulus registered before the stimulation of the FEF (p=.027). Overall, this experiment partly replicated the previously found effects of the Müller-Lyer illusion on amplitude of voluntary saccades, and our interpretation is that cTBS failed to influence that.

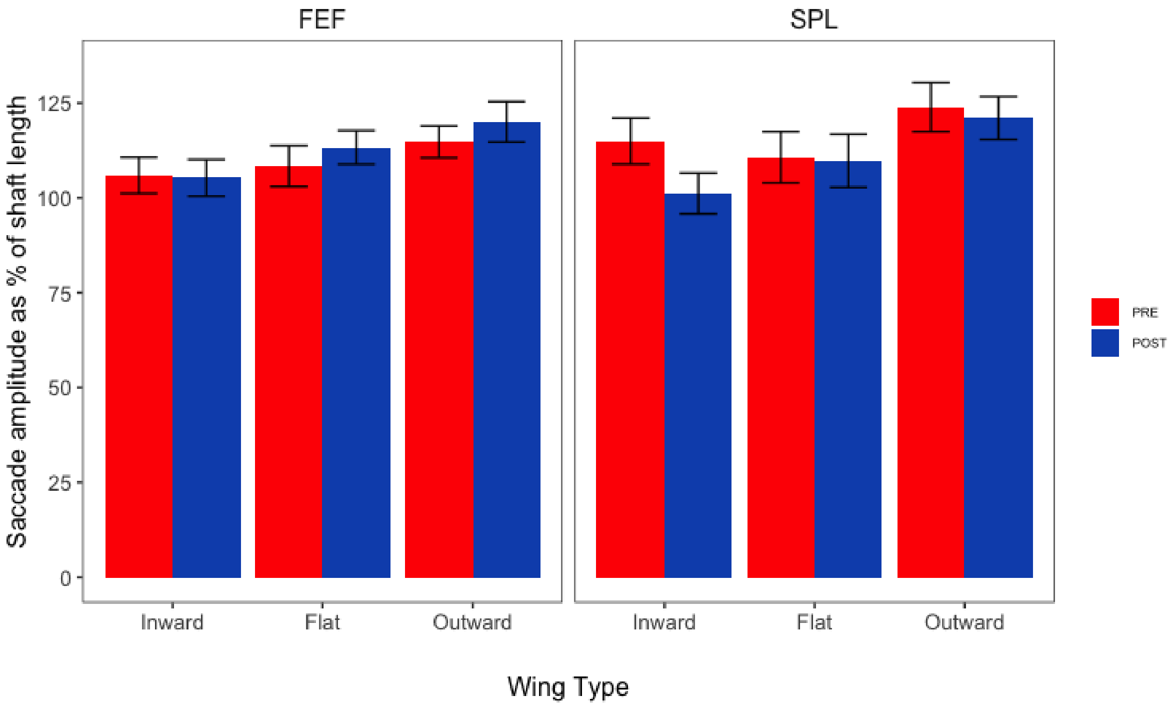

*Figure 4.39 - Bar plot with mean and SE for the stimuli used in Experiment 5.*

### 4.8.4 Discussion

In Experiment 5 we found a significant difference in the amplitude of voluntary saccades depending on the fin type, which meant that in the data the illusion of extent was present. This replicates the previous findings (Binsted et al, 1999; Delabarre et al., 1898; Festinger et at., 1968; Stratton 1906; Yarbus 1967). We also found that in the SPL condition there was a significant difference between the amplitudes recorded for the inward pointing wing when PRE and POST TMS of the SPL were compared. However, we believe that this result is due to an anomaly in the baseline. In the PRE SPLTMS the saccade amplitudes registered for the Inward configuration of the Müller-Lyer were significantly bigger than the amplitudes registered for the same configuration of the stimulus before the FEF TMS.

## 4.9 Experiment 6: Müller-Lyer memory guided saccades

### 4.9.1 Introduction

In the sixth experiment the effect of the cTBS on memeory-guided saccades made in response to Müller-Lyer stimuli was measured

### 4.9.2 Method

In each trial a central fixation cross was initially presented, then a Müller-Lyer stimulus was presented either to the left or to the right of the centre of the screen. The stimulus was presented for 100 ms and was then removed from the screen. During that time participants were asked to keep staring at the centre of the screen and use their peripheral vision to locate the end point of the horizontal shaft of the Müller-Lyer stimulus. After the Müller-Lyer stimulus was removed from the screen, the fixation cross was presented on the screen again, and after 1 second interval in which the target location for the upcoming saccade had to be remembered it was removed, leaving a blank screen. Its removal was interpreted by the participants as the go signal to move their eyes to the end point of the Müller-Lyer stimulus that was previously presented (Figure 4.40).

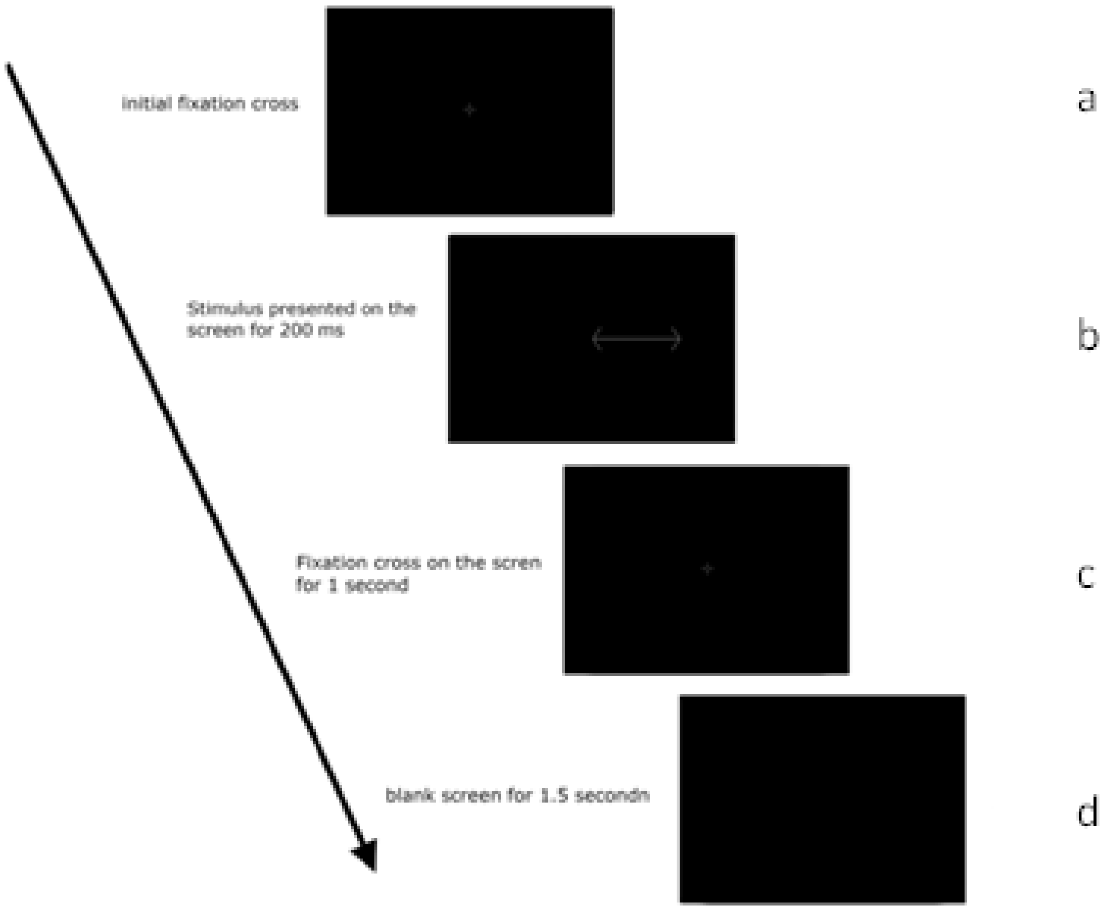

*Figure 4.40 - Procedure for Experiment 6.*

At the beginning of each trial a double fixation cross was presented in the centre of the screen against a black screen. After 1 second a configuration of the Müller-Lyer figure was presented in white for 100 ms. One end of the horizontal shaft was placed in the centre of the screen and the other end was placed either to the left or the right of the centre of the screen. The stimulus was presented on the screen for 100 ms and participants were asked to not move their eyes away from the centre of the screen, but to use their peripheral vision to detect the end of the stimulus. After it was removed, participants were left with just the double fixation cross against the black background. After 1 second a fixation cross was removed from the screen, which was considered as the ‘go-signal’ for the participant. When the fixation cross was removed, there were asked to move their eyes towards the end point of the stimulus further away from the centre of the stimulus previous presented. After 1 second the double fixation cross was presented again on the screen and a new trial started.

Just the outgoing fins and the ingoing fins configurations of the Müller-Lyer illusion (stimuli A and B in Figure 4.15) were presented in this experiment. These 2 configurations were presented in 2 sizes: either the length of the horizontal main shaft was set to 3º, or it was set to 6º. In both sizes each of the arms composing the outer wings of the stimulus was 1/3 of the length of the horizontal shaft. A grand total of 96 trials were presented for this task in a randomised order.

