Effects of Training to an Area-Cue on Human Saccadic Eye Movements

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Abstract

Several recent studies have investigated advanced preparation of oculomotor programs after training to make saccades to a specific location in space. However, in natural visual scenes, we seldom know the precise stimulus location, rather, we often know the general area where target of interest may appear. Here, we investigated how human saccadic reaction time (SRT) and saccade final landing position may be affected by training to attend to an area where a target will appear. Additionally, we looked at how training to an area of one size may influence eye movements to targets presented in a larger area. Subjects were trained to attend to an area-cue of 6° in diameter, always presented in the same quadrant of the visual field, at the same spatial coordinates. During training, targets were presented at random locations inside the cued area. After training, targets were presented inside an area-cue (except for a few catch trials) of either the same size or of a larger size (i.e. 10° diameter). Results show that training-related saccades were directed toward individually distinctive preferred regions inside the trained area, and towards identical regions in relative coordinates inside the larger 10° area. Importantly, training-related saccades were mostly in the anticipatory range, a large proportion of which was followed by the corrective second saccades directed towards the target. Our findings suggest that anticipatory saccades should be considered in the assessment of training-related changes in oculomotor preparation of saccadic programming.

Résumé

Plusieurs études récentes ont investigués la préparation à l'avance de programmes oculomoteurs suite à la pratique à faire des saccades à une location spatiale spécifique. Pourtant, dans l'usage naturel de la vision, on ne connaît pas toujours la location exacte de la cible, plutôt, on connaît la région dans laquelle la cible peut apparaître. Ici, on examine comment le temps de réaction des saccades oculaires (TRS) et la position finale des saccades sont affectés suite à la pratique où une région cible délimite là où la cible peut apparaître. De plus, on examine comment la pratique sur une région cible d'une taille affecte les mouvements oculaires pour une cible présentée dans une région cible d'une plus grande taille. Les sujets se pratiquaient à porter leur attention sur une région cible de 6° de diamètre, toujours présentée dans le même quadrant de l'espace visuel, aux mêmes coordonnées spatiales. Pendant la pratique, les cibles étaient présentées au hasard dans la région cible. Après la pratique, les cibles étaient présentées dans une région cible (à l'exception de quelques essaies truqués) soit de la même taille ou plus grande (i.e. 10° de diamètre). Les résultats montrent que après la pratique, les saccades étaient concentrées vers des régions préférées individuelles, situées à l'intérieur de la région cible, et vers les régions relativement identiques pour la région cible de 10°. Notamment, les saccadés étaient pour la plupart dans la gamme d'anticipation, dont plusieurs étaient suivis par des saccades correctives vers la cible. Nos résultats suggèrent que les saccades anticipatoires devraient être considérées dans l'évaluation des changements reliés à la pratique des saccades dans la préparation des programmes oculomoteurs.

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Abbreviations

Cb   cerebellum

CN   caudate nucleus

dlPFC dorsolateral prefrontal cortex

EEG   electroencephalogram

FEF   frontal eye fields

FEP   final eye position

FP   fixation point

LIP   lateral intraparietal cortex

PEF   parietal eye field

PPC   posterior parietal cortex

SC   superior colliculus.

SEF   supplementary eye fields

SNr   substantia nigra pars reticulata

SRT   saccade reaction time

Th   thalamus

TMS transcranial magnetic stimulation

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Chapter 1: Introduction

1.1. Selection of visual information

A typical visual scene generally contains more information than can be processed at any given time by the visual system. To compensate for its limited capacity, the visual system selects relevant information and disregards irrelevant information. The way in which the organism selects relevant information depends on various factors, such as behavioural goals (search, detection, discrimination), previous experience, and its salience, to name a few. As a result, relevant information can be selected automatically, sometimes not even requiring any conscious awareness, or intentionality. Essentially, selective processing of relevant information involves allocating attention to it by the organism. Therefore, attention is a process through which certain stimuli or locations are given priority over others (Bowman, Brown, Kertzman, Schwartz, and Robinson, 1993). Two types of attention are distinguished: overt attention and covert attention. During overt attention, attention and direction of gaze are aligned (Bowman *et al.*, 1993), i.e. overt attentional shifts are always accompanied by eye movements. In contrast, covert shifts of attention imply that the gaze fixation and the attended targets are distinct, and therefore attention and direction of gaze are not conjoined (Corbetta, 1998). Hence, one can covertly orient attention to the target of interest while fixating on a different target. However, recent studies suggest that the two types of attention are not necessarily mutually exclusive, and in fact could be utilized by the visuo-oculomotor system to augment the processing of relevant visual information (for a review see Clark, 1999).

1.2. Premotor theory of attention

The premotor theory of attention, originally proposed by Rizzolatti (1987), suggests that attention is closely linked to the workings of the oculomotor system (Rizzolatti, Riggio, Dascola, and Umilta, 1987). Specifically, Rizzolatti proposed that both types of attention (overt and covert) are dependent on programming of eye movements (saccades). According to this theory, shifts in visual attention are usually accompanied by associated eye movements; however, the locus of attention can still be shifted even if the movements of the eyes are purposefully suppressed. Therefore, saccadic eye movements get programmed to the attended location, regardless of whether or not they are executed. In the latter case, the programming of a saccade occurs in response to an informative location cue, which if allowed to be executed brings the eye to the target faster than if the target is presented at an unexpected location. In summary, Rizzolatti's premotor theory of attention postulates that overt and covert shifts of attention employ the same mechanism of saccade programming (Rizzolatti *et al.*, 1987).

1.3. Neuronal circuitry of oculomotor system

As stated earlier, saccadic eye movements play a central role in overt visual attention mechanisms. The neuronal circuitry of the saccadic oculomotor system includes both cortical and subcortical structures. Cortical structures include the frontal eye fields (FEF), lateral intraparietal area (LIP), supplementary eye fields (SEF), and dorsolateral prefrontal cortex (dlPFC). Subcortical structures include the superior colliculus (SC), cerebellum (Cb), substantia nigra pars reticulata (SNr), caudate nucleus (CN), and thalamus (Th).

The generation of saccadic eye movements requires visual signals to be conveyed to the brainstem reticular saccade generator; the SC is considered to be its central relay station (Scudder, Kaneko, and Fuchs, 2002). Visual signals reach the SC via either the direct retinal-collicular pathway projecting to its superficial layers (Munoz, Dorris, Paré, and Everling, 2000), or indirect afferent projection from the frontal cortex (FEF, SEF, DLPFC), parietal cortex (LIP), basal ganglia, and cerebellum (Neggers, Raemaekers, Lampmann, Postma, and Ramsey, 2005; Scudder et al., 2002; Snyder, Batista, and Andersen, 2002). In addition, FEF and LIP have extensive reciprocal neuronal projections to SC (Shipp, 2004; Paré and Wurtz, 2001; Gaymard, Ploner, Rivaud, vermersch, and Pierrot-Deseilligny, 1998). Also, SEF and FEF have extensive reciprocal projection to LIP and to each other (Scudder et al., 2002). Notably, while it has been found that the three cortical areas (FEF, SEF, and LIP) have direct descending projections to the brainstem saccade generator (Scudder et al., 2002; Schiller, True, and Conway, 1980), these direct projections are believed to be functionally insufficient for the production of a correct saccade, which in turn seems to require the relay signal via the SC (Scudder et al., 2002; Hanes and Wurtz, 2001; Schiller et al., 1980).

Various human lesion and neuroimaging studies, as well as primate studies indicate that the extent to which any of these areas are involved in saccade generation depends on the nature of the saccade, i.e. reflexive, intentional (planned and guided), or predictive (Abel and Douglas, 2006; Spengler et al., 2006; Broerse, Crawford, and den Boer, 2001; Gaymard et al., 1998; Evdokimidis, Mergner, and Lücking, 1992).

1.4. Characteristics of saccades

1.4.1. Reflexive saccades

The sudden appearance of a visual target in the periphery evokes an automatic oculomotor response – a reflexive saccade toward the target (Broerse *et al.*, 2001; Spengler et al., 2006). Reflexive saccades are characterized by fast velocities (Spengler *et al.*, 2006) and are visually guided (Broerse *et al.*, 2001).

In the laboratory setting, it has been shown that visually guided reflexive saccades have an average saccadic reaction time (SRT) of 170-180 ms (Spengler *et al.*, 2006). Additionally, it has been shown that the extinction of the fixation point (FP) prior to target onset and the presentation of a delay period (gap) between the offset of the FP and the target onset lead to bimodal distribution of SRT (Dorris and Munoz, 1995), with the first peak latency of 100ms or 120ms (depending on target predictability), termed express saccades, and the second peak latency of 140-160 ms, termed regular saccades (Fischer and Boch, 1983).

The superior colliculus is believed to be the main brain structure implicated in the generation of express saccades (Paré and Munoz, 1996). Supporting this conjecture, lesion studies showed that the ablation of the SC leads to the loss of the ability to generate express saccades (Schiller *et al.*, 1987). In addition, studies conducting cell recordings in the SC found distinct neuronal activity associated with express saccade generation (Dorris *et al.*, 1997; Edelman and Keller, 1996).

In contrast, generation of regular latency saccades involves cortical processing of visual information. Clinical lesion studies, human EEG recordings,

and studies examining oculomotor abnormalities linked to psychiatric disorders show that the parietal eye field (PEF)/LIP in the posterior parietal cortex (PPC) is the main cortical structure involved in generation of regular latency reflexive saccades (Spengler *et al.*, 2006; Gaymard *et al.*, 1998; Evdokimidis, Mergner, and Lücking, 1992).

1.4.2. Intentional saccades

In laboratory settings, generation of intentional saccades is studied primarily via two experimental paradigms: antisaccade task and memory guided saccade task. In the antisaccade task, participants are required to suppress a reflexive saccade toward a peripheral target, and instead generate an eye movement toward the mirror location in the opposite visual hemifield. In the memory guided saccade task, a saccade to a target is made after a certain time delay (gap) and therefore the visual information about the target's location is absent during the eye movement (Abel and Douglas, 2006; Broerse *et al.*, 2001).

Because intentional saccades are under voluntary control and involve cognitive processing, their latencies are longer than those of the reflexive saccades. For example, latencies of memory guided saccades are way over 200 ms (Hopp and Fuchs, 2004) and latencies of antisaccades average at around 350 ms (Mort *et al.*, 2003), compared to 170-180 ms for reflexive saccades (Spengler *et al.*, 2006). Also, when intentional saccades are generated in the absence of existing visual information about target location (e.g. memory-guided saccades), they are less accurate than visually guide saccades because they rely exclusively on an internal representation of the target location (White, Sparks, Stanford, 1994;

Gnadt, Bracewell, and Andersen, 1991). Specifically, memory-guided saccades are characterized by an upward bias (systematic error) and a large scatter of the saccade endpoints (variable error) (White *et al.*, 1994).

Given that the generation of both antisaccades and memory-guided saccades requires an active suppression of the initial reflexive eye movement towards the target, generation of the intentional saccades involves cortical processing, and includes areas such as DLPFC, FEF, and SEF (Abel and Douglas, 2006; Neggers *et al.*, 2005; Spengler *et al.*, 2006; Mort *et al.*, 2003; Broerse *et al.*, 2001; Gaymard *et al.*, 1998).

1.4.3. Predictive saccades

When the location and timing of the target's appearance are known in advance, the visual system is able to construct an accurate representation of the future position of the target and generate a saccade with an extremely short latency, often less than 75 ms, termed anticipatory saccade (for review see Broerse *et al.*, 2001). In the laboratory, generation of predictive saccades is achieved through paradigms that involve learning of simple or complex sequences of target presentations, varying the probability of target appearance at a certain locations, presenting the target in the same location over many consecutive trials (training), or indicating target's exact location with a cue (Clohessy, Posner, and Rohbart, 2001; Dorris and Munoz, 1998; Cavegn and d'Ydewalle, 1996; Paré and Munoz, 1996; Evdokimidis *et al.*, 1992; Findlay, 1982; Findlay 1980).

Various imaging studies (see review e.g., Broerse *et al.*, 2001; Gaymard *et al.*, 1998), electrophysiological recordings (Coe, Tomihara, Matsuzawa,

Hikosaka, 2002), and human EEG recordings (Evdokimidis *et al*, 1992), as well as studies on oculomotor abnormalities associated with obsessive-compulsive disorder (Spengler *et al.*, 2006), and Parkinson's disorder (O'Sullivan *et al.*, 1997), demonstrate the involvement of fronto-striatal circuitry in predictive saccade generation, mainly in areas such as the FEF, the SEF, and the basal ganglia. The FEF and basal ganglia are involved in the generation of predictive saccades primarily by means of its inhibitory projections to SNr, thereby disinhibiting the activity in the SC (for review see Hikosaka, Takikawa, and Kawagoe, 2000). Evidently, an increased saccadic latency in the predictive saccade task has been shown in patients with Parkinson's disease (Spenger *et al.*, 2006; Broerse *et al.*, 2002). Furthermore, there is evidence that an overactive circuitry between the FEF and the basal ganglia results in the abnormal reduction of saccadic latencies in the predictive saccade task. For example, patients with obsessive-compulsive disorder (OCD) show a pathophysiological dysfunction of the prefrontal areas (mainly FEF) and the basal ganglia (Busatto *et al.*, 2000). These individuals produce anticipatory saccades with abnormally reduced latencies (Spenger *et al.*, 2006).

1.5. Neuronal circuitry of attention

Covert attentional mechanisms may employ some of the same brain structures that are involved in overt attentional processing (Lomber, 2002; Nobre, Gitelman, dias, and Mesulam, 2000; Corbetta, 1998; Morris, Ohman, and Dolan, 1998). For example, cortical brain structures that are thought to be employed in covert attentional processes are the frontal eye fields (FEF) and the lateral

intraparietal area (LIP). The superior colliculus (SC) is a subcortical structure implicated in covert shifts of attention (Lomber, 2002; Nobre *et al.*, 2000; Corbetta, 1998; Morris *et al.*, 1998).

Various studies using electrophysiological recordings and microstimulation of the cells in the SC provide evidence of its involvement in covert orientation of spatial attention (Ignashchenkova, Dicke, Haarmeier, and Their, 2003; Kustov and Robinson, 1996; Robinson and Kertzman, 1995). For example, a recent study conducted by Ignashchenkova *et al.* (2003) demonstrated the existence of a special subset of neurons (visuomotor neurons) in the SC that are active during covert shifts of attention. Specifically, visuomotor neurons showed a significant discharge during the "attention shift period", defined as 200 ms period preceding the presentation of the target, even though the eventual saccade was not encoded by these types of neurons. The researchers concluded that visuomotor neurons of the SC participate in covert shifts of attention (Ignashchenkova *et al.*, 2003).

The involvement of the FEF in covert visual selection of the saccadic site is more controversial. For example, animal studies using microstimulation of cells indicate that a subthreshold microstimulation of the cells in the FEF at the sites representing the target's location in the visual field, prior to presentation of the target, resulted in an increased sensitivity to changes of the target's luminance (Moore and Fallah, 2004; Moore and Fallah, 2001), i.e. enhanced performance.

However, human studies using transcranial magnetic stimulation (TMS) over the FEF, a technique known to result in the disruption of the activity in the

stimulated site, seem to provide contradictory evidence. On one hand, Smith, Jackson, and Rorden (2005) found that disruption of the activity in the FEF via TMS facilitated attentional processing of relevant visual information by eliminating the cost associated with the presentation of false visual information provided by an invalid cue (Smith *et al.*, 2005).

