Localization of external stimuli during simulated self- and object-motion

Lokalisation externer Reize während simulierter Eigen- und Objektbewegung

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Contents

Erklärung: Eigene Beiträge und veröffentlichte Teile der Arbeit

Gemäß §8, Absatz 3 der Promotionsordnung der Philipps-Universität Marburg (Fassung vom 12.04.2000) müssen bei den Teilen der Dissertation, die aus gemeinsamer Forschungsarbeit entstanden sind, „die individuellen Leistungen des Doktoranden deutlich abgrenzbar und bewertbar sein."

Kapitel 1: Localization of visual targets during optokinetic eye movements

- Planung der Reizapparatur
- Durchführung von 64% der Messungen
- Einarbeitung und Betreuung von Marc Rohe. Marc Rohe war Großpraktikant in unserer Arbeitsgruppe und hat die restlichen Messungen vorgenommen.
- Programmierung sämtlicher Auswertungen und Auswertung sämtlicher Daten
- Verfassen des Manuskripts in Zusammenarbeit (Korrektur) mit Prof. Dr. Frank Bremmer und Prof. Dr. Bart Krekelberg
- Dieses Kapitel wurde in der vorliegenden Form in Vision Research veröffentlicht. (Andre Kaminiarz, Bart Krekelberg, Frank Bremmer (2007) Localization of visual targets during optokinetic eye movements. Vision Research 47: 869-878)

Kapitel 2: Expansion of Visual Space During Optokinetic Afternystagmus (OKAN)

- Planung, Durchführung und Auswertung aller Experimente
- Verfassen des Manuskripts in Zusammenarbeit (Korrektur) mit Prof. Dr. Frank Bremmer und Prof. Dr. Bart Krekelberg
- Dieses Kapitel wurde in der vorliegenden Form im Journal of Neurophysiology veröffentlicht. (Andre Kaminiarz, Bart Krekelberg, Frank Bremmer (2008) Expansion of Visual Space During Optokinetic Afternystagmus (OKAN). J. Neurophysiol. 99: 2470-2478)

Kapitel 3: The Main Sequence of Human Optokinetic Afternystagmus (OKAN)

- Durchführung von 81% der Experimente, die restlichen Messungen wurden von Kerstin Königs durchgeführt

- Auswertung sämtlicher Experimente
- Verfassen des Manuskripts (75%) in Zusammenarbeit mit Kerstin Königs (25%) und Prof. Dr. Frank Bremmer (Korrektur)
- Dieses Kapitel wurde in der vorliegenden Form im Journal of Neurophysiology veröffentlicht. (Andre Kaminiarz, Kerstin Königs, Frank Bremmer (2009) The Main Sequence of Human Optokinetic Afternystagmus (OKAN). J. Neurophysiol. 101(6): 2889-2897)

Kapitel 4: Task influences on the dynamic properties of fast eye movements

- Durchführung von 50% der Experimente, die restlichen Experimente wurden von Kerstin Königs durchgeführt
- Auswertung sämtlicher Experimente
- Verfassen des Manuskripts (75%) in Zusammenarbeit mit Kerstin Königs (25%) und Prof. Dr. Frank Bremmer (Korrektur)
- Dieses Kapitel ist in der vorliegenden Form im Journal of Vision im Druck

Kapitel 5: Control of saccades towards stationary and moving targets: the role of the macaque lateral intraparietal area (LIP)

- Durchführung von 50% der Experimente, die restlichen Experimente wurden von Kerstin Königs und Steffen Klingenhöfer durchgeführt
- Auswertung sämtlicher Experimente
- Verfassen des Manuskripts (75%) in Zusammenarbeit mit Kerstin Königs (25%) und Prof. Dr. Frank Bremmer (Korrektur)

General Introduction

Localizing objects in our environment is one of the key-features of the visual system. Without precise information about the location of objects in our environment goal-directed behavior like reaching for a cup would not be possible. Another, even simpler example, are goal-directed eye-movements. Since our fovea, i.e. the area of vision at highest resolution, covers only about 2° of the visual space, we have to move our eyes around very precisely so that objects of interest are projected onto the fovea. In the past the ability of subjects to localize visual targets has been studied either under static conditions (in the absence of eye movements and self-motion) or during voluntary eye movements. Our knowledge about the ability of subjects to localize stimuli during reflexive eye movements is rather limited. This is surprising given the fact that in everyday life several types of reflexive eye movements are generated as consequence of our self-motion (Lappe and Hoffmann, 2000;Miles, 1998). Therefore, the overall aim of the current thesis was to investigate the ability of subjects to localize visual stimuli during reflexive eye movements which are typically triggered by self-motion.

Accordingly, I will start this introduction by presenting some general findings about the localization of visual targets and its dependence on eye movements. Then I will describe the eye movements investigated within this study and the neural substrate underlying their execution. Thereafter I will introduce the analysis tool which has been used to determine the dynamics of eye movements, i.e. the so called 'main-sequence'. This is followed by an overview of the functional characteristics of a cortical area of the rhesus monkey which is critical for the control of fast eye movements. Finally I will outline the aim of each of the studies being part of this thesis.

Reference frames

Even in the absence of eye movements the localization of an external object is anything but trivial. Depending on the orientation of the eye in the head the image of an object will be projected onto different parts of the retina though it is located at the same position in the outside world. Objects being next to each other in the outside world are also represented adjacent to each other on the retina. The same representation of the outside world can be observed in several cortical areas i.e. adjacent points in the world are represented by neighboring neurons. These areas encode the world in retinal coordinates or a retinal frame of reference. In higher visual and motor areas position information is

often encoded relative to other body-parts like the head or even the body (trunk). Therefore these areas encode position information in a head or body centered frame of reference. Hence a coordinate transformation has to be performed somewhere in the sensorimotor system. To perform such a transformation information about the position of the stimulus on the retina has to be combined with eye- and head-position information (Bremmer et al., 1999;Boussaoud and Bremmer, 1999). This does not seem to be a problem for experiments investigating the ability of subjects to localize a target at first, but depending on how subjects have to indicate where they had perceived the stimulus different transformations might be necessary. For example if the subject reports the perceived position by pointing the information has to be transformed to the reference-system used for the motor-command of the pointing movement (Batista et al., 2007;Bueno et al., 2002;Buneo and Andersen, 2006). When instead verbal reports are used a transformation into a body-centered frame of reference might not be necessary. Furthermore localization can not only be performed relative to a subject's own body but also relative to an external reference like a comparison-stimulus. In general localization is more precise when external references are available (Mapp et al., 2007;Müsseler et al., 1999;Dassonville et al., 1995).

Target characteristics

It has been demonstrated that briefly presented ('flashed') stimuli are mislocalized while targets which were presented for a longer time-period were localized correctly (Adam et al., 1995). Aside from its duration other stimulus characteristics have also been reported to influence localization. Rose and Halpern (1992) demonstrated that localization errors increased as the spatial frequency of the stimulus decreased. For moving stimuli it is known that when two physically aligned dots move in the same direction and they differ in luminance the brighter one is (often) perceived to be ahead of the dimmer one (Hess effect)(Whitney, 2002).

Background characteristics

Under natural viewing conditions objects are in most cases embedded in a rich visual environment. On the one hand localization can benefit from the background as it serves as a reference. On the other hand it has been shown that visual backgrounds can also induce localization errors. When a localization target is presented on a moving

background it will be mislocalized in direction of the background motion (Mateeff et al., 1982). It is not even necessary that the whole background is moving: even if a target is flashed in the vicinity of a moving grating the target will be mislocalized in the direction of the grating motion (Whitney and Cavanagh, 2000;Whitney, 2002).
The effect of background luminance on localization errors during fixation was subject of my PhD work (chapter 2: Expansion of visual space during optokinetic afternystagmus (OKAN)).

Localization during eye movements

Fixation

Localizing an object which is briefly presented in the visual periphery during fixation seems to be an easy task. Yet, still even under these conditions localization errors can be observed. Subjects misperceive the target as being closer to the fovea (centripetal bias) (Mateeff and Gourevich, 1983). Typically the distance between the point of fixation and the target is underestimated by about 10% (van der Heijden et al., 1999). A similar phenomenon can be observed for saccades (see below). When subjects execute a saccade towards a peripheral target the saccade typically falls short by about 10% (Carpenter, 1988). This effect is called 'saccadic undershoot'. It has been hypothesized that both effects have a common origin (Müsseler et al., 1999).

Smooth pursuit eye movements (SPEM)

When subjects pursue a moving visual target and have to localize a briefly flashed target they typically mislocalize it in direction of the eye movement. The size of the localization error depends the eye movement velocity (Mitrani et al., 1979) and on the position of the target relative to the fovea (Mitrani and Dimitrov, 1982). While the error is large in the visual hemifield the eyes are heading for, i.e. ahead of the eyes, only small errors are observed in the other hemifield. Furthermore the error increases with the retinal eccentricity of the stimulus (van Beers et al., 2001).

Saccades

In everyday live we perform about three saccades per second to foveate objects of interest. Saccades belong to the class of fast eye movements (Krauzlis, 2005;Steinman et

al., 1990). They reach peak-velocities of up to 900°/s depending on saccade-type and species. Saccades are ballistic, i.e. they can not be modified after they have been initiated. Several types of saccades can be distinguished. The most common are visually guided saccades. But saccades can also be executed towards auditory or somatosensory targets (Zambarbieri et al., 1982). Other types of saccades often used in the laboratory include anti-saccades and memory guided saccades, which offer the possibility in neurophysiological experiments to differentiate between neural activity caused by the appearance of the saccade target and the activity caused by the execution of the saccade itself. Saccades, like other fast eye movements, are very stereotyped. They adhere to the so called *main-sequence* (see below).

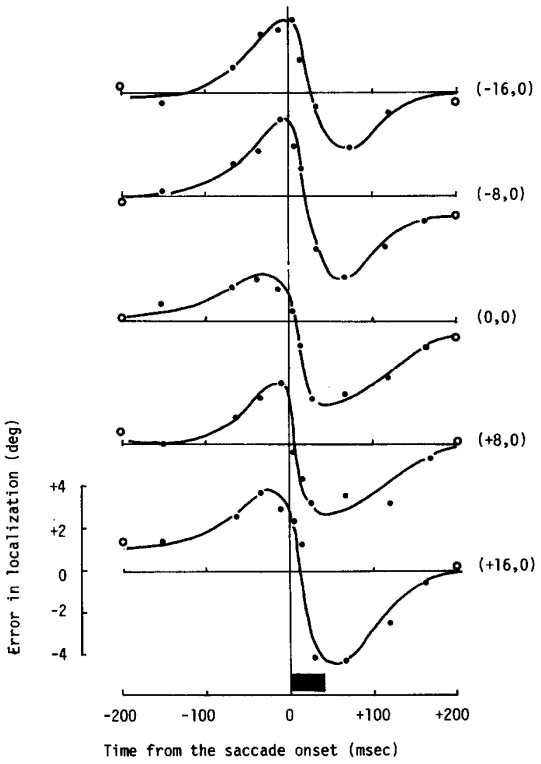

Figure 1: Localization errors during horizontal saccades in darkness. Horizontal errors are displayed as a function of time relative to the onset of the saccade. Positive errors indicate mislocalization in direction of the saccade. The black bar marks the average duration of the saccades. The five curves represent data for five different target positions which are displayed in parenthesis. The saccade start- and end-points were -4/0 and 4/0 respectively. (adapted from Honda, 1993)

The localization errors observed in the temporal vicinity of saccades depend heavily on the exact experimental conditions (Ross et al., 2001;Honda, 1993). In all cases, errors depend on the time of target presentation relative to the onset of the saccade. In complete darkness targets presented briefly before (-100ms) and during the saccade are mislocalized in direction of the eye movement. The error is maximal at saccade-onset. After saccade-offset targets are mislocalized against saccade direction for up to 100 ms (Figure 1). This error pattern is independent of target position and is called 'perisaccadic shift' (Cai et al., 1997;Honda, 1989;Honda, 1993). In the presence of visual references the errors depend heavily on the position of the target relative to the endpoint of the saccade (Figure 2). Targets are mislocalized towards the landing point of the eye i.e. targets which are presented between the saccade–starting point and its endpoint are mislocalized in direction of the saccade while targets which are presented beyond the

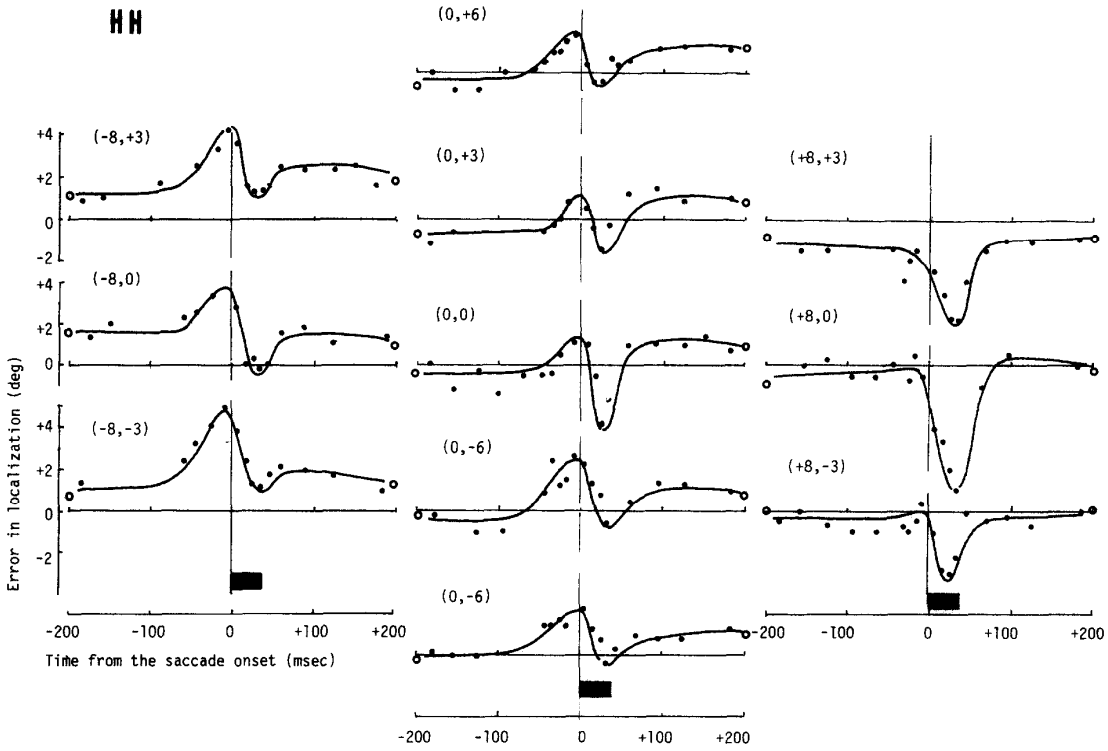

Figure 2: Localization errors during saccades with references available. Horizontal errors are displayed as a function of time relative to the onset of the saccade. Positive errors indicate mislocalization in direction of the saccade. The black bars mark the average duration of the saccades. In each panel data for one target position is displayed. Target coordinates are given in parenthesis. The saccade start- and end-points were -4/0 and 4/0 respectively. (adapted from Honda, 1993)

endpoint of the saccade are mislocalized against the saccade-direction (Honda, 1993). This effect is called perisaccadic compression of space (Ross et al., 1997). Interestingly it is sufficient for compression to occur if the references are present only after the saccade (Lappe et al., 2000).

Optokinetic nystagmus (OKN)

The OKN is a phylogenetically very old, reflexive eye-movement which can be observed in all species with moveable eyes. Together with the vestibulo-ocular reflex (VOR) it serves to stabilize the retinal image during self-motion or head-turning (Carpenter, 1988;Ilg, 1997b). The two systems (OKN and VOR) complement each other depending on the velocity of the self motion. During fast head-movements the compensatory eye movements are mainly caused by the VOR. As head-movement velocity decreases the contribution of the OKN increases (Lappe and Hoffmann, 2000). Both eye movements consist of two alternating phases a slow-phase and a fast-phase. The typical pattern of eye movements which can be observed during reflexive OKN is shown in Figure 3a. When we turn our head to the left the retinal image would move to the right if there

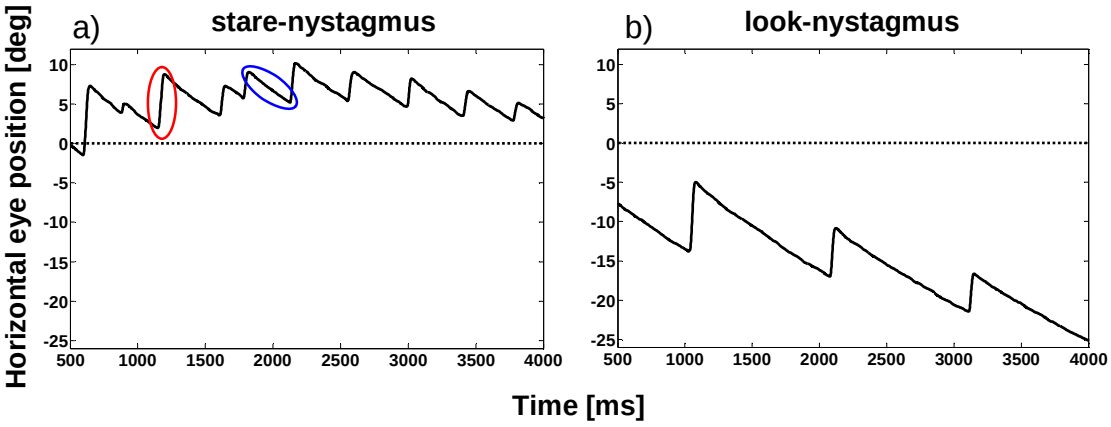

Figure 3: Eye-position traces for different types of OKN. The dotted horizontal line shows the center of the screen. The red ellipse marks a fast-phase while the blue one marks a slow-phase.

weren't any compensatory eye movements. Under natural conditions, however, the movement of the head is compensated for by an eye movement in the opposite direction. The velocity of the eye movement is (almost) identical to the velocity of the head movement and therefore the image on the retina is stabilized. This movement defines the so called slow phase. When the eyes have moved in direction of the stimulus motion for a given time a fast eye-movement in the opposite direction, the so called fast-phase, can be observed. While the VOR is driven by input from the vestibular system, the OKN is driven by visual input. Therefore the two eye movements, OKN and VOR, can easily be studied in the laboratory. Classical studies on the vestibular system have been performed with subjects being turned on a rotating chair. If no visual stimuli are available the velocity of the subjects' slow-phases will decline after some time. This can be explained by the hydrodynamics of the vestibular system. If the subject is rotated with visual input being available no such drop of slow-phase eye-velocity is observed. In this latter case the OKN compensates for the decline of the VOR (Ilg, 1997b). OKN is triggered best by large coherent motion (Cheng and Outerbridge, 1975). Therefore optokinetic eye movements can easily be elicited in the laboratory using large moving patterns of stripes or random dots (RDP). Because the spatial frequency (SF) of stripe-patterns influences the pattern of fast-phases RDPs with their broad spectrum of SFs are preferable (Cheng and Outerbridge, 1974).

Subtypes of OKN

Depending on the instruction given to the subjects two kinds of OKN can be distinguished (Ter Braak, 1936). If the subject is instructed to look at the stimulus attentively without performing any voluntary eye movements the so called stare-

nystagmus can be observed (Figure 3a). It is characterized by a periodic pattern of fast-phases with relatively small amplitudes. During stare-nystagmus the average eye position is shifted opposite to the motion direction i.e. during rightward motion it is shifted to the left and vice versa ('Schlagfeldverlagerung' or 'shift of the beating field'). If the subject is instructed to actively select an element of the stimulus and pursue it for some time and then choose a new element etc., the so called look-nystagmus can be observed (Figure 3b). Typically fast-phases during look-nystagmus are rather large and show no periodicity. During look-nystagmus the mean eye position is shifted in direction of the stimulus motion. It has been suggested that look-nystagmus is closely linked to smooth pursuit or might even be an alternation of voluntary saccades and SPEM (Ilg, 1997b).
In primates stare-nystagmus is composed of two components, an early and a late component (Cohen et al., 1977). When during prolonged OKN the stimulus velocity is increased suddenly the slow-phase eye velocity first increases rapidly and than more slowly until a new steady state is reached. Since the early component can be elicited with small stimuli and depends on the existence of a fovea it is supposed to reflect smooth pursuit. The late component is supposed to reflect optokinetic afternystagmus (see below) (Ilg, 1997b).

Neural substrate of OKN

Since the neural substrate underlying the execution of the OKN differs quite strongly across species I will focus on the optokinetic system of the nonhuman primate (Figure 4; for review see: (Ilg, 1997b)). The main control regions for the OKN, namely the nucleus of the optic tract (NOT) and the accessory optic system (AOS), are located in the pretectum. In the monkey the AOS is composed of the dorsal and lateral terminal nucleus (DTN, LTN; the medial terminal nucleus (MTN) is missing). Neurons in the LTN are selectively activated during upward motion, while neurons in the NOT and the DTN respond during horizontal OKN towards the recording site (ipsiversive) (Ilg, 1997b). Since the properties of NOT- and DTN-neurons are very similar and both structures are hard to differentiate they are often treated as one nucleus and called NOT/DTN. Two major classes of neurons can be distinguished in the NOT/DTN: background velocity cells and target velocity cells (Ilg and Hoffmann, 1996). Target velocity cells are only active when the animal is performing OKN or SPEM while background velocity cells are also active when the monkey fixates a stationary target while the background is moving. As stated above the optokinetic reflex is driven by visual input. While in most species the

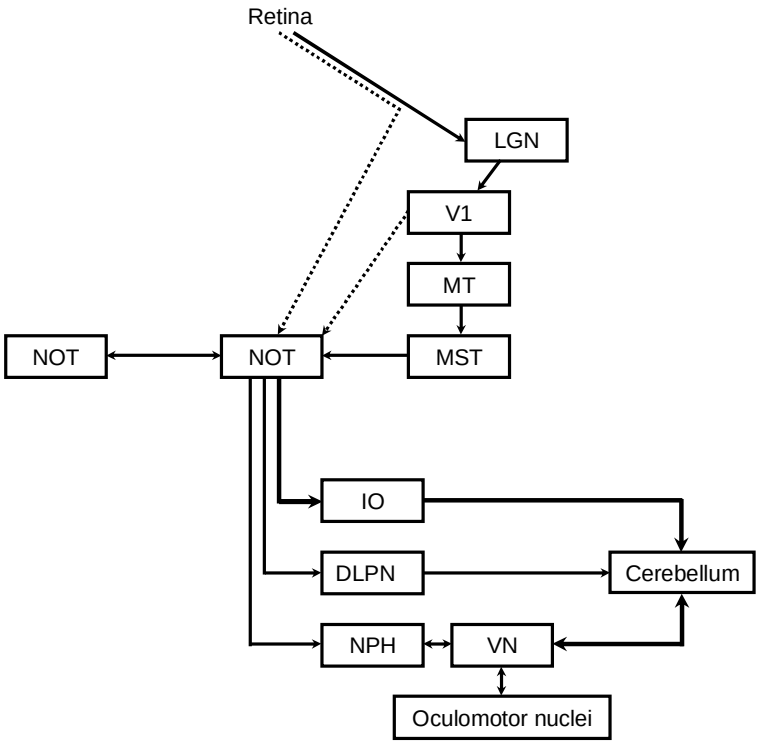

Figure 4: Neural substrate responsible for the execution of OKN. The bold lines represent the cortico-pretecto-olivio-cerebellar pathway. (adapted from Ilg, 1997b)

input to the NOT/DTN is primarily of retinal origin in primates the NOT/DTN receives mainly input from cortical motion selective areas (Hoffmann, 1989). Here, visual motion is processed in the so-called dorsal pathway (Ungerleider, 1982). Motion selective cells in the primary visual cortex (V1) project to the middle temporal area (MT). Area MT is a key-area for visual motion perception with nearly all cells being selective for visual motion. Most of the cells are tuned for the direction and/or the velocity of a stimulus (Albright, 1984). Recordings in area MT showed that neurons are active during the slow phase of the OKN (Ilg, 1997a). MT-neurons project, among other areas, to the medial superior temporal area (MST). Many neurons in area MST respond to stimuli typically induced by self-motion (Bremmer et al., 2000). Neurons with ipsiversive preferred direction project to the NOT/DTN (Hoffmann et al., 2009). Neurons in the NOT/DTN project to nearly all visuomotor regions (Buttner-Ennever and Horn, 1997). Three of them are of special interest for the execution of OKN and OKAN: the dorsolateral pontine nuclei (DLPN), the dorsal cap of the inferior olive (IO), and the nucleus prepositus hypoglossi (NPH). Both, the IO and the DLPN, are connected to the oculomotor nuclei via the cerebellum and the vestibular nuclei (VN) (Ilg, 1997b). The VN comprise neurons showing activity related to different classes of eye movements including OKN (Henn et al., 1974;Miles, 1974;Waespe and Henn, 1977a). The projection from the NOT/DTN to the DLPN consists mainly of target velocity cells. After lesions of the DLPN deficits can be observed for SPEM as well as for the early component of

OKN. The projections to the IO comprise both axons of target- and background velocity cells. Lesions of the IO heavily influence the execution of OKN (Ilg, 1997b). The connections from the NOT/DTN to the NPH consist mainly of background velocity cells. The NPH is connected to the VN via reciprocal connections. This last path is supposed to charge the velocity storage mechanism located in the VN (see below).

Until a few years ago the neural substrate for the programming of different classes of eye movements was thought to be largely separated. More recent studies, however, supported the view that in many cortical and subcortical areas more than one class of eye movement is encoded (Krauzlis, 2004). This is especially true for the networks underlying the execution of OKN and SPEM in primates. In addition the network for the execution of OKN overlaps to some extent with the one encoding saccades.

Optokinetic afternystagmus (OKAN)

When subjects are sitting in complete darkness after performing OKN for several seconds the eye movement pattern of alternating slow and fast-phases continues for some time (Figure 5). This is the so called optokinetic afternystagmus (OKAN). It is characterized by an initial drop of slow-phase eye velocity which is followed by a slower exponential decline (Cohen et al., 1977;Jell et al., 1984). During the execution of OKAN

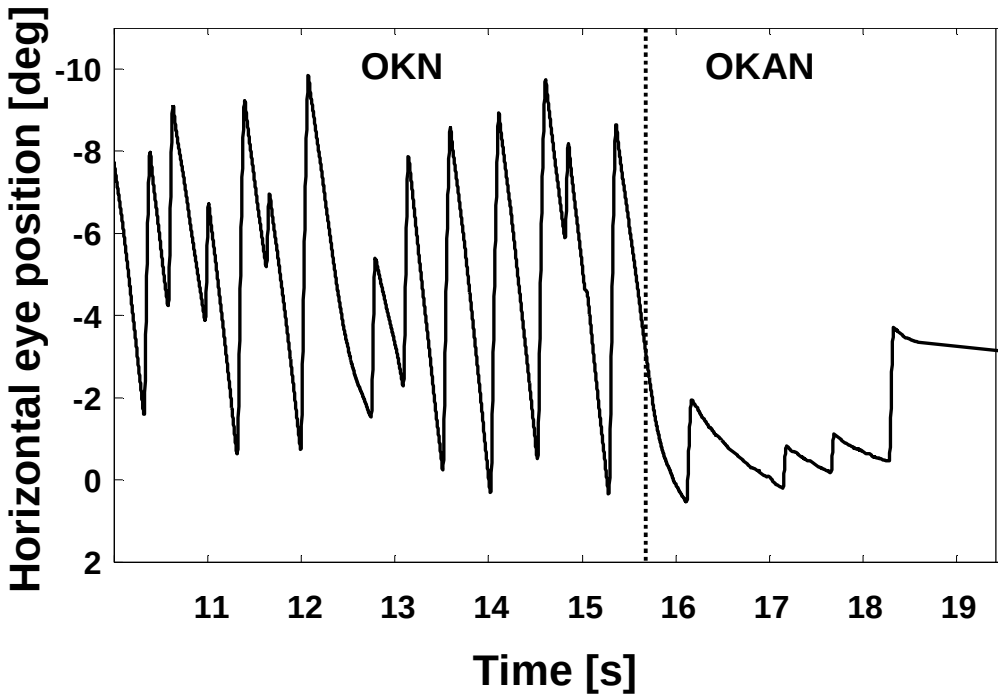

Figure 5: Example for the eye-position trace during the induction of OKAN. The dotted line marks the point in time when the stimulus was extinguished.

at least two phases can be distinguished. Initially the direction of the OKAN slow-phases is the same as during OKN, this is the first phase (OKAN I). During the second phase (OKAN II) the direction of the slow-phases is inverted (Koerner and Schiller, 1972). In the absence of visual references OKAN can not be suppressed voluntarily. Fixation of a stationary target for more than about three seconds abolishes OKAN while after briefer fixation periods OKAN resumes (Cohen et al., 1977).

Neural substrate of OKAN

While during the execution of OKN neurons in many cortical and subcortical areas have been shown to be active (see above) only a very limited number of areas seem to be involved in the execution of OKAN. Ilg et al. (1997a) recording in area MT of the monkey reported OKN but no OKAN related activity. To my best knowledge this is the only study searching for OKAN related activity in cortical areas. However it has been demonstrated that monkeys can perform OKAN even after massive cortical lesions (Tusa et al., 1986).

Waespe and Henn (1977a), recording in the VN of the rhesus monkey, found that all neurons responding to vestibular stimulation were also activated during OKN with neural activity and slow phase eye velocity being correlated. In a second study the authors demonstrated that activity of VN neurons and OKAN decay in parallel (Waespe and Henn, 1977b). According to these results the VN are assumed to be the neural substrate of the OKAN. Boyle et al. (1985) demonstrated that neuronal activity in the VN reflects the late component but not the early component of OKN. This is very likely the reason why OKAN is observed after prolonged OKN only.

Other subcortical areas involved in the generation of OKN like the NOT are not activated during OKAN (Ilg and Hoffmann, 1996;Mustari and Fuchs, 1990).

The main-sequence

The term ‘main-sequence’ was originally defined in astronomy where it is used to classify stars according to the strict dependency of stellar color as a function of actual brightness. In the Neurosciences it is used to describe the relationship between duration and peak-velocity of fast eye movements and their amplitude. The term was introduced by Bahill and Collegues (1975) for though the dependency has been described earlier. Both saccade duration and peak velocity increase as saccade amplitude increases. Several

types of functions have been proposed for regression analysis of main-sequence data. Linear regressions are only useful in a limited range of saccade amplitudes (> 4-5° amplitude for the duration vs. amplitude relationship and < 15-20° for the peak-velocity vs. amplitude relationship. Other models like exponential-, power- or square-root functions give better results (Lebedev et al., 1996). All known types of saccades, e.g. visually guided saccades, memory-guided saccades, antisaccades, etc. have been shown to adhere to a main-sequence, though main-sequences for different types of saccades can vary strongly (Becker and Fuchs, 1969;Smit et al., 1987;Van Gelder et al., 1997). Main-sequence relationships have been described for other types of fast eye movements and in other species than humans. As an example fast phases of the VOR and OKN have been reported to adhere to a main-sequence (Mackensen G. and Schumacher J., 1960;Ron et al., 1972;Sharpe et al., 1975). Though the main-sequence relationship is rather strict it can be influenced by a number of internal and external factors like medication, fatigue, attention or stimulus characteristics (Leigh and Zee, 2006).

The lateral intraparietal area

The execution of saccades is controlled by a large network comprising several cortical and subcortical structures (Munoz, 2002). One of these structures is the lateral intraparietal area (LIP). Area LIP is located in the lateral bank of the intraparietal sulcus (Andersen et al., 1985;Blatt et al., 1990). The activity of the majority of neurons in area LIP is closely related to the execution of saccades (Colby et al., 1996). Since the activity precedes the onset of the saccade in many neurons (Barash et al., 1991) and saccades can be elicited by electrical stimulation of neurons in area LIP (Thier and Andersen, 1998) activity of LIP neurons is believed to be involved in the programming of saccades. Neurons in area LIP have been reported to code the direction and amplitude of saccades (Platt and Glimcher, 1998). Aside from saccades area LIP is also involved in the allocation of spatial attention (Colby et al., 1996) which is closely connected to the execution of saccades. Furthermore, neurons in area LIP are also involved in a variety of other tasks. For example most of them respond to visual stimuli (Barash et al., 1991) and a subpopulation is active during smooth pursuit eye movements (Bremmer et al., 1997). Furthermore eye position has been reported to modulate the activity of neurons in area LIP (Andersen et al., 1990;Bremmer et al., 1997). Of special interest for this thesis are the connections of area LIP to the medial temporal area (MT). LIP receives input from

area MT which is one of the most prominent cortical areas for the analysis of visual motion (see above).

Aim and Scope of the Thesis

Experiment1: Localization of visual targets during optokinetic eye movements

It has been demonstrated in numerous psychophysical studies that briefly flashed targets are mislocalized during voluntary eye movements, namely saccades and smooth pursuit eye movements. The goal of the first study was to investigate localization during the execution of reflexive eye movements, namely optokinetic nystagmus. The observed error patterns were compared to those reported during voluntary eye movements. The analysis of the error occurring during the slow phase of the OKN focused on the effect of the spatial position of the target on the perceptual error. Furthermore I aimed at disentangling the effects of the slow phase eye movement and the background motion on the observed error. The errors occurring in the vicinity of fast-phases were analyzed with regard to both the position of the target and the time of target presentation relative to the onset of the eye movement. Of special interest was the interaction of errors induced by slow- and fast phase.

Experiment 2: Expansion of Visual Space During Optokinetic Afternystagmus (OKAN)

During the execution of OKN a moving, textured background is permanently visible. In the first study I showed that both the slow-phase eye movement and the moving stimulus induce localization errors. Therefore, the aim of the second study was to investigate the error induced by reflexive eye movements in the complete absence of visual stimuli. Therefore localization error during the execution of OKAN were recorded and compared with errors during OKN recorded in the same subjects. As in the first study I investigated the spatio-temporal dependencies of the observed errors.

