Neural correlate of spatial (mis-)localization during smooth eye movements

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Abstract

The dependence of neuronal discharge on the position of the eyes in the orbit is a functional characteristic of many visual cortical areas of the macaque. It has been suggested that these eye-position signals provide relevant information for a coordinate transformation of visual signals into a non-eye-centered frame of reference. This transformation could be an integral part for achieving visual perceptual stability across eye movements. Previous studies demonstrated close to veridical eye-position decoding during stable fixation as well as characteristic erroneous decoding across saccadic eye-movements. Here we aimed to decode eye position during smooth pursuit. We recorded neural activity in macaque area VIP during steady fixation, saccades and smooth-pursuit and investigated the temporal and spatial accuracy of eye position as decoded from the neuronal discharges. Confirming previous results, the activity of the majority of neurons depended linearly on horizontal and vertical eye position. The application of a previously introduced computational approach (isofrequency decoding) allowed eye position decoding with considerable accuracy during steady fixation. We applied the same decoder on the activity of the same neurons during smooth-pursuit. On average, the decoded signal was leading the current eye position. A model combining this constant lead of the decoded eye position with a previously described attentional bias ahead of the pursuit target describes the asymmetric mislocalization pattern for briefly flashed stimuli during smooth pursuit eye movements as found in human behavioral studies.

Introduction

Eye-position signals (‘Gain fields’ or ‘eye-position fields’) are ubiquitous in the visual cortical system of the macaque. They have been found in striate (Trotter & Celebrini, 1999), extrastriate (Galletti & Battaglini, 1989; Bremmer et al., 1997a; Bremmer, 2000), parietal (Andersen & Mountcastle, 1983; Bremmer et al., 1997b, 1999; Morris et al., 2012, 2013) and even in the premotor cortex (Boussaoud et al., 1998). Gain fields are hypothesized to be of critical importance for a stable perception of our environment (Zipser & Andersen, 1988; Bremmer et al., 1998; Snyder et al., 1998; Boussaoud & Bremmer, 1999; Salinas & Abbott, 2001; Blohm et al., 2009; Blohm, 2012).

Eye-position decoding typically has been applied to the stationary case, i.e., the fixating eye. It was only recently that decoding was introduced to the dynamic case (Morris et al., 2012, 2013; Xu et al., 2012). By investigating saccades Morris and colleagues (2013) showed that eye-position signals in four cortical areas of the macaque, among them the ventral intraparietal area (VIP), are precise on short time scales. Yet, eye-position decoding was not veridical in the temporal vicinity of saccades. Instead, the decoded eye position was leading the real eye position briefly before the onset of a saccade, but lagging at the end (Morris et al., 2012). This bi-phasic error pattern resembled results from human psychophysical studies on the localization of perisaccadic visual stimuli. The authors suggested that the erroneous eye-position signal could be the neural basis of the observed behavioral phenomenon.

Localization errors occur also during smooth eye movements: pursuit onset (Blanke et al., 2010), steady-state pursuit (Mateeff et al., 1981; van Beers et al., 2001; Körös & Bremmer, 2010), anticipatory pursuit (Blohm et al., 2003) and optokinetic nystagmus, OKN (Kaminiarz et al., 2007). During OKN, stimulus locations across the whole visual field are perceptually shifted in the direction of its slow phase. During pursuit, however, spatial localization is asymptomatic. Mislocalization occurs only in the hemifield ahead of the pursuit target. The neural bases of these perceptual phenomena are as yet unclear. Given the above described results on saccades, we hypothesized that continuous eye-position decoding across SPEM is possible but likely not veridical. We reanalyzed data from the macaque area VIP which had previously been recorded while monkeys performed SPEMs in otherwise darkness (Schlack et al., 2003). By employing isofrequency decoding (Boussaoud & Bremmer, 1999), we found that decoded eye position was not veridical but leading the actual eye position. Smooth pursuit induces an attention-field centered
ahead of the pursuit target (Khan et al., 2010). Physiologically, attention is known to act on neurons in area VIP (Maunsell & Cook, 2002) and to induce a shift of visual receptive fields toward its center (Ben Hamed et al., 2002; Womelsdorf et al., 2006), leading to a perceptual expansion of space away from its center (Wandak et al., 2011). We show that a model, combining two independent signal sources, i.e., an erroneous eye-position signal and a spatial signal derived from a visual map distorted by attention, can explain localization error during smooth eye movements.

