Perisaccadic encoding of temporal information in macaque area V4

Jakob C. B. Schwenk,1,2* Steffen Klingenhoefer,1* Björn-Olaf Werner,1 Stefan Dowiasch,1,2 and Frank Bremmer1,2

1Department of Neurophysics, Philipps-Universität Marburg, Marburg, Germany and 2Center for Mind, Brain and Behavior (CMBB), Philipps-Universität Marburg and Justus-Liebig-University Giessen, Germany

Abstract

The accurate processing of temporal information is of critical importance in everyday life. Yet, psychophysical studies in humans have shown that the perception of time is distorted around saccadic eye movements. The neural correlates of this misperception are still poorly understood. Behavioral and neural evidence suggest that it is tightly linked to other known perisaccadic modulations of visual perception. To further our understanding of how temporal processing is affected by saccades, we studied the representations of brief visual time intervals during fixation and saccades in area V4 of two awake macaques. We presented random sequences of vertical bar stimuli and extracted neural responses to double-pulse stimulation at varying interstimulus intervals. Our results show that temporal information about very brief intervals of as brief as 20 ms is reliably represented in the multiunit activity in area V4. Response latencies were not systematically modulated by the saccade. However, a general increase in perisaccadic activity altered the ratio of response amplitudes within stimulus pairs compared with fixation. In line with previous studies showing that the perception of brief time intervals is partly based on response levels, this may be seen as a possible correlate of the perisaccadic misperception of time.

NEW & NOTEWORTHY
We investigated for the first time how temporal information on very brief timescales is represented in area V4 around the time of saccadic eye movements. Overall, the responses showed an unexpectedly precise representation of time intervals. Our finding of a perisaccadic modulation of relative response amplitudes introduces a new possible correlate of saccade-related perceptual distortions of time.

area V4; multiunit activity; saccades; temporal processing

INTRODUCTION

Under natural viewing conditions, primates move their eyes more frequently than their heart beats. Each eye movement challenges visual perception as it shifts the image of the outside world across the retina. Although our experience of the world is stable, for a brief time period around saccades our perception is in fact systematically distorted in several domains [for reviews see, e.g., Binda and Morrone (1), Burr and Morrone (2), and Ross et al. (3)], one of which is time. Here, psychophysical studies have mainly described two opposite effects.

The first is a perisaccadic “compression of time” (4, 5), where the interval between two visual stimuli is perceived as shorter than a reference interval if they fall within ~150 ms around saccade onset. This phenomenon also occurs with other types of eye movements, namely, around microsaccades (6) and during smooth pursuit (7). For a proportion of very short intervals, the compression is replaced by an inversion of perceived time, that is, the second stimulus in a pair may erroneously be perceived to have occurred first (5). In the second type of temporal distortion, known as “chronostasis,” intervals presented around the saccade may instead be perceived as longer than a reference interval (8). Unlike temporal compression or inversion, however, chronostasis also occurs when the saccade is only simulated by retinal motion (9) and is not specific to eye movements but can similarly be induced by voluntary movements and external stimuli (10, 11).

Both of these effects show a very similar time course relative to saccade onset as other perisaccadic phenomena, such...
as the perceptual distortion of space and number and direction of self-motion (4, 12, 13). This suggests that the underlying neural mechanisms may be either the same or at least closely related. The study of these mechanisms has focused largely on spatial processing in the macaque monkey, the standard animal model of human sensorimotor processing (14–23; for reviews, see Bremmer and Krekelberg (24), Marino and Mazer (25), Wurtz (26), and Wurtz et al. (27)). The neural substrate of the temporal distortions, however, is less well understood. Broadly, two different mechanisms are conceivable. The first is that the response latency of visual neurons is modulated around the saccade. If, for instance, latencies are reduced, an interval marked by a pair of stimuli immediately before saccade onset will be represented as shorter because the second stimulus occurs closer to the saccade and elicits a response at shorter latency than the first. This reduction in response latency has been observed for neurons in areas MT and MST (28–31) and has been proposed as a correlate of the perisaccadic compression of time. However, the magnitude of this latency reduction does not account for the full amount of compression observed in perceptual studies. From the reported findings in areas MT/MST, it remains unclear if the latency modulation is only augmented further in downstream areas involved in the perceptual readout or if it combines with other perisaccadic modulation to yield the magnitude of perceptual distortion [the latter idea has been put forward by Llobetson et al. (28)].

The second possibility is a modulation of the visual response amplitude. During fixation, the responses to the second of two stimuli are generally reduced in comparison with the first, and this reduction is greater for short intervals (32). Thus, the ratio of response amplitudes provides an additional representation of interval duration. Mayo and Sommer (33) showed that this information is indeed used for temporal discrimination. They recorded from neurons in the frontal eye fields (FEF) and found that the second response peak was larger for those intervals that were judged as longer by the monkey, whereas variability in peak latency showed no correlation with behavior.

Importantly, these two different accounts (latency vs. amplitude modulation) do not preclude each other. The neural basis of temporal perception is likely distributed among many different areas (34, 35), and the saccade-related perceptual distortion of time may well be represented differently between them.

To further characterize the neural correlates of saccade-induced temporal distortions, here we investigated how brief visual temporal intervals presented around the time of a saccade are represented in area V4. The perisaccadic neural dynamics in this area are well studied in the spatial domain (20, 22, 36–39). Given the putative link between the distortions of space and time, we were therefore interested in the possible role of V4 in perisaccadic temporal processing.

To this end, we recorded multiunit activity (MUA) in area V4 of two macaques while they performed a simple saccade task. Throughout the trials, RFs were stimulated using a random noise sequence. We extracted the responses to sequential stimuli presented at varying delays and compared them between fixation and perisaccadic time windows.