At the beginning of each trial a double fixation cross was presented in the centre of the screen against a black screen. After 1 second a configuration of the Müller-Lyer figure was presented in white for 100 ms. One end of the horizontal shaft was placed in the centre of the screen and the other end was placed either to the left or the right of the centre of the screen. The stimulus was presented on the screen for 100 ms and participants were asked to not move their eyes away from the centre of the screen, but to use their peripheral vision to detect the end of the stimulus. After it was removed, participants were left with just the double fixation cross against the black background. After 1 second a fixation cross was removed from the screen, which was considered as the ‘go-signal’ for the participant. When the fixation cross was removed, there were asked to move their eyes towards the end point of the stimulus further away from the centre of the stimulus previous presented. After 1 second the double fixation cross was presented again on the screen and a new trial started.

Just the outgoing fins and the ingoing fins configurations of the Müller-Lyer illusion (stimuli A and B in Figure 4.15) were presented in this experiment. These 2 configurations were presented in 2 sizes: either the length of the horizontal main shaft was set to 3º, or it was set to 6º. In both sizes each of the arms composing the outer wings of the stimulus was 1/3 of the length of the horizontal shaft. A grand total of 96 trials were presented for this task in a randomised order.

### 4.9.3 Results

#### *4.9.3.1 Pre-processing and descriptive statistics*

The eyetracker data for all the participants acquired during Experiment 6, in which participants saccaded towards the end point of the horizontal shaft of the Müller-Lyer figure, was loaded into RStudio and out of all the saccades recorded during this task, just the saccades made when the stimuli were on the screen were selected, for a total of 29890 saccades across all participants and all four sessions. There were a total of 5760 memory guided saccades, and the aim of pre-processing was to identify one saccade for each of these trials.  As an initial step, for each trial just the saccades made in the correct direction (i.e., towards the end point of the horizontal shaft of the Müller-Lyer figure and not the returning saccades) were filtered, reducing the total number of saccades to 14287. We then looked at the histogram of the saccade latency (Figure 34). On the basis of Figure 4.34, we decided to remove all the saccade initiated either before 100 ms or after 750 ms from the cue onset, many of which may have been secondary saccades made after the initial saccade along the shaft of the Müller-Lyer stimulus. This step reduced the number if saccades to 6735. The latency filter used the 750 msec value rather than 500 msec because latencies are expected to be longer in voluntary saccades than reflexive ones.

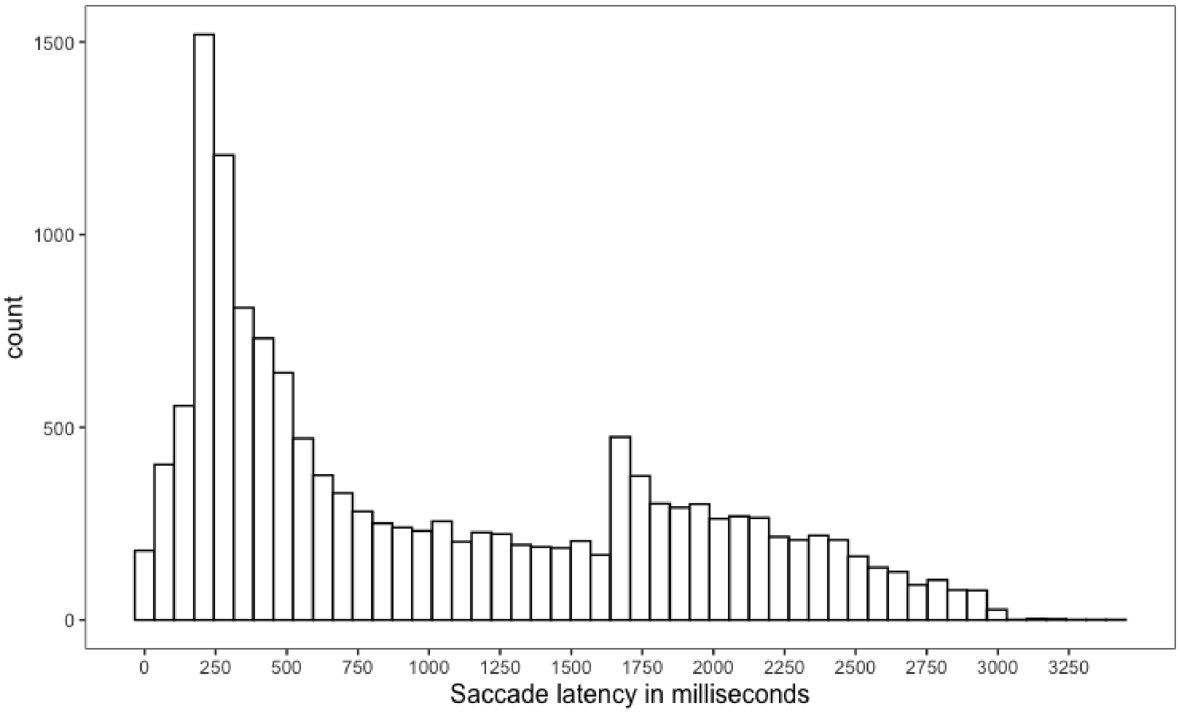

*Figure 4.41 - Histogram for the saccade latency in Experiment 6.*

Then we converted the saccade amplitude into percentage of shaft length, and we produced a histogram (Figure 35). On the basis of Figure 4.35, we removed the saccades either smaller than 35% or bigger than 150% of the shaft length, and this reduced the number of saccades to 4920.

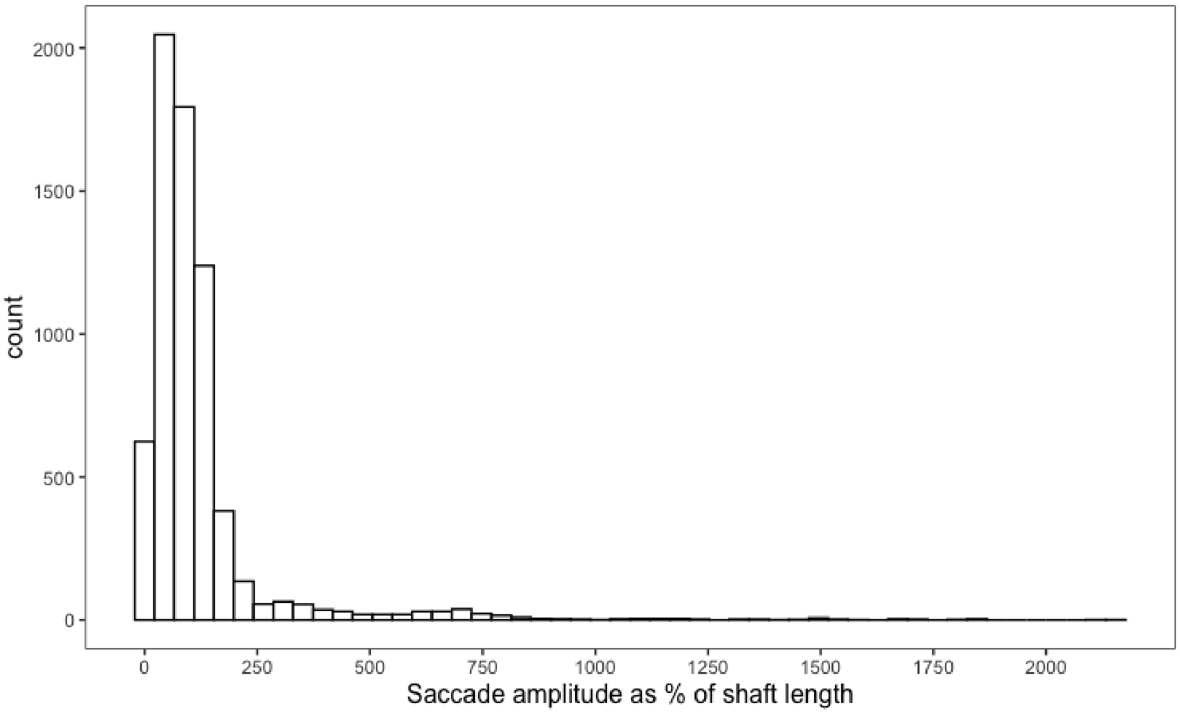

*Figure 4.42 - Histogram for the saccade amplitude in Experiment 6.*

We then calculated for each saccade the angle at which it was produced relative to horizontal (we calculated it by using the arctangent function of the ratio between the horizontal component and the vertical component of the saccade). Figure 4.36 shows the distribution of the saccade angle. On the basis of Figure 4.36, we removed all the saccades with and angle bigger than 15º, and this reduced the number of saccades to 4511.

