Recasting covert visual attention effects from the perspective of fixational oculomotor dynamics: Theory and experiments

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- **XT**, MY and ZH developed the experimental task. **XT**, MY and ZH implemented the human experiments and the model. MY and ZH performed the retinal-image stabilization experiments. **XT** and ZH analyzed the data, and all authors determined final figures. ZH wrote the paper in consultation with **XT** and MY.

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- **XT** and ZH developed the experimental task. **XT** and ZH implemented the animal experiments and model simulations. MY and ZH performed the retinal-image stabilization experiments. **XT** and ZH analyzed the data, and all authors determined the final figures. ZH wrote the paper in the consultation with **XT** and MY.

Content

List of acronyms and abbreviations

FEF: frontal eye field

SC: superior colliculus

MST: medial superior temporal

MT: middle temporal visual area

CTOA: cue-target onset asynchrony

SRT: saccadic reaction time

IOR: inhibition of return

AC: attentional capture

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Abstract

Traditionally, a great many studies of visual attention have used reaction time measures (either with manual button presses or saccadic eye movements) to make inferences about the locus and time course of attentional allocation. One classic example of such studies is the Posner cueing paradigm (Posner 1980), in which subjects maintain fixation and a cue is presented on one side or the other of space; a post-cue target appearing at different times and locations is used to elicit a reaction time and map the spatial and temporal development of cue-induced changes in internal brain state. However, tasks with prolonged fixation inevitably involve fixational eye movements, like microsaccades. Since microsaccades are the same as saccades, and are therefore associated with peri-movement changes in internal brain state, an imperative question we should ask is: how much of performance changes in tasks like Posner cueing may actually be attributable to peri-movement changes in vision associated with microsaccades? And, if this turns out to be a real, plausible possibility, can we predict, on a trial-by-trial basis, when and where microsaccades can occur, and therefore when and where performance changes in Posner cueing might be expected to take place? In order to investigate these questions, we started our Study I, which is a combined study including modeling simulations and behavioral psychophysics. Based on a minimalist model of oculomotor generation (microsaccades) without any other factors (i.e. knowledge about where attention is “supposed” to be allocated), we successfully simulated attentional effects and replicated all detailed observations in the classic Posner cueing paradigm. This means that from a theoretical perspective, classic concepts in cognitive neuroscience like “attentional capture (AC)” and “Inhibition of return (IOR)” become the outcomes of peri-microsaccadic enhancement or suppression of neural visual sensitivity. We next turned to the question of why microsaccades might be modulated in Posner cueing at all; can

we predict when and where microsaccades should be seen? In Study II, we experimentally controlled instantaneous foveal motor error during the presentation of peripheral cues. Post-cue microsaccadic oscillations were severely disrupted, suggesting that microsaccades in Posner cueing occur for oculomotor control over foveal motor error and not necessarily because they form a “dirty” read-out of covert attention, as commonly assumed. We then went one step further in Study III, in which we delved deeper into the mechanisms for fixational eye position dynamics, and how they dictate when microsaccades occur (and therefore when performance changes in Posner cueing might be expected). We discovered a new phenomenon of “express microsaccades” that were highly precise in time and direction. We used this discovery to refine our understanding of why microsaccades might be triggered during Posner cueing, showing that there is an oculomotor “set point” that is very systematically modulated at different times after cue onset, and that the instantaneous relationship between eye position and this set point is sufficient to explain when and where microsaccades would be observed. Overall, our work takes a classic phenomenon in cognitive neuroscience, covert attention as studied with Posner cueing, and significantly recasts it from a completely different perspective related to the highly detailed workings of the oculomotor system during the simple act of gaze fixation. Our work has significant implications on potential neural correlates of covert visual attention and fixational eye position dynamics in the brain.

1. Introduction

Vision is one of the most important human senses, since it provides over 90% of the information that our brain receives from the external world (Booher 1978; Byrnes 1962), and also because it allows us to easily understand and interact with the environments that we are living in. In everyday life, we can quickly react to sudden object appearances, and we can identify objects effortlessly. However, the ease with which we achieve these abilities is in no way due to the simplicity of the tasks at hand; to the contrary, it is proof of the high degree of sophistication of our vision system. Our visual system, by nature, has a built-in mechanism for deciding how to apply limited brain power from moment to moment, which means that the visual system can rapidly select the most relevant information in a scene at any one moment in time. Such selection is often called “attention” and refers to efficient management of visual resources. William James, who is one of the pioneers of the experimental field of psychology, gave it an enduring verbal description. In “Principles of Psychology”, he stated:

Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thoughts. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has real

opposite in the confused, dazed, scatter-brained state which in French is called distraction, and Zerstreutheit in German (James, 1891, p. 403-404).

1.1 Measurement of attention

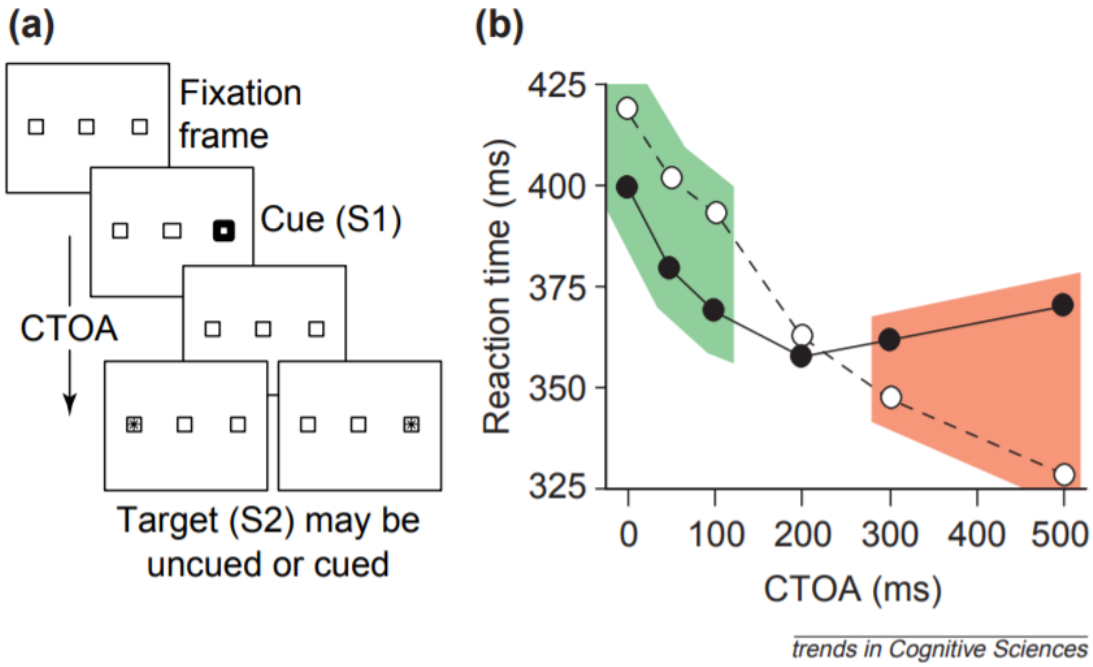

Figure 1. A demonstration of the experimental paradigm for measuring attention proposed by Michael Posner (the so-called classic Posner cueing task) and his findings from this task. The figure is adapted from (Klein 2000b). (a) The Posner cueing task. A fixation display is followed by the first stimulus (S1, cue): appearance in one of two peripheral boxes. After varying intervals (here called cue–target onset asynchronies, CTOAs) from the onset of the cue, a target (S2) is presented at the cued (same) or uncued (opposite) location. The observer has to make a speeded response as soon as the target is detected. (b) Typical results from such an experiment. Filled circles represent the responses to cued targets (same condition); open circles represent the responses to uncued targets (opposite condition). Faster responding to cued targets than opposite targets at the shorter CTOAs (green) reflects the facilitation of reflexive orienting of attention towards the cue (AC effect). This effect flips at longer CTOAs (red). Note, however, that absolute value of reaction time is quite high during AC intervals.

As suggested by William James, everyone knows attention, but no one proposed a reliable way for measurement up to almost 100 years after he wrote his statement. In the 1970's, Michael Posner with his colleagues proposed a very classic paradigm, which has served

as an experimental backbone for eliciting and measuring attention since then, called the "classic Posner cueing paradigm" (Posner 1981; 1980; Posner and Petersen 1990; Posner et al. 1980). Over so many decades, although different researchers made different variations of this task, the typical sequence of events remained the same (shown in Fig. 1a): the subject has to maintain fixation for a while. After the presentation of an attentional cue, a target requiring a response (making a saccade or pressing a button) is shown at either the cued location or at an uncued location after a time delay usually ranging from 100–1000 ms (i.e., cue-target onset asynchronies, CTOAs). By comparing the reaction time across the conditions (i.e. whether the target was the same or opposite the cued location), we can observe relative costs between whether the target appeared at the previously cued location or not (Fig. 1b). When the CTOA is short (i.e., before 200ms from Fig. 1b), performance is slightly better at the cued location than the uncued location in relative terms (called response facilitation, AC). When CTOAs are longer (i.e., since 200ms from Fig. 1b), the opposite occurs (called inhibition of return, IOR) (Klein 2000b). Posner called the early facilitation "attentional capture" and the later flip "inhibition of return", suggesting that attention was initially captured to the cue and then was later inhibited from returning to it. However, note that all of these terms are based on "relative" measurements between same and opposite location. In absolute value, the cue actually caused a major cost in reaction time at short CTOAs, such that it was likely better to present the target without any cue at all. We will get to this point later in our studies.

Based on his results, Posner introduced an analogy of attention as working like a moving *spotlight* (Posner 1981; 1980; Posner et al. 1982; Posner and Gilbert 1999; Posner and Petersen 1990). When a location was being attended to, the spotlight was engaged. In order to pay attention to a new location, this spotlight had to be disengaged from the current location and moved across the display and again engaged at the new location. This cycle of disengage-move-engage characterized the working manner of the attentional system. It also had the advantage that because each process has to take time, there would be a time course to performance modulations as seen in Fig. 1.

1.2 Attention is tightly coupled with eye movements

The metaphor of a spotlight for attention has many similarities with the properties of the saccadic system (or the oculomotor system more generally). For example, foveation brings images of objects of interest into the region of the retina that has preferential neural resources throughout the visual system. Thus, moving the eyes is similar to the concept of using an attentional spotlight to select an object for processing. Likewise, moving the eyes takes time for both pre-movement programming as well as implementation of the movement itself, and looking one way with the eyes incurs a cost on visibility of other locations in a scene not currently being foveated. This means that time courses and spatial benefits and costs would be expected to occur with eye movements.

Therefore, tracking eye movements can be a more direct measure of where attention is deployed. Indeed, there are so many comprehensive and detailed studies to support this

idea. For example, Rizzolatti and his colleagues (Rizzolatti et al. 1987) discovered a *meridian crossing effect*, in which the reaction time cost was greatest when the cue was in a different quadrant from the target. This suggests that there was an additional cost of moving attention that might depend on the extent of motor (saccade) reprogramming required to attend to the new location. The same group also did a further experiment to support their consideration (Sheliga et al. 1995). They asked subjects to make a vertical downward saccade to a box in response to a cue that could appear in a horizontal row of boxes above fixation. They found that saccade trajectories were curved away from the horizontal location of the cue, which means that there was a very close interaction between the attentional allocation and saccade trajectories. Additional support came from studies of patients who apparently had a disorder in their eye movement related brain areas. Patients with damage to the parietal lobe appeared to have a deficit in disengaging attention (Posner et al. 1984); damage to the midbrain appeared to result in a deficit in the ability to move covert attention (Rafal and Posner 1987). However, perhaps the strongest support came from neurophysiological experiments in awake monkeys. Over the last 50 years, there have been extensive studies on the saccadic system, and a lot of brain areas have been identified, including the parietal lobe, frontal eye fields (FEF), superior colliculus (SC) and so on. Interestingly, attentional effects have also been reported in exactly these regions.

Studies by Wurtz and his colleagues are particularly noteworthy. These authors recorded from the superficial layers of the SC in a monkey that was trained either to make a saccade

to a precued light or to attend to the light without making a saccade response (Goldberg and Wurtz 1972; Mohler and Wurtz 1976; Wurtz and Mohler 1976). Cell activity was linked to the onset of the cue and did not occur when a saccade was generated without sensory stimulation. These cells appeared to have responses as a result of attending rather than as a result of generating an eye movement per se. In contrast, when a manual response was required, then the attentional activity from the cells did not occur to the presentation of a cue. Similar studies were also made by the Munoz lab (Bell et al. 2004; Dorris et al. 1999; Fecteau and Munoz 2005). They replicated the cueing paradigm and recorded neuronal activities in the SC. The neural correlates of attentional performance (the costs and benefits of saccadic response times) were identified in the intermediate layers of the SC. The benefit was linked to relatively strong target-related activity when the cue and target appeared at the same location, whereas the cost was associated with relatively weak target-related activity, showing a direct neural correlate of Fig. 1b. All of these evidences show that there is a close coupling between attention and saccade generation, and that both arise from the same basic neural processes.

1.3 Attentional selection occurs via fixation

Given the above, it may be asked how the temporal dynamics of neural selection and eye movement programming proceed. In other words, if attention and eye movements are linked, are there specific phases in an eye movement program in which attentional selection takes place? From the assumption of the spotlight model (Posner 1981; 1980; Posner et al. 1980), there are two stages of information processing. The first is the stage

of preparation, which is computed in parallel with the saccadic system programming, prior to final selection taking place. The second stage is the in-depth processing which is only focused on a restricted part. This later post-attentional stage can be measured by overt eye movements, and its efficiency reflects attentional allocation (i.e. *"where you want to go"*). It has also been shown that it is implemented by peri-saccadic modulation of neural activity in visual areas (Moore and Fallah 2001; 2004). Intuitively, for the first stage, it should take place during the fixation period after the activation of the attentional system (cue onset); during this stage, presumably several locations can be scanned by attention. Therefore, we believe that the simple act of fixation is also a part of the process of paying attention: not only is the final overt movement a measure of attentional selection, but attentional selection itself has also already occurred via fixation.

1.4 Fixational eye movements (microsaccades) are indicators of covert attentional selection

Because of this idea that attentional selection has already occurred via fixation, we need to investigate attention from the perspective of the fixational process itself. Traditionally, it was assumed that fixation is a stable process, and that if there are any changes in fixational eye position, they must be random and therefore inconsequential. However, we now know that fixation is an active process and that tiny eye movements continuously occur (Barlow 1952). Nowadays, there is agreement on the occurrence of three main types of eye movements during fixation: tremor, drifts and microsaccade (Martinez-Conde et al. 2004).

Microsaccades are the most significant among the three types of fixational eye movements, and they are now recognized not to be random. A series of studies investigated the relationship between attention and such miniature saccades, occurring when subjects maintain fixation (Engbert and Kliegl 2003; Hafed and Clark 2002). What they observed was that microsaccades were modulated by the onset of visual stimuli (cues): their rate sharply dropped ~100 ms after stimulus onset and then rebounded to reach a peak at ~200-300 ms before finally returning to baseline rate. Such stimulus-triggered microsaccadic dynamics have been shown to be correlated with attention, such that microsaccade directions relative to the cue location also oscillated (Engbert and Kliegl 2003; Galfano et al. 2004; Hafed and Clark 2002; Hafed et al. 2011a; Rolfs et al. 2005). This and other evidence has led to a strongly accepted view now that microsaccades offer a read-out of attentional selection and can be an index of covert attention (Engbert and Kliegl 2003; Hafed and Clark 2002; Hafed et al. 2011a; Laubrock et al. 2007). This is perhaps the strongest evidence to date that attentional selection already occurs during fixation.

2. Motivation for the thesis

The current view on microsaccades is that they are merely correlated with covert attention shifts and nothing more. At best, they are, thus, viewed as providing a probabilistic likelihood of the average locus of covert attention at any one moment in time after cue onset. In other words, they may be thought of as being a “dirty” read-out of attentional state. However, in this thesis, we would like to question this view. We ask whether it is possible

to envision a deterministic link between each microsaccade occurrence and covert attention. We are motivated by interesting recent developments in the field of microsaccade research.

First, there is mounting interesting evidence in front of us that microsaccades have high similarity with larger saccades in terms of neural generation mechanisms (Hafed et al. 2009; Van Gisbergen et al. 1981). Of particular interest is the idea that, as in the case of saccades, the superior colliculus (SC) plays a casual role in microsaccade generation (Hafed et al. 2009; Hafed and Krauzlis 2012).

