Saccade-related activity in areas 18 and 21a of cats freely viewing complex scenes

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Although saccadic eye movements can radically change the retinal image, perceptually their impact is surprisingly small. Here, we investigate possible neuronal correlates of saccadic suppression in cats freely viewing natural stimuli. By comparing changes attributable to saccadic events with passive stimulus changes, we find that during saccades: (i) evoked and induced activity is reduced in areas 18 and 21a by equal amounts, (ii) the variability of neuronal activity with stimulus category is abolished in both areas, and (iii) the high-power transient induced by stimulus change is not observed. These results present electrophysiological evidence for saccadic suppression at the level of primary and higher visual cortex under natural conditions. *NeuroReport* 18:401–404 © 2007 Lippincott Williams & Wilkins.

Keywords: evoked potential, induced activity, local field potential, natural stimuli, saccades, saccadic suppression

Introduction

Saccadic eye movements are used by humans and many other species to explore rapidly their environment under normal behavioral conditions. During such rapid movements, the retinal image changes quickly. Curiously, we experience neither the rapid change of stimulus resulting from a saccade nor the rapid image transitions themselves. Instead, we have a stable perception of the world.

This striking phenomenon has attracted much research interest and has so far been addressed from two angles. Psychophysics has shown that visual perception during fast eye movements is reduced, an effect known as saccadic suppression [1,2]. Electrophysiological studies have found that neuronal activity in the lateral geniculate nucleus and visual cortex is modulated during eye movements. Several studies, however, have reported different effects: enhancement, facilitation, or suppression of neuronal activity [3–6], or a combination of the above [7,8]. Furthermore, the contribution of early and higher visual areas to these phenomena has not yet been resolved [5,9], an issue of particular relevance for the processing of complex stimuli under natural conditions.

In many studies, the evoked (event-related) activity is measured, which quantifies only the time-locked and phase-locked response to a repeated event, and averages out any nonphase-locked activity. Recent studies have, however, demonstrated the major contribution of ongoing cortical activity to the cortical processes [10]. Such activity not necessarily has a constant phase to a given event, and is therefore missed by investigating only strictly phase-locked responses. Induced activity quantifies responses that are time-locked to an event, but by representing responses in frequency space, it also captures the nonphase-locked activity. Recent studies of visual processing have highlighted the relevance of this induced activity [11,12]. Hence, in investigating the physiological substrate of saccadic suppression, we considered both the evoked and induced components of the responses.

The goal of the present study was to quantify the impact of the changing stimulus structure on neuronal activity in two contrasting cases: first, during eye movements while a static stimulus is presented; and second, during fixation while the stimulus changes from one static image to another. Neuronal activity was recorded in the primary (area 18) and higher (area 21a) visual cortex in freely viewing cats, and evoked and induced activity was analyzed. The stimuli used were presented as a continuous sequence, and included gratings, noise, and uniform images, as well as natural images.

Methods

Experimental procedures

Data were obtained from three alert cats using chronically implanted electrodes [13]. Surgery was performed under sterile conditions using isoflurane anesthesia (0.4–1.5%, mixed in 30% O_2/70% NO_2). Analgesics were delivered during and after surgery. Electrode bundles were placed in

the supragranular, granular, and infragranular layers [14]. Recording sessions were initiated only after the animals had recovered fully. We recorded from a total of 29 sites in area 18 and 18 sites in area 21a. All receptive field locations were well within the central visual field. Electrophysiological signals were passed through a preamplifier (Neurotrack, Budapest, Hungary; $\times 10$ amplification) and digitized at 20 kHz using a Synamp system (Neuroscan, El Paso, Texas, USA) with a 5-Hz high-pass and 3-kHz low-pass analogue filter. The local field potential (LFP) was derived after low-pass filtering and resampling of the electrophysiological signals at 1 kHz.

Eye movements were recorded with a Dual-Purkinje Image eye-tracker (Forward Optical Technologies, Clute, Texas, USA) [15] and were sampled at 1 kHz and analyzed offline.