## MATERIALS AND METHODS

Experiments were performed in two male macaque monkeys (Macaca mulatta, weight 8.5 kg and 9.5 kg) referred to as M and B hereafter. All experimental procedures as well as animal care and housing were approved by the responsible regional government office (Regierungspräsidium Gießen: V54 – 19c2015h01, MR 13/1 Nr. 18/2007) and carried out in accordance with the applicable regulations.

### Animal Preparation and Data Acquisition

Before surgeries, animals were premedicated with atropine. Initial anesthesia was performed using Rompun/ketamine. Subsequently anesthesia was maintained by intravenous injection of propofol. In addition, local analgesics were administered as needed.

After initial training, the monkeys were implanted with a head-holding device. After final training, a recording chamber was implanted above area V4 based on its stereotaxic coordinates (at L = 27 and D = 22 mm in the sagittal plane), which was later confirmed by its topographical and functional properties (40). The chamber was fixed with titanium screws only. Analgesics and antibiotics were applied postoperatively in both monkeys. Recordings started after full recovery of the animals (no sooner than 1 wk after surgery).

We recorded MUA in the left hemisphere of the animals using the Eckhorn system microdrive (Thomas RECORDING GmbH, Germany). This system allows individual positioning of up to 16 quartz-isolated platinum-tungsten electrodes (typical impedances 500–800 kΩ at 1 kHz sine wave) in parallel (41). To obtain the MUA signal, the measured voltage was amplified, band-pass filtered (1–10 kHz), full-wave rectified, and, subsequently, low-pass filtered (140 Hz).

### Experimental Setup and Paradigm

During the experiments, the animals were seated in a dimly lit room 62 cm in front of a CRT monitor subtending 36° × 27° of the visual field (800 × 600 pixels, refresh rate 100 Hz). Animals viewed the stimulus binocularly. Gaze position of the left eye was monitored with an infrared eye-tracker at a sampling frequency of 500 Hz (ET-50, Thomas RECORDING GmbH, Germany).

The animals were trained to fixate a green circular target and to follow displacements of this target with their gaze. A liquid reward was given in trials in which the animals fixated the target correctly throughout the trial and responded to the dimming of the target by the release of a lever. The animals performed sessions that started with 150 trials of a visually guided saccade paradigm and also included a subsequent saccade adaptation paradigm. Unless otherwise noted, we only used data from the saccade paradigm for the analysis presented here. Here, the animals performed horizontal saccades in response to a 12.5° displacement of the fixation target (monkey B always rightward; monkey M rightward or leftward changed on a daily basis). Upon detection of the eye movement by the eye tracker, the saccade target was blanked for 100 ms and then reappeared at the same position. In addition to the 12.5° target displacement, the paradigm also included displacements of smaller amplitude, which followed 500 ms after detection of the primary saccade, either in or against the direction of the primary saccade.
In all conditions, the horizontal extent of the RFs was mapped throughout the trials using random noise stimulation (cf., Random Visual Stimulation section).

**Random Visual Stimulation**

Before the actual experiment, the horizontal and vertical RF positions of all recording sites were coarsely mapped during central fixation using a random noise stimulus. This initial mapping was only used for proper stimulus placement in the subsequent paradigm. In the actual experiment, two vertical bar stimuli were presented throughout the trials in two adjacent but nonoverlapping areas of the monitor (Fig. 1). Each stimulus was composed of a single vertical white bar (75 cd/m², typical height: 4.5°, width: 0.4°) that was repositioned to a random location within the respective stimulation area with every refresh cycle of the CRT (i.e., every 10 ms); the luminance of the display background was 25 cd/m². This means that at any point during the trial, there were always two stimuli on the screen. The precise dimensions of the stimulation areas were chosen for each recording site individually based on the location of the RF, such that together the two areas spanned a continuous region that fully covered the visual field between the pre- and postsaccadic RF positions. This spatial design effectively guaranteed that RF stimulation (stimuli presented inside the RF) was possible throughout the trials. It does not a priori assume the precise location or size of the RF (within the boundaries of the predefined stimulation areas) around the time of the saccade. Importantly, each stimulation area extended beyond the width of the RF to ensure that the random sequence of stimuli inside the RF included variable temporal intervals.

The random sequences used for the two areas were independent.

**Data Analysis**

We included individual recording sites in our analysis based on the signal-to-noise ratio of the responses to stimuli located inside the RF. Specifically, we calculated the ratio between the peak RF response and the standard deviation of the activity at a reference position outside the RF (Z-score). If this ratio was greater than 5, the recording site was included in the analysis.

To investigate perisaccadic dynamics, we first aligned all data to saccade on- and offset (for pre- and postsaccadic analysis, respectively) and then selected stimuli from the realigned stimulus sequence that were presented in certain time bins of 50 ms duration ranging from −500 ms before saccade onset to +200 ms after saccade offset.

We denote these time bins as “time windows” and follow the convention that negative values represent times before saccade onset and positive values times after saccade offset. Once the stimuli presented in a certain time window had been detected, we extracted the MUA within a window of 250 ms duration following the selected stimuli for further analysis. Although in this convention the presentation times of stimuli are restricted to a particular time window, the neural activity evoked by these stimuli extends beyond the respective time window.