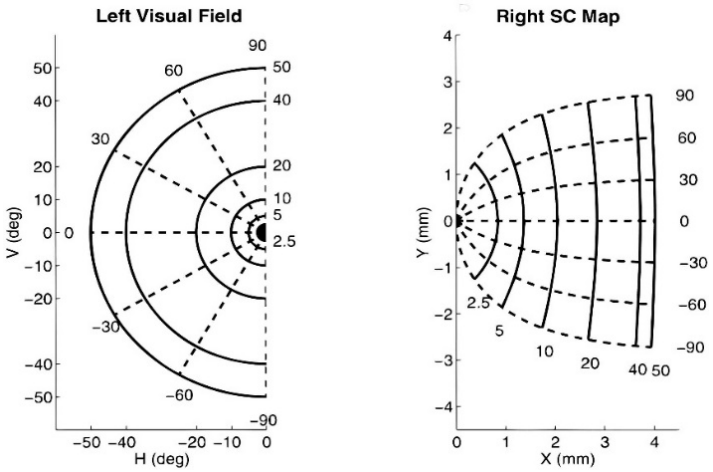

Figure 2. Mapping between visual and collicular reference frames (Quaia et al. 1998). Left figure: left visual hemisfield in polar coordinates. Eccentricities from 2.5° to 50° are drawn for the left hemifield along different directions. Right figure: projection of left visual hemisfield onto the right superior colliculus (SC). The same eccentricities and polar angles are shown as in the visual hemifield map on the left. Solid curves represent constant amplitude (eccentricity in degrees) on both maps; dashed lines represent constant elevation (polar angles in degrees).

The SC contains a representation of retinotopic space that is useful for identifying saccade endpoints (Apter 1946; 1945; Ottes et al. 1986; Robinson 1972), as shown in Fig. 2. In this map, foveal eccentricities are represented rostrally, and the peripheral part of the

contralateral visual field is represented caudally; the upper field is represented medially, and the lower field is represented laterally. It was also found that the retina projects to the colliculus in an orderly fashion (decussate): the right field mapped onto the left colliculus and the left field mapped to the right colliculus (Apter 1946; 1945). Therefore, for a typical large saccade to a peripheral target, peripheral (caudal) neurons in the intermediate and deep layers of the SC exhibit firing rate increases prior to this large saccade onset, a peak of discharge during this movement, and then firing rate decreases back to baseline after this large saccade. In the same way, microsaccade-related activity in the SC was found in the rostral portion of this structure, representing the foveal regions of space. However, such movement-related discharge is indistinguishable from the saccade-related discharge of SC neurons with movement fields tuned for the large saccades (Hafed et al. 2009). From the perspective of this review, this provides strong evidence that: microsaccades and saccades are the same; both are a genuine motor output of the oculomotor system.

Second, it was recently found that microsaccades are associated with peri-movement changes in visual sensitivity and perception identical to those observed for larger saccades (Chen and Hafed 2013b; Chen et al. 2015; Hafed 2013; Hafed et al. 2015; Hafed and Krauzlis 2010). These results were directly motivated by the observation that microsaccades are genuine motor outputs of the oculomotor system and can therefore exhibit modulations similar to active peri-saccadic changes in vision (for large saccades) that are known to dramatically alter the state of the visual system (Sommer and Wurtz 2006; 2002). Thus, during Posner cueing tasks, the target could, in principle, appear at a time

near microsaccade onset, when we now know that there are significant changes in how the visual system operates.

Therefore, an important hypothesis arises out of the above mentioned recent developments. Since microsaccades are not random during Posner cueing (Hafed and Clark 2002), and since they are associated with peri-movement changes in perception (Hafed 2013), then the occurrence of target onset in Posner cueing might coincide with peri-microsaccadic intervals. If so, then performance changes that would be attributed classically to attention would in fact reflect peri-microsaccadic changes in the brain's response to the target, and independently of the prior cue. Specifically, if target onset appears at a phase in which microsaccades are towards its location (regardless of prior cue location), then ‘‘attentional capture (AC)’’ might be observed because of pre-microsaccadic enhancement of visual bursts (Chen et al. 2015). If target onset appears at a phase in which microsaccades are opposite to its location, then “inhibition of return (IOR)” might be observed because of microsaccadic suppression (Hafed and Krauzlis 2010).

The above interpretation of performance changes during Posner cueing paradigms is decidedly different from classic interpretations that ignore the impact of fixational oculomotor activity. However, this interpretation is highly significant because it will recast how we think about the neural mechanisms of attention and eye movements. It is thus imperative to explore this interpretation seriously. To do so, we decided to take a theoretical approach, complemented with experimentation. We asked a simple question: is it

theoretically possible to account for the entirety of the Posner cueing effect (Fig. 1) with a "model" system that only implements peri-microsaccadic changes in vision without needing to invoke a remembered locus of attention at the time of target onset? Such a theoretical approach is exactly what is needed for this kind of interpretation because it allows us to constrain the space of possible solutions to the Posner cueing paradigm down to exactly the mechanism (peri-microsaccadic vision) that we are interested in exploring. Much to our interest and excitement, we found that our hypothesis is indeed plausible. In what follows, we first describe this evidence, coupled with experimental support, and we then switch to deeper questions about why should microsaccades be triggered during Posner cueing. The net result of the thesis is that rather than thinking of microsaccades as providing a "dirty" read-out of attentional state, we can almost predict on a trial by trial basis when microsaccades might happen, and therefore when we can expect to see AC or IOR in Posner cueing.

3. A microsaccadic account of attentional phenomena in Posner Cueing

3.1 Rationale of this study

Based on our hypothesis, we consider that peri-microsaccadic changes are enough to reproduce "attentional effects" in Posner cueing. In order to demonstrate this, we used a combined approach computational modeling and human psychophysics.

The main experimental task that we used is the classic Posner cueing task. In this task, human subjects had to respond as quickly as possible (with a saccade) to a peripheral target, which was preceded by a peripheral cue. The target could appear at either the previously cued location or the opposite one (with 50% likelihood), allowing us to compare performance in conditions where attention was presumably directed to either a given location (attended condition) away from it (unattended condition). This task allowed us to observe both “attentional capture” (AC) and “inhibition of return” (IOR) (Klein 2000b; Posner et al. 1982).

For modeling, we were motivated by a recent concept of how microsaccades can be influenced by random stimulus onsets (like cue onsets). Specifically, the concept states that microsaccades occur repeatedly during fixation in a quasi-rhythmic fashion, and that any stimulus onset (regardless of its task relevance) temporally resets such a process (Hafed and Ignashchenkova 2013). Such a model is sufficient to replicate observations of how microsaccades are modulated in their time of occurrence and direction after cue onset, and it does so without the need to invoke a high-level attentional signal that should affect microsaccades. If we now imagine that the stimulus in the model was the cue onset in a Posner paradigm, then cue onset resets the phase of the microsaccadic system, meaning that subsequent target onsets come at well-defined phases of microsaccade rhythmicity. Therefore, when the second stimulus comes (the post-cue target in our Posner cueing task), it would come at predictable peri-microsaccadic intervals that were earlier reset by

the cue, and based on baseline microsaccadic rhythmicity, the target will either come at a phase in which it is congruent with microsaccade direction or incongruent with microsaccade direction. It is exactly such congruency and incongruency that dictates final performance without the model needing to “remember” where the previous cue was or when it occurred before target onset. AC and IOR would be simple consequences of the reset microsaccadic rhythm, and not a result of a top-down cognitive strategy of attentional allocation.

3.2 Methods

3.2.1 Experimental task

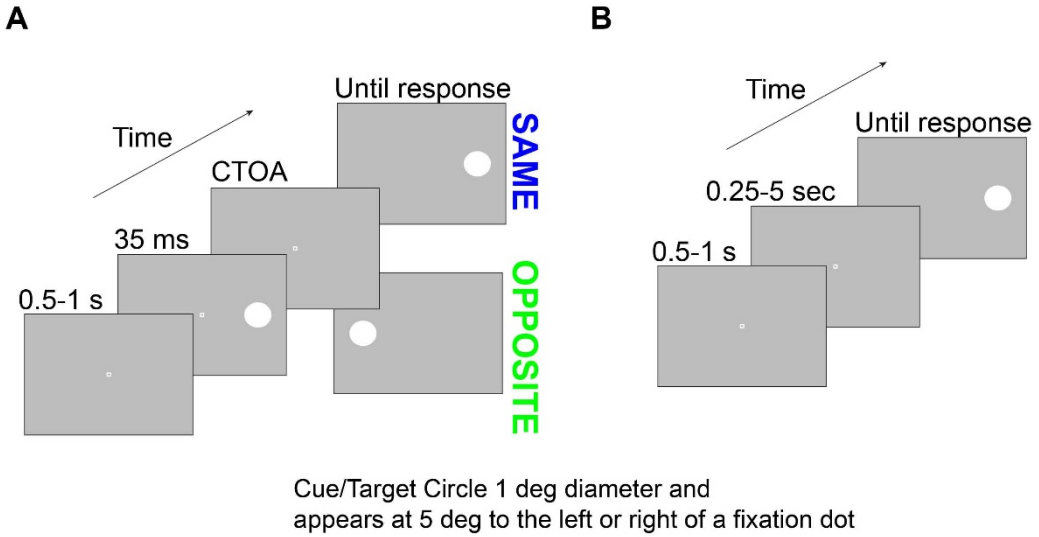

Figure 3. Human psychophysics. (A). Classic cueing task. A horizontal 5° cue appeared followed by a target at either the “same” or “opposite” location and six possible cue-onset-to-target-onset asynchronies (CTOA), which were 47, 94, 141, 247, 541, or 1247ms. (B). Simple button response task without a cue.

For this Study I, the experiments were conducted in a dark room with subjects seated 57cm in front of a CRT monitor (41 pixels/° 85 Hz). The fixation square spot (7.30’ x 7.30’) was

white (97.3 cd/m^2 luminance), and background luminance was 20.5cd/m^2. We tracked eye movements using a high-speed camera (EyeLink 1000, 1 kHz sampling). We fixed subjects' heads at five points using a custom-made fixation device.

Study I had two main human tasks (shown in Fig. 3). The first was a classic Posner cueing task (Figure 3A), and the other was a control experiment of simple button responses (Figure 3B). For the classic Posner cueing paradigm, subjects fixed a central spot with a gray background for 500-1000ms. A cue (1 diameter white circle of similar luminance to the spot) then appeared at peripheral 5°to the right/left of fixation dot for 35 ms. After one of six possible cue-onset-to-target-onset asynchronies (CTOA), 47, 94, 141, 247, 541, or 1247ms, an identical circle (target) appeared at the previously cued location (same) or opposite it and the fixation spot was removed. At this time, subjects had to orient to the target with a saccade as fast as possible. For the second button response task, the stimuli were identical. Subjects merely fixated the same central spot for 0.25-5s. The same target stimulus then appeared at 5° to the right/left, and the subjects had to press a button as quickly as possible. A saccade version of this control task was also tested, in which the subjects looked to the target instead of pressing a button. Thus, there was no cue in these task variants.

3.2.2 Computational model

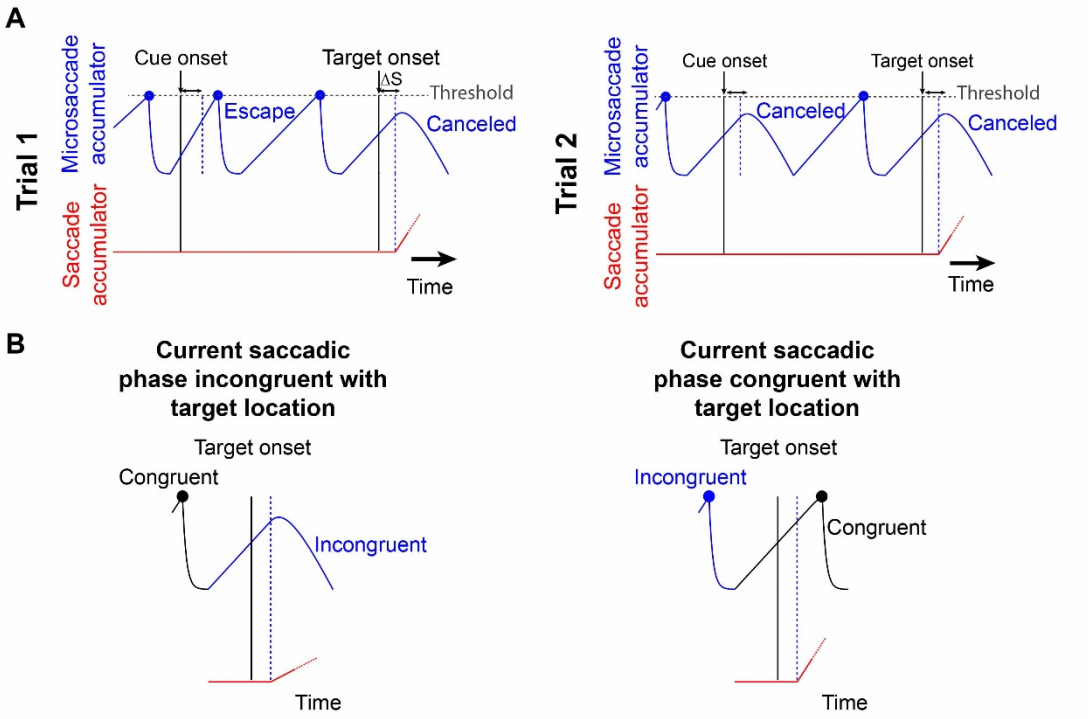

Figure 4. Model of saccadic rhythmicity. (A) In terms of time, we modeled saccade generation using rise-to-threshold processes. During fixation, small saccades repeatedly occurred by rising to threshold (blue accumulator). In this figure, we show two example trials. When a cue/target appears, the microsaccadic rhythm is reset through "countermanding": after a short stimulus processing delay ΔS, the accumulator is slowed down to "cancel" the microsaccade. On some trials (e.g. Trial 2), the movement is successfully canceled. On other trials (e.g. Trial 1 at cue onset), the accumulator was already high enough such that it still reached threshold; an "escape" microsaccade is executed nonetheless. In both trials, red shows the "response" accumulator, which begins to rise after target onset (this accumulator would describe manual RT's on button press versions of the experiment). (B) In terms of space, microsaccades are, on average, anti-correlated in direction. For example, the right column shows a microsaccade before target onset opposite the target (blue) and the subsequent microsaccade being prepared at target onset (rising black accumulator) towards it. Movements towards a stimulus are slightly harder to cancel (e.g. right column "escape") than movements opposite it (e.g. left column successful cancellation). For either case, the final response buildup rate (red) is correlated with the efficacy of microsaccade cancellation.

In our model (Fig. 4A), microsaccades repetitively occur and cues reflexively reset this process. As a result, when the post-cue targets appear, they do so at predictable phases of post-cue oculomotor behavior (Hafed and Ignashchenkova 2013). At the heart of it, the model is the same as that of (Hafed and Ignashchenkova 2013) except for the addition of

a second stimulus onset after cue onset, as well as the implementation of differential microsaccade-related influence on target-related activity (Chen et al. 2015). In producing the final behavior (i.e., RT to the target onset), our model does not use any information about the top–down attentional modulation needed in the task. The model merely simulates a most basic microsaccadic process during fixation, which is both repetitive in time and oscillatory in direction. Orienting efficacy to the target in the model is simply a function of the instantaneous temporal and spatial phase of an ongoing microsaccadic plan at which the post-cue target appears.

The model comprises four elements: (1) a repetitive rise-to-threshold mechanism for generating microsaccades, (2) a reflexive resetting of microsaccades by cue/target onset, (3) an oscillatory directional pattern for microsaccades, (4) a dynamic interaction between reflexive resetting and the direction of the movement being reset by stimulus onset. The first two elements concern the “temporal” aspects of the model (Fig. 4A), and the last two concern the “spatial” aspects (Fig. 4B).

3.2.2.1 Repetitive Rise-to-Threshold Mechanism

The model utilizes a rise-to-threshold process for executing a motor output (Salinas and Stanford 2013a). In our case, we accounted for microsaccadic repetitiveness (Bosman et al. 2009) by repeatedly running this process.