Materials and methods
The current study is an extended computational analysis of neural and behavioral data reported before (Schlack et al., 2003). Accordingly, the procedures described here focus on the analytical treatment of the data and provide only the most relevant specifics of the behavioral and electrophysiological procedures. Full details of experimental methods are provided in our previous report (Schlack et al., 2003).

Animal preparation
Experimental and surgical preparation followed standard procedures. In brief, two monkeys were prepared for recordings under general anesthesia and under sterile surgical conditions. Each animal was implanted with a device for holding the head. Based on structural MRI scans a recording chamber for microelectrode penetrations through the intact dura was placed in a frontal plane at an angle of 45° with respect to the vertical for recordings in area VIP. Additionally, scleral search coils were implanted to monitor eye position (Judge et al., 1980). During the experiment, the animal sat in a primate chair with the head restrained, facing a translucent screen and performing oculomotor tasks for liquid reward. All procedures were in accordance with published guidelines on the use of animals in research (European Council Directive 86/609/EEC) and were approved by the regional ethics committee.

Behavioral paradigm
Oculomotor targets (red LEDs, diameter: 0.8°, luminance: 0.4 cd/m²) were back projected onto a translucent screen (size: 90° × 90°) 48 cm in front of the monkey. All experiments were performed in the dark (luminance < 0.01 cd/m²). To prevent dark adaptation, room lights were briefly switched on prior to a new set of trials for at least a couple of seconds.

In the saccade paradigm, a central fixation target was presented for 1000 ms, followed by a 10° step, pseudo-randomly chosen into one of four directions (left, right, up, and down). The animals’ task was to perform a saccade to the target location within 500 ms and keep fixation until the end of the trial (2.5 s). Smooth pursuit eye movements were induced by a Rashbass’-step-ramp-paradigm’ (Rashbass, 1961). Here, the target moved in pseudo-randomized order at 10°/s into one of four directions (left, right, up, and down). After initial presentation of a central fixation target (800 ms) the target was shifted by 10° in the direction opposite to the following smooth pursuit direction and started to move instantaneously for 1500 ms. Accordingly, each trial had a total duration of 2.3 s.

Binocular eye movements were continuously recorded at 200 Hz in the pursuit task and at 500 Hz in the saccade task. In the pursuit task, only trials without any catch-up saccades were analyzed further. Neurons were isolated and their corresponding spikes were detected on-line. Spike-times were stored for offline analysis with 1 ms resolution. For each neuron recorded, the saccade and pursuit paradigms were performed consecutively with the order counterbalanced across recordings without a specific adjustment of the experimental parameters to the specific functional properties of the neuron (e.g. receptive field location, size, etc.). We recorded at least 20 trials for each neuron and stimulus direction for each paradigm resulting in a minimum total number of 160 trials per neuron.

Data analysis
Eye-movement data and neuronal activity were analyzed with MATLAB 2012a (The MathWorks Inc., Natick, USA). Saccade onset was determined by a velocity criterion with a threshold of 80°/s in a time window of 0–400 ms after target displacement. Spike times were converted into a spike density function, which averaged across all trials for each condition, using a Gaussian smoothing with a standard deviation of the Gaussian kernel of σ = 30 ms and a Gaussian filter with a window size of 6 * σ – 1 (Silverman, 1986). Noise correlations were not analyzed separately. Eye-position signals were smoothed with the same set of filters. Eye movement and neural data were aligned to saccade onset.