The RF of each recording site was stimulated by a vertical bar at random times during each trial (“RF hits”) as determined by the random sequence of the noise stimulus. This allowed us to extract cases in which a bar was presented...
twice inside the RF (but not necessarily at the exact same position) at a given time interval (“double pulse stimulation”). Specifically, for each of the time windows relative to the saccade, we first collected all RF stimulations into a “single pulse” data class and then searched iteratively for stimuli at intervals between 10 ms and 80 ms (stimulus onset asynchrony (SOA)) relative to each initially selected stimulus. We selected intervals defined by subsequent stimuli in the fixation and postsaccadic time windows (“forward” search) and intervals defined by preceding stimuli in the presaccadic time window (“backward” search). Thus, for intervals in the perisaccadic time windows, it was always the stimulus closer to the saccade that had to be presented within the predefined 50 ms window, whereas the other could be presented outside it. This procedure ensures that all stimulus pairs included in the analysis were either presented completely before saccade onset (pre) or after saccade offset (post), that is, the gaze position did not change within a given interval. To distinguish between the alignment relative to the saccade and the temporal order (“first” and “second” stimulus), we denote the initially selected as the “primary” and the other as the “secondary” pulse. In the following, unless noted otherwise, \( t = 0 \) ms on the time axis is aligned to the peak response to the primary pulse. Consequently, temporal intervals will extend toward positive values in the fixation and postsaccadic time windows and toward negative values in the presaccadic time window. A schematic overview of the procedure used for averaging and aligning the data is presented in Fig. 2.

Importantly, our iterative algorithm also included intervals if the RF was stimulated at any time within them, in which case the same data would be collected multiple times for different SOAs. We used responses to all stimuli that were presented in successfully completed trials to determine the horizontal extent of the RF for each site, after confirming that there was no systematic shift in RF position or size in perisaccadic time windows (see RESULTS).

Statistical Analysis

We performed all statistical comparisons based on the mean response across recording sites. Significant differences between two conditions were assessed by testing whether the bootstrapped 95% confidence interval (CI) of the mean difference included zero. Bootstrapped distributions were calculated by drawing with replacement from the set of recording sites with 1,000 repetitions.

RESULTS

We recorded multiunit activity (MUA) in two macaque monkeys while the animals were performing a visually guided saccade paradigm (Fig. 1). The animals performed primary horizontal saccades in response to the displacement of a fixation target of 12.5° amplitude. On average, the saccades were slightly hypometric (mean amplitude: 12.1°), had a latency of 186 ms and a duration of 46 ms. To measure the spatiotemporal response properties of the recording sites, a sparse dynamic noise stimulus was presented throughout the trials. By confining our analysis to only those stimuli of the random stimulation sequence that were presented directly before or after a saccade, we were able to investigate potential perisaccadic changes in the representation of time, assessed by analyzing responses to stimulation sequences of different stimulus-onset asynchronies (SOAs). Based on a signal-to-noise criterion, we included the data of \( n = 128 \) sites from two monkeys in our analysis (\( n = 75 \) from monkey M; \( n = 53 \) from monkey B).

Perisaccadic RFs

To investigate the perisaccadic temporal responses, we first had to establish the corresponding spatial dimensions of the RFs. Previous works have shown that RF positions in V4 can be modulated shortly before a saccade (20, 22, 38). Perisaccadic spatial modulation of visual RFs along the saccade vector has also been found in other areas [e.g., forward remapping; LIP: Duhamel et al. (16), Wang et al. (42), FEF: Umeno and Goldberg (43), SC: Walker et al. (44)]. Accordingly, we anticipated any possible changes in RF position or structure to occur along the horizontal dimension.

Before the saccade task, the RF boundaries for every recording site were mapped in horizontal and vertical dimensions while the animal maintained fixation. In both monkeys, the recorded RFs were positioned in the lower right quadrant of the visual field [average coordinates (hor./vert.): 1.9°/−4.5° and 1.1°/−1.2° for monkey M and B, respectively]. To analyze the perisaccadic RFs, we centered all responses at a given site during the saccade task to the horizontal RF peak (yielding an average or population RF) and then compared the resulting horizontal spatial profile between different 50 ms time bins relative to saccade onset. Results of this analysis are shown in Fig. 3A for the six time windows within ±150 ms around the saccade. In all panels, the response to the stimulus is visible as a transient increase in activity starting at ~64 ms latency. This primary response shows a clear spatial confinement to the RF in all time windows. In fact, activity in response to stimulation at non-RF

![Figure 2](image-url). Summary of data selection and alignment (see text for a detailed description). Multunit activity (MUA) was extracted following stimuli that were presented inside the RF (RF hits) within one of three time windows relative to the saccade (fix, pre, and post). Starting from that “primary pulse” (colored), cases of sequential stimulation at varying stimulus onset asynchrony (SOA) were selected (dashed curves). This search was directed forward for “fix” and “post,” and backward for “pre,” to ensure that no extracted interval extended beyond the time of saccade execution. Note that the “primary pulse” was therefore temporally second in the perisaccadic time window, as illustrated in the bottom row. MUA average curves are illustrations only and do not represent actual data.
locations appears even suppressed during steady fixation (“surround suppression,” blue regions in top panels).

The responses were overall strongly modulated by the saccade in the form of an overall burst in activity. However, the burst was spatially unselective (along the mapped horizontal saccade vector), and after subtraction of this background, the RFs showed no visible modulation of their horizontal position and extent. We quantified this stability by comparing RF position and size at each site in the two perisaccadic time windows. We computed this stability by comparing RF position and size at each site in the two perisaccadic time windows (presaccadic and postsaccadic; see Fig. 3B). The distribution of perisaccadic changes in both parameters did not significantly deviate from zero mean for either monkey (bootstrap test, all P > 0.05, uncorrected). This confirmed that the spatial RFs were stable around the time of the saccade, allowing us to analyze the perisaccadic temporal response profiles in more detail.