Experiment 3: The main sequence of human Optokinetic Afternystagmus (OKAN)

In the two preceding studies the localization errors during different reflexive eye movements have been characterized and compared to each other and to those occurring during voluntary eye movements. It has been shown that the magnitude of the perisaccadic shift depends on the dynamics of the eye movement. Furthermore the dynamics of different types of saccades differ markedly. Given that the localization error induced by fast-phases of OKN and OKAN also depends on the dynamics of the eye movement the comparison made in the first two studies was only valid if the eye

movement dynamics had been sufficiently similar. Accordingly the goal of the study was to characterize the dynamics of OKAN fast-phases for the first time and compare it to the dynamics of OKN fast-phases and saccades.

Experiment 4: Influence of cortical control on the main sequence of human optokinetic nystagmus (OKN)

The comparison of the main-sequences of fast-phases of OKN and saccades revealed large interindividual differences. This reflects the diverse results reported in the literature. Depending on their attitude subjects can perform either the highly reflexive stare-nystagmus or the rather voluntarily controlled look-nystagmus under identical stimulus conditions. In Experiment 3 I had shown that the dynamics of reflexive fast-phases of OKAN and voluntary saccades differ. If look-nystagmus is actually a combination of voluntarily controlled saccades and smooth pursuit eye movements the fast-phases of look- and stare-nystagmus should differ with respect to their main-sequence. Therefore I compared the fast-phases of look- and stare-nystagmus induced with identical visual stimulation.

Experiment 5: Encoding of saccades towards stationary and moving targets within area LIP

During self-motion most saccades are directed towards moving targets. Although computationally demanding, in primates, these saccades have been shown to be very precise. The neural network underlying the execution of saccades has been studied in the awake, behaving monkey mainly utilizing saccades to stationary targets. Therefore very little is known about the encoding of saccades towards moving targets. Neurons in area LIP encode the direction and size of saccades. Furthermore, area LIP receives afferences from areas MT and MST, i.e. two key-areas for the perception of visual motion. Finally, neurons in area LIP project to the superior colliculus, i,e. the midbrain center critically involved in the generation of saccadic eye movements. Neurons in the SC have been shown to fire differently for amplitude-matched saccades to stationary and moving targets. The functional role of area LIP in this context, however, is unknown. Therefore in this study I performed extracellular recordings in area LIP of the rhesus monkey, while the animal executed saccades to stationary and moving targets.

Localization of Visual Targets During Optokinetic Eye Movements

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Localization of visual targets during optokinetic eye movements

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Abstract

We investigated localization of brief visual targets during reflexive eye movements (optokinetic nystagmus). Subjects mislocalized these targets in the direction of the slow eye movement. This error decreased shortly before a saccade and temporarily increased afterwards. The pattern of mislocalization differs markedly from mislocalization during voluntary eye movements in the presence of visual references, but (spatially) resembles mislocalization during voluntary eye movements in darkness. Because neither reflexive eye movements nor voluntary eye movements in darkness have explicit (visual) goals, these data support the view that visual goals support perceptual stability as an important link between pre- and post-saccadic scenes.

Keywords: Localization; Eye movement; OKN; Saccade; Smooth pursuit

1. Introduction

Eye movements challenge visual processing. While the image of external objects moves across the retina during such movements, we perceive the outer world as being stable. Yet, it appears, that this perceptual stability is not complete. Several studies have shown that spatial processing in the temporal vicinity of voluntary eye movements is not veridical. During smooth pursuit eye movements the perceived location of briefly flashed visual stimuli is shifted in the direction of the pursuit (Mitrani, Dimitrov, Yakimoff, & Mateeff, 1979; Mateeff, Yakimoff, & Dimitrov, 1981; Rotman, Brenner, & Smeets, 2004, 2005; van Beers, Wolpert, & Haggard, 2001). This mislocalization is observed mainly in one visual hemifield, i.e. the one the fovea is heading for (van Beers et al., 2001). In addition, the perceptual error increases with increasing retinal eccentricity.

During visually guided saccades different mislocalization patterns can be observed depending on the exact experimental conditions. In total darkness a temporally biphasic perisaccadic mislocalization pattern has been described (Cai, Pouget, Schlag-Rey, & Schlag, 1997; Honda, 1989). Until the start of the eye movement all positions are perceptually shifted in the direction of the saccade. The maximum displacement is typically reached at the onset of the saccade. This shift is followed by a displacement against saccade direction. Approximately 100 ms after the end of the saccade perception is again veridical. This spatio-temporal pattern is completely changed when saccades are performed in the presence of visual references. In such case all perceived locations are shifted towards the endpoint of the saccade, leading to a perceptual compression of space (Lappe, Awater, & Krekelberg, 2000; Ross, Morrone, & Burr, 1997). The strength of this mislocalization is related to the length of the saccade: the longer the saccade vector the larger the localization error (Kaiser & Lappe, 2004; Morrone, Ross, & Burr, 1997).

Both pursuit related and perisaccadic mislocalization have typically been interpreted as a mismatch between the visual system's representation of the eye position and the actual position of the eye (Schlag & Schlag-Rey, 2002, saccades: Dassonville, Schlag, & Schlag-Rey, 1992; Pola, 2004; pursuit: Brenner, Smeets, & van den Berg, 2001; van Beers et al., 2001). In addition for both types of eye movements

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visual mechanisms have been shown to influence localization (Awater & Lappe, 2006; Lappe et al., 2000; Rotman et al., 2004). In other words, these studies show the imperfections of the mechanisms of perceptual stability (Bremmer & Krekelberg, 2003).

Both visually guided saccades and smooth pursuit are voluntary eye movements, which are controlled to a large extent in a number of cortical areas as shown by functional imaging studies in humans (saccades: Corbetta et al., 1998; Kimmig et al., 2001; Konen, Kleiser, Wittsack, Bremmer, & Seitz, 2004, pursuit: Konen, Kleiser, Seitz, & Bremmer, 2005; Nagel et al., 2006; Petit & Haxby, 1999) and single cell recordings in non-human primates (saccades: Barash, Bracewell, Fogassi, Gnadt, & Andersen, 1991a, 1991b; Schall, 1991; pursuit: Bremmer, Ilg, Thiele, Distler, & Hoffmann, 1997; Ilg & Thier, 2003; Newsome, Wurtz, & Komatsu, 1988. For review see: Ilg, 1997; Thier & Ilg, 2005). Reflexive eye movements such as the optokinetic nystagmus (OKN), on the other hand, are phylogenetically much older (Carpenter, 1988). The OKN mainly subserves the stabilization of the whole image on the retina e.g. during head movements. The OKN is an alternation of slow-phases in the direction of the stimulus motion and fast-phases against the direction of stimulus motion. While the fast phases are similar to saccades the slow-phases are considered to be different from smooth pursuit during late OKN while during the early phase of the OKN it is difficult to differentiate between the ocular following reflex, smooth pursuit and OKN (Leigh & Zee, 2006). One notable difference, showing that quite different motor control mechanisms are involved in the control of smooth pursuit and OKN, is the observation of an after-nystagmus. When the full-field stimulus that induces an OKN is turned off, leaving the subject in darkness, OKN-like eye movements with decreasing amplitude are observed. Such an after-effect, called an optokinetic after-nystagmus, is not observed for smooth pursuit eye movements. At the subcortical level, the OKN is mainly controlled by the Nucleus of the Optic Tract (NOT-DTN) (Ilg & Hoffmann, 1991, 1996).

Clearly, the issues that the visual system has to deal with during OKN are quite similar to those during voluntary eye movements. To generate a stable spatial percept, the eye-movements have to be accounted for in some fashion. Given that the motor control of the OKN is quite different from that of the voluntary eye movements (see Section 4), we reasoned that further insight into the mechanisms of perceptual stability could be gained by investigating localization during these reflexive eye movements.

Mimicking the paradigms used to study localization during voluntary eye movements, we asked human subjects to localize briefly flashed visual targets during optokinetic eye movements. We found that, just as during smooth pursuit, flashes are mislocalized in the direction of the eye movement during the slow-phase of the OKN. Contrary to the reported findings during pursuit, mislocalization errors during OKN slow-phase did not depend on the retinal position. During the fast-phases the mislocalization was modulated in a manner that was similar to the mislocalization during voluntary saccades in darkness: the spatial characteristics were identical, while the temporal properties of the two effects were different. In accordance with findings from Tozzi, Morrone, and Burr (2007, 2005) the dynamic error during OKN fast-phase was independent of target position.

These findings are consistent with the view that localization during fast and slow reflexive eye movements relies on similar mechanisms that operate in darkness during voluntary eye movements. Additional mechanisms that rely on the use of visual references seem to be less important during OKN. Preliminary results have been reported in abstract form (Kaminiarz, Rohe, Krekelberg, & Bremmer, 2006).

2. Methods

2.1. Subjects

Nine human subjects participated in the experiments; all had normal or corrected-to-normal visual acuity, and were experienced psychophysical observers. Seven of the subjects were naïve as to the purpose of the study. All subjects gave informed written consent and all procedures used in the present study conformed to the Declaration of Helsinki.

2.2. Stimulus presentation and eye movement recordings

Computer generated stimuli (see below) were presented on a ViewSonic P225f monitor with a spatial resolution of 1152×864 pixels and a frame rate of 100 Hz. The screen was viewed binocularly at a viewing distance of 57 cm. A fixed head position was maintained by a chin and forehead rest. In order to avoid visual reference cues the experiments were carried out in a completely dark room and the monitor casing was occluded with a black cover with a circular aperture 25° in diameter. Eye position was sampled at 500 Hz using an infrared eye tracker (EyeLink 2, SR Research Inc.). The data were stored on hard disk for offline analysis.

2.3. Visual stimuli

The background of the monitor was a homogeneous gray. On top of this background, a visual localization target (white circle, 0.5° in diameter, luminance: 74.2 cd/m^2) was flashed for 10 ms at one of five possible locations in the upper half of the visual field: $[x, y] = [\pm 5°, 0°]$, $[\pm 3.5°, 3.5°]$, $[0, 5°]$ (See Fig. 1c).

To induce optokinetic nystagmus, a random dot pattern (RDP) consisting of black dots (size: 0.17°, luminance: <0.1 cd/m^2, average number of visible dots: 205) moved horizontally in pseudorandomized order either to the left or to the right. All elements of the RDP moved coherently with a speed of 10 deg/s. A new RDP was generated for each trial.

The fixation point consisted of a white (0.35° in diameter) and black circle (0.11°) at the center of the display.

A randomized ruler was used to obtain response-bias free estimates of the perceived position of the flash. This ruler was displayed at the end of a trial only and consisted of a white line with a tick mark at every 0.5 degrees. The tick marks were always in the same position, but they were re-labeled with new random labels (between 10 and 99) every trial. This re-labeling prevented the subjects from acquiring stereotypical response strategies, which could have been induced by the limited number of target positions. Subjects entered the perceived position of the flash (the label of the nearest tick mark) on the keyboard. Offline, these labels were converted back to the appropriate spatial location.

2.4. Free viewing trials

In the 'free viewing' condition, subjects freely viewed a homogeneous gray monitor for 4000 ms. The visual target was flashed after 3500 ms.

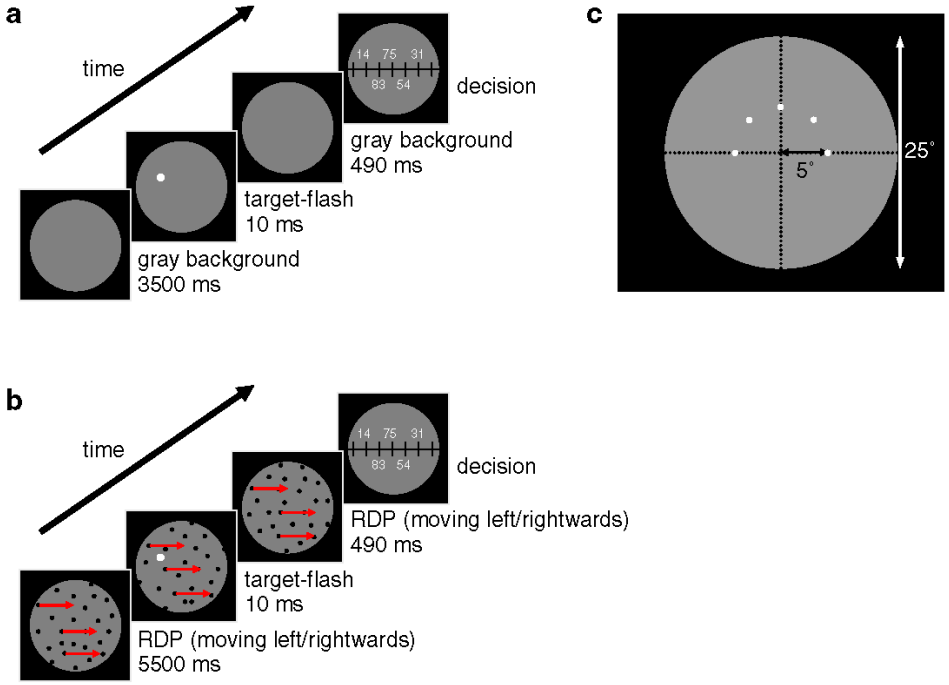

Fig. 1. Schematic illustration of the temporal sequence of a single baseline (a) or OKN (b) trial of experiment 1. During baseline measurements subjects freely viewed a homogeneous gray monitor for 4000 ms. After 3500 ms a target was flashed for 10 ms (1 frame) at one of 5 possible locations. A ruler appeared 490 ms later and subjects had to indicate which number on the ruler was closest to the perceived position of the flashed target. During each session the ruler was oriented either horizontally or vertically. During eye movements trials OKN was triggered using an RDP moving either left- or rightwards for 6000 ms. After 5500 ms the target was flashed for 10 ms. After the end of the movement the ruler appeared and subjects had to indicate the perceived position of the target. (c) Spatial distribution of the 5 targets for all experiments.

2.5. OKN trials

In the OKN condition, the moving RDP was visible for 6000 ms. The localization target was flashed after 5500 ms. Subjects were instructed to attentively watch the display without actively pursuing any elements of the RDP.

2.6. Fixation/background motion trials

During these trials subjects fixated the central fixation point on the gray background (pure fixation), or while the RDP was presented (fixation with background motion). The timing of these trials matched that of the "free viewing" or OKN trials, respectively.

2.7. Procedure

Each experimental session consisted of 100 trials. At the end of each trial, a ruler (see above) was displayed, which could be oriented either horizontally or vertically on the screen. Subjects indicated the perceived location of the flash with respect to this ruler. Ruler orientation was kept constant within sessions.

Each subject performed 4 free viewing sessions, 4 fixation sessions without background motion, and 4 fixation sessions with background motion. Half of these sessions used a vertical ruler, the other half a horizontal ruler. Each subject also performed 6 OKN sessions (4 with horizontal and two with vertical ruler orientation). Fig. 1 shows the temporal evolution of a single trial for free viewing (a) and the OKN-condition (b).

2.8. Data analysis

For the analysis of localization errors during the slow-phase only trials in which no saccade was initiated in a time-window ranging from 100 ms before to 100ms after the onset of the flash were considered. Localization errors were computed independently for the 5 flash locations. Trial-averaged errors in horizontal and vertical directions were combined to a resultant 2-D error vector. In a first step, we determined the errors in the free viewing condition. Then we computed the errors in the OKN condition. Net errors were computed by subtracting the error in the free viewing condition from the error during OKN.

We were also interested in the dynamics of the mislocalization around the time of a fast-phase. To this end, we computed a moving average of the perceived flash location as a function of time relative to the onset of the temporally closest fast-phase from 200 ms before onset of the fast-phase until 200 ms thereafter. These mislocalization errors were smoothed with a Gaussian shaped weighing function ($\sigma = 8$ ms). To verify that the errors were due to the subjects' eye movements and not to the background motion, we tested localization performance during fixation. Again, we determined the localization errors during fixation of a homogenous background and the localization error during fixation and simultaneous background motion. The baseline-corrected error was computed by subtracting the error in the fixation condition from the error during background motion. If not stated otherwise data are presented as means ± SD.

3. Results

We present our results in two parts. First, we demonstrate that during the slow-phase the eye movements of the OKN bias the perception of position in the direction of the eye-movement. Second, we analyze the time course of mislocalization during OKN and show that the fast-phase eye movements modulate this mislocalization in a manner that is reminiscent of the mislocalization during voluntary saccades in darkness.

3.1. Experiment 1

To keep experimental conditions as comparable as possible in this experiment we chose to use localization during free viewing instead of e.g. localization during fixation as baseline condition. The introduction of a fixation point (and the task to precisely fixate it) would probably cause differences in attentional load between the conditions. Furthermore a fixation point could serve as a reference and thereby influence localization.

3.2. Eye movements during free viewing and OKN

Since free viewing is an unconventional condition we will briefly describe eye movements under this condition and compare them with those measured during OKN. Saccade frequency averaged across subjects was 1.73 ± 0.35 Hz during free viewing and increased to 2.79 ± 0.41 Hz during OKN. Total (2-D) saccade amplitude was quite similar under both conditions (2.46 ± 0.99 deg during free viewing and 3.12 ± 0.70 deg during OKN, respectively). While horizontal and vertical saccade components were of comparable magnitude during free viewing (horizontal: 1.80 ± 0.59 deg, vertical: 1.62 ± 0.91 deg; $p > 0.5$, Mann–Whitney Rank Sum Test) they differed significantly during OKN (horizontal: 2.97 ± 0.73 deg, vertical: 0.88 ± 0.27 deg; $p < 0.001$, Mann–Whitney Rank Sum Test). During free viewing the average eye position (calculated from 500 ms after trial-initiation until flash presentation) was slightly above (0.29 ± 0.27 deg) and to the right (0.16 ± 0.13 deg) of the center of the screen (Figs. 2a and d; 3a). During OKN mean eye position differed significantly ($p < 0.001$, Mann–Whitney Rank Sum Test), for leftward and rightward background motion ("shift of the beating-field"). During leftward background motion the average eye position was shifted 3.46 ± 1.24 deg to the right while it was shifted 3.28 ± 1.50 deg to the left during rightward background motion. Vertical eye position was similar under both conditions ($0.12. \pm 0.30$ deg vs. 0.03 ± 0.34 deg for leftward and rightward background motion, respectively).

3.3. Experiment 1a: localization during free viewing

Fig. 2 shows the results of the first experiment for two subjects. The upper graphs (a, d) show localization errors during free viewing. On average, each line represents data from about 70 trials for subject AK and 75 trials for subject AR. Localization was not veridical but biased towards a location below the center of the screen. The same pattern of errors was observed averaged across subjects (Fig. 3a). On average, each data line is based on about 580 trials.

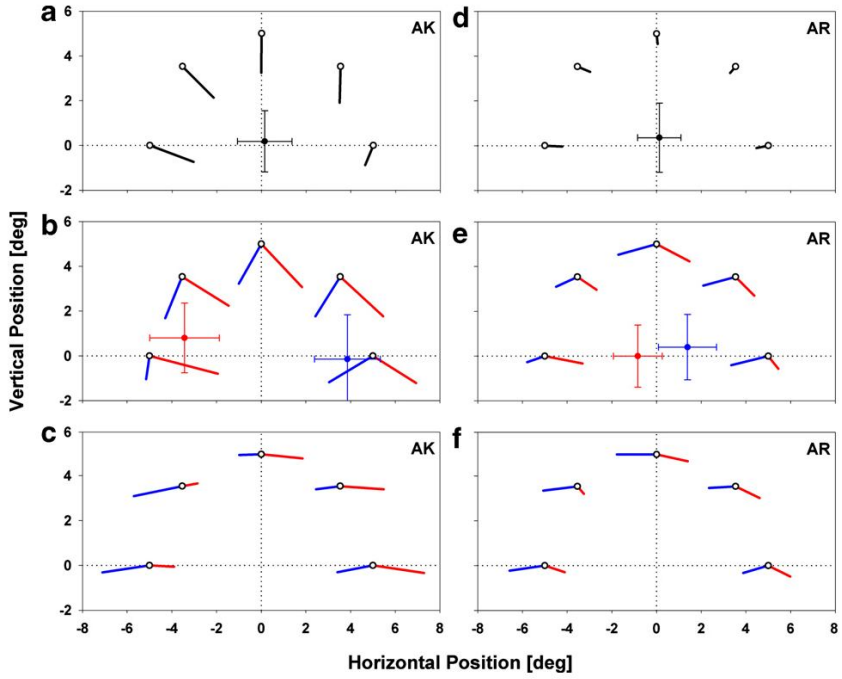

Fig. 2. Localization errors during eye movements. The graphs show the mislocalization during free viewing (a and d) and stimulus induced eye movements without (b and e) and with (c and f) baseline correction for subjects AK and AR. Black circles indicate the flash positions. Lines emanating from these circles point towards the perceived flash position (located at the end of each line). Black lines show localization errors without background motion (free viewing), blue lines show the errors for leftward and red lines for rightward background motion (OKN condition). Crosses mark the average eye position (black: free viewing, blue: leftward background motion and red: rightward background motion). The dashed lines show the horizontal and vertical meridian, respectively, which cross each other at the center of the aperture.

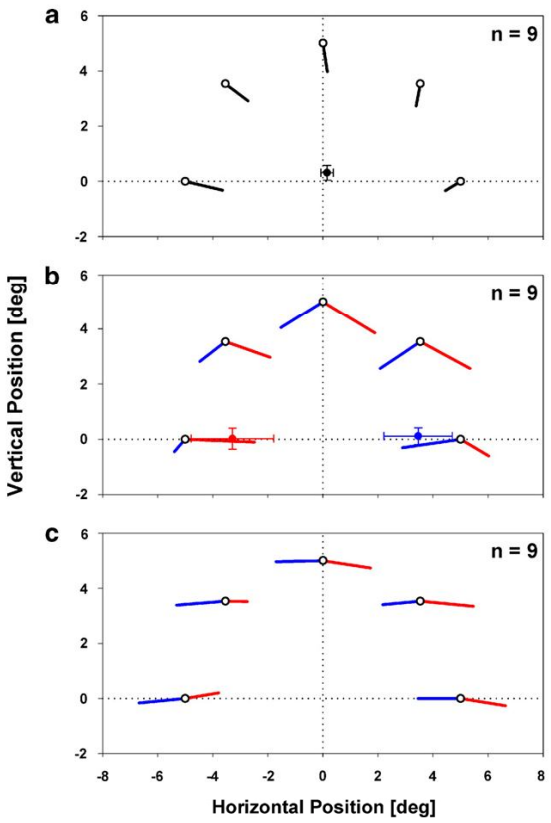

Fig. 3. Localization errors during eye movements. The graphs show the mislocalization during free viewing (a) and eye movement condition without (b) and with (c) baseline correction for the group of $n = 9$ subjects. Other conventions as in Fig. 2.

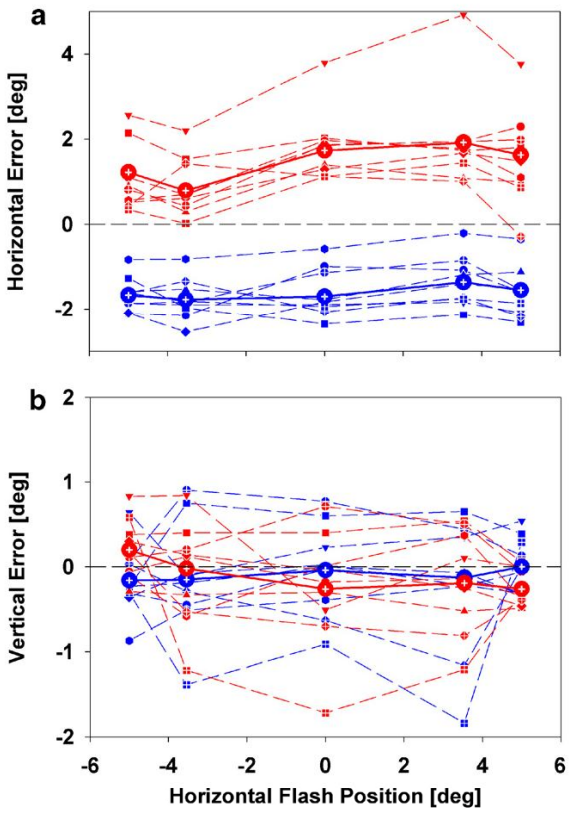

Fig. 4. Corrected horizontal (a) and vertical (b) localization errors as a function of flash position on the screen. Positive errors indicate rightward (upward) mislocalization, negative errors leftward (downward) mislocalization. Dashed curves show single subject data, solid curves show population data. Curve color indicates background motion direction (blue: leftward, red: rightward).

3.4. Experiment 1b: localization during OKN slow-phase

During the slow-phase of the OKN (Fig. 2b and e) we observed a mislocalization in direction of the eye movement. On average, each line represents data from about 24 trials for subject AK and 28 trials for subject AR. After correction for the bias obtained in the baseline condition (i.e. by subtracting the localization errors during free viewing measurements (Fig. 2a and d) from those during OKN slow-phase (Fig. 2b and e)), the remaining shift was clearly in the direction of the slow-phase eye movement (c and f). This perceptual effect was also observed when data were averaged across subjects (Fig. 3b and c). In this case each data line in Fig. 3b is based on about 200 trials.

To investigate the influence of the position of the flash on the localization, we analyzed horizontal (Fig. 4a) and vertical (Fig. 4b) error components independently of each other. Localization errors during OKN slow-phase are plotted as a function of horizontal flash position. The effect of motion direction on the horizontal localization error was significant for all flash positions for each individual subject as well as averaged across subjects (in all cases: $p < 0.001$, Mann–Whitney Rank Sum Test). The (horizontal) OKN, however, had no significant effect on vertical localization errors ($p > 0.9$, Mann–Whitney Rank Sum Test).

Moreover, statistical analysis did not reveal any significant influence of flash position, on vertical localization error ($p > 0.1$ for rightward and $p > 0.8$ for leftward motion, ANOVA on Ranks). While there was no significant influence of flash-position on the horizontal localization error for leftward motion ($p > 0.6$, ANOVA on Ranks) there was some influence for rightward motion ($p < 0.05$, ANOVA on Ranks). To test if the distance of the flash from the fovea could cause this effect we analyzed the relationship between horizontal localization error and the horizontal distance between flash and fovea at the time of the flash (Fig. 5). For leftward motion (a) we found a minimal but significant correlation between the horizontal localization error and the horizontal distance of the flash relative to the fovea ($R^2 = 0.0081$, $p < 0.02$). For rightward motion (b) the correlation was stronger though still small ($R^2 = 0.084$, $p < 0.001$). Linear regression revealed an increase of perceptual error with increasing retinal eccentricity (for fit-parameters see Fig. 5).

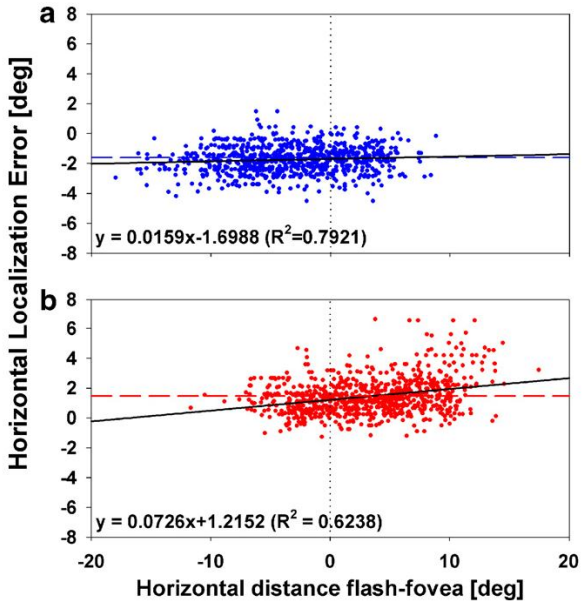

Fig. 5. Corrected horizontal localization errors as a function of stimulus position relative to the fovea for leftward (a) and rightward (b) background motion. Positive errors indicate rightward mislocalization. The dotted lines mark the position of the fovea at the time of the flash. Points to the right of the dotted line depict trials during which the target was presented to the right of the fovea. Solid lines represent linear regressions to the data while dashed horizontal lines show mean errors.

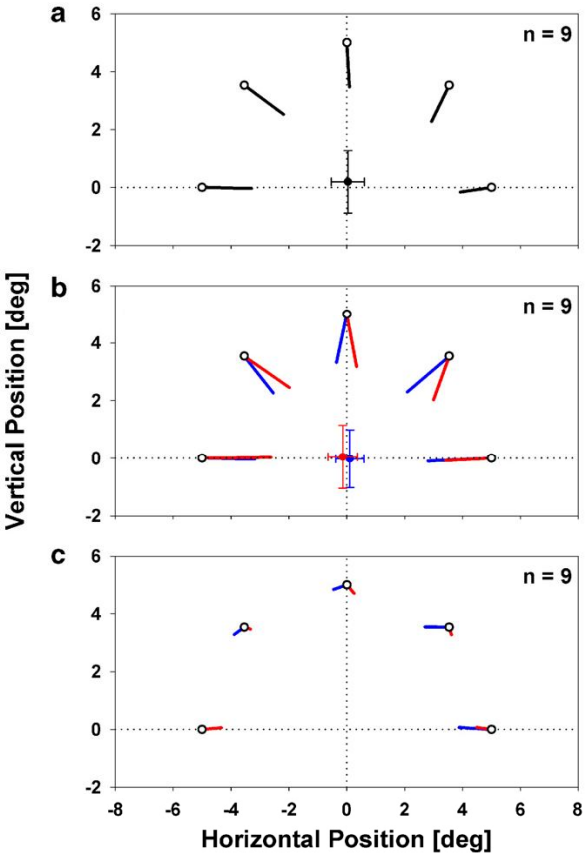

Fig. 6. Localization errors during fixation. The graphs show the mislocalization during baseline (a) and background motion condition without (b) and with (c) baseline correction for the group of $n = 9$ subjects. Other conventions as in Fig. 2.

3.5. Experiment 2

In principle, the mislocalization during the slow-phase eye movements shown in Figs. 2–4 could have been caused by either the eye movements, the presence of background motion, or both. To determine the relative contributions of these sources of perceptual error we introduced a fixation point in the center of the display to suppress optokinetic eye movements while keeping the remaining stimulus conditions identical.

3.6. Experiment 2a: localization during fixation

In the absence of background motion, localization was again biased towards the center of the screen (Fig. 6a), which in this experiment is the same as the fovea. However, mislocalization was significantly larger ($p < 0.001$, Wilcoxon Signed Rank Test) than under free viewing and more uniform across subjects. Lines represent data from about 660 trials each.

3.7. Experiment 2b: localization during background motion

During background motion (Fig. 6b and c) the horizontal component of the localization error was only 17% of the error we observed during OKN. This reduction was statistically significant ($p < 0.001$, Mann–Whitney Rank Sum Test). Nevertheless, it should be noted that the effect of background motion on localization (left vs. right) was significant ($p < 0.001$). In summary, background motion could account for approximately 17% of the mislocalization value during OKN. The remaining 83% of the mislocalization must therefore be attributed to the eye movements themselves. Lines in Fig. 6b represent on average data from about 310 trials each.

3.8. Dynamics of the localization error

OKN is an alternating pattern of slow-phases (in the direction of the stimulus motion) and fast-phases (opposite to the direction of stimulus motion). After showing that most of the localization error was due to the eye movements we were interested if mislocalization was different during the slow and fast-phases. We first calculated the corrected horizontal localization error as a function of time relative to the onset of the temporally closest fast-phase pooling across all flash positions and subjects. Then, we computed a moving average across these data-points independently for both motion directions (Fig. 7). Note that the overall curves are shifted away from zero. This reflects the findings shown in Figs. 2–4; the mean

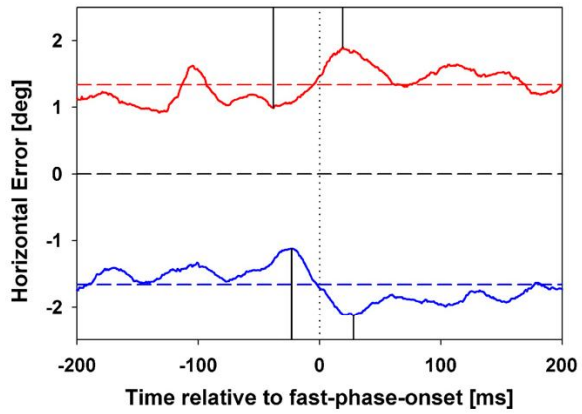

Fig. 7. Horizontal localization errors as a function of time relative to the onset of the temporally closest fast-phase. Positive errors indicate rightward mislocalization. Red and blue dashed horizontal lines represent mean localization errors. The dotted vertical line marks the onset of the fast-phase. Curves are moving averages obtained from the data with a 31 ms wide Gaussian weighted window. Red represents rightward background motion and blue leftward background motion. Solid vertical lines denote the timing of maxima and minima of the curves temporally closest to the onset of the fast-phase.

error points in the direction of the slow eye movement for both motion directions (positive values indicate errors directed to the right, negative values indicate errors to the left). Shortly before a saccade, however, the magnitude of the bias decreased. This modulation was in the direction of the fast-phase. After the fast-phase the bias in the direction of the slow eye movement temporarily increased.

The effect of the fast-phase eye movements can be described as a biphasic, additive mislocalization. This additive mislocalization lasted approximately 100ms, i.e. ±50 ms centered on fast-phase onset. Its effect was first in the direction of the fast-phase (peaking 25 ms before fast-phase onset), crossed zero at fast-phase onset, and then caused a mislocalization against the direction of the fast-phase (peaking 25 ms after onset). This modulatory pattern was the same for all flash positions, i.e. we found no evidence for a perceptual compression of space during the fast-phases.

4. Discussion

We showed that reflexive eye movements cause consistent perceptual mislocalization of briefly presented visual stimuli. These mislocalizations were similar to those observed during smooth pursuit and voluntary saccadic eye movements, but there were some notable differences. This section will discuss our findings in the light of the known properties of perceptual mislocalization during voluntary eye movements.