The process consisted of a “microsaccade accumulator”, $M_{microsaccade}$. Starting from a baseline of zero, the accumulator rose linearly towards threshold. The accumulator’s buildup rate was described by:

$$\frac{dM_{microsaccade}}{dt} = r_B \quad (1)$$

$$r_B = r_{B0} \quad (2)$$

For any given microsaccade, the buildup rate r_B, was a constant, r_{B0}, that was drawn randomly at the beginning of the buildup from a gamma distribution (shape parameter k_m and scale parameter Δ_m). Once the accumulator reached threshold (1000 arbitrary units), a microsaccade was triggered 20 ms later (Salinas and Stanford 2013a). The microsaccade accumulator decayed exponentially after reaching threshold, according to:

$$\frac{dM_{microsaccade}}{dt} = -\frac{M_{microsaccade}}{decay} \quad (3)$$

where *decay* describes the time constant of the dropdown.

When $M_{microsaccade}$ decayed to a value <1 arbitrary units (Hafed and Ignashchenkova 2013), the process started anew with a new r_{B0} for a new microsaccade. Thus, this process resulted in repetitive microsaccade generation, as occurs experimentally. Note that the buildup rate r_B, influences inter-microsaccadic intervals. For subjects with low microsaccade frequencies, this parameter would be lower than for subjects with high frequencies. However, as we show in the chapter of Experimental results, the behavior of the model holds with different parameter values.

3.2.2.2 Resetting by cue/target onset

If a peripheral stimulus appears, it can be thought of as resetting the saccadic system. We implemented such resetting using countermanding. The stimulus acts like a "stop" signal that attempts to "cancel" the ongoing microsaccade accumulator, in order for the saccadic rhythm to restart anew (Fig. 4A). After a brief afferent processing delay ΔS, $M_{microsaccade}$ was now governed by new dynamics because r_B became time varying:

$$\frac{dr_B}{dt} = -\frac{r_{DN} - r_{B0}}{\tau} \quad (4)$$

We set r_{DN} to $-k_m$, and τ was a constant that dictated how much the microsaccade accumulator was slowed down by stimulus onset. ΔS was drawn randomly from a normal distribution (mean $\mu_{stimulus}$ and standard deviation $\sigma_{stimulus}$).

The above countermanding process explains why some microsaccades can still occur after cue/target onset before the characteristic reduction in microsaccade frequency that is normally observed (Rolfs et al. 2008). If the cue/target appears when $M_{microsaccade}$ had risen far enough towards threshold, then the dynamics of equation 4 are not fast enough to prevent $M_{microsaccade}$ from crossing threshold. A microsaccade is thus triggered despite cancellation by stimulus onset, and this microsaccade is called an "escape" microsaccade (Hafed and Ignashchenkova 2013). Note that as a result of this, the direction of an "escape" microsaccade provides an experimentally observable measure of the instantaneous spatial phase of the microsaccadic rhythm that was present at target onset. We exploited this property to test some predictions of our model.

3.2.2.3 An oscillatory direction pattern for microsaccades

The above model results in repetitive microsaccades (i.e. a temporal rhythm), with some microsaccades being canceled by cue/target onset and others escaping. However, microsaccades also oscillate in direction (i.e. a spatial oscillation). For example, square-waves, which are pairs of successive but oppositely directed microsaccades, are prevalent (Bosman et al. 2009; Hafed and Clark 2002). We implemented this spatial oscillation by assigning a direction to each microsaccade. At the beginning of every trial, we picked a random direction. Any subsequent microsaccade (at the beginning of the rise of $M_{microsaccade}$ after the previous decay) was biased away from the previous eye movement's direction. Its direction was drawn from a normal distribution having a mean 180° opposite the previous microsaccade direction and a standard deviation of 70° (Hafed and Ignashchenkova 2013). This large variance allowed our model to generate both square-wave microsaccade pairs as well as single-sided (Hafed and Clark 2002) movements, as observed experimentally. Also, note that our implementation of this oscillation means that only one single small microsaccade can occur at any one time, consistent with the known neurophysiological mechanisms for their generation (Hafed 2011; Hafed et al. 2009).

3.2.2.4 Dynamic interaction between the resetting and the movement being reset

Peripheral stimulus onset generates strong visual bursts in structures like the SC, and this makes it harder to reset (i.e. countermand or cancel) a microsaccade that is being

programmed towards the stimulus compared to a microsaccade that is being programmed opposite the stimulus (Hafed and Ignashchenkova 2013). We implemented this dynamic interaction by multiplying the instantaneous accumulator rise rate (after ΔS) by a scale factor that depended on the microsaccade direction being programmed at stimulus onset: 1.02 for the same direction and 0.98 for the opposite direction. We defined "same" and "opposite" based on the horizontal component of the microsaccade relative to the horizontal location of the stimulus. The result of this interaction is that if stimulus onset happened for a microsaccade that was already being programmed towards the stimulus, the scale factor made $M_{microsaccade}$ ever-so-slightly harder to reset than if the microsaccade was opposite. This explains why early "escape" microsaccades are highly correlated with stimulus location in our data. The dynamic interaction term that we implemented is also consistent with large saccades, for which it was shown that the efficacy of the countermanding process depended on the properties of the saccade being countermanded (Montagnini and Chelazzi 2009).

The above model accounted for microsaccadic modulations. To model the final behavioral output (whether saccade or manual button-press RT, Fig. 4A-B), we assumed that target onset releases a response accumulator $M_{response}$. Thus, after the afferent processing delay ΔS, the microsaccade accumulator was attenuated as usual after stimulus onset (e.g. equation 4), and it was stopped after either a successful cancellation or an "escape" microsaccade. A second "response" accumulator started rising after ΔS. This accumulator represents the recruitment of populations of neurons (other than those needed for

microsaccades) in, say, SC in order to initiate the final eye movement (Munoz and Wurtz 1995) or button decision. The accumulator was identical to equation 1. In this case, r_{B0} was drawn from a normal distribution (mean $\mu_{response}$, standard deviation $\sigma_{response}$). To simulate the influences of microsaccades on behavioral and neuronal responses (Hafed, 2013; Chen et al., 2015), we modulated the sensitivity of the response accumulator by the current phase of the microsaccadic system at which the target appeared. This aspect of the model directly simulates peri-microsaccadic changes in vision that take place around the time of these small eye movements (Chen et al. 2015; Hafed 2013; Hafed and Krauzlis 2010). Specifically, if the microsaccade accumulator at target onset was rising for a microsaccade in the direction of the appearing target, then this meant that the target appeared congruent with the spatial phase of the microsaccadic rhythm. In this case, the randomly drawn response accumulator value r_{B0} was scaled up by a factor of 1.25, modeling an enhanced visual response to the target in structures like the SC (Chen et al., 2015). If, on the other hand, microsaccade accumulator was rising for a movement opposite the target location when the target appeared, then the target appeared in conflict with current spatial phase of microsaccades. In this case, the target was less effective in driving the final decision, and we scaled the response accumulator r_{B0} by a factor of 0.7, modeling a suppressed visual response (Chen et al., 2015). If the microsaccade accumulator was declining at target onset, no modulation of r_{B0} was invoked. It is important to note here that these modulations in r_{B0} are consistent with neurophysiological evidence that SC target-related activity is strong for fast RT's and weaker for IOR (Dorris et al. 2002; Fecteau et al. 2004; Fecteau and Munoz 2005), but they occur in our model

only as a function of microsaccades. Moreover, such modulations appear on initial target-related visual bursts, which explains why the SC (a saccade structure) is causally involved in IOR even when manual responses are used (Sapir et al. 1999). Finally, whether with saccades or with buttons, such SC visual bursts (target-related activity) are a correlate of the slope of rise-to-threshold processes (Boehnke and Munoz 2008; Carpenter and Williams 1995). Therefore, all of the above suggests that a strong prediction of our model is that “strong” and “weak” neural activity in response to target onset would be temporally synchronized with, and significantly modulated by microsaccades.

3.3 Experimental results

3.3.1 Capturing attentional capture and inhibition of return

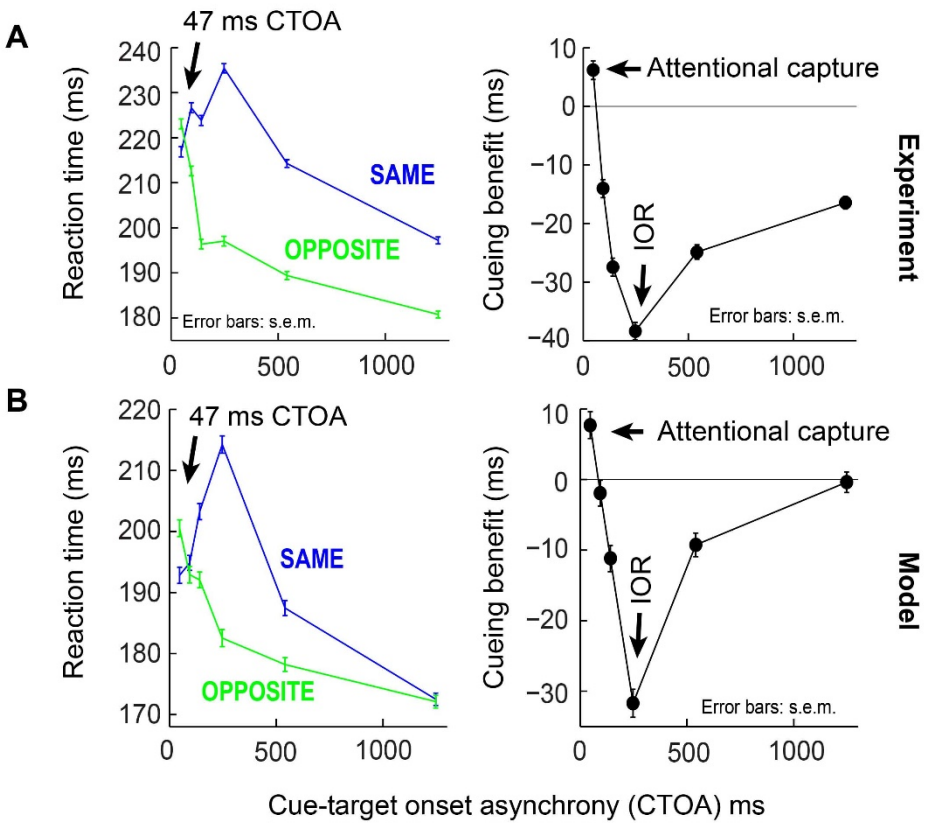

Figure 5. Orienting dynamics in experiment and model. (A) Saccade reaction time (RT) in the cueing task of Fig. 4A as a function of CTOA for “same” and “opposite” trials. RT was faster for “same” at 47 ms CTOA but slower later; cueing benefit defined as the RT difference between “opposite” and “same”. (B) Model results capturing same dynamics of the experimental data in A.

We implemented the Posner cueing task (Posner 1980). Humans fixated a spot while a brief cue appeared. After a cue-to-target-onset-asynchrony (CTOA), the spot disappeared and a target appeared at the cued or opposite location. For the short CTOA’s, subjects oriented to the target faster if it appeared at the cued location than if it appeared at the opposite location (Fig. 5A, 47 ms CTOA, p=1.1*10-4, 2-sided t-test between same and opposite). This phenomenon (“attentional capture”) (Egeth and Yantis 1997; Fecteau and Munoz 2005; Jonides 1981) was short-lived, however, because subjects got much worse later: by 247 ms CTOA, RT was 235 ms at the cued location but only 197 ms opposite (Fig. 6A, 247 ms CTOA, p=1.7*10-141, 2-sided t-test between same and opposite). Therefore, our subjects replicated classic AC and IOR, with similar dynamics as in the previous literature (Fig. 5A).

Such dynamics were also successfully replicated (Fig. 5B) by a model that only takes the concept of microsaccadic repetitiveness into account: a microsaccadic process repeatedly rose towards threshold to trigger a movement. Once the movement was executed, the process rose again to maintain a certain rhythm, which also directionally oscillated (Engbert and Kliegl 2003; Hafed 2013; Hafed and Clark 2002; Hafed and Ignashchenkova 2013; Hafed et al. 2011b). If a cue/target were to now appear, the rhythm was reset after a short delay, ΔS. Subsequent targets then appeared at distinct phases (both temporal and spatial) of the reset rhythm, resulting in predictable behavioral modulations with different CTOA’s.

3.3.2 Time and space in microsaccadic rhythmicity dictate whether attentional capture or inhibition of return are observed

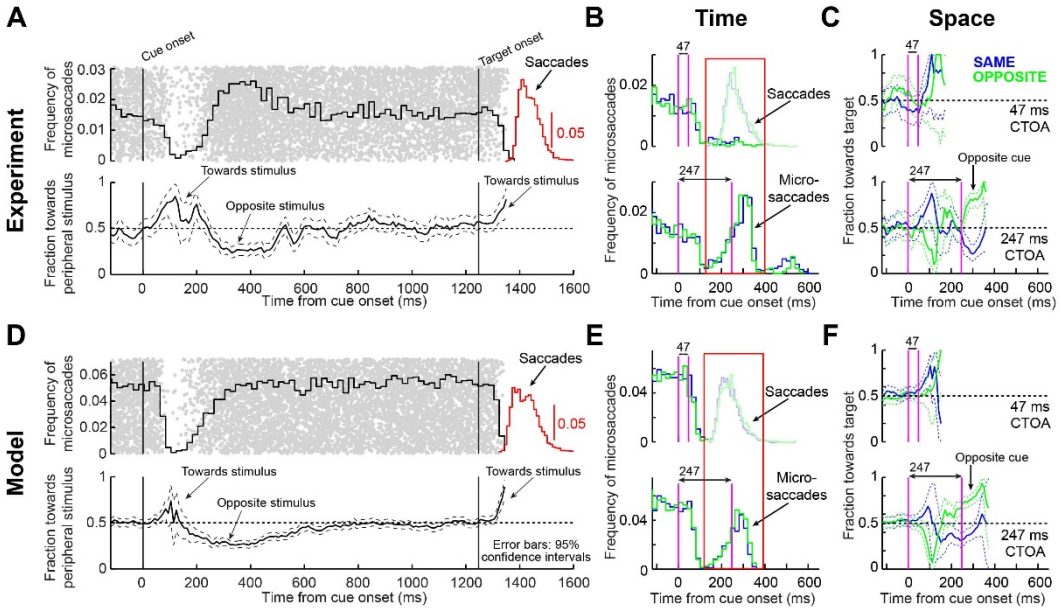

Figure 6. Microsaccade dynamics in the cueing task (experiments and model). (A) Microsaccade frequency (top) and direction (bottom) as a function of time for the longest CTOA 1247 ms (>4000 trials). Top plots the fraction of trials containing microsaccades. Bottom plots the fraction of microsaccades directed towards the peripheral stimulus. Red indicates RT for large saccades (note specific scale bar). Gray dots are rasters of microsaccade onset times across trials. (B) Microsaccade frequency in two CTOA's (top and bottom). Colors refer to the location of the target relative to the cue (blue for "same"). The faint histograms show saccade RT's with similar color coding. Longer CTOA's (bottom) exhibited microsaccades at the time at which large saccades would have occurred if fixation was not enforced (compare to the saccade RT's in the short CTOA's – red rectangle). Magenta lines indicate cue/target onset. (C) Microsaccade directions in the CTOA's of B. When there was sufficient time between cue and target, microsaccades were initially biased towards the cue (thus opposite the target for the green curves in which the cue was opposite the target location). For 247 ms, most microsaccades near target onset were towards the target in the opposite condition because they had flipped from being towards the cue earlier. (D-F) Model simulations from the scheme, capturing all the salient features of the data. All error bars denote 95% confidence intervals. Each experimental condition has N ~2000-3000 trials; simulations: 2000 trials.

Microsaccadic rhythms can replicate cueing dynamics because of the influence of stimulus onsets on such rhythms. Consistent with previous results (Betta et al. 2007; Engbert and Kliegl 2003; Galfano et al. 2004; Hafed and Clark 2002; Hafed and Ignashchenkova 2013; Hafed et al. 2011b), cue onset altered both microsaccade frequency (Fig. 6A, top) and

direction (Fig. 6A, bottom), and microsaccades were biased away from the cue at times of maximal IOR (i.e. ~247 ms).