On the other hand, Grosbras and Pause (2002) demonstrated inter-hemispheric differences associated with the TMS over the FEF, showing that it can result in both facilitation and inhibition of stimulus detection depending on the stimulated hemisphere. Specifically, these researchers showed that when an invalid symbolic cue (arrow) indicates the stimulus's location, transcranial magnetic stimulation of the right FEF added to the detrimental effects of the cue, and therefore resulted in interference with the shifts of attention. However, TMS over the left FEF actually facilitated the responses to targets presented in the contralateral visual field regardless of the cue being valid or invalid (Grosbras and Pause, 2002).

Finally, LIP involvement in the covert attentional mechanisms seems to be specifically prominent when the relevant target is embedded among multiple distracting stimuli, rather than presented alone. Specifically, Wardak, Olivier, and Duhamel (2004) demonstrated a decreased performance in a search task, where the target had to be detected but not explicitly localized (i.e. in the absence of eye movements), following temporary deactivation of the LIP area. Also, there was a positive correlation between the difficulty level of the visual search and the amount of deficit produced by the LIP inactivation, i.e. easy feature search was

less affected than the difficult feature search (Wardak *et al.*, 2004). However, no deficits associated with saccades to a single target were produced following LIP inactivation (Wardak *et al.*, 2004). Therefore, it appears that the LIP is involved in covert shifts of attention when the target selection requires a choice (Wardak *et al.*, 2004; Kusunoki, Gottlieb, and Goldberg, 2000).

1.6. Strategies in saccade generation and planning

In laboratory settings, selective information processing has been studied through cue presentation and training. Studies indicate that training to attend to a specific target location results in a decrease of saccadic latencies (Paré and Munoz, 1996; Fischer and Ramsperger, 1986; Fischer, Boch, Ramsperger, 1984). Particularly, various animal studies showed that training to attend to a target presented in a specific location results in the increased generation of express saccades to that location (Dorris and Munoz, 1998; Paré and Munoz, 1996; Fischer and Ramsperger, 1986; Fischer *et al.*, 1984). For example, Paré and Munoz (1996) demonstrated that training to attend to a specific target position leads to a decrease in the overall saccadic latencies and increased generation of express saccades to the trained location. Also, the percentage of express saccades decreased as spatial proximity relative to the trained target increased (Paré and Munoz, 1996).

Similarly, reduction in SRT associated with training has also been shown in humans; although, human research indicates that training to attend to specific target locations results in the production of even shorter latency saccades – almost exclusively anticipatory saccades. For example, Evdokimidis, Mergner and

Lücking (1992) found that when the target's location is kept constant and its appearance is signalled in advance, the amount of anticipatory saccades reaches 57% within 30 trials, compared to only 3% in the condition where target location is randomized between trials. Likewise, Findlay (1980) demonstrated the production of anticipatory saccades to targets of predictable locations in space.

Also, studies show that human participants can correctly anticipate the target's location of learned complex sequence of target presentation. For example, Clohessy *et al.* (2001) found that after learning a complex sequence of target presentation, adults can correctly anticipate the location of the target on at least 80 percent of trials. Additionally, they found that subjects exhibited correct anticipation of target locations even when they were distracted, indicating that anticipatory visual orienting does not require awareness.

In addition to training, selective information processing has been studied through presentation of a visual cue that signals the location of the target. Attention could be drawn by some sensory or motor stimuli, termed exogenous cue, as well as symbolically defined, termed endogenous cue (Robinson and Kertzman, 1995). In the laboratory settings, exogenous cues are used to indicate the exact location of the target in the visual field, and endogenous cues indicate the area or side (left vs. right) of target's presentation with respect to the FP. Behavioural studies have demonstrated that presentation of an informative cue (i.e. predicting the correct location of a target), either exogenous or endogenous, facilitates the processing of relevant visual information, i.e. the stimuli presented in the expected locations are usually detected faster than the stimuli presented at

unexpected locations. Mainly, cueing the location of the target prior to its presentation shortens both manual and saccadic response time (Shulman, Remington, and McLean, 1979; Posner, Snyder, and Davidson, 1980; Cavegn and d'Ydewalle, 1996; Fischer and Weber, 1998; Kurata and Aizawa, 2004).

In order to explore the role of expectancy in reduction of target detection latencies, Posner et al. (1980) conducted a visual detection task, where the possible spatial position of the target was signalled by the presentation of a cue. Participants had to detect a target presented on the screen following a warning signal of 1 sec. Posner et al. (1980) found that specifying the location of the target, with the presentation of a location cue prior to its presentation, decreased the response time and therefore improved performance. This finding shows that expectancy, expressed in terms of allocation of attention to the cued location, can facilitate visual detection when a valid cue is presented (Posner et al., 1980).

In addition, it has been shown that the benefits associated with specifying the location of the target (cue) and presenting the target always at the same location (training) can be enhanced by presentation of a gap period between the FP offset and the target onset (Cavegn and d'Ydewalle, 1996; Paré and Munoz, 1996). It has been proposed that presentation of a gap period contributes to the build-up of pre-target neuronal activity in the SC, which in turn results in the increased production of express saccades (Munoz et al., 2000).

1.7. Objectives of the study

In the preceding sections I have discussed existing experimental evidence for the congruencies between attentional and oculomotor processing of visual

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information. From the aforementioned studies, it is clear that saccadic types (reflexive, intentional,and predictive) and latencies (anticipatory, express, and regular) vary with experimental conditions (see sections 1.4 and 1.6). However, the experimental techniques that were used in those studies do not necessarily approximate natural conditions. For instance, natural visual scenes are rarely equipped with cues for the precise stimulus location. Hence, there is little practical applicability in learning to attend to a single location in space. However, it is often the case that we know the *area* where the target will appear, rather than its specific location. In our study we wanted to observe the natural progression of training effects on visuo-oculomotor perception. To the best of our knowledge, so far no one looked at how training to attend to a *cued area* would affect saccadic latencies to targets presented randomly inside its boundaries. Such a setup would represent a compromise between random and non-random target presentation, and therefore could result in the production of different types of saccades from those shown in the experiments using training and cueing for the precise target location (Paré and Munoz, 1996; Evdokimidis *et al.*, 1992). Thus, the aim of this study was to investigate in humans the effects of training to attend to an *area-cue* within which the target appears at various locations.

It has been suggested that covert attentional shifts are accompanied by overt attentional shifts (saccades) when an exogenous cue signals the precise stimulus's location, while endogenous central cues induce only covert attentional shifts (Fischer and Weber, 1998; Remington, 1980). Therefore, we set up an

experiment where an exogenous peripheral cue indicates the area of the target's appearance.

First, we wanted to see if training to attend to an area of a specific size (6° circle) would lead to a significant decrease in saccade latency, and result either in (a) a significant increase of express saccade generation towards the targets presented within the trained area, similar to that demonstrated by Paré and Munoz, 1996, or perhaps (b) the area-cue would further enhance the predictive value imposed by the process of training (Clohessy *et al.*, 2001; Dorris and Munoz, 1998; Evdokimidis *et al.*, 1992; Findlay, 1980) and lead to the increase in generation of anticipatory saccades.

Second, we wanted to observe whether training to attend to an area within which the target always appears would result in generation of an effective detection strategy. For instance, He and Kowler (1989) proposed the existence of a high-level saccadic planning mechanism that operates on the probability of target location. According to their findings, the saccade landing position is biased towards the most probable location, based on the past history or the likely future location of the target, regardless of the target's actual location (He and Kowler, 1989). We therefore expected that combined influence of the area-cue presentation and training would indicate a high probability level of target appearance within the trained area, and result in a large percentage of saccades landing inside that area. However, it has been shown that when target appearance is equally probable at multiple target locations, the eyes tend to land at the region that corresponds to what could be considered the centre of the target array

(Vishwanath and Kowler, 2003; Zhou, Chu, Li, and Zhan, 2006), the phenomenon also known as "global effect" (Findlay, 1982). Thus, we wanted to determine whether the initial eye landing position resulting from the training induced saccades within the cued area (He and Kowler, 1989) would be influenced by a "global effect" and the saccades would be made to the centre of the area-cue.

The final goal of this study was to examine whether a training effect would persist if the area of possible target positions would increase in diameter to $10°$. For instance, Paré and Munoz (1996) demonstrated that training to attend to a specific target location resulted in the increase of express saccade generation not only at the trained target location but also at spatially adjacent locations. Similarly, in the present experiment we examined whether training related effects (if any) would persist if the size of the area-cue would increase. Specifically, it is plausible that similar to Paré and Munoz's (1996) findings, the latencies of saccades to targets presented inside a larger ($10°$) area would be in a similar SRT range as to the saccades inside the trained ($6°$) area. Alternatively, increasing the size of the area-cue could decrease the predictive value of target location and result in production of longer latency intentional saccades (Clohessy *et al.*, 2001; Dorris and Munoz, 1998; Evdokimidis *et al.*, 1992; Findlay, 1980). Also, we examined whether in the case of the $10°$ area, the preferred region of the eye gaze would (a) occupy the exact same location, (b) increase in size around the same location, (c) fall into a different region, or (d) perhaps, the training effect might be absent completely.

Chapter 2: Methods

2.1. Participants

Five students (2 male & 3 female, including the first author) participated in this study. All were university graduate students. Their vision was normal or corrected to normal. They were healthy individuals with no history of neurological disorders. Four of the participants had no previous experience in oculomotor studies.

2.2. Apparatus and stimuli

The experiment was controlled by the REX 5.2 software system (designed by the National Institute of Health, US) and 32 I/O-slot interface hardware (PCI-DIO 120 and PCI-AOB 8/12, Kontron). Behavioural paradigm, visual display, and eye movement data collection was controlled by a separate computer running the MATLAB program through the REX I/O interface, which in turn was connected to the projector, which displayed experimental stimuli on the white screen located at a distance of 57 cm from the participants. Monocular (right) eye movements were measured with a high speed (250Hz) eye tracking system (model 501, ASL).

The target consisted of a $0.5°$ dot always presented at random locations on the right top quadrant of the visual display. All targets appeared within 20° vertical and 20° horizontal coordinates from the fixation point presented in the middle of the screen. Stimulus presentation was always preceded by the appearance of an exogenous location cue in form of a circle of one of the two

diameters: 6° and 10°. The cues always appeared at fixed coordinates relative to the FP, with centres positioned at (13, 3) and (13, 5), respectively (Fig. 2-1). The cue was considered valid if the target was subsequently presented within its boundaries, and invalid if the target was presented outside of the cued area. The invalid cue was presented in approximately 12% of trials. Presentation of valid and invalid cues was randomly interleaved between trials. Invalid cue trials were included to encourage target-related saccades.

2.3. Procedure

Prior to each recording session, the gain and offset of the eye position were calibrated while the subject was fixating at various fixed target locations presented in the top quadrant of the right visual field at eccentricities not exceeding 20°.

Testing was separated into the following sessions: pre-training, training, and post-training. The testing procedures during pre-training and post-training sessions were identical in order to observe training effects. No performance feedback was given to the participants at any point during the experiment, a procedure which is known to increase express saccade generation (Kingstone and Klein, 1993).

2.3.1. Pre-training / post-training sessions

Participants were seated in a dark room with their heads restrained by a bite bar. Each trial began with the presentation of the FP alone for 600 ms. After that, an area-cue (either 6° or 10° circle) was presented in the top right quadrant of the visual field simultaneously with the FP for 400 ms. The presentation of the

two area-cues was divided into blocks of 100 trials each. The order of block

presentation was randomized between subjects to control for order effects.

Participants were instructed to maintain their fixation on the FP, and not to make

eye movements toward the cue. The FP and the cue were then extinguished at the

same time, followed by a randomly chosen gap period of 170 ms or 220 ms (Fig.

2-2). Two different gaps were presented in order to reduce the predictability of

target onset. The gaps chosen for this study are very close to the ideal gap

duration that has been shown to increase generation of express saccade (Fischer &

Boch, 1983). During the gap period, subjects had to maintain fixation in total

darkness. On most of the trials, at the end of the gap period, the target was briefly

flashed for 68 ms at a randomly chosen location within the cued-area. However,

in approximately 12% of trials the target was presented outside the cued-area

(catch trials). Participants were instructed to make a saccade toward the target as

soon as they detected it and remain fixated on its position until the trial was over.

At the end of each trial, the room was illuminated for 3000 ms before the start of

the next trail to prevent dark adaptation.

2.3.2. Training session

During the training session the target was presented at random locations

inside only the 6° area, indicated by the 6° area-cue. The target was always

presented within the cued-area, i.e. the cue was valid on 100% of the trials. The

duration of the FP, cue, and target presentation, as well as the task instructions

remained the same as during the pre-training session. The participants were

considered fully trained when the distribution of saccadic latencies was no longer

subjected to change as a result of training.
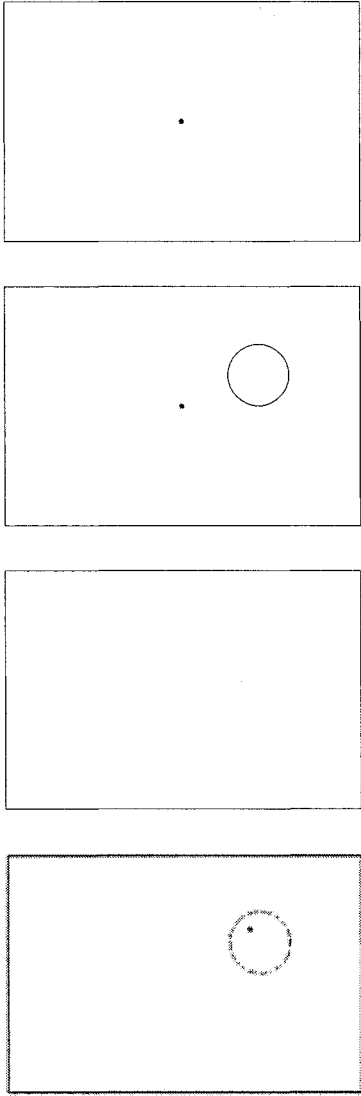
Figure 2-1: A schematic view of a sequence of events. The dashed circle represents the location of the no longer visible area-cue.
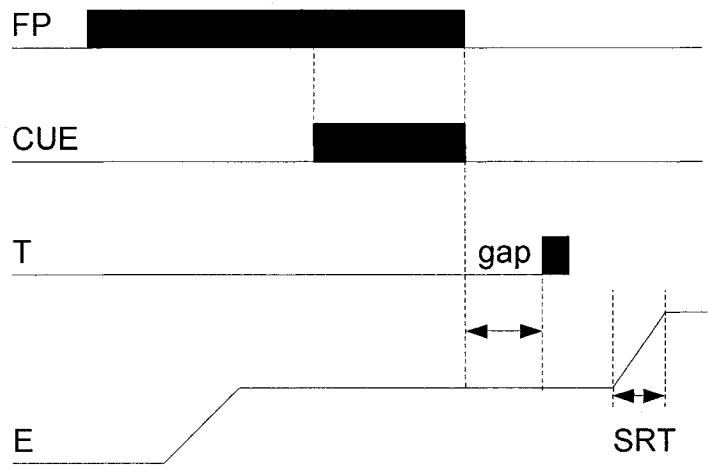
Figure 2-2: Overview of the area-cue task.

Chapter 3: Results

3.1. Data analysis

During each trial, the following experimental quantities were stored: stimulus position and duration, saccadic reaction time (time difference between the target onset and the saccade initiation), saccadic duration and velocity, gap duration, and the error of the final eye position with respect to the target's location.

