Nasal-temporal asymmetries and landing point probability manipulations of saccadic eye movements

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Thesis for the degree of Philosophiae Doctor

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Ómar I. Jóhannesson

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Abstract

The ability of the visual system to follow a moving object is amazing. Imagine that you have just hit a golf ball with your driver and it rushes away with a velocity of more than 230 km/h and you cannot start looking for the ball until you have finished your swing. The visual system is, however, able to find the ball and to follow it until it comes to a stop in the grass about 250 m away. To be able to see the ball, its image has to be kept on the fovea since visual acuity declines fast outside of it. To achieve this, the visual system has to combine movements of the body, the head and the eyes and reaches this goal without any conscious cognitive effort. What makes this task even harder is the fact that the fovea is very small, or just about 1 mm in diameter. The initial eye movements during the tracking are probably saccades, which are the main topic in this thesis. With this in mind it is easy to realize how important eye movements are in our daily lives for a wide variety of tasks.

Eye movements have a very important role in visual perception and research on eye movements can broaden our understanding of attentional functioning, selection and decision processes and neurological disorders. Saccades are very fast eye movements and since the latency, amplitude, peak velocity and accuracy of saccades have been intensely studied their basic characteristics are well known. Saccades have been classified as regular saccades, express saccades and microsaccades. Express saccades are saccades with very short latency and microsaccades are saccades with very low amplitude. The main emphasis in this thesis is on regular saccades, which can be split into anti- and prosaccades. Prosaccade is a saccade towards a stimulus but antisaccade is away from the stimulus.

The neurology of eye movements is rather well understood and it

is known that the frontal lobes play a large role in the generation of eye movements. Eye movements show abnormal characteristics in people with schizophrenia, attention deficit hyperactivity disorder, dyslexia, Parkinson's disease, Tourette's syndrome, Huntington's disease and obsessive-compulsive disorder. Deficits in frontal lobe functioning are also evident in these disorders.

Nasal-temporal asymmetries (NTAs), favoring the temporal visual field, have been found in the latency of the saccades by some authors but not others. NTAs in attentional function have also been found. It is also known that there are NTAs in the retina; the density of ganglion cells declines faster towards the temporal, than the nasal retina. There are also more projections from the nasal, than the temporal retina to the superior colliculi and the lateral geniculate nucleus. Since NTAs exist both in anatomy and attentional functioning it is reasonable to expect that they also exist in saccadic parameters. There is some evidence suggesting that probability manipulations of where the saccadic target appears can modulate the latency of the saccades.

In two studies, which consisted of eight experiments and 74 subjects we investigated NTA in latency, landing-point accuracy and peak velocity of prosaccades, with and with different attentional load and amplitude ranging from 5° to 20°. We found no NTAs in latency and they were only minimal in landing-point accuracy while strong NTAs were observed in peak velocity with higher peak velocity towards the temporal visual field. We concluded that it is the NTA in anatomy that leads to NTA in peak velocity.

In the third study (five experiments and 41 participants) we investigated the supposed modulatory effect of probability manipulations on the latency of anti- and prosaccades where the difference in latency of anti- and prosaccades (the antisaccade cost) was of main interest. The experiments consisted of blocks of prosaccades, blocks of antisaccades and blocks of anti- and prosaccades interleaved. It was not until anti- and prosaccades, horizontal and vertical saccades were interleaved with a visual search task that the probability manipulations resulted in decreased difference between the latency of anti- and prosaccades. Our conclusion

is that the probability manipulation lends its effects upon decision and selection processes, but not on saccadic preparation, per se.

Ágrip

Hæfileiki sjónskynjunar til að fylgja hlut á hreyfingu er stórkostlegur. Ímyndaðu þér að þú sért nýbúinn að slá golbolta með drívaranum þínum og boltinn þýtur af stað á hraða sem er meiri en 230 km/klst. Jafnvel þó þú getir ekki farið að litast um eftir boltanum fyrr en þú hefur lokið sveiflunni getur sjónkerfið fundið boltann og fylgt honum eftir þar til hann stöðvast í grasinu í allt að 250 m fjarlægð. Til að geta séð boltann verður mynd hans að falla á sjóngrófina vegna þess að sjónskerpan minnkar mjög hratt utan hennar. Til að það sé hægt verður sjónkerfið að samræma hreyfingar líkamans, höfuðsins og augnanna og gerir það án þess að við tökum eftir því. Eitt af því sem gerir þetta enn erfiðara er sú staðreynd að sjóngrófin er mjög lítil eða einugis um 1 mm í þvermál. Í þessu ferli eru fyrstu augnhreyfingarnar líklega augnstökk og þau eru megin viðfangsefni í þessari ritgerð.

Hlutverk augnhreyfinga í sjónskynjun er mjög mikilvægt og rannsóknir á þeim geta aukið skilning okkar á því hvernig athygli virkar, hvernig sjónræn áreiti eru valin, hvernig við tökum ákvarðanir og á hinum ýmsu sálfræðilegu röskunum. Augnstökk eru mjög hraðar augnhreyfingar og hafa einkenni viðbragðstíma, lengdar, nákvæmni og hámarkshraða þeirra mikið verið rannsökuð og eðlilegir eiginleikar þessara atriða eru vel þekktir. Augnstökk eru flokkuð í venjuleg augnstökk, örviðbraðgsaugnstökk og örsmá augnstökk. Viðbragðstími örviðbragðsaugnstökka er mjög stuttur og örsmá augstökk eru mjög stutt. Í þessari ritgerð er megin áherslan á venjuleg augnstökk, sem hægt er að skipta í tvo hópa, meðstökk og andstökk. Meðstökk eru í átt að áreitinu en andstökk í átt frá áreitinu.

Taugafræði augnhreyfinga er nokkuð vel þekkt og framheilinn

leikur stórt hlutverk í stjórn augnhreyfinga. Eiginleikar augnhreyfinga hjá fólki með geðklofa, athyglisbrest, lesblindu, Parkinsons veiki, Tourettes heilkenni, Huntingtons veiki og áráttu og þráhyggju eru frábrugðnir eiginleikum augnstökka hjá heilbrigðu fólki. Það sama á við um virkni í framheila. Nokkrar rannsóknir benda til þess að viðbragðstími við áreiti sem birtist gagnaugamegin (hliðlægt áreiti) í sjónsviði sé styttri en við áreiti sem birtist nefmegin (miðlægt áreiti) í sjónsviði en aðrar benda til þess að svo sé ekki. Aftur á móti benda niðurstöður rannsókna á miðlægri-hliðlægri ósamhverfu í virkni athygli skýrt til þess að hliðlæg áreiti fangi athygli hraðar en miðlæg áreiti. Miðlæg-hliðlæg líffræðileg ósamhverfa er vel þekkt og finnst bæði í sjónu og sjóntaug. Þéttni hnoðfruma í sjónu minnkar hraðar í átt að gagnauga en í átt að nefi og taugatengingar frá miðlægri sjónu að efri hólum og hliðlægu hnélíki eru öflugri en frá hliðlægri sjónu. Vegna þess að miðlæg-hliðlæg ósamhverfa er þekkt bæði í virkni athygli og líffræðilegum þáttum er rökrétt að búast við að hún sé einnig til staðar í eiginleikum augnhreyfinga. Að auki eru nokkuð góð rök fyrir því að möndl með líkur á því hvar áreiti augnsökka birtist geti haft áhrif á viðbragðstíma þeirra.

Í tveimur rannsóknum sem samanstóðu af átta tilraunum með samtals 74 þátttakendum rannsökuðum við viðbragðstíma, nákvæmni og hámarkshraða augnstökka. Í þessum tilraunum möndluðum við með álag á athygli og lengd augnstökkanna var frá 5° til 20°. Niðurstöður okkar sýna að miðlæg-hliðlæg ósamhverfa finnst ekki í viðbraðgstíma augnstökka og að hún er mjög óveruleg í nákvæmni þeirra. Aftur á móti er ósamhverfan mjög greinileg í hámarks hraða augnstökka og hraðinn mun meiri í átt að hliðlægu en að miðlægu áreiti. Við teljum okkur hafa mjög góð rök fyrir því að það sé líffræðileg ósamhverfa sem veldur ósamhvefunni í hámarkshraða.

Í þriðju rannsókninni (fimm tilraunir og 41 þátttakandi) rannsökuðum við meint áhrif af líkindamöndli með staðsetningar áreita með áherslu á áhrif möndlsins á viðbragðstíma and- og meðstökka. Í tilraununum voru lotur af meðstökkum, andstökkum og lotur með bæði and- og meðstökkum. Það var ekki fyrr en í tilraun þar sem lóðrétt og lárétt and- og meðstökk,voru samofin við sjónleitarverkefni að líkindamöndlið fór að hafa áhrif og munur á viðbragðstíma and- og meðstökka minnkaði. Vegna þess að áhrif líkindamöndlsins komu ekki fram fyrr en í mjög

flóknu verkefni teljum við ljóst að möndlið hefur ekki áhrif á undirbúning augnstökka sem slíkra heldur hafi það áhrif á þá þætti sem lúta að því að velja (eða finna) markáretið og taka ákvörðun um hvort augnstökkið þarf að vera and- eða meðstökk, lóðrétt eða lárétt.

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I am convinced that I can rightly claim that all the teachers – and the staff – at the Department of Psychology are very good in doing their jobs. There are, however, two teachers – beside my excellent supervisor – that I feel obligated to send my special thanks to, because of their importance in my studies. One of them is Dr. Magnús Kristjánsson and I thank him for very good introduction of the philosophical and historical part of psychology, for his emphasis on critical thinking and for all the interesting chats. The other is Dr. Jörgen L. Pind and I thank him for introducing R to me, which made statistical analyses very enjoyable, and my life so much easier.

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Participating in experiments can be invaluable. In the second half of my master studies I participated in an experiment run by Árni Gunnar Ásgeirsson at Árni Kristjánsson's lab. In this participation I came to know the eyetracker. I was fascinated by this technique and all the programming needed to run eye-tracking experiments and since then I have been using eyetracker in most of my experiments. Thank you, Árni Gunnar, for allowing me to participate and for guiding my first steps in programming eye-tracking experiments.

I finished my matriculation examination rather late with respect to my age – 51 years old – or in the spring of 2007. From the autumn 2004 till then I studied at Menntaskólinn við Hamrahlíð. During this time I came to know psychology as a discipline under the guidance of the excellent teacher, Harpa Hafsteinsdóttir. She explained to us that there were more to psychology than just the clinical part of it and since then, "the other side of psychology" has been the white beam of my studies' lighthouse; thank you very much for this Harpa!

The last two and a half year have been very enjoyable and quite busy. But I am used to being busy and I like it. Although my doctoral studies were on eye movements I had some side projects quite different from my main research field including visual search, foraging, evaluation of erroneously chosen targets and picture naming experiments. But the side projects were certainly worth the effort. Besides gaining valuable experience three of those experiments have already led to published papers and two more papers are in preparation. Well, now my doctoral studies are finished but I am not leaving the field …

Bela Julesz: "So tell me George, what do you think happiness is?"

George Von Bekésy: "That's easy, Bela. Happiness is a good experiment".

(Julesz, B. (1995). *Dialogues on perception*. MIT Press.)

Table of content

List of abbreviations

ACC	Anterior cingulate cortex
ADHD	Attention-deficit hyperactivity disorder
AIC	Akaike information criterion
ANOVA	Analyses of variance
BG	Basal ganglia
BN	Burst neuron
CRT	Cathode ray tube
DLPFC	Dorsolateral prefrontal cortex
EBN	Excitatory burst neuron
FEF	Frontal eye field
GB	Gigabyte
GHz	Gigahertz
Hz	Hertz
IBN	Inhibitory burst neuron
LCD	Liquid-crystal display
LED	Light emitting diode
LGN	Lateral geniculate nucleus
LIP	Lateral intraparietal area
LLBN	Long-lead burst neuron
LMM	Linear mixed model
MD	Medial dorsal nucleus of the thalamus
MedRF	Reticular formation
ML	Maximum likelihood
MRI	Magnetic resonance imaging
ms	Millisecond
nm	Nanometer
NTA	Nasal-temporal asymmetry
OCD	Obsessive–compulsive disorder

OPN	Omnipause neuron
PET	Positron emission tomography
PPC	Posterior parietal cortex
PPRF	Paramedian pontine reticular formation
px	Pixel
REML	Maximum restricted likelihood
riMLF	Rostral interstitial nucleus of medial longitudinal fasciculus
RT	Response time
s	Second
SAI	Stratum album intermediale
SAP	Stratum album profundum
SC	Superior colliculi
SCi	Intermediate layer of the superior colliculus
SCs	Superficial layer of the superior colliculus
SD	Standard deviation
SEF	Supplementary eye field
SGI	Stratum griseum intermediale
SGP	Stratum griseum profundum
SGS	Stratum griseum superficiale
SO	Stratum opticum
SOA	Stimulus onset asymmetry
TAN	Tonically active neuron
SZ	Stratum zonale
μ	The mean of the Gaussian part of the ex-Gaussian distribution
σ	The standard deviation of the Gaussian part of the ex-Gaussian distribution
τ	The mean and standard deviation of the exponential part of the ex-Gaussian distribution

List of figures

List of papers included only in the printed version of the thesis

Jóhannesson, Ó. I., Ásgeirsson Á., G., and Kristjánsson, Á. (2012). Saccade performance in the nasal and temporal hemifields. *Experimental Brain Research 219*(1), 107–120, DOI 10.1007/s00221-012-3071-2.