However, based on our model we were able to understand how microsaccade/saccade generation itself could be sufficient to replicate cueing dynamics. Two concepts, one concerned with time (Fig. 6B) and the other with space (Fig. 6C), can be enough to reproduce cueing dynamics. In terms of time, microsaccade frequency abruptly "stops" and then recovers (e.g. Fig. 6A, top). This stop represents a cue-induced temporal-frequency "phase resetting", and we implemented it through countermanding (Hafed and Ignashchenkova 2013; Salinas and Stanford 2013b). The implication of this resetting is that during fixation, microsaccades will still occur after the resetting event such that the saccadic system's temporal structure (Bosman et al. 2009; Gaarder et al. 1966; Hafed and Ignashchenkova 2013) is still maintained. For example, with 247 ms CTOA's, a population of tiny microsaccades occurred at roughly the same time after cue onset as the 5° targeting saccades of the shorter 47 ms CTOA trials when fixation was released (Fig. 6B, red rectangle): the saccadic system still generated motor outputs after cues, but the movements were small with a persistent foveal stimulus instead of large when fixation was released. As a result of this, and given saccade/microsaccade repetitiveness (Bosman et al. 2009; Drewes and VanRullen 2011; Gaarder et al. 1966; Hafed and Ignashchenkova 2013), final RT clearly depended on the previous microsaccadic temporal structure.

The second concept has to do with space. On average, microsaccades in our model oscillate in direction (Bosman et al. 2009; Engbert and Kliegl 2003; Hafed 2013; Hafed and Clark 2002; Hafed and Ignashchenkova 2013; Hafed et al. 2011b), and such oscillations are also cue-reset: early microsaccades "escaping" the temporal-frequency phase resetting are more likely to be toward the cue than opposite, resulting in coherent post-cue direction oscillations (Fig. 6C, bottom). This phenomenon is consistent with earlier evidence of an interaction between the "escape" movements and the countermanding (Hafed and Ignashchenkova 2013; Montagnini and Chelazzi 2009). In the model, the dynamics of this phenomenon (i.e. its speed and duration) were dictated by the efficacy of cue-/target-related sensory processing (ΔS), as well as the efficacy with which sensory inputs countermanded the microsaccadic buildup accumulator (τ). These dynamics means that, relative to the final target position, "same" and "opposite" cue onsets in our task caused counterphase direction oscillations (Fig. 6A, bottom and Fig. 6C). When the target later appeared, it could do so when the saccadic system was either preparing to move in the direction of the cue or opposite it (Fig. 6C), which ultimately affected final RT.

Using both time and space, we can understand why 247 ms CTOA showed the strongest IOR (Fig. 5A). For 247 ms "same" trials, the target appeared at a spatial phase in which the saccadic system had already flipped away from preparing movements towards the cue to preparing ones opposite (Fig. 6C, 247 ms CTOA, blue), and the timing of this flip was dictated by the dominant microsaccadic rhythm speed (or accumulator buildup rate in Fig. 4).

3.3.3 Entire saccadic/microsaccadic activity matters even if microsaccades are rare

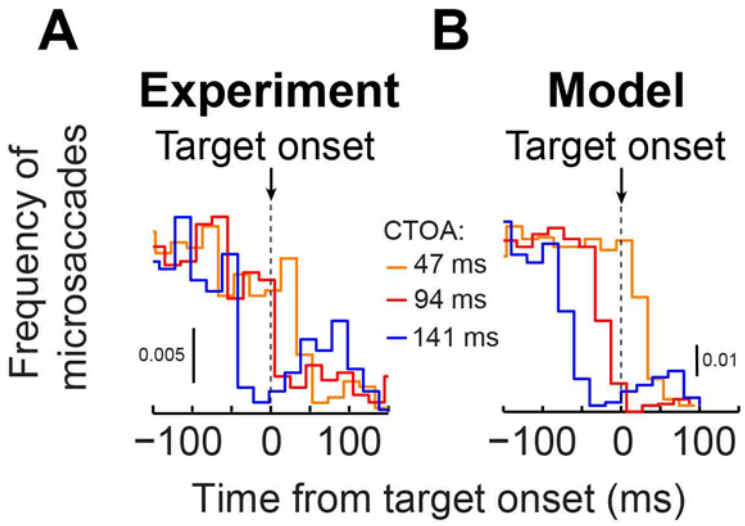

Figure 7. Our model can replicate cueing dynamics even if microsaccades are rare. (A). Microsaccade frequency around target onset for the shortest 3 CTOA's in "same" trials. Virtually identical curves were obtained from "opposite" trials. Each curve shows data from >2000 trials. The timing between target and cue onset caused modulations in microsaccade frequency as a function of CTOA. For example, there were extremely few microsaccades near target onset in 94 ms CTOA trials even though RT in these trials was markedly different from RT in other CTOA's. (B). Model microsaccades showed similar modulations. In this case, we ran the model for 2000 trials per CTOA.

It may be argued that microsaccades occur too infrequently in cueing tasks to be of much importance. However, we observed that our model exhibited an interesting emergent property; it explained how microsaccades can sometimes be quite infrequent but still influential. Target onset occurred at different phases relative to the previous cue-resetting event in these (and other) CTOA's. As a result, these CTOA's caused marked microsaccade frequency modulations, such that 94 and 141 ms CTOA's had rare microsaccades at target onset (Fig. 7A). Despite these modulations, which our model

captured (Fig. 7B), our model still exhibited markedly different RT's at these 3 CTOA's, as in the experiments (Fig. 5).

3.3.4 Variability of microsaccadic rhythms correlates with the variability in cueing effects across subjects

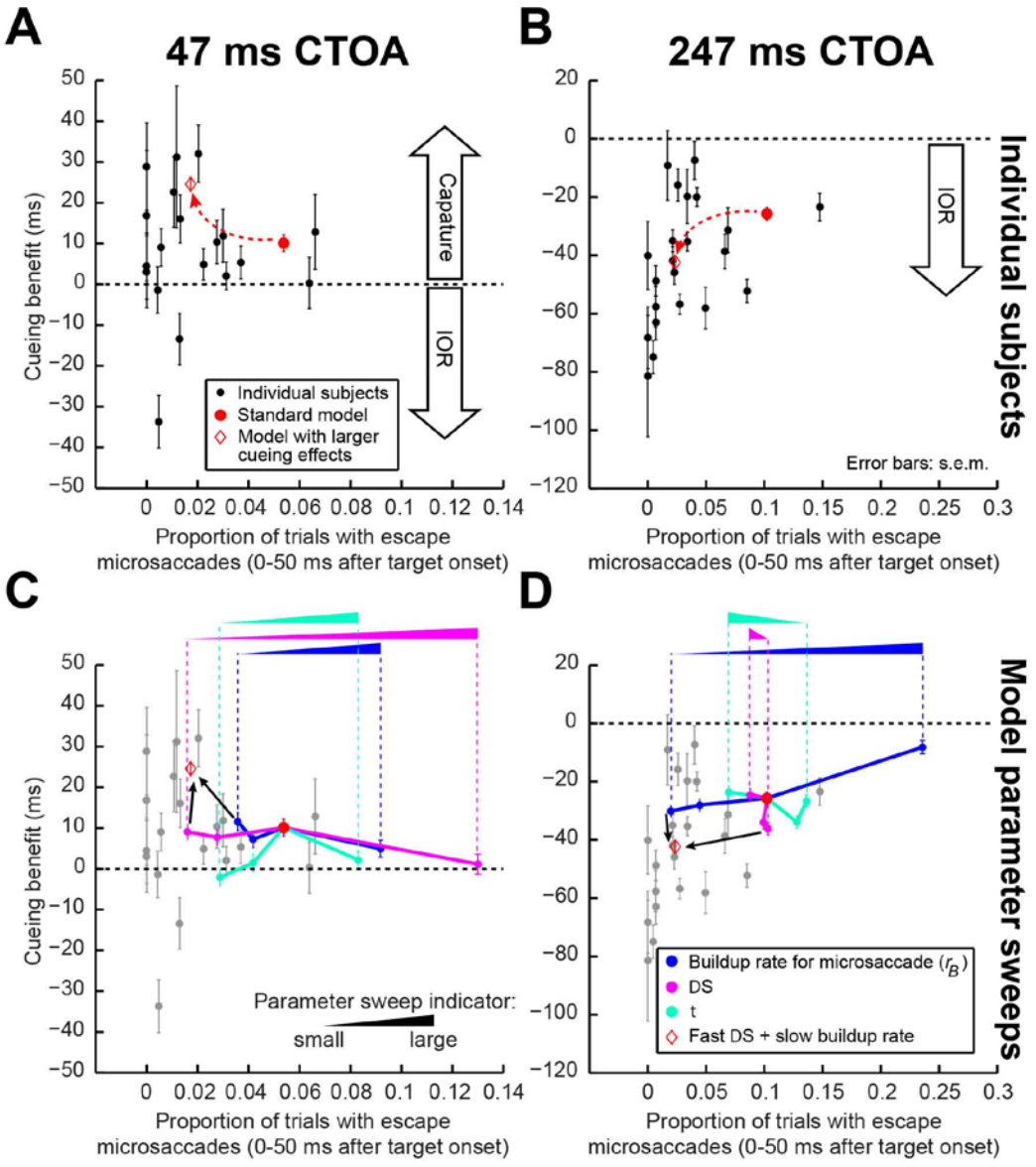

Figure 8. Exploring individual subject variability. (A, B) In each panel, we plotted each subject's cueing benefit (as defined in Fig. 6) as a function of his/her proportion of trials with "escape" microsaccades <50 ms after target onset. Each dot represents a subject, and each panel shows his/her performance at one CTOA. The red circle shows model performance when run as in Results, and the red diamond shows it when run with fast ΔS ($\mu_{stimulus}$ 1/4 of the standard model) and slow buildup rate (k_m 1/4 of the standard model, Methods). Cueing effects were stronger for lower "escape" microsaccade frequency. With simple

parameter changes, the model could exhibit similar changes. (C, D) Model parameter sweeps allowing us to explore model robustness. Starting from the standard model (red circle), we changed one parameter at a time while holding all other parameters constant. We changed the dominant buildup rate (k_m, blue), the dominant ΔS processing delay ($\mu_{stimulus}$, magenta), or the countermanding time constant (τ, cyan). Model performance moved in systematic ways as parameters changed (the latter were indicated by the ramp icon where the height of a ramp correlates with the size of the parameter being swept). For short CTOA's (C), ΔS was a primary determinant of performance changes. For long CTOA's (D), buildup rate played a prominent role. When two parameters were changed at a time (red diamond with the smallest $\mu_{stimulus}$ and k_m), the model moved along a non-linear trajectory like our subjects. Error bars denote s.e.m. The gray dots in C, D show individual subject data for easier comparison to the model trajectories. In each parameter set, the model was run for 2000 trials.

To further investigate this idea, we asked whether our model could help us understand inter-individual differences in cueing dynamics. We reasoned that subjects with different microsaccadic rhythms might exhibit different cueing effects. For each subject and CTOA, we measured the frequency of trials containing "escape" microsaccades within 50 ms after target onset. Since "escape" microsaccades depend on intrinsic microsaccadic rhythm dynamics (Hafed and Ignashchenkova 2013), this allowed us to relate each subject's individual microsaccade dynamics to his/her cueing effects. Across subjects, there was a (non-linear) relationship between "escape" microsaccade frequency and cueing-effect magnitude: the fewer the "escape" microsaccades, the stronger the cueing effects (Fig. 8A, B). Our model captured this relationship when buildup rate and sensory-processing delay ΔS, were altered. This second model exhibited both fewer "escapes" and stronger capture/IOR (Fig. 8A, B). Therefore, simple parameter changes captured the apparently complex relationships between microsaccadic rhythms and cueing effects across individuals.

3.3.5 Microsaccadic rhythmicity influences behavior in different response modalities

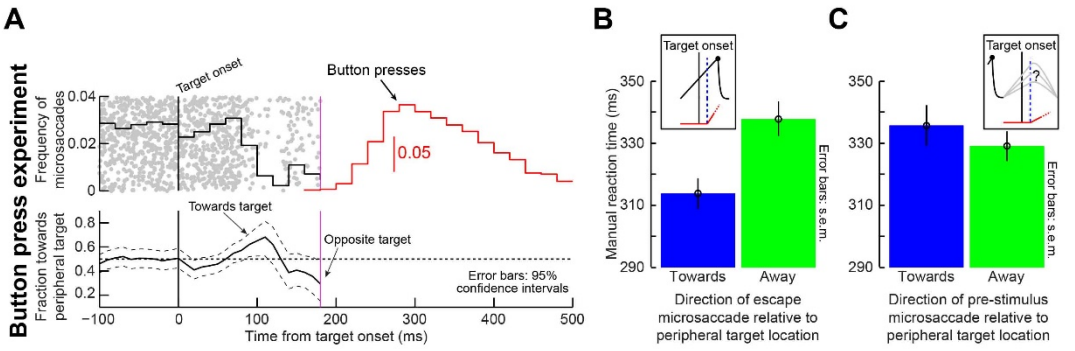

Figure 9. An influence of microsaccades on manual RT's. (A) Microsaccade frequency (top panel) and direction (bottom panel) in a simple fixation task (inset). Human subjects fixated and pressed a button as fast as possible when a target appeared. Near target onset, microsaccade frequency behaved similarly to microsaccade frequency near target onset in our earlier cueing task with saccades as the response modality (Fig. 3). Microsaccade direction also behaved similarly, showing an early bias towards the target and then a later bias opposite. N=3628 trials. All conventions similar to Fig. 7A. (B) We tested the prediction that current microsaccadic phase at target onset influences manual RT's. Experimentally, the current microsaccadic phase is unambiguously revealed on trials with "escape" microsaccades (inset). We therefore analyzed manual RT on trials with these microsaccades. Manual RT was faster if the target was congruent with microsaccadic phase (blue) than if it was opposite (green) (p=0.0015, t-test, N=187 same, N=192 opposite). (c) This effect disappeared when the microsaccade ended before target onset (p=0.412, N=214, N=210). This is so because current microsaccadic phase at target onset was ambiguous (inset). Error bars denote 95% confidence intervals in A and s.e.m. in B, C.

A strong prediction of our model is that instantaneous microsaccadic rhythm phase at target onset should be sufficient to modulate orienting efficacy (i.e. the response accumulator): if a peripheral target appears at a spatial phase of microsaccades in which movements are already being prepared in one direction, orienting efficacy (response accumulator slope) would be higher than if movements were being prepared opposite, and this is a function of peri-microsaccadic changes in visual sensitivity (Hafed 2013; Hafed and Krauzlis 2010; Zuber and Stark 1966). Therefore, we performed a simple RT experiment (i.e. without cueing) but with button presses (Fig. 9A). We asked 8 human subjects to press a button

as soon as a target appeared, and without any prior cueing. We measured microsaccade frequency and direction around target onset and found virtually indistinguishable patterns from those in our original cueing task with saccades (compare Fig. 9A to Fig. 6A around target onset). Most importantly, on trials with “escape” microsaccades towards the target, manual RT’s were significantly faster than when the “escapes” were opposite the target (Fig. 10B, p=0.0015, 2-sided t-test, N=187 trials for same, N=192 for opposite). If microsaccades had ended before target onset, meaning that the instantaneous microsaccadic spatial phase at target onset was uncertain (Fig. 9C, inset), the effect disappeared (p=0.412, 2-sided t-test, N=214 for same, N=210 for opposite). Thus, the presence of microsaccades near target onset had measureable impacts on RT, whether with saccades or manual presses. Combined with known changes in microsaccade times and directions after cue onset using manual responses (Engbert and Kliegl 2003; Hafed 2013; Hafed and Clark 2002; Hafed et al. 2011b), these results all suggest that our framework can account for both classic ways of studying IOR (with saccade or manual RT’s), and that a primary factor of attentional capture or IOR effects may be the instantaneous state of ongoing saccadic activity at which targets appear.

3.4 Short summary

In this Study I, through comparison between the results of computational simulations and experimental psychophysics, we can see that based on peri-microsaccdic modulation alone, coupled with rhythmic microsaccade generation, it is possible to re-produce both attentional effects, AC and IOR, in classic Posner tasks. However, this leads to the next

question, which is why should microsaccades occur in the cueing task at all? Therefore, we started the second study.