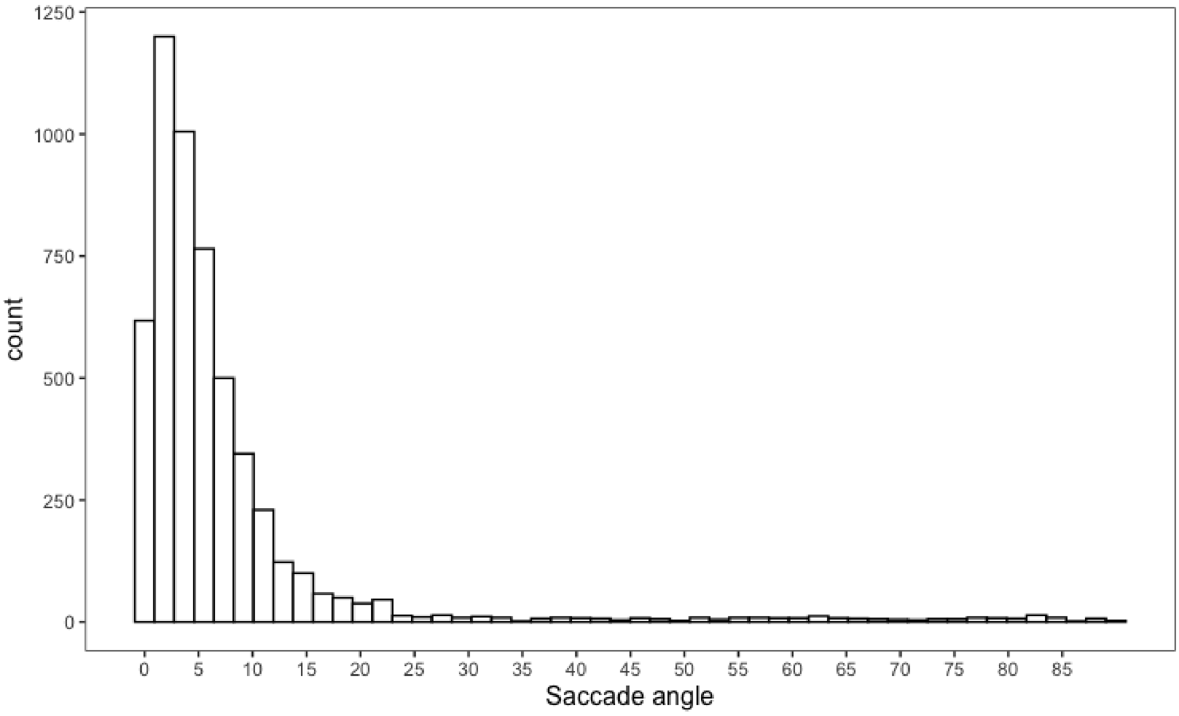

*Figure 4.43 - Histogram for the saccade angle in Experiment 6.*

Inspection of the remaining raw data revealed that some saccades remained that had starting points distant from the fixation point. For this reason, all the saccades that were initiated more than 100 pixels away from the centre of the screen in any direction were removed. The exception to this was when inspection of plots of saccades for some individual participants in some sessions strongly suggested that the eye tracker calibration had drifted in either the X or Y dimension. Where this happened, we adjusted the 100 pixel window. This reduced the sample to 2814 saccades. We also checked that the end point of all the saccades was within 200 pixels vertically from the centre of the screen, and all the saccades satisfied this criterion. These filtering steps were based on those used by de Brouwer and colleagues (2014), and the one used by McCarley and colleagues (2003). After the filtering procedure the biggest saccade recorded in each trial was obtained for each participant. Three participants (ID-3, ID-11, ID-12) were removed from the data set because less than 5% of the initial number of trials survived the filtering procedure (Figure 4.37). Pirate plots showing the effects of

TMS on the mean, 95% CI and distribution of the saccade amplitudes in the 3 experimental conditions are presented in Figure 4.38.

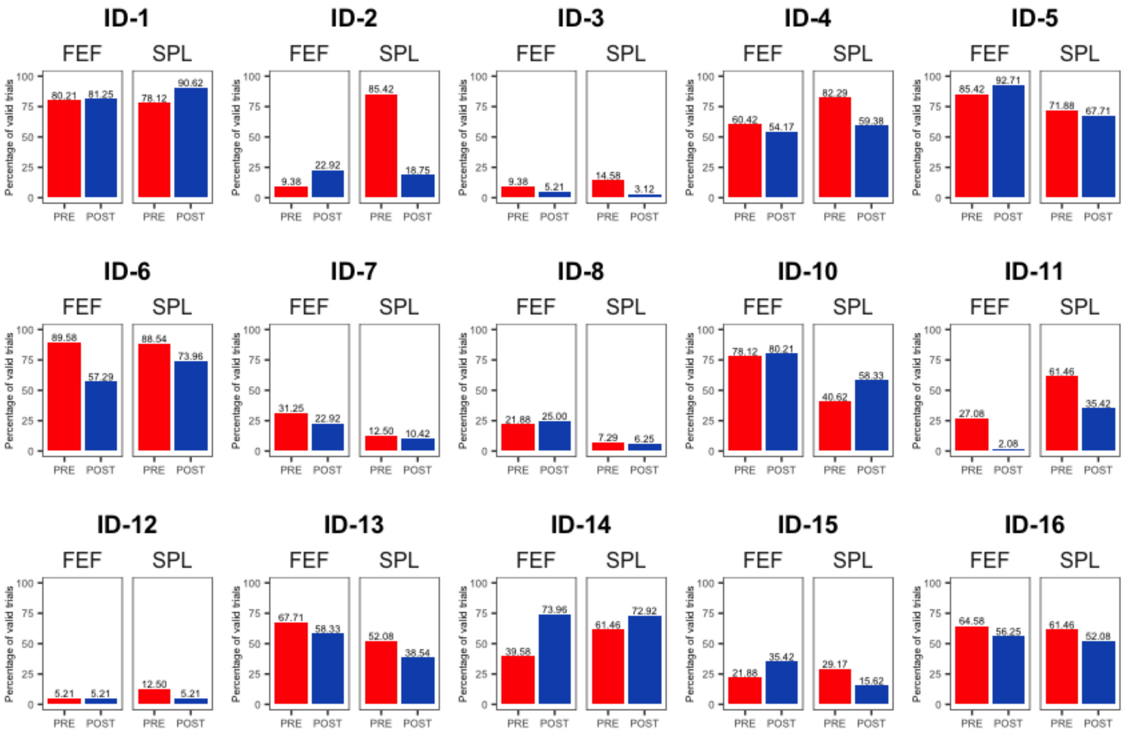

*Figure 4.44 - Number of valid trials for each participant in Experiment 6.*

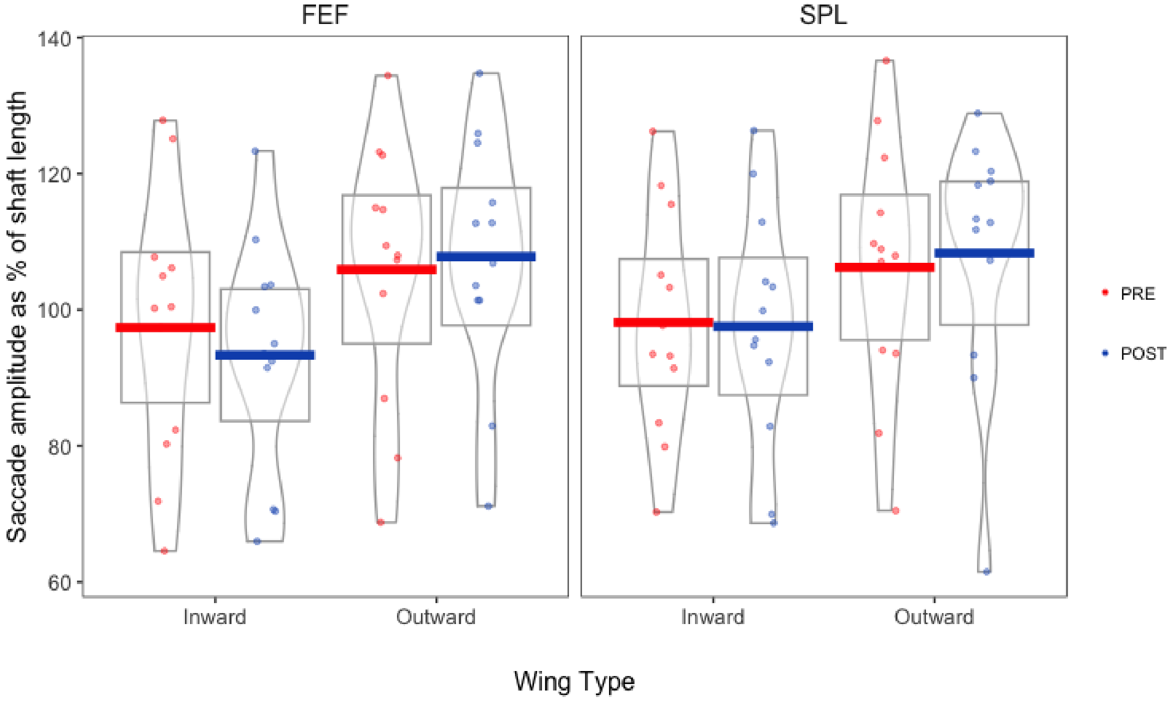

*Figure 4.45 - Pirateplots with means and 95% CIs for the line saccade amplitudes in Experiment 6.*

#### *4.9.3.2 Statistical analysis*

We expected to find that cTBS would reduce the influence of the Müller-Lyer illusion on saccade amplitudes.  Means and SE for the saccade amplitudes recorded in Experiment 6 are presented in Figure 4.46.

In order to test our prediction, a 2 (cTBS: FEF vs SPL) x 2 (Session: Pre vs Post) x 2 (Wing: Inward vs Outward) repeated measure ANOVA was run.