Responses to Sequential Stimulation

For the temporal analysis, we included only those stimuli that were presented inside the RF at each site. In other words, we took cross sections at the RF locations (averaged across the extent of the RFs) of the activity maps shown in Fig. 3 for the single pulse case and analyzed them as single traces over time. Our aim was to characterize the perisaccadic representation of two sequentially presented stimuli at varying SOA. Thus, for every stimulus presentation, we first collected the single-pulse response and then searched iteratively for stimuli following (fix/post-sacc) or preceding (pre-sacc) at SOAs between 10 ms and 80 ms in steps of 10 ms. We compared the resulting temporal response profiles across the same time bins relative to saccade onset as section Perisaccadic RFs.

Figure 4 shows the temporal MUA response profiles for single-pulse stimulation and three exemplary SOAs. Here, the time axis is aligned to the peak response induced by a single-pulse presentation. This means that the time of the secondary peak in each panel will correspond to the presented SOA if the response latency is stable across the given time window. Note also that the secondary pulse in the presaccadic time window is the (temporally) first pulse since the data are aligned to the stimulus closest to the saccade.

The mean recorded responses are shown in black, with the shaded area indicating the bootstrapped 95% confidence interval (CI). For all SOAs > 20 ms, the MUA showed a clear separation of the responses to the primary and secondary pulse. We subtracted from each response curve the single-pulse response (dashed lines and left column) to isolate the incremental response to the secondary pulse (colored solid line).

The saccade-related burst of activity described under Perisaccadic RFs above is similarly visible here in the presaccadic time windows as a general increase in the baseline (single-pulse) activity (cf., Fig. 3; note that due to the shorter time scale in this figure the subsequent decrease in activity is not visible in most panels). Yet, the isolated secondary response shows a comparatively reliable representation of the presented SOA in each case.

To analyze the temporal accuracy of this representation, we collected the incremental secondary peak from each condition (except the single-pulse data) and aligned the activity profiles to their corresponding SOA (Fig. 5A). This revealed that the secondary responses were highly consistent across different SOAs, both in the overall waveform shape and the time of their peak. The interval durations as derived from the response peak times showed on average a very small positive offset with respect to the veridical SOA (residuals across time windows and monkeys: mean = 2.086 ms, SD = 2.492 ms). However, this offset was found for both, the fixation and perisaccadic time windows [i.e., the bootstrapped 95%
We extracted onset latencies by setting a threshold (95% quantile of the baseline activity) to the MUA after subtraction of the perisaccadic burst (onsets marked by triangles in Fig. 4). For intervals shorter than 60 ms, the onset to the second response cannot be reliably isolated due to large overlap of the responses (open triangles). We, therefore, only used SOAs 60, 70, and 80 ms for our estimation of the latency changes (filled).

The resulting interval residuals are shown in Fig. 5C, analogous to the residuals based on peak times presented in Fig. 5B. In monkey B, onset latencies were reduced in the presaccadic time window by 5.11 ms on average relative to steady fixation (P = 0.005, uncorrected) but unchanged in the postsaccadic time window. In monkey M, there was no significant modulation of onset latency across time windows.

Notably, the observed presaccadic reduction in latencies in monkey B again did not depend on SOA (shorter SOAs are represented as open triangles in Fig. 5C to approximate the trend but were not included in calculating the mean values). This pattern, that is, a constant offset between time windows, could likely be due to slight differences in the MUA traces obtained from the single-pulse stimulation, even if there is no neural modulation of latency, for example, as a result of differences in the signal-to-noise level. This is because the onset time detected for the single-pulse category is necessarily used as a delimiter for all intervals within the respective time window and will therefore add a constant offset to the residual for each SOA.
In summary, our analysis of response onsets did not reveal a consistent modulation of latency across time windows. However, given the limitations of our data with regard to this analysis, the discrepancy in the findings between monkeys is difficult to interpret.

As outlined in the INTRODUCTION, it has been shown previously that the perceived duration between two visual events may depend on the amplitude ratio of the two response peaks. Along this line, the spatially unspecific burst of activity we observed around the time of the saccade (cf., Figs. 3 and 4) could lead to a perisaccadic misrepresentation of time. We, therefore, reanalyzed our data with respect to peak amplitudes.

We extracted the ratio of amplitudes between response peaks from the mean recorded data (black lines in Fig. 4), now based on the temporal order, that is, second to first pulse. We limited this analysis to SOAs > 20 ms because the two peaks were not separable for shorter intervals. The resulting peak ratios are shown in Fig. 6A. During steady fixation, the second response peak showed either the same or a reduced amplitude. This was clearly modulated by the background activity in the perisaccadic time windows, where relative amplitudes of the second peak were increased in both time windows in monkey B and post-saccade in monkey M (all $P < 0.05$). As expected, the slightly different patterns between the monkeys were explained directly by the individual slopes of the perisaccadic burst within each time window (Fig. 6B). The burst was narrower in monkey M and did not extend as much into the mapped time period (0–80 ms) in the presaccadic time window as in monkey B. Consequently, the peak ratios were modulated only in the postsaccadic time window in monkey M.

**DISCUSSION**

We investigated the influence of saccadic eye movements on the spatiotemporal response characteristics of neurons in area V4 of the macaque monkey. Our results show that brief time intervals between two sequential stimuli were reliably represented by the separation of MUA response peaks. Response amplitudes were, however, modulated by a (stimulus-unspecific) burst of activity in perisaccadic time windows. Assuming that subsecond time perception is partly based on activity levels, the observed effect could in principle account for previously described perisaccadic distortions of time perception.