4. Microsaccades reflect oculomotor control over foveal motor error

4.1 Rationale of this study

The previous study has taught us that it is possible to account for Posner cueing dynamics in their entirety based on peri-microsaccadic alterations in visual perception. However, what is still not clear is why there is microsaccadic rhythmicity in the first place during Posner cueing. Historically, it would have been argued that peripheral attention might oscillate in time, and this somehow “leaks” into the oculomotor system such that microsaccades might also oscillate. However, an alternative possibility is that microsaccades are serving an important oculomotor function: they reduce foveal motor error away from the foveal fixation spot. After all, the task is keep the eye on the fixation spot, and it would be expected that microsaccades, like larger saccades, would be used to “acquire” the relevant target (in this case, the foveal fixation spot). To test for this, we carefully measured foveal motor error before microsaccades at different times after cue onset, and we then causally perturbed such error using real-time retinal image stabilization of stimulus position, such that we minimize foveal motor errors. During simple fixation, previous studies have proposed a possibility that microsaccades are just corrective movements for foveal error (Guerrasio et al., 2010; Ko et al., 2010). In our present study, we found that this function is surprisingly still maintained after cue osnet, even though it

might look like microsaccades are oscillating in a coherent manner relative to peripheral cue location. For this study, we used two monkeys implanted with scleral search coils because real-time retinal image stabilization would be most accurate when high quality tracking data is available even during fixation periods in between individual microsaccades.

4.2 Methods

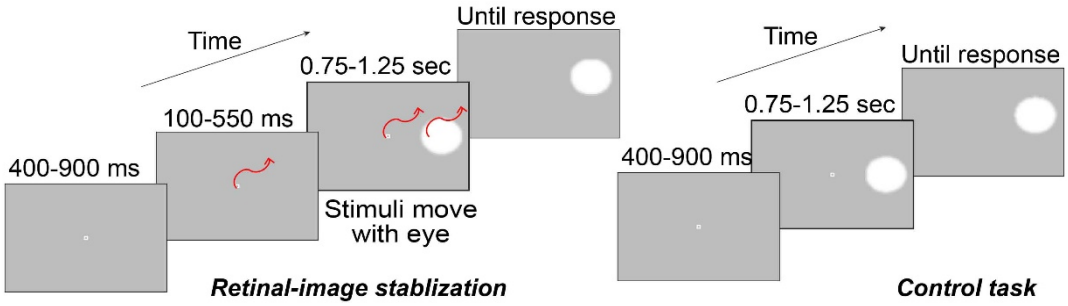

Figure 10. Monkey psychophysics. Retinal-image stabilization and its control task.

For this Study II, we implemented the experiments on monkeys (Fig.10). Eye movement data came from two (*N and P*) adult, male rhesus monkeys (Macaca mulatta) that were 6-11 years of age and weighed 9 –13 kg. All experimental protocols for the monkeys were in accordance with the guidelines for animal experimentation approved by the local governing committee of Tuebingen city, Germany. The monkeys sat 45cm in front of a CRT monitor (22 pixels/° and 120 Hz) and were measured eye movements with high temporal and spatial precision technique of the scleral search coils by 1 kHz sampling frequency (Judge et al. 1980; Robinson 1972).

For the retinal-image stabilization task, the monkeys fixated a central spot (8.50’ x 8.50’; 72 cd/m^2) presented over a gray background (21 cd/m^2). After a random fixation interval

(400-900ms), a cue appears at 5°horizontally or vertically. The cue was a disk that was white at the center and gradually approached background luminance according to a Gaussian profile with 1°standard deviation. The cue remained on for 750-1250 ms, after which the fixation spot disappeared instructing the monkeys to make a saccade to the cue. On randomly interleaved trials, retinal-image stabilization was applied. After the fixation interval, the fixation spot was translated in register with the monkeys' eye position. This stabilization lasted for 100-550 ms, after which the cue appeared. The cue and fixation spot remained stabilized for the same interval as in the regular condition (750-1250 ms), after which the peripheral stimulus froze and the fixation spot was removed. The monkeys had to orient to the stimulus with a 5°saccade. During stabilization, there was no constraint on eye position, since the foveal stimulus was always moved with eye. Success at the end of the trial only depended on bringing the eye within 2° from the now-stationary cue location. In additional interleaved trials, we also applied retinal-image stabilization but now forcing the fixation spot to remain ~2.70' to the right or left of current gaze position. Thus, if the cue was to the right and the fixation spot was stabilized ~2.70' to the left of current gaze, then this was a condition in which foveal motor error was opposite the cue direction. If the cue was to the left, then foveal motor error was toward the cue. Since search coil systems can drift, we applied an offset correction at the beginning of every trial to ensure proper calibration across trials. In addition, we used high-speed Ethernet connections for display updates, and we checked whether we missed frames due to communication delays. Using our real-time system, we never missed display update (~millions of updates).

4.3 Results

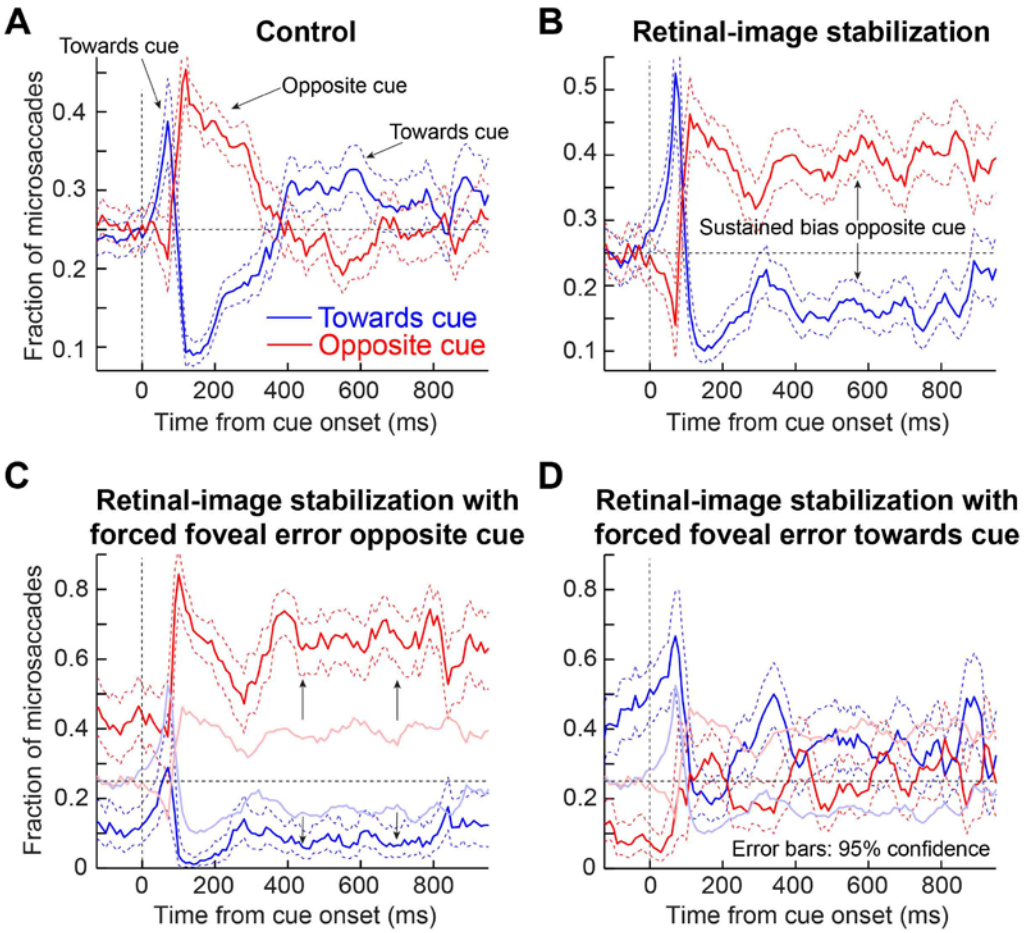

Figure 11. Disrupting post-cue microsaccade direction oscillations by simply controlling foveal motor error. (A) Microsaccade directions in the control condition (repeated from Fig. 7A to facilitate comparison to the other panels). (B) With retinal-image stabilization, after the initial cue-directed “escapes”, microsaccades became constantly biased opposite the cue. A persistent peripheral cue causes an imbalance in the oculomotor system that is rebalanced if persistent saccades are generated in the opposite direction. (C&D) Similar to (B), but when forcing the fixation spot ~2.7’ away from gaze (either opposite the cue (C), or towards it (D)). Microsaccade direction was strongly influenced by foveal motor error, and in all cases, the control oscillations were disrupted. The faint colors are those in b but included to facilitate comparison. Error bars denote 95% confidence intervals.

In the control condition, microsaccade directions oscillated (Fig. 11A), consistent with our results in the original attentional task of Study I (Fig. 6A). Note that there was no attentional requirement in the present experiment, but the same oscillations occurred. This confirms our hypothesis that the microsaccade modulations in Posner cueing are reflexive, and

explained by simple phase resetting (Hafed and Ignashchenkova 2013). More interestingly, when we simply controlled instantaneous foveal motor error, without any other change to the task, the microsaccade direction oscillation was disrupted entirely. Instead, microsaccades had a sustained bias opposite the cue and the effect has been magnified compared to the control condition (Fig. 11B; compare to Fig. 11A). This means that microsaccade direction oscillations are not necessarily due to reflexive peripheral covert attentional oscillations. Instead, they are highly sensitive to the tiny instantaneous foveal motor errors away from the fixation spot that might occur due to fixational eye movements. Experimentally reducing these foveal motor errors did away with the oscillations continuously. Concerning why there was a long-term sustained bias of microsaccade directions away from the peripheral stimulus, we think that this reflects the idea of fixation as balance in the SC (Goffart et al. 2012b; Hafed et al. 2008). Specifically, with everything stabilized on the retina, corrective movements do not allow recentering gaze; this results in a persistent influence of the peripheral cue, which the oculomotor system counteracts by biasing itself to make more microsaccades in the opposite direction.

We also found more evidence that tiny foveal motor errors are what drive microsaccadic oscillations in cueing. In the same experiment, with a forced foveal error (~2.7') opposite the cue (Fig. 11C), the effect of a sustained bias opposite the cue was appeared and significantly lasted for a long time; with a forced foveal error (~2.7') towards the cue (Fig. 11D), the effect of initial cue-directed "escapes" was significant. In all of these cases,

microsaccade directions were strongly modulated by a tiny foveal motor error and the role of microsaccades is only serviced for the foveal error correction.

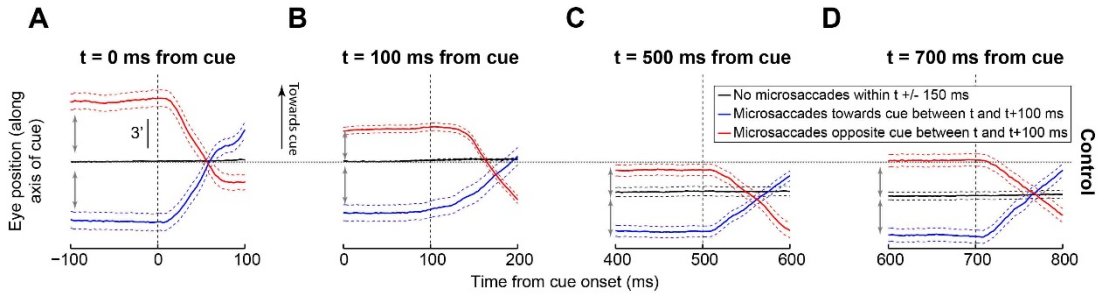

Figure 12. Eye position at different times in the control trials of retina-image stabilization. For each time t, we measured average eye position when there were no microsaccades within t+/-150 ms. This was deemed the preferred retinal locus at t (black). We then measured average eye position when there were microsaccades between t and t+100 ms towards (blue) or opposite (red) the cue. Error bars denote s.e.m.

The above results also receive support from analyzing the patterns of foveal motor errors driving microsaccades in the control condition of this study. In this control condition, the fixation spot was stable on the display. Thus, if the eye drifted away from it, then this increased foveal motor error. A microsaccade would therefore be expected to reduce such an error. The question is: does this relationship hold true for different post-cue times? We picked all microsaccades to or away from cue location happening at different time samples relative to cue onset. We then plotted the foveal motor error leading to such microsaccades (Fig. 12). Before cue onset (Fig. 12A), microsaccades were triggered to bring gaze closer to the optimal foveal locus indicated by the black line. Interestingly, this same relationship held for all other times after cue onset (Fig. 12B-D). Thus, regardless of time after cue onset, microsaccades were still doing their normal function of reducing instantaneous foveal motor error. The oscillations in direction relative to cue location (e.g. Fig. 11A) are

essentially an epi-phenomenon of the phase resetting process, and not necessarily reflection of the idea that microsaccades are providing a “dirty” read-out of top-down signals related to attention.

4.4 Short summary

In order to maintain fixation well, the saccadic system triggers microsaccades to correct eye position error and let the eyes keep the optimal foveal retinal locus. Combined with Study I, this means that based on instantaneous foveal motor error, one can predict whether a microsaccade in one direction is likely, and one can therefore predict whether there would be “attentional” effects if a target were to now appear. This is a powerful advance in our understanding of Posner cueing, and it creates several interesting neurophysiological hypotheses about the mechanisms of attention. In the third and final study of this thesis, we go one step further in elucidating how and why microsaccades might be triggered, and we discover a new microsaccade phenomenon in the process. The starting point for our investigation was the observation in Fig. 12 that the black optimal foveal locus was not constant at all post-cue times, but systematically shifted away from the cued location. This indicates that fixational eye position itself, independent of microsaccades, is yet another intriguing additional variable to consider in studies of covert visual attention.

5. Beyond microsaccades: dynamics of fixational eye position and what they imply

5.1 Rationale of this study

A thus-far neglected factor in studies of the links between spatial cueing and microsaccades has been the influence of fixational eye position per se. The implications of microsaccades in cueing tasks on fixational eye position dynamics are not explored even though microsaccades alter gaze position; conversely, the conditions of fixational gaze position that may or may not increase microsaccade likelihood in cueing tasks are unknown. This gap in our understanding exists because most modern studies of microsaccades have relied on video-based eye trackers, making it hard to reach reliable inferences about the role of fixational eye position dynamics. Here, we used spatially and temporally precise scleral search coils combined with real-time retinal-image stabilization (Chen and Hafed 2013a; Tian et al. 2016) to investigate exactly these questions.

We uncovered a highly systematic relationship between instantaneous foveal eye position error (a direct consequence of instantaneous fixational eye position) and microsaccade occurrence in cueing tasks, and we discovered a new phenomenon of “express microsaccades” that critically depends on such a relationship. More importantly, we additionally found that cue onset causes reliable drifts in eye position to new foveal “set points” of the oculomotor system that microsaccades are directed towards. Instantaneous

fixational eye position after cue onset is thus not a random variable. Instead, besides microsaccadic influences on performance alluded to above, retinal-image position changes associated with foveal eye position itself may be relevant for performance in spatial cueing tasks.

5.2 Methods

We collected eye movement data from three (*N, P and F*) adult, male rhesus monkeys (Macaca mulatta) that were 6-11 years of age and weighed 9 –13 kg. All experimental protocols for the monkeys were in accordance with the guidelines for animal experimentation approved by the local governing committee of Tuebingen city, Germany. The monkeys sat 45cm in front of a CRT monitor (22 pixels/° and 120 Hz) and were measured eye movements with high temporal and spatial precision technique of the scleral search coils by 1 kHz sampling frequency (Judge et al. 1980; Robinson 1972).

There were two experimental tasks in this study. The first task was same as that in our Study I, which is a classic spatial (Posner) cueing task (Fig. 4A), but performed by monkeys. For this task, the monkeys fixated a central spot with a gray background for 500-1000ms. A cue (1 diameter white circle of similar luminance to the spot) appeared at a peripheral 5° to one of the cardinal directions (right, left, up or down) for 35 ms. After a random waiting time 8-1508ms, an identical circle (target) appeared at the previously cued location (same) or symmetrically opposite it. When the fixation spot was removed, monkeys had to orient to the target with a saccade as fast as possible. We analyzed 8195 trials from monkey *P*,

6990 trials from monkey *N*, and 4083 trials from monkey *F* in this task. The second task was similar to the task of Study II but with real-time control of foveal motor error during initial gaze fixation only (i.e. before cue onset). Only in monkeys *P* and *N*, this second experiment compared a control condition similar to that of the first experiment to a retinal-image stabilization condition. The detailed procedures of this experiment are as follows. The control condition was identical to that described in Study II (right panel of Fig. 10). However, for the retinal-image stabilization trials, compared with Study II (left panel at Fig. 10), we only stabilized the fixation spot and the rest was the same. Across both monkeys, we analyzed a total 13973 control trials and compared them to 5123 retinal-image stabilization trials.