Animals were head-fixed and they freely viewed the stimuli and no reward or any other kind of feedback was given. Recording sessions lasted for an average of 15–20 min per day. During the sessions, the state of alertness of the animal was monitored continuously using an infrared camera and an online examination of LFP and eye movement traces. All procedures complied with university and governmental regulatory guidelines for experimental animal care (Kantonales Veterinäramt Zürich).

Visual stimuli

Stimuli were presented on a 19″ CRT monitor (Hitachi, 120 Hz refresh rate, 8-bit grey scale) in an otherwise darkened room. The monitor horizontally covered 53° and vertically 40° of the central visual field of the cat. This provides a sufficient screen size for the $\pm 25°$ oculomotor range of cats and hence all fixations were well within the limits of the screen.

Five stimulus categories and one control condition (complete darkness) were used. All stimuli were normalized for contrast and brightness and had a spatial resolution of 640×480 pixels. The five stimulus categories were: natural images acquired from a cat's perspective [16]; sine wave gratings, which were vertically oriented with a spatial frequency of 0.2 cycles/degree and varied only in phase; pink pixel noise, which had the same frequency spectrum as the natural images; wavelet noise [12] and a uniform grey image. We did not record stimulus changes for the grey image but only saccadic eye movements while presenting this category (see Fig. 1c and d), as brightness was fixed for all images. To allow the investigation of neuronal activity during stimulus changes, 10 different images from each of the first four stimulus categories were presented consecutively, with each image presentation lasting 2 s. This meant that the transitions between images were to another image of the same type. For the saccade condition, stimuli were presented for 25 s during which saccades were detected.

Data analysis

Saccades were defined with respect to a velocity threshold [16]. Electrophysiological data were analyzed both by alignment to stimulus onset (change condition) and by alignment to the onset of a saccadic eye movement (saccade condition). In the case of the saccade condition, only those saccades that occurred more than 1000 ms before or after an image transition were included in our analysis. In the stimulus change condition, we ensured that no saccade occurred within the same time window of an acceptable