Only data collected from the pre-training and post-training sessions were examined. On the pre-training session (i.e. day 1), data from all five participants was included in the analysis. On the post-training session (after approximately 2 training sessions), data of 4 participants were analyzed together, while the 5th participant's data were examined separately due to the considerable difference in the subject's post-training performance from the rest of the subjects. Also, subject 5 was excluded from all of the t-tests and ANOVAs because this person failed to achieve the same level of training as the rest of the participants. However, this person's data were analyzed independently (for description see section 4.9).

Participants completed between 100 and 150 trials for each experimental condition. For analysis purposes, data from the two gap periods were pooled together, since no differences in latencies associated with each gap were present. Only non-catch trials were included in all the analyses.

SRT was divided into three categories: anticipatory (<75 ms), express (75-125 ms), and regular (>75 ms) saccades. The saccades with latencies larger than 500 ms are presumably not target related (Paré and Munoz, 1996) and were

excluded from the analysis. The amount of saccadic eye movements in the anticipatory and express ranges was calculated for each subject in each condition. Analyses of SRT were performed by using various repeated-measures factorial ANOVAs and paired samples t-tests.

Mean systematic error for each participant in each condition was computed and analyzed using various repeated-measures factorial ANOVAs and paired samples t-tests. Estimates of systematic, as opposed to variable error (the scatter of the endpoint of each saccade toward a particular target position) were chosen as a dependent measure because it has been shown that, contrary to the variable error, systematic error does not augment with the gap increase, and therefore might reflect a non-memory related error (White, Sparks, and Standford, 1994).

Even though no specific instructions pertaining to generation of second saccades were given to the participant, second saccades were analyzed to detect possible training effects related to multiple saccade generation. Only those second saccades that were corrective in nature were included in the analysis. Saccades were labelled as corrective if they reduced the error associated with the first saccade.

3.2. Training effects on saccadic latency distribution

Fig. 3-1 plots histograms of pooled latencies from all 5 participants for each area-cue on each experimental session. From the histograms, it is clear that the overall latency distribution was shifted towards the anticipatory SRTs after training. Specifically, a two factor (session x area-cue) within subject ANOVA on

SRT yielded significant main effect for session type, $\underline{F}$ (1, 19) = 19.75, $\underline{p}$ = .0113.

The interaction term was not significant, $\underline{F}$ (1, 19) = 0.05, $\underline{p}$ = .8390. Paired t-tests

confirmed an increase of the proportion of anticipatory saccades from pre- to

post-training sessions p < .05 (one tailed) for all participants in both 6° and 10°

area-cue conditions, except subject 5, t (150) = -0.49, p < .05 (one tailed).

The percentage of express saccades increased with training for 2 of the 5

participants. Specifically, paired t-test for subjects 4 and 5 revealed that the

proportion of express saccades relative to the total number of valid trials increased

significantly from the pre- to post-training session, both in the 6° and 10°

conditions (t (179) = -3.8, p < .05, and t (150) = -3.78, p < .05, respectively).

3.3. Training effects on saccadic error distribution

In order to determine the effects of training to the 6° area on the accuracy

of saccades to specific targets presented within that area, the error was computed

as the distance between the target location and the 1st saccade endpoint. Training

to the 6° area-cue did not have an effect on the overall error associated with the

initial saccade in either the 6° area-cue condition (t (3) =.03, p = .9751 (two

tailed)) or the 10° area-cue condition (t (4) =.04, p = .9704 (two tailed)).

3.4. Training effects on the saccade-end position concentration of the 1st saccades

The distance (Δr) of the saccade endpoints from the centre of the cued area

was calculated using the Pythagorean Theorem:

$$\Delta r = \sqrt{\Delta x^2 + \Delta y^2}$$

where Δr is the distance from the centre of the cue, and Δx and Δy are distances along the vertical and horizontal axes.

The results indicate that training significantly reduced mean distance (Δr) of saccade endpoints from the centre of both 6° and 10° area-cues (t_s (3) = 3.08 and 2.78, p < .05 respectively). Table 3-1 summarizes the mean distance (Δr) from the centre of each area-cue in each condition for each participant.

Fig. 3-2 shows the final eye positions of all the 1st saccades on the pre-training and post-training sessions for 6° and 10° area-cues across all participants (excluding subject 5 from post-training session). It is clear that there is a higher concentration of the saccade endpoints inside the area-cues after training, compared to before training, in both conditions. Fig. 3-3 shows that, in the post-training session, the areas of concentration of the final eye positions within 6° and 10° cues overlap, but only to a small degree. However, when both the 6° area-cue and the 10° area-cue were normalized (scaled to a circle with a radius of 1), the areas of concentration of the final eye positions within the normalized 6° and 10° area-cues show almost complete overlap in the post-training session (Fig. 3-4 A), except in the case of subject 5 who showed no overlap of saccade endpoints (Fig. 3-4 B). The 6° and 10° area-cues were normalized to a circle with a radius of 1°, using the Cartesian coordinate system, according to the following formula:

$$\text{normalized target (x)} = \frac{[\text{target (x)}] - [\text{cue center (x)}]}{\text{cue radius}} \times \text{normalized circle radius } (r)$$

$$\text{normalized target (y)} = \frac{[\text{target (y)}] - [\text{cue center (y)}]}{\text{cue radius}} \times \text{normalized circle radius } (r)$$

3.5. Training effects on the production of secondary saccade

A two factor (session x area-cue) within subject ANOVA on the amount of secondary saccades, yielded no significant main effect for session type, F (1, 9) = 1, p = .3434. The interaction term was also not significant, F (1, 9) = 1, p = .3434.

Fig. 3-5 and Fig. 3-6 (6° area-cue and 10° area-cue conditions, respectively) show that in both cue conditions, only the 1st saccades that fell into the latency range of < 20 ms with respect to the target's onset were followed by the 2nd corrective saccade, i.e. the error resulting from the 1st saccade was reduced by the subsequent 2nd saccade. Grouped data from each session in each condition were analyzed by separate paired one-tailed t-tests. The analyses revealed significant reduction in error of 1st saccades in the range of latencies < 20 ms with respect to target onset by the subsequent 2nd saccades, at p < .0001. This error reduction associated with the 2nd corrective saccade resulted because the majority of the initial anticipatory 1st saccades landed within the cued-area when the target was still visible, which permitted the 2nd saccades to be visually triggered.

The difference between the proportions of the amount of secondary *corrective* saccades to the total amount of secondary saccades during the pre-versus-post-training sessions was calculated using the following formula:

$$t = \frac{p_1 - p_2}{s_p}$$

where p_1 is the proportion of corrective saccades on the pre-training session, p_2 is the proportion of corrective saccades on the final session, and s_p is the standard error of the proportion (Bradley et al, 1979). The proportion of 2nd *corrective*

saccades significantly increased after training for both the 6° area-cue (t (262) = -8.84, p < .05) and the 10° area-cue (t (315) = -5.59, p < .05). Specifically, during the post-training session in the 6° area-cue condition, 77.5 % of secondary saccades were corrective compared to only 22.9% during the pre-training session, and 70.9% versus 39.6% in the pre- and post-training sessions, respectively, in the 10° area-cue condition (Fig. 3-7).

Also, the proportion of the secondary *corrective* saccades following the initial anticipatory saccades of the *total* amount of secondary saccades following the initial anticipatory saccade was significantly larger in the post-training session compared to the pre-training session in both the 6° area-cue and the 10° area-cue conditions (t (172) = -3.97 and t (226) = -2.98, respectively, p < .05 (one-tailed)).

3.6. Overall training effects: 1st + 2nd saccades

3.6.1. Overall time to target

Overall time to target was calculated as the sum of SRT and saccade duration. In cases where the initial saccades were followed by secondary corrective saccades, only the SRT and saccade duration of the latter was considered. The analyses of one-tailed paired t-tests revealed marginal significant decrease in the overall time to target after training in the 6° area-cue condition (at p = .055), and a statistically significant decrease in the overall time to target in the 10° area-cue (at p = .035) (Fig. 3-8).

3.6.2. Overall error to target

In order to determine the effects of training to the 6° area on the overall accuracy of saccades to targets presented within the 6° and 10° area-cue

conditions, the error was computed as the distance between target location and the final saccade endpoint. The results indicate that training did not have a significant effect on the final error in either the 6° or the 10° area-cue conditions (at $p_s = .07$ and .16, respectively (one tailed)) (Fig. 3-9).

3.7. Individual differences related to training

Fig. 3-10 depicts the initial saccade endpoint concentrations of the individual participants for the 6° and 10° area-cues in the post-training session. These graphs show that 4 out of 5 participants generated the initial saccades inside the cued area; the saccade landing points of subject 5 were mostly distributed outside of the cued area. Also, subjects 1-4 generated the initial saccades to a preferred region within the cued area. Although, for all of these participants, the preferred region was located near the centre of the area, the exact location of the preferred region was slightly different for each participant.

3.8. Saccade endpoint representation in the collicular map

The SC is a critical structure for triggering saccades. In order to calculate the representation of saccade vectors on the SC motor map, we used a set of formulas described in detail elsewhere (Optican, 1995; Ottes, Van Gisbergen, and Eggermont, 1986). In brief, we converted the polar coordinates (R, θ), of the saccade vectors in the visual space into the Cartesian coordinates (X, Y), in mm, on the SC motor map. Then retinotopic coordinates (R, θ) were translated into the collicular coordinates in mm using the following equations:

$$X = B_x \log_e \left(\frac{\sqrt{R^2 + 2AR\cos(\theta) + A^2}}{A} \right)$$

$$Y = B_y a \tan \left(\frac{R\sin(\theta)}{R\cos(\theta) + A} \right)$$

where A = 3.0 deg, B_x = 1.4 mm, B_y = 1.8 mm (Optican, 1995).

The resulting collicular representations of the retinotopic coordinates of the initial saccade vectors are depicted in the Fig. 3-11 for the 6° area-cue condition and Fig. 3-12 for the 10° area cue condition. These graphs show that the saccade endpoint concentration is primarily located inside the collicular shape in the post-training session, compared to the highly dispersed saccade endpoint distribution during the pre-training sessions in both 6° and 10° area-cue conditions.

In addition, Fig. 3-13 shows the distribution of saccade endpoints in retinal and collicular coordinates for 6° and 10° area-cues, along with the outline of the cues, during the post-training session. Statistical analysis revealed that on average, saccade endpoints were further from the center in the retinal plane than in the collicular plane, relative to the cued-area size. Specifically, the average distance away from the center is a factor of 1.8 and 1.6 times further in visual than in collicular coordinates, in 6° and 10° area-cue conditions, respectively (Table 3-2).

Finally, Fig 3-13 shows that the collicular activity is more evenly distributed around the center-point of the 6° collicular shape (A), as opposed to the saccade endpoints being positioned largely to the left of the center of the 6° circle (B), after training. A chi-square (χ^2) test for independence was performed to examine the relation between the side of distribution (left vs. right) and plane type (collicular vs. visual). The relation between these variables was significant at a

distance of 20% of the radius away from the center-point, $\chi^2(1) = 6.6$, p < .025.

The collicular activity distribution on either side of the area-cue's center, within

20% of its radius, did not differ in collicular coordinates, whereas there were more

saccade endpoints to the left in retinal coordinates (see Fig. 3-14). However, a

chi-square (χ^2) test for independence in the 10° area-cue condition showed no

significant relation between the variables at any distance from the center-point (at

p>.05), indicating an uneven distribution of the collicular activity/saccade

endpoints to the left and to the right away from the center.
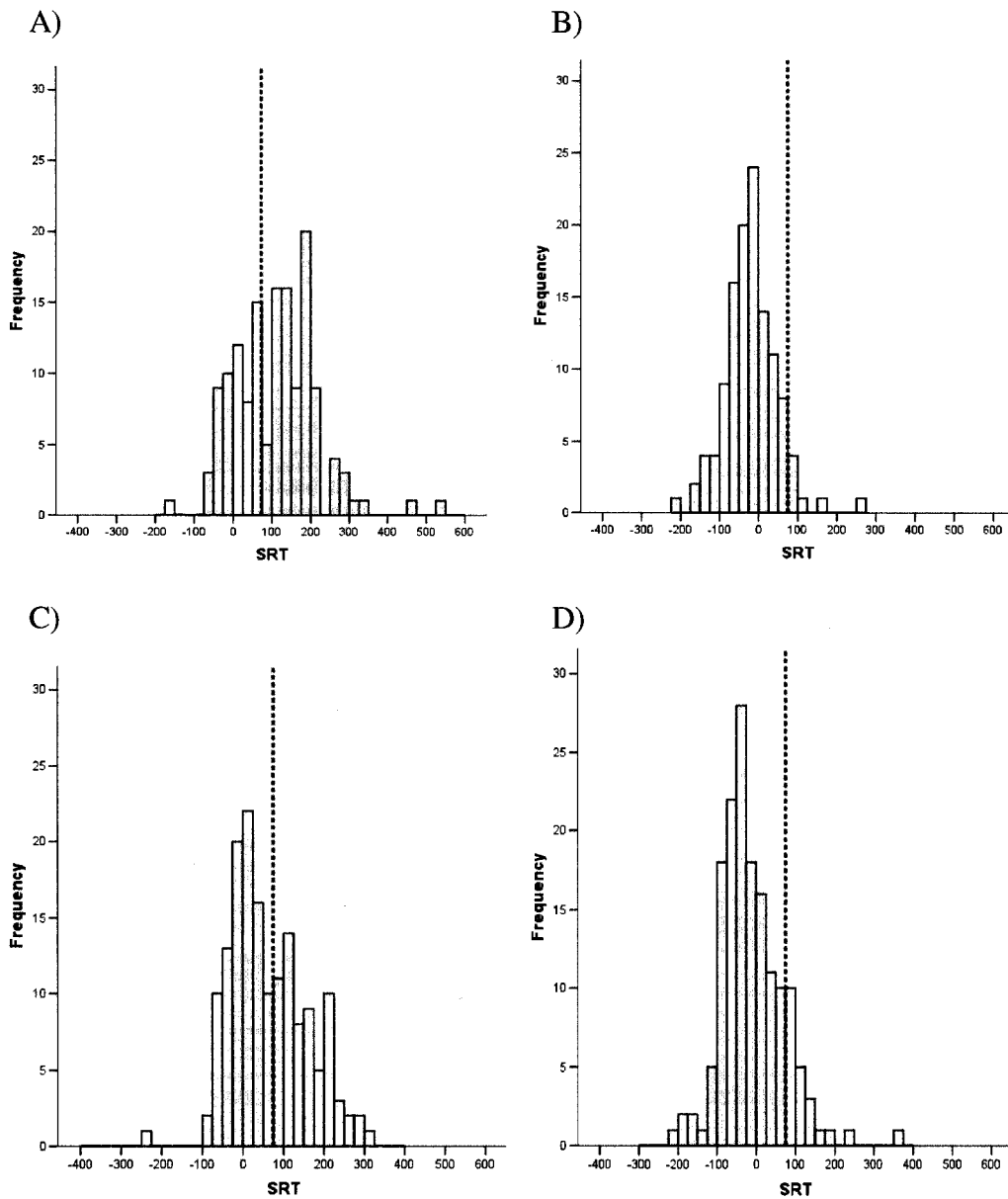
Figure 3-1: SRT distribution. A) SRT distribution in the 6° area-cue during the pre-training session; B) SRT distribution in the 6° area-cue during the post-training session; C) SRT distribution in the 10° area-cue during the pre-training session; and D) SRT distribution in the 10° area-cue during the post-training session. The dashed line marks the beginning of express latency range (75 ms); 0 ms marks the time of target onset.