5.3 Results

5.3.1 A new phenomenon - express microsaccades

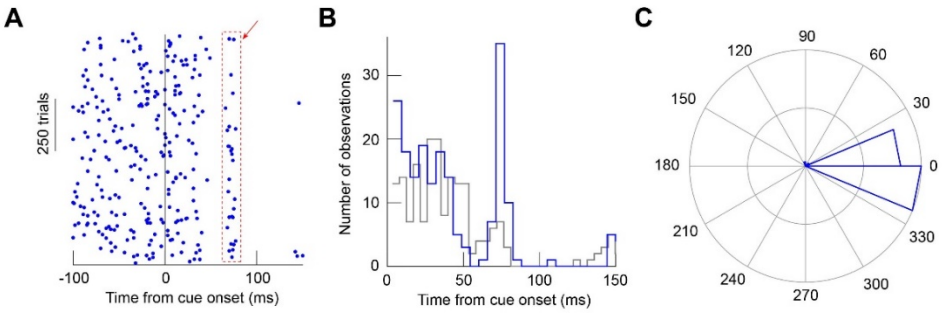

Figure 13. Express microsaccades. (A) Each row of dots is a trial from a sample monkey (P) with a sample cue location (upward), and each dot indicates the onset time of a microsaccade. Shortly after cue onset, microsaccade frequency abruptly decreased to zero, as expected. However, there was a population of subsequent “express” movements triggered with latencies from cue onset of <100 ms (highlighted by the dashed rectangle). (B) Same data as in panel A but presented as a frequency histogram, demonstrating the distinct population of movements with express latencies shortly after the onset of microsaccadic inhibition. For comparison, the gray histogram shows similar analyses for another cue location (downward) from the same monkey. Even though the express movements were fewer, they still occurred and shared properties with those observed for the upward cue. (C) Direction histogram of the express movements

(with latencies of 60-100 ms from cue onset) shown in A, B. We plotted the difference in direction between a given microsaccade and the direction of the cue relative to the fixation spot, such that a value of zero indicates perfect alignment between microsaccades and the cue. The directions of express microsaccades were highly aligned with cue location.

We observed microsaccadic inhibition right after cue onset in the first experiment, but closer inspection of the data revealed a distinct population of microsaccades that were triggered within a narrow time window of ~60-100 ms after cue onset, and shortly after the onset of the microsaccadic inhibition phase. For example, in Fig. 13A, each dot represents the onset time of a microsaccade relative to cue onset (in this case, for the upward cues) in one of our monkeys (monkey *P*), with trials from the same monkey and cue location stacked as rows. Microsaccadic inhibition started at ~50 ms after cue onset, and it was followed on some trials (53/1311; 4.02%) with a population of eye movements reminiscent of “express saccades” that can be observed in larger visually-guided saccade tasks (Carpenter and Williams 1995; Fischer and Breitmeyer 1987). That is, these movements, highlighted in red rectangle in the figure, formed a distinct population of movements from the microsaccades occurring in the pre-inhibition phase, and they had very short latencies relative to stimulus onset. These observations can be better appreciated with the same data plotted as a frequency histogram of microsaccade latencies from cue onset (Fig. 13B, blue): there was a steady rate of microsaccade occurrence early after cue onset, followed by the onset of an inhibition phase, and then followed once again by a distinct peak of microsaccades with “express” latencies (highlighted by the red arrow). Importantly, these microsaccades were also highly congruent in direction with the location of the cue. Specifically, Fig. 13C plots the distribution of angular differences between cue location and

these microsaccades' directions (i.e. for the same movements highlighted by red arrows in Fig. 13A, B), and it shows that these movements had directions that were almost entirely within +/- 30 deg from the direction of the cue (the average directional difference between the microsaccades and cue direction was 2.14 deg +/- 2.04 deg s.e.m., and it was not significantly different from zero; p=0.299, t-test, N=53 microsaccades). Because these movements were clearly triggered by cue onset both in time (Fig. 13B) and in direction (Fig. 13C), and because they had very short latencies reminiscent of those associated with larger express saccades (Fischer and Ramsperger 1986; 1984), we referred to these movements here as "express microsaccades".

5.3.2 The generation of express microsaccades

5.3.2.1 Eye position error dictates the occurrence of express microsaccades

Express microsaccades did not occur with equal likelihood across all trials. We explored the conditions that could contribute to the occurrence of these eye movements. Based on our hypothesis after Study II (Fig. 12), we believed that the instantaneous eye position error from the optimal locus would play a significant role. Specifically, we hypothesized that if the eye was already near the optimal foveal locus, then the oculomotor system was close to balance, make it easier for cue onset to trigger a quick and reflexive movement. Indeed, we found that express microsaccades were on average >3x the size of normal

microsaccades. Thus, they most definitely increased foveal motor error rather than decreasing it. We explored this increase further.

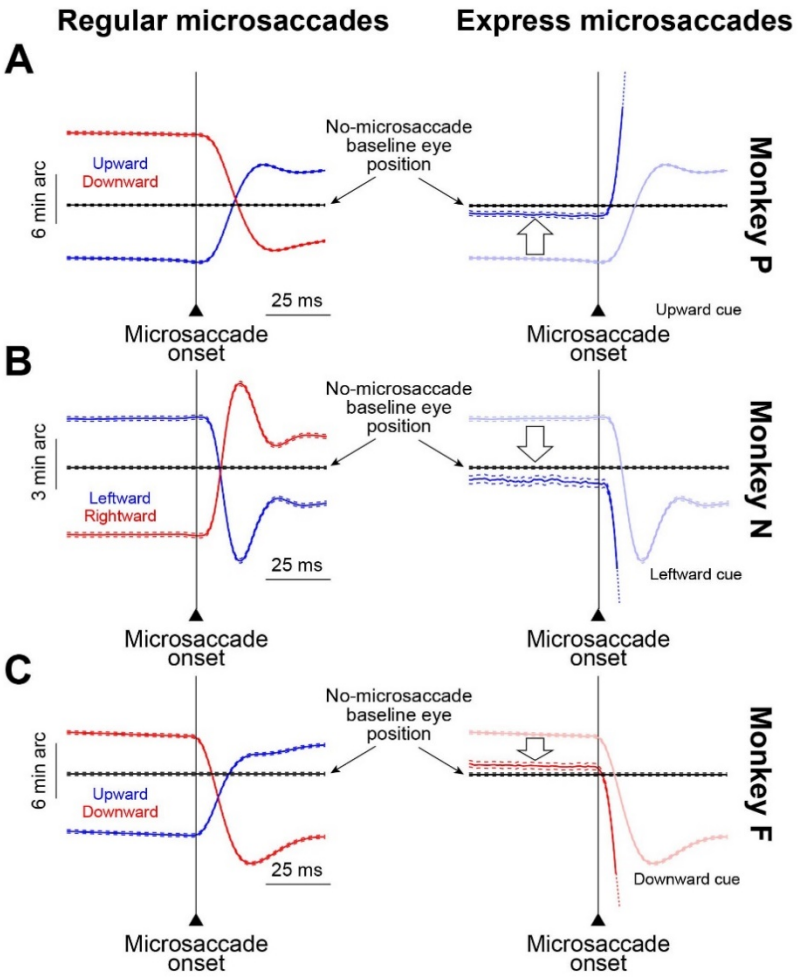

Figure 14. Spatially, express microsaccades occurred when there was minimal eye position error to correct for at fixation. (A) For monkey P, the left panel shows the relationship between eye position error during baseline fixation and microsaccade direction. The black line shows average vertical eye position (+/- s.e.m.) during microsaccade-free fixation before cue onset (we ensured that there were no microsaccades 0-300 ms before cue onset, and we plotted the middle of this interval in this figure). We next plotted average vertical eye position (+/- s.e.m.) aligned on microsaccade onset for all upward (blue) or all downward (red) microsaccades. Microsaccade directions were dictated by the sign of eye position error that existed before movement triggering. However, when express microsaccades happened (right panel), they did so when the eye was already almost "balanced" at its optimal fixation position. That is, the cue happened to appear when the eye was already at its optimal position, making the cue much more effective in triggering an eye movement away from this position. The faint blue curve in the right panel is a replica of the blue curve in the left panel to facilitate comparison between regular and express microsaccades (black arrow). (B, C) Similar analyses for monkeys *N* and *F*. In all cases, express microsaccades were triggered when there was minimal eye position error at fixation when the cue appeared (express microsaccades were also much bigger than regular ones). Note that for each monkey, we analyzed eye positions along the direction resulting in the highest proportion of express microsaccades; it is for these

directions that the eye was most likely to be near a balance point at the time of cue onset, and therefore most likely to be captured by cue onset in an express manner.

We specifically measured eye position carefully while the monkeys fixated steadily without any microsaccades for 300 ms before cue onset. This eye position was deemed the current "set point" for the oculomotor system, and it was probably dictated by the preferred foveal retinal locus for fixation. We then measured eye position for express microsaccades and regular microsaccades (shown at Fig. 14). For example, in monkey *P*, for which express microsaccades were most likely for upward cues, we analyzed vertical eye position before and after cue onset. Before cue onset, upward microsaccades (blue in the left panel of Fig. 13A) were triggered when vertical eye position was below the set point established without any microsaccades (black curve). Thus, upward microsaccades acted to reduce eye position error during baseline fixation, similar to our recent observations; for comparison, eye position for downward microsaccades in the same animal are also shown in red and again demonstrate the corrective nature of regular, pre-cue microsaccades. However, after cue onset, when there was an upward express microsaccade (rightward panel in Fig. 14A), there was minimal foveal eye position error from the baseline oculomotor set point (the faint blue curve is a replica from the left panel to facilitate comparison of the express microsaccades to the regular ones). The same results were also replicated in other two monkeys (Fig. 14B-C). Therefore, in all three monkeys (Fig. 14), express microsaccades were triggered when the eye was at an equilibrium position near the preferred retinal locus of fixation at the time of cue onset, meaning that the cue could easily tip the balance of fixation and trigger a large, cue-directed express microsaccade. This evidence adds further

support to our conclusions from Study I and Study II that the state of foveal motor error dictates microsaccade properties, and therefore attentional effects in Posner cueing.

5.3.2.2 Time since the last microsaccade dictates the occurrence of express microsaccades

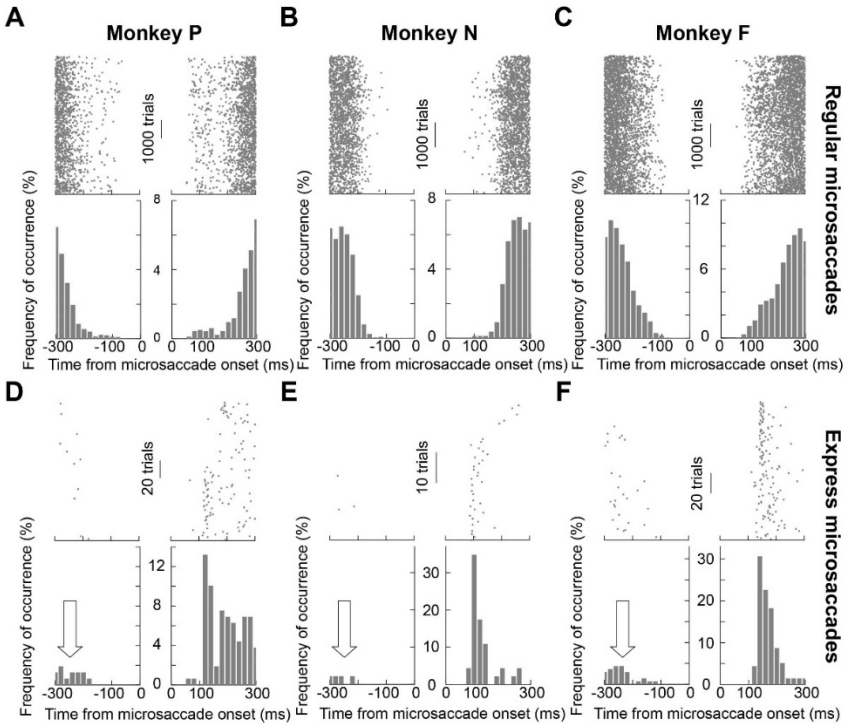

Figure 15. Microsaccadic temporal structure influenced the likelihood of observing express microsaccades. (A, B, C) For each monkey, we measured microsaccade probability either before (left histogram in each panel) or after (right histogram in each panel) the occurrence of a given microsaccade (akin to computing a microsaccadic autocorrelation function), and we did this for regular microsaccades occurring during a baseline fixation interval before cue onset (-500~0 ms from cue onset). As expected, microsaccade probability increased ~100 ms before or ~100 ms after a given movement. The panels above each histogram show the raw rasters of microsaccade onset times across repetitions of this analysis. (D, E, F) Repeating the above analysis but for express microsaccades (occurring 60-100 ms after cue onset) revealed that express microsaccades were most likely to occur if there was a particularly long interval of no microsaccades during fixation (see the downward black arrows and the raster plots above each histogram). Note also that express microsaccades were often followed by a second population of low-latency microsaccades that were corrective back to the fixation spot given how big express microsaccades were. Thus, a particularly long fixation interval with no prior microsaccades is among the temporal conditions that can increase the likelihood of observing express microsaccades.

Besides foveal retina locus, we also observed that a second important factor for predicting when express (and regular) microsaccades are expected to occur is time since the last microsaccade. We compared the temporal relationship between successive microsaccades during baseline fixation (before cue onset) to this relationship for express microsaccades in particular. For each baseline microsaccade (i.e. occurring before cue onset), we plotted a frequency distribution of the times of all previous movements to the selected microsaccade and a similar frequency distribution of the times of all subsequent movements. The result, akin to a microsaccade-aligned autocorrelation function, revealed that during baseline fixation, microsaccade probability increased ~100 ms before or ~100 ms after the occurrence of any given movement, and this was true in all three monkeys (Fig. 15A-C). However, this expected behavior of microsaccades was strongly violated for express microsaccades. In each of the monkeys (Fig. 15D-F), there was a noticeable scarcity of microsaccades occurring before any given express microsaccade, meaning that the latter movements were triggered when the cue appeared at a time in which no recent microsaccades had occurred for a substantial amount of time. Note that the analyses in Fig. 15D-F revealed that express microsaccades were followed by additional microsaccades with shorter average latencies than during baseline fixation before cue onset (compare the rightward histogram in each panel to the corresponding histogram above in Fig. 15A-C). These additional subsequent movements likely occurred to correct for the large fixation error caused by express microsaccades, because these express movements could be as large as 1 deg in amplitude in all three monkeys.