Isofrequency decoding
Extracellular neural activity as obtained during steady fixation in the saccade paradigm was used to determine an eye-position field for each of the 180 neurons recorded. Many previous studies have shown the eye-position effect to be linear along the horizontal and vertical eye position, also in area VIP (Bremmer et al., 1999). Accordingly, we fitted two-dimensional linear regression functions to the neuronal discharges (Fig. 1). A regression plane represents the tuning of a cell for eye position: the gradient represents the direction of the steepest increase in activity with eye position, the intercept determines the average discharge of the neuron. Regression planes were fitted into the average neural discharges obtained long before (pre-saccadic: −700 to −200 ms) and long after saccade onset (post-saccadic: +300 to +900 ms). During these epochs, the eyes were constantly positioned either at the screen center (pre-saccadic: [x, y] = [0°, 0°]) or at one of the four eccentric fixation locations (post-saccadic: [x, y] = [± 10°, 0°], [0°, ± 10°]). By choosing these analysis windows, we excluded interference of eye-position-dependent neuronal discharges with saccade planning and/or execution. This is supported by the analysis of the mean activity of the 180 neurons during saccades in each of the four directions. Figure 2 shows, that up to 200 ms before saccade onset and from 300 ms after saccade onset on, the firing rate of the population of neurons was not significantly different from baseline activity. This is in line with previous studies in area VIP which showed that excitability of VIP neurons is back to normal about 300 ms after saccade onset (Bremmer et al., 2009). For each cell, the values of the regression plane as determined from the saccade paradigm were applied to neural activity recorded in the pursuit paradigm. This allowed us to decode eye position continuously across the SPEM by employing an iso-frequency decoding regime, which has been employed as an analytical tool to extract eye-position signals from neuronal recordings in various brain regions before (Boussadou & Bremner, 1999). This population decoder is based on the planar tuning of the eye-position signals. For a given eye position, a neuron fires at a specific frequency. Yet, due to the planar tuning, this discharge occurs not only for one single eye position, but for a whole range of eye positions. In a mathematical sense, the discharge occurs for an infinite number of eye positions, all located along a straight line perpendicular to

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the gradient of the regression plane, the so-called ‘isofrequency line’. Accordingly, discharges from a single neuron are not sufficient to decode eye position unequivocally. Considering discharges from a second neuron, however, theoretically would be sufficient, given that the second neuron would have a different tuning for eye position. In such case, also for this second neuron an isofrequency line on its regression plane could be found. This line, however, would be differently oriented in the 2-D eye-position space. The only point located simultaneously on both isofrequency lines is the point of intersection (PI) of these lines, which represents the current eye position.

This scenario reflects the ideal case of a perfect linear fit of a 2-D regression plane to the neuronal discharges and constant discharges over time. Due to temporal fluctuations of the neural signal and due to imperfect 2-D linear fits, the PI obtained from two single neurons is typically only a coarse measure of the current eye position. Hence, the isofrequency regime considers the PIs obtained from a whole population of neurons, constructed from a sequence of serial recordings: for \( n \) neurons, these are \( (n \times (n+1)/2) \) PIs. The decoded eye position is computed as the median of the distribution of all PIs.

**Attention and localization during smooth pursuit**

Localization of briefly flashed stimuli during smooth pursuit induces an attentional field which is broadly ahead of the pursuit target (Khan et al., 2010). Attention induces (or is based on) a shift of visual receptive fields toward the attended location (Ben Hamed et al., 2002; Womelsdorf et al., 2006). This shift of visual RFs in turn leads to a perceptual expansion of visual space (Wardak et al., 2011). We modeled such an expansion based on the structure of the attentional field during smooth pursuit as given by Khan et al. (2010), i.e., their equation for saccade reaction times during smooth pursuit, given in the legend of their Fig. 8. These authors found that attention is broadly ahead of the pursuit target and that this attentional field could be fitted by a 2-D sigmoid with a superimposed Gaussian:

\[
L_{\text{attention}} = -0.010 + 0.065/(1 + \exp(0.328 \times (x - 4.24))) + 0.05 \times \exp(-((x - 4.734)^2 + (y - 0.081)^2)/5.8032)) \tag{1}
\]

Boundary conditions of our model of perceptual expansion of space due to attention resulted from behavioral data in humans showing (i) almost no mislocalization during SPEM in the visual hemifield behind the pursuit target and (ii) smaller localization error in the directions perpendicular to the pursuit direction (van Beers et al., 2001; Königs & Bremmer, 2010). In our model, overall localization error then results from superimposing two signals: (i) decoded eye position and (ii) a visual map, distorted by attention.