Jóhannesson, Ó. I., and Kristjánsson, Á., (2013). Violating the main sequence: asymmetries in saccadic peak velocities for saccades into the temporal versus nasal hemifields. *Experimental Brain Research, 227*(1), 101-110, DOI 10.1007/s00221-013-3490-8

Jóhannesson, Ó. I., Haraldsson, H. M., and Kristjánsson, Á., (2013). Modulations of antisaccade costs through manipulation of landing-point probability: Only under decisional uncertainty. *Vision Research, 93(C)*, 62-73, DOI 10.1016/j.visres.2013.10.010

List of papers in appendix B in the printed version of the thesis

Jóhannesson, Ó. I., Sigurdardottir, K. Ó., and Kristjánsson, Á., (2013). Searching for bumps and ellipses on the ground and in the sky: No advantage for the ground plane. *Vision Research, 92(C)*, 26-32, DOI 10.1016/j.visres.2013.09.001

Kristjánsson, Á., Jóhannesson, Ó. I., and Thornton, I.M. (2014). Common Attentional Constraints in Visual Foraging. *PLOS ONE 9*(6): e100752. doi:10.1371/journal. pone.0100752

Kristjánsson, Á, and Jóhannesson, Ó. I. (2014). How priming in visual search affects response time distributions: Analyses with ex-Gaussian fits. *Attention, Perception, & Psychophysics*, DOI 10.3758/s13414-014-0735-y

Declaration of contribution

Paper I and study 1: Saccade performance in the nasal and temporal hemifields

Experimental design: Jóhannesson and Kristjánsson. Programming of the experiments: Jóhannesson and Ásgeirsson. Data collection: Jóhannesson. Eyetracker data and statistical analyses: Jóhannesson. Paper writing: Jóhannesson under the supervision of Kristjánsson.

Paper II and study 2: Violating the main sequence: asymmetries in saccadic peak velocities for saccades into the temporal versus nasal hemifields

Experimental design: Jóhannesson and Kristjánsson. Programming of the experiments: Jóhannesson. Data collection: Jóhannesson. Eyetracker data and statistical analyses: Jóhannesson. Paper writing: Jóhannesson under the supervision of Kristjánsson.

Paper III and study 3: Modulations of antisaccade costs through manipulation of landing-point probability: Only under decisional uncertainty

Experimental design: Jóhannesson and Kristjánsson. Programming of the experiments: Jóhannesson. Data collection: Jóhannesson. Eyetracker data and statistical analyses: Jóhannesson. Paper writing: Jóhannesson under the supervision of Kristjánsson and Haraldsson.

1. Introduction

When we open our eyes, photons enter through the pupil, inducing chemical reactions in cells in the retina, which in turn sends signals to the brain causing us to perceive the environment. But, importantly, visual acuity declines rather fast outside the fovea and into the periphery of the retina. The fovea is very small or just about 1 mm in diameter (Kandel, Schwartz, & Jessel, 2000) and at 2° outside of the fovea visual acuity has declined by about 50% (Leigh & Zee, 2006). Somehow the visual system, with help from the movements of the eyes, is able to interpret the scene as if everything it contains is sharp and in focus. If we, however, need to see something clearly, information from the point of interest must enter the fovea and we move our gaze towards it, without thinking about moving the eyes. Eye movements play a very important role in our visual perception in more ways than moving our gaze to what interests us. Eye movements compensate for the movements of the head and the body and even though we are moving around, the point of interest can be kept on the fovea, where visual acuity is highest.

1.1. Why study eye movements?

> "The oculomotor paradigm has additional features as well: it allows perimetric mapping of memory to targets throughout the visual field, precise control over the staging and timing of task events, and exact measurement of the response latency, trajectory, and amplitude of the response." (Goldman-Rakic, 1995, page 478).

Eye movements are very interesting in themselves and play a very important role in visual perception. Eye movement studies can also broaden our understanding of brain and attentional functioning, decision processes and neurological disorders. The characteristics of eye movements are well known and the biological processes of generating them are rather

well understood. The frontal lobes in the brain play a large role in eye movement generation but also in attention and executive function. Eye movements show abnormal characteristics in people with schizophrenia (Haraldsson et al., 2008), attention deficit hyperactivity disorder (Munoz, Armstrong, Hampton, & Moore, 2003), dyslexia (Biscaldi, Fischer, & Hartnegg, 2000), Parkinson's disease (Chan, Armstrong, Pari, Riopelle, & Munoz, 2005), Tourette's syndrome (Farber, Swerdlow, & Clementz, 1999), Huntington's disease (Lasker, Zee, Hain, Folstein, & Singer, 1987), obsessive-compulsive disorder (Rosenberg, Dick, O'Hearn, & Sweeney, 1997), as further discussed below.

1.2. Types of eye movements

There are several types of eye movements and all have a different role (Leigh & Zee, 2006). *Vestibular* eye movements keep the image of the world steady on the retina while we briefly move our head but under sustained rotation *optokinetic* movements keep the image steady on the retina. The role of *fixation* is to hold a stationary object on the fovea so we can see it clearly. When we follow a moving object with our eyes *smooth pursuit* movements keep the object on the fovea. During prolonged rotation of the head, body, or head and body, saccade-like movements called *nystagmus*, which are part of the optokinetic response, reset the position of the eyes and direct gaze towards the oncoming scene. *Vergence* movements are different from other eye movements in that they involve movements of the two eyes in opposite directions, i.e. moving both eyes toward the center or both eyes towards the periphery. *Saccades* are very fast eye moments, which shift the center of gaze from one point to another. Saccades are the main topic of this thesis in which experiments focusing on their latency, landing-point accuracy and their peak velocity are presented.

1.3. Measuring eye movements

Since the eye is a sphere and lies in a socket at the front of the head, the movements of the eyes are rotations and it is therefore both rational and convenient to measure their movements in degrees (or minutes for very short rotations) but even though the movements of the eyes are rotations it is traditional to refer to amplitude that is measured in degrees and applies also to the size or magnitude of the saccades. Saccades can be horizontal, vertical or oblique movements, but in this thesis the emphasis is on horizontal and vertical saccades. The main characteristic of saccades

is their velocity profile. When a saccade is initiated the acceleration of the movement can be more than 10000°/sec^2 and at the end of the saccade a similar negative acceleration can be seen (Leigh & Zee, 2006). The peak (maximum) velocity of the saccades can be several hundreds of degrees per second and as an example, the peak velocity of 20° saccades can be as high as 450°/sec (Leigh & Zee, 2006). The onset of the saccade is usually defined as the last point before the velocity, the acceleration or both, of the movement exceed a predefined limit and its offset when the velocity or acceleration drops below a specific limit. When Purkinje image eyetrackers are used, small movements back and forth of the eye are usually seen at the end of the saccade. These apparent movements are not movements, per se, but oscillations caused by the inertia of the lens (Deubel & Bridgeman, 1995) and have been termed *post saccadic oscillations* (Eizenman, Frecker, & Hallett, 1984; Nyström, Hooge, & Holmqvist, 2013). The amplitude range of the post saccadic oscillations has been found to be 0.5°–1° and can last for 30–40 ms (Nyström et al., 2013).

1.4. Saccades

Saccades can be classified into three types, regular saccades, express saccades and microsaccades. Microsaccades share the same characteristics as regular saccades but are very short and typically between 0.33° and 1° (Leigh & Zee, 2006). The latency of express saccades is between 80 and 110 ms (Fischer & Ramsperger, 1984) but despite this short latency they are reflexive, and not anticipatory (Edelman, Kristjánsson, & Nakayama, 2007). Express saccades share the same characteristics as regular saccades but tend to be more hypometric, at least in the monkey (Edelman & Keller, 1996) and are thought to be initiated when visual signals are directly transformed into motor commands in the superior colliculus (Dorris, Paré, & Munoz, 1997; Edelman & Keller, 1996). One can therefore speculate that express saccades are the only saccades that are purely stimulus driven, or bottom-up. Since microsaccades and express saccades are not part of our studies they will not be discussed further. Regular saccades or often classified as prosaccades and antisaccades, but the difference between these two classes is mainly a consequence of task instruction, not the saccades, per se.

A prosaccade is a saccade towards a peripherally presented stimulus

but antisaccades are saccades in the opposite direction of prosaccade (away from a peripheral stimulus) but of the same amplitude, see Figure 1. It is considerably more complex to elicit anti- than prosaccade. To perform a prosaccade the visual system has to locate the stimulus and compute the direction and the distance to it (in fact it is the velocity needed to the reach the landing-point that is computed, see below). In the antisaccade task the computations are the same with the addition of computing the antisaccade landing-point in the opposite visual field and mirroring the direction. Furthermore, the visual system has to overcome the tendency to make a saccade to a suddenly appearing stimulus which may involve attentional effort (Yantis & Jonides, 1984). There is some good evidence supporting the view that the supplementary eye field has a significant role in the execution of antisaccades (Amador, Schlag-Rey, & Schlag, 2004; see discussion of it below).

1.5. Saccadic latency

The latency of a saccade is the time from the appearance of the target until the saccade is initiated and is about 180–220 ms (Fischer & Weber, 1992; Haraldsson et al., 2008) for prosaccades but considerably longer for antisaccade (Evdokimidis, Constantinidis, Liakopoulos, & Papageorgiou, 1996; Fischer & Weber, 1992) and have been found to be about 270–300 ms (Haraldsson et al., 2008; Vergilino-Perez et al., 2012) and the error rate of antisaccades is higher than of prosaccades (Haraldsson et al. 2008; Munoz & Everling, 2004). The difference between anti- and prosaccades latencies has been termed *the antisaccade cost*. When a novel stimulus suddenly appears people have a strong tendency to saccade to it (sometimes called *the visual-grasp reflex*) and it can be very difficult not to saccade to the target (Everling, Dorris, & Munoz, 1998; Theeuwes, Kramer, Hahn, & Irwin, 1998). To initiate an antisaccade this tendency has to be overcome and the consequence of this results in longer latency and more errors. When the fixation stimulus disappears before the target appears the latency of both anti- and prosaccades is shorter than when this happens simultaneously or when the presentation of fixation stimulus and the target overlap (referred to here after as *overlap* or *overlap condition*). This effect has been termed *the gap effec*t (Saslow, 1967) and is thought to be because the fixation neurons in SC release their "grip" on the eye when there is nothing to fixate on (Dorris & Munoz, 1995), see below. Other factors that might affect saccadic latency are probability manipulations

of target location (Carpenter & Williams, 1995; Dorris & Munoz, 1998; Koval, Ford, & Everling, 2004; Liu et al. 2010; Noorani & Carpenter, 2012) and attentional load (Kristjansson, Chen, & Nakayama, 2001).

1.6. Saccadic peak velocity and duration

The peak velocity of the saccades increases with increased amplitude and, as mentioned above, the peak velocity of saccades with amplitude of 20° is about 450°/sec. The close relationship between amplitude and peak velocity is well known and is often referred to as *the main sequence* (Bahill, Clark, & Stark, 1975; Leigh & Zee, 2006). The the saccadic command includes information about the velocity (Sparks, 2002). At 20° amplitude this relationship starts to level off and the peak velocity reaches an asymptotic value of about 500°/sec at 30° amplitude. The main sequence holds also for microsaccades. There is also a close relationship between saccade duration and their amplitude (from 1°–50°) with typical duration of 100 ms for 20° amplitude (Leigh & Zee 2006). There can, however, be considerable variability in both saccadic peak velocity and duration for saccades of similar size from day to day for the same individual and many factors have modulatory effects on these parameters. The peak velocity of antisaccades tends to be lower than of prosaccades

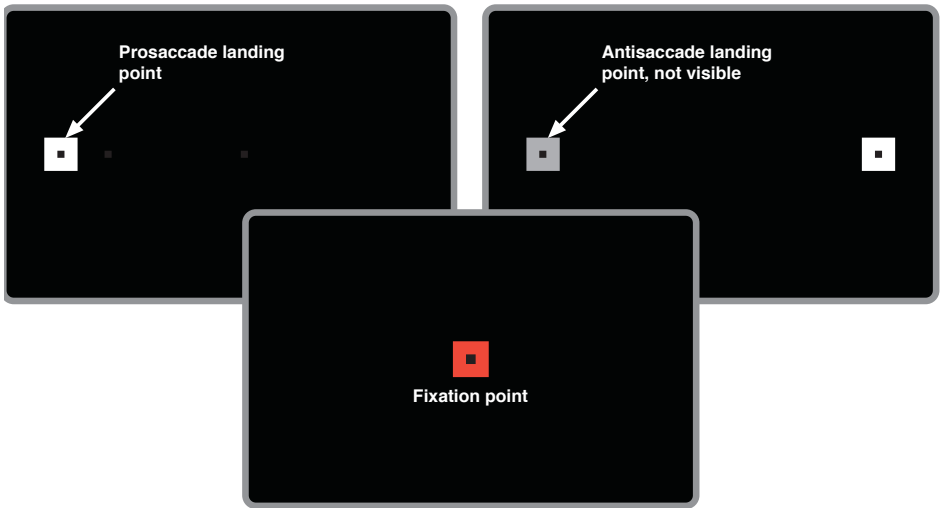

Figure 1. Pro- and antisaccades. When the fixation point disappears and the task is to make a prosaccade the observer moves the gaze to the left towards the prosaccade landing-point. When an antisaccade is to be made the observer moves the gaze towards a location equally far from the fixation point as the target but in the opposite direction.

and higher if the antisaccades are made to visual than non-visual targets (Edelman, Valenzuela, & Barton, 2006). According to Edelman et al. (2006) the main reason for the observed difference of peak velocity between anti- and prosaccades is that the goal of traditional antisaccades does not have a visual target. There is also some evidence for higher peak velocity of anti- (Fischer, Weber, 1992) and prosaccades (Pratt, 1998) in the gap-paradigm than in the no-gap paradigm. Furthermore, centripetal saccades (towards the center) are usually faster than centrifugal saccades (Leigh & Zee, 2006). Since the duration of the saccades is very short, visually guided information can not be used to modulate the saccade after it has been initiated but if the information reaches the control stations of the saccade while it is being prepared and before the eye starts to move the saccade can be modified after it's initiation (Leigh & Zee, 2006; Ludwig, Mildinhall & Gilchrist, 2007).