4.1. Mislocalization during smooth pursuit and OKN slow-phase

Visual targets presented during smooth pursuit eye movements are mislocalized in the direction of pursuit (Brenner et al., 2001; Mateeff et al., 1981; Mitrani et al., 1979). This is clearly very similar both in sign and in magnitude (Mateeff, Mitrani, & Stojanova, 1982; Mitrani & Dimitrov, 1982; Mitrani et al., 1979) to our findings. Differences become apparent when the spatial properties of the error patterns are compared. During smooth pursuit, targets flashed in the visual hemifield for which the fovea is headed are subject to strong mislocalization. Target locations in the other hemifield (i.e. where the fovea comes from) are mislocalized less markedly (Mitrani & Dimitrov, 1982; Rotman et al., 2004; van Beers et al., 2001). This was not the case during OKN. In our experiments we tested a horizontal range of target positions of 10°. Due to the spatial arrangement of the targets, not all target locations were projected into the same retinal hemifield. Depending on the length of the OKN-slow-phase and the previous shift of the beating-field, the target could be projected onto a parafoveal or more peripheral part of the retina, being either within the nasal or temporal half of the retina. Yet, different from the results during smooth pursuit, we observed substantial localization errors in both hemifields. In addition we found only minimal (leftward background motion) or minor (rightward background motion) dependencies of the localization errors on retinal eccentricity. The observed error could be interpreted as a slight overestimation of the retinal eccentricity which has also been observed during smooth pursuit (Rotman et al., 2004).

Mislocalization during pursuit is often explained by a temporal mismatch between the visual and the eye position signal (Brenner et al., 2001; Schlag & Schlag-Rey, 2002). The spatial dependence of the perceptual error during pursuit, however, suggests that this is either not the only error-component during pursuit (Mitrani & Dimitrov, 1982; Rotman et al., 2004) or that eye position signals and retinal signals are matched differently for different parts of the visual field (van Beers et al., 2001). Since misperception during OKN slow-phase was (predominantly) independent of target position in our experiments our results could be explained simply by the combination of an erroneous eye position signal with the visual signal.

The neural systems underlying OKN and smooth pursuit have been well studied. Early studies emphasized the differences between these systems (Carpenter, 1988) and as such one might expect a difference in localization during OKN and pursuit. More recent studies, however, have revealed a much tighter link. For instance, a lesion of the most important subcortical structure for the control of the OKN, the Nucleaus of the Optic Tract (NOT-DTN), also affected pursuit performance (Ilg, Bremmer, & Hoffmann, 1993). Moreover, imaging studies showed that the same cortical networks were active during smooth pursuit and OKN (Konen et al., 2005). In this context, our finding that localization during OKN does not depend on target position while localization during smooth pursuit does, is somewhat surprising. As we will discuss below in the context of fast-phase OKN, one important factor may be the absence of an explicit visual target during OKN.

4.2. Mislocalization during saccades and OKN fast-phase

A number of studies have shown mislocalization of briefly presented visual targets during visually guided saccades (for review see: Ross, Morrone, Goldberg, & Burr, 2001; Schlag & Schlag-Rey, 2002). The exact pattern of perisaccadic spatial distortion heavily depends on the exact environmental conditions. A unitary shift of perceived stimulus locations is observed in total darkness (Cai et al., 1997; Lappe et al., 2000). In the presence of visual references, however, the same spatial arrangement of target positions leads to a perceptual compression of space (Ross et al., 1997).

In our experiments the error pattern observed during fast-phase OKN was independent of position. Moreover, the modulation of perceived position by the fast-phases revealed a biphasic pattern that has also been observed for visually guided saccades in total darkness (Honda, 1989). Yet, the time course of the observed effects was different in the two cases: during visually guided saccades, the peak mislocalization in the direction of the saccade occurred at saccade onset, while for OKN fast phases the peak mislocalization was observed about 25 ms prior to fast-phase onset. Taken together the error pattern we observed is somewhat similar to the perisaccadic shift even though the stimulus conditions led us to expect a compression of space.

The prime candidate mechanism for perisaccadic shifts is a mismatch between the actual eye position and a sluggish or damped neural eye position signal (Dassonville et al., 1992; Honda, 1991). Given the spatial similarity in the perceptual effects, this mechanism could underlie mislocalization during fast-phase OKN as well. The different time courses of the effects during OKN and visually guided saccades might be indicative of different lengths of neural processing being necessary in the one or the other case. The question, however, arises why the mechanism that causes saccadic compression does not seem to be active during OKN. One explanation could be that – unlike during voluntary saccades – there is no clearly defined target position for the fast phase eye movement. In the two-step model of perisaccadic localization (Awater & Lappe, 2006) such uncertainty about the position of the eye abolishes the compression. At the neural level, perceptual stability and perisaccadic localization are far from understood, but a number of studies have shown that receptive field properties change before voluntary saccades in many visual areas (LIP: Duhamel, Colby, & Goldberg, 1992, V3–V1: Nakamura & Colby, 2002, V4: Tolias et al., 2001, MT/MST: Krekelberg, Kubischik, Hoffmann, & Bremmer, 2003). Recently, we have shown that such RF shifts in MT can also be observed during OKN (Hartmann, Bremmer, Albright, & Krekelberg, 2006).

Our data also show an enhanced perceptual error in the direction of the slow eye movement briefly after the fast-phase. This effect is reminiscent of the increased sensitivity to optokinetic stimulation briefly after a voluntary saccade (Kawano & Miles, 1986), which has recently been linked to an enhanced postsaccadic neural response in area MT (Ibbotson, Price, Crowder, Ono, & Mustari, 2006). It is, however, also possible that the large retinal slip that occurs during this period affects the mislocalization in a purely visual manner (as the background motion did in experiment 2b).

4.3. Mislocalization during fixation and free viewing

Localization during fixation was not veridical. Perceived flash positions during free viewing were shifted towards a point below the center of the display, while subjects on average looked at a point slightly above and to the right of the center of the display. This is in contrast to previous experiments which reported mislocalization towards the point of fixation (van der Heijden, van der Geest, de Leeuw, Krikke, & Musseler, 1999). During active fixation, perception was shifted towards the fixation point. Interestingly, the mislocalization was stronger than during free viewing. One explanation could be that the eye position of the subjects at the time of the flash was less consistent in the free viewing condition (x: 0.51 ± 1.44 deg, y: 0.7 ± 1.85 deg; averaged across all trials) than in the fixation condition (x: 0.07 ± 0.73 deg, y: 0.23 ± 1.30 deg). Although speculative, another explanation might be based on differential receptive field (RF) properties of cortical neurons during free viewing and active fixation. When a macaque monkey freely views a homogeneous gray monitor, LIP RFs have a smaller maximum response and a more peripheral center of gravity than during active fixation (Ben Hamed, Duhamel, Bremmer, & Graf, 2002). In other words, active fixation shifts the average LIP RF toward the straight ahead position. Currently, it is not clear whether such RF changes also occur in the putative human homologue of macaque area LIP (Konen et al., 2004). Recently an influence of attention on the position of RFs in macaque area MT has been demonstrated (Womelsdorf, Anton-Erxleben, Pieper, & Treue, 2006). In about two thirds of the cells the center of mass of the RFs is shifted in direction of the focus of attention. Similar results have been observed in area V4 (Connor, Preddie, Gallant, & van Essen, 1997). Though we did not explicitly vary attention in our experiment these results are interesting with regard to our study since they suggest that active/attentive fixation of a visual stimulus (here: the fixation point) may have shifted visual receptive fields.

5. Conclusion

In summary, we showed that briefly flashed visual targets are mislocalized during reflexive eye movements. This mislocalization is similar to that observed during voluntary eye movements in darkness and did not show the typical spatial variation observed when voluntary eye movements are performed in the presence of visual references. In other words, the localization mechanisms operating during reflexive eye movements appear not to use visual references even though some are available. We speculate that the reason for

this may be that the strongest of visual references – the visual target of an eye-movement – is absent during reflexive eye movements. One could even say that these reflexive eye movements have no (conscious) target at all. This interpretation provides further confirmation of the importance of the eye movement target, as a reference, in the linking of pre- and postsaccadic coordinate systems (Awater & Lappe, 2006; Deubel, 2004; Deubel, Bridgeman, & Schneider, 1998).This work was supported by the DFG (Research Group 560 "Perception and Action" and Research-Training-Group-885 "NeuroAct").

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Expansion of Visual Space During Optokinetic Afternystagmus (OKAN)

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Expansion of Visual Space During Optokinetic Afternystagmus (OKAN)

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Kaminiarz A, Krekelberg B, Bremmer F. Expansion of visual space during optokinetic afternystagmus (OKAN). *J Neurophysiol* 99: 2470–2478, 2008. First published February 27, 2008; doi:10.1152/jn.00017.2008. The mechanisms underlying visual perceptual stability are usually investigated using voluntary eye movements. In such studies, errors in perceptual stability during saccades and pursuit are commonly interpreted as mismatches between actual eye position and eye-position signals in the brain. The generality of this interpretation could in principle be tested by investigating spatial localization during reflexive eye movements whose kinematics are very similar to those of voluntary eye movements. Accordingly, in this study, we determined mislocalization of flashed visual targets during optokinetic afternystagmus (OKAN). These eye movements are quite unique in that they occur in complete darkness and are generated by subcortical control mechanisms. We found that during horizontal OKAN slow phases, subjects mislocalize targets away from the fovea in the horizontal direction. This corresponds to a perceived expansion of visual space and is unlike mislocalization found for any other voluntary or reflexive eye movement. Around the OKAN fast phases, we found a bias in the direction of the fast phase prior to its onset and opposite to the fast-phase direction thereafter. Such a biphasic modulation has also been reported in the temporal vicinity of saccades and during optokinetic nystagmus (OKN). A direct comparison, however, showed that the modulation during OKAN was much larger and occurred earlier relative to fast-phase onset than during OKN. A simple mismatch between the current eye position and the eye-position signal in the brain is unlikely to explain such disparate results across similar eye movements. Instead, these data support the view that mislocalization arises from errors in eye-centered position information.

INTRODUCTION

Space constancy during eye movements is a major challenge for the visual system. Objects move across the retina with speeds up to several hundred degrees per second as a consequence of saccadic eye movements. Nevertheless we perceive the world as being stable. However, visual stability is not perfect, at least when transient stimuli are considered. Many studies have demonstrated spatial misjudgments of stimuli flashed during voluntary eye movements (pursuit and saccades). During smooth pursuit such stimuli are mislocalized in the direction of the eye movement and the magnitude of the error depends on the position of the target relative to the fovea (Mitrani and Dimitrov 1982; Rotman et al. 2004; van Beers et al. 2001). During voluntary saccades localization errors follow a characteristic spatiotemporal pattern, which heavily depends on experimental conditions (Ross et al. 2001; Schlag and Schlag-Rey 2002). In complete darkness, transient stimuli are mislocalized in the direction of the eye movement from about 100 ms before saccade onset (shift) (Cai et al. 1997; Honda 1989). The maximum shift is observed around saccade onset. Mislocalization is then inverted and stimuli are perceived as being shifted opposite to the saccade direction for $\leq$100 ms. In contrast, when visual references are available, the mislocalization strongly depends on the position of the target relative to the saccade goal and all stimuli are shifted toward the landing point of the eye, resulting in a perceptual compression of visual space (Kaiser and Lappe 2004; Lappe et al. 2000; Ross et al. 1997).

Mislocalization is commonly interpreted as a temporary mismatch between the actual eye position and eye-position signals in the brain (Dassonville et al. 1992; Honda 1991). Given this context it is of interest to determine how different eye movements, with very similar kinematics, affect localization. Recently, two studies investigated mislocalization of transient visual stimuli during optokinetic nystagmus (OKN) (Kaminiarz et al. 2007; Tozzi et al. 2007). OKN is a reflexive eye movement evoked by large-field moving patterns. OKN consists of two alternating phases: a slow phase in the direction of the stimulus motion and a fast phase opposite to the stimulus motion. Stimuli presented during OKN slow phase were found to be mislocalized in the direction of the eye movement. However, contrary to smooth pursuit, the size of the error did not depend on the position of the target relative to the fovea. The error pattern observed during the OKN fast phase resembled the one described for voluntary saccades in darkness (perisaccadic shift). The biphasic mislocalization pattern during OKN, however, occurred earlier with respect to fast-phase onset.

In this study we continue our investigation of mislocalization during reflexive eye movements. Most important, we sought to address the issue that during OKN a moving textured background is permanently visible. This background in itself might contribute to the observed localization errors. Hence, to show that perceptual errors occur in the complete absence of visual stimulation, we tested localization during optokinetic afternystagmus (OKAN), which is an alternation of slow and fast phases observed in total darkness in subjects who previously performed prolonged OKN.

METHODS

Subjects

Nine subjects participated in the experiments. Six were naive as to the purpose of the experiment. All subjects had normal or corrected-to-normal visual acuity and gave informed written consent. All procedures used in this study conformed to the Declaration of Helsinki.

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Stimulus presentation and eye-movement recordings

Experiments were carried out in a completely dark experimental room to avoid visual references that otherwise could *1*) prevent OKAN and/or *2*) influence visual localization. Computer-generated stimuli were projected onto a large tangent screen using a CRT projector (Marquee 8000, Electrohome) running at a spatial resolution of 1,152 × 864 pixels and a frame rate of 100 Hz. The screen was viewed binocularly at a distance of 114 cm and subtended 70 × 55° of visual angle. During the experiments each subject's head was supported by a chin rest. Eye position was sampled at 500 Hz using an infrared eye tracker (Eye Link 2, SR Research). The system was calibrated prior to each session using a 9 (3 × 3) point calibration grid. During sessions drift correction was performed before each trial. Recording sessions lasted between 5 and 10 min, depending on experiment and subject. Eye movement and behavioral data were stored on hard disk for off-line analysis.

Visual stimuli

To induce OKN/OKAN we presented a random-dot pattern (RDP) consisting of black dots (size: 2.0°, luminance <0.1 cd/m^2, number of visible dots: 250) moving left- or rightward on the screen. All dots moved coherently and a new RDP was generated for each trial. The visual localization target [white circle, 0.5° (OKAN) or 1.0° (OKN) in diameter, luminance 22.5 cd/m^2] was flashed for 10 ms at one of three positions (x = −8°, 0°, +8°) on the horizontal meridian. In all experiments different target positions were displayed with equal probability in pseudorandom order. To determine the perceived position of the target a horizontal ruler was displayed on a gray background (luminance 12.5 cd/m^2) at the end of each trial (see also Kaminiarz et al. 2007). The ruler's tick-mark positions were equally spaced, but random numbers were assigned to the tick marks for each trial to prevent subjects from developing stereotypical response strategies due to the limited number of targets. Subjects reported the perceived position of the target by entering the number of the tick mark closest to the target flash.

Baseline trials

In OKAN baseline trials, subjects freely viewed a white (luminance 22.5 cd/m^2) screen for 3,000 ms. Thereafter the screen turned black for another 3,000 ms. The target was flashed 2,500 ms after the luminance change (Fig. 1*B*). This background luminance change mimicked the change that occurred in the actual OKAN trials (see following text). Here and in all other cases, the ruler was displayed 490 ms after target presentation and the trial ended once the subject entered the perceived position on the keyboard. In OKN baseline trials, subjects freely viewed a homogeneous gray (luminance 12.5 cd/m^2) screen for 4,000 ms. The target was presented after 3,500 ms (Fig. 1*D*). Each baseline session consisted of 30 trials.

OKN trials

In the OKN condition, the RDP moved across a gray background (luminance 12.5 cd/m^2) for 4,000 ms. The target was flashed after 3,500 ms (Fig. 1*C*). The RDP velocity in the OKN condition was set individually for each subject such that the amplitudes of the fast phases during OKN and OKAN matched as closely as possible. Thirty trials were recorded per session.

OKAN trials

In the OKAN condition the RDP moved on a white background (luminance 22.1 cd/m^2) at a speed of 80°/s. After 15 s of stimulus motion the screen turned completely dark. After 2,500 to 4,500 ms (depending on subject and session) in darkness, the target was flashed. The ruler was displayed 490 ms later (Fig. 1*A*). A single session consisted of 15 trials.

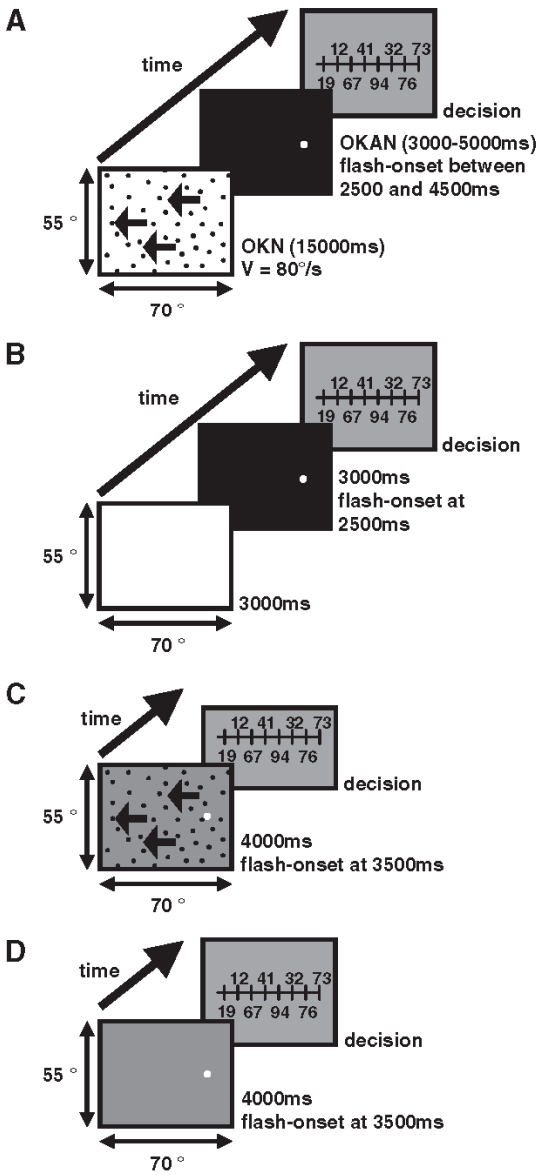

FIG. 1. Schematic illustration of the temporal sequence of an optokinetic afternystagmus (OKAN, *A*), OKAN baseline (*B*), optokinetic nystagmus (OKN, *C*), or OKN baseline trial. *A*: during OKAN trials a random-dot pattern (RDP) moved left- or rightward for 15 s. Thereafter the background turned black. After 2,500 to 4,500 ms the target was flashed and a ruler appeared 490 ms later. Subjects indicated which number on the ruler was closest to the perceived position of the flashed target. *B*: during OKAN baseline measurements subjects freely viewed a screen for 6,000 ms. The initially white screen turned black after 3,000 ms. The target was flashed 2,500 ms after the luminance change. *C*: in the OKN condition, the RDP moved leftward for 4,000 ms. The target was flashed after 3,500 ms. Again, the ruler was used at the end of the trial to indicate the perceived target position. *D*: during OKN baseline trials, subjects freely viewed a gray screen for 4,000 ms. The target was presented after 3,500 ms and the ruler appeared 490 ms after the target offset.

Data analysis

Data were analyzed using Matlab 7.3.0 (The MathWorks) and SigmaStat 3.10 (Systat Software). Eye-position data for all OKN/OKAN trials were inspected off-line. Trials were excluded from

further analysis if *1*) subjects had not performed any systematic OKN/OKAN, *2*) the fast phase closest to the target flash did not match the previously defined velocity/acceleration criterion, or if *3*) the fast phase closest to the flash was in the same direction as the slow eye movement and was initiated <100 ms after the target flash. Due to these criteria 38% of all OKAN and 21% of all OKN trials were excluded from further analysis.

For the remaining valid trials, we determined as a first step the error in the free-viewing condition (baseline error). Then we computed the errors during OKN/OKAN slow phases. For this analysis only trials in which no fast phase was initiated in a 200-ms time window centered on the onset of the flash were considered. Net errors were estimated by subtracting baseline errors from OKN/OKAN slow-phase errors.

To determine the dynamics of the localization error around the fast phases of the OKN/OKAN we first identified the fast phase closest (in time) to the flash. Then we determined the (baseline-corrected) localization error as a function of the time of the flash relative to the onset of the fast phase and computed a moving average for this data set. The moving average was smoothed with a Gaussian-shaped weighing function (σ = 7 ms). Data were recorded until data from 150 valid trials in the relevant time window were available for each subject.

RESULTS

Eye movements during OKN and OKAN trials

During OKN trials (leftward pattern motion only) fast-phase frequency averaged across subjects was 2.41 (SD 0.34) Hz with fast phases having a mean horizontal amplitude of 5.3 (SD 1.2) deg. The slow-phase gain (gain = [eye velocity/stimulus velocity]) was 0.89 (SD 0.04) at an average stimulus velocity of 14.54 (SD 1.50) deg/s. Mean preflash slow-phase velocity (determined in the last 50 ms before flash onset) was 12.85 (SD 1.15) deg/s, whereas the average eye position at flash onset was 5.33 (SD 1.73) deg. The analysis was based on 8,545 fast phases in 930 trials.

During leftward/rightward OKAN trials mean fast-phase frequency during optokinetic stimulation (80°/s) was 3.07/3.17 (SD 0.5/0.49) Hz with an average horizontal fast-phase amplitude of 13.7/14.4 (SD 2.8/2.9) deg. Mean slow-phase gain was 0.66/0.72 (SD 0.06/0.04). During OKAN the fast-phase frequency and the horizontal fast-phase amplitude dropped to 1.5/0.97 (SD 0.23/0.33) Hz and 3.32/4.8 (SD 0.97/1.96) deg, respectively. Average preflash slow-phase velocity was −4.07/4.58 (SD 0.82/2.16) deg/s and the average horizontal eye position at flash onset was −2.71/4.46 (SD 2.41/3.36) deg. The analysis was based on 101,987 and 5,977 fast phases during OKN and OKAN, respectively, performed during 1,388 valid trials.

To summarize, we achieved our goal to match the fast-phase amplitudes during OKN and OKAN; they were within 1SD from each other. We could not, however, simultaneously match the slow-phase velocities; they were slower during OKAN than during OKN.

Localization during OKAN slow phase

Figure 2 (*left column*) shows the results of the first experiment in head-centered coordinates. During free viewing in darkness (Fig. 2, *top left*) perception was not veridical. Instead, we observed a heterogeneous pattern of misperceptions. Three subjects (1, 2, and 8) showed an outward bias (centrifugal shift), whereas two subjects (5 and 9) showed an inward bias (centripetal shift). The remaining subjects showed a tendency for an overall shift either to the left (subjects 4, 6, and 7) or to the right (subject 3). Across subjects (mean) we found no consistent bias in any direction.

During the slow phase of the OKAN (Fig. 2, *middle left*) perception was biased toward larger eccentricities at the population level (mean). Yet, after correction for the baseline bias (Fig. 2, *bottom left*), the remaining shift revealed no clear bias. Two (7, 8) subjects showed a significant ($P < 0.05$) mislocalization opposite to the direction of the slow-phase eye movement. Four subjects (1, 2, 3, and 5) mislocalized targets toward larger eccentricities, whereas two (4 and 6) showed no systematic bias. Only a single subject (9) revealed a shift in the direction of the slow-phase eye movement as we have previously reported for localization during OKN (Kaminiarz et al. 2007).

These results show that there is a large degree of intersubject variability. To confirm this finding, we repeated the experiment with rightward OKAN for seven of nine subjects (Fig. 3). Again, we found no bias in any particular direction when data were averaged across all subjects. Visual comparison of the baseline-corrected findings for leftward and rightward OKAN, however, showed that subjects were consistent in their mislocalization. For instance, subject 7 mislocalized against the direction of the slow-phase eye movement for both leftward and rightward OKAN. Similarly, subject 3 showed a clear centrifugal effect irrespective of whether the OKAN slow phase was leftward or rightward.

We will subsequently show that much of the intersubject variability can be understood by analyzing the data in retinal coordinates. Before turning to that explanation, however, we first compare localization during OKAN with that during OKN.

Localization during OKN slow phase

The kinematics of the eye movements during OKAN are quite similar to those during OKN; thus it is instructive to directly compare mislocalization during OKAN and OKN. Our previous OKN study used small-field (monitor size: circular aperture with 25° diameter) rather than the large-field visual stimulation (screen size: 70 × 55°) of the current study. To exclude this factor as a possible cause for any differences, we repeated some of the OKN experiments in the large-field setup.

The results for localization during OKN are shown in Fig. 2, *right column*. In the control condition (*top right*) we observed for all but one subject (8) a centripetal shift of perceived target locations. This confirms our previous findings and matches errors of mislocalization found in the absence of eye movements (Müsseler et al. 1999) but is clearly different from our findings for the OKAN baseline in total darkness where we observed a much more heterogeneous error pattern (*top left*). Mislocalization during OKN slow phase, however, closely matched results from our previous study; position perception during the OKN slow phase was biased in the direction of the eye movement (*right middle* and *bottom*). This error was independent of flash position ($P = 0.71$, ANOVA on ranks).

Error as a function of retinal eccentricity

We determined the effect of retinal eccentricity on localization error for OKAN and large-field OKN as well as during free viewing in darkness and in light. To do so we calculated

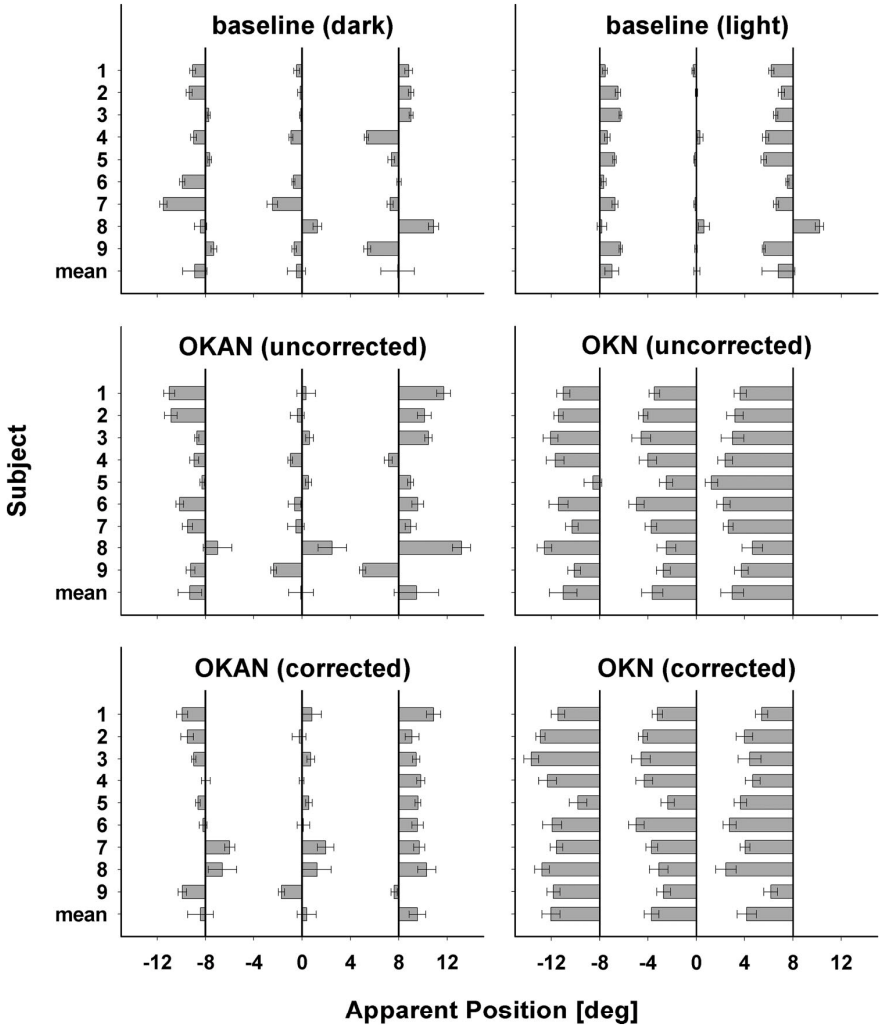

FIG. 2. The graphs show the apparent target position during baseline (*top row*) and OKAN/OKN slow phase without (*middle row*) and with baseline correction (*bottom row*) for leftward OKAN (*left column*) and OKN trials (*right column*). Bars show localization errors. Error bars are 95% confidence intervals.

localization errors as a function of retinal stimulus eccentricity independently for each subject and performed linear regressions for all three stimulus positions (see Fig. 4 for data from a single subject). In Fig. 5 regression lines for all single subjects (thin lines) as well the population mean (thick lines) are shown. Extending our earlier findings for both free viewing in light (*top right*) and OKN (*middle right*), respectively, mislocalization did not depend on retinal eccentricity as indicated by the flat regression curves. However, the localization errors during both free viewing in darkness (*top left*) and slow-phase OKAN (*middle left*) depended strongly on the retinal eccentricity of the flashed target. To further analyze this behavioral difference we performed for each individual subject an eccentricity-dependent baseline correction by subtracting the baseline fits from the corresponding OKAN fits (*bottom left*). The data clearly show that on average when a target is flashed on the lagging side of the retina (i.e., on the right when the eye moves to the left and vice versa), it is mislocalized in a direction opposite that of the eye movement. When a target is flashed on the leading side of the retina, however, it is mislocalized in the direction of the eye movement. The OKAN data were obtained during leftward slow phases, but the same effect was found for rightward slow phases (not shown). Hence, we can rephrase this finding as showing a horizontal expansion of visual space in retinal coordinates during horizontal OKAN. The linear regressions of the single-subject data provide us with a quantification of this expansion. First, we can determine the focus of the expansion by calculating the eccentricity for which the mislocalization is zero. When averaged across all subjects and all stimulus positions, the focus was found to lie at $x = 0.2^{\circ}$. Across subjects, this focus of expansion ranged from $x = -1.6^{\circ}$ to $x = 0.76^{\circ}$. Second, the slope of the regressions quantifies the foveofugal mislocalization error per degree of retinal eccentricity. Averaged across subjects the mislocalization increased by 0.12°/degree eccentricity. This measure was somewhat more variable across subjects (range: [0.03, 0.26]). Importantly, the correlation between eccentricity and mislocalization was positive and significant ($P < 0.01$; Spearman rank order) for all but one subject. These data confirm that horizontal OKAN slow phases consistently lead to a horizontal expansion of visual space in retinal coordinates.

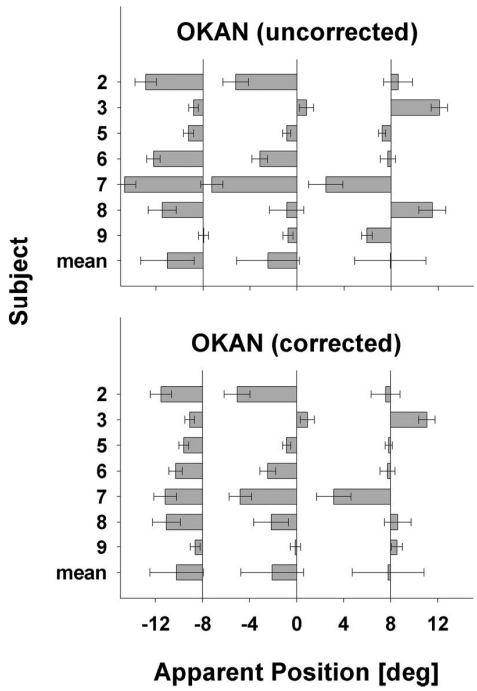

FIG. 3. Localization errors during rightward OKAN slow phase without (*top*) and with (*bottom*) baseline correction. Conventions as in Fig. 2.

Accordingly, the explanation of the intersubject variability found in Fig. 2 (data in head-centered coordinates) can be found in the differences in average eye position across OKAN phases in the different subjects. For instance, subject 5 performed leftward OKAN with eye positions mainly on the left side of the screen. Obviously, this shift in eye position has consequences for the average retinal position of the targets that were flashed at fixed positions on the screen. First, the left target was closer to this subject's fovea than it was to the fovea of subjects 2 or 6 who performed OKAN mainly with gaze located at the center of the screen. According to our retinal expansion model, a flash nearer the fovea will be mislocalized less, thus explaining the relatively small leftward mislocalization of subject 5 as shown in Fig. 2. Similarly, for subject 5 the central target almost always landed on the lagging side of the retina (and not foveally), thus evoking a much stronger mislocalization.

This perceptual expansion of visual space was found only during OKAN. The baseline-corrected OKN data (Fig. 2, *bottom right*) clearly show no such effect of retinal stimulus eccentricity on visual localization.