The main effect for Wing type was significant (F(1, 11)=32.691, p< .001, η2=.748), while the simple main effect of cTBS (F(1,11)=.317, p=.585, η2=.028) and the simple main effect of Session (F(1,11)=.008, p=.93, η2=.008) were not significant. Also, none of the 2-way interactions, nor the 3-way interaction were significant. This indicates that we found an effects of the Müller-Lyer illusion on the amplitude of memory guided saccades, but cTBS failed to influence that.

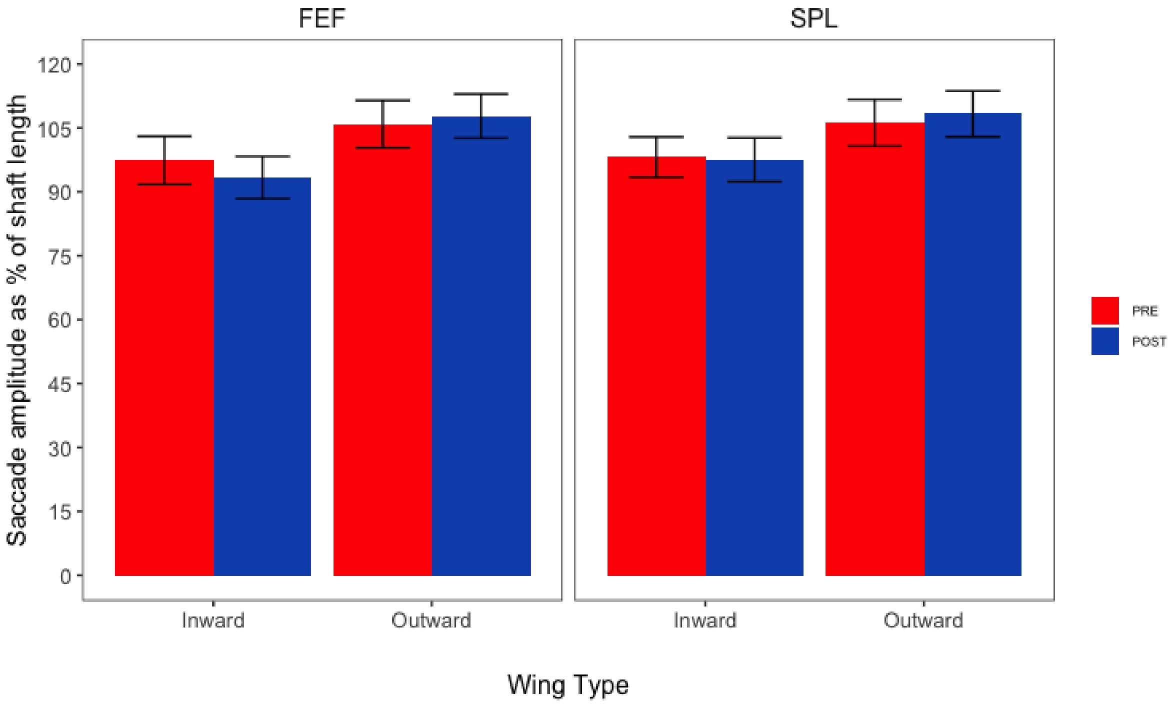

*Figure 4.46 - Bar plot with mean and SE for the stimuli used in Experiment 6.*

### 4.9.4 Discussion

In Experiment 6 we found a significant difference in the amplitude of the voluntary saccades depending on the fin type, which meant that in the data the illusion of extent was present. This replicates previous findings (Binsted et al, 1999; Delabarre et al., 1898; Festinger et at., 1968; Stratton 1906; Yarbus 1967) However, we found that the cTBS stimulation did not significantly affect the amplitude of memory-guided saccades.

## 4.10 Analysis of saccade latencies in Experiments 4,5, and 6

Because some previous studies have found that TMS to the FEF increases saccade latency, especially of voluntary saccades, in Experiment 4, Experiment 5, and Experiment 6 we analysed the saccade latency. For each experiment we used the same filtering criteria we used for obtaining the amplitude of the first saccade, but this time we focused on the latency of the first valid saccade produced in each trial. Pirate plots showing the effects of TMS on the mean, 95% CI and between participant distribution of the saccade latency in the 3 different experiments are presented in panel A in Figure 47, while means and SE for the saccade latencies recorded in the 3 different experiments are presented in panel B in Figure 47.

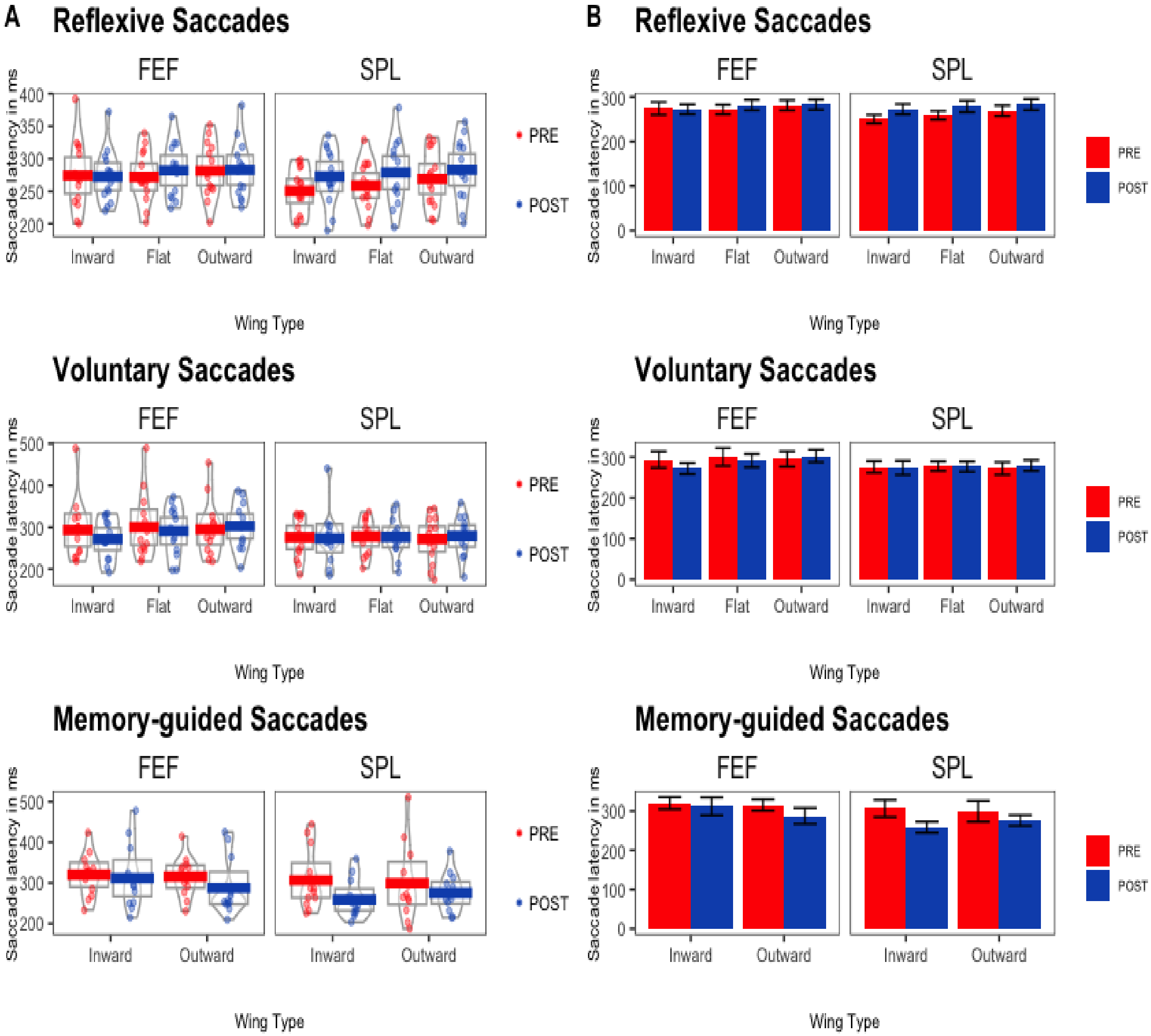

*Figure 4.47 - Plots for saccade latencies recorded for Experiment 4, Experiment 5, and Experiment 6. Panel A shows pirateplots with means and 95% CIs for the saccade latencies recorded for the 3 experiments. Panel B shows bar plots with mean and SE for the saccade*

For Experiment 4 (reflexive saccades) a 2 (cTBS: FEF vs SPL) x 2 (Session: Pre vs Post) x 3 (Wing: Inward vs Flat vs Outward) repeated measure ANOVA was run. The main effect of cTBS was not significant (F(1,12)=1.289, p=.278, η2=.097), while both the main effect of session (F(1,12)=8.034, p=.015, η2=.401), and the simple main effect of Wing type (F(1.383,16.59)=4.08, p=.049, η2=.254) were significant. None of the 2-way interactions, nor the 3-way interaction were significant. This indicates that the cTBS affected the latency of reflexive saccades, moreover it was found that after the cTBS the saccade latencies were significantly higher. In addition to that, it was also found that configuration of the Müller-Lyer stimulus that produced saccades with bigger amplitudes, also had relatively delayed latency.