**Amplitude Modulation of Double-Pulse Responses in V4**

As outlined in the INTRODUCTION, information about the relative timing between two unitary stimuli is theoretically available through either latency or the ratio between response amplitudes. Assuming that the saccade-related misperception of temporal intervals is based on one (or both) of these measures, our data suggest that the correlate in V4 is a global modulation of response amplitudes. In both time windows immediately neighboring saccade on- and offset (pre/post),
addition, also from visual activity caused by the saccade, that
relayed from the saccade network (corollary discharge) or, in
ground activity in our data primarily represents activity
simulated (9). It is not clear whether the perisaccadic back-
larly induced by fast retinal motion when a saccade is only
nostasis does not speci-
depend on stimulus features and spatial position relative to
temporal judgements (i.e., expansion vs. compression) may
determined (5). Furthermore, which of the two effects determines
temporal properties previously [LIP: Jazayeri and Shadlen (49)
and Leon and Shadlen (50), FEF and SC: Mayo and Sommer
(33, 51)]. Importantly, FEF feedback onto area V4 has been
shown to play a role in attentional and spatial modulation of
V4 activity (52–54). Likewise, such feedback projections might
also be functionally relevant for the representation of time in
area V4.

The account of perisaccadic temporal distortions pre-
sented above rests to a large part on the evidence pre-
sented by Mayo and Sommer (33). Although their findings
suggest that relative response amplitudes and perceived
duration are linked, it is not yet clear whether that assump-
tion holds generally true. More specifically, it remains to
be shown if variability of response amplitudes that extends
beyond noise (such as the perisaccadic activity in our data)
could even evoke temporal misjudgments. A modulation
such as this could be induced experimentally in a psycho-
physical study, for example, through a systematic varia-
tion of stimulus contrast. The latter seems particularly
promising given that both latency and amplitude of neural
responses at low processing stages covary with stimulus
contrast [e.g., LGN: Maunsell et al. (55)]. This may lead to
internal correction mechanisms at higher stages that use
amplitude levels to recalibrate stimulus onsets, which
could contribute to the link between response amplitudes
and perceptual judgements. Alternatively, the correlation
observed by Mayo and Sommer may instead relate exclu-
sively to neural adaptation [as suggested by the authors;
see also Mayo and Sommer (51)]. In either case, characteriz-
ing the link between relative response amplitudes and per-
ceived duration in psychophysical studies will facilitate
interpretation of physiological results like ours in the
future.

The general and spatially unspecific increase of the saccade-
related activity led to an increase in amplitude of the second
of the two response peaks as compared with the same
response during steady fixation. Following the results of
Mayo and Sommer (33), this increase of amplitude of the sec-
ond response peak would be indicative of an expansion of per-
ceived time, that is, in line with the phenomenon of
chronostasis (8). The timing of the saccade-related increase of
neural activity in our data is indeed roughly aligned with the
period of maximum perceptual expansion of time (9).
However, it seems unlikely that the two observations, that is,
the activity increase and chronostasis, are causally related.
First, if this was the case the perceptual expansion should be
followed by a time period of compression caused by the
decreasing activity at around 150 ms post-saccade. Such a
postsaccadic rebound effect to chronostasis, that is, a compres-
sion of perceived time, has not been described in the litera-
ture. Instead, compression was observed only presacca-
dically (5). Furthermore, which of the two effects determines
temporal judgements (i.e., expansion vs. compression) may
depend on stimulus features and spatial position relative to
the saccade target (9, 45). As a second caveat, it should be
noted that, unlike temporal compression, expansion or chro-
nostasis does not specifically require a saccade, but is simi-
larly induced by fast retinal motion when a saccade is only
simulated (9). It is not clear whether the perisaccadic back-
ground activity in our data primarily represents activity
relayed from the saccade network (corollary discharge) or, in
addition, also from visual activity caused by the saccade, that
is, extensive retinal blur. Our finding of a spatially unspecific
presaccadic increase of activity, that is, while the eyes were
still fixating, speaks for a saccade related mechanism. Yet, we
cannot rule out additional visual mechanisms as there were
always two stimuli present on the screen during any given
frame cycle. Even though both effects may contribute to the
perceptual outcome of chronostasis, these will be crucial to
disentangle in future studies. This is because temporal com-
pression is selectively associated with the saccade itself, and
a neural account of how the two opposite phenomena (chrono-
stasis and compression) can be reconciled is still lacking. If
augmented activity, as described here, indeed leads to a per-
ceptual overestimation of time, time compression may con-
versely be attributable to a phase of suppression. Although we
did not observe saccadic suppression in our V4 MUA data, it
has been reported for V4 single-unit activity (SUA) (46) and
consistently been found in SUA in dorsal stream areas [see, e.
g., Bremmer et al. (14), Ibbotson and Krekelberg (47), and
Thiele et al. (48)]. Thus, both types of temporal mispercep-
tions could in principle be accounted for by known patterns of
perisaccadic activity. However, the ubiquity of saccade-related
activity throughout areas within the visual system (as well as
beyond it) implies that the neural correlate of these misper-
ceptions is widely distributed. Although the present study sug-
gests that area V4 could be involved, the activity patterns in
the core areas of the saccade network might be considered
more likely to be causal to the perceptual outcome. Indeed,
these areas have also been implicated in the representation
of temporal properties previously [LIP: Jazayeri and Shadlen
(49) and Leon and Shadlen (50), FEF and SC: Mayo and Sommer
(33, 51)].
No Consistent Modulation of Response Latencies

Our analysis of sequential stimulus presentations showed that in the (neural) temporal domain all intervals were reliably represented, surprisingly even those with SOAs as short as 20 ms. We did not expect this level of temporal discrimination within neural responses in V4 given that this area is primarily associated with the selection/extraction of attended features in object recognition (56). Although the reverse correlation procedure likely enhanced the temporal precision additionally, our data nonetheless show that the information about very brief time intervals is at least available in the ventral stream at the level of V4.