**Statistical analysis**

To statistically evaluate the mean relative error of the decoded eye-position signal over time we calculated a moving average using a bootstrap analysis with 50 000 iterations (Efron, 1979). As the real and the decoded eye position were sampled with 200 Hz, we randomly took samples with replacement from the relative error of the decoded eye-position signal in the four different stimulus directions (left, right, up, and down) within a time-window of ±25 ms around each 5 ms time step. We chose this short time window in order to have a sufficient number of spikes available for the bootstrapping to provide robust results. This analysis provided 95% confidence intervals, which were used to assess significance levels.

**Results**

This study is based on recordings from 180 neurons in area VIP of two macaque monkeys. The discharges related to smooth pursuit eye-movements have been described in detail before (Schlack et al.,

\[
z = 15.3 + 0.06 \times t + 0.19 \times y
\]

\[
R^2 = 0.89; \text{RMSE} = 0.82
\]
Continuous decoding of eye position

In a second step, we analyzed the accuracy of the decoded eye position outside steady fixation, i.e., across the saccades. Confirming previous results (Morris et al., 2012, 2013), our analysis revealed a bi-phasic perisaccadic error pattern (Fig. 3). A subtle increase in error in the direction of the upcoming saccade was followed by a large error in the direction opposite to the saccade.

In a third step of our analysis, we aimed to decode eye position during smooth pursuit. Eye movements had been recorded in a classical Rasshann paradigm (Rasshann, 1961). After initial fixation, the target stepped in pseudo-randomized order into one of four directions (right, up, left, or down) and instantaneously started to move in the opposite direction. Critically, for decoding, we applied the regression plane values as obtained from the saccade paradigm to the neuronal discharges recorded during smooth pursuit. In other words: the neural signals, from which the fit parameters were obtained, were different from the samples, to which the decoding algorithm was applied.

Well before pursuit onset, i.e., in a temporal window from t = 400 to 200 ms before onset of the initial catch-up saccade, the mean relative error of the decoded eye position was minimal (ε = 0.06°) and not significantly different from zero (95% confidence interval = [−1.78°, 1.72°], bootstrapped with 50 000 iterations). After a minimal negative blip, it increased markedly in direction of the upcoming pursuit around the time of the catch-up saccade (Fig. 4A). As the initial saccade was in the opposite direction to the pursuit, this effect equals the pattern observed in the saccade paradigm. After the catch-up saccade and its related decoding error, the relative error decreased to an almost constant level. Around 300 ms after the onset of the catch-up saccade, the gain of the smooth pursuit eye movement reached an almost constant value for the duration of the eye movement with a mean of 0.97 (95% confidence interval = [0.95, 0.98], bootstrapped with 50 000 iterations; Fig. 4B). During this steady-state pursuit, i.e., in the time window from t = 300 to 1000 ms after saccade onset, the mean decoding error was 1.38°. A positive value indicates a lead of the decoded eye position in the direction of the pursuit as compared to the actual eye position. This lead of decoded eye position was statistically significant (95% confidence interval = [0.21°, 2.68°], bootstrapped with 50 000 iterations; Fig. 4A). Even when shifting the time window marking the steady-state pursuit by the mean duration of the catch-up saccades (60 ms), the lead of the decoded eye position was statistically significant with a mean of 1.26° (95% confidence interval = [0.09°, 2.54°], bootstrapped with 50 000 iterations).

Furthermore, we analyzed the influence of the distance between the actual eye position and the pursuit target during steady-state pursuit and performed a multiple regression analysis with this parameter and the steady state pursuit gain as well as the relative error of the decoded eye position (Fig. 4C). On average, the actual eye position was 0.13° behind the pursuit target. If the actual eye position lagged behind the pursuit target, the gain was generally higher and the relative error of the decoded eye position was smaller. If the actual eye position was leading the pursuit target, the gain was smaller and the relative error of the decoded eye position was larger. A stepwise examination of this multiple regression showed that using all three parameters generated the best fit of the data (R² = 0.46; RMSE = 3.09; P = 4.65 × 10⁻⁷) as compared to a single linear regression of distance and relative decoding error (R² = 0.43; RMSE = 3.16; P = 1.82 × 10⁻⁷), the sole linear regression of distance and Gain (R² = 0.28; RMSE = 0.043; P = 1.11 × 10⁻⁴), or
relative decoding error and Gain ($R^2 = 0.043$; RMSE = 4.1024; $P = 8.13 \times 10^{-5}$).