For Experiment 5 (voluntary saccades) a 2 (cTBS: FEF vs SPL) x 2 (Session: Pre vs Post) x 3 (Wing: Inward vs Flat vs Outward) repeated measure ANOVA was run. The main effect of cTBS showed a trend towards significance (F(1,12)=3.702, p=.078, η2=.236), while neither the main effect of Session (F(1,12)=.124, p=.731, η2=.01), nor the main effect of Wing (F(2,24)=2.06, p=.149, η2=.146) were significant. Just the 2-way interaction between Session and Wing type showed a trend toward significance (F(2,24)=2.804,p=.08, η2=.189), while the other 2-way interaction and the 3-way interaction were not significant. This means that cTBS did not reliably affect the latency of voluntary saccades.

For Experiment 6 (memory guided saccades) a 2 (cTBS: FEF vs SPL) x 2 (Session: Pre vs Post) x 3 (Wing: Inward vs Outward) repeated measure ANOVA was run. The simple main effect of cTBS was significant (F(1,11)=7.402, p=.02, η2=.402), while the simple main effect of Session showed a trend towards significance (F(1,11)=4.459, p=.058, η2=.288), and the simple main effect of Wing (F(1,11)=2.116, p=.174, η2=.161) was not significant. None of the 2-way interaction was significant, while the 3 way interaction was significant (F(1,11)=7.109, p=.022, η2=.393).This indicates that the participants overall made quicker saccades on the days where the target of the cTBS was the SPL compared to the one recorded on the FEF days. Although not quite significant, we also found that cTBS had an effect on saccade latency for both SPL and FEF, in which after the cTBS stimulation the saccade latency was reduced. Regarding the significant 3-way interaction, this occurred because the effect of TMS for the inward facing stimulus was stronger for SPL than FEF.

## 4.11 General Discussion

The main purpose of this study was to investigate whether SPL and FEF might be part of a network supporting a common metric for spatial perception and saccade planning. In order to do so, a 2-day cTBS experiment was carried out. On one day of the study the cTBS stimulation was delivered over the right SPL before and after stimulation several experiments were presented: a reaction time task, where participants had to press the spacebar as soon as they noticed a white square presented on the screen; an interception task, where participants had to press a spacebar when they thought that a moving square was exactly on top of a white dot; 2 tasks where participants had to adjust the length of a straight line to match the length of the horizontal shaft of a Müller-Lyer figure, a reflexive saccade task, where participants were asked to move their eyes from one and to the other of the horizontal shaft of the Müller-Lyer figure; a voluntary saccade task, where participants were asked to look at a cue and then decide whether to move their eyes from one end to the other of the horizontal shaft of the Müller-Lyer illusion, or to move their eyes in the hemifield where the stimulus was not presented; and finally a memory-guided saccade task, where participants were asked to move their eyes to the end point of the horizontal shaft of a Müller-Lyer figure that was previously presented.

On the other day of the experiment cTBS was delivered over the right FEF and the same tasks were presented before and after stimulation. We predicted that if the TMS to either SPL or FEF was found to reduce the effects of the Müller-Lyer illusion on perceived extent or saccade landing position compared to the performances recorded before the TMS, or to disrupt or enhance performance in the interception task then this would implicate the region in neural processing related to 2D visual separation. The data failed to support our prediction and do not implicate SPL or TMS in processes producing spatial perception.

Although it was not related to our main hypothesis, we also looked at the saccade latency for Experiments 4, 5, and 6 because previous literature has shown effects of TMS to FEF on voluntary and memory-guided saccades in particular and effects of SPL TMS on reflexive saccades in SPL (Müri, & Nyffeler, 2008; Pierrot-Deseilligny, Milea, & Müri, 2004). We found that cTBS stimulation of either the SPL or the FEF increased the latency of reflexive saccades, and also that Müller-Lyer stimuli that produced saccades with bigger amplitudes also produced saccades with longer latencies. This finding goes against previous studies where the TMS stimulation of the FEF did not affect the latency of reflexive saccades (Müri et al., 1991; van Donkelaar et al., 2009, Gurel, Castelo-Branco, Sack, & Duecker, 2018). However, it is consistent with other papers such as Nagel, Sprenger, Lencer, Kömpf, Siebner, & Heide (2008) and Priori, Bertolasi, Rothwell, Day, & Marsden (1993), where TMS to the FEF resulted in longer latencies for reflexive saccades.

We found that cTBS of either the SPL or the FEF did not have an effect on the latency of voluntary saccades in Experiment 5. This goes against a previous finding by Thickbroom and colleagues (1996), but it seems to be consistent with a more recent finding by Gurel and colleagues (2018), where they delivered cTBS over the FEF and measured the latency of voluntary saccades. They found that the cTBS over the FEF did not reduce the latency.

For memory-guided saccade we found a reduction of latency after TMS to either SPL or FEF. This is in line with previous finding of Wipfti and colleagues (2001), where TMS stimulation of the FEF resulted in shorter saccade latency. However, our finding that this also occurs for SPL TMS appears to be the first report of this happening. We also found that overall latencies of memory guided saccades were significantly lower for the SPL day compared to the FEF day. However, this effect was not true only for the session after the stimulation, but also for the baseline. Overall, using an offline TMS paradigm for studying the effect of stimulation on saccade latency is probably not the most desirable solution, as a matter of fact the majority of TMS study that investigate the saccade generation use online TMS, which can be delivered at specific time points in the saccade planning process, instead (Gurel et al., 2018). Overall, the stimulation of either SPL or FEF did not have an effect on the latencies of the voluntary saccade but had an opposite effect between reflexive and memory-guided saccades. Reflexive saccades were delayed after the TMS stimulation, and the memory guided were facilitated by it. We do not have a hypothesis that can explain this finding.

An improved design would have incorporated an additional no-TMS or sham control condition, which would have allowed us to establish whether FEF or SPL cTBS had any effect on our behavioural tasks. Without a no/sham-cTBS condition, the only patterns of results that can be confidently attributed to TMS are ones where SPL TMS and FEF TMS produce different patterns of results. When they produce similar patterns of results order of testing effects cannot be ruled out as alternative explanation. With the addition of a no/sham TMS condition then it would also be possible to confidently determine when FEF and SPL cTBS both have similar effects.

Another methodological limitation is that in this study we defined the regions of interest using structural MR image from the Brainsight software. According to a previous study this a legitimate method of localisation of cortical areas (Boroojerdi, Foltys, Krings, Spetzger, Thron, & Töpper, 1999; Neggers, Langerak, Schutter, Mandl, Ramsey, Lemmens, & Postma, 2004). However, a study conducted by Sparing, Buelte, Meister, Paus, & Fink (2008) has showed that the structural MR image is not very reliable. In their study Sparing and colleagues compared 5 different modalities of localisation of the left motor cortex: the 10-20 EEG system, the standardized function-guided procedure, the structural MR image, the individual functional MRI data and the group functional MRI data and they measured both MEP amplitudes and spatial accuracy of cortical regions. They discovered that out of the 5 modalities, the structural MR image gave one of the lowest MEP amplitudes and spatial accuracy of cortical regions, while the best results were found after the localisation guided by individual functional MRI data (Sparing et al., 2008). Therefore, the results we obtained need to be considered with caution, because we cannot be totally convinced that the cTBS stimulation was exactly delivered over the Superior Parietal Lobule and the Frontal Eye Field. However, the significant results we obtained for saccade latencies do provide a degree of confidence that TMS was targeted sufficiently well to test our main hypothesis.

Another consideration is the fact that the cTBS stimulation was delivered only over the right Superior Parietal Lobule. Corbetta, Shulman, Miezin, & Petersen (1995) found that a bilateral activation of the Superior Parietal Lobule occurs during the early spatial shift of attention, which is a covert form of eye movement “readiness”. So, a possible explanation for the lack of significant results is that targeting just the right Superior Parietal Lobule is not enough to reduce the centre of gravity effect that may underly the ML illusion. A possible solution for this problem would be using cTBS bilaterally on the Superior Parietal Lobule. Such bilateral cTBS studies are technically feasible, having been done in the past, for example, for treating tinnitus and auditory hallucinations (Schraven, Plontke, Rahne, Wasserka, & Plewnia, 2013), to study how learning new vocabulary happens (Sliwinska, Elson, & Pitcher, 2021), or to study the attentional network (Vesia, Niemeier, Black & Staines, 2015).

In this study we opted for an offline TMS paradigm so that we did not have to worry about the difficulties of TMS online paradigms (such as inter-pulse interval and participant's head movement). However, this might have been the reason why we did not find behavioural effects. The effect of offline TMS is weaker compared to the effect that a single pulse/a train of pulses delivered at the optimal period of relevant processing is (Gurel et al., 2018), it might be that our cTBS paradigm had an effect on the neuropsychological level that was too weak to be seen at the behavioural level. In addition to that, Sack and colleagues (Sack, Camprodon, Pascual-Leone, & Goebel, 2005) showed that offline TMS has a higher probability of allowing compensatory brain mechanisms to occur. It might be that the brain "adjusted" after the cTBS stimulation and therefore no change in behaviour was shown in the experiments we presented. Also, studies in the human motor cortex have shown that the effects of offline TMS can depend on the current brain state, a process known as metaplasticity (Gentner, Wankerl, Reinsberger, Zeller, & Classen, 2008; Iezzi, Conte, Suppa, Agostino, Dinapoli, Scontrini, & Berardelli, 2008; Goldsworthy, Müller-Dahlhaus, Ridding, & Ziemann, 2014). This means that asking participants to perform the experiments before the delivery of TMS in the way that we did might have affected the direction and/or magnitude of the stimulation effect. Possible future studies should look into presenting experiments were the effects of 2D visual extent illusions are measured while participants receive online TMS stimulation.