Table 3-1: Mean distance (Δr) and standard deviation from the centre of the 6°
and 10° area-cues.

Subject	Session	Δr (S.D.) of 6° area	Δr (S.D.) of 10° area
1	pre	3.1 (1.7)	4.6 (2.5)
1	post	1.6 (1.1)	3.5 (1.6)
2	pre	4.6 (2.8)	7.1 (2.6)
2	post	2.3 (1.1)	2.8 (1.4)
3	pre	2.5 (1.9)	4.3 (2.6)
3	post	1.8 (1.1)	3.3 (2.2)
4	pre	2.6 (1.6)	4.4 (2.7)
4	post	2.02 (1.6)	3.3 (1.8)
5	pre	3.2 (1.6)	5.4 (2.8)
5	post	6.7 (3.8)	5.4 (3.5)

Table 3-2: Relative distance of the average saccade endpoint/retinal activity from
the centre-point of the area-cue in the visual and collicular planes.

Area Cue	Retinal distance (%)	Collicular distance (%)	Factor difference
6 deg	36.70	20.91	1.8
10 deg	35.78	22.08	1.6
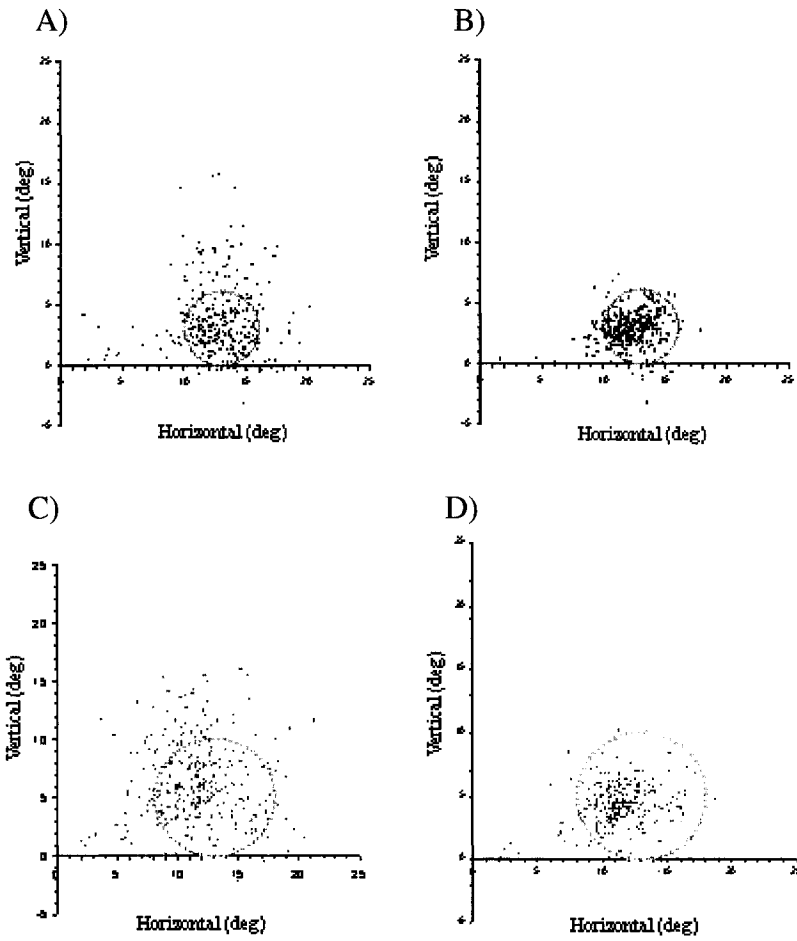
Figure 3-2: The final-eye positions of the 1st saccades on the pre-training and post-training sessions for 6° and 10° area-cues across all participants (excluding subject 5). A) 6° pre-training; B) 6° post-training; C) 10° pre-training; and D) 10° post-training.
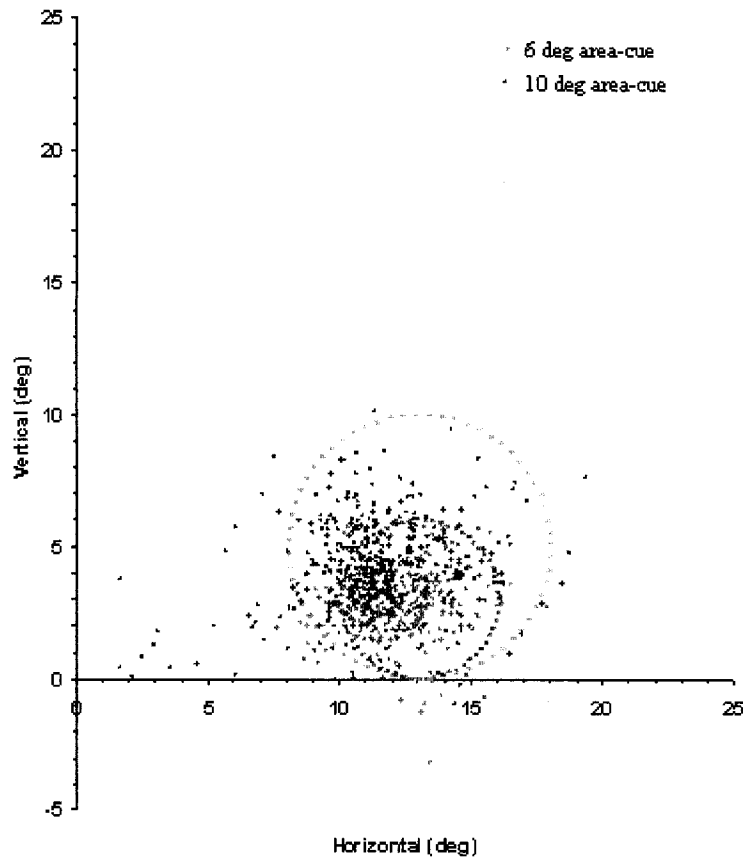
Figure 3-3: The areas of concentrations of the final-eye positions within 6° and 10° area-cues during post-training session.
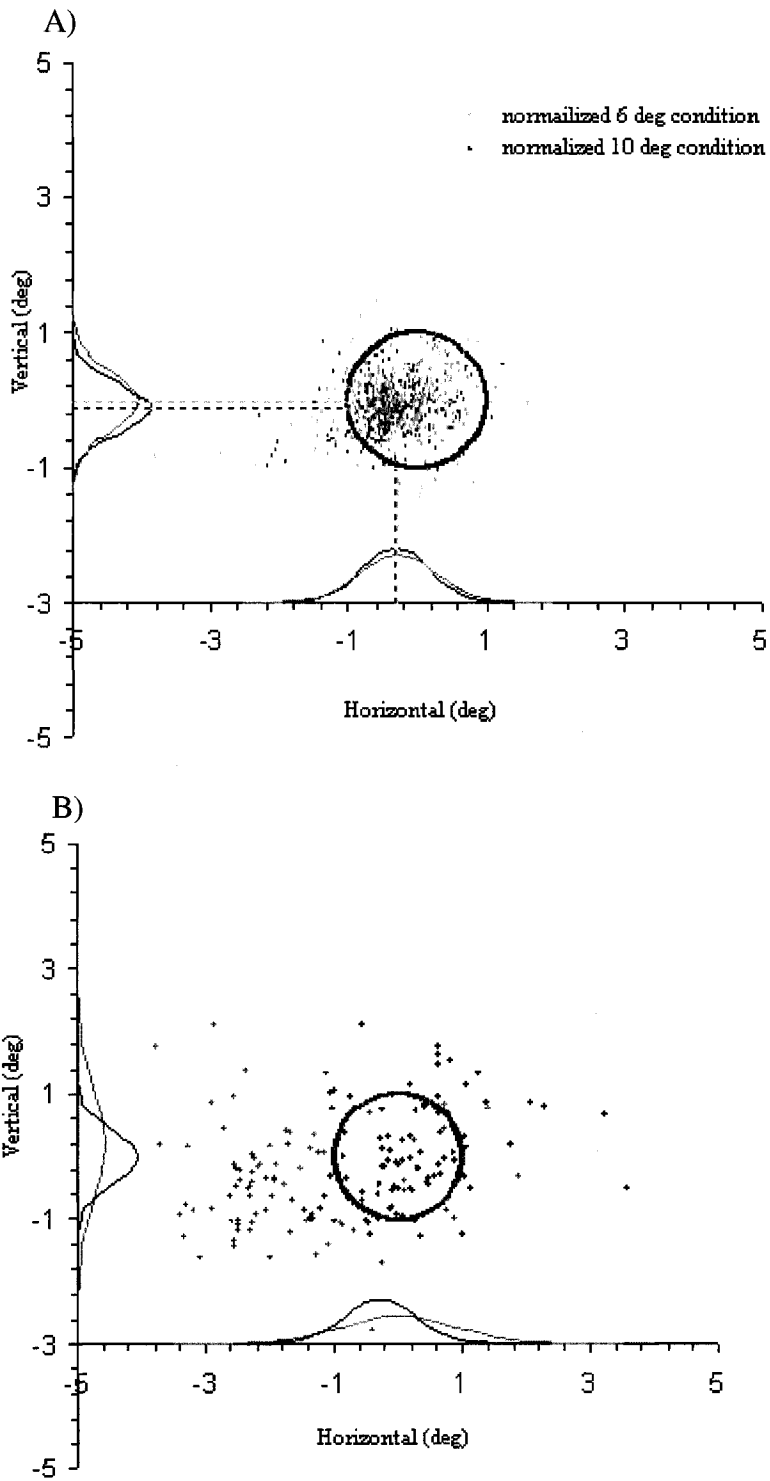
Figure 3-4: The areas of concentrations of the final-eye positions within the "normalized" 6° and 10° area-cues. A) all of the participants, excluding subject 5; B) Subject 5.
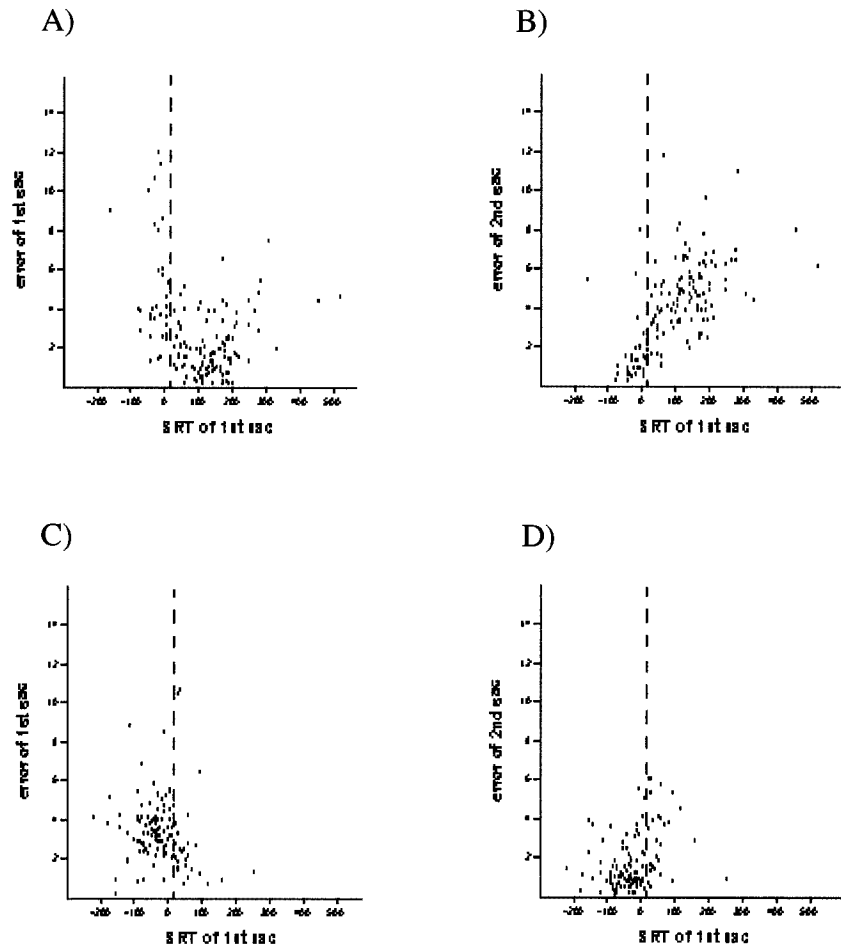
Figure 3-5: Error in the 6° area-cue condition of the 1st (A,C) or 2nd saccade (B,D) by the SRT of the 1st saccade during the pre- (A,B) or post-training session (C,D).
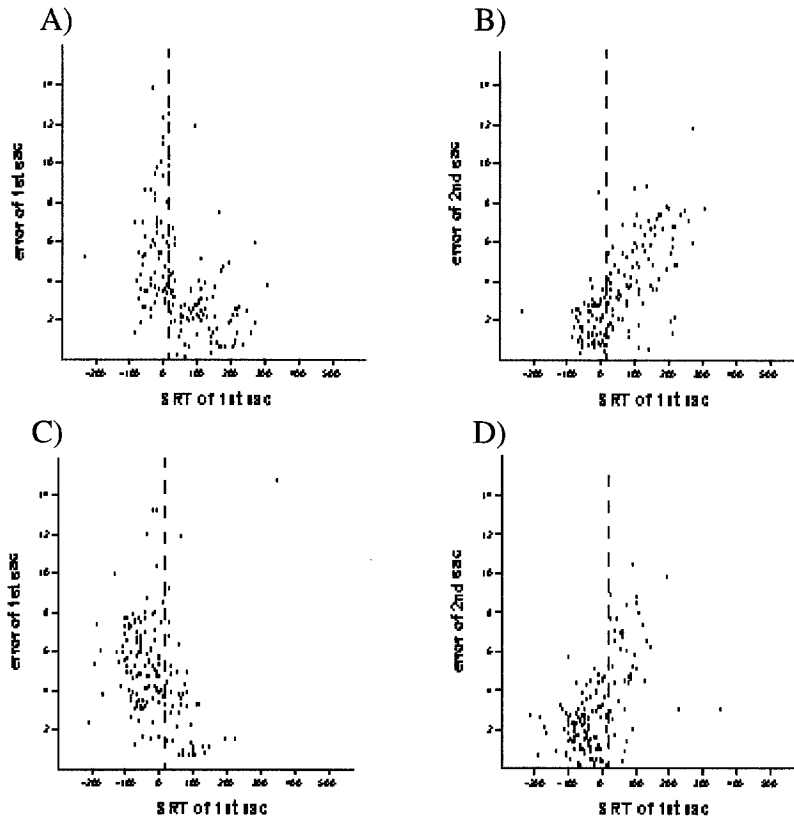
Figure 3-6: Error in the 10° area-cue condition of the 1st (A,C) or 2nd saccade (B,D) by the SRT of the 1st saccade during the pre- (A,B) or post-training session (C,D).