We analyzed the perisaccadic modulation of temporal representations based on two different quantifications of response latency: the response peak and its onset. The temporal representations as defined between peaks were unchanged between fixation and both perisaccadic time windows. When defining intervals between response onset times for SOAs with sufficient separation of the two responses, we found an inconsistent pattern of perisaccadic modulation. Here, intervals were selectively compressed (relative to fixation) in the presaccadic time window in one monkey, whereas the other showed no significant changes. This result is difficult to interpret. Theoretically, the observed reduction could be representative of a perisaccadic compression of perceived time that was limited to this time window and monkey. We would argue, however, that it is more likely an artifactual effect arising from the analysis; as noted under Responses to Sequential Stimulation in RESULTS, the thresholding procedure necessary to define response onset times is vulnerable to differences in the signal-to-noise ratio between time windows. Lending support to this explanation is the lack of a modulation of the effect by SOA. Moreover, the latency reduction reported previously occurred for stimuli presented between 30 ms and 250 ms after saccade onset (28), whereas latencies for our post-saccadic time window (0–50 ms) were similar to those during steady fixation.

Given these results, we conclude that our data do not sufficiently indicate that neural response latencies were systematically modulated by the saccade.

This contrasts with the pattern of results reported by Ibbotson et al. for areas MT and MST, where latencies were reduced shortly after saccade onset (28–31). The difference between these findings and our own has several possible explanations. First, the neurons in MT/MST characterized by Ibbotson et al. showed strong suppression of response amplitudes during the ~100 ms directly preceding saccade onset ("saccadic suppression"). The reduction in latency followed this suppression and was accompanied by a period of amplitude enhancement. Ibbotson et al. proposed that this second phase ("short-latency, high-gain") may be necessary to compensate for the gap in reliable information caused by the saccade. For areas MT and MST, which predominantly process visual motion information, these mechanisms (suppression and compensatory enhancement, or release from inhibition) are of particularly high relevance. This is because 1) the retinal movement from the saccade produces wide-field background motion, and 2) motion information is often relayed to motor output in feedback loops (e.g., smooth pursuit eye movements) that are time sensitive. This is arguably not the case for the visual information processed in area V4, which may be the reason why our data showed no latency modulation. In line with this explanation, we did not observe saccadic suppression of response amplitudes in our paradigm (but note that, as mentioned above, it has been described in V4 SUA previously) (46). It would be interesting to explore in future studies whether saccadic suppression and modulation of response latencies are indeed linked.

Although our data did not show classical suppression, the large perisaccadic increase in baseline activity led to a considerable reduction in the signal-to-noise ratio of responses within these time windows. This effect is particularly visible in the post-saccadic data from monkey M (Fig 4B, bottom). Here, the first of the two responses was aligned with the time of the steepest increase in activity and exceeded this baseline only marginally. Indeed, the full perisaccadic burst showed both a higher relative peak as well as higher peak increase in activity in monkey M than in monkey B (cf., the two panels in Fig. 6B; note that the scaling is normalized to the peak amplitude of the primary responses in each time window).

Still, the responses to the secondary pulse (after subtraction of the baseline) were robust, despite the overall noisy pattern. Thus, the information about the temporal interval was still contained in the responses and merely obscured by signal-independent noise. The open question remains if and how well the brain is able to compensate for this in a perceptual read-out of time. A possible corrective mechanism might compare the activity to a corollary discharge signal relayed from the saccade network, thus essentially performing the same baseline correction we applied in our analysis. If, on the other hand, such a correction was not implemented or could not fully compensate for the perisaccadic burst, the baseline activity may be erroneously interpreted as part of the response, leading to misestimations of stimulus onset times in higher areas (e.g., the frontal cortex).

As an alternative explanation for the discrepancy of our results with previous studies, it has to be considered that our paradigm may not be suited to evoke latency modulations in V4. The random noise stimulation procedure effectively generated a constant flicker, lacking any stable or salient stimuli apart from the fixation/saccade target. Given the role of area V4 in object recognition, a putative mechanism of perisaccadic latency modulation may not be engaged under these circumstances simply because it was not relevant (possibly mediated by top-down attentional processes). To further investigate perisaccadic processing in V4, future studies could thus employ stimulation paradigms that include single identifiable objects or a task that requires separation by stimulus features [for an overview see Roe et al. (56)].

In a similar vein, the possible influence of attentional deployment may also be considered. The saccade task in our paradigm did not include an additional attention task and, importantly, saccade direction was not randomized across trials. As a result, the attentional focus was likely invariably located around the future saccade target across trials. It has been shown previously that spatial attention can modulate activity in V4 independent of individual features or objects and that these effects can spread to irrelevant stimuli in spatial proximity to the attended object (57, 58). This mechanism may have enhanced responses to stimuli closer to the saccade target in the present study. Importantly, this possible
enhancement was present across all trials and, hence, is unlikely to have other stimulus-specific effects.

Lastly, it is important to note that the present study characterized multunit responses, whereas previous studies in this context [including the work by Ibbotson et al. (28–31)] in MT/MST have mostly investigated single neurons. If only a smaller subset of V4 neurons showed a change in latencies, this modulation could have been masked in the aggregate MUA response. We would argue, however, that the impact of such a hidden modulation on perception would likely be small when the activity of the population is read out, particularly in comparison to the more consistent modulation in response amplitudes.