Finally, the statistical power of the study for detecting cTBS effects was relatively low (power = 0.8 to detect an effect size of d = 0.75 for a two tailed prediction). In conclusion, further studies with greater statistical power and methodological improvements discussed above should be conducted to test the hypothesis that SPL and/or FEF are brain regions that support the common metric for saccades and spatial perception.

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# Chapter 5. General Discussion

## 5.1 Overview of Results

The overall aim of this thesis was to investigate how perception of visual extent is supported in the brain. Specifically, the three core aims were: use TMS to investigate the role played by the Superior parietal Lobule in the processing and perception of visual separation; use TMS to investigate the role played by the Superior Parietal Lobule in the processing and perception of eye movement and visual extent in the Müller-Lyer illusion; and use TMS to investigate the role played by the Superior Parietal Lobule and the Frontal Eye Field in the processing and perception of eye movements and perception of extent and visual separation.

We used Transcranial Magnetic Stimulation (TMS) to induce virtual lesions in healthy subjects and then presented tasks that were designed to measure the perception of visual extent. The TMS was delivered over the Superior Parietal Lobule (SPL) in all three experiments because previous evidence suggested that this region of the brain plays a significant role in the perception of 2D visual separation. In the final experiment we also delivered TMS to the FEF, which is heavily connected to the SPL.

### 5.1.1 Chapter 2: The role of the Superior Parietal Lobule in the perception of the visual separation between stimuli: an rTMS study

In chapter 2 we wanted to test the hypothesis that the Superior Parietal Lobule (SPL) was involved in supporting the perception of the 2D visual separation between two points. In order to test this hypothesis, we presented a psychophysical visual separation judgment task while we delivered high frequency rTMS stimulation over the left SPL. We also presented a control task, which had cognitive and motor aspects identical to those in the visual separation judgment task, but relative contrast of two Gabor patches was judged. This was an online TMS experiment, in which TMS was delivered on each trial during the stimulus presentation. In the experimental task two pairs of dots were presented and participants had to indicate in which pair the distance between the dots was larger. We also presented a control experiment which shared many of the generic features of the experimental task but did not require judgment of visual spatial separation. To increase methodological rigor, we also delivered the same pattern of TMS to a control region (the vertex) while both tasks were presented.

Our first prediction was that the TMS over the left SPL should reduce the precision of judgment in the visual separation judgment task compared to TMS over the vertex. However, when we looked at the slopes obtained by fitting psychometric functions to the data for the visual separation task, we found no significant differences between the slopes obtained during the TMS over the SPL and those obtained during the TMS over the vertex. Therefore, we failed to support/find evidence for the hypothesis that SPL supports the perception of visual extent.

We also predicted that TMS over the SPL would have not reduce the precision of judgment in the control experiment compared to TMS over the vertex. However, when we looked at the slopes obtained for the control task, we noticed a significant increase in accuracy (i.e., steeper slope) when the TMS was delivered over the SPL compared to the vertex.  We did not predict this and had assumed that only TMS of earlier visual areas such as V1 would influence processing of low-level visual properties such as contrast. However, we subsequently found two studies in which TMS to the right FEF was found to influence contrast sensitivity, and in this context our result appears less surprising because of the strong connections between SPL and FEF. Specifically, Ruff and colleagues (Ruff, Blankenburg, Bjoertomt, Bestmann, Freeman, Haynes, Rees, Josephs, Deichmann, & Driver, 2006) delivered TMS stimulation over the right FEF and simultaneously presented a psychophysical task in which participants had to judge the perceived contrast of two concurrent Gabor patches. One stimulus was presented in the centre of the screen and the other was peripheral (either to the left or right of the screen). It was found that peripheral Gabor patches had stronger perceived contrast relative to central Gabor patches when stimulation of the FEF was compared to stimulation of the Vertex. This implies that the FEF is involved in the perception of low-level visual properties.  Lensing further support to this idea, Chanes, Chica, Quentin, & Velero-Cabre (2012) reported a similar result.

### 5.1.2 Chapter 3: The role of the Superior Parietal Lobule in the Muller Lyer illusion: a TMS study

In chapter 3 we tested the proposal that the Superior Parietal Lobule (SPL) was critical for the processing of eye movements and the perception of visual extent in the Muller-Lyer illusion. In order to do so, we used an offline TMS paradigm in which we delivered continuous theta burst (cTBS) stimulation over the electrode CP1 (used as a proxy for the left SPL) for 40 seconds and after that we presented three different behavioural experiments. In the control condition, cTBS was instead delivered over the vertex. In the first experiment, an eye movement task, we presented participants a configuration of the Muller-Lyer stimulus, and we asked them to move their eyes back and forth from one end to the other of the horizontal shaft while an eye tracker was recording their eyes movement. In the second experiment, a perceptual bisection task, participants were asked to bisect (divide in half) a Judd variant of the Muller-Lyer, and in the third experiment, another perceptual bisection task, participants were asked to bisect a Brentano version of the Muller-Lyer.

Our first prediction was that the cTBS over the SPL should have affected the amplitudes of the eye movements elicited by the different configurations of the Muller-Lyer stimuli. In particular we predicted that cTBS over the SPL should have affected the effect of the illusion on eye movements by reducing the amplitude of the eye movements recorded during the presentation of the Muller-Lyer with the wings pointing inwards and should have increased the eye movements for the version of the stimulus with the wings pointing outwards. The data showed that there was a significant difference between the amplitude of the eye movements recorded for the different type of stimuli, meaning that the illusion of visual extent that is normally associated with the Muller Lyer figure was obtained with this task. However, when we compared the performance obtained after the stimulation over the left SPL to that obtained after vertex stimulation, we found no difference in saccade amplitude for SPL compared to Vertex. This failed to support our hypothesis.

Our second prediction was that cTBS over the SPL should have affected the bisection bias that is normally induced by the Judd variant of the Muller-Lyer stimulus. The data showed that, for all 4 configurations of the Judd variant where the middle fin was not flat, a bisection bias was obtained after cTBS stimulations, meaning that the stimuli used successfully induced a bisection bias. However, none of the 6 configurations of the Judd variant showed a reduction in the bisection bias when the data recorded after the cTBS stimulation of the SPL was compared to the data recorded after the cTBS stimulation of the vertex. Only stimulus E (presented in Figure 3.5) showed a trend towards significance.

Our third prediction was that the cTBS over the SPL should have affected the bisection bias that is normally induced by the Brentano version of the Muller-Lyer stimuli. The data showed that for all the configurations a bisection bias was induced.

However, when the data obtained after the cTBS of the SPL was compared with the data obtained after the cTBS of the vertex there was not a significant difference.

### 5.1.3 Chapter 4: Using TMS to investigate the role of the Superior Parietal Lobule and the Frontal Eye Field in the perception of spatial separation

In chapter 4 we investigated the role played by the Superior parietal Lobule (SPL) and the Frontal Eye Field (FEF) in the perception of spatial separation. In order to do so, we delivered continuous theta burst (cTBS) stimulation over the SPL or FEF for 40 seconds and we presented several experiments before and after said stimulation: a reaction time task, where participants had to press the spacebar as soon as they noticed a white square presented on the screen, an interception task where participants had to press a spacebar when they thought that a moving square was exactly on top of a white dot, two tasks where participants had to adjust the length of a straight line to match the length of the horizontal shaft of the Muller Lyer illusion, a reflexive saccade task where participants moved their eyes to the end of the horizontal shaft of the Muller Lyer illusion, a voluntary saccade task where participants had first to look at a cue and then decide whether to move their eyes to the end point of the horizontal shaft of the Muller Lyer illusion, or to move their eyes in the hemifield where the stimulus was not presented, and finally a memory-guided saccade task, where participants had to move their eyes to the end point of the horizontal shaft of the Muller Lyer illusion that we previously presented. It was hoped that Muller-Lyer tasks used in this Experiment would be more sensitive to TMS effects than those used in Chapter 2. The perceptual tasks were improved by isolating the Standard and Comparison stimuli into separate visual hemifields; if the TMS effect was selective to one visual field this would help reveal it compared to the task used in Chapter 2 where the Muller-Lyer stimulus was presented in central vision. The eye movement tasks in Chapter 3 were designed to isolate a single saccade, and to separately measure reflexive, voluntary, and memory guided saccades; the eye movement task used in Chapter 2 was not targeted in any of these ways.

If the TMS to either FEF or SPL was to disrupt or enhance the performance in the interception task, this would then implicate that the region was involved in the neural processing related to 2D separation because performance on the task relied on visually picking up how a visual angle was changing. The data showed that after TMS stimulation to either SPL or FEF participants responded less accurately (i.e., they produced later interception responses) for the faster velocities in the stimulus set. This pattern of result could be explained by the fact that the task relied on attending the 2D visual separation, and because FEF and SPL are heavily connected, TMS to either of these regions might be expected to produce a similar effect. However, the design of this study does not allow us to rule out the possibility that this pattern of results might also be observed in the absence of TMS due to order of testing effects.