A)

B)
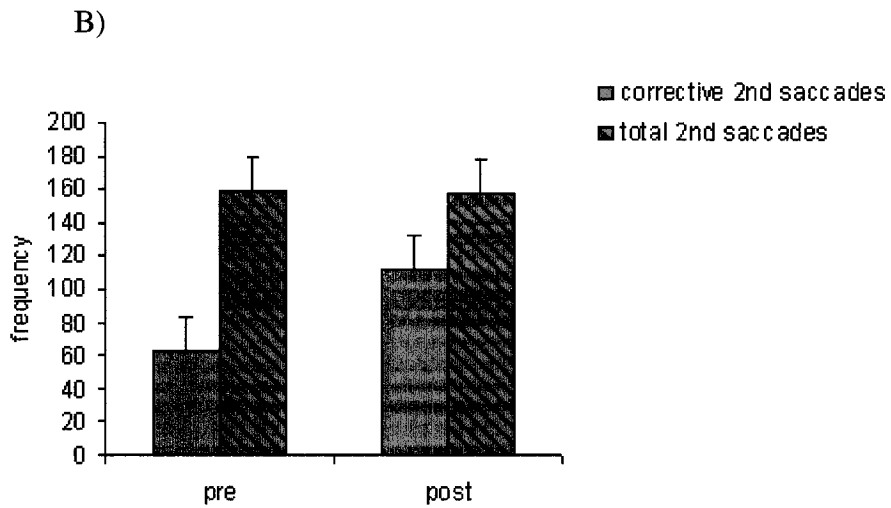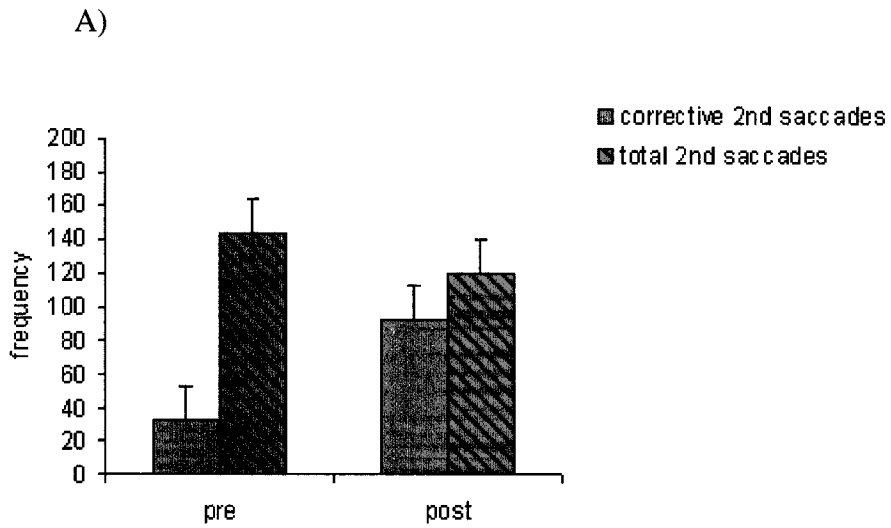
Figure 3-7: The proportions of the amount of secondary corrective saccades to the total amount of secondary saccades during the pre- versus-post-training sessions in the 6° area-cue (A) and the 10° area-cue (B) conditions.
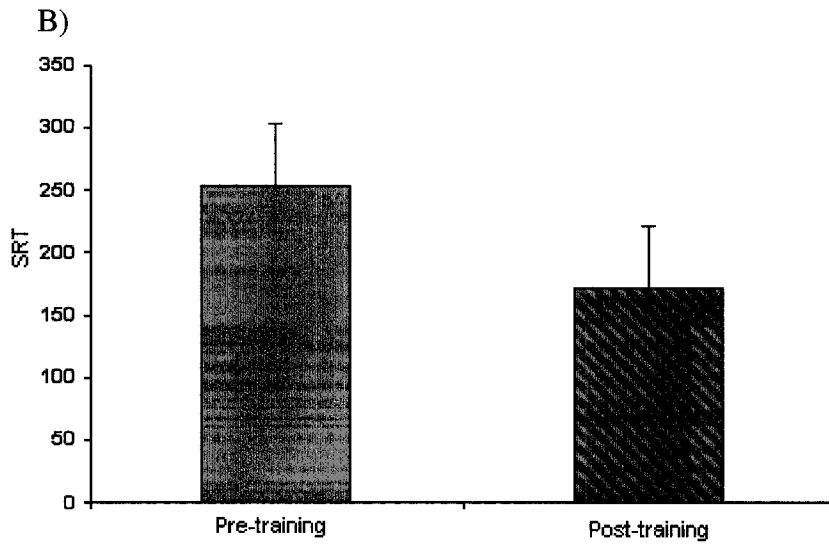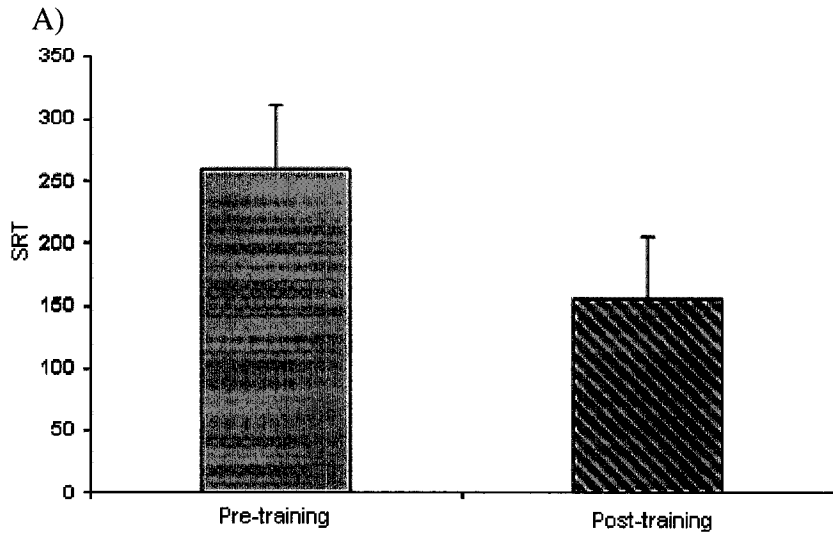
Figure 3-8: Overall time to target in 6° area-cue (A) and the 10° area-cue (B) conditions.

A)

B)
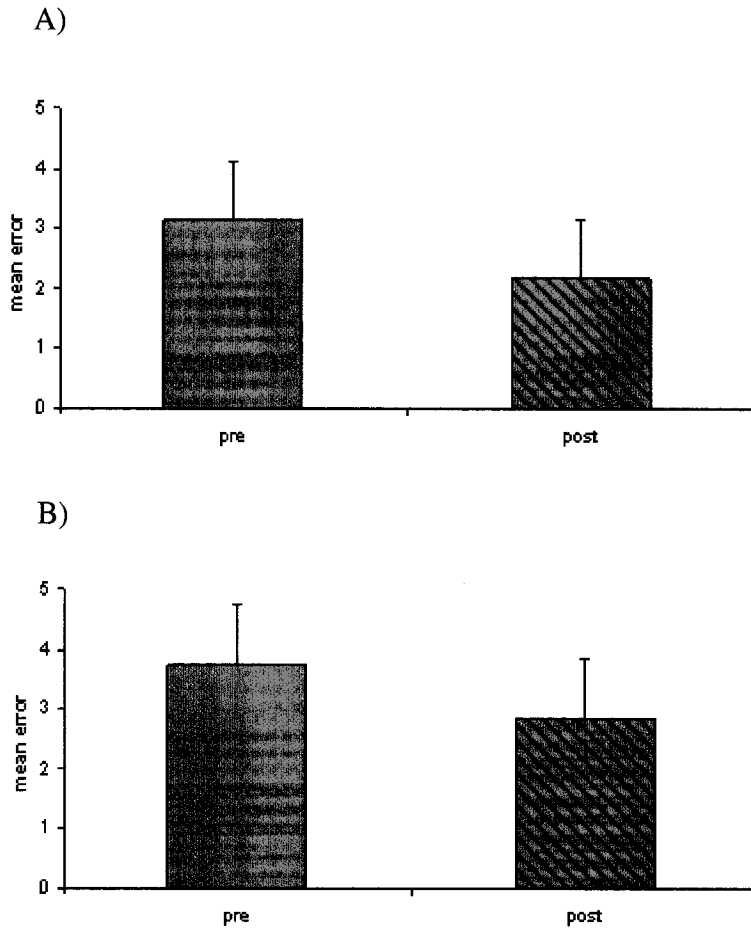
Figure 3-9: Overall error to target in 6° area-cue (A) and the 10° area-cue (B) conditions.
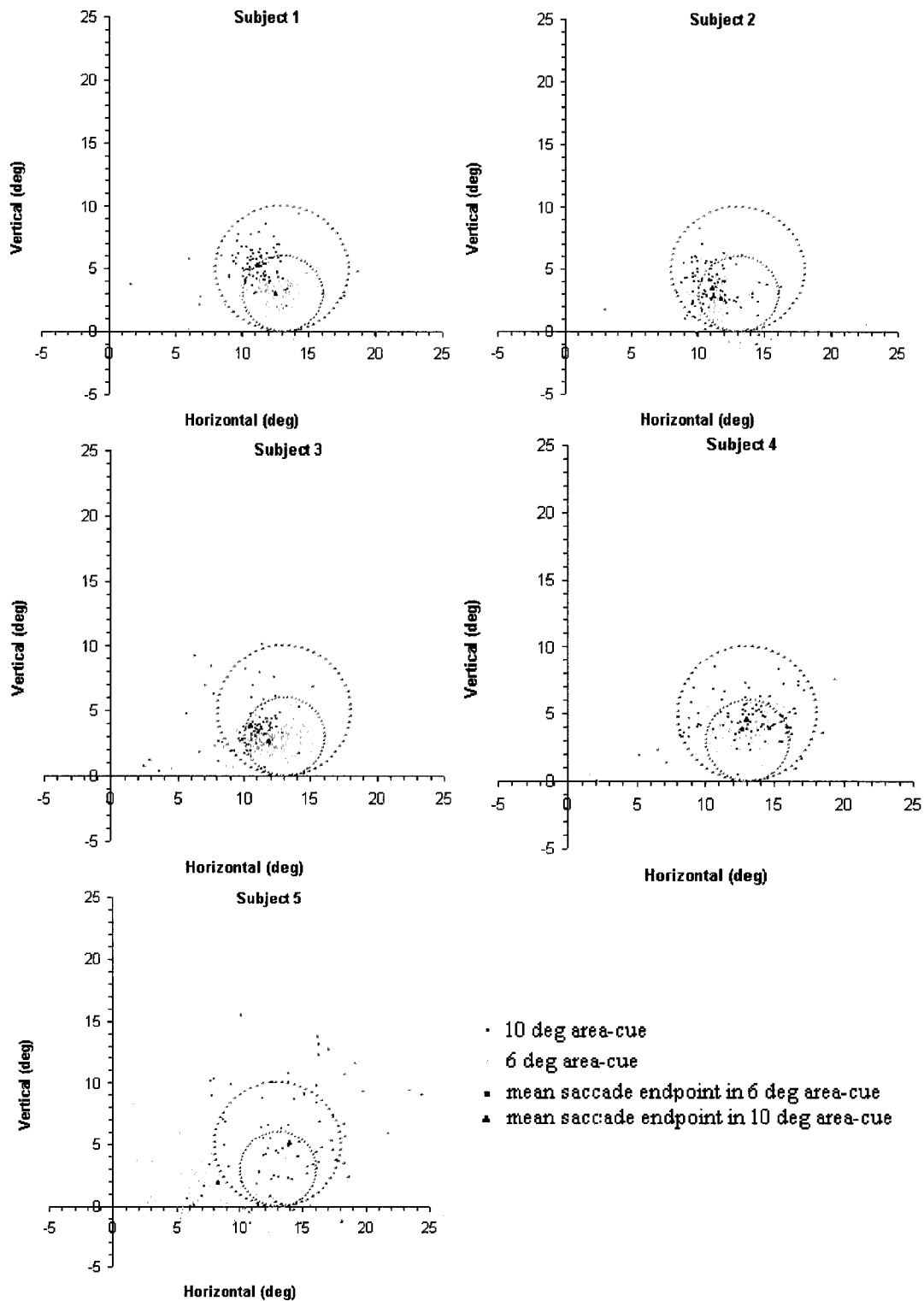
Figure 3-10: 1st saccade endpoint concentrations of individual participants for the 6° and 10° area-cues on the post-training session.
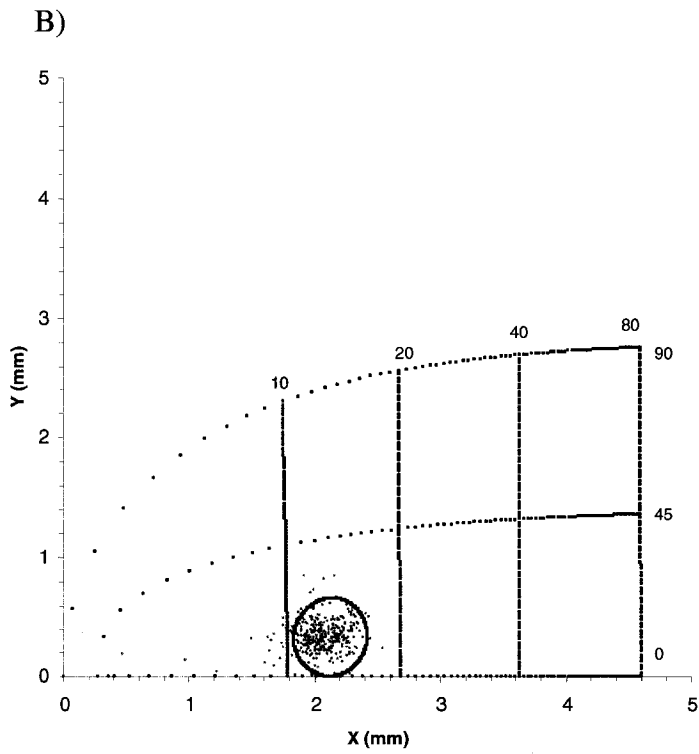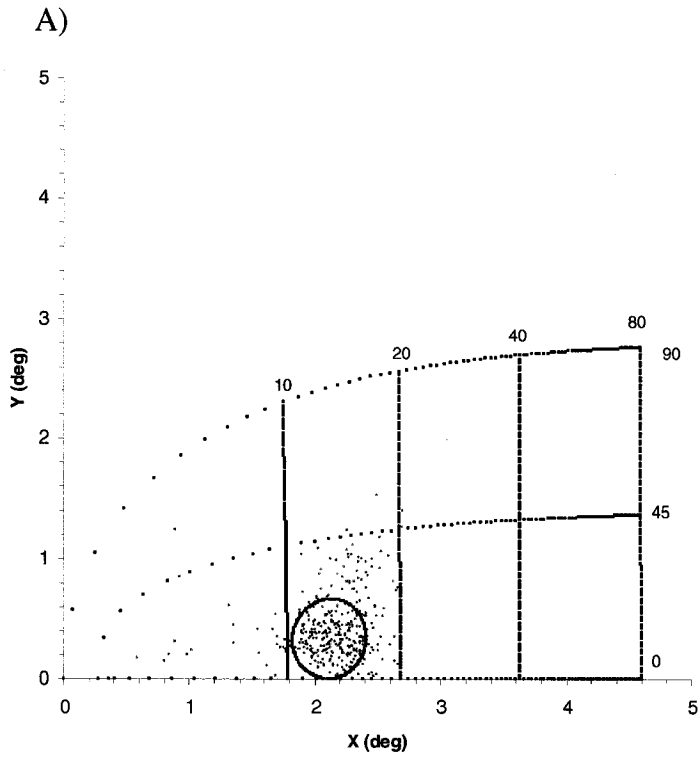
Figure 3-11: Collicular representations of the retinotopic coordinates of the initial saccade endpoints in the 6° area-cue condition. A) pre-training, B) post-training.
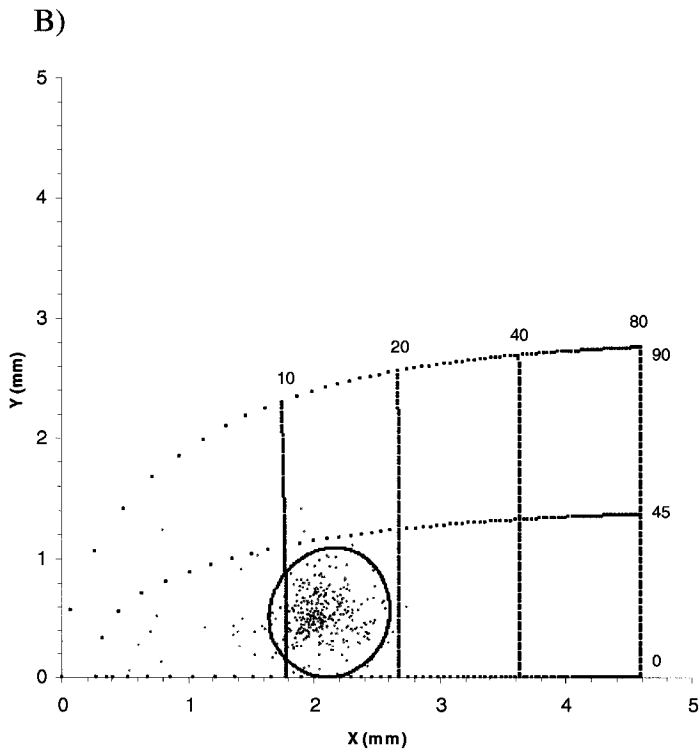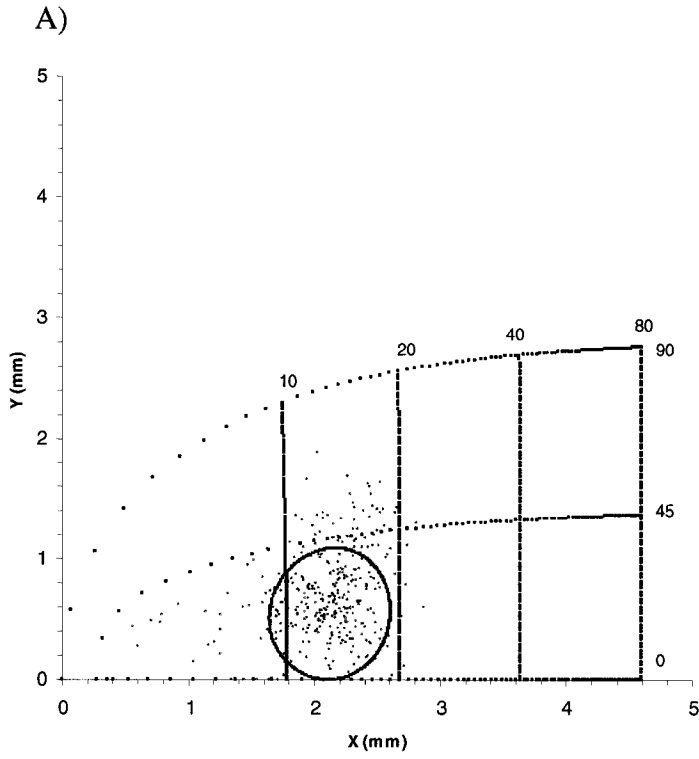
Figure 3-12: Collicular representations of the retinotopic coordinates of the initial saccade endpoints in the 10° area-cue condition. A) pre-training, B) post-training.