1.7. Anatomy of eye movements

1.7.1. Nasal-temporal asymmetries in anatomy

The terms – nasal and temporal – become very important when discussing the anatomy of the eyes and measuring their movements under monocular viewing. These terms are explained visually in figure 2.

The photoreceptors in the fovea are mostly cones with only a few rods but outside of the fovea this ratio is reversed. The number of ganglion

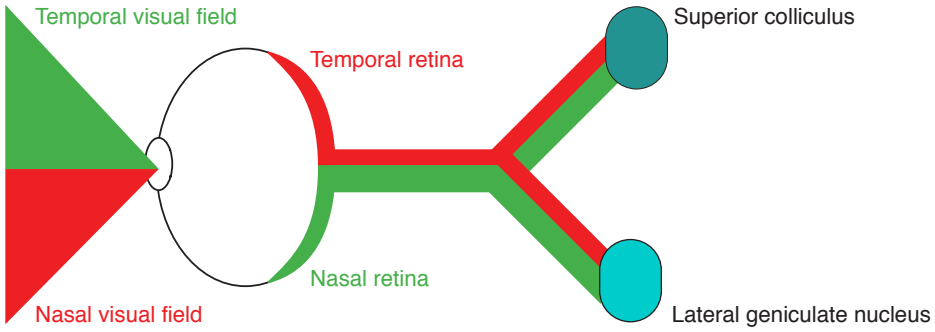

Figure 2. The terms *nasal* and *temporal* explained. Visual information in the temporal visual field (green on the figure) is projected onto the nasal retina and vice versa for what is in the nasal visual field (red on the figure). This color code will be used on all figures in this thesis when appropriate. The neural projections from the nasal retina are about 1.5 times denser than from the temporal retina (based on Williams, Azzopardi, & Cowey, 1995).

cells is also much higher in the fovea than outside of it and their density declines faster towards the temporal than nasal periphery (see Figure 3; replotted from Curcio, & Allen, 1990). Consistent with this, Vernier acuity declines faster for the temporal, than nasal, retina outside of the ± 5° of the center of the retina, where acuity declines rather symmetrically. At 20° eccentricity the Vernier acuity is about 70% higher for the temporal visual hemifield (nasal retina) than for the nasal visual hemifield (temporal retina; Fahle, & Schmid, 1988). The main purpose of the ganglion cells is to collect information from rods and cones and convey this information through the optic nerve to the brain.

The nasal-temporal asymmetry found in the retina is also evident in the optic nerve. Neurophysiological work on cats (Hubel, LeVay. & Wiesel, 1975; Sterling 1973) old world (Itaya & Van Hoesen, 1983) and new world monkeys (Tigges & Tigges, 1981) has revealed asymmetries in projections from the retina to the SC. This NTA might also exist for projections to the lateral geniculate nucleus (LGN). Williams, Azzopardi, & Cowey, (1995) found that the ratio of nasal cells compared to temporal cells in rhesus monkeys was 1.54 when all major cell types were included (i.e. cells that project to the LGN and SC). For projections to the SC the variability between the four monkeys was high and in two of them the nasal-temporal ratio was high while it was low for the other two. It is, however, notable that according to Table 1 in Williams' et al. (1995) the nasal-temporal ratio is significantly higher for nasal than temporal projection in all cases but for the pooled data. This supports the NTAs

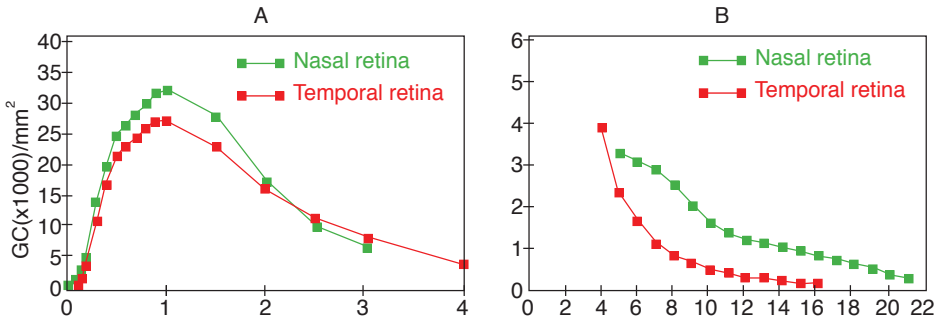

Figure 3. Ganglion cells in the retina. The density of ganglion cells decreases faster in temporal than nasal retina as can be seen on the figure. Note that the difference in density is most pronounced at 8° eccentricity. The scale on the y-axis represents number of ganglion cells (in thousands) per mm^2. Reproduced from Curcio and Allen, 1990.

found in the optic nerve by Hubel et al. (1975) Sterling (1973), Itaya and Van Hoesen (1983) and Tigges and Tigges (1981). From the eye about 10% of the optic nerve projects to the SC and about 90% to the LGN (Perry & Cowey, 1984).

1.7.2. The motor circuit.

The eye rotates around three axes and the rotations are controlled by six muscles, which are directly connected through cranial nerves III, IV and VI to the brain. Cranial nerve VI controls the lateral rectus; all other eye movement muscles are controlled through cranial nerves III and IV. Of the three axes, two are horizontal (x and y axes) and one is vertical (the z axes). The x-axis is rostral-caudal (sagittal) and the y-axis is medial-lateral (transverse). Around these three axes the eye can be rotated in any direction. The six oculomotor muscles are in three pairs and one pair (the medial rectus and lateral rectus) is for horizontal movements only and rotates the eye around the z-axis. In rotations around the x-axis and y-axis the two other pairs cooperate to control vertical and oblique rotations. The lateral rectus receives signals through the abducens nerve (cranial nerve VI) from a nucleus in the brain stem and the medial rectus gets its signals through the oculomotor nerve (cranial nerve III) from the midbrain (Kandel et al., 2000). When a horizontal saccade to the right temporal visual field is made, the lateral rectus of the right eye contracts and the medial rectus relaxes. For the left eye the role of the lateral and medial muscles is reversed. The saccade signal to these muscles is made-up of two parts, the step and the pulse command. The step command includes the location of the landing-point and the tension – or pulling force – of the agonist muscle needed to overcome the elastic forces of the antagonist muscle so the eye can be kept in the desired position. The pulse command contains information about the force needed to overcome the viscosity of the orbit and the velocity of the saccade (Sparks, 2002). Furthermore, the inertia of the eyeball has negligible effect on saccadic generation (Robinson, 1964). There is some evidence suggesting that the step command is derived from the pulse command (Arnold & Robinson, 1997; Leigh & Zee, 2006).

In the motor circuit there are mainly three types of neurons, omnipause neurons (OPNs), burst neurons (BNs) and tonically active

neurons (TANs). The BNs are further divided into three groups, excitatory burst neurons (EBNs), inhibitory burst neurons (IBNs) and long-lead burst neurons (LLBNs), all with a different role in saccadic generation that are all part of the brainstem saccadic pulse generator (Sparks, 2002). The BNs and IBNs are active during a saccade and the OPNs are silent, but during fixation the OPNs are active keeping the BNs silent (Rucker et al. 2011). The TANs are active during fixation and are the main source of the step command. The TANs for horizontal position signals are located in the nuclei prepositus hypoglossi (NPH) and medial vestibular nuclei (MVN) and TANs for vertical and torsional positions are located in the interstitial nucleus of Cajal (Scudder, Kaneko, & Fuchs, 2002). When a saccade is to be initiated, e.g. to the left, the lateral rectus of the left eye and the medial rectus of the right eye contract but the medial rectus of the left eye and the lateral rectus of the right eye relax. This process (the pulse command) is controlled by EBNs (for horizontal saccades in the paramedian pontine reticular formation, PPRF; for other saccades in the rostral interstitial nucleus of medial longitudinal fasciculus, riMLF) and IBNs (for horizontal saccades in the medullary reticular formation, MedRF; for other saccades in the interstitial nucleus of Cajal and riMLF). The ipsilateral EBNs send excitatory signals to the left eye's lateral rectus and to the right eye's medial rectus while the contralateral IBNs send inhibitory signals to the medial rectus of the left eye and to the lateral rectus of the right eye. When the saccade ends, this process is reversed and all these muscles are commanded to adjust their pulling forces to keep the eyes in the desired position (the step command). There is good reason to believe that the OPNs control the interaction of the EBNs and the IBNs (Leigh & Zee, 2006) since the OPNs stop firing ≈ 16 ms prior to the saccade and are silent during saccades but active during fixations (Leigh & Zee, 2006). Furthermore, if the OPNs are exogenously stimulated (e.g. by electrical stimulation) during a saccade the saccade is terminated (Rucker et al. 2011). According to Rucker et al. (2011) it is possible, under normal operation, that the OPNs do not terminate saccades but that it is the cerebellar caudal fastigial nucleus (cFN, which is sometimes called the fastigial oculomotor region or FOR) that terminates the saccades by activation of the IBNs. The main role of OPNs might therefore be to keep the BNs silent after the eye has come to a stop (Rucker et al. 2011).

1.7.3. Superior colliculus

The superior colliculi are located in the midbrain and are one of the major brain areas in controlling eye movements, projecting directly to the brainstem saccade generator (Leigh & Zee, 2006). There are, however, several higher cortical areas – both in the frontal and parietal lobes – that participate in saccadic generation. Among these areas, according to Leigh and Zee (2006), are the frontal eye field (FEF), the supplementary frontal eye field (SEF), and both the dorsolateral prefrontal cortex (DLPFC) and the posterior parietal cortex (PPC; White & Munoz, 2011). The superior colliculus consists of seven layers, which can be split into superficial and deep layers (Sparks, & Hartwich-Young, 1989; White, & Munoz, 2011) The superficial layers (SCs) of the SC consist of three layers: the stratum zonale (SZ), the stratum griseum superficiale (SGS), and the stratum opticum (SO). The deeper layers are the stratum griseum intermediale (SGI), the stratum album intermediale (SAI), the stratum griseum profundum (SGP), and the stratum album profundum (SAP; Sparks, & Hartwich-Young, 1989). The deep layers are sometimes divided into the intermediate layers (SGI and SAI) to which we refer as SCi, and the deeper layers (SGP and SAP; White & Munoz, 2011).

The two layers, SCs and SCi, seem to play very different roles in saccade generation. The neurons in SCs are organized retinotopically so that each neuron has a receptive field that responds to a restricted region of the contralateral visual field. The SCi has a retinotopic motor map and if neurons at a specific location are stimulated they cause the eye to move to the corresponding location in the contralateral visual field (White & Munoz, 2011). The neurons in layers below SCs are thought to be multisensory but the exact location of the border between motor map neurons and multi sensory neurons is not clear. According to Sparks et al. (1999) the SGI (the deeper layer of the SCi) receives somatosensory input and the SGP (the upper layer of the deep layers) receives auditory input. Recent evidence suggest that the main role of the SCs is to locate the stimulus and convey this information down to the SCi enabling the conversion of sensory signals to motor signals (Phongphanphanee et al. 2014).

The SCs receives mainly input from the retina and the primary

visual cortex (V1) and projects to SCi (Helms, Özen, & Hall, 2004; White & Munoz, 2011) and to the pulvinar, which further projects to the lateral intraparietal area (LIP). The SCi receives input from SCs, LIP, anterior cingulate cortex (ACC), FEF, supplementary eye field (SEF) and from DLPFC via the basal ganglia. There are direct projections from the FEF to SCi and also via the basal ganglia. The projections from SCi to FEF are mediated through the medial dorsal nucleus of the thalamus (White & Munoz, 2011). While V1 sends mostly bottom-up information, the FEF and DLPFC are assumed to mediate top down information, especially the DLPFC. The main outgoing projection of the SCi is to the reticular formation (RF; White & Munoz, 2011), which houses some aspects of the saccadic motor controls.

SCs neurons show short high frequency bursts about 40 ms after a stimulus appears in their receptive field, which corresponds to the location of the stimulus in the retina. Neurons deeper in the SCs behave similar except that after the initial burst of action they show sustained low frequency firing while the stimulus is in their receptive field but no bursts of action potentials when a saccade is triggered. It is not known whether those neurons belong to the lowest part of SCs or the uppermost part of SCi (White & Munoz, 2011).

Visuomotor neurons in the SCi fire action potentials about 50 ms (10 ms later than neurons in the SCs) after a stimulus appears in their receptive field and again when a saccade occurs. Some saccadic related neurons in the SCi fire for all amplitudes equal or greater than their location while others fire when the amplitude is in accordance with their location on the motormap. There is good correspondence between the visual receptive fields of the neurons in SCi and the receptive fields of the saccade related neurons, which ensures that the signals from SCi to the saccadic generator correctly code the saccadic parameters needed (White & Munoz, 2011).

In the rostrolateral part of SCs there are neurons with small receptive fields representing the foveal and parafoveal visual field and in the SCi a motor map with similar receptive fields continues. Among the neurons in the rostral pole (which represents the fovea) of the SCi are neurons that fire in relationship with fixations (fixation neurons) and those neurons stop or decrease firing if the target disappears, e.g. the fixation point in the

gap paradigm (Dorris & Munoz, 1995; Munoz & Wurtz, 1992; White & Munoz, 2011) but their activity is increased while an antisaccade is being prepared (Everling, Dorris, Klein, & Munoz, 1999). There is, however, some evidence indicating that the role of the "fixation neurons" in the rostral SCi is not solely to maintain fixation but that its role is similar to neurons more caudal in the SCi, i.e. that they might code the difference between the point of gaze and the location of the stimulus but for smaller amplitude (Krauzlis, Basso, & Wurtz, 1997). The behavior of those neurons has also been shown to be similar in smooth pursuit and saccadic eye movements (Krauzlis, 2003).