Localization during OKAN/OKN fast phase

To analyze the dynamics of the perceptual error in the temporal vicinity of the fast phases we computed the perceived stimulus position as a function of time between flash onset and the initiation of the temporally closest fast phase. To increase our data yield per time window, we merged data from all subjects and flash positions and calculated a moving average across these data points. The solid lines in Fig. 6 show the results for OKAN (*top*) and OKN (*bottom*), respectively. Dashed lines depict the underlying average eye-position traces (trials in which the time interval between flash onset and fast-phase onset was >100 ms were not considered for calculating the average eye-position trace). Although during OKN targets were on average mislocalized 4° in the direction of the slow-phase eye movement (thin straight horizontal line), no such shift was observed during OKAN. This mirrors the

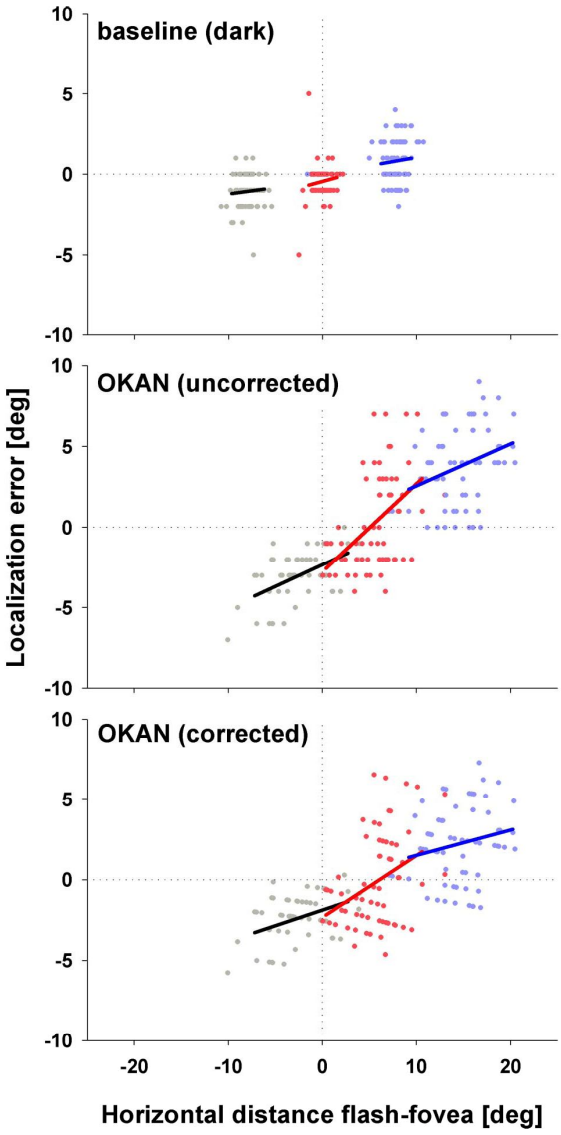

FIG. 4. The graphs show localization errors as function of retinal stimulus eccentricity during free viewing in darkness (*top*) and OKAN slow-phase without (*middle*) and with (*bottom*) baseline correction for subject 1. Positive errors indicate rightward mislocalization (i.e., against the direction of the slow-phase eye movements). Stimulus positions are color-coded: black: x = −8°; red: x = 0°; blue: x = +8°. Solid lines are linear regressions to the data. The line length codes the data distribution with respect to the underlying eye position, with lines ranging from 5 to 95% of the horizontal eye-position values. The vertical dotted lines mark the position of the fovea at the time of the flash, whereas the horizontal ones mark correct localization. Points to the right of the dotted line depict trials during which the target was presented to the right of the fovea.

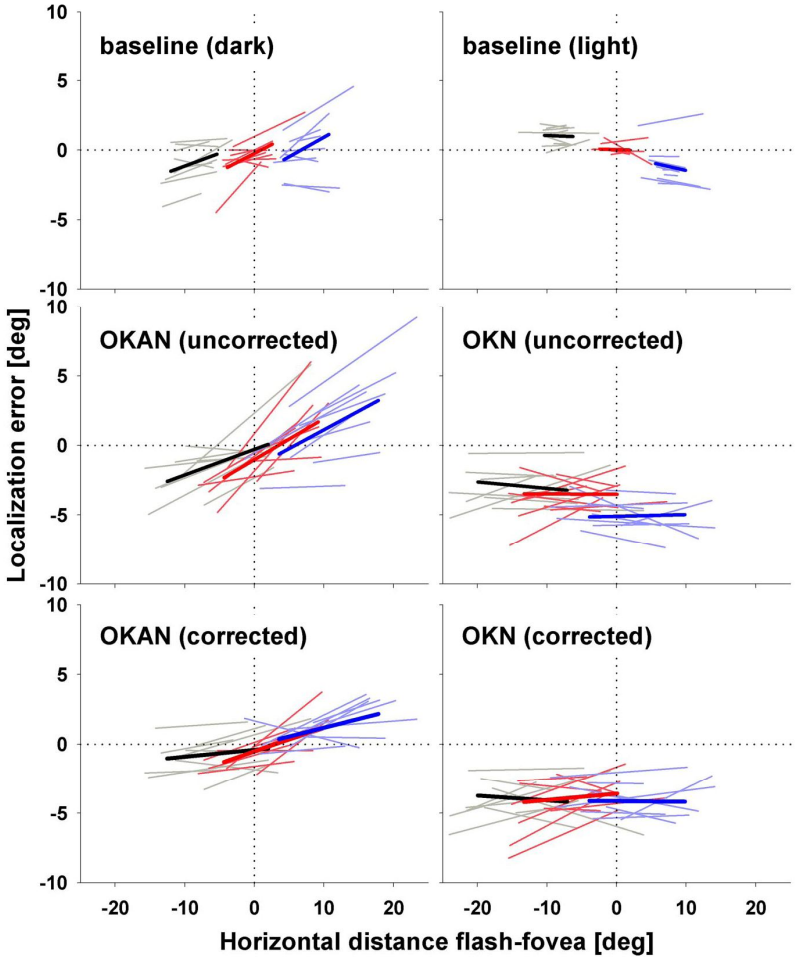

FIG. 5. The graphs show linear regressions to the localization error as function of stimulus position relative to the fovea during baseline (*top row*) and OKAN/OKN slow phase without (*middle row*) and with baseline correction (*bottom row*) for leftward OKAN (*left column*) and OKN trials (*right column*). Thin lines display single subject data, whereas thick lines show data averaged across subjects.

findings shown in Figs. 2 and 5. For both eye movements the observed bias depended on the time interval between stimulus presentation and the onset of the fast phase.

During OKAN flashes were mislocalized in the direction of the fast phase starting 150 ms before fast-phase onset with a peak error 51 ms prior to fast-phase onset. Starting at about 20 ms before fast-phase onset, stimuli were slightly mislocalized in the opposite direction. This mislocalization returned back to its steady-state level 100 ms after fast-phase onset at the latest.

During OKN we observed a mislocalization in the direction of the fast phase before its onset and mislocalization in the opposite direction about 50 ms after fast-phase onset. This fast-phase effect was superimposed on the general shift in the direction of the slow-phase eye movement. Contrary to the OKAN, however, the error in direction of the fast phase peaked 37 ms before fast-phase onset.

Error patterns during both OKAN and OKN fast phases were independent of target position; i.e., we did not observe any evidence for a compression of space around the fast phase (data not shown). As can be inferred from the eye-position traces the average amplitude of the saccade closest (in time) to the flash was nearly identical for both types of eye movements [OKAN: 3.7° (SD 2.7); OKN: 3.5 (SD 2.2)]. Statistical analysis comparing mean fast-phase amplitudes across subjects revealed no significant difference ($P = 0.69$, Mann–Whitney rank-sum test). Surprisingly, however, the amplitude of the biphasic modulation in perceived position induced by the fast phase was considerably larger during OKAN (3.8°) than during OKN (2.15°).

DISCUSSION

We demonstrated systematic mislocalization of briefly flashed visual targets during optokinetic afternystagmus (OKAN). The observed error pattern varied widely across subjects when expressed in head-centered coordinates, but was highly consistent when expressed in retinal coordinates. In the latter reference frame our data can be summarized as a horizontal expansion of visual space during slow-phase horizontal OKAN. Localization in the temporal vicinity of the fast phases of the OKAN was modulated. A mislocalization in the direction of the fast phase was observed prior to fast-phase onset. This perceptual effect was followed by a weak transitory shift into the opposite direction. The perceptual error returned to its steady-state level about 100 ms after fast-phase onset.

In this discussion we first compare our OKAN findings to those previously reported on other fast and slow eye movements. Second, we discuss the role of visual references in localization. Third, we discuss the claim that a combination of

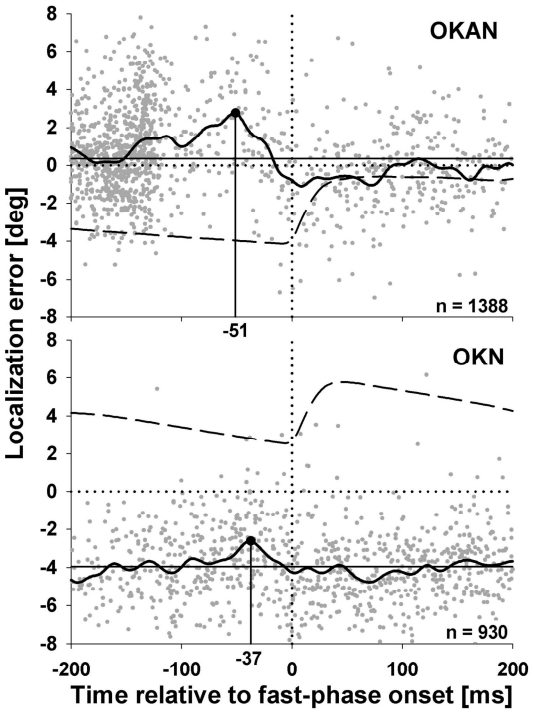

FIG. 6. Localization errors as a function of time relative to the onset of the temporally closest fast phase during leftward OKAN (*top*) and OKN (*bottom*). Positive errors indicate rightward mislocalization. The dotted horizontal lines indicates unbiased localization, whereas solid horizontal lines represent mean localization errors. The dotted vertical line marks the onset of the fast phase (t = 0 ms). Solid curves are moving averages obtained from the raw data (gray dots) smoothed with a Gaussian-shaped weighing function (σ = 7 ms). Black dots mark the peak mislocalization in direction of the fast phase. Dashed curves are mean eye position traces during OKAN and OKN.

erroneous eye position signals and veridical retinal signals could underlie these phenomena.

Mislocalization around slow eye movements

OKN, OKAN, and smooth pursuit share similar phases of slow eye movements. Mislocalization during these eye movements, however, is quite different. During smooth pursuit and OKN slow phase, but not OKAN slow phase, stimuli are mislocalized in the direction of the eye movement. During pursuit and OKAN the error pattern depends on the retinal position of the flash (Mateeff et al. 1982; Mitrani and Dimitrov 1982; Rotman et al. 2004; van Beers et al. 2001), whereas the error is independent of retinal position during OKN (Kaminiarz et al. 2007). This clearly shows that the kinematics of the eye movements alone are not sufficient to account for the observed mislocalizations.

There are two clear differences that may in principle account for the disparate localization errors. First, the visual scene is quite different during OKN, smooth pursuit, and OKAN and these visual factors may contribute to mislocalization in various ways (see following text for further discussion). Second, the eye-movement control networks involved in OKN, OKAN, and pursuit are distinct and thus they may interact in different ways with the visual system. To be specific, smooth pursuit and OKN are accompanied by neural activity within identical cortical areas or networks (Bremmer et al. 2002; Dieterich and Brandt 2000; Konen et al. 2005; Schlack et al. 2003), but with stronger activation during smooth pursuit (Konen et al. 2005). OKAN, on the other hand, is driven by the so-called velocity storage mechanism whose neuronal substrate is located in the vestibular nucleus (Leigh and Zee 2006; Waespe and Henn 1977). Although we are not aware of any functional MRI study investigating human brain activity during OKAN, studies in the macaque suggest that OKAN is not accompanied by specific cortical activity at all (Ilg 1997). Furthermore, the subcortical nucleus of the optic tract/dorsal terminal nucleus is active during OKN but not during OKAN (Ilg and Hoffmann 1996). This raises the possibility that the involvement or absence of cortical as well as specific subcortical processing may contribute to the observed perceptual differences during slow eye movements.

Mislocalization around fast eye movements

A temporally biphasic mislocalization has been found during voluntary saccades (Dassonville et al. 1992; Honda 1991), fast-phase OKN (Kaminiarz et al. 2007; Tozzi et al. 2007), and now also fast-phase OKAN. In the spatial domain, these biphasic mislocalizations are quite similar, although a direct comparison across all three fast eye movements is difficult given that the sizes of the fast movements in the different studies were not matched. In our study, however, the OKN fast phases matched the OKAN fast phases and we nevertheless found a much larger spatial modulation during OKAN. This is in line with reports showing that localization errors during voluntary saccades increase when fewer visual references are available (Dassonville et al. 1995; Honda 1999). In other words, the relatively large effects found during OKAN, compared with OKN, may be due to the complete absence of visual references. Interestingly, the errors during OKAN are not only larger than those during OKN but are also larger than those found during voluntary saccades in darkness. During saccades errors are in the range of ≤50% of the saccadic amplitude. During OKAN the error is about 100% of the fast-phase amplitude. Analogous to the preceding line of arguments this could be due to the total absence of visual references. In saccade experiments two visual references are available for the subjects: the initial fixation point and the saccade target. Even if both are not present at the time of the flash they allow subjects to build up an internal representation of the environment. During OKAN, on the other hand, subjects performed eye movements without visual goal or feedback for ≥2,500 ms, which should severely constrain the buildup of a representation of the environment. Summarizing, this line of arguments suggests that perceptual bias increases when the internal visual representation of the environment is poor.

In the temporal domain, the biphasic mislocalization differs considerably across eye movements. For visually guided saccades, the peak error generally occurs at saccade onset (Honda 1991), whereas during OKN it occurs about 40 ms before fast-phase onset and even earlier during OKAN.

Localization and visual references in the absence of OKAN/OKN

As noted earlier, differences in visual input could be an important factor affecting mislocalization. This has been suggested

before (Lappe et al. 2000) and our current data provide further evidence in favor of this view. Not only do we find very different patterns of mislocalization during OKAN (no visual references) and OKN (with some visual references), our free-viewing baseline trials support a similar view. We tested the same subjects during free gaze in light and in darkness and found a systematic centripetal (inward) bias in light but a centrifugal (outward) bias in complete darkness. This may also explain why previous studies reported disparate results concerning localization of targets during fixation. Some reported an overall centripetal bias (Kaminiarz et al. 2007; Mateeff and Gourevich 1983; Müsseler et al. 1999), whereas others reported a centrifugal bias (Honda 1989; Königs et al. 2007). Our data suggest that the details of the visual references are critical in those experiments and may explain some of the observed discrepancies.

Neural basis of visual mislocalization

It has been argued that localization errors during smooth eye movements could be due to sluggish or delayed eye-position signals that combine with veridical retinal signals to determine the (world) position of the flashed stimulus (Schlag and Schlag-Rey 2002). However, as discussed earlier, different patterns of mislocalization are observed during fast and slow eye movements with very similar kinematics. To explain all mislocalizations with the same mismatch between eye-position signals and veridical retinal signals, one would have to assume that the eye-position signals generated by these three eye movements are very different. For smooth pursuit mislocalization, the eye-position signal should be sluggish, but the sluggishness/delay should vary with retinal eccentricity; for slow-phase OKN, the eye-position signal should be sluggish throughout the visual field; and for slow-phase OKAN, the eye-position signal should be veridical foveally, whereas it should lead on the leading side of the retina and lag on the lagging side of the retina. For fast phases, these eye-position signals should then be modulated appropriately to account for the spatiotemporal mislocalization around fast eye movements.

We cannot exclude that such complex eye-position signals exist, but note that there is no evidence beyond that gathered in mislocalization experiments that supports their existence. Accordingly, based on our current results, we believe that mislocalization is not caused by the algebraic summation of a veridical retinal signal with an erroneous eye-position signal. Instead, these findings support the view that the underlying retinal signals are distorted. When distorted retinal position information is combined with (veridical or otherwise) eye-position signals, perceptual mislocalization in head-centered coordinates occurs. Explicit support for errors in eye-centered neural position signals comes from recordings in the middle temporal (MT) and medial superior temporal (MST) areas of the macaque. Neurons in MT and MST encode position information, although this information is distorted around saccades in a manner that mimics the perisaccadic compression of space (Krekelberg et al. 2003). The fact that a neural correlate of space compression is already found in an area encoding eye-centered position information suggests that the effect is not caused by a combination of retinal and eye-position information. Our current finding—that mislocalization during slow-phase OKAN is best understood in retinal rather than in head-centered coordinates—also suggests that it arises from distortions of the representation in early visual areas, with a retinocentric encoding of space. These changes of the early visual representation may be related to mechanisms whose aim is to hide retinal motion that is caused by the eye movements themselves (Kleiser et al. 2004). Such an early, purely visual basis for mislocalization would also be consistent with the fact that the details of the visual scene have such a great influence on mislocalization.

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The Main Sequence of Human Optokinetic Afternystagmus (OKAN)

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The Main Sequence of Human Optokinetic Afternystagmus (OKAN)

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Kaminiarz A, Königs K, Bremmer F. The main sequence of human optokinetic afternystagmus (OKAN). *J Neurophysiol* 101: 2889–2897, 2009. First published March 18, 2009; doi:10.1152/jn.00114.2009. Different types of fast eye movements, including saccades and fast phases of optokinetic nystagmus (OKN) and optokinetic afternystagmus (OKAN), are coded by only partially overlapping neural networks. This is a likely cause for the differences that have been reported for the dynamic parameters of fast eye movements. The dependence of two of these parameters—peak velocity and duration—on saccadic amplitude has been termed "main sequence." The main sequence of OKAN fast phases has not yet been analyzed. These eye movements are unique in that they are generated by purely subcortical control mechanisms and that they occur in complete darkness. In this study, we recorded fast phases of OKAN and OKN as well as visually guided and spontaneous saccades under identical background conditions because background characteristics have been reported to influence the main sequence of saccades. Our data clearly show that fast phases of OKAN and OKN differ with respect to their main sequence. OKAN fast phases were characterized by their lower peak velocities and longer durations compared with those of OKN fast phases. Furthermore we found that the main sequence of spontaneous saccades depends heavily on background characteristics, with saccades in darkness being slower and lasting longer. On the contrary, the main sequence of visually guided saccades depended on background characteristics only very slightly. This implies that the existence of a visual saccade target largely cancels out the effect of background luminance. Our data underline the critical role of environmental conditions (light vs. darkness), behavioral tasks (e.g., spontaneous vs. visually guided), and the underlying neural networks for the exact spatiotemporal characteristics of fast eye movements.

INTRODUCTION

Saccades are fast eye movements that can be characterized by a tight relationship between several of their kinematic parameters. Saccade duration and peak velocity increase with saccade amplitude. This relationship has been termed "main sequence" (Bahill et al. 1975) and has been shown for different types of saccades, including visually guided saccades (Bahill et al. 1975; Baloh et al. 1975), memory-guided saccades (Becker and Fuchs 1969; Smit et al. 1987), antisaccades (Smit et al. 1987; Van Gelder et al. 1997), and catch-up saccades (Van Gelder et al. 1997). Although all these types of saccades adhere to a main sequence, the individual main sequences for different kinds of saccades show considerable variability. For example, memory-guided saccades and antisaccades have lower peak velocities (and longer durations) than those of visually guided saccades of identical amplitude (Smit et al. 1987). In addition, factors like fatigue (Bahill and Stark 1975; Riggs et al. 1974) and drug usage (Bittencourt et al. 1981) influence the main sequence. Concerning other factors like saccade direction and background luminance/structure the reports in the literature are less consistent (Bahill et al. 1975; Becker and Jurgens 1990; Boghen et al. 1974; Garbutt et al. 2003a; Hyde 1959; Pelisson and Prablanc 1988; Robinson 1964). Considering specific characteristics of the backgrounds across which saccades had to be made several studies reported faster saccades on illuminated (Henriksson et al. 1980; Riggs et al. 1974; Sharpe et al. 1975) compared with dark backgrounds, whereas others reported no such difference (Becker and Fuchs 1969; Ilg et al. 2006). Furthermore significant inter- and intraindividual differences have been reported (Bollen et al. 1993).

Aside from saccades a main sequence relationship has also been demonstrated for the fast phases of different kinds of nystagmus in several species (Garbutt et al. 2001, 2003a; Gavilan and Gavilan 1984; Henriksson et al. 1980; Mackensen and Schumacher 1960; Ron et al. 1972; Sharpe et al. 1975). Studies comparing saccades and fast phases of the vestibuloocular reflex (VOR) reported identical or very similar main sequences (Guitton and Mandl 1980; Ron et al. 1972; Sharpe et al. 1975), but lower velocities for the VOR have also been reported (Gavilan and Gavilan 1984). Fast phases during visually guided optokinetic nystagmus (OKN) have either been reported to follow the same main sequence as that of visually guided saccades (Mackensen and Schumacher 1960; Sharpe et al. 1975) or to be slower than saccades (Garbutt et al. 2001, 2003a; Gavilan and Gavilan 1984; Henriksson et al. 1980).

In primates the OKN is composed of two components: a direct/early/fast component and an indirect/late/slow component (Cohen et al. 1977). After an increase in stimulus velocity slow phase eye velocity first increases rapidly and, afterward, more gradually until a steady state is reached. The early component is supposed to reflect smooth pursuit (Pola and Wyatt 1985), whereas the late component charges the velocity storage mechanism located in the vestibular nucleus and is therefore essential for the execution of optokinetic afternystagmus (OKAN). OKAN can be observed in subjects who performed OKN for some time and are put in complete darkness thereafter. Like OKN, it consists of slow and fast phases, but amplitude of the fast phases is reduced in the dark.

It is widely accepted that the differences between OKN and OKAN slow phases are the origin of (partially) different neural structures underlying the execution of both types of eye movements. In this study we asked whether the different mechanisms controlling OKN and OKAN also influence their fast-phase characteristics.

Furthermore, we aimed at disentangling the relative influence of cortical control and stimulus characteristics on the main sequence by comparing main sequences for OKAN, OKN, spontaneous, and visually guided saccades.

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METHODS

Subjects

In total, 10 healthy subjects [2 male and 8 female, 22–31 yr, mean age 25.7 yr (3.37 SD)] participated in the study. All had normal or corrected-to-normal visual acuity and gave informed written consent. All procedures used in this study conformed to the Declaration of Helsinki.

Experimental procedure

All experiments were carried out in a dark, sound-attenuated chamber. Stimuli were projected onto a tangent screen (70 × 55°) via a CRT projector (Marquee 8000, Electrohome) running at 100 Hz and a resolution of 1,152 × 864 pixels. The screen was viewed binocularly at a distance of 114 cm, with the subject's head stabilized by a chin rest. Eye movements were monitored and recorded at 500 Hz with an infrared eye-tracking system (Eye Link II, SR Research). The system was calibrated at the beginning of each session using a 3 × 3 point calibration grid. The data were stored on hard disk for off-line analysis.

Experiment 1: OKAN

Eight subjects participated in this experiment [one male and seven female, 22–30 yr, mean age 24.5 yr (SD 2.5)]. Optokinetic eye movements were recorded while the subjects performed a visual localization task. A detailed description of the experimental paradigm can be found elsewhere (Kaminiarz et al. 2008). In brief, OKAN was induced by means of a random-dot pattern (RDP) consisting of black dots (size: 2.0°, luminance <0.1 cd/m^2, mean density: 0.065 dots/deg^2, unlimited lifetime) moving across a white background (22.1 cd/m^2) at a speed of 80°/s for 15 s. Afterward the screen turned black for several seconds and the reflexive OKAN was recorded.

Experiment 2: OKN

The same eight subjects as in the first experiment and two of the authors participated in this experiment. OKN was recorded while the same RDP as in the OKAN experiment moved across a gray background (12.5 cd/m^2) for 4,000 ms. The RDP velocity was adapted for each subject to match fast-phase amplitudes for OKN and OKAN. The average RDP velocity was 12.4 (SD 2.16) deg/s.

Experiment 3: spontaneous saccades

The same eight subjects as in the first experiment served as observers. Spontaneous saccades were recorded while subjects performed a localization task. In sessions with background illumination subjects freely viewed a homogeneous gray (luminance 12.5 cd/m^2) screen for 4,000 ms. After 3,500 ms a localization target was presented. At the end of the trial a ruler was presented and the trial ended once the subject entered the perceived position on the keyboard. In the remaining sessions, subjects freely viewed a white (luminance 22.1 cd/m^2) screen for 3,000 ms. Thereafter the screen turned black for another 3,000 ms (luminance <0.01 cd/m^2). The target was flashed 2,500 ms after the luminance change. The perceptual data from this study were recently published (Kaminiarz et al. 2008).

Experiment 4: visually guided saccades

Seven subjects, five of whom also participated in the experiments described earlier, and two of the authors served as observers [one male and six female, 22–31 yr, mean age 26.1 yr (SD 4)].

Each trial started with subjects fixating a central green fixation target for 1,000 ms. Afterward the target jumped purely horizontally to the left or right. Five different step amplitudes were used (1.5, 3, 4.5, 6, and 7.5°). Two different backgrounds were used in different sessions. For comparison with OKN fast phases a moving RDP with identical spatial properties as in the OKN experiment served as background (Fig. 1*A*). The RDP moved either left- or rightward at 10°/s throughout the trial. Saccades could be either in the same or in the opposite direction as the background motion. Accordingly subjects could not anticipate the direction of the upcoming saccade. A black background was used to control for a possible influence of background characteristics on the main sequence (Fig. 1*B*). Subjects were instructed to follow the target as fast and as accurately as possible by an appropriate eye movement.

Data analysis

Data were analyzed using Matlab R2007b (The MathWorks) and SigmaStat 3.10 (Systat Software).

Eye-position data for all trials were inspected off-line. Trials were excluded from further analysis if *1*) fast phases/saccades were contaminated by (partially suppressed) blinks that had not been detected automatically (all experiments), *2*) subjects did not perform systematic OKN/OKAN (OKN/OKAN trials only), or *3*) a saccade not directed toward the target was executed in the analyzed time window (see following text; experiment on visually guided saccades only). The first 500 ms of eye movement data recorded on OKAN, OKN, and spontaneous saccade trials were discarded since we cannot exclude that the onset (OKN and spontaneous saccades with background illumination) or the change of the stimulus (OKAN and spontaneous saccades in darkness) influenced the eye movements. Additionally, all eye movements after presentation of the localization target were not considered for further analysis. For the experiment on visually guided saccades only the first saccade in a time window from 100 to 400 ms after the target step was analyzed.

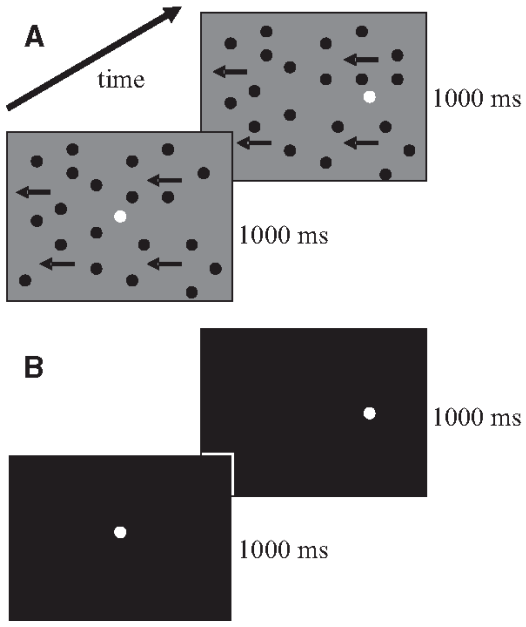

FIG. 1. Illustration of the reflexive saccade paradigm. Each trial started with subjects fixating a central target for 1,000 ms. Then the target jumped either to the left or to the right (±1.5, 3, 4.5, 6, and 7.5°) and remained at the new position for another 1,000 ms. Two different types of background were used on different sessions. During background motion sessions (*A*) a random-dot pattern (RDP) consisting of black dots on a gray background was moving at 10°/s, either in the same or the opposite direction as the target step. On sessions without background motion (*B*) a uniform black background was used.

Saccade detection

Eye velocity was derived from unfiltered eye position data by differentiation. Saccades were detected using a flexible velocity criterion. Mean eye velocity was calculated in a 40-ms time window (v_{mean}). Whenever the eye moved faster than v_{mean} + 24°/s for three consecutive samples a saccade onset was detected. Saccade offset was detected when eye velocity dropped below the threshold for three consecutive samples.

Correction for slow eye movement components

Whereas earlier work suggested that fast and slow eye movement components do not add up when saccades are executed during pursuit (Carpenter 1988) some newer studies proposed that slow and fast eye movement components could be added during saccades to moving targets (Blohm et al. 2003; de Brouwer et al. 2002). Since during steady state OKN/OKAN fast phases are always temporally surrounded by slow eye movements we removed slow eye movement components from the eye-velocity traces. To do so we first determined the mean eye velocity in time windows before (−50 to −10 ms) and after (10 to 50 ms) the saccade. Then we performed a linear interpolation for the time in between and subtracted this slow component from the velocity trace. Corrected saccadic/fast-phase peak velocity was calculated from the corrected velocity traces. Corrected saccadic/fast-phase amplitude was calculated by adding the additional change in eye position, which would have resulted from the slow-phase movement during this temporal interval.

Main sequence analysis

Peak velocity and duration of the fast phases/saccades were plotted as a function of their amplitude. The range of fast-phase/saccade amplitudes recorded varied for the different conditions. Lebedev and colleagues (1996) showed that fit parameters are substantially influenced by the amplitude range used, even in the same data set. Therefore we matched the data sets for all comparisons with respect to the fast-phase amplitude. To do so, we calculated the 95% percentiles for the amplitudes of each data set and used the smallest as the maximum amplitude for the comparison. Afterward we fitted power functions to the data using least-squares procedures according to: $y = ax^b$. Power functions were chosen since they are especially well suited for data sets with small amplitudes (Lebedev et al. 1996).

To test for significant differences between conditions at the single-subject level we performed bootstrap analyses and fitted a power function to each of the data sets created by this means. Afterward we calculated the 5% and 95% percentiles of the curves fitted to the bootstrapped data sets. Wilcoxon signed-rank tests were used to compare the parameters of the power functions fitted to the data at the population level for significant differences.

Analysis of velocity traces

Mean velocity traces were computed from individual velocity traces after sorting saccades/fast phases in 1-deg-wide bins according to their amplitude and aligning the individual velocity traces to saccade/fast-phase onset. Only bins that contained at least 10 fast phases/saccades were used for further analysis. From the mean velocity traces we determined the duration of the acceleration and deceleration periods as well as the total duration. The skewness of the velocity traces was calculated as the duration of the acceleration period divided by the total duration of the saccade/fast phase.

RESULTS

In the following we will show main sequence plots (raw data) for only one single subject (the same subject for all plots). For comparison of the effects across subjects we will show the parameters of the power functions fitted to the data.

OKAN versus OKN main sequence

Figure 2 shows duration (*A*) and peak velocity (*B*) for fast phases as a function of fast-phase amplitude during OKAN (black) and OKN (blue) for a single subject. For this subject, OKAN fast phases last longer and reach a lower peak velocity than OKN fast phases of the same amplitude. For the duration versus amplitude relationship this was also the case for the remaining seven subjects. Statistical analysis showed the difference in the scaling factor (*a*) but not the exponent (*b*) of the power function to be significant (*a*: $P = 0.008$; *b*: $P = 0.742$; Wilcoxon signed-rank test) at the population level. Fit parameters for all eight subjects under both conditions are displayed in Fig. 3. The differences between OKAN and OKN concerning the relationship of the peak velocity and amplitude were less consistent (data not shown). Only two subjects exhibited higher peak velocities for OKN fast phases than those for OKAN fast phases; for one subject the opposite was true, whereas the remaining five subjects exhibited no clear difference. Statistics revealed no significant differences in the parameters of the power functions (*a*: $P = 0.148$; *b*: $P = 0.945$; Wilcoxon signed-rank test).

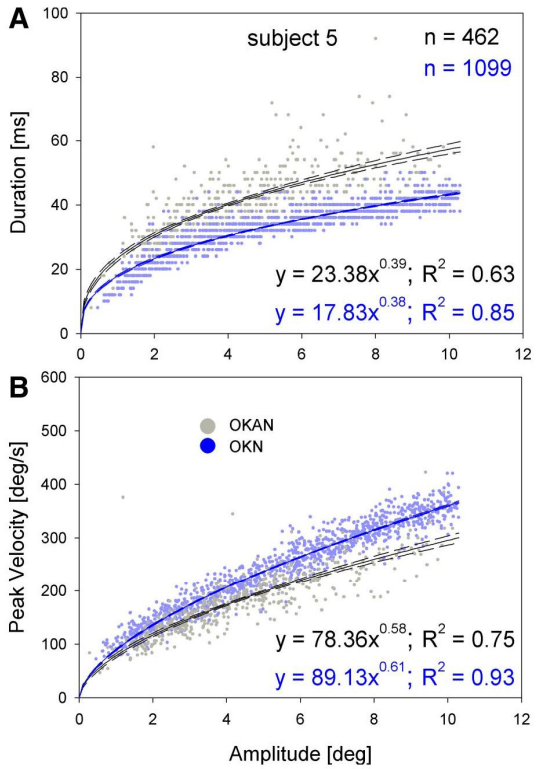

FIG. 2. Comparison of main sequences for optokinetic afternystagmus (OKAN) and optokinetic nystagmus (OKN) fast phases. The graphs show duration/amplitude (*A*) and peak velocity/amplitude (*B*) relationships for OKN (blue) and OKAN (gray, black). OKAN was induced by a RDP moving for 15 s at 80°/s, whereas OKN was induced by an RDP moving at an average speed of 13.6°/s. Dots represent data from individual fast phases, whereas solid lines depict power functions fitted to the data. Dashed lines represent 5% and 95% percentiles (see METHODS for details).

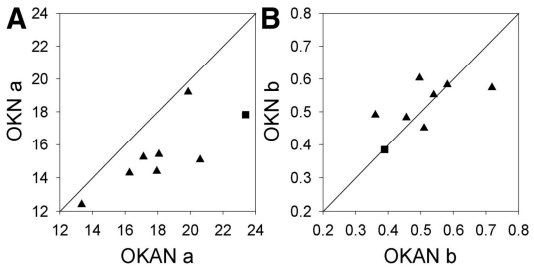

FIG. 3. Comparison of fit parameters *a* and *b* of the power functions fitted to the main sequences for OKAN and OKN fast phases. The square represents data from subject 5, whereas triangles represent individual data points from the remaining subjects. The solid black lines represent the identity lines.

In a next step we compared the mean velocity traces for OKAN and OKN fast phases. In Fig. 4 the mean velocity traces are depicted for the same subject as before. As described in METHODS, these velocity traces were corrected for the velocity of the preceding and the following slow phases by linear interpolation. Solid lines represent data from OKAN fast phases, whereas dashed lines represent data from OKN fast phases. Fast phases of similar amplitudes are color-coded. As already shown in the main sequence plots, OKAN fast phases of a given amplitude are slower and last longer than OKN fast phases of the same amplitude. In addition, Fig. 4 indicates that for small-amplitude OKAN fast phases the peak velocity is reached later than that for OKN fast phases. That means that during OKAN fast phases the eyes accelerate less rapidly compared with OKN fast phases. Seven of the eight subjects showed longer acceleration intervals for small OKAN fast phases compared with OKN fast phases. Next we calculated the skewness (duration of the acceleration period/total duration of the fast phase) of the velocity traces and compared the skewness for OKAN and OKN fast phases. For both OKAN and OKN skewness increased with amplitude. The ratio $OKAN_{skew}/OKN_{skew}$ was 0.93 (0.15 SD), indicating that velocity traces were skewed more strongly for OKAN fast phases.