Finally, we investigated the influence of smooth pursuit velocity on the relative error of the decoded eye position. To this end, we computed the relative decoding error in a subset of 78 neurons for three different pursuit velocities (5°/s, 10°/s and 20°/s). These neurons were only tested during pursuit in the preferred direction of each neuron (Fig. 5). The mean relative error during steady-state pursuit was positive for all three pursuit velocities and could be explained by a constant temporal lead of the internal eye-position signal of about 200 ms. To estimate the maximum achievable accuracy of a whole population of neurons in area VIP, we computed the mean error of the decoded eye position as a function of the number of cells contributing to the isofrequency coding (Fig. 6).

This was done by randomly selecting 100 000 subsets of neurons from the 180 measured neurons. This procedure was repeated for each of the given population sizes. Figure 6 shows that the absolute error of the decoded eye position decreases with an increasing number of cells approximately following an inverse square-root function. Using this correlation, we can calculate the theoretically needed number of neurons to achieve a defined accuracy, e.g. about 900 neurons are needed for a continuous representation of eye position during SPEM with a mean absolute error < 2°.

**Decoded eye position and attention**

Given that a functional equivalent of macaque area VIP has been identified in the human parietal cortex (Bremmer et al., 2001;...
Sereno & Huang, 2006), erroneous eye-position signals most likely also exist in the human visual cortical system. Accordingly, if spatial localization would rely among other signals on an estimate of eye position, a constant lead of decoded eye position would suggest a shift of perceived spatial locations in the direction of pursuit across the whole visual field. Such a constant perceptual shift has been described for the slow phases of optokinetic nystagmus (Kaminiarz et al., 2007). During pursuit, however, mislocalization is only found in the visual hemifield ahead of the fovea. In order to explain this asymmetry in spatial localization during SPEM, we suggest an additional mechanism to act in concert with the erroneous eye-position signal: attention. Attention has been shown to lead to a perceptual distortion of space, i.e., an expansion of perceived locations away from the focus of attention (Wardak et al., 2011). Khan and colleagues (2010) have mapped the attentional field during the presentation of briefly flashed targets during pursuit, which could be fitted by a 2-D sigmoid with a superimposed Gaussian, and found attention centered broadly ahead of pursuit, resulting in an asymmetry with respect to the fovea. We hence modeled the effect of attention on spatial localization by transforming the attentional map as given by Khan et al. (2010) into a (mis-)localization map:

\[ L_{\text{attention}} = -65 \times (0.0848 + 0.065/(1 + \exp(0.328 \times (x - 4.24)))) + 0.05 \times \exp(-(x - 4.734)^2 + (y - 0.081)^2)/5.8032) \]  

(2)

In this Eqn 1, only the scaling factors (highlighted in bold) were changed as compared to the findings of Khan et al. (2010). These factors were adjusted to meet the boundary condition of localization, i.e., only a marginal error in the hemifield behind the fovea. According to our hypothesis, localization during smooth pursuit should be given by a superposition of the erroneous eye-position signal and the spatial map, which is distorted by attention:

\[ L = L_{\text{eye pos.}} + L_{\text{attention}} \]  

(3)

The resulting 2-D error pattern for localizing stimuli during smooth pursuit is shown in Fig. 7. Horizontal localization error starts to build up at the vertical meridian. Vertical localization error is directed away from the focus of attention. This error pattern qualitatively resembles the behavioral data observed in humans (van Beers et al., 2001; König & Bremmer, 2010).