Since it is only possible to saccade to one target at a time and the selection process in the SC is thought to be "winner-takes-all" mechanism, it is necessary to inhibit a saccade to other portions of space. There is some neurophysiological (Dorris, Olivier, & Munoz, 2007), anatomical and pharmacological evidence supporting inhibitory mechanisms inside the SCi but external inhibitory signals might be projected through the nigrotectal pathway (e.g. from the substantia nigra pars reticulata; White & Munoz, 2011).

There are usually many interesting things in the visual scene and one of them often of a special interest to us and becomes the target of our visual inspection, e.g. the odd-one-out in visual search. In visual search the visual system has to select the target among the distractors and that is not a simple process The winner-takes-all mechanism is not able to do this selection on its own so some top down guidance is needed (e.g. from the LIP, Paré & Dorris, 2011). There are many areas in the brain that participate in the selection process and selection related activity has been found in the SCi but not in the SCs (White & Munoz, 2011). When a visual search task is presented, the neurons that participate in the selection process become active and respond equally to all stimuli but after a while the neurons that are tuned to the distractors start to decrease their activity while the neurons tuned to the target increase their firing reflecting the top down process (White & Munoz, 2011). When a cue is displayed at a location where a target subsequently appears the latency of a saccade towards the target is shorter than if the location is not cued, provided that the time between the cue and the target is not too long (≈ 100) but if it is long enough (> 500 ms) the response is delayed (inhibition of return,

Klein, 2000). Since the same pattern is observed in the sensory neurons in the SC, the effect of the cue is probably more related to bottom up than to top down processes (White & Munoz, 2011).

1.7.4. The frontal eye field.

The frontal eye field (FEF) is located in the frontal cortex anterior to the arcuate sulcus. Among the brain areas that FEF receives projection from are the SCs, SCi (mediated through the medial dorsal thalamus, Lynch, Hoover, & Strick, 1994), and LIP. The FEF projects to BG, MD and to SC, mainly, but not exclusively, to its' ipsilateral side. There are reciprocal projections between FEF, SEF, DLPFC and LIP. An inoperative FEF does neither abolish regular nor express saccades (Johnston & Everling, 2011) consistent with the proposal that express saccades mostly reflect activity in the SC (Dorris et al, 1997; Edelman & Keller, 1996). It seems that there are no direct projections from FEF to premotor burst neurons of the brainstem saccadic generator (Johnston & Everling, 2011) or that they are not sufficiently strong to elicit saccades without contribution from the SC (Hanes & Wurtz, 2001) but the FEF projects directly to the OPNs (Johnston & Everling, 2011). The projections from the FEF to the OPNs can only silence the OPNs however. Since the role of the OPNs is inhibition, the projections from the FEF to them cannot provide any information about the amplitude or direction of the saccade. About 40% of the neurons in FEF show only visual activity (visual neurons) and another 40% both visual and movement related activity (visuomotor neurons) and 20% of the neurons show only movement related activity (motor neurons) and fire before purposeful saccades. Movement related neurons also fire before aurally guided saccades (Johnston & Everling, 2011). The firing of neurons in FEF might reflect task instruction related activity. Indeed, Everling and Munoz (2000) found that those neurons behaved differently after monkeys were instructed (by a central cue, differently colored for anti- vs. prosaccades) to elicit anti- than prosaccades before the target was displayed. This difference in neuronal activity was found in the gap paradigm as well as in a no-gap paradigm. At the end of the gap (in the gap paradigm) the neuronal activity was higher for express, than for regular saccades. Everling and Munoz take this as evidence for the involvement of the FEF in generating express saccades. It is, however, important to keep in mind that the exact latency limits of express saccades is not

precisely defined and saccades with a latency of 125 ms (as in the study of Everling and Munoz, 2000) could be on the border between express and regular saccades. Express saccades in the gap paradigm have, indeed, been classified to be in the range of 80–110 ms in humans (Fischer & Ramsperger, 1984) and shorter in monkeys.

1.7.5. The supplementary eye field.

The supplementary eye field (SEF) is dorsal and medial to FEF, in area 6. The SEF is different from FEF in many important aspects. Inactivation of SEF has milder effects on saccadic generation than inactivation of FEF. According to Johnston and Everling (2011) it is likely that the SEF codes the saccadic endpoint in head cantered coordinates. Repeated microstimulation at the same location in the FEF produces multiple saccades of the same amplitude but the saccades evoked by the same stimulation process in the SEF ends at a specific location in the visual field (Johnston & Everling, 2011) or more precisely, with respect to the head (Tehovnik, Slocum, Tolias, & Schiller, 1998). Tehovnik et al. conclude that the SEF codes the point of gaze in head-centered coordinates. It seems, however, not to be clear what kind of coordinates the SEF uses and the results from Russo and Bruce (1993) do not support the head-centered hypothesis. Furthermore, the signal from the SEF might be a combination of head-centered and eye-centered coordinates (Martinez-Trujillo, Wang, & Crawford, 2003). There is also some evidence suggesting that the neurons of the SEF code the saccades in object-centered coordinates (for an overview see e.g. Olson, 2003) and that the SEF combines object-centered locations and saccadic directions (Moorman & Olson, 2007). The SEF directly projects to many brain areas involved in saccadic generation and among them are the SC and the brain stem saccadic generator. Whereas the FEF is directly involved in saccadic generation it seems that the effect of SEF is indirect and might mediate executive effects on saccadic generation (Johnston & Everling, 2011). People with SEF lesions seem unable to make memory-guided sequence of saccades but the lesions seem not to affect other aspects of saccadic performance (Gaymard, Ploner, Rivaud, Vermersch, & Pierrot-Deseilligny, 1998). Further links between SEF and cognition have been found in the antisaccade task. The activity of SEF's neurons is higher in relation with task instruction and saccades on antisaccades trials than on prosaccade trials. Furthermore, the activity of those neurons

is less on erroneous antisaccade trials (i.e. when a prosaccade is made instead of antisaccade) than on prosaccade trials (Munoz & Everling, 2004). Visuomotor and motor neurons in the SEF have two firing bursts, the first as response to the stimuli and the second peaks in activity just before the saccade is initiated. During antisaccades the neurons coding for the antisaccade landing-point do not fire when the target appears because it is not in the receptive field of the neurons. Interestingly, however, the neurons at the antisaccade landing-point increase their firing rate about 200 ms before the onset of the saccade (Amador et al., 2004). Amador et al. (2004) conclude that these patterns of activity support the hypothesis that the SEF plays an important role in antisaccade generation.

1.7.6. The dorsolateral prefrontal cortex.

The role of the DLPFC in saccadic generation is only indirect. It has been shown that saccades cannot be evoked by low current electrical stimulation of DLPFC and that saccade related activity is not always evoked in it until after the saccade has been initiated. Furthermore, the neuronal activity in DLPFC does not correlate well with saccadic latency, even not of the neurons that project directly to oculomotor areas. The activity in DLPFC correlates with learning, working memory, attention, decision-making, response strategies, rewards and more. Three types of DLPFC processes are highly related to oculomotor control: working memory, flexible control and response suppression (Johnston & Everling, 2011), which might not be suppression of improper responses but facilitation of proper responses (Everling & Johnston, 2013).

Besides having reciprocal projections to almost all sensory systems the DLPFC projects to the majority of motor areas, including oculomotor areas. There are also reciprocal projections between DLPFC and LIP but the LIP is not assumed to play a direct role in generating saccades but to inform the saccadic system of potential targets (Paré & Dorris, 2011). The DLPFC projects to the BG, which further projects to the intermediate layers of SC and through those projections the DLPFC might be able to modulate the motor response of neurons in the SCi. The role of DLPFC in eye movements has been assumed to be inhibitory but recent evidence suggests that this is not the case. According to Everling and Johnston (2013) the main role of the DLPFC is to facilitate the desired response but

not to inhibit improper responses. But since the DLPFC projects to the BG the inputs projected to SCi can be inhibitory depending on which part of BG receives excitatory inputs from DLPFC (Everling & Johnston, 2013).

One of the main tasks of the DLPFC is flexible mapping between sensory inputs, goals and the tasks needed to achieve the goals (Johnston & Everling, 2011). To make this mapping possible the information needed for the task, e.g. to initiate antisaccades rather than prosaccades and the location of the target, needs to be available for the cognitive processes involved and that fits nicely to the role of Baddeley's definition of working memory.

According to Baddeley (2007) one of the tasks of working memory is to maintain information concerning the current task, keeping it available for other cognitive processes. Information to be maintained in working memory can either come directly through the senses (e.g. the eyes), from the environment or can be retrieved from and mediated to long-term memory (Baddeley, 2007). It has been shown that monkeys with temporary lesions (e.g. by cooling) of the DLPFC perform badly on the oculomotor delayed response task (also known as memory guided saccades) and the same deficit, on the same task, is found in the performance of people with schizophrenia (Lewis, 2000). Lesions in human DLPFC seem not to affect prosaccades but increase error rates in the antisaccade task and decrease the accuracy of memory-guided saccades (Gaymard et al., 1998). This indicates that lesions in the DLPFC do neither affect motor control of the saccades nor sensory processes but affect working memory (Gaymard et al., 1998). Evidence from PET and MRI studies further suggests that the DLPFC plays a significant role in working memory (Kane, & Engle, 2002).

1.7.7. The lateral intraparietal area

The LIP receives projections from V1 and from both SCs and SCi via the pulvinar and projects directly to SCi. There are reciprocal projections between LIP, FEF and SEF (for a review see e.g. Bisley, Mirpour, Arcizet, & Ong, 2011). Because of those projections, the LIP has ample opportunity to influence attentional and saccadic activity. It is, however, not thought to play a direct role in allocating attention or the generation of saccades (Bisley et al., 2011). According to Bisley et al. (2011) the main

role of the LIP is to create *priority maps* of the visual scene to guide covert attention and eye movements. The LIP achieves this goal by combining top down and bottom up information and the stimulus that receives the highest priority is chosen as the target. Those authors prefer to use the term priority map, not salience map, to emphasize the role of top down processes in generating the map. Furthermore the LIP has been found to code the location of a salient stimulus even though it is task irrelevant (Constantinidis & Steinmetz, 2005).

Neurons in the LIP respond more to salient, than non-salient, stimuli even though those stimuli are task irrelevant but the difference is small. If the salient stimuli are task relevant the activity of neurons in LIP are greatly elevated representing top down modulation (Bisley et al., 2011). It has been shown that the time needed to find the stimulus of highest priority correlates with the latency of the saccade to that stimulus, at least in the monkey (Thomas & Paré, 2007). In feature visual search the neurons in LIP initially respond equally to all the stimuli in the scene but before a saccade is initiated to the chosen stimulus (i.e. the singleton) the activity of the neurons changes and the most actively firing neurons represents the target. This effect was found in the monkey when the singleton was identified by color (Thomas & Paré, 2007).

1.8. Eye movements and visual attention

We do have some very good reasons to expect a close relationship between visual attention and eye movements since they share some brain areas. Among brain areas where visual attentional and saccadic activity has been found to coexist are DLPFC, FEF, ACC (Johnston & Everling, 2011), LIP (Paré & Dorris, 2011) and SC (Ignashchenkova, Dicke, Haarmeier, & Thier, 2003). The expected relationship could take several forms, e.g. attention could precede eye movements or eye movements could precede attention. The premotor theory of attention holds that attention follows the track, which has been planned for eye movements (Kristjánsson, 2011; Rizzolatti, Riggio, Dascola, & Umiltá, 1987). We know we can move the focus of attention from one spot to another without moving the eyes but that does not mean that the premotor theory is wrong since eye movements have to be planned before the eyes start to move. Allocation of attention to a secondary task, e.g. discrimination, can alter anti- and prosaccadic latency differently with respect to time interval between saccadic and

discrimination target (Kristjansson et al., 2001). This is further discussed in *Modulation of the antisaccade cost* (page 21).

In a clever experiment Deubel and Schneider (1996) investigated the relationship between visual attention and saccades. The fixation screen consisted of fixation point and two strings (one on each side of the fixation point) of five letters surrounded by ovals. The three ovals in the middle were red, green or blue. After the fixation period the fixation point changed to a colored triangle pointing either to the left or to the right. The color of the triangle and the direction it pointed in informed the observer where the saccadic target subsequently appeared but the discrimination target could appear in any of the three colored ovals. The observer was instructed to fixate the triangle until it disappeared and then saccade to the primed location. The content of the ovals changed to distractors and the discrimination target 60 ms after the triangle disappeared and the target was visible for 120 ms. The task was to determine whether the target was an "E" or a mirrored "E". Performance was by far the best when the saccadic and the discrimination target shared the same location indicating that attention had shifted to the landing-point of the upcoming saccade. In another experiment with a similar procedure, except that the observer always knew were the discrimination target would appear, the results were the same (Deubel & Schneider, 1996). Deubel and Schneider concluded that the results showed that there is a tight temporal and spatial relationship between saccades and attention. During the saccadic preparation period attention can be shifted to the saccadic target early or late but if attention is allocated to the saccadic target immediately before the initiation of the saccade the performance in discrimination tasks is always best when the discrimination target and the saccadic target share the same location (Deubel, 2008). The results from Deubel and Schneider (1996) and Deubel (2008) show that there is a tight coupling between attention and saccadic preparation and can be taken as a support for the premotor theory of attention since it seems that covert attention goes to the same point as the saccade.