In the first experiment we demonstrated that OKAN fast phases have a longer duration than that of OKN fast phases. OKAN is performed in total darkness, whereas during OKN a moving, structured background is permanently visible. Since saccade main sequence has been reported to depend on background illumination we asked whether the longer duration of the OKAN fast phases could simply originate from the different lighting conditions in the two experiments. In the literature OKN fast phases have mainly been compared with saccades to visual targets. In contrast, fast phases of OKAN and (stare-) OKN are not directed to a visual target. Therefore we recorded both spontaneous and reflexive saccades in darkness and across a gray background for comparison with OKAN and OKN fast phases.

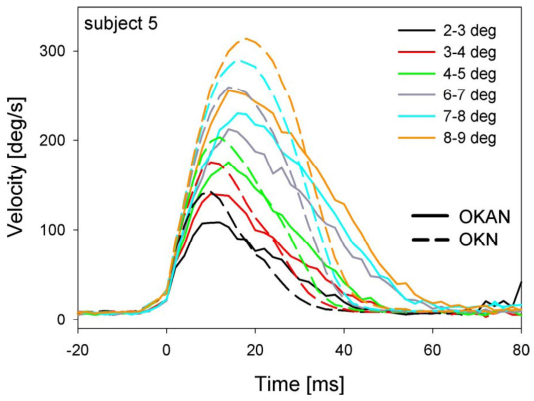

FIG. 4. Average velocity traces of OKAN and OKN fast phases for subject 5. Velocity is plotted against time from fast-phase onset ($t = 0$ ms). Solid lines represent OKAN fast phases, whereas dashed lines represent OKN fast phases. Fast-phase amplitude is color-coded. Each curve represents the mean of ≥10 individual velocity traces.

Spontaneous saccades under different lighting conditions

Figure 5 shows the main sequence plots for the same subject as before. For this subject spontaneous saccades in darkness lasted longer and reached a lower peak velocity than those across a gray background for the considered range of amplitudes. Six of the eight subjects exhibited longer durations during saccades in darkness, whereas the remaining two subjects showed no such difference. Fit parameters for all eight subjects are depicted in Fig. 6. At the population level the difference for the scaling factor just failed to reach significance (*a*: $P = 0.055$; *b*: $P = 0.641$; Wilcoxon signed-rank test). Five of the eight subjects showed higher peak velocities for saccades in darkness. Statistical analysis revealed no significant difference at the population level (*a*: $P = 0.25$; *b*: $P = 0.461$; Wilcoxon signed-rank test).

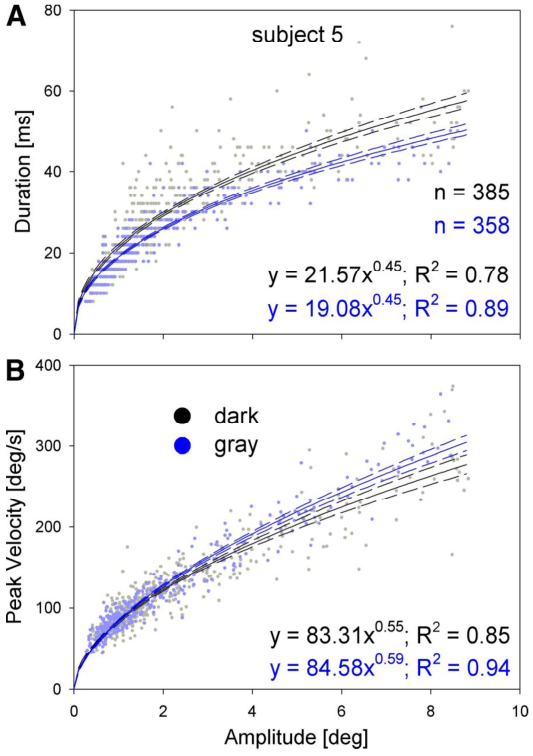

FIG. 5. Main sequence plots for spontaneous saccades across a uniform gray background and in darkness. Data for saccades in darkness are depicted in gray/black; data for saccades on gray background are depicted in blue. Other conventions as in Fig. 2.

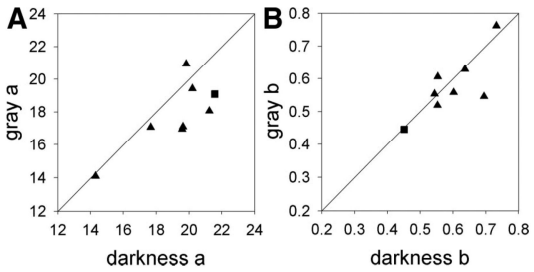

FIG. 6. Comparison of fit parameters for spontaneous saccades on gray background and in darkness. Conventions as in Fig. 3.

Analysis of the velocity traces for OKAN and OKN showed faster acceleration of the eyes during OKN. Given the similarity of the results for spontaneous saccades and OKN/OKAN fast phases so far, we next analyzed the velocity traces for spontaneous saccades. Figure 7 shows the data for the same subject as before. Clearly the acceleration intervals are of similar length under both conditions. The duration of the acceleration intervals differed by <1% for the whole population ($n = 8$), indicating no differences in eye acceleration for spontaneous saccades in different environments. The ratio dark-sac_{skew}/gray-sac_{skew} was 0.94 (0.14 SD), indicating that velocity traces tended to be skewed more strongly for saccades in darkness. This result is analogous to our results for OKAN and OKN fast phases.

Visually guided saccades under different lighting conditions

Four of the seven subjects performing visually guided saccades did not show any significant influence of environmental luminance on the main sequence. For two subjects saccades in darkness had longer durations than saccades across a moving structured background, whereas for the last subject the opposite was the case. At the population level ($n = 7$) fit parameters (Fig. 8) were not significantly different for the duration versus amplitude relationship (*a*: $P = 0.688$; *b*: $P = 0.938$; Wilcoxon signed-rank test) and the peak velocity versus amplitude relationship (*a*: $P = 0.938$; *b*: $P = 0.938$; Wilcoxon signed-rank test). Analysis of velocity traces revealed that on average the acceleration interval lasted 3.2% longer for saccades in darkness. The ratio dark-sac_{skew}/gray-sac_{skew} was 1.02 (0.08 SD), indicating similarly skewed velocity traces for visually guided saccades under different lighting conditions.

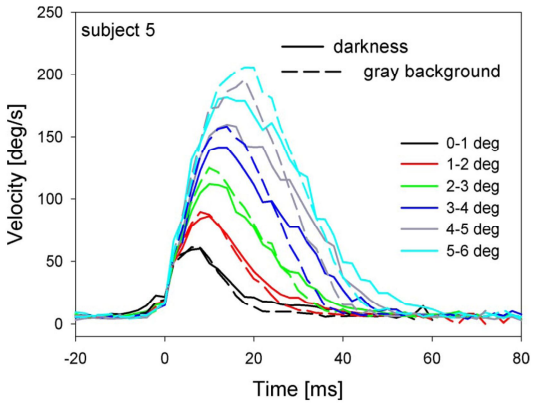

FIG. 7. Average velocity traces of spontaneous saccades across uniform gray background and in darkness. Solid lines are velocity traces for saccades in darkness, whereas dashed lines represent data from saccades across a gray background. Other conventions as in Fig. 4.

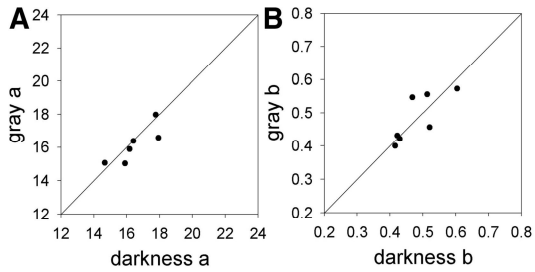

FIG. 8. Comparison of fit parameters for reflexive saccades on gray background and in darkness. Circles represent individual data points. Other conventions as in Fig. 3.

OKN/OKAN versus spontaneous saccades

After having shown that spontaneous saccades are influenced by the background characteristics similarly to OKN/OKAN fast phases we directly compared the two types of eye movements. Comparison of the main sequences for OKN fast phases and spontaneous saccades across a gray background revealed longer durations for spontaneous saccades in all eight subjects (see Fig. 9, *A* and *B* for fit parameters). For seven subjects spontaneous saccades had lower peak velocities. Group analysis revealed significant differences for both duration versus amplitude and peak velocity versus amplitude relationships (duration vs. amplitude: *a*: $P = 0.008$; *b*: $P = 0.195$; peak velocity vs. amplitude: *a*: $P = 0.008$; *b*: $P = 0.039$; Wilcoxon signed-rank test).

Comparison of OKAN fast phases and spontaneous saccades in darkness revealed longer durations for spontaneous saccades in four of the eight subjects. Another three subjects did not show any difference and for the remaining subject fit quality

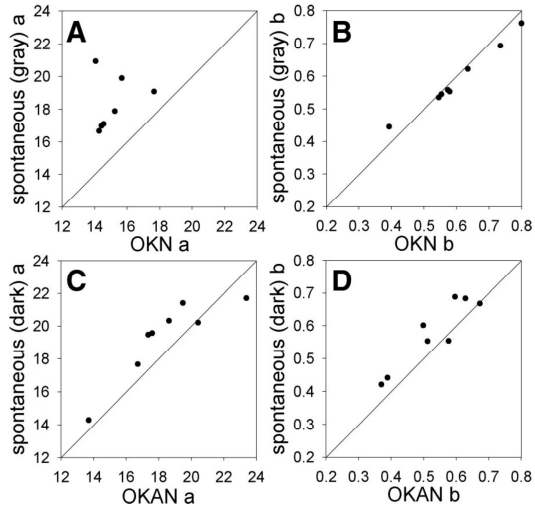

FIG. 9. Comparison of fit parameters for spontaneous saccades and fast phases. *Top row*: comparison of OKN fast phases and spontaneous saccades across a gray background. *Bottom row*: comparison of OKAN fast phases and spontaneous saccades in darkness. Circles represent individual data points. Other conventions as in Fig. 3.

was insufficient (Fig. 9, *C* and *D*). The signed-rank test performed on the seven subjects whose data allowed a curve fit of sufficient quality showed a significant difference for the exponent and a tendency for the scaling factor (*a*: $P = 0.078$; *b*: $P = 0.039$; Wilcoxon signed-rank test). Three of the eight subjects had lower peak velocities for spontaneous saccades than for fast phases. In the remaining four subjects we observed no significant difference. At the population level fit parameters were not significantly different (*a*: $P = 0.148$; *b*: $P = 0.742$; Wilcoxon signed-rank test).

Taken together spontaneous saccades and fast phases performed in luminance-matched environments are not on the same main sequence. Rather, spontaneous saccades typically last longer and have lower peak velocities.

OKN/OKAN versus visually guided saccades

For three of the seven subjects OKN fast phases had longer durations and lower peak velocities than those of visually guided saccades. One subject showed no difference, either for duration or for peak velocity. For the remaining two subjects OKN fast phases lasted slightly shorter than visually guided saccades (Fig. 10, *A* and *B*), whereas the peak velocities were similar. Population analysis ($n = 7$) revealed no significant difference for the scaling factor. The exponent was different for both conditions in the duration versus amplitude relationship (*a*: $P = 0.813$; *b*: $P = 0.031$; Wilcoxon signed-rank test) and showed a tendency for the peak velocity versus amplitude relationship (*a*: $P = 0.297$; *b*: $P = 0.078$; Wilcoxon signed-rank test).

Fast phases of OKAN had longer durations than those of visually guided saccades on a black background in all five subjects (Fig. 10, *C* and *D*). In two subjects we also observed higher peak velocities for saccades. Both effects were not significant at the population level (duration–amplitude relationship: *a*: $P = 0.125$; *b*: $P = 0.625$; peak velocity–amplitude relationship: *a*: $P = 0.438$; *b*: $P = 0.188$; Wilcoxon signed-rank tests).

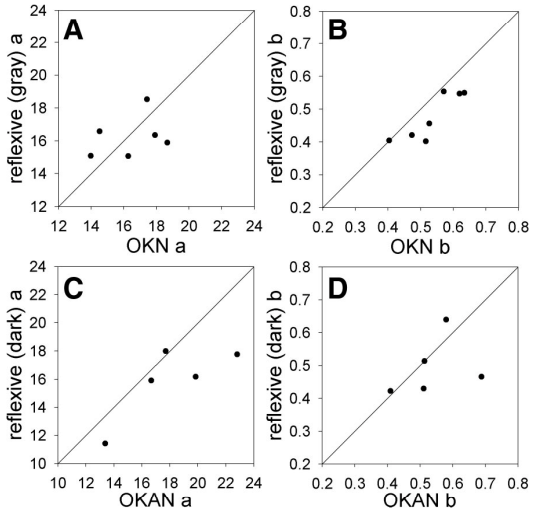

FIG. 10. Comparison of fit parameters for reflexive saccades and fast phases. *Top row*: comparison of OKN fast phases and reflexive saccades across a gray background. *Bottom row*: comparison of OKAN fast phases and reflexive saccades in darkness. Circles represent individual data points. Other conventions as in Fig. 3.

Effects of correction for slow-phase velocity

Since we do not know for certain whether eye velocity during fast phases of OKN is modified by the slow-phase eye velocity we finally tested to what extent the correction for the slow-phase eye velocity influences the data and whether the observed effect can still be observed without correction. For OKAN and OKN correction for slow-phase eye velocity on average resulted in higher peak velocities and shorter durations. At the population level statistical analysis revealed significant differences between parameters of the power functions fitted to the data for corrected and uncorrected data for fast phases of OKN (duration vs. amplitude: *a*: $P = 0.008$; *b*: $P = 0.008$; peak velocity vs. amplitude: *a*: $P = 0.016$; *b*: $P = 0.008$). For OKAN this difference did not reach significance (duration vs. amplitude: *a*: $P = 0.25$; *b*: $P = 0.74$; peak velocity vs. amplitude: *a*: $P = 0.95$; *b*: $P = 0.55$). The reason that we observed no significant effect for OKAN is probably that slow-phase velocities were about twice as high during OKN compared with that during OKAN. Since the effect of slow-phase correction differs between conditions we next tested whether the observed difference between OKAN and OKN can be observed in the uncorrected data set.

Statistical analysis showed the difference in the scaling factor but not the exponent of the power function to be significant for the duration versus amplitude relationship (*a*: $P = 0.039$; *b*: $P = 0.688$; Wilcoxon signed-rank test) at the population level. For the peak velocity versus amplitude relationship statistics revealed no significant differences in the parameters of the power functions (*a*: $P = 0.313$; *b*: $P = 0.945$; Wilcoxon signed-rank test). This is the same result as observed for the corrected data; therefore the observed difference between the main sequences of OKAN and OKN is not an artifact of correction for slow-phase eye velocity. Similarly we analyzed the data without correction for all other experiments. Although for single subjects results were sometimes different for corrected and uncorrected data sets, the results were the same at the population level for all experiments (data not shown).

DISCUSSION

We have tested and compared various types of saccades and fast phases in the same human subjects. Our data clearly show that fast phases of OKAN and OKN are not on the same main sequence. Instead, OKAN fast phases lasted longer and had lower peak velocities compared with those of OKN fast phases. Similarly, spontaneous saccades on a black background lasted longer and had lower peak velocities than did spontaneous saccades in darkness. Although for spontaneous saccades this effect was very robust, it was absent in most subjects for saccades toward a visual target and, if present, it was much weaker.

Visually guided saccades

The main sequence of visually guided saccades has been the topic of various studies. In some studies power functions have been used to describe the main sequence. Comparing our

results to those of Lebedev et al. (1996) and Garbutt et al. (2003b) we see that the exponents of the power functions are similar in all three studies. However, the factors denoting the duration/peak velocity of a 1° saccade indicate higher peak velocities and shorter durations in our study. One likely reason could be the different techniques used for measuring eye position. Lebedev et al. (1996) used electrooculography, whereas Garbutt et al. (2003b) used the scleral search coil technique, both of which were reported to underestimate peak velocity (Boghen et al. 1974; Byford 1962; Frens and van der Geest 2002). Two other likely reasons are that we *1*) did not filter our eye data prior to analysis and *2*) used a different algorithm to detect saccades. Since we are mainly interested in main sequence differences between experimental conditions measured in the same setup and analyzed with identical techniques in the same human subjects these differences are negligible. The main sequence of visually guided saccades was weakly influenced by the environmental luminance in one third of our subjects. This reflects the heterogeneous results reported in the literature. Although some authors reported faster saccades in the light (Henriksson et al. 1980; Riggs et al. 1974; Sharpe et al. 1975), others found no influence of background luminance (Becker and Fuchs 1969; Ilg et al. 2006).

Spontaneous saccades

We found spontaneous saccades to be slower than visually guided saccades under (nearly) identical luminance conditions. The main sequence of spontaneous saccades depended heavily on background illumination. We observed lower peak velocities and longer durations for spontaneous saccades in darkness. This is in accordance with studies demonstrating lower peak velocities and longer durations for voluntary saccades in darkness (Barton and Sharpe 1997; Riggs et al. 1974; Sharpe et al. 1975). However, the results of some of the studies have to be handled with care because the authors did not compare voluntary saccades in light and darkness, but instead compared voluntary saccades directed toward a visual target, with memory-guided saccades in total darkness (Henriksson et al. 1980; Sharpe et al. 1975), which have been shown to be significantly slower (Smit et al. 1987).

Comparison of OKN and OKAN fast phases

OKAN fast phases have a longer duration compared with that of OKN fast phases, lower peak velocities, slower acceleration, and stronger skewness. For both eye movements skewness increased with amplitude, which has also been shown for reflexive saccades (Smit et al. 1987). During OKN a moving RDP is constantly visible, whereas OKAN is performed in the absence of visual stimulation. Although it seems likely that the RDP causes the difference it is not possible to determine which aspect of the stimulus causes the difference. Two likely candidates are the difference in environmental luminance and the motion per se. We showed that spontaneous saccades are heavily influenced by the background luminance. Spontaneous saccades and fast phases of OKAN and (stare-) nystagmus are not deliberately directed to a visual target and are similarly influenced by cortical lesions (Tusa et al. 1986). Therefore the main sequence difference could be simply caused by the luminance difference.

Comparison of OKN and visually guided saccades

We observed higher peak velocities for saccades in half of our subjects. In the literature OKN fast phases have been compared with several types of saccadic eye movements. Garbutt and colleagues (2001) found OKN fast phases to be of slightly longer duration and to have lower peak velocity than those of reflexive saccades. Voluntary saccades have been reported to be faster than OKN with respect to peak velocity (Garbutt et al. 2003a; Henriksson et al. 1980) and average velocity (Gavilan and Gavilan 1984). Other authors reported similar peak velocities for OKN fast phases and voluntary saccades (Mackensen and Schumacher 1960; Sharpe et al. 1975). Therefore our data are in accordance with the literature.

As previously discussed by Garbutt (2001) one likely reason for the discrepancies in the literature is that various types of saccades were used for comparison, which have been shown to differ with respect to their main sequence. Another likely cause is the different background characteristics during OKN and saccades in some of the studies. For example, Henriksson and colleagues (1980) compared OKN fast phases with voluntary saccades performed in darkness. In our study we kept background properties identical and still observed significantly longer durations for fast phases in some subjects. As mentioned earlier, fast phases of stare-nystagmus are not deliberately directed toward a visual target, whereas visually guided saccades are. We did not use limited lifetime RDPs in our study. Therefore subjects presumably performed a mixture of look- and stare-nystagmus, adding a voluntary component to the fast phase. Under the assumption that the main sequence depends on the intentionality of the performed eye movement we expect (nearly) identical main sequences for look-nystagmus and visually guided saccades, whereas fast phases of pure stare-nystagmus, evoked by limited lifetime dots, should be slower and last longer than visually guided saccades.

Comparison of OKN and spontaneous saccades

Spontaneous saccades had longer duration and lower peak velocity compared with those of OKN fast phases. We compared spontaneous saccades across a uniform gray background and OKN fast phases. During OKN the background was obviously *not* uniform but instead an RDP moved across the screen. Since we showed that the main sequence of spontaneous saccades depends on background illumination the two conditions are therefore not completely identical. We nevertheless decided to use a uniform background because using the same structured background as that during OKN would have caused subjects to perform visually guided saccades between the elements of the RDP.

Neuronal basis of the observed effects

Saccades and fast phases are both generated by the same premotor network located in the brain stem (Leigh and Zee 2006). Burst neurons in the paramedian pontine reticular formation show identical firing characteristics before saccades and fast phases of OKN and VOR (Cohen and Henn 1972; Henn and Cohen 1976). Omnipause neurons stop firing previous to fast phases and saccades (Cohen and Henn 1972), whereas electrical stimulation inhibits the execution of saccades and VOR fast phases (Westheimer and Blair 1973).

Recordings from single units in the vestibular nucleus (VN) of the rhesus monkey demonstrated that neural activity and slow-phase activity are correlated during OKN (Waespe and Henn 1977a) and OKAN (Waespe and Henn 1977b). Boyle et al. (1985) demonstrated that neuronal activity reflects the late component of OKN but not the early component. According to these results the VN is assumed to be the neural substrate of the velocity storage mechanism. Interestingly, saccade-related activity has also been reported for VN neurons (Boyle et al. 1985; Waespe et al. 1992). Studies using single-cell recordings reported neurons in monkey nucleus of the optic tract (NOT) being activated during OKN slow phases. Activity returned to the spontaneous level during OKAN and shortly after fast phases (Ilg and Hoffmann 1996; Mustari and Fuchs 1990).

After extensive unilateral cerebral cortical lesions OKN, OKAN, and spontaneous saccades could still be elicited, whereas reflexive and voluntary saccades directed to the contralateral hemifield were abolished (Tusa et al. 1986). Interestingly, peak velocity of OKN fast phases, OKAN fast phases, and spontaneous saccades was reduced similarly after the lesion. Single-cell recordings revealed OKN- but not OKAN-related activity in the medial temporal area (Bremmer et al. 2002; Ilg 1997). For both areas activity was not related to the execution of fast phases.

The cortical network underlying the execution of OKN in humans has been investigated using functional imaging (Bucher et al. 1997; Dieterich et al. 1998, 2003; Galati et al. 1999; Konen et al. 2005). The activated network is reminiscent of the networks activated during smooth-pursuit eye movement (SPEM) and saccades (Dieterich and Brandt 2000; Petit and Haxby 1999). One study directly comparing OKN and SPEM found largely overlapping patterns of activation, especially with respect to the oculomotor regions (Konen et al. 2005). Interestingly these regions were activated only in subjects performing a combination of look- and stare-nystagmus. In subjects performing pure stare-nystagmus no activation in frontal eye field (FEF), supplementary eye field, and the ventral intraparietal area could be observed. This finding was confirmed in a recent study comparing activation patterns during stare-nystagmus and combined look- and stare-nystagmus (Schraa-Tam et al. 2008). Saccadic activity within FEF has also been reported to depend on the intentionality of the executed saccade. Although FEF is strongly activated during voluntary saccades (antisaccades), it is less active during visually guided saccades (Gaymard et al. 1998; Mort et al. 2003; Pierrot-Deseilligny et al. 2004). We therefore hypothesize that FEF is part of the neural network causing higher peak velocities and shorter durations for voluntary fast eye movements compared with those of unintentional fast eye movements. FEF is also active during pursuit. Due to its low temporal resolution, functional magnetic resonance imaging (fMRI) cannot differentiate between activity related to slow and fast phases. Therefore differences could also be related to the execution of the slow phase of the eye movement.

Phylogenetic/ontogenetic aspects of OKN

Our results emphasize the importance of the cortical influence on OKN in humans. In adult cats, nonhuman primates, and probably humans input to the NOT is dominated by the cortex. In all three species OKN is symmetrical—i.e., if only one eye is stimulated, OKN is equally strong for nasal and temporal stimulation. In contrast, OKN is asymmetrical in species like rabbits and rats, where cortical input is less dominant or absent (Carpenter 1988). Furthermore, directional asymmetries can be observed in newborn humans, monkeys, and kittens. It has been hypothesized that after birth the NOT receives retinal input only and that, while cortical input increases, OKN becomes more symmetrical (Hoffmann 1989). Taking into account our results one could hypothesize that in humans, monkeys, and cats the dynamics of OKN fast phases should change with increasing cortical influence in the first months after birth.

Conclusions

We showed that OKAN and OKN differ with respect to their main sequence. This could be caused by the different environmental conditions or by (partially) different neural networks underlying the execution of both types of eye movements, which have already been proposed to be the origin of the differences between OKN and OKAN slow phases (Cohen et al. 1977). Knowledge about the cortical network underlying the execution of OKN/OKAN is still rather limited. This is particularly problematic since OKN fast phases are routinely used as a diagnostic tool (Garbutt et al. 2001, 2003a; Leigh and Zee 2006). Since fMRI cannot differentiate between activity related to slow and fast phases, electrophysiological studies in cortical areas revealed to be active during OKN should be performed to provide the required information.

GRANTS

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Task Influences on the Dynamic Properties of Fast Eye Movements

Task Influences on the Dynamic Properties of Fast Eye Movements

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Abstract
It is widely debated whether fast-phases of the reflexive optokinetic nystagmus (OKN) share properties with another class of fast eye movements, visually guided saccades. Conclusions drawn from previous studies were complicated by the fact that a subject's task influences the exact type of OKN: stare- vs. look nystagmus. With our current study we set out to determine in the same subjects the exact dynamic properties (main sequence) of various forms of fast eye movements. We recorded fast-phases of look- and stare-nystagmus as well as visually guided saccades. Our data clearly show that fast-phases of look- and stare-nystagmus differ with respect to their main sequence. Fast-phases of stare-nystagmus were characterized by their lower peak-velocities and longer durations as compared to fast-phases of look-nystagmus. Furthermore we found no differences between fast phases of stare-nystagmus evoked with limited and unlimited dot-lifetime. Visually guided saccades were on the same main-sequence as fast-phases of look-nystagmus, while they had higher peak-velocities and shorter durations than fast-phases of stare-nystagmus.
Our data underline the critical role of behavioral tasks (e.g. reflexive vs. intentional) for the exact spatio-temporal characteristics of fast eye movements.

Keywords: main sequence, optokinesis, nystagmus, saccade

Introduction

Fast eye movements can be characterized by a tight relationship between several of their kinematic parameters. Duration and peak velocity increase with amplitude. This relationship has first been described for voluntary saccades and was termed the '*main sequence*' (Bahill et al., 1975). Since then the existence of a main sequence has been shown for different types of saccades including: reflexive saccades (Baloh et al., 1975), memory guided saccades (Becker and Fuchs, 1969;Smit et al., 1987), antisaccades (Smit et al., 1987;Van Gelder et al., 1997), and catch-up saccades (Van Gelder et al., 1997). However, the individual main sequences for different kinds of saccades show considerable variability. For example, visually guided saccades are faster than memory-guided saccades and antisaccades of identical amplitude (Smit et al., 1987). Concerning other factors like saccade direction the reports in the literature are less consistent. While some studies reported centripetal saccades to be faster then centrifugal ones (Hyde, 1959;Pelisson and Prablanc, 1988;Becker and Jürgens, 1990), others reported the opposite (Garbutt et al., 2003a;Robinson, 1964), described differences only for large amplitudes in a subset of subjects (Boghen et al., 1974) or found no difference at all (Bahill et al., 1975). Another group of fast eye movements which have been shown to adhere to a main sequence are the fast phases of different kinds of reflexive, compensatory eye movements (Mackensen G. and Schumacher J., 1960;Garbutt et al., 2001;Garbutt et al., 2003a;Ron et al., 1972;Sharpe et al., 1975;Gavilan and Gavilan, 1984). Studies comparing saccades and fast-phases of the vestibulo-ocular reflex

(VOR) reported identical or very similar main sequences (Ron et al., 1972;Sharpe et al., 1975;Guitton and Mandl, 1980), but lower velocities for the VOR have also been reported (Gavilan and Gavilan, 1984). Fast phases of optokinetic nystagmus (OKN) have either been reported to follow the same main sequence as visually guided saccades (Mackensen G. and Schumacher J., 1960;Sharpe et al., 1975;Kaminiarz et al., 2009a) or to be slower than saccades (Garbutt et al., 2001;Garbutt et al., 2003a;Henriksson et al., 1980;Gavilan and Gavilan, 1984). Aside from the type of saccade performed factors like fatigue can influence the main sequence (Bahill and Stark, 1975;Riggs et al., 1974). Depending on the subjects' attitude regarding the task two kinds of OKN can be distinguished (Ter Braak, 1936). When subjects watch the stimulus attentively without intentionally foveating any element a so called stare-nystagmus can be observed, which is characterized by small fast-phase amplitudes and high fast-phase frequencies. If subjects intentionally follow single elements of the stimulus they perform a so-called look-nystagmus which is typically characterized by a low frequency but large amplitude of fast-phases. The slow-phases of look-nystagmus have often been linked to voluntary pursuit, but to our best knowledge the fast-phases occurring during the different types of OKN have not been classified.

In this study we aimed at disentangling the relative influence of task/cortical control and input/stimulus characteristics on the main sequence by comparing in individual subjects the main sequences of stare-nystagmus, look-nystagmus, and visually guided saccades. Preliminary results have been published in abstract form (Kaminiarz et al., 2009b).

Methods

Subjects

In total, 18 healthy subjects (6 male and 12 female, 22-30 years, mean age 26.3 (SD 4.7)) participated in the experiments. All had normal or corrected to normal vision and gave informed written consent. All procedures used in this study conformed to the declaration of Helsinki.

Experimental procedure

All experiments were carried out in a dark, sound attenuated chamber. Eye movements were monitored and recorded at 500 Hz with an infrared eye tracking system (Eye Link II, SR Research). The system was calibrated at the beginning of each session and a so-called drift correction (compensating for potentially occurring small drifts of the eye position signal) was performed before every third (visually guided saccades) or before each trial (other experiments). The subjects' heads were stabilized by a chin rest with their eyes leveled at the center of the screen.

Visual stimuli were projected onto a tangent screen (70° × 55°) via a CRT projector (Marquee 8000, Electrohome) running at 100 Hz and a resolution of 1152 x 864 pixels. The screen was viewed binocularly at a distance of 114 cm.

OKN

A random dot pattern (RDP) consisting of black dots (size: 2.0 deg, luminance < 0.1 cd/m^2, mean density: 0.065 dots/deg^2) moving across a white background (22.1 cd/m^2) for 4 seconds was used to elicit OKN. In the main experiment dots moved at 10°/s while speeds of 10, 15 and 20°/s were used in a second experiment on the interaction of slow and fast eye movements. Dot lifetime was either infinite or limited to 80 ms. Each dot that reached its maximum lifetime was displaced to a new, randomly assigned position on the screen. During

sessions with unlimited dot lifetime subjects were either instructed to intentionally follow single dots with their eyes (look-nystagmus) or to watch the screen attentively without tracking individual dots (stare-nystagmus).

Visually guided saccades

Each trial started with subjects fixating a central green fixation target for 1000 ms. Afterwards the target jumped purely horizontally to the left or right. Five different step amplitudes were used (1.5, 3, 4.5, 6, and 7.5 deg). Since it has been reported that background characteristics can influence the main sequence (Henriksson et al., 1980) we used a moving RDP with identical spatial properties as in the large field OKN experiment served as background. The RDP moved either left- or rightwards at 10 deg/s throughout the trial. Saccades could be either in the same (Fig 1a) or in the opposite direction (Fig 1b) as the background motion. Accordingly subjects could not anticipate the direction of the upcoming saccade. Subjects were instructed to follow the target as fast and accurately as possible by an appropriate eye movement.

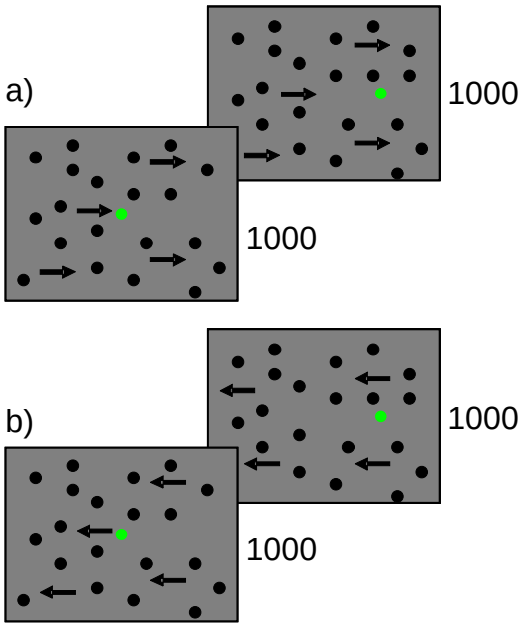

Figure 1. Illustration of the saccade-paradigm. Each trial started with subjects fixating a central target for 1000ms. Then the target jumped either to the left or right (±1.5, 3, 4.5, 6, and 7.5 deg) and remained at the new position for another 1000ms. A Random Dot Pattern (RDP) consisting of black dots on a gray background was moving at 10deg/s either in the same (a) or the opposite (b) direction as the target step.

Data analysis

Data was analyzed using Matlab R2007b (The MathWorks, Inc.) and SigmaStat 3.10 (Systat Software, Inc.).

Eye-position data for all trials were inspected offline. Trials were excluded from further analysis if (i) fast-phases/saccades were contaminated by (partially suppressed) blinks which had not been detected automatically, (ii) subjects did not perform systematic OKN, or (iii) a saccade not directed towards the target was executed in the analyzed time window (experiment on visually guided saccades only). In total 22.6% (ranging from 1.7% to 80.7% for different subjects) of the trials had to be excluded from further analysis.

The first 500 ms of eye movement data recorded on OKN-trials were discarded since we cannot exclude that the stimulus-onset influences fast eye movement characteristics. For the experiments on visually guided saccades only the first saccade in a time window from 100 to 500 ms after the target step was analyzed.