Discussion

Efference copy vs. proprioception

Over the last three decades, numerous studies have shown that neurons in many visual cortical areas of the macaque carry an eye-position signal (e.g. Andersen & Mountcastle, 1983; Galletti & Battaglini, 1989; Bremmer et al., 1997a,b; Trotter & Celebrities, 1999; Bremmer, 2000), among them also area VIP (Duhamel et al., 1997; Bremner et al., 1999; Morris et al., 2012, 2013). A number of different approaches have shown that the functional characteristics of these modulatory influences of eye position on neuronal discharge are suited to decode eye position from the activity of a population of neurons within each of these areas: a back-propagation network (Andersen & Mountcastle, 1983), splitting a population into sub-populations with opposite tuning properties (Bremner et al., 1998), an iso-frequency decoding (Busseau & Bremner, 1999), as well as a maximum likelihood approach (Morris et al., 2012, 2013).

Eye-position signals have also been documented for neurons in the primary somatosensory cortex (Wang et al., 2007; Xu et al., 2011). Based on this finding, it was suggested that eye-position signals result from proprioception rather than from an efference copy or from corollary discharge. In line with this hypothesis, it was shown that the strength of visual responses of a number of neurons from area LIP visually stimulated briefly after the end of a saccade was more compatible with pre-saccadic rather than post-saccadic eye positions (Xu et al., 2012). These findings are in contrast to
results from two other recent studies (Morris et al., 2012, 2013). Here, Morris and colleagues tested the time course of the pure eye-position signals without any further visual stimulation in four different cortical areas of the macaque dorsal visual pathway: areas MT, MST, LIP, and VIP. The authors unequivocally showed that eye position as decoded from population activity within each of these areas started to change prior to saccade onset. Such a predictive change cannot be based on proprioception but rather would be indicative of an efference copy or corollary discharge signal. Our findings on decoded eye position leading the actual eye position during smooth pursuit are in agreement with the results from Morris and colleagues on saccades.

Continuous decoding of eye position

The result on the accuracy of decoded eye position during steady fixation in our study was in line with those of previous studies on dorsal visual areas (Boussaoud & Bremmer, 1999; Morris et al., 2013). To decode the eye position during smooth pursuit eye movements, we used the 2-D linear tuning of each cell as computed from the saccade paradigm and applied it to the neuronal discharges as recorded during SPEM. The error of the decoded eye position during the initial fixation and the saccade to the pursuit target was in the same range and direction as in the saccade paradigm.

In line with previous studies, our data show that eye-position signals in area VIP are accurate and sufficiently fast to serve as a possible candidate for representing the actual eye position not only during steady fixation, but also during ongoing eye movements. The analysis of absolute decoding error as a function of population size showed, that there is a relationship between these parameters proportional to the inverse square root, which has been shown suitable for population coding of other parietal areas (Bremmer et al., 1998; Morris et al., 2013) as well as premotor areas (Boussaoud & Bremmer, 1999) and primary visual cortex (Vogels, 1990). This functional approach suggests a highly accurate and reliable efference copy signal during SPEM available from the whole population of VIP neurons. Hence, they provide viable information for a coordinate transformation of visual signals from an eye-centered to a head-centered frame of reference at the population level. Such a transformation is thought to be necessary not only for a stable perception of our environment (Zipser & Andersen, 1988; Salinas & Abbott, 2001; Bremmer, 2005), but also for the computation of pursuit motor commands in the correct reference frame (Blohm & Lefèvre, 2010; Murdison et al., 2015). It remains to be determined, if explicit head-centered representations at the single cell level, which have been shown for area VIP during steady fixation (Duhamel et al., 1997; Avillac et al., 2005; Schlack et al., 2005), can also be found across eye movements.

During steady-state pursuit, the relative error of the decoded eye position was positive. Such a positive error indicates that the internal representation of eye position was slightly leading the actual eye position. However, it is unlikely that this lead is due to an underestimating of eye eccentricity, which has been found in extrastriate cortex (Morris et al., 2013). Such an underestimation would produce a lead of the decoded eye position when the pursuit target moves toward the center of the screen and would turn into a lag when the target moves away from the center. Yet, as shown in Fig. 4A, the lead of the decoded eye position remained almost constant for the entire duration of steady-state pursuit, even after crossing the center of the screen at around 800 ms after saccade onset, due to the mean latency of 200 ms of the initial catch-up saccade.