In the experiments discussed above, the relationship between voluntary saccades and attention was studied and the results suggest that attention – at least covert attention – precedes saccades. In an interesting study conducted by Peterson, Kramer, and Irwin (2004) the relationship

between both voluntary and involuntary saccades and covert attention was investigated. In Peterson's et al. study (2004) six circles (one target and five distractors), which all contained the digit 8 (as a seven segments figure) were presented on an imaginary circle. At the beginning of each trial the observer fixated the center of the imaginary circle. After the fixation period all the distractor circles (five of the six stimuli), changed color, the "8" was changed to letters and a seventh additional stimulus (what Peterson et al. termed "the onset") appeared 90° or 150° away from the target. The target (in the circle that did not change color) was always a C or a mirrored C and too small to be identified without saccading to it. A cue, which was always a C or mirrored C (congruent or incongruent with the target) but big enough to be identified without fixating it, appeared either in the onset circle or at the saccadic target circle. The task was to judge whether the target C was mirrored or not. After the saccade was initiated the cue was changed. If it had appeared on the onset it was changed to a neutral item, otherwise the cue was changed to be the response target. The primary saccade could be to the onset or to the saccadic target, which happened significantly more often. In trials when a secondary saccade was elicited it could therefore either be from the target to the onset or vice verse, which happened more often. The results suggest that when a saccade was made to the target the observer did not attend to the onset but when the saccade went to the onset and then to the target the result suggest that the observer attended to both. Peterson et el. (2004) concluded that when the primary saccade was to the onset and the secondary to the target, covert attention preceded the saccades, first to the onset and then to the target. When the saccade went only to the target, covert attention did also precede the saccade and went only to the target.

There is considerable evidence supporting the view that saccadic neurons participate in attention, at least covert attention. If attention - whether it is overt or covert - is allocated to an object it is easier to recognize it and discriminate between different features of it (Deubel, 2008; Deubel & Schneider, 1996; Peterson et al., 2004). Microstimulation of visuomotor neurons in FEF enhances discrimination of neurons in V4 in the monkey (Armstrong & Moore, 2007). The visuomotor neurons in FEF behave differently with respect to saccadic task type (Everling & Munoz, 2000) which can be taken as evidence for their participation in saccadic preparation. Armstrong and Moore (2007) take the enhancement

from the FEF on discriminational ability of neurons in V4 as evidence for the role of saccadic related neurons in the allocation of attention.

1.9. Nasal-temporal asymmetry in saccadic behavior under monocular viewing

Because of the anatomical NTAs in the eyes, in the optic nerve and in projections to SC and LGN it is reasonable to expect some NTAs in saccadic behavior, and in fact, such NTAs have been found. In experiments where people are free to choose whether to saccade into nasal or temporal visual fields (with one of their eyes covered), and targets are presented simultaneously in both fields, they show a clear preference for the temporal field (Bompas, Rafal, & Sumner, 2008; Posner & Cohen, 1980). Bompas et al. (2008) also found similar preferences for the temporal visual field for s-cone stimuli that are thought to be invisible to the non color-opponent retinotectal neurons. Valid and invalid cues[1] have different effects on saccadic latency with respect to the nasal and temporal visual fields. When a valid cue is presented in the temporal visual field, the benefits of the cue are greater than when it is presented in the nasal visual field. Accordingly, the cost of an invalid cue in the temporal visual field is greater than when it is presented in the nasal visual field (Rafal, Henik, & Smith, 1991). This seems also hold for the inhibition of return effect (Rafal, Calabresi, Brennan, & Sciolto, 1989).

Evidence for NTAs in both anti and prosaccade latency has also been reported (Kristjánsson, Vandenbroucke, & Driver, 2004). The stimulus in their experiments 1 and 2 were LEDs and the targets located 8° to the left and right of the fixation LED. Below the fixation LED were two LEDs (red and green; the saccade type indicator) used to indicate whether to make anti- or prosaccade. All the LEDs were visible throughout the experiments. After turning on the saccade type indicator, either the left or the right LED was switched on in experiment 1 (in experiment 2 it remained unlit) and the observer made either a prosaccade towards the LED or antisaccade away from it, depending on the color of the saccade type indicator. Prosaccades into the temporal visual field had shorter latencies

1 A valid cue provides correct information about the location of, or the direction to the target whereas invalid cues provided incorrect information. It has been shown that a valid cue shortens the reaction time needed to respond to a subsequently presented target, e.g. Posner and Cohen, 1980.

than prosaccades into the nasal visual field but the opposite pattern was observed in the antisaccade task. But, as Kristjánsson et al. (2004) pointed out the direction of the saccades was always towards the temporal visual field. In a second experiment where the peripheral LEDs were never turned on and included only prosaccades, Kristjánsson et al. (2004) found no NTA in saccadic latency and concluded that stimuli presented in the temporal visual field trigger stronger prosaccade tendency than stimuli in the nasal visual field resulting in shorter latency of prosaccades into the temporal, than into the nasal visual field and longer latency of antisaccades away from temporal than nasal visual field. In experiment 1 Kristjánsson et al. (2004) found that the peak velocity of prosaccades towards the nasal visual field to be higher than towards the temporal visual field.

The evidence for NTAs in saccadic latency is, however, unclear since some have found such asymmetries (Kristjánsson et al., 2004; Walker, Mannan, Maurer, Pambakian, & Kennard, 2000) while others have not (e.g. Bompas et al., 2008).

1.10. Modulation of the antisaccade cost

The difference in the latency of anti- vs. prosaccades is well established and has been termed the antisaccade cost. It seems, however, that both attentional load and landing-point probability can modulate the cost. In an experiment with anti- and prosaccades run in separate blocks, with and without a discrimination task, a difference in the time interval (SOA) between the presentation of the discrimination stimuli and the saccadic target in the periphery modulated the antisaccade cost (Kristjansson et al. 2001). When the discrimination stimuli were presented 100 ms before the saccadic target there was no modulation of the antisaccade latency but the latency of the prosaccade increased significantly resulting in decreased antisaccade costs.

The probability of saccade target location has been found to modulate the antisaccade cost. In an experiment with the left/right probability of the targets locations ranging from .50/.50 to .95/.05 Carpenter and Williams (1995) found that the latency of prosaccades was shorter towards high, than low, probability locations. Dorris and Munoz (1998) found similar effects of probability manipulations for the saccadic performance of rhesus monkeys. Similar effects of probability manipulations on antisaccade

performance have also been reported. Koval, Ford, and Everling (2004) found, using landing-point probabilities of .80/.20, .50/.50 and .20/.80 that the latency of antisaccade towards high probability locations was shorter (and error rates lower, i.e. prosaccades towards the target instead of antisaccade away from it) than towards low probability locations. Noorani and Carpenter (2012) found similar effects on antisaccade performance as Koval et al. (2004) using the same probabilities and further supporting the modulatory effects of probability manipulations on saccadic latency. It is not clear, however, whether the probability manipulations modulated the antisaccade cost but Liu et al. (2010) found some modulatory effects on the antisaccade cost with probability manipulation of targets locations. Liu et al's (2010) paradigm was quite different from the above-mentioned methods, and included anti- and prosaccades as well as horizontal and vertical saccades but only the probability of horizontal prosaccade targets was manipulated. In one block of 322 trials the high probability prosaccade target appeared on 74.1% of the trials to the left and in the other block this was reversed. The antisaccade targets appeared on 25% of the trials in each location. Their results were that the difference (i.e. the antisaccade cost) in latency of high probability prosaccades and low probability antisaccades was significant while the difference in latency between low probability anti- and prosaccades was not, i.e. there was no antisaccade cost (Liu et al., 2010). The latency of high probability prosaccades was significantly shorter than the latency of low probability prosaccades. Furthermore the latency of antisaccades away from the high probability prosaccade target locations was significantly longer than away from low probability locations (Liu et al. 2010). One can, however, speculate whether the probability manipulation lends it effects upon saccadic preparation, per se, or on attentional and decisional processes.

1.11. Saccadic abnormalities and psychological disorders

1.11.1. Obsessive-compulsive disorder

People with obsessive–compulsive disorder (OCD) tend to obsessively repeat thoughts and actions in a way that considerably affects their daily functioning and life quality. OCD is thought to be a consequence of dysfunction in frontal brain areas and in the basal ganglia (Spengler et al., 2006). The roles of these areas in generation of eye movements are rather

well understood and we might therefore expect that investigations of the eye movements of people with OCD might deepen our understanding of OCD. Rosenberg et al. (1997) found that the peak velocity was lower and the error rate higher in the antisaccade task in people with OCD compared with healthy people but this decreased with increased eccentricity. Furthermore, females made more errors than males and the control group. Rosenberg et al. (1997) found, however, no difference in latency and landing-point accuracy. The higher error rate for people with OCD than without it was found in a previous study (Tien, Pearlson, Machlin, Bylsma, & Hoehn-Saric, 1992) in which the ratio of antisaccades that deviated more than 20° from the target locations was also higher in the OCD group than in the control group but no other significant differences were found. The task was only run for 45 sec, which resulted in very few trials. In study conducted by Spengler et al. (2006) people with OCD, people with schizophrenia and healthy people participated but no differences in antisaccade performance were found. When the participants in Spengler's et al. (2006) study made prosaccades from 8° left of the center to 8° right of the center (or vice verse), the ratio of anticipatory saccades was significantly higher for OCD and schizophrenia than for controls but the amplitude gain[2] was lower. In this study eye movements were only recorded for 20 sec in the prosaccade task and 60 sec in the antisaccade task. Caution should be taken when the results from the two above studies are interpreted since both of them consist of very few trials but they, however, suggest that abnormal saccadic characteristics might be found in OCD. There is also some evidence suggesting that first-degree relatives of people with OCD show some abnormality in saccadic performance (Kloft, Reuter, Riesel, & Kathmann, 2012). The participants in Kloft's et al. study were people with OCD, their unaffected first-degree relatives and healthy people, 22 observers in each group. When subjects were to make prosaccades randomly to the left or right, the latency of both the OCD group and their relatives were significantly longer than of healthy people.

2 Amplitude gain is the ratio between the amplitude of the saccade and the distance of the target from the fixation point. If the amplitude gain is < 1 then the saccade does not reach the target (is hypometric) and if it is > 1 then the saccade passes the target (is hypermetric).

1.11.2. Attention-deficit hyperactivity disorder

The characteristics of attention-deficit hyperactivity disorder (ADHD) include hyperactivity and problems in attentional control. Since it is known that frontal brain areas are involved in attention and self control it is reasonable to expect some deficit in these areas in people with ADHD (Munoz, Armstrong, Hampton, & Moore, 2003). Furthermore since the frontal brain areas are known to have important and rather well known roles in eye movements it is reasonable to expect that research on eye movements in people with ADHD might broaden the understanding of ADHD. Munoz et al. (2003) studied people from 6–16 years and 18–59 years old (total 294 participants), with and without ADHD and used prosaccades, antisaccades and fixation tasks to evaluate the participants' performance. In the prosaccade task the latency was significantly longer, and individual variance was higher in the ADHD group than in the control group in all age groups. Munoz et al. (2003) also found that the peak velocity was lower and the duration longer in people with ADHD than in healthy people. In the antisaccade task Munoz et al. found the error rates to be higher among participants with ADHD than in the control group. Interestingly, the gap effect was larger for both adults and children with ADHD than for their corresponding control group. The individual variance differed between groups and was higher in the ADHD, than in the control group in accordance with what was found in the prosaccade task (Munoz et al. 2003).

1.11.3. Dyslexia

The role of eye movements in dyslexia is not well understood but there is some evidence showing that there are differences in some aspects of eye movements in dyslexics compared to people without dyslexia. There is, however, not a general agreement about whether dyslexia causes deficits in eye movements or whether deficit in eye movements contributes to dyslexia (Bednarek, Tarnowski, & Grabowska, 2006). But whereas the neurology of eye movements is rather well known, the investigation of the interaction of eye movements and dyslexia might shed an important light on what brain areas are involved in dyslexia. Biscaldi et al. (2000) used prosaccades with an overlap and antisaccades with a gap in their experiment, testing 200 trials in each condition. In the experiment 254 dyslexics and 114 controls, aged from 7–17 years, participated. There

were no significant differences in the prosaccade tasks. In the antisaccades task they found significant differences between dyslexics and controls, except for 7 and 8 year old children. The dyslexics made more errors, corrected fewer errors and their saccadic latency was longer in the oldest group (16 years old and older). In the antisaccade task Biscaldi et al. (2000) found that the differences between dyslexics and controls increased with age. This is an interesting finding since the performance of healthy children and adolescents improves into their twenties. It has been shown that latency and error rates change with age, especially the latency and error rates of antisaccades and reach their minima when people are in their early twenties (Munoz, Broughton, Goldring, & Armstrong, 1998). Furthermore, this finding suggests that the development of brain areas, which the antisaccade task relies on, is delayed in dyslexics compared to healthy young people. In the double step paradigm the latency of orthogonal prosaccades from the first target to the second has been found to be longer in dyslexics than in controls (Ram-Tsur, Faust, Caspi, Gordon & Zivotofsky, 2006). There might, however, be some inconsistency in findings on the modulatory effects of dyslexia on saccadic latency since Bednarek et al. (2006) found the latency of horizontal prosaccades to be shorter in young dyslexic children (9 to 10.5 years old) than their age matched controls.

1.11.4. Schizophrenia

Schizophrenia is a brain disorder that affects about 1% of the population and usually begins in the late adolescence or early adulthood. It consists of both positive and negative symptoms. Among the positive symptoms are delusions, hallucinations, and thought disorganization but negative symptoms are impaired motivation and decreased emotional expression (Lewis, 2000). In both MRI (Suddath, Christison, Torrey, Casanova, & Weinberger, 1990) and postmortem studies on schizophrenia patients an enlargement of the ventricles has been found and reduction of total brain tissue (about 3–5% and mostly the gray matter of the cerebral cortex; Lewis, 2000). The largest reduction has been found to be in the medial temporal lobe, the superior temporal gyrus, and the prefrontal cortex (see e.g. Beasley, Zhang, Patten, & Reynolds, 2002, for detailed description of the reduction in DLPFC). Among tasks, in which people with schizophrenia show impaired performance on, are tasks that tap on working memory and

oculomotor delayed response task (Lewis, 2000) and these individuals tend to have longer antisaccade latencies and their antisaccade error rates are higher than of healthy people (Haraldsson et al., 2008).