Saccade detection

Eye velocity was derived from unfiltered eye position data by discrete differentiation of the raw data set which had been sampled at 500 Hz. In other words: the speed of sample n was computed as the difference of position samples pos_{n+1} and pos_n ; this difference was then divided by the temporal difference of these two samples $t_{n+1} - t_n$ = 2ms: $v_n = \frac{pos_{n+1} - pos_n}{t_{n+1} - t_n}$ Saccades were detected using a flexible velocity criterion. Mean horizontal eye velocity was calculated for a 40 ms time window (v_{mean}). Whenever eye velocity deviated from v_{mean} (calculated for the preceding 40ms) by more than 24 deg/s for three

consecutive samples (i.e. 6 ms) a saccade onset was detected. Saccade offset was detected when eye-velocity dropped below the same threshold for three consecutive samples.

Main-sequence analysis

Peak-velocity and duration of the fast eye movements were plotted as a function of their amplitude. The range of fast-phase/saccade amplitudes recorded varied for the different conditions. Lebedev and colleagues (1996) showed that fit-parameters are substantially influenced by the amplitude-range used, even in the same dataset. Therefore we matched the datasets for all comparisons with respect to the fast-phase amplitude. To do so, we calculated the 95 percentiles for the amplitudes of each dataset and used the smallest of them as the maximum amplitude for the comparison. We then fitted power functions to the data using least squares procedures according to: $y = ax^b$. Power functions were chosen since they are especially well suited for datasets with small amplitudes (Lebedev et al., 1996).

To test for significant differences between conditions at the single subject level we performed a bootstrap analysis and fitted a power function to each of the new data sets created by this means. Afterwards we calculated the 5% and 95% percentiles of the curves fitted to the bootstrapped datasets. Wilcoxon Signed Rank Tests were used to compare the parameters of the power functions fitted to the data at the population level for significant differences.

Analysis of velocity traces

Mean velocity traces were computed from individual velocity traces after sorting saccades/fast-phases in 1 deg wide bins according to their amplitude and aligning the individual velocity traces to saccade/fast-phase onset. Only bins that contained at least ten fast-phases/saccades were used for further analysis. From the mean velocity traces we determined the duration of the acceleration and deceleration periods as well as the total duration. The skewness of the velocity traces was calculated as the duration of the acceleration period divided by the total duration of the saccade/fast-phase.

Results

Fast phases of look and stare-nystagmus (unlimited dot lifetime)

The slow-phases of look-nystagmus are often compared to smooth pursuit eye movements. In addition, fast-phases during look-nystagmus aim at specific elements of the moving stimulus and hence are similar to visually guided saccades. Therefore we analyzed fast-phases of both stare- and look-nystagmus since the grade of reflexiveness of these eye movements varies under otherwise

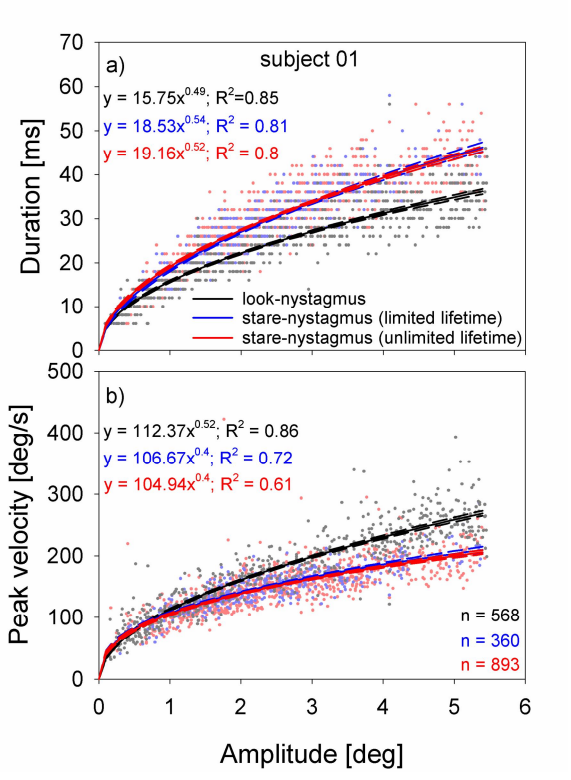

Figure 2. Comparison of main-sequences for look- and stare-nystagmus. The graphs show duration vs. amplitude (a) and peak-velocity vs. amplitude (b) relationships for stare- (red symbols: unlimited dot lifetime, blue symbols: limited dot lifetime) and look-nystagmus (gray, black). Dots represent data from individual fast-phases while solid lines depict power functions fitted to the data.

identical stimulus conditions due to the subjects' task.

The amplitudes of fast-phases executed during look- and stare-nystagmus trials differed considerably. The 95 percentiles used for amplitude matching had a range of 13.7 deg (2.4 SD) for look-nystagmus, 9.23 deg (1.7 SD) for stare-nystagmus, and 6.8 (1.6 SD) for stare-nystagmus evoked with limited dot lifetime respectively. During stare-nystagmus (unlimited dot lifetime) mean eye-position, averaged across subjects, was shifted 7.6 deg (5.0 SD) opposite to the direction of the slow-phase ('shift of the beating field'). This shift decreased to 4.1 deg (3.5 SD) during stare-nystagmus evoked with limited dot lifetime. During look-nystagmus we observed a shift in direction of the slow-phase component (3.1 deg (6.4 SD)). Slow-phase gain (eye-velocity/ RDP-velocity) was 1.0 (0.03 SD) for look-nystagmus, 0.90 (0.06 SD) for stare-nystagmus with unlimited dot-lifetime, and 0.60 (0.13 SD) for stare-nystagmus with limited dot lifetime.

Figure 2 shows duration (a) and peak-velocity (b) for fast-phases as a function of fast-phase amplitude during look- (black symbols) and stare-nystagmus (red symbols: unlimited dot lifetime, blue symbols: limited dot lifetime) for a representative subject. As can be clearly seen, stare-nystagmus fast-phases lasted longer and reached a lower peak-velocity than look-nystagmus fast-phases of identical amplitude. This functional relationship was found in all eight subjects. Statistical analysis proved the difference in the scaling-factor but not the exponent of the power function to be significant for the duration vs. amplitude relationship and the peak-velocity vs. amplitude relationship (duration vs. amplitude: a: $p = 0.008$; b: $p = 0.148$; peak-velocity vs. amplitude: a: $p = 0.008$; b: $p = 0.25$; Wilcoxon Signed Rank Test). Fit-parameters for all subjects under both conditions (look-nystagmus and stare-nystagmus with unlimited lifetime) are displayed in Figure 3.

In a next step we compared the mean velocity-traces for fast-phases of look- and stare-nystagmus (unlimited dot lifetime). In Figure 4 these mean velocity-traces are depicted for the same subject as before. Solid lines represent data from look-nystagmus fast-phases while dashed lines represent data from

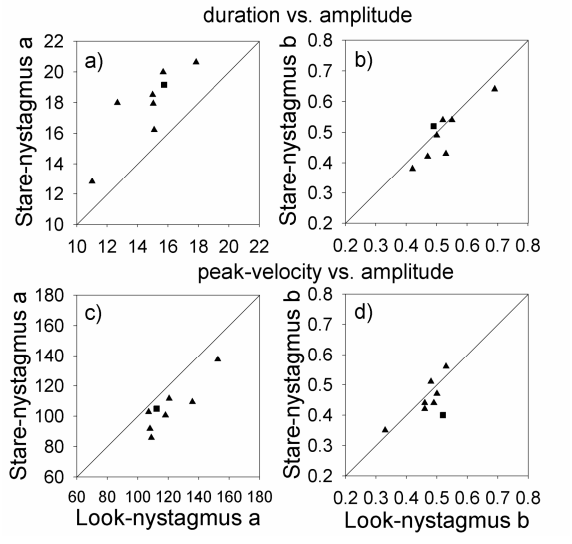

Figure 3. Comparison of fit-parameters scaling factor (a) and exponent (b) of the power-functions fitted to the main sequences for fast-phases of look- and stare-nystagmus (unlimited dot lifetime). The square represents data from subject 01 (whose data were shown also in Figure 2) while triangles represent data points for all other subjects. The solid black lines represent the identity-lines.

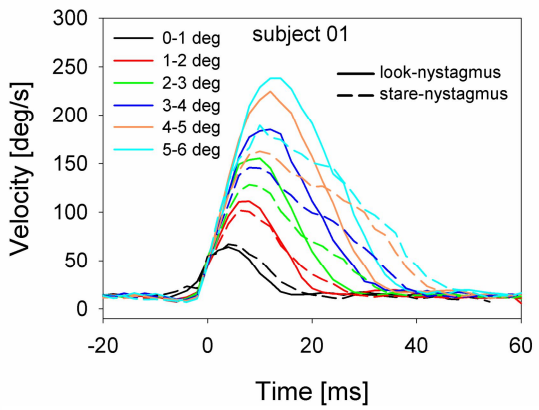

Figure 4. Average velocity traces for fast-phases of look- and stare-nystagmus (unlimited dot lifetime) for subject 01. Velocity is plotted against time from fast-phase onset (t = 0 ms). Solid lines represent look-nystagmus fast-phases while dashed lines represent stare-nystagmus fast-phases. Fast-phase amplitude is color coded. Each curve represents the mean of at least 10 individual velocity traces.

stare-nystagmus (unlimited dot lifetime) fast-phases. Fast-phases of similar amplitudes are color-coded. As already shown in the main sequence plots, stare-nystagmus fast-phases of a given amplitude were slower and lasted longer than fast-phases of look-nystagmus with a similar amplitude. For both look- and stare-nystagmus skewness (duration of the acceleration period / total duration of the fast-phase) of the velocity-traces increased with amplitude.
The skewness was larger for fast-phases of stare-nystagmus as compared to fast-phases of look-nystagmus. The ratio $look_{skew}/stare_{skew}$ was 1.11 (0.15 SD). While for both eye movements the acceleration-interval was not significantly different ($p>0.05$, Wilcoxon Signed Rank Test) the eyes decelerated more slowly during fast-phases of stare-nystagmus.

Effects of limited dot lifetime
In the experiment described above we demonstrated that stare-nystagmus fast-phases last longer and have a lower peak velocity as compared to look-nystagmus fast-phases. Yet, we had not used a limited dot lifetime in the stare-nystagmus condition. So, in principle, subjects could have performed a combination of look- and stare-nystagmus. Such a mixture of eye movements could have resulted in an underestimation of the differences between the two eye movements. Therefore, we decided to record stare-nystagmus with limited and unlimited lifetime as well as look-nystagmus in the same subjects.
For fast phases of stare-nystagmus evoked with limited lifetime dots we observed the same effect as for those evoked with unlimited dot lifetime (Figure 2, data depicted in blue). As for fast-phases of stare-nystagmus evoked with unlimited lifetime dots the difference in the scaling-factor but not the exponent of the power function was significant for the duration vs. amplitude relationship and the peak-velocity vs. amplitude relationship (duration vs. amplitude: a: $p = 0.016$; b: $p = 0.383$; peak-velocity vs. amplitude: a: $p = 0.008$; $b = 0.938$; Wilcoxon Signed Rank Test). The ratio $look_{skew}/stare_{skew}$ was 1.11 (0.18 SD) indicating that velocity traces were skewed more strongly for fast-phases of stare-nystagmus. The direct comparison of fast-phases of stare-nystagmus evoked with unlimited and limited dot lifetime revealed significant differences for the scaling factor of the duration vs. amplitude relationship only (duration vs. amplitude: a: $p = 0.023$; b: $p = 0.742$; peak-velocity vs. amplitude a: $p = 0.109$; $b = 0.578$; Wilcoxon Signed Rank Test).

Effects of fast-phase direction/initial eye position
Studies comparing the main-sequences of centrifugal and centripetal saccades have reported inconsistent results. Centripetal saccades have been reported to be faster than centrifugal ones by some authors while others reported the opposite (see introduction). We compared the main-sequence of centripetal and centrifugal fast-phases of look-nystagmus. Fast-phases consisting of both centripetal and centrifugal components (i.e. fast-phases crossing the vertical meridian) were not considered for the analysis. Statistical analysis revealed no significant differences between the power-functions fitted to the data ($p > 0.05$, Mann-Whitney Rank Sum Test).
In a second step we asked if the main-sequence of centrifugal fast phases depends on the eye position at the time of initiation of the fast phase. To do so we performed a median split with respect to the initial eccentricity of the eye at the onset of the fast phase and compared the main sequence for fast-phases starting at smaller or larger eccentricities. Statistical analysis revealed no significant differences between the power-functions fitted to the data for fast-phases of look- as well as of stare-nystagmus (in all

cases: $p > 0.05$, Mann-Whitney Rank Sum Test).

Interaction of fast- and slow phase eye movements

To quantitatively test for an interaction of the slow and fast-phases of OKN we recorded look- and stare-nystagmus evoked with different stimulus velocities (10°/s, 15°/s, and 20°/s). Five subjects, who already participated in the previous experiments served as observers. We observed a slight but statistically not significant increase of fast-phase peak-velocity with stimulus velocity for fast-phases of look-nystagmus only ($p > 0.05$; ANOVA on Ranks).

Fast-phases versus saccades

In the past OKN fast-phases have often been compared with visually guided saccades. Fast-phases were reported to be either similar to saccades or to have lower peak-velocities/longer durations. In none of the studies, however, stimuli with limited lifetime had been used. Considering our results it might be the case that in those studies reporting different main sequences subjects had performed pure stare-nystagmus while in the studies reporting no differences subjects had performed a mixture of look- and stare-nystagmus. Therefore we asked subjects to perform visually guided saccades and compared these with fast-phases of look- and stare-nystagmus (limited dot lifetime). Data for the same subject as before are displayed in Figure 5. This subject shows relatively similar main-sequences for look-nystagmus and reflexive saccades while the main-sequence of stare-nystagmus fast-phases was clearly different. Corresponding mean velocity traces are displayed in Figure 6. Six of the eight subjects exhibited a similar behaviour, one subject showed larger similarities between saccades and stare-nystagmus as compared to look-nystagmus while for the last subject saccades were not similar neither to fast-phases of stare- nor look-nystagmus for the range of amplitudes recorded. Statistical analysis revealed significant differences between saccades and fast-phases of stare-nystagmus (limited dot lifetime) for the scaling factor but not the exponent for both the

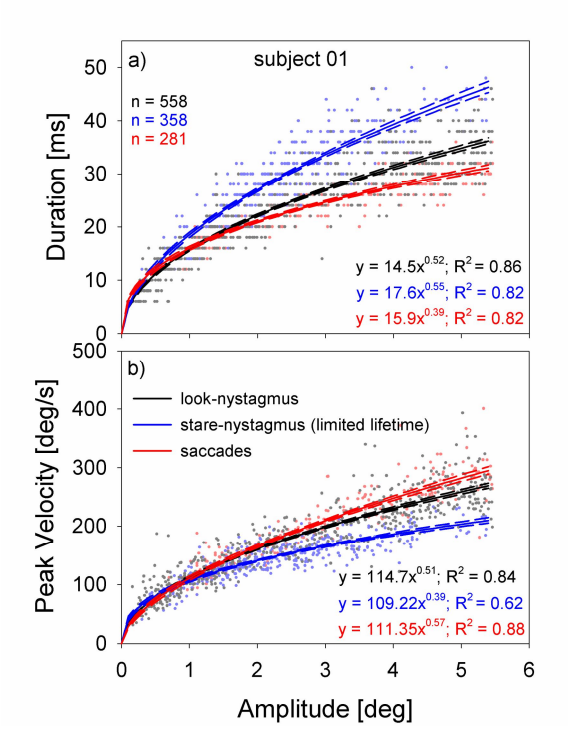

Figure 5. Comparison of main-sequences for saccades and fast phases of look- and stare-nystagmus evoked with limited lifetime dots. The graphs show duration vs. amplitude (a) and peak-velocity vs. amplitude (b) relationships for stare-nystagmus (blue), look-nystagmus (gray, black), and saccades (red). Dots represent data from individual fast-phases while solid lines depict power functions fitted to the data.

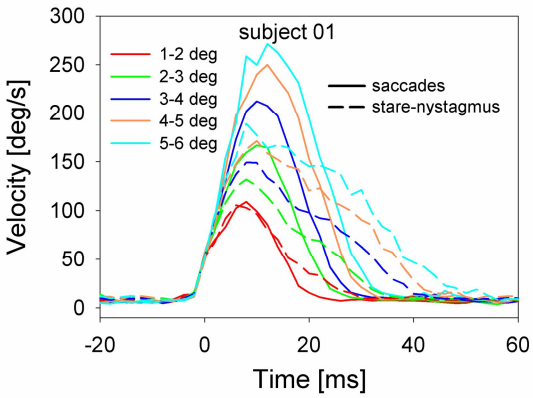

Figure 6. Average velocity traces for fast-phases of stare-nystagmus (limited dot lifetime) and saccades for subject 01. Velocity is plotted against time from fast-phase onset (t = 0 ms).

duration vs. amplitude (a: p = 0.016; b: p = 1; Wilcoxon Signed Rank Test) and the peak-velocity vs. amplitude relationship (a: p = 0.016; b = 0.563; Wilcoxon Signed Rank Test). Statistical analysis revealed no significant differences between saccades and fast-phases of look-nystagmus (duration vs. amplitude relationship: a: p = 0.641; b: p = 0.148; peak-velocity vs. amplitude relationship: a: p = 0.383; b = 0.297; Wilcoxon Signed Rank Test). For the distribution of fit-parameters see figure 12.

Taken together our results demonstrate that saccades and fast phases of look-nystagmus are on the same main sequence, while fast phases of stare-nystagmus are clearly different from saccades.

Discussion

We have tested and compared fast-phases of look- and stare-nystagmus and visually guided saccades in the same human subjects. Our data show clearly that fast-phases of look- and stare-nystagmus are not on the same main sequence. Instead, fast-phases of stare-nystagmus lasted longer and had lower peak-velocities as compared to fast-phases of look-nystagmus. The main-sequence of stare-nystagmus was largely independent of the lifetime of the dots used to induce nystagmus. We observed no differences between the main-sequences of visually guided saccades and fast-phases of look-nystagmus while clear differences exist for saccades and fast-phases of stare-nystagmus.

Saccades

The main sequence of visually guided saccades has been the key topic of various studies. In some studies power functions have been used to describe the main sequence. Comparing our results to those of Lebedev et al. (1996) and Garbutt et al. (2003b) we see that the exponents of the power functions are similar in all three studies. However, the scaling factor indicates higher peak velocities and shorter durations in our study. One likely reason could be the different techniques used for measuring eye-position. Garbutt et al. (2003b) used the scleral search coil technique while Lebedev et al. (1996) used electro-oculography, which both have been reported to underestimate peak velocity (Boghen et al., 1974;Byford GH, 1962;Frens and van der Geest, 2002). In addition we (i) did not filter our eye data prior to analysis and (ii) used a different algorithm to detect saccades. But since we are mainly interested in main sequence differences between experimental conditions measured in the same setup and since we analyzed our data with identical techniques in the same human subjects these differences are negligible.

Comparison of fast-phases of look- and stare-nystagmus

Fast-phases of stare-nystagmus had a longer duration, lower peak-velocity, and stronger skewness as compared to fast-phases of look-nystagmus. Since the visual stimulus was identical (using unlimited dot-lifetime) under both conditions these differences are likely caused by the different neural networks underlying the execution of the eye-movements. While fast-phases of stare-nystagmus are not deliberately directed to a visual target, subjects actively choose a single dot during look-nystagmus. Therefore areas active during the execution of voluntary goal-directed eye movements are probably more strongly involved during look- as compared to stare-nystagms. This interpretation would be in line with findings from previous imaging studies (Schraa-Tam et al., 2008;Konen et al., 2005).

Effects of limited dot-lifetime

Main-sequences for stare-nystagmus evoked with unlimited and limited (80 ms) dot lifetime were almost identical for our sample of subjects. Therefore the

dynamics of OKN fast-phases are not or only slightly influenced by the different stimulus characteristics, while the slow-phase gain (averaged across subjects) was reduced from 0.9 for stare-nystagmus evoked with unlimited lifetime dots to 0.6 for stare-nystagmus evoked with limited lifetime dots. Mackensen and Schumacher (1960) reported that the main-sequence of OKN fast-phases is independent of the stimulus velocity. Slow-phase gain, on the other hand, depends on stimulus velocity with lower gains for higher velocities (Abadi et al., 2005). In our view the fact that fast- and slow phase characteristics are differentially influenced by stimulus-characteristics demonstrates that both eye movements are controlled by largely independent neural networks. An interesting question arising is how the two systems interact e.g. how and when a fast-phase is initiated during the execution of a slow-phase.

Fast-phases versus saccades

Visually guided saccades and fast-phases of look-nystagmus turned out to be on the same main-sequence while the main-sequences of saccades and fast-phases of stare-nystagmus were quite different. Similarly the skewness of fast-phases of stare nystagmus was much more pronounced than that of saccades and fast-phases of look-nystagmus. These differences are one likely reason for the discrepant results in previous studies comparing the main-sequence of saccades and nystagmus. Saccades have either been reported to be faster with respect to peak-velocity (Garbutt et al., 2001;Garbutt et al., 2003a;Henriksson et al., 1980) or average velocity (Gavilan and Gavilan, 1984) or to be on a similar main-sequence (Sharpe et al., 1975;Mackensen G. and Schumacher J., 1960). Since none of these studies had used limited lifetime dots to induce OKN it seems likely that in studies reporting no differences subjects had performed a mixture of look- and stare-nystagmus or pure look-nystagmus. On the other hand, in the studies reporting differences subjects had probably performed pure stare-nystagmus. Other reasons are different types of saccades which have been used for comparison with fast-phases, and which have been reported to differ with respect to their main-sequence (visually guided, memory guided, etc). Furthermore in some studies the background characteristics during OKN and saccades had been quite different. Our results highlight the relevance of an explicit visual target and/or the behavioral task of the subject for the dynamics of fast-eye movements.

Interaction of fast- and slow phase eye movements

While earlier work suggested that fast and slow eye movement components do not add up when saccades are executed during pursuit (Carpenter, 1988) some more recent studies proposed that slow and fast eye movement components might add during saccades towards moving targets (de Brouwer et al., 2002;Blohm et al., 2003). During steady state OKN fast-phases alternate with slow eye movements. Since look-nystagmus is closely linked to smooth pursuit slow- and fast phase eye velocities might add up during OKN. We did not observe a significant influence of slow-phase eye velocity on the main-sequence neither for look-nystagmus nor for stare-nystagmus. For look-nystagmus peak-velocity increased slightly but not significantly with stimulus velocity. Such an increase could in principal be caused by a linear addition of the slow and fast-phases (de Brouwer et al., 2002).

Neuronal basis of the observed effects

While for a long time the neural networks underlying the execution of voluntary saccades and smooth pursuit eye movements have been assumed to be anatomically separated more recent findings show that both eye movements are controlled by largely overlapping

neural networks (for reviews see: (Krauzlis, 2004;Krauzlis, 2005;Orban de Xivry and Lefevre, 2007)). Our knowledge about the neural networks underlying the execution of slow and fast-phases during OKN is more limited, especially when different forms i.e. look- and stare-nystagmus, are considered.

Saccades and fast phases are both generated by the same premotor network located in the brainstem (Leigh and Zee, 2006). Burst neurons in the paramedian pontine reticular formation (PPRF) show identical firing characteristics before horizontal saccades and fast phases of OKN and VOR (Henn and Cohen, 1976;Cohen and Henn, 1972). Omnipause neurons stop firing previous to fast phases and saccades (Cohen and Henn, 1972) while electrical stimulation of these neurons inhibits the execution of saccades and VOR fast phases (Westheimer and Blair, 1973).

Recordings from single units in the vestibular nucleus (VN) of the rhesus monkey, demonstrated that neural activity and slow phase activity are correlated during OKN (Waespe and Henn, 1977). Interestingly, saccade related activity has also been reported for VN neurons (Boyle et al., 1985;Waespe et al., 1992). Studies employing single cell recordings reported neurons in the nucleus of the optic tract (NOT) of the monkey to be activated during OKN slow-phases (Ilg and Hoffmann, 1996;Mustari and Fuchs, 1990).

Lesions of the oculomotor vermis influence the dynamics of saccades in the monkey (Takagi et al., 1998). Similar lesions of the fastigial nucleus influence the main sequence in the cat (Goffart et al., 1998) an in the monkey (Robinson et al., 1993). Helmchen et al. recording from the fastigial nucleus (Helmchen et al., 1994) and in the vermis (Helmchen and Buttner, 1995) of the monkey reported similar activity related to spontaneous saccades and fast phases of OKN. Functional imaging studies in humans also reported cerebellar activation during OKN (Dieterich et al., 2000;Bense et al., 2006;Konen et al., 2005).

After extensive unilateral cerebral cortical lesions OKN, OKAN and spontaneous saccades could still be elicited, while reflexive and voluntary saccades directed to the contralateral hemifield were abolished (Tusa et al., 1986). Interestingly, peak velocity of OKN fast phases, OKAN fast phases and spontaneous saccades was reduced similarly after the lesion. Single cell recordings revealed activity during OKN in the medial temporal area (MT) (Ilg, 1997). The activity was not related to the execution of fast phases.

The cortical network underlying the execution of OKN in humans has been investigated using functional imaging (Bucher et al., 1997;Dieterich et al., 1998;Dieterich et al., 2003;Galati et al., 1999;Konen et al., 2005;Schraa-Tam et al., 2008). The activated network is reminiscent of the networks activated during SPEM and saccades (Petit and Haxby, 1999;Dieterich and Brandt, 2000). One study directly comparing OKN and SPEM found largely overlapping patterns of activation especially with respect to the oculomotor regions (Konen et al., 2005). Interestingly these regions were only activated in subjects performing a combination of look- and stare-nystagmus. In subjects performing pure stare-nystagmus no activation in the frontal eye field (FEF), the supplementary eye field (SEF), and the ventral intraparietal area (VIP) could be observed. This finding was confirmed in a recent study comparing activation patterns during stare-nystagmus and combined look- and stare-nystagmus (Schraa-Tam et al., 2008). Saccadic activity within FEF has also been reported to depend on the intentionality of the executed saccade. While FEF is strongly activated during voluntary saccades (antisaccades) it is less active during visually guided saccades

(Gaymard et al., 1998;Pierrot-Deseilligny et al., 2004;Mort et al., 2003). In addition neurons in FEF of the monkey show no build-up activity before spontaneous saccades that is typical for voluntary saccades (Bruce and Goldberg, 1985). We therefore hypothesize that FEF is part of the neural network causing higher peak velocities/shorter durations for voluntary fast eye movements, including fast-phases of look-nystagmus, as compared to unintentional fast eye movements. FEF is also active during pursuit. fMRI, due to its low temporal resolution, cannot differentiate between activity related to slow and fast phases. Therefore differences could be also related to the execution of the slow phase of the eye-movement.

Conclusions

We showed that fast-phases of look- and stare-nystagmus differ with respect to their main sequence. Furthermore, saccades and fast-phases of look-nystagmus are on the same main sequence while fast-phases of stare-nystagmus show different spatiotemporal characteristics. Our results highlight the relevance of an explicit visual target and/or the behavioral task of the subject for the dynamics of fast-eye movements. The observed differences could be caused by (partially) different neural networks underlying the execution of the eye movements. Knowledge about how the cortical networks underlying saccades and fast-phases differ is still rather limited. This is particular problematic since OKN fast phases are routinely used as a diagnostic tool (Garbutt et al., 2001;Leigh and Zee, 2006;Garbutt et al., 2003a). Since fMRI cannot differentiate between activity related to slow and fast phases, electrophysiological studies in cortical and subcortical areas (i.e. the FEF and Cerebellum) of non-human primates are needed in order to provide the required information.

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Control of Saccades towards Stationary and Moving Targets: The Role of the Macaque Lateral Intraparietal Area (LIP)

Control of Saccades towards Stationary and Moving Targets: The Role of the Macaque Lateral Intraparietal Area (LIP)

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Primates perform saccadic eye movements in order to bring the image of an interesting target onto the fovea; this target might be either stationary or moving. Yet, saccades towards moving targets are computationally more demanding since the oculomotor system must use speed and direction information as well as internal knowledge about its processing latency to program an adequate saccade. In non-human primates different brain regions have been implicated in the control of voluntary saccades. One of these regions is the lateral intraparietal area (LIP). While the tuning of LIP neurons for the saccade metric (length and direction) has been described before (e.g. Barash et al., 1991), it is not known whether LIP neurons show differential activation related to the control of saccades towards stationary as compared to moving targets.
To this end we recorded single unit activity in area LIP of two monkeys (*Macaca mulatta*). First we determined the preferred saccade direction. In the following experiments saccades were always along this preferred direction. Then monkeys performed visually guided saccades to either stationary targets located at different positions or moving targets (step ramp paradigm) in pseudo-randomized order. Stationary saccade targets were located such that the amplitudes of saccades towards moving and stationary targets were identical.
Confirming previous results, many LIP neurons showed saccade related discharges that were tuned for amplitude and direction. Yet, given identical saccade metrics, discharge varied depending on whether saccades were followed by stable fixation or smooth pursuit in about one third of these neurons. We conclude that area LIP is involved in the control of saccades towards stationary and moving targets.

Keywords: saccade, pursuit, monkey, LIP

Introduction

Primates perform saccadic eye movements in order to bring the image of an interesting target onto the fovea; this target might be either stationary or moving. Although computationally demanding, saccades to moving targets have been shown to be spatially precise in monkey (Keller and Johnsen, 1990;Newsome et al., 1985) and in man (Gellman and Carl, 1991;Kim et al., 1997), though some studies reported the opposite (Ron et al., 1989;Heywood and Churcher, 1981). Furthermore, it has been shown that information about target position is only used until about 70 to 80 ms before the onset of a saccade (Becker and Jürgens, 1979). The degree of precision which has been observed for saccades to moving targets can not be explained by the use of a position that has been sampled 70 to 80 ms before the saccade. Therefore it has been suggested that the oculomotor system must use speed and direction information as well as internal knowledge about its processing latency to program an adequate saccade (Keller and Johnsen, 1990;Newsome et al., 1985;Gellman and Carl, 1991;Kim et al., 1997). This hypothesis is supported by the finding that after lesions in the medial temporal

area (MT) of the macaque, which is known to be one of the key-areas for the processing of visual motion, the accuracy of saccades towards moving targets is reduced (Newsome et al., 1985;Schiller and Lee, 1994).
Keller et al. (1996) recorded from neurons in the superior colliculus (SC) of the monkey while the animal performed saccades to stationary targets or targets moving in the same direction as the saccade. They observed a shift of the center of the neurons' movement fields in direction of the eye movement, i.e. the saccade amplitude eliciting the maximal neuronal response was shifted towards higher amplitudes for targets moving in direction of the saccade.
In primates several cortical regions have been implicated in the control of saccades (Munoz, 2002;Gaymard et al., 1998). One of these regions is the lateral intraparietal area (LIP) (Barash et al., 1991a;Colby et al., 1996). Located in the lateral bank of the intraparietal sulcus (Andersen et al., 1985) neurons in LIP also respond to visual stimuli (Barash et al., 1991a;Colby et al., 1996) and some of them are active during smooth pursuit eye movements (Bremmer et al., 1997). Furthermore activity within LIP is modulated by a number of factors like eye-position (Bremmer et al., 1997;Andersen et al., 1990), attention (Colby et al., 1996), and intention (Mazzoni et al., 1996). While the tuning of LIP neurons for the saccade metric (length and direction) has been described before (Barash et al., 1991b;Platt and Glimcher, 1998) it is not known whether LIP neurons show differential activation related to the control of saccades towards stationary as compared to moving targets. But since LIP receives strong input from area MT (Blatt et al., 1990) and has outgoing connections to the intermediate layers of the superior colliculus (Lynch et al., 1985) it seems likely that area LIP is involved in the programming of saccades to moving targets. Therefore, in this study we recorded from single neurons in area LIP of the rhesus monkey while the animal performed amplitude-matched saccades to stationary and moving targets. In about one third of the cells we found differential activation for the two types of saccades. Therefore, a subpopulation of LIP-neurons encodes not only the metric of the saccade but is also involved in programming saccades towards moving targets.

Material and Methods

Extracellular recordings were performed in 2 hemispheres of two male macaque monkeys (Macaca mulatta; monkey K: 10.4kg and monkey C: 9.5 kg). All procedures were in accordance with guidelines on the use of animals in research (European Communities Council Directive 86/609ECC).

Animal preparation and experimental equipment

Before surgeries animals were pretreated with atropine. Initial anaesthesia was performed using Ketamin (monkey C) or Rompun/Ketamin (1:4) (monkey K) respectively. Subsequently anaesthesia was maintained by i.v. injection of either pentobarbital sodium (Nembutal; monkey C) or propofol (monkey K). Additionally local analgesics were administered as needed.
After initial training monkeys were implanted with a head holding device and (monkey C only) two scleral search coils (Judge et al., 1980). After final training a recording chamber was implanted above the intraparietal sulcus in a second surgery. In monkey C a stainless steel chamber was placed at P 3 L 15 at an angle of 45 deg relative to the vertical on the basis of a presurgical MRI scan. Both chamber and head holding device were fixed with self-tapping screws and covered in dental acrylic (Technovit 4004). In monkey K the chambers (custom build) were placed at the same coordinates. Implants were fixed with titanium screws only. Analgesics and

antibiotics were applied postoperatively in both monkeys. Recordings started after full recovery of the animal (at least one weak after surgery).

During training and experiments the monkeys were seated in a primate chair with their heads fixed. Eye position was measured using the scleral search coil technique (monkey C) or an infrared camera system (ET50; TREC, Gießen) (monkey K). In both cases eye-position was sampled at 250 Hz. Animals were rewarded with liquid (water or apple juice) for each correct trial. Data acquisition and visual stimulation was controlled using PC-based in-house software (NABEDA). For monkey K all stimuli were generated using PC-based software Neurostim and presented on a 20`` CRT display covering the central 25.6×19.2 deg of the visual field which was placed 0.89 m in front of the animal. For monkey C stimuli were generated using a mirror galvanometer backprojecting targets (red dot diameter: .8°, luminance: .4 cd/m^2) on a translucent screen placed 0.48 m in front of the monkey. The screen subtended the central 90×90 deg of the monkey's visual field.