The multiple regression analysis of the three parameters ‘distance between actual eye position and pursuit target’, ‘pursuit gain’ and ‘relative decoding error’ revealed further insight into how the
decoded eye position might be influenced by other eye movement parameters. First of all, the smooth pursuit eye movement in our study showed a typical feature of ringing (Robinson et al., 1986), i.e., a lead of the actual eye position relative to the pursuit target induced a gain below one, whereas a lag of the actual eye position lead to a gain higher than one. Yet, the mean pursuit gain of 0.97 averaged across all trials was well within the usual range of a typical smooth pursuit task (e.g. Lisberger et al., 1981; Lencer et al., 2004; Konen et al., 2005). Furthermore, the comparison of the distance between the actual eye position and the pursuit target with the relative decoding error showed that the decoded eye position was leading the pursuit target on average by 1.27°. Yet, our results show, that pursuit velocity influences the relative decoding error. Although the data is quite noisy because of the smaller number of neurons in the velocity dependent measurement and because there is no one-to-one mapping between the 10°/s measurement in all cardinal directions vs. the preferred direction, the relationship between relative decoding error and pursuit velocity can be translated into a constant temporal lead of the internal representation of eye position of about 200 ms. This phenomenon, historically called ‘perception time’ (Hazelhoff & Wiersma, 1924; Mita et al., 1950), has been described by previous psychophysical studies and was reported to be within the same range (Brenner et al., 2001; Rotman et al., 2002, 2005; Kerzel et al., 2006). In addition, this timing fits nicely with the time which the saccadic system needs to account for future changes of the pursuit target and perform a catch-up saccade (de Brouwer et al., 2001, 2002; Orban de Xivry & Lefèvre, 2007). Thus, it seems that eye position coding in VIP predicts the location of the target about 200 ms into the future, which might be used for the programming of catch-up saccades during the steady-state pursuit.

On the other hand, the finding of a lead of the decoded eye position in relation to the actual eye position could explain, at least in part, the behaviorally observed mislocalization of briefly flashed stimuli during SPEM (Mateeff et al., 1981; van Beers et al., 2001; Königs & Bremmer, 2010) or related smooth eye movements like the slow phase of optokinetic nystagmus (Kaminiarz et al., 2007): if the erroneously decoded eye position would be combined with information about the location of a visual stimulus on the retina, it could induce the above mentioned mislocalization. Similarly, a possible neural substrate of the mislocalization during saccades had been identified (Morris et al., 2012).

Indeed, the mean relative error of about 1.4° for the whole population of 180 neurons measured with a velocity of 10°/s in our current study greatly matches the mean localization error reported during the slow phase of look nystagmus (Kaminiarz et al., 2007; Tozzi et al., 2007). In these experiments, visual stimuli were presented during ongoing OKN. When stimulus presentation fell in a slow phase of the OKN, stimuli were mislocalized in the direction of the eye movements. Stimulation, which were presented shortly before, during or after a fast phase of the OKN were mislocalized according to a saccade-like error pattern. These results were very different from results during stare-nystagmus or during Optokinetic Afternystagmus (OKAN), which can be induced by prolonged optokinetic stimulation. In such a case, mislocalization during the slow phase was not in the direction of the eye movements, but directed away from the fovea, resulting in a perceptual expansion of space (Kaminiarz et al., 2008). Interestingly, only SPEM and look nystagmus are associated with very similar cortical activation patterns in motion sensitive and eye-movement areas (Konen et al., 2005), which is not the case for stare-nystagmus and OKAN. These results suggest that visual localization during eye movements, which are under cortical control, relies (at least in part) on decoded eye-position signals.

Decoded eye position and attention

If localization was based only on an erroneous eye-position signal, perceived positions of briefly flashed stimuli should always be shifted in the direction of the eye movement, irrespective of the position of this stimulus in the visual field. Yet, different from look nystagmus, mislocalization during smooth pursuit is asymmetric with respect to an eye-centered visual field: it is found almost exclusively in the visual hemifield ahead of the pursuit target (or the fovea) (van Beers et al., 2001; Königs & Bremmer, 2010). There it increases from about 2° for stimuli close to the fovea to a maximum value of up to 5° for stimuli presented further away from the fovea. This suggests an additional signal contributing to the mislocalization during SPEM in addition to the erroneously decoded eye position.