The DLPFC has a significant role in many cognitive processes and some of them are highly related to oculomotor control, e.g. working memory, flexible control (Johnston & Everling, 2011) and, according to Everling and Johnston (2013), facilitation of correct responses instead of inhibition of incorrect responses as previously suggested (see e.g. Johnston & Everling, 2011). Deficits in DLPFC are one of the major deficits in schizophrenia (Bertolino, et al., 2000; Mirnics, Middleton, Marquez, Lewis, & Levitt, 2000).

In many aspects the characteristics of the eye movements of people with schizophrenia are different from the characteristics of healthy people, e.g. in latency, accuracy and error rates. These differences are more pronounced in the anti- than in the prosaccade tasks. The latency of prosaccades of people with schizophrenia has been found to be longer and landing-point accuracy lower compared to healthy people but in both cases the error rates are low and not significantly different (Haraldsson et al., 2008). In the antisaccade task the error rate of the patients can be twice as high as of controls and the patients' latency is longer and their accuracy is lower than of the controls (Haraldsson, et al., 2008). Haraldsson et al. (2008) studied 113 patients and 108 controls and their findings are consistent with what Fukushima et al. (1990) found except that Fukushima et al. did not find any difference in prosaccade performance between participants with schizophrenia and healthy participants.

In a study of monozygotic twins, Ettinger et al. (2006) compared the performance of schizophrenia twins to the performance of their unaffected twins and found the performance to be similarly affected in accuracy and latency but worse than of healthy comparison group. Calkins, Curtis, Iacono, and Grove, (2004) found the antisaccade error rates of the participants with schizophrenia to be similar to the antisaccade error rates of their symptom free first-degree relatives but higher than of healthy participants. There are more studies reporting similar concordance between people with schizophrenia and their relatives and different from healthy people. It seems, however, that there are reasons to interpret this

with caution. According to a meta analyses performed by Levy et al. (2004) the effect found might be mostly because of different inclusion/exclusion criteria for relatives of schizophrenic people and healthy controls. Levy et al. (2004) conclude that the inclusion/exclusion criteria are more liberal for relatives than for controls in experiments reporting large and significant differences between relatives and healthy people.

1.11.5. Parkinson's disease

Among the characteristics of Parkinson's disease are slowness of movements and muscle rigidity and patients often show impaired ability in suppressing automatic responses. In a study of 18 people with Parkinson's disease and 18 healthy people as controls Chan et al. (2005) used a task involving immediate responses and delayed responses (also a delayed memory-guided sequential task, not discussed here) in anti- and prosaccade tasks with gap and overlap conditions. In the immediate prosaccade task the patients made more express saccades in the gap paradigm than controls and in both gap and overlap conditions the patients' variability in latency was higher than of controls. The results from the immediate antisaccade tasks were similar with the addition of longer latency, higher antisaccade cost and higher error rates in the patients than in the controls. Furthermore, the amplitude of the prosaccades was shorter in the patients than in the control group. In the delayed anti- and prosaccade tasks no significant differences were found in latency but the error rates were higher in the patient group than in the control group in both tasks (Chan et al., 2005). In a previous study, similar effects of Parkinson's disease on saccadic parameters have been found in the gap paradigm (Briand, Strallow, Hening, Poizner, & Sereno, 1999) and with multiple amplitudes (White, Saint-Cyr, Tomlinson, & Sharpe, 1983). There might, however, be some difference in latency between patients with Parkinson's disease and healthy people, since Briand, Hening, Poizner, & Sereno (2001) found their patients to have shorter latency than healthy people in the prosaccade task.

1.11.6. Tourette's syndrome

The main symptoms of Tourette's syndrome are chronic motor and vocal tics and are often associated with emotional and behavior problems (Singer, & Minzer, 2003). A variety of brain areas is associated with

Tourette's syndrome and among them are the frontal and supplementary eye fields, DLPFC and the anterior cingulate cortex (Singer, & Minzer, 2003). Since both the supplementary and frontal eye fields, and also the DLPFC, are associated with Tourette's syndrome it is reasonable to expect some abnormal activity in eye movements. In a study of 21 observers with Tourette's syndrome and same number of healthy people in a control group, Farber et al. (1999) found the patients to have shorter duration and higher peak velocity of prosaccades in the overlap condition than controls but no difference in prosaccadic latency. In the prosaccade gap task, the patients generated more anticipatory saccades (RTs < 90 ms) and more saccades on the catch trials (on which no target was presented) than people in the control group but their rate of express saccades was not different. In the antisaccade task patients made more errors than the comparison group, otherwise, no significant differences between patients and healthy people were found. The differences in experimental conditions in Farber's et al. (1999) are notable. In the prosaccadic overlap condition the amplitude ranged from 5° to 35° (in 5° steps) left/right of fixation while in the gap paradigm the target appeared always 4° to left or right. In the antisaccade task the target appeared 8° or 16° left/right of fixation. After the target had been visible for 1000 ms, a stimulus was flashed for 100 ms at the antisaccade landing-point (Farber et al., 1999). In similar experiment but with the target appearing always 20° to the left or right in the immediate and delayed anti- and prosaccade tasks, LeVasseur Flanagan, Riopelle, & Munoz (2001) found the saccadic latency in the patients group to be longer than of controls in all tasks, except when the fixation point overlapped the target in the prosaccade trials. Interestingly, they found no significant difference in error rates in the antisaccade task. In the delayed condition the latency of prosaccades in the Tourette's group was significantly longer than of controls. In a recent study (Jung, Jackson, Nam, Hollis, & Jackson, 2014) the latency was longer and the peak velocity lower in the patients group, than in the control group in prosaccade blocks. But in blocks with anti- and prosaccades interleaved there were no significant differences in latency but the error rates in the patients group were lower than in the control group.

1.11.7. Huntington's disease

Huntington's disease is a slowly progressive, genetic neurological

degenerative disorder, resulting in cognitive decline and involuntary movements of the limbs. It is an autosomal dominant disorder and the causative gene provides the genetic information for a protein (found for about two decades, Li et al., 1995) which causes pathological changes in certain areas of the brain (Lasker & Zee, 1997). It has been proposed that among affected brain areas in Huntington's disease are the frontal eye field, the superior colliculi and the basal ganglia (Lasker & Zee, 1997).

In an interesting study from 1987, Lasker et al. (1987) studied eye movements in 22 people[3] with the Huntington's disease and their results were intriguing. Lasker et al. (1987) used four paradigms and in all of them there were three different amplitudes. In the first paradigm that Lasker et al. called *novel stimulus* the fixation point disappeared simultaneously with the appearance of the target. In the second paradigm, *continuous stimulus*, the peripheral target was illuminated but the observer had to wait for awhile before he/she initiated the saccade. The third paradigm was *remembered stimulus* and was similar to second, except that the observer had to remember the location of the target since it was turned off 1–2 s before the saccade was to be initiated. The forth paradigm, *mirror stimulus*, was a traditional antisaccade task (all other were with prosaccade tasks) except that after 750 ms presentation of the target, a cue was illuminated where the antisaccade landing-point should be. In all the prosaccade tasks the latency of the experimental group was longer than of the control group. In the antisaccade task Lasker et al. (1987) contrasted the difference in the latency of erroneous antisaccades (i.e. prosaccades) and correct antisaccades between groups and the difference was significantly larger for the experimental, than the control group (203 ms vs. 67 ms, respectively). Otherwise, the latencies of correct antisaccades were similar in both groups. The error rates in the experimental group were substantially higher than in the control group.

3 The control group consisted of 10 healthy observers, 8 with the Tourette's syndrome and 4 with developmental dyslexia.

2. About the studies in this thesis

The experiments in this thesis are presented in three published papers, which are included in the thesis.

2.1. Studies 1 and 2

Studies 1 and 2 are presented in paper I (*Saccade performance in the nasal and temporal hemifields*) and paper II (*Violating the main sequence: asymmetries in saccadic peak velocities for saccades into the temporal versus nasal hemifields*), respectively. There is considerable evidence for NTAs in anatomy and attention but the evidence for NTAs in saccadic behavior, per se, has been contradictory as some have found such asymmetries (Kristjánsson et al., 2004; Walker et al., 2000) while others have not (e.g. Bompas et al. 2008). The experiments in study 1 were solely designed to investigate any putative NTAs in saccadic performance, with an emphasis on latency and landing-point accuracy, and to try to discriminate between NTAs in saccadic preparations and the role of attentional NTAs in the saccadic behavior NTAs under scrutiny. In study 2 our emphasis was on the peak velocities of the saccades. To investigate the possibility of NTA in peak velocity we reanalyzed the data from study 1 with one additional experiment run to collect data from binocular viewing whereas the data from study 1 included only monocular viewing conditions.

2.2. Study 3

Study 3 is presented in paper III (*Modulations of antisaccade costs through manipulation of landing-point probability: Only under decisional uncertainty*). The role of the experiments in this study was initially to compare the effect of landing-points probability manipulations on performance of people with schizophrenia and healthy people. There were considerable evidence supporting the idea that probability manipulations

would modulate saccadic latency and would be able to decrease the antisaccade cost but it was not until we replicated experiment 2 from Liu et al. (2010) that we found some modulation of antisaccade costs from probability manipulations. We speculated however, that the task in Liu's et al. experiment was too complicated for people with schizophrenia and therefore we abandoned our initial goal and investigated the general modulation of probability manipulation upon saccadic latency.

3. General methods

3.1. Equipment

3.1.1. Eyetracker

In all eye tracking experiments we used a high speed (250 Hz, one datapoint every fourth ms) monocular video eyetracker from Cambridge Research Systems. The spatial accuracy of the eyetracker is between 0.125° and 0.25°. Its horizontal range is ± 40° and the vertical range is ± 20° (Cambridge Research Systems, 2006). To keep track of gaze the eyetracker uses infrared technology and dual first Purkinje reflection. The infrared light (930 nm) comes from 2 diodes identically positioned on each side of the infrared camera and provides two sets of the first Purkinje image, each opposite to the corresponding diode. When the eye rotates, the length from the centre of the pupil (which the eyetracker software computes) to both of the first Purkinje image changes and these changes are used to compute the point of gaze. As with most eyetrackers based on similar technology, the movement of the head has to be restricted and in all our eye tracking experiments we used a chin and forehead stabilizer, although our eyetracker can compensate for head movements up to ± 10 mm (Cambridge Research Systems, 2006).

When using an eyetracker, two aspects of its accuracy have to be kept in mind. First, how accurate the eyetracker is in locating the point of gaze, what Holmqvist et al. (2011) refer to as the accuracy of the eyetracker. Second, how precisely the eyetracker locates the point of gaze repeatedly at the same location, what Holmqvist et el. (2011) refer to as the precision of the eyetracker. Both accuracy and precision are of great importance but their importance differs with respect to experimental design. In long runs both accuracy and precision tend to decrease (drift) so recalibration

is necessary every now and then. In our experiments we recalibrated the eyetracker after ≈ 10 minutes of tracking. Since it is of great importance to know the pros and cons of ones equipment we tested the accuracy, precision and the drift of our eyetracker, see appendix A.

3.1.2. Computer and monitors

All our experiments were run on the same Dell computer (Intel Core Duo 2.33 GHz, working memory: 1.95 GB, operating system: Microsoft Windows XP 2002) but three different types of monitors were used. In experiments 1 and 2 in study 1 we used 85 Hz, 19" Dell CRT monitor (model P992 with maximal resolution of 1140 X 900 px) and in experiments 6 and 7 in study 1 we used a 60 Hz, 24" Dell LCD monitor (model 2407WFP, with maximal resolution of 1920 x 1200 px). The maximum amplitude in experiments 6 and 7 was 20° and the CRT monitors used in the other experiments were too small for this amplitude, and since we wanted to keep the same viewing distance as in other experiments we needed a bigger monitor. In all other experiments we therefore used a 100 Hz, 19" Hansol CRT monitor (model 920D with maximal resolution of 1280 x 1024 px). Exactly when the target stimulus appears on the screen a signal is sent to the eyetracker. This signal is the timestamp of the appearance of the stimulus. This means that the x and y coordinates of the gaze when the stimulus appeared are known with 4 ms precision. In experiments as ours, the temporal resolution of the monitors is therefore not of great importance.

3.1.3. Software

The main software used in all the experiments was Matlab (v. 7.11.0, 2010b, 32 bit) in which the experiments were programmed and a custom made program written to analyze the eyetracker data. We used PsychToolbox (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007; Pelli, 1997) to display the stimuli and to keep track of the timing of their appearance and disappearance. The PsychToolbox was designed to be used in psychophysical and psychological experiments and is used in many laboratories around the world. To control the eyetracker a toolbox for Matlab from Cambridge Research System (2006) was used. The eyetracker toolbox provides information about the x and y coordinates

(and their timestamps) of the gaze relative to the center of the screen with 4 ms interval (sampling rate = 250 Hz).

3.2. Analyses

3.2.1. Eyetracker data analyses

We wrote a program in Matlab to analyze the eyetracker data. In all analyses the saccade was considered to have started at time point N – 1 when the velocity of the movement of the eye exceeded 30°/sec (Leigh & Zee, 2006) at time point N and when the angular distance between N and N – 1 exceeded 1° (Rolfs, Knapen, & Cavanagh, 2010). A saccade was valid if it was made in the right direction and the amplitude exceeded half the distance to the target stimulus in all experiments except the experiments in study 3 where the saccade was valid if its landing-point was within 4° around the intended target location. An antisaccade was valid if the initial movement was in the opposite direction of the target and classified as corrected if it was first towards the target and then in the opposite direction of the target. A corrected antisaccade consists therefore of two saccades: the initial saccade is a prosaccade and the second one is the antisaccade.