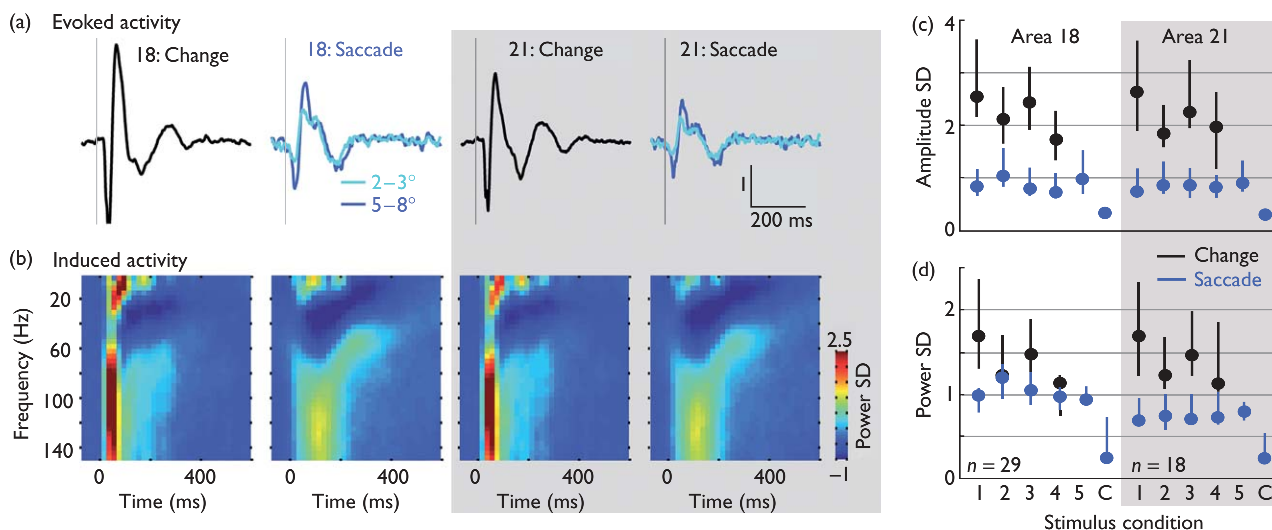

Fig. 1 Example graphs of evoked and induced activity owing to stimulus change and saccade. (a) Evoked activity aligned to stimulus change (black lines) and saccade onset (blue lines depict large saccades, cyan lines small saccades) in areas 18 (white background) and 21a (grey background), averaged over a single recording site in each area. Activity is averaged over all stimuli conditions in each case. The grey vertical bar represents the point of alignment. The abscissa represents time in milliseconds, and the ordinate SD from baseline. (b) Induced activity is presented in normalized spectrograms derived from the same data used in the evoked activity analysis of panel (a). The abscissa represents time in milliseconds and the ordinate represents frequency, whereas the color scale codes for the variation of power with respect to baseline. The recording sites in (a) and (b) are from cat Q. Influence of different stimuli on evoked and induced activity. (c) Circles represent the median amplitude and lines depict the 25–75 percentiles of the evoked activity of change (black) and saccade (blue) conditions. The abscissa shows stimulus condition and the ordinate shows the amplitude of the evoked activity in units of SD from baseline activity. (d) Circles represent median power and lines represent the 25–75 percentiles of the induced activity of change and saccade conditions averaged over frequencies, separated for stimulus condition (abscissa); ordinate indicates the power of the induced activity given as SD from baseline. Stimuli categories: 1, natural images; 2, gratings; 3, pixel noise; 4, wavelet noise; 5, grey; C, complete darkness. Data shown is from all cats and all trials.

stimulus change event. Evoked potentials were obtained by averaging the LFP traces across trials for a given condition. Induced oscillations were analyzed using spectral analysis [11,12]. This involves a transformation to the Fourier domain, computation of the power as a nonlinear step, and only after averaging across trials, again for a given condition. This can be carried out repeatedly for different segments of a trial. Hence, even if an increase of neuronal activity is not strictly phase-locked, it can be detected with this method. Fourier analysis was performed with a 100-ms data window and a 80-ms window overlap. Normalization was performed relative to a baseline value defined by the 50 ms period before the saccade or stimulus event. Hence, evoked and induced activities are quantified as z-scores (standard deviations, SD) relative to baseline. To give a statistical measure of size-independent variance, we used the coefficient of variation, which is computed here as the standard deviation of a stimulus category divided by its mean.

Results

Evoked activity

Evoked activity was measured in areas 18 and 21a of alert cats during saccadic eye movements executed while viewing a stationary stimulus, and during stimulus changes in the absence of eye movements. The evoked potentials display the pattern typical for visual responses: a prominent sequence of positive and negative peaks (Fig. 1a). The average amplitude, defined as the difference between the first positive and negative peaks, is significantly stronger in both areas for the change condition than that for the saccade condition: 2.37 ± 1.17 (mean $\pm$ SD across recording sites) compared with 0.89 ± 0.33 in area 18, and 2.13 ± 0.82 compared with 0.85 ± 0.28 in area 21a ($P < 0.001$ for both areas, paired t-tests). In addition, there is no significant difference between areas for both the change condition ($P = 0.443$) and the saccade condition ($P = 0.671$). Hence, evoked activity is weaker during saccadic eye movements than during changes in the stimulus, and this finding holds to a similar degree in both areas.

Comparing saccade-evoked potentials for small (defined as 2–4°) and large (defined as 8–18°) saccades, we find that the size of the evoked potential, as well as its duration, is dependent on saccade amplitude (Fig. 1a, second and fourth panels). The average evoked potential for large saccades is 1.50 in area 18 and 1.33 in area 21a. This is significantly different to small saccades, with an evoked potential of 0.80 in area 18 and 0.82 in area 21a ($P < 0.001$ for both areas, paired t-tests). Hence, the evoked potential increases with the size of saccades to a similar degree in both areas.