· Centre
· Average saccade endpoint/collicular activity
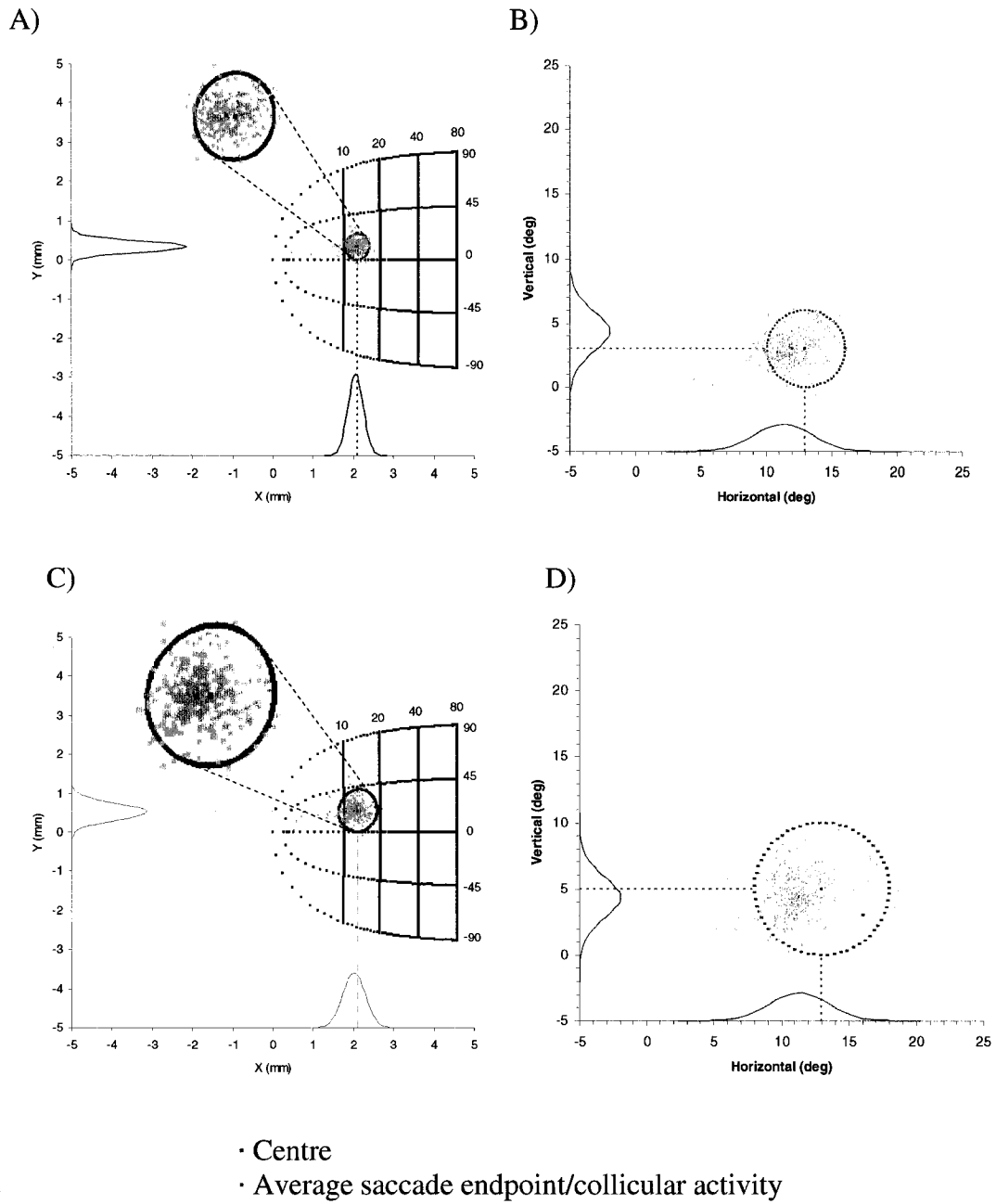
Figure 3-13: Visual and collicular representations of the initial saccade endpoints in the post-training session. A) collicular representation of the 6° area-cue condition, B) visual representation of the 6° area-cue condition, C) collicular representation of the 10° area-cue condition, D) visual representation of the 10° area-cue condition.

Collicular Plane

distance of 20% away from the center

distance of 25% away from the center

distance of 30% away from the center

distance of 40% away from the center

Visual Plane

distance of 20% away from the center

distance of 25% away from the center

distance of 30% away from the center

distance of 40% away from the center

Figure 3-14: Saccade endpoint distribution in the collicular and visual planes in the 6° area-cue condition.

Chapter 4: Discussion

4.1. Summary of general findings

The results of our study produced several clear outcomes. First, we have shown that for human subjects, training to attend to an area-cue of a certain size resulted in the production of almost exclusively anticipatory saccades. Second, the anticipatory saccades produced after training are different from the anticipatory saccades produced before training, in that they are spatially selective and occur within a time range most favourable for being followed by corrective saccades. Third, we found that training-related saccades were generated towards a preferred region within the cued area, which is located near its centre, consistent with the "global effect". Fourth, our findings show that, even though no training to the 10° area-cue ever took place, the participants generated the majority of the initial saccades in the anticipatory latency range towards the preferred default region, within the 10° area as well. Finally, similar to saccades generated within the 6° area, the region of the landing positions of the initial saccades was in close proximity to the centre of the 10° area, suggesting that training dependent "global effect" is transferable to larger areas.

4.2. Effects of training on the initial saccades

Our finding that training results in the increase of anticipatory saccades is in agreement with the study conducted by Evdokimidis *et al.* (1992). In their experiment, researchers presented the target either randomly to the left or to the right of the FP at an eccentricity of 8°, or always at a constant location on one side

for 30 consecutive trials. The time of the target's presentation was signalled by the extinction of the FP. Therefore, both the location and the time of target appearance were known in advance (FP duration was constant across trials). Their results showed a mono-modal distribution of SRT, with the peak at 0ms with respect to target onset. Also, when the target location was kept constant, the percentage of anticipatory saccades was significantly higher than when it was randomised between the left and right visual fields (57% vs. 3%, respectively) (Evdokimidis *et al.*, 1992).

In our study, the target's position was partially predictable, as the area in space and its location in the top quadrant of the right visual field were known, but the specific target location within the area was not. These factors alone were sufficient to result in a multimodal distribution of SRT during the pre-training session, with saccades being produced not only in the regular range, but also both in the anticipatory and express latency ranges. However, after training, practically all of the saccades were produced in the anticipatory range, similar to Evdokimidis's *et al.* (1992) findings, even though the precise time and location of the target appearance were not known in advance. Thus, it appears that training was the critical factor, as training enhanced the predictive value of the area-cue to the same level as if the target locations were certain (Findlay, 1980; Dorris and Munoz, 1998; Clohessy *et al.*, 2001), and resulted in the generation of predominantly anticipatory saccades. Additionally, there was no speed-accuracy trade off, as there was no overall error increase after training.

Nonetheless, our results are in disagreement with those obtained from some other animal and human studies. For example, Paré and Munoz (1996) found that in rhesus monkeys, training to attend to a particular target position resulted in the increase of express saccade generation toward the trained target location. They reported that only a very small amount of anticipatory saccades was produced throughout the entire set of the experiments. However, the animals in their study were not given a reward if they could not accurately get on target, and the non-rewarded trials were discarded from the analysis. It is possible that, to maximize their chances of getting the reward, monkeys would wait until the target would appear in order for the saccade to be accurate. Therefore, the discrepancy between the results found in Paré and Munoz's (1996) study and our findings might be due to the fact that monkeys were actually indirectly trained to not produce anticipatory saccades.

Similarly, Fischer and Ramsperger (1986) showed that in human subjects, training resulted in an increased amount of express saccades, while the number of anticipatory and regular saccades significantly decreased. However, in their experiment, subjects were given a trial-by-trial immediate feedback on the latency of their saccades, a procedure known to increase the likelihood of express saccade generation (Kingstone and Klein, 1993). Moreover, such trial-by-trial feedback, not unlike the reward system used in the animal studies, might discourage production of anticipatory saccades. Since we wanted to observe the natural progression of training effects on visuo-oculomotor perception, no such performance-related feedback was given to any of the participants in our study.

We believe that the absence of the reward/feedback component, which is representative of a natural setting, could have contributed to the difference in the results obtained in our study.

Lastly, the results of our study provide evidence that training resulted in the generation of predictive saccades. While, technically, the experimental paradigm was designed to elicit volitional saccades, this type of eye movement was produced only during the pre-training session, characterized by the longer overall latencies. Consequently, it appears that the repetitive presentation (training) of the targets within the same area elevates the predictive value of the area-cue and results in the generation of predictive saccades, characterized by their anticipatory latencies. Therefore, our results suggest that training to attend to the cued area compensates for the target's location uncertainty, and leads to the occurrence of predictive saccades similar to those generated when the exact location and time of onset of the target are known in advance (Broerse *et al.*, 2001; Evdokimidis *et al.*, 1992; Findlay, 1980).

4.3. Gaze-attraction position

Our results are in agreement with He and Kowler's (1989) suggestion that past history and expected future location of the target influence saccadic programming. Particularly in our study, as a result of training to attend to the 6° area, the majority of the initial saccades were generated inside that trained area. Moreover, training resulted in a much smaller dispersion of the saccade endpoints, compared to the highly dispersed landing positions of saccades before training.

Because, training resulted in the generation of saccades mostly in the anticipatory range, the initial saccades were triggered before the information about target location could be processed. Mainly, these saccades were generated towards a distinct location in the cued-area that was different for each participant. Particularly, as Fig. 3-10 illustrates, after training only subject 1 landed initial saccades around the centre of the circle; the rest of the participants' preferred gaze-attraction position was located at the less central location, although still near the centre.

Our finding of the preferred gaze-attraction position being located at a slightly less eccentric location with respect to the centre of the cued area, than predicted by the classic "global effect" (Findlay,1982), is in agreement with the results obtained in the Coëffé and O'Regan's (1987) study. These researchers found that the participants tend to aim at the 3^d or 4th letter in the nine letter string, which does not land exactly in the middle of the letter string (the middle being between the 4th and 5th letters). The entire range of target eccentricities was from 3.5° to 10°, which is comparable to the size of our area-cue used in the training. In their study, participants aimed 1° to 2° away from the medial distance in the letter string (Coëffé and O'Regan, 1987), which is comparable to a range of 1.6°-2.3° in our study, for the 6° area-cue. So, our results are in agreement with those found in Coëffe and O'Regan's experiment, in that the preferred eye landing position is located at a less central region than the classic "global effect" would predict.

In a different experiment, Coëffé and O'Regan (1987) showed that when the response time is delayed, and therefore sufficient amount of time is given to

process information about the target's location, the accuracy of saccades is increased and the "global effect" is diminished. Similarly, in our experiment, during the pre-training session, most of the saccades were generated in the non-anticipatory range and therefore a sufficient amount of time elapsed for saccades to be target-driven. As a result, area-cue presentation failed to produce the "global effect". Contrary to the pre-training session, the initial anticipatory saccades in the post-training session were triggered before the information about target location could be processed, and therefore they were under the influence of the "global effect", similar to that which was found in Coëffé and O'Regan's (1987) study.

Taken together, the reduction of the distance from the centre of the cued area and the reduced dispersion of the saccade endpoints provide evidence for the occurrence of the "global effect" as a result of training (Coëffé and O'Regan, 1987; Findlay, 1982).

4.4. Transfer of the "global effect" to a larger area

Our findings show that, even though no training to the 10° area-cue ever took place, participants generated the majority of their initial saccades in the anticipatory latency range (except for the participant who showed no learning effects in the 6° condition). Moreover, similar to the saccades generated within the 6° area, the initial saccades within the 10° area were generated towards the preferred default region, which was in a close proximity to the centre of the 10° area, but spatially distinct from that generated in the 6° area.

The "global effect" found in the 10° area was a result of the spatial transformation of the 6° area's training-related "global effect", as is evident from

the finding that when both 6° and 10° areas were scaled to a circle with a radius of 1, the two resulting default regions completely overlapped (see Figure 3-4 (A)). Hence, the training dependent "global effect" is transferable to larger areas. Therefore, it appears that training-related spatial transformation takes into account the overall extent of the area of target presentation, and the saccade landing positions are calculated relative to the boundaries of the cued area. These results are consistent with the shape-based localization model proposed by McGowan, Kowler, Sharma, and Chubb (1998). This model implies that the computation of the centre of gravity takes into account the overall extent of the attended shape.