3.2.2. Statistical analyses

In all statistical analyses we used the statistical program R (R Core Team, 2013) and the corresponding libraries. In all experiments in study 1 and study 3 we used repeated measure ANOVA (the aov function in R; R Core Team, 2013) to compare the differences in the dependent measures with respect to factors (the experimental conditions) and their levels. When appropriate, we used Bonferroni correction to adjust the p-values of the post-hoc comparisons. One drawback to repeated measure ANOVA is that it is based on the mean of each participant in each condition, which may reduce the power of the analyses. To compensate for this we also used linear mixed model (LMM; the lmer function in R; Bates, Maechler, Bolker, & Walker, 2014) in the experiments in studies 2 and 3 (presented in papers II and III). The LMM takes within subjects' difference into account (see e.g. Kliegl, Wei, Dambacher, Yan, & Zhou, 2010) and uses the maximum restricted likelihood method (REML or the maximum likelihood, ML) to estimate the corresponding parameters. Both REML and ML are considered to be more efficient than the traditional ANOVA method, especially if

group sizes differ (Snijders & Bosker, 2012). Even though there were always equal number of participants in all conditions the number of data points might have been different because of the exclusion criteria, i.e. it is highly likely that the criteria excluded different number of data points in different conditions. We used the default REML parameter estimation because it is more efficient if the sample size is small (which is usually the case in experiments like ours) than the ML method (Snijders & Bosker, 2012). In statistical analyses of data from the experiments in studies 1 and 3 (presented in papers I and III) we also used distribution analyses. It is well known that response times tend to be positively skewed (Luce, 1986; McGill, 1963), which automatically violates the normal distribution assumption of ANOVA and by fitting the ex-Gaussian distribution to RTs a better description of the data can be obtained (Dawson, 1988; Hockley, 1984; Hohle, 1965; Ratcliff, 1979; Ratcliff & Murdoch, 1976). The ex-Gaussian distribution is described with 3 parameters in contrast to the 2 parameter description of the frequently used Gaussian distribution. The ex-Gaussian distribution is a convolution of a Gaussian and an exponential distribution, which means that the right tail of the distribution is longer than the left tail and therefore has a shape similar to the distribution of RTs (Dawson, 1988; Ratcliff & Murdock, 1976). The three parameters used to describe the ex-Gaussian distribution are μ, σ and τ. The μ-parameter is the mean of the Gaussian part of the ex-Gaussian distribution and the σ-parameter it's standard deviation. The τ-parameter represents the mean and the standard deviation of the exponential part of the ex-Gaussian distribution. The mean of the RT distribution is therefore defined as $\mu + \tau$ and it's variance by $\sigma^2 + \tau^2$ (Burnham, 2013; Luce, 1986; Yap, Balota, Cortese & Watson, 2006) but since the ex-Gaussian parameters are ML estimate there is no obvious ways to compute a confidence interval for the estimated parameters (Yves Lacouture, personal communication 06.05.2104). To estimate the ex-Gaussian parameters we used the egfit.m functions (Lacouture & Cousineau, 2008) in Matlab.

If the latency of the saccade was shorter than 80 ms (100 ms in experiment 4A and 4B in study 3) it was considered anticipatory, but not stimulus driven, and was therefore excluded from all analyses. To find the upper limit of valid saccades we computed the mean of each task for each participant and saccades that deviated more than 3 SD from the corresponding mean were excluded from all analyses but in experiments

4A and 4B in study 3 the upper limit was at 2500 ms following the procedure of Liu et al (2010).

3.3. Participants

All observers that participated in our experiments were unpaid volunteers and students at the University of Iceland. In the experiments of study 1, 54 observers participated (10 excluded because their error rates exceeded our criteria) and their mean age was 27.9 years ranging from 19–55 years. Of those 54 observers 44 had a right dominant eye. In study 2 we only ran one experiment in which 20 observers participated and their mean age was 26.6 years ranging from 20–53 years. The observers in study three were 41 and their mean age was 27.0 years ranging from 20–53 years.

4. Study 1

Saccade performance in the nasal and temporal hemifields

4.1. Experimental procedure

In this study we investigated nasal-temporal asymmetries (NTA) in the latencies of prosaccades and the accuracy of their landing-points. All experiments were run with an eye-patch over the non-dominant eye to be able to compare nasal versus temporal saccade performance. In experiment 1 and 2 we tested saccades from center to both left and right (amplitude = 5°), from the periphery to the center (amplitude = 5°) and from left/right to right/left (amplitude = 10°). In experiment 1 there were 3 target locations but in experiment 2 we added one possible target location to each periphery to minimize the influence of motor preparation, which could have affected the results from experiment 1 (see paper I fore detailed description). In all other experiments there were 3 target locations and the saccades were always from the center to the periphery. The task in experiments 3 (amplitude = 8°), 6 (amplitude = 20°) and 7 (amplitudes = 5°, 10° and 20°) was a traditional saccadic task but in experiment 4 (amplitude = 8°) we added attentional load and a discrimination task in experiment 5 (amplitude = 8°). For more detailed description of the experimental procedures see paper I.

4.2. Results

The main result with regard to our experimental questions of possible NTAs in saccade performance is that no such asymmetries were observed in latency or accuracy. In experiment 1 the only significant difference in latency was between low (5°) and high (10°) amplitude saccades with shorter latency for the high amplitude saccades. But landing-point accuracy was better for low than high amplitude saccades. In experiment

2 the landing-point accuracy was significantly better for saccades towards temporal than nasal stimuli. In experiments 3 through 5 there was a trend for better accuracy of saccades towards temporal than nasal stimuli but no NTA in latency was found. Experiment 6 did not reveal any evidence of NTAs in saccade performance, generally consistent with what we have seen in the 5 preceding experiments. In experiment 7 we found the landing-point accuracy of the highest amplitude saccades to be better towards temporal than nasal targets and the interaction between hemifield and eccentricity for landing-point accuracy and latency was significant. This significant interaction suggests that NTAs in latency might be found at eccentricities larger than 20° because the between hemifield difference in ganglion and cone density increases with eccentricity. For details see the corresponding results sections in paper I.

4.3. Discussion

Our study was the first to directly investigate the supposed NTAs in saccadic performance. In other studies this had been a secondary aim (e.g. Bompas et al. 2008; Kristjánsson et al. 2004; Rafal et al. 1991; Walker et al. 2000). The only significant NTA we found was in landing-point accuracy and only in some of the experiments. There are good reasons to expect NTAs in latency since there is considerable NTA in the anatomy of the retina and the optic nerve (Curcio, & Allen, 1990; Hubel et al. 1975; Itaya & Van Hoesen, 1983; Sterling 1973; Tigges & Tigges, 1981; Williams et al., 1995), at least in projection to the SC. Another reason to expect NTAs in saccadic performance comes from the fact that there is NTA in attentional functioning (e.g. Bompas et al., 2008, Rafal et al., 1991) and from experiments in which people were free to choose whether to saccade to nasal or temporal visual fields (Bompas et al., 2008, Posner & Cohen, 1980). Express saccades are mainly controlled by the SC (Dorris, Paré, & Munoz, 1997; Edelman & Keller, 1996) and NTAs in saccadic latency might show up in these saccades but we are not aware of any studies investigating this possibility and future experiments could shed light on this hypothesis. One factor that could minimize the effect of NTA in anatomy and attention on saccadic latency and accuracy might be that only about 10% of projections from the retina is to the SC. It is therefore quite possible that higher cortical areas minimize the consequences of the anatomical differences between nasal and temporal seen in the retina and in the optic nerve. Another factor that could minimize the effect of

anatomical NTAs is that it might be the peak velocity that is coded for by the brain stem saccadic generator (Leigh & Zee, 2006), but neither latency nor amplitude, when a saccade is planned. In study 2 this question was addressed.

5. Study 2

Violating the main sequence: asymmetries in saccadic peak velocities for saccades into the temporal versus nasal hemifields

5.1. Experimental procedure

Since the main purpose of this study was to reanalyze the data from experiment 1 to find out if there were nasal-temporal asymmetries in the peak velocity of the saccades we ran only 1 experiment in this study using a traditional saccadic task with amplitude of 8°. For details see paper II.

5.2. Results

In this study we investigated NTAs in saccadic peak velocity and found that for monocular viewing the peak velocity was higher towards the temporal than towards the nasal visual field for saccades with an amplitude of 5°, 8° and 10° but no difference was found for 20°. Under binocular viewing conditions and amplitude of 8°, the peak velocity of the dominant eye was higher towards the temporal than the nasal visual field but the difference was considerably smaller than under monocular viewing. Our conclusion of higher peak velocity towards the temporal than the nasal visual field is based on comparison of 3 types of multiple mixed-effects models. In the base model the only factor was amplitude, in the second model we used amplitude and hemifield as factors and added latency to the third one. The model with the lowest AIC (Akaike information criterion; Akaike, 1974) is considered to have the best fit to the data (Akaike, 1974; Burnham & Anderson, 2004). For all amplitudes, a model with amplitude and hemifield as predictors had the best fit indicating that both hemifield and amplitude – but not latency – had modulatory effects on peak velocities. The effect of amplitude on peak velocity is well known (the main sequence; Bahill et al., 1975) but what is new here is the effect of hemifield on peak velocity

resulting in NTA in peak velocity. More detailed description of the results can be found in the results sections in paper II.

5.3. Discussion

In study 2 we found clear evidence of differences in peak velocity of saccades towards the temporal and nasal visual fields. The peak velocity of monocular saccades towards the temporal visual field was significantly higher than of saccades towards the nasal visual field. The same pattern was observed for binocular saccades but the difference was much smaller. The saccades into the nasal visual field were on average more hypometric than saccades into the temporal visual field, which means that the amplitude of the saccades into the nasal visual field was, on average, lower than of saccades in the opposite direction. The main sequence therefore predicts higher peak velocities of saccades into to the temporal, than into the nasal visual field (Bahill et al. 1975) but as we controlled for the difference in amplitude in our analyses the main sequence does not explain the observed NTA in peak velocity.

The observed NTA in peak velocity is in good accordance with NTAs in attention (Bompas et al., 2008; Rafal et al., 1991) and the higher preference people seems to have for the temporal vs. the nasal visual field when they are free to choose whether to saccade into the temporal or nasal hemifield (Bompas et al., 2008; Posner & Cohen 1980). The NTAs in ganglion cells in the retina are most pronounced at 8° eccentricity (see Figure 3) where we found the highest NTA in peak velocity. The observed NTA is therefore in good accordance with anatomical differences in the retina (Curcio & Allen, 1990) and the optic nerve (Hubel et al. 1975; Itaya & Van Hoesen, 1983; Sterling 1973; Tigges & Tigges, 1981; Williams et al., 1995) and we concluded that the anatomical NTAs lead to NTAs in peak velocity.

Why should NTAs in peak velocity be a consequence of NTAs in anatomy since no NTA in latency was observed? One of the answers to this question might be that the signal from the nasal retina is stronger than from the temporal retina but the time it takes the signals to go from nasal and temporal retina to the saccadic generators might be the same. When the signals enter the saccadic control stations the stronger signal from the nasal retina might code for higher peak velocity than the weaker signal

from the temporal retina. This is a reasonable explanation since it is the peak velocity that the brain stem saccadic generator computes for the given amplitude but not the amplitude itself (Leigh & Zee, 2006). Furthermore, the direct projections from SCs to SCi (Helms et al. 2004) might contribute to the observed NTA in peak velocity and these projections strengthen our hypothesis that the anatomical NTA is the main reason for NTA in peak velocity.

6. Study 3

Modulations of antisaccade costs through manipulation of landing-point probability: Only under decisional uncertainty

6.1. Experimental procedure

In this study we ran 5 experiments and 2 of them (4A and 4B) were replications of experiment 2 conducted by Liu et al. (2010). Experiments 1 through 3 consisted of 3 blocks each of horizontal saccades only. The first block in each of these experiments included only prosaccades, the second block consisted of antisaccades and in the third block anti- and prosaccades were interleaved. In all these experiments the probability of the target to the left of center were .25, .50 and .75 (or vice versa). In experiment 3 the observer had to find the target (the oddly colored stimuli) among 3 distractors. In experiments 4A and 4B, which consisted of two blocks, with horizontal and vertical saccades, anti- and prosaccade were interleaved and the target (defined by color, different from the distractors) appeared among 3 distractors. The probability manipulations only applied to the horizontal prosaccades: The probability that the target would appear to the left in one block and to the right in the other, was .741. The probability of the prosaccade target in all other locations was therefore .086 in each but .25 for the antisaccade target. In both blocks observers were to perform equal numbers of anti- and prosaccades. In all the experiments all trials began with a fixation cross and when it disappeared the saccade-type indicator appeared instructing the observer to make either anti- or prosaccades. In blocks of only antisaccades and only prosaccades the saccade-type indicator was displayed even though observers knew the saccade type, to ensure that the procedure was the same in all blocks. In experiments 1 and 3 the target appeared simultaneously with the disappearance of the saccade-type indicator. In experiment 2 we

used the gap-paradigm (Saslow, 1967), i.e. the target appeared 200 ms after the saccade-type indicator disappeared. In experiments 4A and 4B the fixation stimulus appeared as the saccade-type indicator disappeared and was visible throughout each trial. In studies 1 and 2 there were 2 target locations, 8° left or right of the center whereas in experiment 3 there were 4 locations (6° and 8° left or right of the center). The first 3 experiments consisted of horizontal saccades only while experiments 4A and 4B included also vertical saccades. For detailed description of the experimental procedures see paper III. There were considerably fewer trials in experiment 1 through 3 than in experiments 4A and 4B in which some modulation of antisaccade costs were found. Furthermore, Koval et al. (2004) and Noorani and Carpenter (2012) found some evidence of effects of probability manipulations on saccadic latency in blocks of 200 and 400 trials, respectively. To test if longer blocks would reveal effects of probability manipulations on the antisaccade cost we ran the 5th experiment with 3 blocks of antisaccades and 3 blocks of prosaccades and the same task as in experiment 1 but with 300 trials in each block.