Induced activity

The induced activity of each condition quantifies the average power of different frequency bands at a given time, regardless of their phase. The time course of induced activity for each condition is comparable in both recorded areas (Fig. 1b). In the change condition, a high-power transient at stimulus onset dominates (first and third spectrograms). The power rises sharply over all frequencies for a short time, similar to the first peak of the evoked potential, and reaches values of 1.84 and 1.20 in the frequency band of 64–128 Hz, in areas 18 and 21a, respectively. In contrast, induced activity measured in the saccade condition rises more slowly and reaches lower peak values (0.78 and 0.81 at 64–128 Hz, second and fourth spectrograms). There is, however, a more prominent suppression of γ-frequencies (20–60 Hz) in the saccade condition –visible as dark blue regions in the spectrogram well as a higher level of sustained induced activity. This specific impact of saccades on induced activity reaches durations of up to 400 ms, constituting a significant fraction of the intersaccadic interval. To better quantify the induced activity, we averaged the power across the whole frequency spectrum. Induced activity is significantly stronger for the change condition compared with the saccade condition in area 18 (1.49 and 1.05, respectively) and in area 21a (1.34 and 0.81). These differences across conditions are highly significant ($P < 0.001$ for both areas, paired t-tests). In summary, the activity induced by a saccade is much lower than that induced by a pure change of stimulus, and displays a characteristic distribution of power across different frequency bands. These properties differ little between areas 18 and 21a.

Influence of stimulus condition on evoked and induced activity

So far, the analysis has been calculated over all stimuli categories. Now, to compare the influence of stimulus structure on neuronal activity during saccade and change conditions, we measured evoked and induced activity for each of the five different stimulus sets and the control condition, and quantified the variability of the activity across stimulus categories (Fig. 1c and d).

First, we examine evoked activity (Fig. 1c). The coefficient of variation across stimulus categories was significantly larger for the change condition (0.27 in both areas) than that for the saccade condition (0.19 in area 18, 0.13 in area 21a; $P < 0.01$ for both areas, paired t-tests, sign test). Hence, evoked activity during saccades is modulated to a lesser degree by the particular type of stimulus that is being viewed.

Next, we examined induced activity (Fig. 1d). Again, the coefficient of variation is significantly larger for the change condition (0.27 and 0.35 in areas 18 and 21a) than that for the saccade condition in both areas (0.10 and 0.08; $P < 0.001$ for both areas, paired t-tests, sign test). Together, these results demonstrate that the impact of stimulus structure on neuronal activity is significantly reduced when the change in retinal stimulation is due to a saccade.

In addition, the control condition involved measuring the neural activity of animals making saccades during complete darkness, that is, in the complete absence of visual stimulation. For the evoked activity, we find small amplitudes during darkness, which are less than half of those found during visual stimulation (0.40 in area 18 and 0.36 in area 21a). Similarly, the activity induced by saccades during darkness is weaker, with an induced power of 0.48 and 0.38 in areas 18 and 21a, respectively. Thus, the strength of saccade-related activity is much reduced during darkness, demonstrating the crucial relevance of visual stimulation to saccade-related activity.

Discussion

During active vision, we have a stable perception of the world. How this temporal and spatial constancy is achieved despite high-speed eye movements is the topic of some

debate. This study is concerned with the impact of saccades on neural activity in primary and higher visual areas. We find characteristic differences between change and saccade conditions in terms of both evoked and induced activity. Importantly, these signatures of neuronal activity are expressed to a similar degree in the primary (area 18) and higher (area 21a) visual cortex. We also find a low variability in saccade-related activity owing to the structure of the different stimuli used, and this again holds for both areas. These results suggest that the neuronal correlates of saccadic suppression are fully expressed in the primary visual cortex.

Saccadic suppression is the reduction in visibility of various factors such as spatial frequency and luminance. Testing the neuronal response to different stimuli may therefore elucidate this perceptual phenomenon. Kleiser *et al.* [5] tested brain areas for color-selective saccadic suppression using colored or noncolored dot stimuli, and found that hMT, V7 and V4 are likely candidate areas for the neuronal correlates of saccadic suppression. By presenting continuous sequences of structured stimuli without the interruption of a blank screen, we were able to show that in the feline homologue areas V1 and V4 [17], neuronal activity during saccades is not selective for a particular stimulus structure. Thus, even for complex and natural stimuli, we observe correlates of saccadic suppression in higher areas, albeit to the same degree as in the primary visual cortex.