Paradigms

All experiments were performed in complete darkness. For each cell we first determined the preferred saccade direction (left, right, up, down). In all subsequent recordings saccades were always in the preferred direction of the neuron under investigation. The monkeys performed saccades to either stationary or moving targets. Each trial started with the fixation of a peripheral target (monkey C: 10°; monkey K: 6.4°). After 1000ms the target either jumped to one of five (monkey K) or eight (monkey C) different positions and remained stationary (step-paradigm, Figure 1a) or jumped to the center of the display and immediately started to move either in the same (forward saccade, Figure 1b, monkey K only) or opposite (backward saccade, Figure 1c) direction (as compared to the initial jump) (monkey C: v = 10°/s; monkey K: v = 6.4°/s) for another 1000ms.

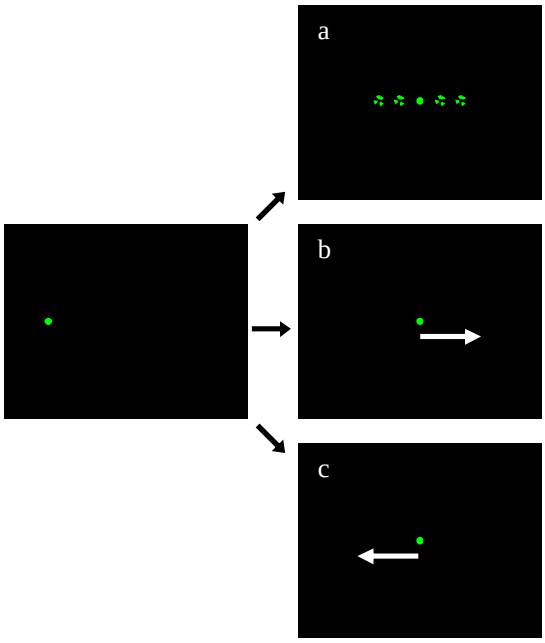

Figure 1. Illustration of the saccade paradigm. Each trial started with monkeys fixating a central target for 1000ms. Afterwards the target either jumped in the preferred direction of the cell with one of 5 (monkey K) or 8 (monkey C, not shown) different amplitudes and remained stationary for another 1000ms (a) or jumped to the center of the display and immediately started to move either in (b. Forward saccade) or against (c. Backward saccade) the direction of the saccade.

Data analysis

Data were analyzed using Matlab R2007b (The Math Works). Saccades were detected using a velocity criterion (200°/s). Saccade onset was defined as the point in time when the eye velocity exceeded this criterion for three consecutive samples (12 ms). All data were aligned to saccade onset. First we determined if neural activity depended on the saccade amplitude for saccades to stationary targets. To that end a response window was defined for each cell. The mean activity within this time window across different conditions was compared using a Kruskal-Wallis ANOVA. Second we determined whether or not the activity for saccades to stationary and moving targets was identical. To do so we

compared the mean activity within the same time window as before for saccades to moving targets and amplitude-matched saccades to stationary targets by means of a t-test.

Main-sequence analysis

We quantified and compared saccades in the different conditions considering the so-called main sequence (Bahill et al., 1975). To that end, peak-velocity and duration of saccades were plotted as a function of their amplitude and statistically approximated by power functions. The range of saccade amplitudes recorded varied for the different conditions. Lebedev and colleagues (1996) had shown that fit-parameters are substantially influenced by the amplitude-range used, even in the same dataset. Therefore we matched the datasets for all comparisons with respect to saccade amplitude. We calculated the 95 percentiles for the amplitudes of each dataset and used the smallest of them as the maximum amplitude for the comparison. We then fitted power functions to the data using least squares procedures according to: $y = ax^b$. We only analyzed data from monkey C since the acuity of the infrared camera use with monkey K was insufficient for this type of analysis.

Analysis of velocity traces

Mean velocity traces were computed from individual velocity traces after amplitude matching and aligning the individual velocity traces to saccade onset. Only bins that contained at least ten saccades were used for further analysis. From the mean velocity traces we determined the duration of the acceleration and deceleration periods as well as the total duration. The skewness of the velocity traces was calculated as the duration of the acceleration period divided by the total duration of the saccade/fast-phase.

Results

We recorded from 58 (38 from monkey K and 20 from monkey C) neurons in area LIP exhibiting a clear saccade-related activity. Figure 2 shows the distribution of preferred saccade directions for the 58 neurons with saccade-related activity. In both monkeys the recording chamber was implanted over the right hemisphere, therefore ipsiversive indicates saccades to the right while contraversive indicates saccades to the left. As can be seen in figure 2 preferred directions were not distributed uniformly.

In total 37 (64 %) of these neurons exhibited presaccadic activity (monkey K: 20/38 cells or 52%, monkey C: 17/20 cells or 85%) while the remaining neurons showed postsaccadic activity. At the population level, mean latency of activity relative to the onset of the saccade was -66 ms (SD 65.3) for monkey C and -17.90 ms (SD 107.33) for monkey K.

In figure 3 data for a representative neuron showing differential activity for saccades to stationary and moving targets is depicted. Spike rasters for individual trials are shown at the top of each panel, response histograms are shown in the middle and eye position traces are shown at the bottom. The dashed vertical lines indicate the temporal window used for

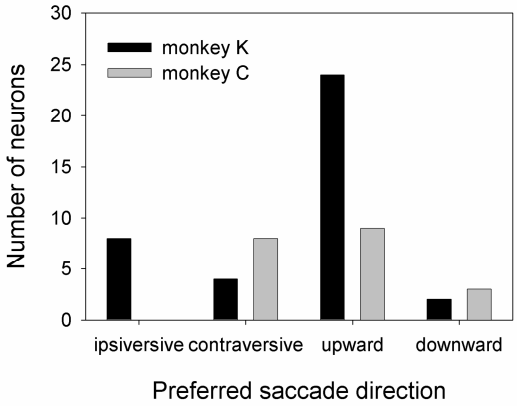

Figure 2. Distribution of preferred saccade directions. Preferred horizontal direction (ipsi- and contraversive) is given relative to the hemisphere (right) the chamber was placed above.

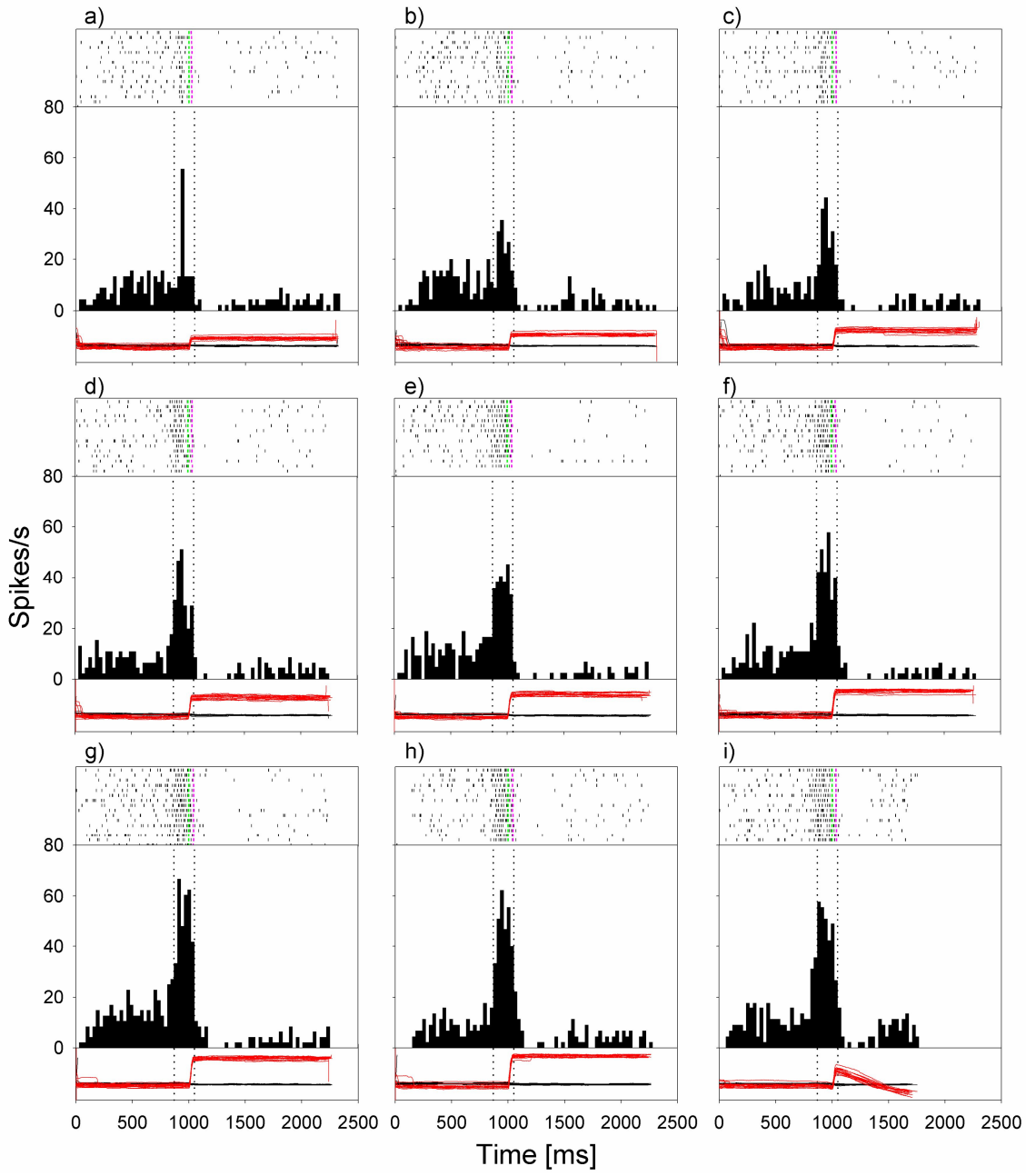

Figure 3. Data from an individual LIP neuron exhibiting differential activity for saccades towards stationary (panels a to h) and moving (panel i) targets. In each panel, spike rasters for individual trials are shown at the top, response histograms are shown in the middle and eye position traces are shown at the bottom (black curve: horizontal eye position; red curve: vertical eye position). In the spike rasters, the green lines indicate saccade onset, and the pink lines saccade offset. The dashed vertical lines indicate the temporal window used for the analysis. All data in each panel are aligned to saccade onset.

the analysis. All data in each panel are aligned to saccade onset. Panels a) to h) show data recorded during trials in which the monkey executed saccades of different amplitudes directed towards stationary targets. In panel i) data recorded while the monkey performed a saccade towards a backward moving target ('backward saccade') is shown. This neuron was tuned for upward saccades and exhibited clear presaccadic activity (latency: -130 ms). Statistical comparison of the activity within the temporal window denoted by the dashed vertical lines showed that the neuron was significantly tuned for saccade amplitude ($p < 0.001$; ANOVA on ranks) for saccades to stationary targets. This can also be inferred from figure 4. Here the mean activity of the neuron is depicted as a function of the actual saccade amplitude. Circles represent data for

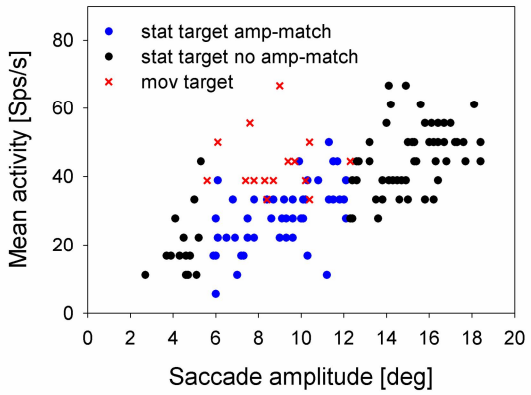

Figure 4. Neural activity as a function of saccade amplitude. Mean activity in the temporal window denoted by the dashed lines in Figure 3 is depicted as a function of actual saccade amplitude. Crosses show activity for saccades towards moving targets. Open circles represent discharges for saccades towards stationary targets with matching amplitude while filled circles represent discharges for saccades towards stationary targets with non-matching amplitude.

saccades towards stationary targets while data for saccades to moving targets is represented by crosses. For saccades to stationary targets activity increased with saccade amplitude. For comparison of saccades towards stationary and moving targets we used only those saccades to stationary targets covering the same amplitude range (blue circles) as the backward saccades (red crosses). The neuron showed stronger activity before backward saccades as compared to stationary targets of the same amplitude. This effect was statistically significant ($p<0.001$; t-test).

In figure 5 data for another neuron are depicted. Similar to the neuron described above this cell exhibited presaccadic (latency: -70 ms) activity and was tuned for the direction (upward) and amplitude ($p<0.001$; ANOVA on ranks) of saccades. But as can be seen in Figure 6 this cell showed no differential activation for saccades towards stationary and moving targets. This was confirmed by statistical analysis ($p>0.05$; t-test).

In total 18 of the 58 (monkey C: 10/20; monkey K: 8/38) neurons exhibited differential activation for saccades to stationary and moving targets. Twelve of these neurons were active presaccadically.

In figure 7 mean activity for saccades to moving targets is depicted as a function of mean activity for amplitude-matched saccades to stationary targets for those 18 neurons showing differential activation under both conditions. For backward saccades (black symbols) most data points (10/14) lie above the identity line. This indicates that most neurons show stronger activity for a backward saccade as compared to a saccade towards a stationary target of the same amplitude. We have data for only four neurons showing differential activity during forward saccades and those directed to stationary targets (red symbols) yet. Two of these four neurons show greater activity for saccades towards moving targets. While being statistically irrelevant, we report this latter data only for the sake of completeness.

Saccade dynamics

Different dynamics for saccades towards stationary and moving targets have been reported in some studies. Therefore we compared the main-sequences of both types of saccades. Figure 8 shows duration (a) and peak-velocity (b) for saccades as a function of saccade amplitude during saccades to stationary (black symbols) and moving (red symbols) targets for monkey C. While there was no difference for the amplitude-duration relationship saccades to moving targets had slightly higher peak velocities. In Figure 9 average velocity traces for three different amplitude bins (see methods for details) are depicted. The shapes of the velocity traces are rather similar for both types of saccades. In order to quantify this (dis-) similarity we compared the skewness of the velocity traces for backward saccades and saccades to stationary targets for each amplitude bin. For only one of the thirteen amplitude bins (9-10°) skewness was significantly different ($p = 0.46$) for

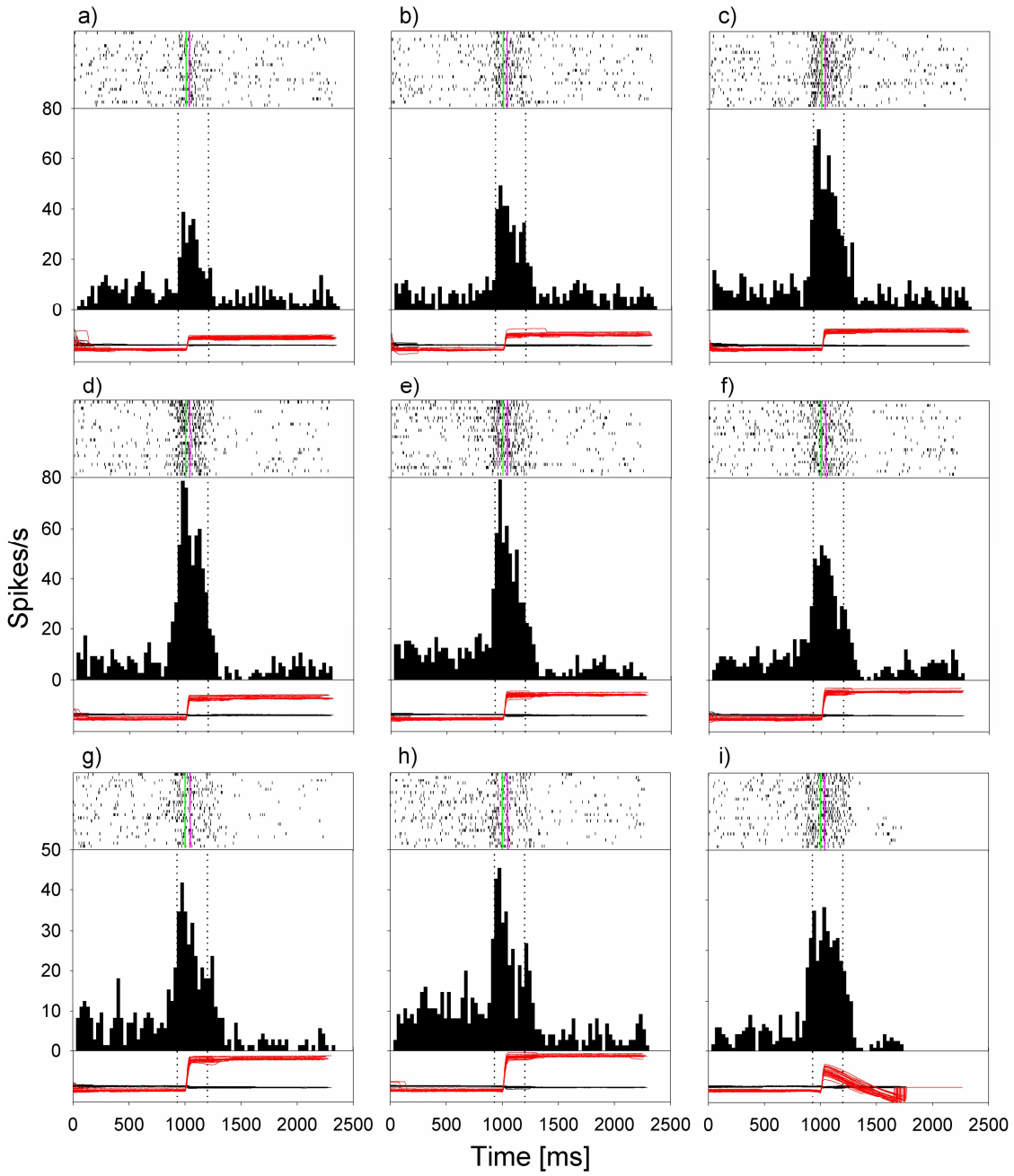

Figure 5. Data from an individual LIP neuron exhibiting similar activity for saccades towards stationary and moving targets. Conventions as in figure 3.

all other bins we observed no significant differences ($p>0.05$).

Discussion

We have recorded activity of neurons in area LIP of the rhesus monkey while the animals performed saccades to stationary and moving targets. We found differential activation for the two types of saccades in about one third of the cells. Therefore, we conclude that neurons in area LIP encode not only the metric of the saccade, but are also involved in controlling saccades towards moving targets.

Neural control of saccades

The neurons in this study had average latencies of -66 ms (SD 65.3) for monkey C and -17.90 ms (SD 107.33) for monkey K. This is in good agreement with data from the literature (-10,5 ms, (Barash et al., 1991a)).

Keller et al. (1996) recorded from neurons in the superior colliculus (SC) of

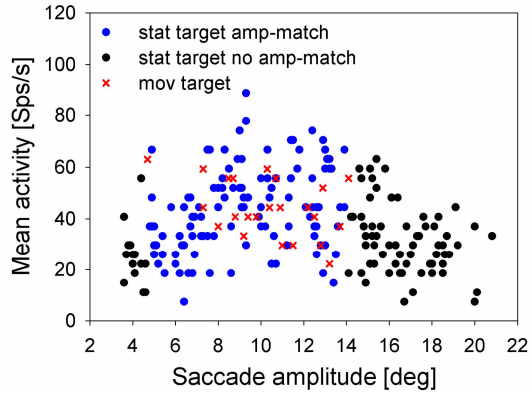

Figure 6. Neural activity as a function of saccade amplitude. Mean activity in the temporal window denoted by the dashed lines in Figure 4 is depicted as a function of actual saccade amplitude. Conventions as in figure 4.

the monkey while the animal performed saccades to stationary and moving targets. In nearly all cells they observed a shift of the center of the neurons' movement field in direction of the eye movement, i.e. a forward saccade would elicit less activity as compared to a saccade to a stationary target of the same amplitude. The authors argued that this would happen if the forward saccade, from the perspective of the SC, had been planned as a smaller saccade and conclude that the SC is not involved in the programming of saccades to moving targets. The majority of our cells exhibited higher activity for backward

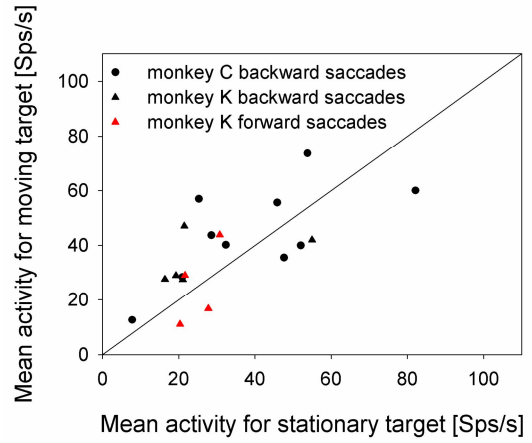

Figure 7. Mean activity for amplitude-matched saccades to stationary and moving targets. Each symbol represents data from one neuron. Data for backward saccades is represented in black, while red represents data for forward saccades. Circles show data from monkey C while triangles depict data for monkey K. The solid line represents the identity-line.

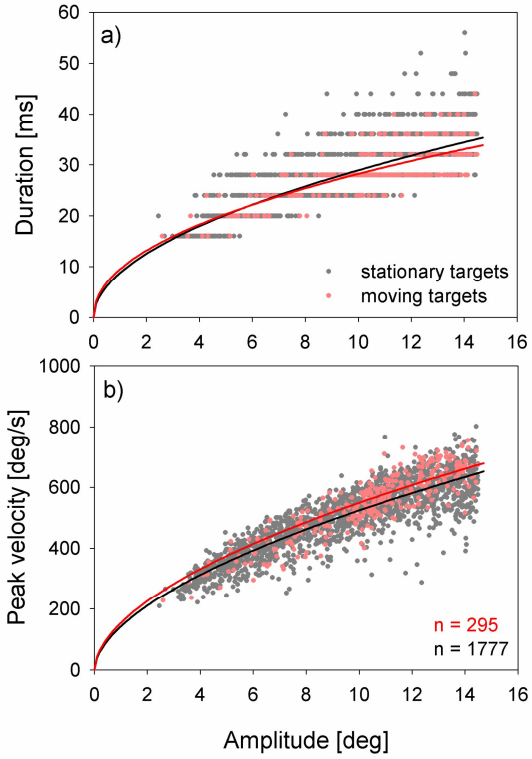

Figure 8. Comparison of main-sequences for saccades to stationary and moving targets. The graphs show duration vs. amplitude (a) and peak-velocity vs. amplitude (b) relationships for saccades to stationary targets (gray, black) and backward moving targets (red). Dots represent data from individual fast-phases while solid lines depict power functions fitted to the data.

saccades as compared to amplitude-matched saccades to stationary targets. This could be interpreted in the same way as the results of Keller and colleagues. However, we believe that this line of arguments does not apply to area LIP for the following reasons. For monkey K we tested backward as well as forward saccades. Four neurons exhibited differential activity for forward and stationary saccades. Two of them exhibited lower activity for forward saccades, as expected if the hypothesis formulated by Keller et al would hold for area LIP, while the other two exhibited higher activity. It has to be noted, however, that due to this rather limited number of neurons further recordings are needed to test this line of arguments. More important, in monkey K we tested forward and backwards saccades within the same neurons. Only in one cell we observed a significant difference between

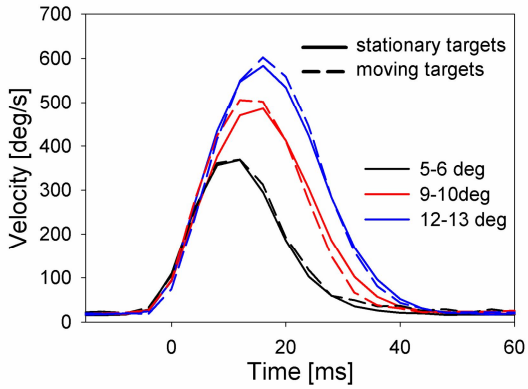

Figure 9. Average velocity traces for saccades to stationary and moving targets. Velocity is plotted against time from saccade onset (t = 0 ms). Solid lines represent saccades to stationary targets while dashed lines represent backward saccades. Fast-phase amplitude is color coded. Each curve represents the mean of at least 10 individual velocity traces.

saccades to stationary targets and forward saccades *and* backward saccades. The other seven cells showed differences for only one of the two types of saccades. Furthermore about two thirds of the cells did not show any differences between saccades to stationary and moving targets. We therefore believe that LIP - in contrast to the SC - contains cells that are part of the neural network controlling saccades towards moving targets.

Saccade dynamics

We observed largely identical dynamics for saccades to stationary targets and to backward moving targets. The latter were characterized by a slightly higher peak-velocity. Keller et al. (1996) analyzed the dynamics of forward saccades (i.e. both the step and the ramp were in the same direction) and found lower peak velocities and longer durations for forward saccades as compared to saccades to stationary targets. This finding was replicated later by Guan and colleagues (2005). These latter authors also investigated backward saccades. They reported slightly higher peak velocities for backward saccades as compared to saccades to stationary targets. This is very similar to our observations.

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General Discussion and Outlook

In the general discussion I will mainly focus on discussing my findings with respect to models made to explain localization error during voluntary eye movements. Furthermore I will highlight the importance of an explicit visual target for perception and eye movement characteristics.

Localization during fast eye movements

As stated in the introduction objects can be localized within different reference frames and using different strategies. When localization in darkness is considered no external references are available. Therefore, it seems very likely that subjects use an egocentric frame of reference. This means that during eye movements the most likely way to calculate the position of an object is to combine the visual information (where is the stimulus on the retina) or 'retinal signal' (R) with information about the movement of the eye called 'extraretinal signal' (exR). Several studies have used different versions of a simple mathematical model to obtain information about the exR signal (Hershberger, 1987;Mateeff et al., 1982;Pola, 2004). According to formula 1 the exR signal can be calculated as,

$$exR(t) = PL(t) - RL(t) \quad (1)$$

with exR(t) being the exR signal at the time t, PL(t) being the perceived location of the flashed target at time t, and RL(t) being the retinal location stimulated by the target flash. The individual versions of the model differ with respect to the assumed characteristics of the retinal and/or extraretinal signal. The retinal signal for example may be delayed, dampened or persistent (i.e. last longer than the target is visible). The classical models build on the assumption that the retinal signal is available instantaneously (no delay) and lasts exactly as long as the stimulus lasts (no low-pass like dampening) (Honda, 1991;Pola, 2004;Dassonville et al., 1992). Under these assumptions the resulting exR starts to change long before the saccade and continues to change for during and for some time after the saccade i.e. it is dampened (Figure 6). These models were very influential for a long time though it was known that i) retinal signals reach the brain areas involved in localization with considerable delay (Schmolesky et al., 1998) and ii) a brief visual signal is perceived to last longer than it actually does (Bowen et al., 1974) and causes a neural response that typically lasts much longer. Furthermore, the extraretinal signal

starts to change either during (Sommer and Wurtz, 2004) or after the saccade (Wang et al., 2007) but not before saccade onset as predicted by the models.

Neurons in parietal areas LIP, VIP, MT, and MST have been shown to carry an accurate eye position signal. Interestingly the signal is lost about 100 ms before the onset of a saccade (Morris et al., 2009). Recent research has demonstrated that models consisting of the same components and making more realistic assumptions about parameters like latency and neuronal persistence can also simulate the observed localization errors (Pola, 2004;Teichert et al., 2009).

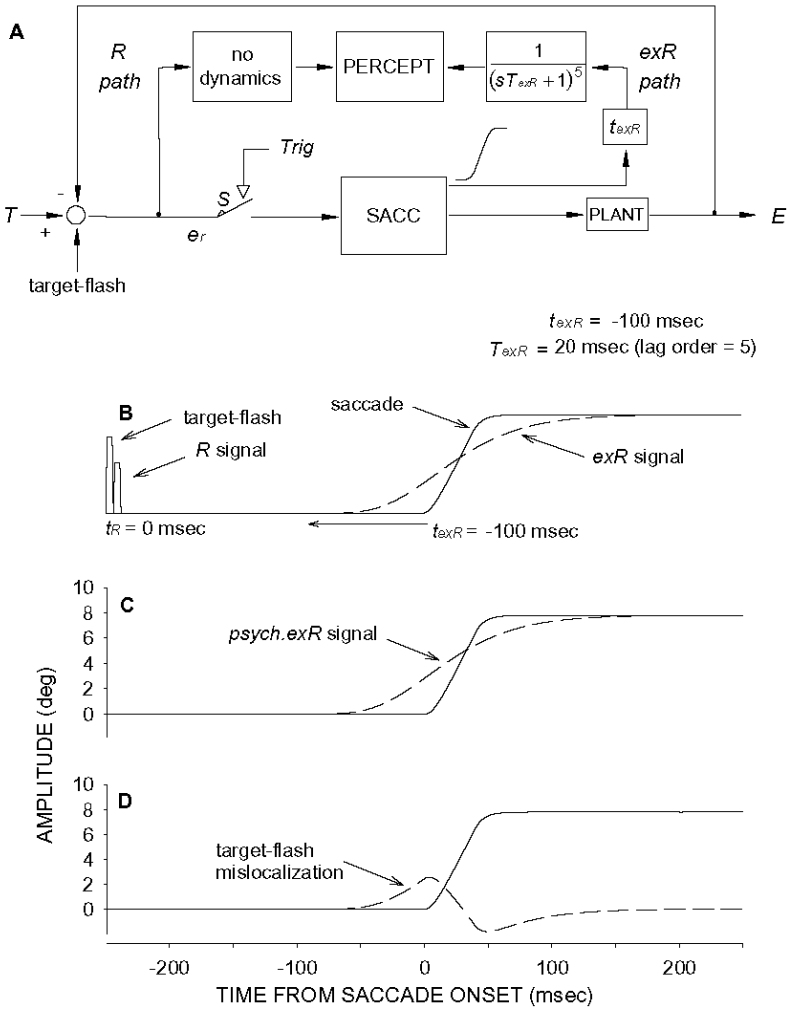

Figure 6: Classical model for perceived location. (adapted from Pola, 2004)

Since the biphasic error pattern observed during fast-phases resembles that observed during saccades these models can also explain the basic error patterns observed during OKN and OKAN. Localization errors get maximal at eye-movement onset for saccades while the peak is reached several tenths of milliseconds earlier during OKN/OKAN. Different latencies for the R signal during voluntary and reflexive eye-movements seem unlikely as long as stimulus contrast is identical. Therefore the models would predict shorter latencies of the exR signal for reflexive eye-movements as compared to voluntary eye movements. No physiological data comparing the latencies of the corollary discharge for voluntary and reflexive eye movements in the primate are available yet. Further results of experiment 2 showed that the magnitude of the localization error was larger

during OKAN as compared to saccades in darkness. We argued that this could be due to the complete absence of visual references during OKAN while during saccades some references (the fixation-point and the saccade target) serve as visual landmarks. Interestingly the models predict that the localization errors increase when the latency of the exR signal decreases. One aspect the models can not explain are the localization errors observed in the absence of eye movements. Since these errors depend also on the availability of visual references (e.g. a fixation point) it seems likely that also other (retinal) factors influence localization.

Hamker and colleagues (2008) suggested a model (Figure 7) which could explain perisaccadic compression, which is observed during saccades in the presence of visual references. Their model utilizes the fact that many sensory as well as motor areas are organized in a retinotopic way (i.e. cells representing neighboring areas of space are located next to each other and therefore form an orderly map). In brief, the visual stimulus evokes an activity-profile within the input stage of a sensory area. Similarly in the oculomotor map an activity hill is exerted at the representation of the saccade target. The cells of the input-stage are connected via a gain-stage to a pooling-stage. Oculomotor feedback controls the gain of the gain-stage, which results in a shift of the peak of the population response of the sensory area towards the saccade target. If the shifted peak is used for localization targets are perceived as being closer to the saccade target. The authors do not explicitly consider what happens in the absence of eye movements within their study. Yet, due to its architecture, the model could also explain the localization errors observed in the absence of eye-movements. In the model the activity in the oculomotor map rises at the saccade target position briefly before the saccade is executed. Under the assumption that this rise in activity, or part of it, lasts until the eyes move to a new position and continuously modifies the gain of the sensory neurons the model would predict a shift of perceived position towards the fixation point, which is exactly what we observed. In the absence of a fixation point i.e. during free viewing we observed a centrifugal localization error. Different from our results, the model would predict no localization error during free viewing.