5.3.3 Express microsaccades are functionally relevant for attentional task performance

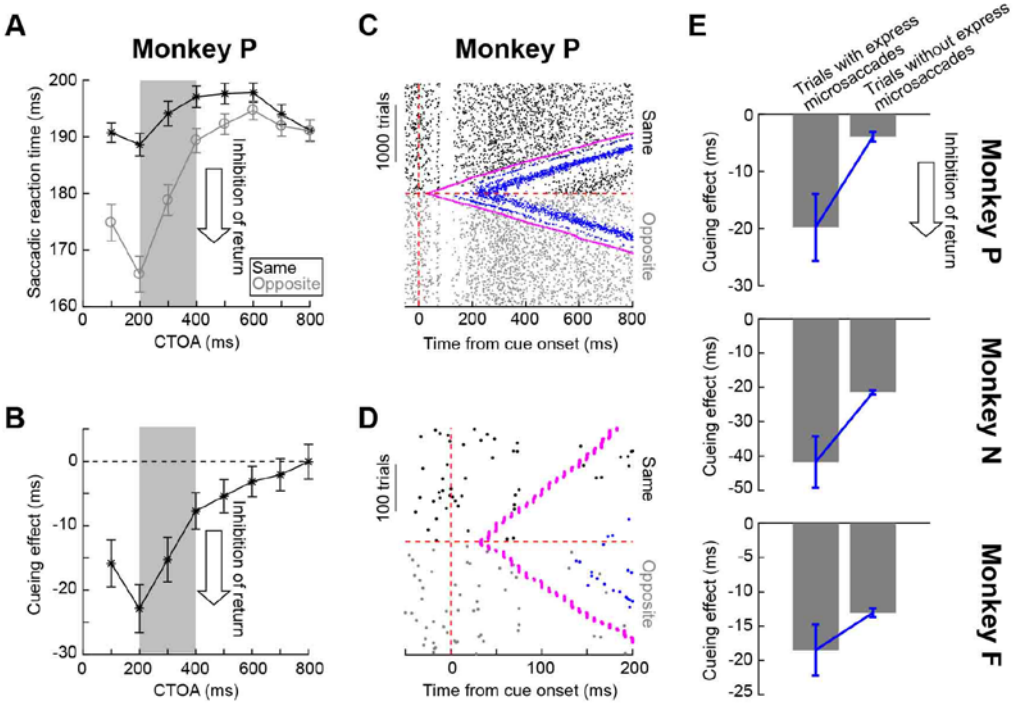

Figure 16. Express microsaccades were associated with magnified cueing effects. (A) Saccadic RT as a function of CTOA for an example monkey (P). RT was faster for opposite than for same target locations, especially for CTOA's around ~200 ms, consistent with well-known inhibition of return. Note that with CTOA randomization like in our case, it is unlikely to observe short-CTOA RT benefits for same trials compared to opposite ones, and this also depends on microsaccadic behavior (Tian et al. 2016). Thus, the primary cueing effect that we could relate express microsaccades to in our data was inhibition of return. Error bars denote 95% confidence intervals, and the shaded rectangle defines an interval in which we explored the influence of express microsaccades on RT. (B) Cueing effect, defined as the RT difference between opposite and same trials (Materials and Methods), for the data in A. Error bars denote 95% confidence intervals. (C) Raster of microsaccade onset times as a function of CTOA for the same data in A, B. Each black or gray dot is a microsaccade onset, and each row is a trial. Magenta dots indicate target onset, and blue dots indicate response saccades. Trials were sorted by CTOA and target location relative to the cue (black means same); trials with no magenta dots had longer CTOA than shown in the figure. (D) Magnification of the short CTOA subset of data from C, demonstrating how microsaccadic inhibition precludes analyzing relationships between express microsaccades and RT on very short CTOA trials. Moreover, for such trials, microsaccades are replaced by the real response saccades. Also note how RT was already shorter for opposite than same trials for early CTOA's in this figure (compare blue dots for same and opposite trials). (E) For all three monkeys, the cueing effect during the interval 200-400 ms after cue onset (shaded region in A, B) was magnified on trials with express microsaccades (error bars denote 95% confidence intervals). Note that for this analysis, we only considered horizontal cue and target locations. This is because vertical saccades have strong saccadic RT asymmetries (Hafed and Chen 2016;

Schlykowa et al. 1996; Zhou and King 2002). Thus, for a given cue location, “same” and “opposite” saccades would necessarily be upward versus downward, or vice versa, complicating any interpretation of cueing effects without RT asymmetry contamination.

We next turned to the question of attentional task performance. As we showed in Study I, microsaccades can influence performance in the Posner cueing task, perhaps even accounting for the entire phenomenon. If this is the case, then the larger express microsaccades that we discovered here should be even more relevant, so we asked whether the occurrence of express microsaccades has magnified cueing effects on the trials in which these eye movements occurred. As we know, in this classic cueing task, different CTOAs are known to cause differential saccadic RT effects for targets in the same and opposite cued locations; moreover, a measure of “cueing effect” is the best indicator for the attentional benefit or costs (Klein 2000a; Lupianez et al. 2006; Posner 1980; Posner and Cohen 1984; Posner et al. 1985; Tian et al. 2016). In the example of 1 monkey (*P*), we found that the cueing effect was most negative ~200 ms after cue onset (Fig. 16A-B), indicating strong IOR (Klein 2000a; Lupianez et al. 2006; Posner 1980; Posner and Cohen 1984; Posner et al. 1985; Tian et al. 2016). Because express microsaccades were not very frequent in our experiment (N=97 trials out of N=3911 trials in the example data of Fig. 16C), and also because of microsaccadic inhibition reducing the number of microsaccades in very-early CTOA trials (Fig. 16D), we could not measure the cueing effect for very short CTOAs with enough express microsaccade trials (microsaccades might be replaced with response saccades for short CTOA’s). It was therefore hard to relate the occurrence of express microsaccades to short-CTOA cueing effects. However, during well-known IOR epochs (200-400 ms after cue onset; shaded regions in Fig. 16A-B), we had sufficient trials

with express microsaccades to compare cueing effects with and without these movements. In all three monkeys (Fig. 16E), trials with express microsaccades had significantly stronger cueing effects (in this case, IOR) than trials without (error bars in Fig. 16E denote 95% confidence intervals). This means that RT's on opposite trials got significantly faster when an express microsaccade was triggered earlier by the cue. We think that the effect of express microsaccade triggering lingered until 200-400 ms after cue onset because express microsaccades were almost always followed by an opposite movement (see Fig. 15) ~100 ms later. Thus, by the time of target onset in our analysis interval of Fig. 16E, the saccadic system had already "flipped" towards the opposite location, and the target onset now appeared in the temporal vicinity of a directionally congruent microsaccade. This is the exact result that is known to maximize microsaccadic influences on peripheral performance from our Study I (Fig. 6). These observations of magnified cueing effects (Fig. 16E) clearly indicate that express microsaccades contribute to it.

5.3.4 The oculomotor set point is itself variable

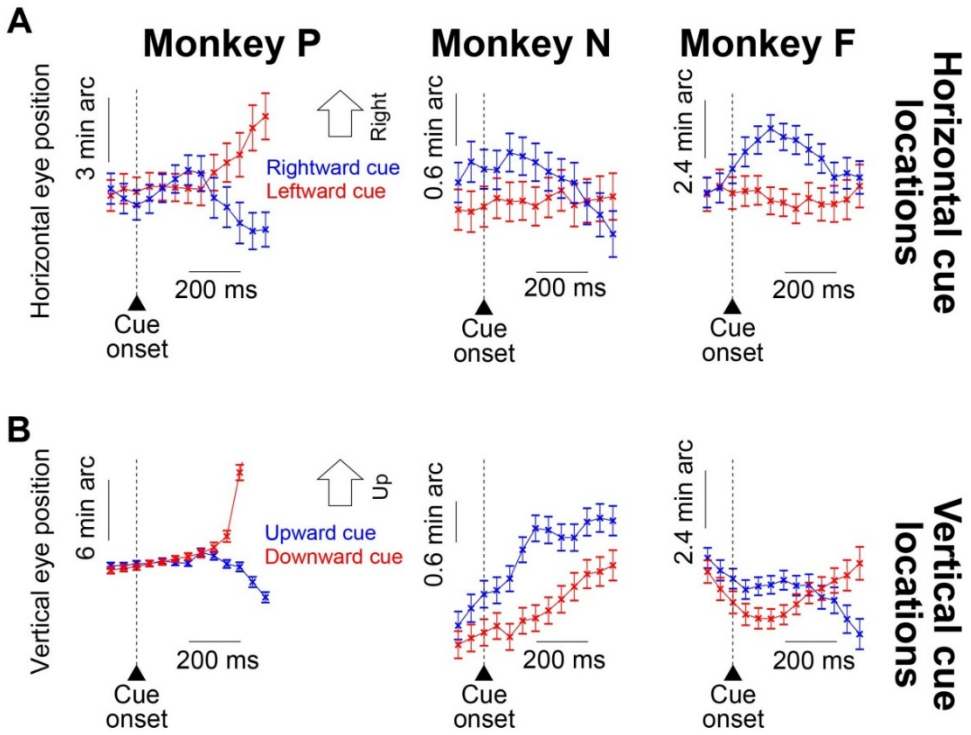

Figure 17. Optimal baseline eye position was deviated away from cue location in the longer term after cue onset. (A) For each monkey (across columns), we picked successive 100-ms fixation intervals that did not contain any microsaccades in them, and we measured mean (+/- s.e.m.) eye position during these intervals. Eye position was not static after cue onset. For example, for times longer than ~200 ms after cue onset, eye position began to shift leftward for rightward cue locations in all 3 monkeys (i.e. opposite the cue location). Similarly, in monkey P, eye position shifted rightward for leftward cue locations, with a weaker trend in the other 2 animals. Thus, the “baseline” to which microsaccades attempted to balance gaze was not a static entity, but it changed with time several hundred milliseconds after cue onset. (B) Similar analyses for vertical eye positions after vertical cue onsets. Note that in monkeys P and F, a clear reversal opposite cue location was evident (as in the horizontal cue conditions), such that eye position shifted upward for downward cues and downward for upward cues long after cue onset. Monkey N’s modulations were masked by consistent nystagmus-like shifts in eye position. Upward deflections in the curves of A denote rightward eye position deflections, and upward deflections in B denote upward eye position deflections.

Given the new phenomenon of express microsaccades, we are now ready to explore the point about optimal foveal locus that we alluded to by comparing the black lines in the different panels of Fig. 12. Is the optimal set point of the oculomotor system constant? We

picked successive 200ms intervals of no microsaccades, and plotted the average eye position in these intervals. For example, in Fig. 17A, each data point relative to cue onset plots the average horizontal eye position after a horizontal cue onset, but subject to the constraint that there were no microsaccades within +/- 100 ms from that particular data point. Similarly, Fig. 17B repeats this analysis for vertical eye position after vertical cue onsets. In all monkeys, eye position was not a stable entity after cue onset. For example, in monkey *P*, after ~300 ms from cue onset, eye position systematically shifted away from cue location for both horizontal and vertical cues. While this effect might reflect the fact that most microsaccades are known to bias away from cue location at these times (shown in Fig. 7D), it does still nonetheless mean that eye position is not a static entity in spatial cueing tasks. The other two monkeys also showed similar reversals in eye position relative to cue location. For example, in monkey *N*, rightward cues eventually caused more leftward eye positions than leftward cues at the end of the shown interval, and in monkey *F*, upward cues caused more downward eye positions than downward cues at the end of the shown interval. For vertical cues in monkey *N* and horizontal cues in monkey *F*, changes in the "direction" of eye position modulations as a function of time were consistent with a reversal away from the cue, although they were masked by systematic changes in position that were present even before cue onset (whether due to nystagmus-like drifts or to microsaccade asymmetries, or both). For example, in monkey *N*, the rate of upward drift was slowed down after >300 ms for upward cue locations but accelerated for downward cue locations. Similarly, in monkey *F*, a rightward drift in position switched to being leftward >300 ms after rightward cues. Thus, cue onset systematically deviated eye

position towards its location with short latencies; for longer latencies, the net effect of both microsaccades and slow control meant that eye position was not a static entity, but dynamically shifted away from the cue location under most circumstances, i.e., such an "away" shift was also observed in our previous study II (Fig. 12).

5.3.5 The oculomotor set point depends on more than just microsaccades

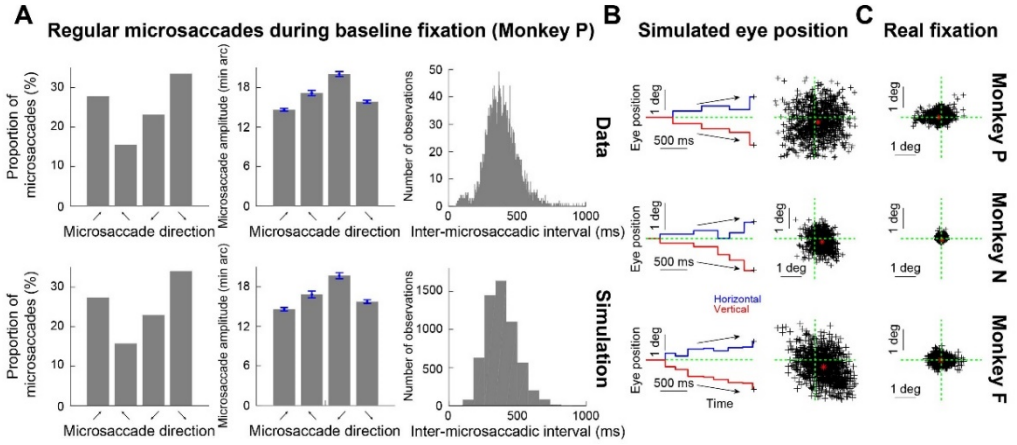

Figure 18. Optimal baseline eye position was not a simple outcome of the aggregate influence of successive microsaccades. (A) For each monkey (P shown as an example), we classified baseline microsaccades according to their direction (into one of the four quadrants), and we measured their intrinsic direction (leftmost histogram) and amplitude (middle histogram) biases. This monkey made more microsaccades towards the upper and lower right quadrants, but these movements were smaller than those into the upper and lower left quadrants. We also measured inter-microsaccadic intervals (rightmost histogram). We then created simulated data sets (bottom row) in which a microsaccade could occur in a given simulated trial at random with the same biases as in the monkey, and with the same inter-microsaccadic interval distribution. (B) For each monkey, we simulated 2-second fixation trials in which the sole determinant of eye position was the outcome of microsaccades with intrinsic biases and times like those shown in A. The left column shows example simulated trials, demonstrating how eye position would increasingly deviate with time if the sole determinant of eye position were microsaccade amplitudes, directions, and times. The right column of scatter points shows the ending positions of simulated eye position after 2 seconds of fixation from 1000 simulated trials. As can be seen, simulated eye position had a large amount of scatter and was biased away from "center". (C) In contrast, real eye position at the end of the fixation period before cue onset was much more constrained in each of the monkeys. Thus, eye position, an important determinant of express microsaccade occurrence (Figs. 15-16), was not a simple outcome of successive microsaccades shifting gaze in particular directions, but it was optimized despite microsaccade biases.

Based on the above result, we would also ask what the relationship between this foveal eye position and microsaccades is. Are the results of Fig. 12 just an aggregate outcome of microsaccades? When we inspected the distribution of microsaccade directions and amplitudes during steady-state baseline fixation before cue onset, we found that there were persistent asymmetries that were present in each monkey. Such asymmetries are illustrated in the top row of Fig. 18A for monkey *P*. In the leftmost histogram, we divided microsaccades according to whether they were directed into one of the four quadrants around the fixation spot, and we measured the proportion of all microsaccades that were directed into a given quadrant. This monkey did not have perfectly uniformly distributed microsaccade directions, but it made more microsaccades towards the right visual field (upper and lower right quadrants). Similarly, microsaccade amplitudes were not the same in all four quandrants, but the monkey made slightly larger microsaccades into the left visual field (upper and lower left quadrants; middle histogram in the top row of Fig. 18A). Might it be the case that these asymmetries in microsaccade amplitudes and directions dictate the eye position set points in the pre-cue interval?

To test this, we created simulated data in which eye position was solely dictated by microsaccadic displacements in eye position. For each monkey, we measured direction and amplitude asymmetries as above, and we also measured inter-microsaccadic interval distributions (e.g. the third histogram in the top row of Fig. 18A). We then created simulated trials in which eye position was perfectly stable, except that microsaccades happened at

random times, but with inter-microsaccadic distributions and direction/amplitude biases that were the same as in the real data (bottom row in Fig. 18A). We then simulated 2 seconds of fixation (left eye position traces in Fig. 18A with simulations matched to each monkey's asymmetries). The right cloud of dots in Fig. 18B shows the final eye position after 2 seconds of simulated fixation from 1000 simulated trials in each monkey. As can be seen from Fig. 18B, if eye position was solely dictated by microsaccades, then asymmetries like those shown in Fig. 18A would result in runaway fixation. In the real data, eye position at the end of the pre-cue interval was much tighter than predicted by the aggregate sum of prior microsaccades (Fig. 18C). Thus, the eye position set points are independent of microsaccades, which is also consistent with our considerations from Study II. This means that eye position alone, independently of peri-microsaccadic influences, represents and additional factor that is worthy of consideration in the priority process of attention.