In the reaction time task (i.e., the control task for Experiment 1), we found that TMS to either FEF or SPL increased the reaction times. However, due to the design of this study we cannot rule out the possibility that this just an order of testing effect. Only by adding a control condition (i.e., sham TMS) on a third day can the alternative explanations of the interception task and reaction time task results can be tested and potentially ruled out.

Our prediction for Experiment 2 was that TMS over the SPL should affect the illusion of extent on perceptual judgment that is normally induced by the Muller Lyer figures. The data showed that there was a significant difference in apparent length of horizontal shaft of the Muller Lyer figure depending on the wing type, meaning that the stimuli used successfully induced a perceptual judgment illusion. We also found that the

TMS to either the SPL or the FEF reduced the length setting of the comparison line for all stimuli. However, because this result is not specific to the stimulation of the SPL or FEF, and because it also occurred for the stimulus with flat fin (i.e., the control configuration of the Muller Lyer stimulus), once again we cannot rule out the possibility that the pattern of result, we found is an order of testing effect.

Our prediction in Experiment 3 was that the TMS over the SPL should affect the illusion of extent on perceptual judgment that is normally induced by the Muller Lyer figures. The data showed that the final length of the comparison line was significantly different depending on the configuration of the Muller Lyer figure that was presented. This meant that the stimuli used in this experiment successfully induced an illusion of extent on perceptual judgment. However, the TMS stimulation failed to affect the illusion.

Our prediction for Experiment 4 was the TMS over the SPL should have affected the illusion of extent on the amplitude of reflexive saccades, which is normally induced by the Muller Lyer figures. The data showed that there was a significant difference on the amplitudes of reflexive saccades depending on the configuration of the Muller Lyer presented, which meant that the stimuli used in this experiment successfully induced the illusion of extent. However, the stimulation failed to affect the illusion on amplitude of reflexive saccades.

Our prediction for Experiment 5 was that the TMS over the SPL should have affected the illusion of extent on the amplitude of voluntary saccades, which is normally induced by the Muller Lyer figures. The data showed that there was a significant difference in the amplitudes of voluntary saccades depending on the configuration of the Muller Lyer presented, which meant that the stimuli used in this experiment successfully induced the illusion of extent. We also found a significant reduction in amplitudes for the voluntary saccades elicited by the inward configuration of the stimulus (Figure 4.8, Stimulus B) after the TMS of the right SPL. However, this result is most likely due to an anomaly in the baseline before the stimulation of the SPL,

Our prediction for Experiment 6 was that TMS over the SPL should have affected the effect of the illusion of extent on the amplitude of memory-guided saccades, which is normally induced by the Muller Lyer figures. The data showed that there was a significant difference in the amplitudes of memory-guided saccades depending on the configuration of the Muller Lyer presented, which meant that the stimuli used in this experiment successfully induced the illusion of extent. The effect of the Muller-Lyer on memory guided saccades replicated the findings of de Brouwer and colleagues (de Brouwer, Brenner, Medendorp, & Smeets 2014). However, the stimulation of the SPL did not affect the illusion.

We also looked at the latency of saccades generated in Experiments 4, 5, and 6, in order to see if TMS over either the SPL or FEF had an effect on the saccade latency for reflexive, voluntary or memory-guided saccades. The data showed that, after TMS over both FEF and SPL, the latency of reflexive saccades increased, and saccades with bigger amplitudes, induced by the Muller-Lyer illusion, also had longer latencies. It was found that the latencies of voluntary saccades were not affected by TMS over either the FEF or SPL. Finally, it was found that TMS over either the FEF or SPL reduced the saccade latencies for memory-guided saccades. Moreover, it was found that the effect of SPL TMS on memory guided saccades was greater than that of FEF TMS. It is noteworthy that an opposite effect was found for the latencies of reflexive saccades and memory guided saccades, with the former being delayed by the cTBS over either SPL or FEF, and the latter being facilitated by the stimulation. We do not have a hypothesis that can explain this finding.

## 5.2 Strengths and Limitations

In the three studies included in this PhD thesis, we investigated the role played by the Superior Parietal Lobule (SPL) in the perception of 2D visual extent. We have done so by using a combination of psychophysics, behavioural tasks, and eye movement tasks and online and offline TMS stimulation. However, the design used in the three different studies have some limitations.

In Study 1 we located the left SPL by entering into the Brainsight software MNI coordinates based on a series of fMRI studies running concurrently in the lab. For half of the participants, we used T1w images, while for the remaining participants we used a standardised 2mm T1w that came with the Brainsight software. In Study 2 we decided to target the left SPL by using the 10-20 EEG system, and we identified the electrode CP1 as the closest to our region of interest. In Study 3 we once again used MNI coordinates and standardised 2mm T1w to locate the right SPL and the right Frontal Eye Field (FEF). Although these are legitimate methods to localise brain regions, they are far from the gold standard. In a study conducted by Sparing and colleagues (2008) the left primary motor cortex (left M1) was located using 5 different neuronavigation modalities (i.e., 10-20 EEG system, standardised function guide procedure, structural MR, individual function MRI and group functional MRI data), and then the result was compared to a TMS-based map of the primary motor cortex (which has high spatial accuracy), and motor-evoked potentials (MEP) were calculated. The result showed that the 10-20 EEG system was the least accurate of all tested approaches, and the MEP amplitudes were significantly lower than the other conditions. The localisation based on the structural MR image gave better accuracy, but the best localisation was an individual functional MRI. As we have chosen to use neuronavigation methods that have been shown to give less accurate locations, this might be a contributing factor to the lack of significant findings in our studies.

Another limitation of the three studies presented in this thesis are the designs of the individual studies. In Study 1 and 2 we considered the Vertex to be the control region for the TMS stimulation. We did this assuming that delivering TMS over the Vertex would not have an effect on the behavioural tasks we presented, and therefore we could rule out the possibility that any significant difference was due to the use of TMS regardless of location of stimulation. However, in a recent study conducted by Jung and colleagues (2016) it was showed that when TMS stimulation at 120% of the resting motor threshold was delivered inside an MRI scanner to the Vertex, there was a significant deactivation in several brain regions including the SPL. The stimulation of the Vertex caused a deactivation in the ‘default mode network’, which might have had a knock-on effect on the salience network. This means that when we delivered the TMS over the Vertex we might have influenced the normal brain activity of the SPL, and this might have affected the behavioural tasks we presented. Therefore, we cannot realistically assume that the Vertex was a good control region for the TMS stimulation. A better design would have also included an additional no-TMS control condition, which would have allowed us to establish whether Vertex TMS had any effect on the behavioural tasks.

In Study 3, for the reasons given above, we decided to not use the Vertex as a control region, and instead experimental control was provided by repeating the task battery before and after the TMS. We also introduced an extra experimental condition – TMS to the Frontal Eye Field. Whenever the effects of TMS differed between SPL and TMS this would provide an additional form of experimental control. However, in most of the experiments we presented in Study 3 we obtained a similar pattern of result after the TMS of both the SPL and FEF. Because the pattern of results was similar for the performances recorded after the TMS of SPL/FEF it was not possible to rule out the possibility that what we observed was an order of testing effect (i.e., performances changed simply because the tasks were presented a second time). It was also not possible to conclude whether the pattern of result was specific for the TMS stimulation of either region, or if the results were due to the use of TMS (i.e., targeting any area of the brain would have given the same pattern of results). A better design would have also included a control condition on a different day (i.e., sham TMS), which would have allowed us to see whether the pre-post changes in performance were specific to TMS to SPL/FEF, or if they were just a by-product of the TMS over the brain. This also would have allowed us to see if the results were due to an order of testing effect.

Another limitation of the three studies included in this thesis is the nature of the TMS stimulation. In Study 1 we used online high frequency rTMS (4 pulses at 20Hz in each trial), while in Study 2 and Study 3 we have used offline continuous theta burst stimulation (3 pulses at 50Hz for a total of 600 pulses). The problem we noticed in Study 1 was the accuracy of the stimulation in what was a lengthy study for participants. Because we opted for an online TMS, after locating the region of stimulation for the day we used a robotic arm to hold the coil in place for us. However, using a robotic arm does not take into account any slight head movements that a participant might make over the course of the experiment, and therefore we cannot be confident that all pulses were delivered over the target region we identified. In addition to this problem, we had to introduce a 5 second ITI between each trial in order to avoid any add up effect of the TMS (Hamidi, Johson, Feredoes, & Postle, 2011). Because we used a psychophysics approach and included 960 trials (30 trials for each configuration of the stimulus), the inclusion of a 5 second ITI considerably increased the duration of the experiment, compounding the problem we identified above. An alternative design would have not used a psychophysics approach so that the number of trials would be reduced, and also would have measured the head movements of the participant head in relation to the coil, in order to be able to discard from the analysis the trials in which the pulses were not delivered to the target region.