Spatial Stability of RFs

Aside from the aforementioned considerations about temporal processing, it is also noteworthy that our data showed spatially highly stable RF positions around the time of the saccade. This is in contrast with previous studies showing that neurons in V4 (among other areas) shift their RF position toward either the future RF or the saccade target immediately before saccade onset (“saccadic remapping” (20, 22, 38)). Notably, however, these studies used RF mapping based on one single or few stimuli per trial. A dense configuration with multiple stimuli on the screen at any given time on the other side might elicit weak or no remapping (46, 59). These results suggest that remapping may be dependent on stimulus saliency, which is well in line with evidence from other areas [LIP: Gottlieb et al. (60), FEF: Joiner et al. (61), and SC: Churan et al. (62)]. Our finding of perisaccadically stable RF positions lends further support to this previous result. It should be noted, however, that these findings on the cellular level do not necessarily translate directly to a perceptual outcome. Human psychophysical studies using a reverse-correlation approach based on classification images were able to characterize different perisaccadic perceptual effects despite a dense multistimulus array [spatial distortion: Panichi et al. (63), saccadic suppression of displacement: Joosten and Collins (64)]. Similarly, future investigations focusing on how the perisaccadic distortion of time depends on stimulus parameters could help to establish links between the neural level and perception.

CONCLUSION

In summary, our results highlight the perisaccadic representation of brief visual intervals in area V4. We found that reliable temporal information about intervals as short as 20 ms was contained in the separation of MUA-response peaks at all time points relative to the saccade. Our findings point to a modulation of relative response amplitudes rather than latency in area V4 as a neural correlate of perisaccadic perceptual distortions of time.

ACKNOWLEDGMENTS

We are grateful to Yvonne Velte and Katharina Martin for animal care and Alexander Platzner for technical support.

GRANTS

This work was supported by the German Research Foundation: FOR-1847, IRTG-1901, and CRC/TRR-135 (Project No. 222641018).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

S.K. and F.B. conceived and designed research; S.K. and S.D. performed experiments; J.C.B.S., S.K., and B-O.W. analyzed data; J.C.B.S., S.K., B-O.W., S.D., and F.B. interpreted results of experiments; J.C.B.S. and S.K. prepared figures; J.C.B.S. and S.K. drafted manuscript; J.C.B.S., S.K., B-O.W., S.D., and F.B. edited and revised manuscript; J.C.B.S., S.K., B-O.W., S.D., and F.B. approved final version of manuscript.

REFERENCES

1. Binda P, Morrone MC. Vision during saccadic eye movements. Annu Rev Vis Sci 4: 193–213, 2018. doi:10.1146/annurev-vision-091517-034317.
2. Burr DC, Morrone MC. Perception: transient disruptions to neural space–time. Curr Biol 16: 847–849, 2006. doi:10.1016/j.cub.2006.08.075.
3. Ross J, Morrone MC, Goldberg ME, Burr DC. Changes in visual perception at the time of saccades. Trends Neurosci 24: 131–132, 2001. doi:10.1016/S0166-2236(00)01685-4.
4. Burr DC, Ross J, Binda P, Morrone MC. Saccades compress space, time and number. Trends Cogn Sci 14: 528–533, 2010. doi:10.1016/j.tics.2010.09.005.
5. Morrone MC, Ross J, Burr D. Saccadic eye movements cause compression of time as well as space. Nat Neurosci 9: 950–954, 2005. doi:10.1038/nn1488.
6. Yu G, Yang M, Yu P, Doris MC. Time compression of visual perception around microsaccades. J Neurophysiol 118: 415–424, 2017. doi:10.1152/jn.00229.2017.
7. Schutz AC, Morrone MC. Compression of time during smooth pursuit eye movements. Vision Res 50: 2702–2713, 2010. doi:10.1016/j.visres.2010.07.022.
8. Yarrow K, Haggard P, Heal R, Brown P, Rothwell JC. Illusory percepts of space and time preserve cross-saccadic perceptual continuity. Nature 414: 302–305, 2001. doi:10.1038/35104551.
9. Knoll J, Morrone MC, Bremmer F. Spatio-temporal topography of saccadic overestimation of time. Vision Res 83: 56–65, 2013. doi:10.1016/j.visres.2013.02.013.
10. Park J, Schlag-Rey M, Schlag J. Voluntary action expands perceived duration of its sensory consequence. Exp Brain Res 149: 527–529, 2003. doi:10.1007/s00221-003-1376-x.
11. Yarrow K, Rothwell JC. Manual chronostasis: tactile perception precedes physical contact. Curr Biol 13: 1134–1139, 2003. doi:10.1016/S0960-9822(03)00413-5.
12. Binda P, Morrone MC, Bremmer F. Saccadic compression of symbolic numerical magnitude. PLoS One 7: e49587, 2012. doi:10.1371/journal.pone.0049587.
13. Bremmer F, Churan J, Lappe M. Heading representations in primates are compressed by saccades. Nat Commun 8: 920, 2017. doi:10.1038/s41467-017-01021-5.
14. Bremmer F, Kubischik M, Hoffmann KP, Krekelberg B. Neural dynamics of saccadic suppression. J Neurosci 29: 12374–12383, 2009. doi:10.1523/JNEUROSCI.2908-09.2009.
15. Chen X, Zirnsak M, Moore T. Dissonant representations of visual space in prefrontal cortex during eye movements. Cell Rep 22: 2039–2052, 2018. doi:10.1016/j.celrep.2018.01.078.
16. Duhamel JR, Colby CL, Goldberg ME. The updating of the representation of visual space in parietal cortex by intended eye movements. Science 255: 90–92, 1992. doi:10.1126/science.1553535.
17. Krekelberg B, Kubischik M, Hoffmann KP, Bremmer F. Neural correlates of visual localization and perisaccadic mislocalization. Neuron 37: 537–545, 2003. doi:10.1016/S0896-6273(03)00003-3.
18. Moore T, Tolias AS, Schiller PH. Visual representations during saccadic eye movements. Proc Natl Acad Sci USA 95: 8981–8984, 1998. doi:10.1073/pnas.95.15.8981.
Electrodes, fine wires, needles and microsensors. J Neurosci Methods 49: 175–179, 1993. doi:10.1016/0165-0270(93)90127-1.