5.3.6 Controlling fixational eye position set points at cue onset modulates the statistics of early cue-induced microsaccades

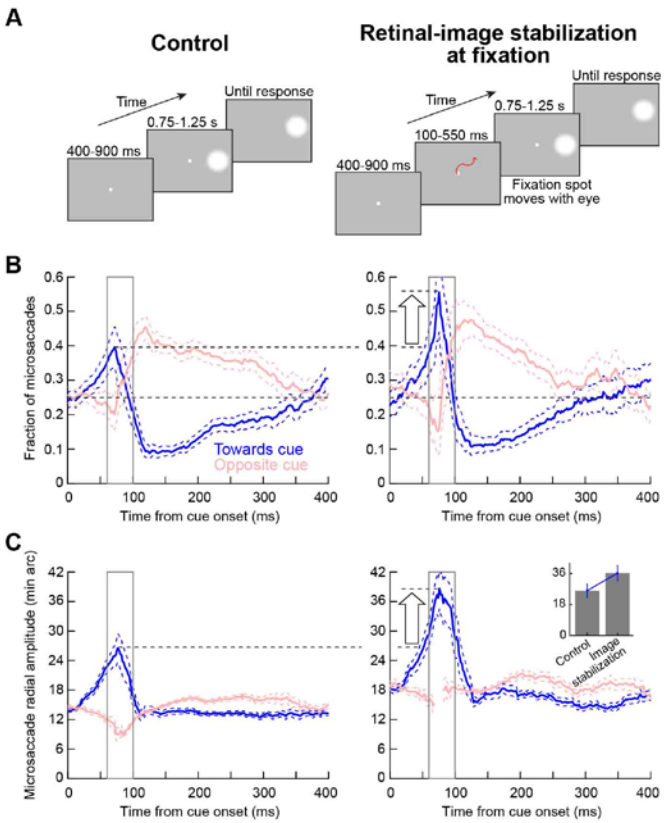

Figure 19. Causally manipulating the properties of early cue-induced microsaccades by real-time stabilization of the instantaneous retinal-image position of the fixation spot. (A) In monkeys P and N, we ran control trials interleaved with retinal-image stabilization trials, similar to Study II. Monkeys fixated, and a peripheral cue appeared for a variable duration. In retinal-image stabilization trials, the fixation spot was moved with gaze in real-time such that foveal eye position error at the time of cue onset was minimized (squiggly red line). When the cue appeared, retinal-image stabilization was stopped. (B) Time course of microsaccade directions after cue onset. The left column shows control trials, and the right column shows retinal-image stabilization trials; error bars denote 95% confidence intervals. In each condition, there was an increase in microsaccades towards the cue in the highlighted rectangles. However, in the retinal-image stabilization condition, the increase was significantly stronger (black arrow), consistent with the mechanism of Fig. 11. That is, with foveal gaze position error in balance, the cue's attractive influence on gaze was more effective. All analysis details in this figure are identical to figure 11. (C) Similar time course analyses but for microsaccade amplitude. The right panel shows that early cue-directed microsaccades were bigger when instantaneous foveal error was controlled than when it was not (black arrow). The inset shows microsaccade amplitudes in the interval 60-100 ms after cue onset, showing an increase in the retinal-image stabilization condition. Error bars denote s.e.m. (p=0.034, ranksum test). Thus, controlling instantaneous foveal eye position error at the time of cue onset has a significant impact on the efficacy of the cue to influence subsequent microsaccades, consistent with the mechanism of Fig. 11.

Finally, we did a causal experiment to demonstrate that express microsaccades can be triggered under the appropriate conditions. We randomly interleaved control trials (Fig. 19A, left) with retinal-image stabilization trials. The latter trials employed techniques, which we

have used in Study II that allowed us to artificially move the fixation spot in real-time with gaze position before cue onset (Fig. 19A, right). This ensured minimizing gaze position error at the time of cue onset. If such minimization was sufficient to trigger express microsaccades (as in Fig. 14), then we should have seen more cue-directed microsaccades 60-100 ms after cue onset than in the control condition, and these microsaccades should have also been significantly larger in amplitude. This is exactly what we found. In Fig. 19B (left), we plotted a time course of microsaccade directions after cue onset in the control condition. As we did in Fig. 11, we divided microsaccades into movements towards the cue, opposite the cue, or orthogonal to the cue (Materials and Methods). This means that before cue onset, there was a 25% chance that microsaccades towards the cue occurred. Such movements then increased in likelihood early on after cue onset, as expected from prior studies, before a reversal of microsaccade directions occurred. Such a reversal can be seen by the increase in movements opposite the cue shown in faint red color in the figure. Importantly, with experimental control over eye position error at the time of cue onset in the retinal-image stabilization trials (Fig. 19B, right), the increase of movements towards the cue in the critical interval of 60-100 ms was significantly dramatic (black arrow). Similarly, the amplitudes of these movements were also larger than in control, as can be seen from the time courses of microsaccade amplitudes shown in Fig. 19C. Thus, experimentally placing the oculomotor system at a point of equilibrium, albeit an unstable one (Fig. 20), was sufficient to increase the likelihood of express cue-directed microsaccades (and with larger amplitude), even though

the manipulation was only a subtle and very brief manipulation at the fixation spot with all other stimulus conditions being identical to those in the control trials.

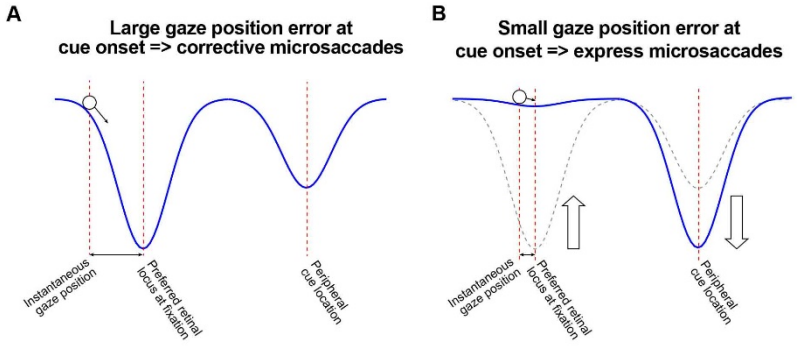

Figure 20. Express microsaccade occurrence as an outcome of an "energy potential" landscape associated with instantaneous foveal eye position error at fixation. (A) Energy landscape analogy explaining the importance of gaze position at the time of cue onset. When there is a relatively large foveal eye position error at cue onset (like in Fig. 14A, left), there is a substantial local minimum that attracts gaze (ball in this analogy) to the optimal position needed to align the fixation spot with the preferred retinal locus in the fovea. Thus, even with the attractive influence of cue onset, microsaccades behave in a primarily corrective manner like the regular ones shown in Fig. 14A, left. (B) On the other hand, when gaze is almost balanced at the optimal preferred retinal locus for fixation, the local minimum associated with this locus is all but abolished, and cue onset exerts a much stronger attractive influence on eye movements. The dashed gray lines indicate the "energy potential" when gaze is not at its preferred locus (as in A). Thus, near-optimal gaze fixation along with a remaining foveal error that is congruent with cue location are associated with the highest likelihoods of express microsaccades.

5.4 Short summary

In the current Study III, we extended our research and explored the prediction of attentional modulations through the example of "express microsaccades". Besides the validation of all of our hypothesis from Studies I and II, we also found that optimal foveal eye position is another important factor in this process. From this perspective, it paves a new way to help us to understand more how higher cognitive processing (attention) works.

6. Closing Remarks

6.1 Summary

The starting point of my thesis was very simple and just to investigate the effects of peri-microsaccadic changes in vision on the classic cueing paradigm, and more specifically, on how much such peri-microsaccadic changes can help us to understand such a broadly studied cognitive function. In Study I, we embarked on a theoretical investigation and found that a simple model invoking motor repetitiveness and pre-microsaccadic alteration of vision sufficiently accounts for AC and IOR in Posner cueing. Unlike other models, at the time of dictating its final behavior, our model knows nothing about the previous cue location or what top–down covert attentional strategies are needed. All it does is react to stimuli, with the spatial and temporal phase of these stimuli determining how efficient the response to them is. Moreover, microsaccade direction oscillations, a critical component of the model, reflect oculomotor control over foveal motor error (Study II) and are independent of peripheral covert attentional oscillations. We then started the in-depth Study III and tested whether it can predict attentional performance in the example of extreme “express microsaccades”. In this study, based on the rule of foveal error, we explored the mechanism of express microsacade generation and also observed a change in microsaccade-free fixational gaze position immediately after cue onset (Fig. 17). These results are particularly intriguing because they demonstrate fine stimulus-induced control over non-saccadic ocular drifts during fixation, and also because they show that dynamic changes in fixational eye position during spatial cueing tasks are not entirely accounted for by cue-induced

changes in microsaccade directions and amplitudes alone (Fig. 18). Therefore, in conjunction with eye position measurements, we could predict accurately in real-time whether microsaccades are expected to occur in response to visual stimuli or not, and also the related behavioral performance “attentional” scenarios.

6.2 Discussion

6.2.1 The physiological implications

The physiological implications of our studies are intriguing, especially in light of prior IOR research. In the SC, which is the most important brain area for the saccade generation, target-related visual bursts are enhanced for short CTOAs and suppressed for longer ones (Bell et al. 2004; Dorris et al. 1999; Fecteau and Munoz 2005). According to my studies, such modulations should be synchronized with microsaccades, and independent of cueing. This is indeed what we found in both SC and FEF which are also important brain areas for the saccade/microsaccade generation (Chen et al. 2015): without cueing, stimulus onsets before microsaccades elicit enhanced visual bursts if microsaccade directions are congruent with stimulus location and suppressed bursts if microsaccades are incongruent. These results suggest that peri-microsaccadic changes may be sufficient to account for attentional effects in classic cueing paradigm.

Recent findings also provide compelling evidence to support such possibility (Lovejoy and Krauzlis 2010; Zenon and Krauzlis 2012). When these authors inactivated a small region of the SC corresponding to the cued location, they found that monkeys ignored the cued

motion change and reported the motion change occurring at the foil location. Conversely, when the foil signal appeared in the inactivated region of the SC, the monkeys ignored this and transferred to report the motion change from the cued location. This effect was constant no matter which kind of response modality, saccade or manual response, was used. However, during this task, when they recorded from neurons in cerebral cortical areas MT and MST, which are relevant brain areas for attention, they found that while the monkeys were impaired at performing the task, all the cortical neural signatures of attention remained even after SC inactivation.

6.2.2 The premotor theory of attention

Indeed, our framework does not deny the “need” for attention in general, since it is already well-known that a tight link exists between attention and saccade motor preparation (Posner and Petersen 1990; Rafal and Posner 1987). What I want to re-state here is that the explanation of attention by the classic pre-motor theory for attention is reasonable: before saccades, preparatory signals are expected to modulate visual representations and attentional performance (Kustov and Robinson 1996; Rizzolatti et al. 1987). Since microsaccades are generated using similar mechanisms as larger saccades, it stands to reason that fixation is still an important factor given that microsaccades continuously occur. Thus, merely peri-microsaccadic modulations could be enough to provide a simple, yet mechanistic, account of cueing effects. Corbetta and his colleagues reviewed a range of studies of the attentional task by means of neuroimaging (Corbetta et al. 2000; Corbetta and Shulman 1998). The massive data has confirmed the notions that attention is not a

unitary concept and that attention works at the system level and with several brain areas involved. The fronto-parietal network, including frontal and supplementary frontal eye field (important nodes of the saccadic system), are the most active brain areas and such anatomical overlapping is consistent with the assumptions of the pre-motor theory.

6.2.3 The idea of momentary oculomotor balance

Concerning the important role of foveal motor error in dictating when peri-microsaccadic modulations might occur (Study II), we think that it suggests that foveal processing centered by the error has substantial contributions to attentional performance changes. However, because of the existence of error, the idea of balance becomes important and how this balance is maintained and updated. This idea of balance, of course, does mean that the balance is only momentary, because it has been proven in Study II and Study III that eye position continuously changes by minute amounts and the triggered microsaccades always served for it (Figs. 12, 17). Therefore, the balance may be thought of as an unstable equilibrium state, such that any perturbation of this state can push it away from balance. This is exactly what cue onset does. In Study III, we found that this accounts for express microsaccades and how they act to increase foveal eye position error as opposed to reducing it; the eye was already at the balance point before cue onset (Figs. 13, 15).

The idea of momentary balance would also indicate that significant trial-to-trial variability in behavior in cueing tasks can be related to the instantaneous state of the oculomotor

system. For example, the momentary reductions of neural activity in the rostral SC, a region related to the small eccentricities associated with microsaccades, are associated with increased visual bursts in more eccentric regions (Jagadisan and Gandhi 2016). If such reductions are correlated with the oculomotor balance, then stronger visual bursts could contribute to express microsaccade generation and magnified cueing effects. This would be consistent with the notion that SC visual bursts have high correlation with saccadic RT (Chen and Hafed 2017; Hafed and Krauzlis 2010).

6.2.4 Gaze fixation as equilibrium

Because of the above conclusions, we could develop a simple idea. That is, whether due to a lingering visual effect of the cue or due to a top-down signal associated with the cued location, the landscape of fixation is disrupted by cue onset, causing an imbalance in favor of the cued side. The eyes have to rebalance fixation given this imbalance. This is exactly consistent with how the SC is believed to contribute to gaze fixation through balanced population activity (Goffart et al. 2012a; Hafed et al. 2009; 2008). This can explain our perturbation effects in Study II.

An additional question related to this topic is on how eye position can be controlled beyond the SC balance idea just mentioned, and on what such control of eye position implies. Neurons in several brain areas, like parietal cortex (Andersen et al. 1990; Andersen et al. 1985), premotor cortex (Boussaoud et al. 1998), and prefrontal cortex (FEF/SEF) (Boussaoud et al. 1993; Cassanello and Ferrera 2007; Schall 1991), exhibit so-called eye

position gain fields. These neurons' various sensitivities are modulated as a function of absolute eye position. It could be that the neurons with gain fields can contribute to establishment of the new fixational eye position set points at different times after cue onset, and given the small changes in eye positions that we observed, our results suggest that the resolution of eye position control, whether from parietal areas or elsewhere, has to be quite high. In a complementary fashion, it could be the case that fixational eye position set point shifts are implemented exactly to alter neurons' various sensitivities by exploiting these neurons' eye position gain fields. Either way, it would be interesting to better understand the detailed role of position control circuitry on, not just eye position in cueing tasks, but also on how the retinal implications of eye position can affect task performance. In the Study I and II, one of my primary foci was on the influence of peri-microsaccadic changes on performance changes in attentional tasks, but in study III we went further and in the center of foveal error we uncovered the contribution of eye position and its associated drifts in eye position, are important in their own right. Based on it we could precisely predict the attentional performance (Fig. 16).

6.3 Future work

Until now, we have already given a clear summary for my finished studies, but in this section, we still introduce some programs which are still ongoing based on the outcomes of the experiments described in this thesis.

The first aim of this series of follow-up experiments is necessary to understand the express saccade. According to the SC map (Fig. 2), neurons in the rostral area of the SC have originally been considered to be involved to maintain fixation and engaged in a push–pull interaction with saccade-related neurons elsewhere in the SC (Munoz and Wurtz 1993a). Because of this, mutual inhibition between neurons in the rostral area and the rest of the SC for saccades was thought to implement a winner-take-all mechanism for determining whether fixation was maintained or a saccade was initiated (Munoz and Wurtz 1993b). From our results of Study III, this scheme is too simplistic. In fact, we found that perfect balance, a situation ideal for the “fixation zone” hypothesis, is exactly when express microsaccades would be triggered. We would like to extend this evidence further by studying larger express saccades.

The second necessary study is that we have to know the possible physiological support for all of our studies. We need to look for a specific population of neurons for eye position control to support our findings. Indeed, we have already used the laminar electrode to record SC. According to previous literatures (Dorris et al. 1999; Fecteau and Munoz 2005), there is a type of “build up” neurons in it (Glimcher and Sparks 1992; Kim and Basso 2008) and it has high possibility to contribute to this process. In addition, as we know, different information is coded in different SC layers (Basso and May 2017; Moschovakis and Highstein 1994; Moschovakis et al. 1988a; b). It is worthwhile for us to explore how different neurons coordinate with each other based on the SC’s layer structure (Fig. 2) and how this coordination is related to the changes in foveal eye position that we observed during

fixation. From our studies, we have a strong assumption that foveal regions have a strong and substantial influence on peripheral representations.

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