4.5. Neuronal circuitry

Although, the present study was behavioural in nature, the results shed some light on the possible changes in neuronal activity as a result of training to attend to a cued area.

This experiment was designed to elicit volitional saccades. Specifically, reflexive saccades towards a peripheral area-cue had to be initially suppressed for a delay period, and then be generated towards a briefly flashed target in the periphery. In the pre-training session, the resulting distribution of SRT (see Fig. 3-1) shows a majority of saccades being generated in the non-anticipatory latency range, which provides evidence that a large amount of these saccades were intentional eye movements. Furthermore, our participants also produced a significant amount of reflexive saccades, represented by the eye movements in the express latency. On the other hand, after training, saccade latency distribution was heavily shifted towards the anticipatory saccade range, indicating that training to

make saccades to targets presented at random locations within the cued 6° area, resulted in predictive saccade generation. Therefore, our results indicate that different brain circuitries were recruited during the pre- and post-training sessions.

4.5.1. Neural control during the pre-training session

Based on the anatomical and electrophysiological evidence reviewed below, it appears that the main brain areas involved in the processing of the visual information during the pre-training stage of the experiment are the FEF, SEF, and SC (Abel and Douglas, 2006; Neggers *et al.*, 2005; Spengler *et al.*, 2006; Mort *et al.*, 2003; Broerse *et al.*, 2001; Gaymard *et al.*, 1998). Neggers *et al.* (2005) conducted an fMRI study using a "gap" paradigm in order to investigate the role of the SC and frontal areas (FEF and SEF) in oculomotor control in humans. Similar to animal studies, the results of their study showed a large activation of the SC when the fixation point was removed and a short delay was introduced prior to the presentation of the target. Importantly, they found a negative correlation between the activity level in the SC and the subsequent saccadic latencies. Conversely, the activity in the frontal cortical areas, the FEF and SEF, was positively correlated with the saccadic latencies. The researchers concluded that in humans (similarly to animals) the cortical areas FEF and SEF send inhibitory projections to the SC, thereby suppressing generation of reflexive saccades (Neggers *et al.*, 2005). Experimental evidence suggests that the FEF and SEF extend projections to the SC through the basal ganglia, involving substantia nigra pars reticulata (Neggers *et al.*, 2005; Scudder *et al.*, 2002), thereby inhibiting its activity (Hikosaka and Wurtz, 1983). It follows that the activity in

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the SC is closely related to the generation of reflexive saccades (Neggers *et al.*, 2005). Therefore, our finding of express saccade generation during the pre-training session is consistent with the theory that presentation of the area-cue resulted in saccade generation via subcortical circuitry, without requiring the use of cortical areas (Paré and Munoz, 1996; Schiller *et al.*, 1987).

4.5.2. Neural control during the post-training session

As was mentioned earlier (see section 1.4.3.) studies on obsessive-compulsive and Parkinson's disorders, electrophysiological recordings, human EEG recordings, and imaging studies demonstrate the involvement of the FEF, the SEF, the basal ganglia, and the SC in production of predictive saccades. (Spengler *et al.*, 2006; Coe *et al.*, 2002; Broerse *et al.*, 2001; Gaymard *et al.*, 1998; O'Sullivan *et al.*, 1997; Evdokimidis *et al.*, 1992).

It has been shown that the activity in the SEF is mainly correlated with the programming of saccades towards targets that are presented in memorized sequences (Gaymard *et al.*, 1998). In the present experiment, the targets were presented always at random locations and in no specific sequence. Therefore, the involvement of the SEF in the generation of training related predictive saccades may not account for the post-training outcome of our study.

It is reasonable to assume that the main areas involved in the generation of predictive saccades, as a consequence of training to attend to the 6° area, are the FEF and the SC. It is known that the FEF has both direct projections to the brainstem oculomotor saccades generator and indirect projections via the SC (Schiller *et al.*, 1980). However, a recent study conducted by Hanes and Wurtz

(2001) demonstrated the inability of the FEF to generate saccades upon inactivation of the SC; particularly when the inactivated SC region represented eye movements of the same vector as the saccades generated from the FEF. Therefore, these results provide evidence that the signal from the FEF to the brainstem saccade generator has to be relayed via the SC (Hanes and Wurtz, 2001).

Furthermore, Dorris and Munoz (1998) demonstrated behavioural correlate to the heightened pre-target activity of motor responses in the intermediate layers of the SC, i.e. they showed an inverse relationship between pre-target neuronal activity and subsequent saccadic latency. These researchers found that when the target location was highly predictable, the pre-target neuronal activity was especially heightened. This phenomenon has been explained by proposing that training to a specific location causes elevated motor preparation of neurons in the intermediate layers of the SC, thereby lowering the threshold for neuronal response, which in turn leads to subsequent reduction of saccadic reaction time (SRT) (Paré and Munoz, 1996).

Based on the aforementioned evidence, we propose that training to attend to a cued 6° area, positioned in fixed spatial coordinates, within which targets appear at random locations (i.e. no learned sequence), leads to production of predictive saccades due to changes in neuronal activity in the FEF and the SC. However, our results suggest that it is unlikely that motor preparation activity can occur for saccades to multiple locations in the area-cue. Rather motor preparation favours a single saccade vector to the default position inside the cued area.

4.6. Topographical representation of the saccade endpoints in the SC

Our finding that training resulted in the saccade endpoints being concentrated near the centre of the cued area (both 6° and 10°), brings about a question as to why the preferred region is positioned at a point less eccentric than the centre of the area-cue. Coëffé and O'Regan (1987) proposed that this might be because the calculation of the centre of gravity is done not based on the retinal representation of the attended configuration, but on its cerebral representation. Similarly, we propose that the centre of the attended cued area was calculated based on its representation in the SC.

The collicular representation of the area cue was computed because it appears to be the final structure in the neuronal chain of the visuo-oculomotor information processing before the visual signal is sent to the brainstem saccade generator (see section 4.5.2). In addition, the SC's anatomical characteristics make it a perfect structure to be responsible for the "global effect" (Vitu, Lancelin, Jean, and Fariolli, 2006; McGowan et al., 1998; Lee, Rohrer, and Sparks, 1988). Specifically, the neurons in the SC have large well-defined receptive fields that code for retinal coordinates of the visual stimuli presented in the contralateral visual hemifield (Munoz et al., 2000). Moreover, these sensory topographical maps are closely linked to the motor maps that code for direction of gaze in space associated with the presentation of specific visual (or other sensory modality) stimuli (King, 2004). Therefore, each point on the motor map codes for a specific vector in retinal coordinates. Specifically, stimuli presented in the foveal locations are coded in the rostral part of the SC, whereas stimuli displayed

in the peripheral visual field are coded in the contralateral caudal regions of the SC (King, 2004; Munoz *et al.*, 2000). The metrics of a single saccade are coded by a population of neighbouring cells, rather than a single neuron, due to the overlap in the receptive fields of the SC neurons (Munoz *et al.*, 2000; McIlwain, 1991; Lee *et al.*, 1988). Finally, the neurons in the superficial layers receive inputs from retinal ganglion cells that are only involved in low acuity vision (Lomber, 2002; Munoz *et al.*, 2000; Morris, Ohman, and Dolan, 1999), as evidenced by the SC processing strictly low spatial frequency information, such as global feature discrimination (Vuilleumier, Armony, Driver, and Dolan, 2003; Lomber, 2002).

Our results showed a non-circular collicular representation of the circular area-cues, where the shape of the 10° area seems more distorted than that of the 6° area (see Fig. 3-11 and 3-12). These distortions are due to the logarithmic representation of the visual field in the SC map (Optican, 1995).

Importantly, Fig. 3-11 and Fig. 3-12 demonstrate how the activity in the SC would be modulated by training. Specifically, there is an enhancement of the activity within a small area of the collicular map, compared to the highly dispersed activation in the pre-training session in both the 6° area-cue and the 10° area-cue conditions. Also, on average, the collicular activity was closer to the center of the collicular shape than its corresponding visual representation by a factor of nearly two (Fig. 3-13). Finally, the saccade endpoints were more evenly distributed around the central region of the 6° area-cue in collicular coordinates than in retinal coordinates, for the 6° area-cue. However, there was no difference between saccade endpoint and collicular activity distributions around the centre in

the 10° area-cue condition (see section 3.8; Fig. 3-14). Therefore, training related "global effect" might have been more pronounced in the trained area (6° area-cue) at the level of the SC.

The "oculomotor training hypothesis" states that training to a specific location causes elevated motor preparation of the neurons coding for the trained target coordinates, thereby lowering the threshold for neuronal response (Paré and Munoz, 1996). Moreover, another hypothesis states that the saccade metrics are determined by a weighted average of the signals from the entire active population of neurons within the attended region (Vitu *et al.*, 2006; McGowan *et al.*, 1998; Lee *et al.*, 1988). Accordingly, we can make some predictions about neuronal activity in the SC. First, during pre-training sessions, saccade metrics would code eye movements towards the actual individual targets, accounting for the scattered collicular activation. Second, training to attend to a cued area results in elevated motor preparation in SC neurons, around the central region of the collicular representation of the area-cue. Third, because the training effect increases preparedness to the entire cued area, a larger population of neurons would be active than there would be for a single target. Finally, the metrics of post-training initial saccades would be biased by a weighted average of the entire active population (Lee *et al.*, 1988), which in our experiment correspond closely to the centre of the collicular configuration.

However, this representation of saccade endpoints in the SC is based on the assumption that there is a direct relationship between the extrinsic locations of saccade endpoints and the intrinsic neuronal activity in the SC. It might be the

case that the metrics of the resulting eye movements undergo further transformation at the oculomotor relay stations downstream of the SC, such as premotor saccade generation circuitry in the mesencephalic, pontine, and medullary reticular formations, as well as the fastigial oculomotor region in the cerebellum that send efferent projections to the saccade burst generator, as well as reciprocally connected with the SC (Scudder *et al.*, 2002).

Therefore, our spatial coding of the saccade endpoints on the collicular map is perhaps a rough and global estimation and should only be considered as a template for future neurophysiological studies.

4.7. Effects of training on the secondary saccades

Even though our study was not specifically designed to measure corrective saccade generation, we performed the analyses of the secondary saccades in order to detect possible training effects manifested through multiple saccade generation.

Our finding that the percentage of secondary saccades did not increase after training (Fig. 3-7), despite a large increase in the production of anticipatory saccades, might seem to be counterintuitive. However, Prablanc and Jeannerod (1975) proposed that the occurrence of the corrective saccades is dependent upon retinal re-afferent signal. Specifically, they found that when the stimulus was presented briefly and never reappeared again, almost no corrective saccades occurred. However, when the stimulus reappeared at the same location after a delay of 50 ms or more, systematic generation of corrective saccades was observed (Prablanc and Jeannerod, 1975). Similarly, Prablanc, Masse, and Echallier, (1978) found that when no visual feedback was given, of the 86% of

initial saccades that were inaccurate, only 28% were followed by corrective saccades. Similarly, in our experiment the target was briefly flashed for 69 ms, a time period too short for visual feedback.

Nevertheless, our findings indicate that the nature of the secondary saccades changed as a result of training. Specifically, the majority of training related initial anticipatory saccades occurred at a time window that allowed the target to be visible during the execution of the second saccade, which ensured its corrective quality. Mainly, only those initial anticipatory saccades that fell into the latency range of less than 20 ms with respect to the target onset were followed by a corrective saccade, i.e. the error of the initial saccade was significantly reduced. Thus, it appears that while the amount of second saccades following the initial anticipatory saccades generated before and after training did not change, a significantly larger percentage of them led to the reduction of error after training. Consequently, training to attend to a cued area resulted not only in the generation of a spatially specific initial anticipatory saccade, but also increased the likelihood of corrective saccades for initial saccades occurring within a specific time window.

Our results seem to be in disagreement with those reported by Findlay (1980). Indeed, Findlay (1980) reported that 50-70% of anticipatory saccades were followed by secondary saccades. However, in that experiment the stimulus remained stationary at any given position for an average of 500 ms, and therefore was visible during the saccade execution, providing the retinal re-afferent signal necessary for corrective saccade generation (Prablanc and Jeannerod, 1975). Also,

the stimulus was randomly moved in a series of steps between three positions in a sequence of centre-left/right-centre-left/right (Findlay, 1982). Hence, the error produced by the anticipatory saccades was measured in both distance and direction from the stimulus. Therefore, a lot of the secondary saccades could have been correcting the directional error, such as jumping to the right of the centre rather than to the left of the centre, a distinction important to the differences with our results. In our experiment, the direction of the target's presentation was always kept constant and therefore the error was measured only in terms of the distance of saccade endpoint from the location of the target. Therefore, due to methodological differences in our experiments, the quantity of corrective saccades can not be readily compared.

4.8. Overall training effects: 1st + 2nd saccades

The results obtained in the present study indicate that with training, participants developed a search strategy, thereby selecting a default position within the cued area from which corrective saccades were subsequently made. Moreover, the development of this detection strategy proved to be of some benefit, indicated by the reduction of the overall time taken to get to the target. This benefit was more apparent with respect to targets presented in the 10° area than 6° area. In addition, there was no speed-accuracy trade off, as indicated by the same overall error to target, before and after training.

4.9. Training effect

Our findings indicate that human subjects might have individual variability in the required duration of training, as one of the participants (subject 5) did not reach the same results despite undergoing as much training as other participants. Specifically, contrary to the results associated with training from the previous studies (Broerse et al., 2001; Evdokimidis et al., 1992; Findlay, 1980) and the results obtained in the present experiment from the rest of the participants, this individual: (a) did not produce more anticipatory saccades after training, (b) did not concentrate his saccade endpoints inside either of the area-cues, (c) did not decrease his mean distance from the centre of the area-cue in either conditions (see Table 3-1), and (d) did not show an increased overlap in the concentration of saccade endpoints of the "normalized" 6° and 10° area-cues. This participant performed similarly to others during the pre-training session, thus, differences are unlikely to be due to an exaggeration of initial differences, and are more likely due to a lack of sufficient training.

4.10. Conclusion

Results obtained in this study shed more light on training related oculomotor preparation of saccades in human subjects. Specifically, our data show that pre-target oculomotor preparation can be extended to small areas and not just to a single target location (Evdokimidis et al., 1992; Fischer and Ramsperger, 1986). Moreover, our findings provide some evidence of training-related plasticity in the SC resulting from training to attend to an area. Furthermore, it appears that the oculomotor system takes into consideration the

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dimension of the entire attended area when calculating the metrics of the training related initial saccades.

Herein, we provide evidence that anticipatory saccades are perhaps a lot more meaningful than previous oculomotor research suggests. Specifically, the distinction between pre- and-post-training anticipatory saccades, such as spatial and temporal selectivity, indicates that training related changes could be measured at much earlier latencies than the express range. Further investigation of training- and non- training related anticipations might contribute to our understanding of perceptual learning.

References

1. Abel, L.A. and Douglas, J. (2006). Effects of age on latency and error generation in internally mediated saccades. *Neurobiology of Aging*, 1-11.

2. Bowman, E. M., Brown, V. J., Kertzman, C., Schwartz, U., and Robinson, D. L. (1993). Covert orienting of attention in macaques I. Effects of behavioural context. *Journal of Neurophysiology*, 70 (1): 431-443.