So far no neural model can explain both perisaccadic shift and perisaccadic compression. While both models presented above use some kind of extraretinal signal the information conveyed by the signal is different in both models. The model by Hamker et al. (2008) uses only the information about the endpoint of the saccade. How the eyes reached the target is not represented within the model. In contrast the models on perisaccadic shift

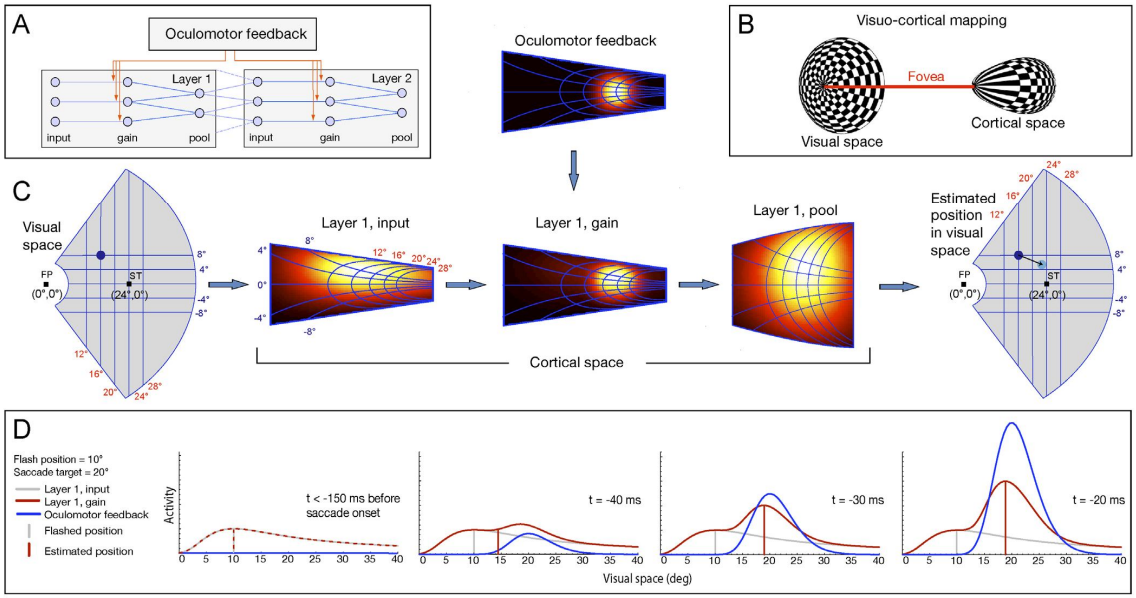

Figure 7: Computational Model for the Oculomotor Modulation of Visual Processing
(A) Hierarchical view of visual processing where each cell implements a specific feature detector with a localized receptive field. Each layer consists of three stages (input, gain and pool). The oculomotor system feeds the encoded saccade target position back to multiple layers and increases the gain of the cells prior to spatial pooling.
(B) Illustration of the mapping from visual space to cortical space.
(C) Detailed view of computations within a single layer. We illustrate the effect on the population response exerted by a peri-saccadically flashed dot at position (16°, 8°) while executing a 24° saccade. The activity distributions in the model are shown in cortical space. The depicted area of cortical space refers to the gray surface highlighted in the visual space. The spatial distortion due to cortical magnification is illustrated by the projection of the grid in the visual space into the cortical space. Using functions of receptive field size, cortical magnification and gaze position, we first determine the cortical population response in the input stage evoked by the flashed dot. The feedback signal determines the gain factor according to its activity profile. The gain modulated population response is distorted towards the saccade target. This population is then spatially pooled to obtain increasing spatial invariance. The perceived position of the stimulus is decoded from the activity in the neural ensemble.
(D) Population responses along the horizontal meridian in layer 1, input and layer 1, gain from a flashed dot at position (10°, 0°) before a 20° saccade. Long before saccade onset (t < -150 ms) no oculomotor feedback has been built up and the population responses in layer 1, input and layer 1, gain are identical. The decoding of the stimulus position from the population response leads to the true position. At t = -40 ms oculomotor feedback is sufficiently strong to distort the population response so that the decoded value is already shifted towards the saccade target. As the occurrence of the flash gets closer to saccade onset, the feedback signal, and thus the gain, increases further and the estimated perceived position is close to the saccade. (adapted from Hamker et al., 2008)
target. However, a further increase of the gain (e.g., flash occurrence at t ¼_20 ms) does not lead to a larger mislocalization. (adapted from Hamker et al. 2008)

use the dynamics of the eye movement to calculate localization errors (Hershberger, 1987;Mateeff et al., 1982;Pola, 2004). Up to now our knowledge about the actual nature of the corollary discharge is rather limited, but numerous feedback loops exist. Therefore different types of feedback might be used for localization depending on environmental conditions. Currently, however, we have very little knowledge about how and where the different signals are used for localization within the cortex.

Localization during slow eye movements

Localization errors during smooth pursuit eye movements are thought to be the result of (different) latencies within the visual system (Figure 8). When a target is flashed while the subject performs smooth pursuit it takes some time until the flashed target is perceived. At the time the flash is perceived the eyes have moved some distance. If the target is localized at the position in space the subject is looking when the target is perceived this will result in a mislocalization of the target in direction of the eye movement (Schlag and Schlag-Rey, 2002). This 'model' can explain a unitary shift like the one observed during OKN slow-phases, but it can not explain the hemifield-asymmetry which has been described during smooth pursuit (van Beers et al., 2001). A very interesting result in light of the model was the expansion of space during the slow-phase of OKAN as observed in Experiment 2. This result clearly showed that during slow eye movements targets are not necessarily mislocalized in direction of the eye movement. The main difference between smooth pursuit and OKAN slow-phases is the complete absence of visual references during the latter eye movement. Therefore information about eye-position in space at the time the flashed target is perceived could only originate from an extraretinal signal. It has been suggested that during reflexive eye movements no such exR signal is available. If this was true the localization errors occurring during OKAN slow-phases should be by far larger as compared to those we (experiment 2) and others (Bedell, 1990) observed. Still the way how the retinal signal and the extraretinal signal are combined seems to be different for voluntary and reflexive slow eye movements.

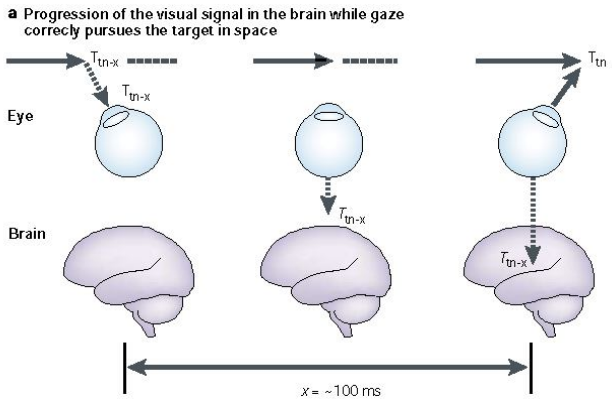

Figure 8: Effect of visual delay in smooth pursuit. Schematic representation of the progression of the visual signal generated by moving target T while the eyes pursue it. From left to right are shown three selected snapshots in the course of this progression. On the left the physical signal of target T impinges on the retina at time tn-x. In the center, the signal has been processed by the retina. This has taken ~40ms, during which the eye has moved as shown. On the right, the image *T* of the target T, as it was at time tn-x, reaches the hypothetical level of perception. But now the eye is looking at T_{tn}. (adapted from Schlag and Schlag-Rey, 2002)

The importance of an explicit visual target for visuomotor processing

The results of the 3rd and 4th study revealed the importance of an explicit visual target for the dynamics of fast eye movements. Fast eye movements not directed to an explicit visual target i.e. fast-phases of OKAN and stare-nystagmus are slower and last longer than fast eye movements directed to visual targets i.e. fast-phases of look-nystagmus and visually guided saccades. We hypothesise that this difference is indeed caused by the absence of an explicit visual target and not simply by the fact that stare-nystagmus and OKAN are truly reflexive eye movements while saccades and look-nystagmus are voluntarily controlled. This view is supported by studies investigating the main-sequence of different types of saccades. Anti-saccades and memory guided saccades which are clearly under voluntary control are characterized by lower peak velocities and longer durations as compared to saccades directed to a visual target (Becker and Fuchs, 1969;Smit et al., 1987;Van Gelder et al., 1997). Similarly saccades directed to auditory targets are slower and last longer than saccades to visual targets (Zambarbieri et al., 1982). In addition the data presented in the 3rd study show that the dynamics of saccades towards visual targets are not or only slightly influenced by the background luminance while saccades in the absence of a visual target are heavily influenced by the background luminance. Not only the dynamics of saccadic eye movements depend on the existence of a visual target. Also localization errors are influenced by the existence of a fixation target as I showed in the first study. In the absence of eye movements localization errors were larger when a fixation point was available as compared to localization without a fixation point. Furthermore we showed that during OKN the error pattern induced by the fast-phases is similar to a perisaccadic shift, though for visually guided saccades perisaccadic compression can be observed under similar background conditions. We argued that the reason might be the absence of an explicit visual target for the eye movement, which is probably among the strongest references available. This hypothesis could easily be tested by recording localization errors during the execution of look-nystagmus.

Neural substrate underlying different eye movement dynamics

Differential activity during eye movements with different dynamics has been shown for several cortical and subcortical areas. For example using fMRI in humans Konen et al. (2005) showed that the frontal eye field (FEF), the supplementary eye field (SEF) and the ventral intraparietal area (VIP) are activated during the execution of look- but not stare-

nystagmus. The FEF is also more active during antisaccades as compared to visually guided saccades. Fast-phases of look-nystagmus are faster than those of stare-nystagmus while anti-saccades are slower than visually guided saccades. Hence FEF-activity does not determine the dynamics of fast-eye movements. Instead it seems likely that the FEF is involved in the programming of voluntarily controlled eye movements irrespective of their dynamics.

At the subcortical level cerebellar lesions have been reported to affect saccade dynamics. After lesions of the oculomotor vermis or the fastigial nucleus in the monkey horizontal saccades were slower than normal (Robinson and Fuchs, 2001;Takagi et al., 1998). Therefore neurons in the cerebellum might be part of the network responsible for the different dynamics of fast eye movements. One surprising finding is that burst neurons in the paramedian pontine reticular formation (PPRF) of the monkey exhibit similar activity before horizontal saccades and fast-phases of OKN and VOR (Cohen and Henn, 1972;Henn and Cohen, 1976). Since these neurons project directly to the motor neurons it is very unlikely that the signal coding the saccade dynamics is modified at a later stage. Therefore firing characteristics of the burst neurons should be reinvestigated to determine which aspect of the activity pattern encodes the dynamics of the eye movements.

Encoding of saccades towards stationary and moving targets within area LIP

This study has not been finished yet, so results are preliminary. For monkey C anatomical investigation of the brain confirmed that the recording sites were located in area LIP. For monkey K the observed latencies of the cells fit well to latencies reported for neurons in area LIP in the literature (Barash et al., 1991). Since neurons in neighboring areas 7a, AIP, VIP, and PIP exhibit no saccade related activity (AIP, VIP, and PIP) or are on average active postsacadically (7a) it is very likely that the cells we recorded from in monkey K were located in area LIP. In monkey C we recorded saccades towards stationary targets and saccades towards targets that moved in the opposite direction as the saccade direction. The majority of these cells exhibited higher activity for saccades to moving targets as compared to saccades (with identical amplitude) to stationary targets. According to Keller at al. (1996) this could be interpreted as if the saccade would have been planned as a larger one and was reduced to its actual size at a later stage. To test for this hypothesis in future recordings we plan to ask the monkey to perform saccades towards targets that move either in the same or in the opposite direction as the saccade direction. If the hypothesis was correct neurons should be less active

during saccades towards targets moving in the same direction as the saccade direction as compared to saccades to stationary saccades. We already started recordings, but the number of neurons available right now is too small for a statistical analysis.

Conclusion

The data presented in this thesis demonstrate for the first time that briefly flashed targets are systematically mislocalized during reflexive eye movements, namely OKN and OKAN. Though the error patterns observed during reflexive eye movements show some similarities to those found during voluntary eye movements the observed differences implicate (partially) different neural networks underlying the localization of visual targets during reflexive and voluntary eye movements. The dynamics of reflexive eye movements differ from those of voluntary eye movements. These differences, however, are not large enough to be the origin of the different localization errors. They imply though that not only the neural substrate underlying target localization but also that the underlying encoding of eye movements is (partially) different for voluntary and reflexive eye movements. The existence of an explicit visual target seems to be crucial for both perception of space and eye movement dynamics. Finally, neurons in area LIP of the rhesus monkey encode not only the metrics of saccades but are also involved in the computationally more complex encoding of saccades towards moving targets.

Zusammenfassung

Die Leistung des visuellen Systems wurde in den letzten Jahrzehnten in einer Vielzahl von Experimenten untersucht. In den meisten Studien geschah dies unter statischen Bedingungen, das heißt während der Experimente wurden Augen- und Kopfbewegungen der Versuchspersonen bzw. der Versuchstiere weitestgehend unterbunden, um andere als visuelle Eingangssignale zu minimieren. Dies entspricht nicht der Situation, mit der unser visuelles System normalerweise konfrontiert ist. Im Alltag bewegen wir uns aktiv durch unsere Umgebung. Diese Bewegung verkompliziert die Situation für das visuelle System in mehrerlei Hinsicht. Selbst wenn die Umwelt ausschließlich aus statischen Objekten bestünde, induzierte die Eigenbewegung auf der Retina ein ‚Flussfeld' genanntes optisches Bewegungsmuster. Flussfelder lösen reflexive, kompensatorische Augenbewegungen aus, die dazu dienen, das Bild der Umwelt auf der Retina zu stabilisieren. Eine dieser Augenbewegungen ist der Optokinetische Nystagmus (OKN). Dieser besteht aus zwei Phasen: der langsamen Phase, während der die Augen sich mit dem visuellen Stimulus bewegen und diesen so auf der Retina stabilisieren, und der schnellen Phase in die Gegenrichtung. Die beiden Phasen des OKN wurden in der Vergangenheit häufig mit willentlichen Augenbewegungen verglichen. Es wurden Parallelen zwischen der langsamen Phase des OKN und glatten Augenfolgebewegungen sowie der schnellen Phase und Sakkaden gezogen. Sowohl für Sakkaden als auch glatte Augenbewegungen ist bekannt, dass sie Fehler bei der Lokalisation von Objekten in unserer Umgebung induzieren. Zusätzlich zu den durch das Flussfeld ausgelösten Augenbewegungen beeinflusst auch das Flussfeld selbst die Lokalisation von Objekten im Raum. Diverse Studien haben gezeigt, dass bewegte Stimuli und damit auch Flussfelder zu einer Fehllokalisation in Richtung der Bewegung führen. Ziel der ersten beiden Studien dieser Arbeit war, zu untersuchen, ob die während willentlicher Augenbewegungen auftretenden Lokalisationsfehler auch während durch simulierte Eigenbewegung ausgelöster reflexiver Augenbewegungen (OKN/OKAN) auftreten. Es stellte sich heraus, dass sich die Lokalisationsfehler während reflexiver und willentlicher Augenbewegungen in einigen Aspekten unterscheiden. Da bekannt ist, dass Lokalisationsfehler durch die Dynamik der Augenbewegung beeinflusst werden können, habe ich in zwei weiteren psychophysischen Studien untersucht, ob reflexive und willentlich ausgeführte schnelle Augenbewegungen die gleiche Dynamik aufweisen.

Da sich während einer (simulierten) Eigenbewegung fast alle Ziele für Augenbewegungen ebenfalls bewegen, aber gleichzeitig wenig über die Steuerung von Augenbewegungen auf bewegte Ziele bekannt ist, habe ich in einer fünften Studie die Kodierung von Sakkaden auf stationäre und bewegte Ziele im Parietalcortex des Rhesusaffen mittels extrazellulärer Einzelzellableitungen untersucht.

Kapitel 1: Lokalisation von visuellen Zielen während optokinetischer Augenbewegungen. (Localization of visual targets during optokinetic eye movements)

In diversen psychophysischen Studien wurde gezeigt, dass kurzzeitig eingeblendete Stimuli während willentlicher Augenbewegungen (Sakkaden und glatten Augenfolgebewegungen) nicht an ihrem tatsächlichen Ort lokalisiert werden. In dieser Arbeit habe ich nun untersucht, ob es auch während reflexiver Augenbewegungen, nämlich dem optokinetischen Nystagmus, zu einer Fehllokalisation von kurzzeitig eingeblendeten Stimuli kommt. Der OKN dient der Stabilisierung des Bildes auf der Retina während langsamer Kopfbewegungen und setzt sich aus zwei Phasen zusammen, der langsamen Phase und der schnellen Phase. Die langsame Phase wir häufig mit einer glatten Augenfolgebewegung verglichen, während die schnelle Phase häufig mit Sakkaden verglichen wird.

Während der langsamen Phase des OKN wurden alle Ziele in Richtung der Hintergrund-/Augenbewegung verschoben wahrgenommen. Kontrollexperimente belegten, dass der Fehler hauptsächlich durch die Augenbewegung induziert wurde. Der Fehler stieg schwach aber signifikant mit der retinalen Exzentrizität des Ziels an. Dieses Fehlermuster spiegelt mit einer Ausnahme das während glatter Augenfolgebewegungen beobachtete Fehlerschema wider. Während glatter Augenfolgebewegungen ist der Lokalisationsfehler im foveopetalen Halbfeld, d.h. dem Halbfeld, in das sich die Augen bewegen werden, deutlich größer als im foveofugalen Halbfeld. Einen solchen Halbfeldeffekt gibt es während der langsamen Phase des OKN nicht.

Die zeitaufgelöste Analyse zeigte, dass auch die schnelle Phase des OKN die Lokalisation beeinflusst. Kurz vor Beginn der schnellen Phase nahm der Fehler in Richtung der langsamen Phase zunächst ab. Danach stieg der Fehler in Richtung der langsamen Phase vorübergehend an. Diese biphasische Modulation des Lokalisationsfehlers dauerte insgesamt etwa 100ms. Das Maximum in Richtung der schnellen Phase lag ca. 25ms vor deren Beginn, während das Maximum in der entgegengesetzten Richtung ca. 25ms nach deren Beginn lag. Dieses Modulationsschema

war für alle Stimuluspositionen identisch. Das während der schnellen Phase des OKN beobachtete biphasische und positionsunabhängige Modulationsschema entspricht dem für Sakkaden in Dunkelheit beschriebenen perisakkadischen Shift. Allerdings liegt das Maximum der Misslokalisation in Richtung der schnellen Augenbewegung 25ms vor deren Beginn und nicht, wie bei Sakkaden, genau zu deren Beginn. Ferner ist während des OKN permanent das bewegte Punktemuster sichtbar. Unter solchen Hintergrundbedingungen würde bei Sakkaden kein perisakkadischer Shift, sondern die so genannte perisakkadische Kompression auftreten.

Insgesamt konnten wir mit dieser Studie erstmals zeigen, dass kurzzeitig eingeblendete Stimuli auch während reflexiver Augenbewegungen fehllokalisiert werden. Die Fehler unterscheiden sich dabei von den während willentlicher Augenbewegungen unter gleichen Umgebungsbedingungen beobachteten Fehlern. Dies deutet darauf hin, dass visuelle Referenzen während reflexiver Augenbewegungen nicht oder nur teilweise zur Lokalisation externer Reize verwendet werden.

Kapitel 2: Ausdehnung des visuellen Raums während optokinetischem nachnystagmus (OKAN). (Expansion of visual space during optokinetic afternystagmus (OKAN))

Während optokinetischer Stimulation ist permanent ein strukturierter Hintergrund sichtbar. Die erste Studie (Kapitel 1) hatte gezeigt, dass die Hintergrundbewegung den Lokalisationsfehler beeinflusst. Ziel der zweiten Studie war daher, den durch die Augenbewegungen allein induzierten Lokalisationsfehler zu untersuchen. Hierzu wurde bei den Versuchspersonen der so genannte optokinetische Nachnystagmus (OKAN) induziert. Der OKAN setzt sich wie der OKN aus einer langsamen und einer schnellen Phase zusammen. Er tritt in vollständiger Dunkelheit auf, wenn die Versuchsperson zuvor für einige Sekunden einen OKN ausgeführt hat. Zum direkten Vergleich wurde neben dem Lokalisationsfehler während OKAN auch der während OKN auftretende Fehler bestimmt.

Es stellte sich heraus, dass beide Komponenten des OKAN (schnelle und langsame Phase) Lokalisationsfehler auslösen. Während der langsamen Phase des OKN kam es bei allen Versuchspersonen zu einer Fehlwahrnehmung in Richtung der Augenbewegung. Dieser Fehler hing nicht von der Exzentrizität des Stimulus ab. Während der langsamen Phase des OKAN zeigte sich kein einheitliches Fehlerschema. Allerdings wurde deutlich, dass der Lokalisationsfehler während der langsamen Phase des OKAN mit zunehmender retinaler Exzentrizität des Zielreizes deutlich ansteigt. Ein solcher Anstieg entspricht

einer perzeptuellen Ausdehnung des visuellen Raumes. Dieses Fehlerschema unterscheidet sich von den während glatter Augenfolgebewegungen und OKN auftretenden Fehlern. Zwar wurde auch für andere langsame Augenbewegungen ein Einfluss der retinalen Exzentrizität beobachtet, allerdings trat gleichzeitig immer eine Verschiebung wahrgenommener Positionen in Richtung der langsamen Phase auf. Sowohl die schnellen Phasen von OKN als auch OKAN modulieren den während der langsamen Phase auftretenden Fehler. Bei beiden Augenbewegungen trat eine biphasische Modulation des Lokalisationsfehlers auf. Kurz vor Beginn der schnellen Phase wurden die Stimuli in Richtung der schnellen Phase verschoben wahrgenommen. Dieser Fehler erreichte sein Maximum beim OKAN 51ms vor Beginn der schnellen Phase (OKN 37ms). In den letzten Millisekunden vor und während der schnellen Phase nahmen die Versuchspersonen den Zielreiz entgegen der Richtung der schnellen Phase verschoben wahr. Die Amplitude der durch die schnelle Phase ausgelösten Modulation war während OKAN größer als während OKN, obwohl die mittlere Amplitude der beiden Augenbewegungen identisch war. Das während der schnellen Phase des OKAN beobachtete biphasische Modulationsschema entspricht dem für Sakkaden in Dunkelheit beschriebenen perisakkadischen Shift. Allerdings lag das Maximum in Richtung der schnellen Augenbewegung ca. 50ms vor deren Beginn und damit noch früher als während OKN.

Insgesamt konnten wir mit dieser Studie zeigen, dass die Existenz eines bewegten visuellen Stimulus nicht nur die Amplitude der Lokalisationsfehler beeinflusst, sondern dass sich die während OKN und OKAN auftretenden Lokalisationsfehler massiv unterscheiden. Dies unterstreicht die herausragende Bedeutung visueller Referenzen für die Lokalisation von Objekten in der Umgebung.

Kapitel 3: Die main-sequence des menschlichen Optokinetischen Nachnystagmus (OKAN) (The main sequence of human Optokinetic Afternystagmus (OKAN))

Der Vergleich der Wahrnehmungsfehler während willentlicher und reflexiver Augenbewegungen in den beiden vorangegangenen Studien (Kapitel 1 und 2) beruhte auf der Annahme, dass deren Dynamiken ähnlich oder sogar identisch sind. Ein zur Charakterisierung schneller Augenbewegungen häufig verwendetes Instrument ist die so genannte ‚main-sequence'. Sie bezeichnet den für schnelle Augenbewegungen charakteristischen Anstieg der Dauer bzw. Maximalgeschwindigkeit der Bewegung mit ihrer Amplitude. Studien, die die main-sequence von schnellen Phasen des OKN und

Sakkaden verglichen hatten, kamen zu widersprüchlichen Ergebnissen. Ziel dieser Studie war, zu untersuchen, ob reflexive und willentliche schnelle Augenbewegungen ähnlich Dynamiken aufweisen. Daher wurde die main-sequence von spontanen und visuell geführten Sakkaden mit der von schnellen Phasen des OKN und OKAN verglichen.

Die schnellen Phasen von OKN und OKAN unterschieden sich bezüglich ihrer main-sequence. Schnelle Phasen des OKAN dauerten bei gleicher Amplitude länger.

Der Vergleich von Sakkaden über einen strukturierten Hintergrund mittlerer Helligkeit und in Dunkelheit ergab, dass die main-sequence von spontanen Sakkaden, nicht aber die von visuell geführten Sakkaden von den Hintergrundeigenschaften abhängt. Spontane Sakkaden dauern in Dunkelheit länger als solche über einen strukturierten Hintergrund.

Der Vergleich von Sakkaden und schnellen Phasen ergab deutliche Unterschiede: spontane Sakkaden auf grauem/schwarzem Hintergrund sind langsamer und dauern länger als schnelle Phasen des OKN/OKAN. Visuell geführte Sakkaden in Dunkelheit hingegen dauerten weniger lang als schnelle Phasen des OKAN. Visuell geführte Sakkaden und schnelle Phasen des OKN unterschieden sich auf Populationsebene statistisch nicht voneinander. Bei der Hälfte der Versuchspersonen zeigte sich aber dennoch ein deutlicher Unterschied zwischen den Augenbewegungen. Hier dauerten die schnellen Phasen länger als die Sakkaden.

Wir konnten erstmals zeigen, dass auch die schnellen Phasen des OKAN einer main-sequence folgen. Die unterschiedlichen main-sequences für schnelle Phasen des OKN und OKAN könnten z.B. aus den unterschiedlichen Hintergrundeigenschaften oder (teilweise) unterschiedlichen neuronalen Netzwerken zur Steuerung dieser Augenbewegungen resultieren. Die Tatsache, dass spontane Sakkaden und schnelle Phasen in ähnlicher Art und Weise durch die Hintergrundhelligkeit beeinflusst wurden und dass beide Augenbewegungen kein explizites visuelles Ziel haben, lässt eine Verwandtschaft der beiden Augenbewegungen wahrscheinlich erscheinen. Trotzdem unterscheiden sie sich deutlich in ihrer main-sequence. Die uneinheitlichen Ergebnisse beim Vergleich der main-sequence von schnellen Phasen des OKN und visuell geführten Sakkaden spiegelt die uneinheitlichen Befunde der Literatur wider. Bezüglich der Fragestellung der Studie ist festzustellen, dass sich die Dynamiken von reflexiven und willentlichen Augenbewegungen unterscheiden. Da aber alle untersuchten schnellen Augenbewegungen einer main-sequence folgen und die Unterschiede zwischen reflexiven und willentlichen Augenbewegungen relativ gering sind, ist ein Vergleich der

Lokalisationsfehler während Sakkaden und schneller Phasen von OKN und OKAN zulässig.

Kapitel 4: Einfluss der Aufgabenstellung auf die dynamischen Eigenschaften schneller Augenbewegungen (Task influences on the dynamic properties of fast eye movements)

Die Ergebnisse für den Vergleich der main-sequence von willentlichen Sakkaden und schnellen Phasen des OKN waren sowohl in unserer Studie wie auch in der Literatur sehr heterogen. In Abhängigkeit vom Verhalten der Versuchsperson kann man beim OKN zwischen 2 Subtypen – dem eher willentlichen Schaunystagmus und dem eher reflexiven Stiernystagmus - unterscheiden. Aufgrund der Beobachtung, dass sich die Dynamik von eindeutig willentlichen (Sakkaden) und eindeutig reflexiven Augenbewegungen (schnelle Phasen des OKAN) unterscheidet, war das Ziel der vierten Studie, zu untersuchen, ob sich die Dynamiken der schnellen Phasen von Schau- und Stiernystagmus unterscheiden.
Die Analyse der Daten zeigte, dass schnelle Phasen des Stiernystagmus länger dauern und eine geringere Maximalgeschwindigkeit haben als schnelle Phasen des Schaunystagmus. Dies ist unabhängig davon, ob der Stiernystagmus mit einem Punktemuster mit limitierter oder unlimitierter Lebensdauer ausgelöst wird. Der direkte Vergleich der schnellen Phasen von mit limitierter bzw. unlimitierter Lebensdauer ausgelöstem Stiernystagmus zeigte einen signifikanten Unterschied. Der Vergleich von Sakkaden und schnellen Phasen ergab einen signifikanten Unterschied zwischen der main-sequence von Sakkaden und schnellen Phasen des Stiernystagmus. Schnelle Phasen dauerten länger und wiesen eine geringere Maximalgeschwindigkeit als Sakkaden auf. Sakkaden und schnelle Phasen des Schaunystagmus unterschieden sich hinsichtlich ihrer main-sequence nicht voneinander.
Wir haben damit erstmals gezeigt, dass sich die schnellen Phasen von Schau- und Stiernystagmus in ihrer Dynamik unterscheiden. In den Studien, die in der Vergangenheit die main-sequence von Sakkaden und schnellen Phasen des OKN verglichen hatten, wurden keine Punktemuster mit limitierter Lebensdauer verwendet. Es wäre daher möglich, dass die Resultate dieser Studien sich unterschieden, weil die Versuchspersonen nicht immer einen reinen Stiernystagmus ausgeführt hatten. Die main-sequence der schnellen Phasen des Schaunystagmus entspricht der von visuell geführten Sakkaden. Dies stützt die in der Literatur verbreitete These, dass es sich beim Schaunystagmus um eine Abfolge willentlicher Sakkaden und glatter Augenfolgebewegungen handelt.

Kapitel 5: Die Kontrolle von Sakkaden auf stationäre und bewegte Ziele: Die Rolle des lateralen intrparietalen Areals (LIP) des Makaken (Control of saccades towards stationary and moving targets: the role of the macaque lateral intraparietal area (LIP))

Neben reflexiven Augenbewegungen treten während Eigenbewegungen auch willentliche Augenbewegungen auf, u.a. Sakkaden. Das neuronale Netzwerk, das zur Steuerung von Sakkaden dient, wurde in der Vergangenheit intensiv untersucht. In den meisten Studien wurden dabei aber ausschließlich Sakkaden auf stationäre Ziele untersucht. Während Eigenbewegungen sind aber fast alle Objekte in der Umgebung in Bewegung. Primaten sind in der Lage, Sakkaden auch auf solch bewegte Ziele präzise auszuführen. Ein wichtiges kortikales Areal, das an der Steuerung der Metrik von Sakkaden beteiligt ist, ist das laterale intraparietale Areal (LIP). Ziel dieser Studie war deshalb, zu untersuchen, ob Zellen im Areal LIP an der Kodierung von Sakkaden auf bewegte Ziele beteiligt sind. Hierzu wurden extrazelluläre Ableitungen im Areal LIP des Rhesusaffen (*Macaca mulatta*) durchgeführt.

Dieser Versuch ist zum jetzigen Zeitpunkt noch nicht abgeschlossen. Insbesondere fehlen noch Daten von einem dritten Tier sowie einige Kontrollexperimente.

Die Analyse der Sakkadendynamik der bislang vorliegenden Daten zeigte, dass Sakkaden auf Ziele die sich entgegen der Sakkadenrichtung bewegen eine etwas höhere Maximalgeschwindigkeit aufweisen als Sakkaden auf stationäre Ziele (Affe C). Dies stimmt mit dem in der Literatur beschriebenen Effekt überein. Die Qualität der für Affe K aufgenommenen Augenpositionsdaten ist nicht ausreichend für eine Analyse der Augenbewegungsdynamik. Zum jetzigen Zeitpunkt liegen Daten zu 58 Zellen mit sakkadenbezogener Aktivität vor (Affe K: n=38, Affe C: n=20). Alle Neurone, die während Sakkaden auf stationäre Ziele aktiv waren, zeigten auch während Sakkaden auf bewegte Ziele eine erhöhte Aktivität. Insgesamt waren 37 der 58 Neurone (64%) präsakkadisch aktiv. Die mittlere Latenz relativ zum Beginn der Sakkade lag bei -66,0 ms (SD = 65,3) für Affe C und -17,9 ms (SD = 107.3) für Affe K. Daher kann man davon ausgehen, dass die hier betrachtete Neuronenpopulation an der Planung von Sakkaden beteiligt ist. Achtzehn der 58 Neurone (31%) zeigten ein unterschiedliches Antwortverhalten für Sakkaden auf stationäre und bewegte Ziele identischer Amplitude. Zwölf dieser Zellen waren präsakkadisch aktiv. Es wurde für 14 Zellen die Aktivität während Sakkaden auf entgegen der Sakkadenrichtung bewegte Ziele gemessen. Für zehn dieser Zellen war die Aktivität in dieser Bedingung größer als während Sakkaden auf stationäre Ziele mit gleicher Amplitude. Sollte sich dieser Trend verstärken,

entspräche das dem im SC beobachteten Antwortschema. Hier zeigen nahezu alle Zellen eine geringere Aktivität für Sakkaden auf Ziele die sich in Richtung der Sakkade bewegen als für Sakkaden auf stationäre Ziele mit gleicher Amplitude.

Zusammenfassend kann man festhalten, dass eine Subpopulation der Zellen im lateralen intraparietalen Areal des Rhesusaffen nicht nur die Metrik einer Sakkade kodiert, sondern darüber hinaus auch an der Planung von Sakkaden auf bewegte Ziele beteiligt ist.

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ABSTRACTS (SELECTED)

- Modulation of human direction discrimination by cognitive demands; Kaminiarz A. & Bremmer F.; Göttingen Neurobiology Conference 2003; Göttingen, Germany – poster
- Localization of visual targets during optokinetic eye movements; Kaminiarz A., Rohe M. & Bremmer F.; Göttingen Neurobiology Conference 2005; Göttingen, Germany – poster
- Localization of visual targets during optokinetic eye movements; Kaminiarz A., Rohe M., Krekelberg B.& Bremmer F. ; Society for Neuroscience, 35th Annual Meeting 2005; Washington DC, USA - poster
- Localization of visual targets during optokinetic eye movements; Kaminiarz A., Rohe M., Krekelberg B.& Bremmer F.; Vision Sciences Society 6th Annual Meeting 2006; Sarasota Florida, USA - talk

- Control of saccades towards stationary and moving targets: the role of the macaque lateral intraparietal area (LIP); Kaminiarz A., Klingenhoefer S., Koenigs K. & Bremmer F.; Society for Neuroscience, 36th Annual Meeting 2006; Atlanta, USA - poster
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- Localization of visual targets during optikinetic afternystagmus (OKAN); Kaminiarz A., Krekelberg B. & Bremmer F.; ESF-EMBO Symposium: Three Dimensional Sensory and Motor Space: Perceptual Consequences of Motor Action 2007;Sant Feliu de Guixols, Spain – poster
- The main sequence of human optokinetic nystagmus; Kaminiarz A., Königs K. & Bremmer F.; Vision Sciences Society 9th Annual Meeting 2009; Naples, USA - poster

Marburg, _____ _____

Andre Kaminiarz

Erklärung

Ich versichere, dass ich meine Dissertation

Localization of external stimuli during simulated self- and object-motion
(Lokalisation externer Reize während simulierter Eigen- und Objektbewegung)

selbstständig, ohne unerlaubte Hilfe angefertigt und mich dabei keiner anderen als der von mir ausdrücklich bezeichneten Quellen und Hilfen bedient habe.

Die Dissertation wurde in der jetzigen oder einer ähnlichen Form noch bei keiner anderen Hochschule eingereicht und hat noch keinen sonstigen Prüfungszwecken gedient.

Marburg, _____ _____

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