Wang X, Fung CCA, Guan S, Wu S, Goldberg ME, Zhang M. Perisaccadic receptive field expansion in the lateral intraparietal area. Neuron 90: 400–409, 2016. doi:10.1016/j.neuron.2016.02.035.

Umeno MM, Goldberg ME. Spatial processing in the monkey frontal eye field. I. Predictive visual responses. J Neurophysiol 78: 1373–1383, 1997. doi:10.1152/jn.1997.78.3.1373.

Walker MF, FitzGibbon MA, Goldberg ME. Neurons in the superior colliculus predict the visual result of impending saccadic eye movements. J Neurophysiol 73: 1988–2003, 1995. doi:10.1152/jn.1995.73.5.1988.

Georg K, Lappe M. Spatio-temporal contiguity of saccade-induced chronostasis. Exp Brain Res 180: 535–539, 2007. doi:10.1007/s00221-007-0876-5.

Zanos TP, Mineault PJ, Guitton D, Pack CC. Mechanisms of saccadic suppression in primate cortical area V4. J Neurosci 36: 9227–9239, 2016. doi:10.1523/JNEUROSCI.1015-16.2016.

Ibbotson MR, Krekelberg B. Visual perception and saccadic eye movements. Curr Opin Neurobiol 21: 553–558, 2011. doi:10.1016/j.conb.2011.05.012.

Thiele A, Henning P, Kubischik M, Hoffmann KP. Neural mechanisms of saccadic suppression. Science 295: 2460–2462, 2002. doi:10.1126/science.1066813.

Jazayeri M, Shadlen MN. A neural mechanism for sensing and reproducing a time interval. Curr Biol 25: 2599–2609, 2015. doi:10.1016/j.cub.2015.08.038.

Leon MI, Shadlen MN. Representation of time by neurons in the posterior parietal cortex of the macaque. Neuron 38: 317–327, 2003. doi:10.1016/S0896-6273(03)00003-7.

Mayo JP, Sommer MA. Neuronal adaptation caused by sequential visual stimulation in the frontal eye field. J Neurophysiol 100: 1923–35, 2008. doi:10.1152/jn.00549.2008.

Armstrong KM, Fitzgerald JK, Moore T. Changes in visual receptive fields with microstimulation of frontal cortex. Neuron 50: 791–798, 2006. doi:10.1016/j.neuron.2006.05.010.

Moore T, Armstrong K. Selective gating of visual signals by microstimulation of frontal cortex. Nature 421: 370–373, 2003. doi:10.1038/nature01341.

Noudoost B, Clark KL, Moore T. A distinct contribution of the frontal eye field to the visual representation of saccadic targets. J Neurosci 34: 3687–3698, 2014. doi:10.1523/JNEUROSCI.3824-13.2014.

Maunsell JHR, Ghose GM, Assad JA, Mcadams CJ, Boudreau CE, Noerager BD. Visual response latencies of macaque single V4 neurons. Vis Neurosci 16: 1–14, 1999. doi:10.1017/S095252399156177.

Roe AW, Chelazzi L, Connor C, Conway BR, Fujita I, Gallant JL, Lu H, Vanduffel W. Toward a unified theory of visual area V4. Neuron 74: 12–29, 2012. doi:10.1016/j.neuron.2012.03.011.

Connor CE, Preddie DC, Gallant JL, Van Essen DC. Spatial attention effects in macaque area V4. J Neurosci 17: 3201–3214, 1997. doi:10.1523/JNEUROSCI.17-03-0201.1997.

Mcadams CJ, Maunsell JHR. Attention to both space and feature modulates neuronal responses in macaque area V4. J Neurophysiol 83: 1751–1755, 2000. doi:10.1152/jn.2000.83.3.1751.

Marino AC, Mazer JA. Saccades trigger predictive updating of attentional topography in area V4. Neuron 86: 429–438.e4, 2018. doi:10.1016/j.neuron.2018.03.020.

Gottlieb JP, Kusunoki M, Goldberg ME. The representation of visual salience in monkey parietal cortex. Nature 391: 481–484, 1998. doi:10.1038/35135.

Joiner WM, Cavanaugh J, Wurtz RH. Modulation of shifting receptive field activity in frontal eye field by visual salience. J Neurophysiol 106: 1179–1190, 2011. doi:10.1152/jn.01054.2010.

Churan J, Guitton D, Pack CC. Context dependence of receptive field remapping in superior colliculus. J Neurophysiol 106: 1862–1874, 2011. doi:10.1152/jn.00388.2011.

Panichi M, Burr D, Morrone MC, Baldassi S. Spatiotemporal dynamics of perisaccadic remapping in humans revealed by classification images. J Vis 12: 1–15, 2012. doi:10.1167/12.4.1.

Joosten ERM, Collins T. Probing transsaccadic correspondence with reverse correlation. J Vis 18: 1–14, 2018. doi:10.1167/18.3.10.