6.2. Results

The main purpose of this study was to investigate the effect of different probability of target location on saccadic latency and especially on the antisaccade cost. In the traditional anti- and prosaccade tasks in experiment 1 we found no modulatory effects of the probability manipulations of target location. In experiment 2 we found the well known gap effect (Saslow, 1967), i.e. the latency of saccades were shorter than in experiment 1 but no modulation of anti- versus prosaccade latencies from target-location probability manipulation were seen. In experiment 3 the observers had to find the target (and in the interleaved block, decide whether to make anti- or prosaccades) among 3 distractors. We found only very limited modulation of antisaccade costs from probability manipulations in this experiment. The error rates were, however, very high indicating the difficulty of the tasks, which is further supported by the longer latency (289 ms, SD = 95.4 ms) than in experiment 1 (172 ms, SD = 31.1 ms). Because of the lack of modulation of probability manipulations on antisaccade cost it was reasonable to replicate experiment 2 conducted by Liu et al. (2010) in which they found that landing-point probability manipulations decrease the antisaccade costs. The difference in the latency of antisaccades vs. prosaccades was significant in the high probability, but not in the low

probability conditions. Furthermore, the latency of prosaccades towards the high probability location was shorter than of prosaccades towards the low probability locations. The opposite effect of probability was observed on the antisaccades latency, i.e. it was longer away from high, than low probability locations. We therefore ran two additional experiments (4A and 4B). These experiments included both horizontal and vertical saccades as well as anti- and prosaccades in the same block. The task in experiments 4A and 4B was similar to the task in the interleaved block of experiment 3 in that observers had to decide whether to make anti- or prosaccades and then find the target among 3 distractors. Furthermore, the observer had to find out – after the experimental display appeared – whether to make horizontal or vertical saccades, i.e. whether the target was in the horizontal or vertical direction from the fixation point. In experiments 4A and 4B we found similar effects on antisaccade costs for the low probability locations as Liu et al. (2010), i.e. the antisaccade cost was reduced. The very long latencies for both anti- and prosaccades are very notable as they are twice as long as the latencies in experiment 3 which, in turn, was considerable longer than in experiment 1. This very long latency may suggest that the probability manipulations did not modulate the saccadic preparation process, per se, but the decision process of which saccade type – anti or pro, horizontal or vertical – the observer had to perform. In experiment 7 we found the usual main effect of saccade type (longer latency for anti- than prosaccades) and a small effect of probability but this did not reduce the antisaccade costs. For detailed information about the results from study 3 see the results sections in paper III.

6.3. Discussion

In the experiments of this study the task demands varied from very low to very high as is reflected in big differences in latency. The latency of anti- and prosaccades, in experiment 1, was 172 ms and 274 ms, respectively with equal probability of left and right targets and increased to 626 ms and 631 ms for anti- and prosaccades, respectively, in the low probability condition in experiment 4A. The latency of prosaccades can be as low as 80 ms (express saccades; Edelman et al. 2007; Fischer & Boch, 1983) and the latency of regular prosaccades is usually between 170 and 200 ms (Leigh & Zee, 2006). Because of this big increase in saccade latency it is reasonable to propose that other factors, than saccadic preparation per se, explain the longer latency in experiments 4A and 4B. The task

in experiment 1 was very simple, especially in the blocks of anti- and prosaccades only where the only decision needed was whether to initiate a saccade or not. The task in experiments 4A and 4B was, on the other hand, highly complex and involved visual search and decisions. When the saccade type indicator appeared, the observer had to decide whether to make an anti- or prosaccade. In the next step, observers had to find the target among three distractors and it was not until the target was found that the observer knew whether to make a horizontal or vertical saccade. In experiment 1, the observer could start to prepare the saccade as soon as the target appeared but in experiments 4A and 4B the preparation could not start until the target was found.

We can be pretty confident that both experiment 3 and experiments 4A and 4B include feature visual search since the target is defined by color and has to be found among three distractors. Given that the role of LIP is to combine top down and bottom up activity and its role in covert visual search (Bisley et al. 2011) it is reasonable to expect that LIP is involved in the tasks in all the experiments in this study but the time needed to build the priority map was quite different between experiments. In experiment 1 the neurons in LIP had only to find a singleton that pops out in the display and this process is very likely mostly bottom-up and might rely more on selection processes in SC than in LIP. In experiments 4A and 4B top down guidance is involved to a much larger extent than in experiment 1. The observer knows that he/she has to look for the oddly colored singleton and the task of LIP is to combine those top down instructions with bottom up information (e.g. the different feature of target and distractors) before that saccadic target can be selected. The time needed to prepare a saccade can at least be split up into the time needed to select the target and the time needed to compute the direction and peak velocity (which in turn represents its' amplitude) of the saccade. In tasks as complicated as in experiments 4A and 4B there are at least two more steps (anti- or prosaccade; horizontal or vertical saccade) involved before the saccade can be initiated as mentioned above. If probability manipulations of landing-point locations would affect preparation of the saccade itself, these effects would have been observed in experiments 1 and 2. But since the probability manipulations effects on saccadic latency were only observed in experiments 4A and 4B we conclude that the probability manipulations modulated decisions and selection processes but not saccadic preparation per se.

7. General discussion

Our results from study 1 show that there are no NTAs in the latency of regular prosaccades in the amplitude range from 5°–20° and only minimal in landing-point accuracy. Whether any NTA might show up in express saccades is not known yet but we consider this not unlikely, since they are probably initiated directly from SC (Dorris et al., 1997; Edelman & Keller, 1996). We did not look for NTAs in antisaccadic latency but it is unlikely that it would be found since higher brain areas – in which anatomical NTAs are not known to exist – are more involved in the anti- than prosaccade generation. In the investigations of peak velocity in study 2 we found, however, clear evidence for NTAs of saccades with the amplitude of 5°–10° under monocular viewing and even to some extent of binocular saccades with an amplitude of 8°. As with latency, future studies will have to determine if NTAs in peak velocity are found for express saccades but with respect to anatomical NTAs in early visual pathways it is reasonable to expect such asymmetries would be seen and perhaps even larger than in the peak velocity of regular saccades. The results from study 3 clearly suggest that probability manipulations of landing-point locations do not affect the preparation of saccades per se, but the time needed to choose between saccade types and to select the target.

The results of our studies emphasize the importance of taking all the different steps in saccadic generation into account when designing eye movement experiments and interpreting the results. In blocks with anti- and prosaccade trials interleaved the observers has to keep the meaning of the saccade type indicator in working memory (likely involving DLPFC), decide which saccade type to initiate and send the decision to FEF and SEF. When the stimulus appears, it has to be found (likely involving LIP) and attention has to be allocated to it (involving LIP and FEF). If the task

is a prosaccade then a "go" signal can be sent to the SCi confirming that the saccadic endpoint should be where the location of stimulus has been coded. If the task is an antisaccade then the DLPFC, FEF and SEF have to "tell" the neurons in SCi to compute the landing-point in the opposite direction of the stimulus. Adding visual search and interleaved horizontal and vertical saccades to the task requires still more cognitive effort and taps more on higher cortical areas than the simpler tasks.

It has been shown that saccadic characteristics in people with different psychological disorders are in many aspects different from healthy people (Biscaldi et al., 2000; Chan et al., 2005; Farber et al., 1999; Haraldsson et al., 2008; Lasker et al., 1987; Munoz et al., 2003; Rosenberg et al., 1997). In clinical research of eye movements it is even more important to take task complexity into account than in basic research. Another aspect of this is the importance of balance between the number of trials needed for reliable statistical analyses and the ability of the patients to participate in the experiments. It is surprising how few data points were collected in some of the above discussed studies and in some of them, data was only collected fore 60 s or less (Spengler et al. 2006; Tien, et al. 1992).

In most, if not all, the studies reviewed above traditional statistical analyses were performed, i.e. ANOVAs and t-tests. Analyses with random effects models might in many cases be more powerful since they can take individual differences into account to a greater extent than the traditional methods. As described in the statistical analyses section, distribution analyses should provide better description of RTs with three parameters than the traditional two parameters descriptions. It has been shown that different task types in visual search differently modulate the parameters of the ex-Gaussian distribution (Kristjánsson & Jóhannesson, 2014, see Appendix B). It is therefore reasonable to expect that different task types - and different psychological disorders - also differently modulate the ex-Gaussian parameters in eye movement research. It is also worthwhile to analyze express saccades and regular saccades separately since the former might be elicited directly from the SC, with higher cortical areas only minimal involved.

It is clear that eye movement research is of great importance in basic research as well as in clinical studies and many important questions are

awaiting answers. It would be very interesting to get better knowledge of what are the exact roles of the FEF, SEF, DLPFC and the LIP in the generation of eye movements and the time it takes the signals from the retina to reach these areas.

8. References

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Appendix A

Accuracy and precision

To test the accuracy and precision of our eyetracker we used method suggested by Holmqvist et al. (2011). After calibration of the eyetracker the testing procedure began and each trial consisted of 5 targets, one at screen center and the other four in 0°, 90°, 180° and 270° direction from the center. The distance from the center of the screen to the targets was 8° and only 1 target was visible at a time.

At the beginning of each trial a white dot (0.4° measured at screen center) was displayed on the screen and the observer moved the mouse-pointer to the dot, pressed the space-bar and then the dot changed to a much smaller one (0.07° measured at screen center) and the observer pointed with the mouse at the dot while fixating it and when he/she was satisfied with his/her accuracy he/she clicked the mouse, the pointed at target disappeared and the next target was instantly displayed.

To address the drift in accuracy we ran two blocks of eye tracking experiment and each block lasted for ≈ 10 minutes. Before, after the first block and after the second block accuracy trials were run. In this measure only the author participated.

Before the first block the horizontal and vertical differences between targets positions and the gaze points were – 0.14° and 0.20°, after tracking for ≈ 10 minutes the difference was – 0.03° and 0.13° and after ≈ 20 minutes of tracking the difference was – 0.28° and 0.15°, respectively. The results are depicted on figure A1.

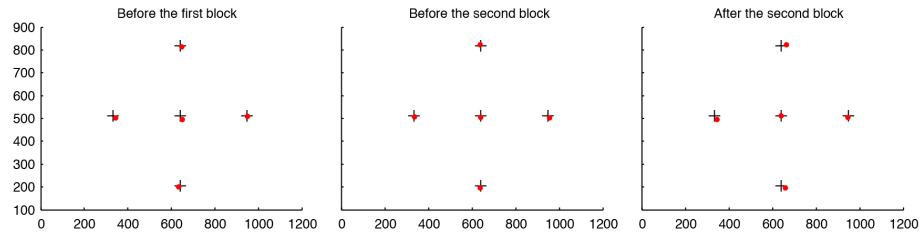

Figure A1. Accuracy and drift. The "+" on the figure represents the locations of the targets and the red dots the point of the gaze. The figure clearly shows that the accuracy of the eyetracker is good and the drift of the accuracy is small.

To test the precision of the eyetracker we ran 6 trials with 2 subjects. In trial 1 the average deviations of the point of gaze from the horizontal and vertical locations of the targets were 0.21° and 0.06°, respectively. In trial 6 the deviations of the point of gaze from the horizontal and vertical locations of the targets were 0.06° and 0.3°, respectively. The precision of the eyetracker is visualized on figure A2.

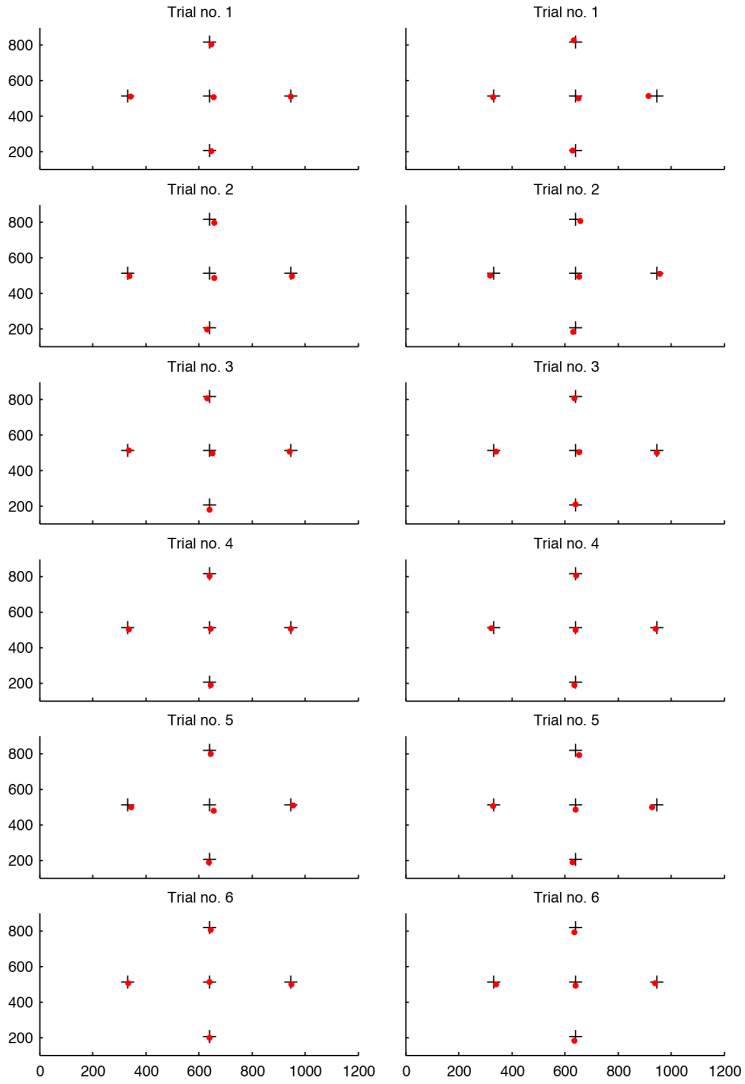

Figure A2. The precision of the eyetracker. The "+" on the figure represents the locations of the targets and the red dots the point of the gaze. The plots on the left are for subject 1 and on the right for subject 2. The figure clearly shows that the precision of the eyetracker is good.