3. Bradley, D. R., Bradley, T. D., McGrath, S. G., and Cutcomb, S.D. (1979) Type I error rate of the chi square test of independence in r x c tables that have small expected frequencies. *Psychological Bulletin*, 86: 1200-1297.

4. Broerse, A., Crawford, T.J., and den Boer, J.A. (2001). Parsing cognition in schizophrenia using saccadic eye movements: a selective overview. *Neuropsychologia*, 39: 742-756.

5. Busatto, G.F., Zamignani, D.R., Buchpiguel, C.A., Garrido, G.E.J., Glabus, M.F., Rocha, E.T., Maia, A.F., Rosario-Campos, M.C., Castro, C.C., Furuie, S.S., Gutierrez, M.A., McGuire, P.K., and Miguel, E.C. (2000). A voxel-based investigation of regional cerebral blood flow abnormalities in obsessive-compulsive disorder using signal photon emission computed tomography (SPECT). *Psychiatry Research Neuroimaging Section 99*, 15-27.

6. Cavegn, D. and d'Ydewalle, G. (1996). Presaccadic attention allocation and express saccades. *Psychological Research (Historical Archive)*, 59 (3): 157 – 175.

7. Clark, J. J. (1999). Spatial attention and latencies of saccadic eye movements. *Vision Research*, 39: 585-602.

8. Clohessy, A. B., Posner, M. I., and Rothbart, M. K. (2001). Development of the functional visual field. *Acta Psychologica*, 106: 51-68.

9. Coe, B., Tomihara, K., Matsuzawa, M., and Hikosaka, O. (2002). Visual and anticipatory bias in three cortical eye fields of the monkey during an adaptive decision-making task. *The journal of Neuroscience*, 22 (12): 5081-5090.

10. Coëffé, C. and O'Regan, J. K. (1987). Reducing the influence of non-target stimuli on saccadic accuracy: predictability and latency effects. *Vision Research*, 27 (2): 227-240.

11. Corbetta, M. (1998). Frontoparietal cortical networks for directing attention and the eye to visual locations: Identical, independent, or overlapping neural systems? *Proceedings of the National Academy of Sciences of the United States of America*, 95: 831-838.

12. Dorris, M.C. and Munoz, D.P. (1995). A neural correlate for the gap effect on saccadic reaction time in monkey. *Journal of Neurophysiology*, 73: 2558-2562.

13. Dorris, M.C. and Munoz, D.P. (1998). Saccadic probability influences motor preparation signals and time to saccadic initiation. *The Journal of Neuroscience*, 18 (17): 7015-7026.

14. Dorris, M. C., Paré, M., and Munoz, D. P. (1997). Neuronal activity in monkey superior colliculus related to the initiation of saccadic eye movements. *The Journal of Neuroscience*, 17 (21): 8566-8579.

15. Edelman, J. A. and Keller, E. L. (1996). Dependence on target configuration of express saccade-related activity in the primate superior colliculus. *Journal of Neurophysiology*, 80: 1407-1426.

16. Evdokimidis, I., Mergner, T., and Lücking, C.H. (1992). Dependence of presaccadic cortical potentials on the type of saccadic eye movements. *Electroencephalography and clinical Neurophysiology*, 83: 179-191.

17. Fischer, B. and Boch, R. (1983). Saccadic eye movements after extremely short reaction times in the monkey. *Brain Research*, 260: 21-26.

18. Fischer, B., Boch, R., and Ramsperger, E. (1984). Express-saccades of the monkey: effect of daily training on probability of occurrence and reaction time. *Experimental Brain Research*, 55: 232-242.

19. Fischer, B. and Ramsperger, E. (1986). Human express saccades: effects of randomization and daily practice. *Experimental Brain research*, 64: 569-578.

20. Fischer, B. and Weber, H. (1998). Effects of pre-cues on voluntary and reflexive saccade generation. I. Anti-cues for pro-saccades. *Experimental Brain Research*, 120: 403-416.

21. Findlay, J.M. (1980). Spatial and temporal factors in the predictive generation of saccadic eye movements. *Vision Research*, 21: 347-354.

22. Findlay, J.M. (1982). Global visual processing for saccadic eye movements. *Vision Research*, 22: 1033-1045.

23. Gaymard, B., Ploner, C.J., Rivaud, S., Vermersch, A.I., and Pierrot-Deseilligny, C. (1998). Cortical control of saccades. *Experimental Brain Research*, 123: 159-163.

24. Gnadt, J.W., Bracewell,R.M., and Andersen, R.A. (1991). Sensorimotor transformation during eye movements to remembered visual targets. *Vision Research*, 31 (4): 693-715.

25. Grosbras, M.-H. and Pause, T. (2002). Transcranial magnetic stimulation of the human frontal-eye field: Effects on visual perception and attention. *Journal of Cognitive Neuroscience*, 14 (7): 1109-1120.

26. Hanes, D.P. and Wurtz, R.H. (2001). Interaction of the frontal eye fields and superior colliculus for saccade generation. *The Journal of Neurophysiology*, 85 (2): 804-815.

27. Hikosaka, O., Takikawa, W., and Kawagoe, R. (2000). Role of basal ganglia in the control of purposive saccadic eye movements. *Physiological Reviews*, 80 (3): 953-978.

28. Hikosaka O, and Wurtz RH. (1983). Visual and oculomotor functions of monkey substantia nigra pars reticulata. IV. Relation of substantia nigra to superior colliculus. *Journal of Neurophysiology*, 49: 1285-301.

29. He, P. and Kowler, E. (1989). The role of location probability in the programming of saccades: Implications fro "centre-of-gravity" tendencies. *Vision Research*, 29 (9): 1165-1181.

30. Hopp, J. J. and Fuchs, A. F. (2004). The characteristics and neuronal substrate of saccadic eye movement plasticity. *Progress in Neurobiology*, 72: 27-53.

31. Ignashchenkova, A., Dicke, P. W., Haarmeier, T., and Their, P. (2003). Neuron-specific contribution of the superior colliculus to overt and covert shifts of attention. *Nature Neuroscience*, 7 (1): 56-64.

32. King, A. J. (2004). The superior colliculus. *Current Biology*, 14 (9): R335-R338.

33. Kingstone, A. and Klein, R.M. (1993). What are human express saccades? *Perception and Psychophysics*, 54 (2): 260-273.

34. Kurata, K. and Aizawa, H. (2004). Influences of motor instructions on the reaction times of saccadic eye movements. *Neuroscience Research*, 48: 447-455.

35. Kustov, A. A. and Robinson, D. L. (1996). Shared neural control of attentional shifts and eye movements. *Nature*, 384: 74-77.

36. Kusunoki, M., Gottlieb, J., and Goldberg, M.E. (2000). The lateral intraparietal area as a salience map: the representation of abrupt onset, stimulus motion, and task relevance. *Vision Research*, 40: 1459-1468.

37. Lee, C., Rohrer, W.H., and Sparks, D. L. (1988). Population coding of saccadic eye movements by neurons in the superior colliculus. *Nature*, 332: 357-360.

38. Lomber, S. G. (2002). Learning to see the trees before the forest: Reversible deactivation of the superior colliculus during learning of local and global visual features. *Proceedings of the National Academy of Sciences of the United States of America*, 99 (6): 4049-4054.

39. McGowan, J.W., Kowler, E., Sharma, A., and Chubb, C. (1998). Saccadic localization of random dot targets. *Vision Research*, 38 (6): 895-909.

40. McIlwain, J.T. (1991). Distributed spatial coding in the superior colliculus: a review. *Vision Neuroscience*, 6 (1): 3-13.

41. Moore, T. and Fallah, M. (2001). Control of eye movements and spatial attention. *PNAS*, 98: 1273-1276.

42. Moore, T. and Fallah, M. (2004). Microstimulation of the frontal eye field and its effects on covert spatial attention. *Journal of Neurophysiology*, 91: 152-162.

43. Morris, J. S., Ohman, A., and Dolan, R.J. (1998). Conscious and unconscious emotional learning in the amygdala. *Nature*, 393: 467-470.

44. Morris, J. S., Ohman, A., and Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proceedings of the National Academy of Sciences of the United States of America*, 96: 1680-1685.

45. Mort, D.J., Perry, R.J., Mannan, S.K., Hodgson, T.L., Anderson, E., Quest, R., McRobbie, D., McBride, A., Husain, M., and Kennard, C. (2003). Diffrenetial cortical activation during voluntary and reflexive saccades in man. *NeuroImage*, 18: 231-246.

46. Munoz, D. P., Dorris, M. C., Paré, M., and Everling, S. (2000). On your mark, get set: Brainstem circuitry underlying saccadic initiation. *Canadian journal of physiology and pharmacology*, 78: 934-944.

47. Neggers, S.F.W., Raemaekers, M.A.H., Lampmann, E.E.L., Postma, A., and Ramsey, N.F. (2005). Cortical and subcortical contributions to saccade latency in the human brain. *European Journal of Neuroscience*, 21: 2853-2863.

48. Nobre, A. C., Gitelman, D. R., Dias, E. C., and Mesulam, M. M. (2000). Covert visual spatial orienting and saccades: Overlapping neural systems. *NeuroImage*, 11: 210-216.

49. Optican, L.M. (1995). A field theory of saccade generation: Temporal-to-spatial transformation in the superior colliculus. *Vision Research*, 35 (23-24): 3313-3320.

50. Ottes, F.P., Van Gisbergen, J.A.M., and Eggermont, J.J. (1986). *Vision Research*, 26 (6): 857-873.

51. O'Sullivan, E.P., Shaunak, S., Henderson, L., Hawken, M., Crawford. T.J., and Kennard, C. (1997). Abnormalities of predictive saccades in Parkinson's disease. *Neuroreport*, 8: 1209-1213.

52. Paré, M. and Munoz, D. P. (1996). Saccadic reaction time in the monkey: advanced preparation of oculomotor programs is primarily responsible for express saccade occurence. *Journal of Neurophysiology*, 76: 3666-3681.

53. Paré, M. and Wurtz, R.H. (2001). Progression in neuronal processing for saccadic eye movements from parietal cortex area LIP to superior colliculus. *The American Physiological Society*, 2545-2562.

54. Posner, M. I, Snyder, C. R. R., and Davidson, B. J. (1980). Attention and the detection of signals. *Journal of Experimental Psychology: General*, 109: 160-174.

55. Prablanc, C. and Jeannerod, M. (1975). Corrective saccades: Dependence of retinal reafferent signals. *Vision Research*, 15: 465-469.

56. Prablanc, C., Massé, D., and Echallier, J.F. (1978). *Vision Research*, 18: 557-560.

57. Rizzolatti, G., Riggio, L., Dascola, I., and Umilta, C. (1987). Reorienting attention across the horizontal and vertical meridians: Evidence in favour of a premotor theory of attention. *Neuropsychologia*, 25 (1A): 31-40.

58. Remington, R.W. (1980). Attention and saccadic eye movements. *Journal of Experimental Psychology. Human perception and Performance,* 6 (4): 726-744.

59. Robinson, D. L. and Kertzman, C. (1995). Covert orienting of attention in macaques. III. Contributions of the superior colliculus. *Journal of Neurophysiology*, 74 (2): 713-721.

60. Schiller PH, Sandell JH, and Maunsell JH. (1987). The effect of frontal eye field and superior colliculus lesions on saccadic latencies in the rhesus monkey. *Journal of Neurophysiology*, 57: 1033-49.

61. Schiller PH, True SD, and Conway JL. (1980). Deficits in eye movements following frontal eye-field and superior colliculus ablations. *Journal of Neurophysiology*, 44: 1175-89.

62. Scudder, C.A., Kaneko, C.R.S., and Fuchs, A.F. (2002). The brainstem burst generator for saccadic eye movements. A modern synthesis. *Experimental Brain Research*, 142: 439-462.

63. Shipp, S. (2004). The brain circuitry of attention. *TRENDS in Cognitive Science*, 8 (5): 223-230.

64. Shulman, G.L., Remington, R.W., and McLean, J.P. (1979). Moving attention through visual space. *Journal of Experimental Psychology: Human Perception and Performance*, 5 (3): 522-526.

65. Smith, D.T.., Jackson, S.R., and Rorden, C. (2005). Transcranial magnetic stimulation of the left human frontal eye fields eliminates the cost of invalid endogenous cues. *Neuropsychologia,* 43: 1288-1296.

66. Snyder, L.H., Batista, A. P., and Andersen, R.A. (2000). Intention-related activity in the posterior parietal cortex: a review. *Vision research*, 40: 1433-1441.

67. Spengler, D., Trillenberg, P., Sprenger, A., Nagel, M., Kordon, A., Junghanns, K., Heide, W., Arolt, V., Hohagen, F., and Lencer, R. (2006). Evidence from increased anticipation pf predictive saccades for a dysfunction of fronto-striatal circuits in obsessive-compulsive disorder. *Psychiatry Research*, 143: 77-88.

68. Vishwanath, D. and Kowler, E. (2003). Localization of shapes: eye movements and perception compared. *Vision Research*, 43: 1637-1653.

69. Vitu, F., Lancelin, D., Jean, A., and Fariolli, F. (2006). Influence of foveal distractors on saccadic eye movements: A dead zone for the global effect. *Vision Research*, 46: 4684-4708.

70. Vuilleumier, P., Armony, J., Driver, J., and Dolan, R. J., (2003). Distinct spatial frequency sensitivities for processing faces and emotional expressions. *Nature Neuroscience*, 6 (6): 624-631.

71. Wardak, C., Olivier, E., and Duhamel, J.-R. (2004). A deficit in covert attention after parietal cortex inactivation in a monkey. *Neuron*, 42: 501-508.

72. White, J. M., Sparks, D. L., and Stanford, T. R. (1994). Saccades to remembered target locations: an Analysis of systematic and variable errors. *Vision Research*, 34 (1): 79-92.

73. Zhou, X., Chu, H., Li, X., and Zhan, Y. (2006). *NeuroReport*, 17 (1): 85-88.

Appendix: Human Ethics Approval

Centre universitaire de santé McGill
McGill University Health Centre

September 15, 2005

D. Guitton, PhD
C/o Toula
Neurobiology Unit
Room : 776, MNI

RE: **GUID 2001/1**
Oculomotor Control in Hemidecorticate Patients (CIHR #202670)
PI: Dr. Guitton
- REB correction letter dated April 26, 2005;
- Application for Continuing Review date April 13, 2005;
- English Consent form dated April 11, 2005;

Dear Dr. Guitton,

Thank you for submitting your Application for Continuing Review for the above-cited research protocol.

The above submission, reviewed by the full REB at the April 25, 2005 meeting # 5.1., was found to be acceptable for continuation at the McGill University Health Centre (MUHC). This was entered accordingly into the minutes of the REB meeting.

The approval of the study is valid until September 13, 2006.

All research involving human subjects requires review at recurring intervals. To comply with the regulation for continuing review of "at least once per year," it is the responsibility of the investigator to submit an Application for Continuing Review to the REB prior to expiry. However, should the research conclude for any reason prior to approval expiry, you are required to submit a Termination Report to the board once the data analysis is complete to give an account of the study findings and publication status.

The Research Ethics Boards (REBs) of the McGill University Health Centre are registered REBs working under the published guidelines of the Tri-Council Policy Statement, in compliance with the "Plan d'action ministériel en éthique de la recherche et en intégrité scientifique" (MSSS, 1998) and the Food and Drugs Act (2001.06.07), acting in conformity with standards set forth in the (US) Code of Federal Regulations governing human subjects research and functioning in a manner consistent with internationally accepted principles of good clinical practice.

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