In Study 2 and Study 3 we opted to use offline theta burst stimulation in an attempt to overcome the difficulties we had in Study 1, such as participants head movements and duration of the experiments. However, offline TMS is not exempt from limitations. The effects of offline TMS are weaker compared to the immediate disruption that online TMS offers (Gurel et al., 2018). Because of this, it might be that the impact of the stimulation is too weak to be seen on the behavioural measures we recorded in Study 2 and Study 3. Moreover, online TMS can be delivered at the optimal period of the relevant processing, while offline TMS does not offer that feature. In addition, using offline TMS leads to a higher probability of compensatory brain mechanisms being engaged (Sack, Camprodon, Pascual-Leone, & Goebel, 2005). It could be that the brain “adjusts” to the stimulation, by recruiting more or other neuronal resources from other brain regions.

Recent studies of offline cTBS over the human motor cortex have shown that the effect of the stimulation depends on the brain state at the time of stimulation; a process known as metaplasticity. Gentner and colleagues (Gentner, Wankerl, Reinsberger, Zeller, & Classen, 2008) delivered different pattern of cTBS over the motor cortex and measured the amplitudes of MEP at the abductor pollicis brevis (APB) muscle. They found that delivering cTBS for 20 seconds (i.e., total of 300 pulses) facilitated MEP recorded from APB muscle. The pattern of results was opposite (i.e., MEP were reduced) if the 20 seconds of cTBS was preceded by voluntary activity of the APB muscle for sufficient duration (1.5 to 5 minutes). The same reduction in MEP size was also observed if the cTBS was delivered for 40 seconds (i.e., 600 pulses). The fact that there is an opposite effect on MEP size depending on the presence of muscle activation before TMS stimulation indicates that presenting the tasks before delivering the TMS in Study 3 might have influenced the direction and/or magnitude of the TMS. Given that the same results that were observed for motor functioning can be expected also for cognitive functions of the brain, the fact that in Study 3 we presented the tasks before the cTBS, might be considered as ‘voluntary activation’ of those regions that later we targeted with TMS, and this might have influenced the direction and/or magnitude of the stimulation, which might be a contributing factor to the lack of significant findings in our study.

Finally, in the three studies presented above, we targeted either the left SPL (Study 1 and 2) or the right SPL (Study 3). However, a study conducted by Corbetta and colleagues (Corbetta, Shulman, Miezin, & Petersen, 1995) found a bilateral activation of SPL for early spatial shifts of attention. The lack of significant findings in our studies might explained by the fact that the stimulation of an individual SPL is not enough to see an effect on behavioural measures, and instead a bilateral stimulation is needed. A better design would have addressed this problem by delivering bilateral cTBS over the SPL. Bilateral cTBS studies are possible and have been done in the past, for studying how learning new vocabulary happens (Sliwinska, Elson, & Pitcher, 2021), or for studying the attentional network (Vesia et al 2015), or to treat tinnitus and auditory hallucinations (Schraven, Plontke, Rahne, Wasserka, & Plewnia, 2013). Further suggesting that bilateral TMS might be a more appropriate way to test our theory is the comparison between two neuropsychological conditions that can arise from damage to the parietal lobe. Bilateral damage to the superior parietal lobe results in Balint’s syndrome, which is characterised by simultagnosia and oculomotor ataxia (Balint, 1909). This means that the patient has difficulty perceiving more than one object at a time or the spatial relations between objects, and also difficulty initiating saccades between objects (‘sticky fixation’). Our theory that the SPL is crucial for processing visual separation is quite consistent with this pattern of deficits caused by bilateral parietal damage. However, unilateral parietal damage produces visual neglect, which has symptoms much less related to our theory. Therefore, the unilateral TMS we used may have been inappropriate.

Covid-19 had a big impact on the studies included in this thesis. Study 3 was affected by the restrictions caused by the spread of the virus. As a result of this, the sample size in the study was reduced, in order to accommodate for the restriction, put in place by the University of Reading. This resulted in the study being underpowered, and for this reason some analyses were not run. For example, in previous studies investigating the role of the FEF in saccades using TMS, it has been noticed that the effect of unilateral stimulation of the FEF resulted in impaired contralateral saccades. For this reason, we planned to run analysis comparing rightward saccades (i.e., ipsilateral) versus leftward saccades (i.e., contralateral) for reflexive, voluntary, and memory-guided saccades. However, the reduced sample size (when combined with our data filtering procedures) did not allow us to run such analysis. With more participants, some would have been excluded by the filters, but enough would have remained to run the analysis. Furthermore, in studies 3 Covid-19 restricted access to the MRI scanner, this prevented us from acquiring fMRI data to be used to locate brain regions to be targeted with TMS. Therefore, we had to change the experimental design of the study by dropping the fMRI element, which resulted in a less optimal design.

## 5.3 Future Directions

The studies included in this thesis do not fully answer the question of whether the Superior Parietal Lobule (or FEF) is involved in the perception of 2D visual extent, and for this reason further research is suggested.

Aside from the practical limitations of the studies mentioned above (such as a better neuronavigation technique and the inclusion of a sham TMS day), further studies should try to approach the question of whether the SPL is involved in the perception of 2D visual extent from a different angle, following the example of previous research into human perception of velocity and acceleration. Smith (1987) has shown that in the brain there exists a specific mechanism that allows us to be very good at judging velocities. As a matter of fact, in MT there are neurons that are tuned to specific velocities (Maunsell & Van Essen, 1983; Orban, Kennedy, & Maes, 1981), and therefore participants asked to discriminate between different velocities are usually very good at that task. The same is not true for accelerations. The human brain does not have neurons in the MT (or in any other brain region) that are tuned to different accelerations, and therefore participants asked to discriminate between different accelerations are usually poor at the task (Schmerler, 1976). It might be that a similar pattern is true for visual separation relative to visual position. The visual system has neurons that are tuned to specific positions in the visual field, but it may lack neurons that are specifically tuned to separation between points in visual field. In order to test this hypothesis a future study should include the two following conditions: a position judgment task, where participants are asked to judge the position of an element in the visual field; a separation judgment task, where participants are asked to judge the visual separation between points in the visual field. If the same principle found by Smith is also valid for visual separation, we expect to find precise judgements (steep psychophysical functions) for the position judgment task, and shallow psychophysical functions for the visual separation task. If the two task were done in an fMRI study, and there is a dedicated neural mechanism for separation judgement, then a possible pattern of results might be an activation in V1 for the position judgment task and an activation in SPL for the visual separation task.

A similar methodology was used by Morgan (2005) to investigate if there is a specific mechanism in the brain to support the perception of the 2D area of a rectangle, or alternatively that participant judgments of 2D area are supported by cognitively combining the separate perceptions of height and width. If the latter was true, then the precision (noise) of the area judgements should be at least equal to the result of multiplying the precision (noise) of the height and width judgements together. But if there was a dedicated mechanism it would be less than that. To test these ideas Morgan made the relevant psychophysical measurements in a series of experiments. It was concluded that participants do not have a specific mechanism for computing the area, but instead the 2D area arises from heuristics derived from the height and width perceptions. Morgan's methodology could be used to quantify the precision of visual separation judgments and compare them to those found for position.

Another possible future direction would be to study relevant patient populations with parietal lobe damage. For example, patients with Balint's syndrome seems to be excellent candidates to test the role played by the Superior Parietal Lobule in the perception of visual extent. Balint's syndrome is a rare condition that is caused by a bilateral parietal-occipital lesion, which includes the SPL. Patients with Balint's syndrome suffer a discrepancy between visual input and motor output, and they usually show three symptoms: simultagnosia (i.e., they cannot identify multiple objects simultaneously); oculomotor apraxia (i.e., they cannot move their eyes to an object of interest), and optic ataxia (a deficit in reaching to a target). This pattern of deficits suggests that Balint’s patients would also perform poorly in tasks that require them to judge the magnitude of visual separation between two stimuli. A possible study with Balint’s syndrome patients might use a psychophysical approach to present a visual separation judgment task, with elements (e.g., pairs of horizontal lines) presented simultaneously at two screen locations, and then ask participants to judge which one of the two lines was longer, which is an equivalent task to judging visual separation. If performance recorded for patients with Balint’s syndrome are worse than performances recorded for matched stroke control patients, it might be possible to argue that the Superior Parietal Lobule is directly involved in the perception of visual extent. A further prediction that could be tested is that in a similar psychophysical task where what is judged is tied to a single retinal location, e.g. colour of a patch or orientation of single line, then Balint’s patients should not perform worse than the control patients because these tasks rely on early visual areas that are intact in Balint’s patients, and do not require any spatial processing.

## 5.4 Conclusions

The body of work contained within this thesis aimed to expand on the available literature regarding the role played by the parietal lobe in the perception of 2D visual extent. Firstly, we investigated if the Superior Parietal Lobule was involved in the perception of 2D visual separation between points by delivering online high frequency rTMS while participants performed a separation task. In chapter 3 we investigated if an offline cTBS over the left SPL would affect the illusion of visual extent generated by the Muller Lyer illusion and the bisection bias induced by the Judd and Brentano versions of the Muller Lyer figure. In chapter 4 we investigated the effects of offline cTBS over the SPL and the FEF on an interception task, a reaction time task, a line adjustment task, and on the amplitudes for reflexive, voluntary, and memory-guided saccades generated by the Muller Lyer illusion. None of these experiments provided support for the role for the SPL in the perception of 2D visual extent, but due to limitations of the experiments the idea was not conclusively refuted either. Improved TMS studies could be carried out to address these limitations, as well as fMRI studies and studies on patients with Balint's syndrome.

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