Visual receptive fields have been shown to shift toward the location where attention is allocated (Ben Hamed et al., 2001; Womelsdorf et al., 2006). If the spotlight of attention coincides with the fovea, the receptive fields shift toward the fovea. According to a labeled line coding, this centripetal shift must result in a centrifugal shift of perceptual localization with respect to the fovea. Such a centrifugal shift away from the focus of attention has recently been demonstrated in behavioral experiments in humans (Wardak et al., 2011). During smooth pursuit, however, attention is not always where the fovea is. Instead, a study of Khan et al. (2010) found that attention during SPEM is allocated broadly ahead of the pursuit target. By mapping response latencies to visual stimuli presented around the pursuit target, a peak of attention was found at about 4° ahead of the pursuit target. By considering different eye velocities, the authors found that there was a constant lead of attention in time, not in space, i.e., the faster the eye velocity, the further ahead was attention. Accordingly, this spatial attention most likely induces an asymmetric distortion of perceptual space with perceived locations directed away from the center (or focus) of attention. Figure 7A shows the function of the attentional field during SPEM found by Khan et al. (2010) converted to represent (mis-)localization under the assumption that the location with the highest attention shows the least mislocalization. This attentional landscape can be considered a potential field implying a centrifugal force always directed away from its center. Importantly, this spatially asymmetric signal alone would not be sufficient to explain mislocalization during pursuit: in such case, stimulus positions in the hemifield the eye comes from should be mislocalized in the direction opposite to the pursuit direction. Hence, we suggest that this distorted representation of perceptual space is superimposed onto the erroneously decoded eye-position signal. The combination of a spatial map, distorted by attention, and a constant lead of the decoded eye position would add up to a joint localization map.

In this map, the effects of attention and decoded eye position add to each other in the visual hemifield ahead of the focus of attention, but antagonize each other in the hemifield behind the fovea (Fig. 7B). The resulting error map qualitatively resembles the asymmetric localization error during smooth pursuit as found in behavioral experiments in humans (van Beers et al., 2001; Königs & Bremmer, 2010). The mislocalization studies during smooth pursuit eye movements to which we refer all used flashed targets as localization stimuli. We thus only used established results from the attention literature that are compatible with this paradigm, i.e., Blohm et al. (2005), Kanai et al. (2003), Tanaka et al. (1998), Van Donkelaar & Drew (2002) and Khan et al. (2010). Other paradigms such

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as a target discrimination task (Khurana & Kowler, 1987; Souto & Kerzel, 2008; Lovejoy et al., 2009) might lead to different attentional allocations and therefore different localization patterns for which our model might not be suitable. Further discussion of this topic can be found in Khan et al. (2010).

As OKN is a reflexive eye movement, it is assumed that attention is uniformly allocated across the whole visual field. Without a specific attentional contribution only the constant lead of the decoded eye position would induce a uniform mislocalization pattern across the visual field. Indeed, such an error pattern has been shown for the slow phase of look-OKN (Kaminiarz et al., 2007). Accordingly, our data suggest that it should be possible to decode eye position from neural activity in the macaque area VIP (and most likely further visual cortical areas with eye-position-dependent activation) during the slow phases of look nystagmus. Most likely, this decoded signal would not be veridical but rather show a lead with respect to real eye position.

To the best of our knowledge, this is the first study to show the predictive nature of eye-position signals during smooth pursuit eye movements at a neuronal level. Simultaneously, we used this finding to provide a potential physiological explanation for the behaviorally observed localization errors of flashed targets during smooth eye movements. Whether such a mechanism is actually used by the brain to determine a spatial representation across smooth eye movements and what brain areas contribute the most, however, cannot be answered by currently available data sets.

Conflict of interest

The authors declare no conflict of interests.

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Abbreviations

LIP, lateral intraparietal (area); MRI, magnetic resonance imaging; MST, medial superior temporal (area); MT, middle temporal (area); OKAN, optokinetic affermynystagmus; OKN, optokinetic nystagmus; PI, point of intersection; RF, receptive field; RMSE, root mean square error; SPEM, smooth pursuit eye movement; VIP, ventral intraparietal (area).

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