Saccade-induced activity is remarkably sustained, lasting up to 400 ms, but does not show the high-power transient seen in the change condition. Areas 18 and 21a display a highly similar pattern of activation for each condition, which emphasizes the radical difference in cortical processing owing to active as opposed to passive stimulus change. Although saccades have a duration of 30–50 ms in humans [16,18] and 100–150 ms in cats [16,19], saccadic suppression in humans begins 40–60 ms before saccade onset and ends 50–100 ms after saccade offset [20,21]. Taken together with the current findings, this means that saccade-induced activity is present not only during the saccade itself but also during saccadic suppression. The duration of the sustained induced activity found in this study makes up an extensive part of the intersaccadic interval and, by bridging the time from one saccade to the next, it may potentially contribute to the stable subjective perception of the world.

The reported reduction in neuronal response sensitivity to stimulus structure is surprisingly similar in primary and higher visual cortex even for natural stimuli, and might well be a reason for the lower perceptual sensitivity and performance during saccadic eye movements, for example [1,2]. The altered perceptual sensitivity, which is reduced but not abolished [2], may also be related to the qualitatively similar but weaker responses found in the saccade condition as compared with the change condition.

In conclusion, extending the research into the physiological substrate of saccadic suppression by including an analysis of induced activity, we are able to show a distinct difference between active and passive viewing, as well as the substantial impact that saccades have on ongoing neuronal activity in the primary and higher visual cortex.

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References

1. Dodge R. Visual perception during eye movement. *Psychol Rev* 1900; **7**:454–465.
2. Volkmann FC. Vision during voluntary saccadic eye movements. *J Opt Soc Am* 1962; **52**:571–578.
3. Wurtz RH. Response of striate cortex neurons to stimuli during rapid eye movements in the monkey. *J Neurophysiol* 1969; **32**:975–986.
4. Noda H. Depression in the excitability of relay cells of lateral geniculate nucleus following saccadic eye movements in the cat. *J Physiol* 1975; **249**:87–102.
5. Kleiser R, Seitz RJ, Krekelberg B. Neural correlates of saccadic suppression in humans. *Curr Biol* 2004; **14**:386–390.
6. Gross EG, Vaughan HG Jr, Valenstein E. Inhibition of visual evoked responses to patterned stimuli during voluntary eye movements. *Electroencephalogr Clin Neurophysiol* 1967; **22**:204–209.
7. Reppas JB, Usrey WM, Reid RC. Saccadic eye movements modulate visual responses in the lateral geniculate nucleus. *Neuron* 2002; **35**: 961–974.
8. Lee D, Malpeli JG. Effects of saccades on the activity of neurons in the cat lateral geniculate nucleus. *J Neurophysiol* 1998; **79**:922–936.
9. Thilo KV, Santoro L, Walsh V, Blakemore C. The site of saccadic suppression. *Nat Neurosci* 2004; **7**:13–14.
10. Fiser J, Chiu C, Weliky M. Small modulation of ongoing cortical dynamics by sensory input during natural vision. *Nature* 2004; **431**:573–578.
11. Tallon-Baudry C, Bertrand O. Oscillatory gamma activity in humans and its role in object representation. *Trends Cogn Sci* 1999; **3**:151–162.
12. Kayser C, Salazar RF, König P. Responses to natural scenes in cat V1. *J Neurophysiol* 2003; **90**:1910–1920.
13. Kayser C, König P. Stimulus locking and feature selectivity prevail in complementary frequency ranges of V1 local field potentials. *Eur J Neurosci* 2004; **19**:485–489.
14. Siegel M, König P. A functional gamma-band defined by stimulus-dependent synchronization in area 18 of awake behaving cats. *J Neurosci* 2003; **23**:4251–4260.
15. Körding KP, Kayser C, Betsch BY, König P. Non-contact eye-tracking on cats. *J Neurosci Methods* 2001; **110**:103–111.
16. Moeller GU, Kayser C, Knecht F, König P. Interactions between eye movement systems in cats and humans. *Exp Brain Res* 2004; **157**: 215–224.
17. Payne BR. Evidence for visual cortical area homologs in cat and macaque monkey. *Cereb Cortex* 1993; **3**:1–25.
18. Bahill AT, Adler D, Stark L. Most naturally occurring human saccades have magnitudes of 15 degrees or less. *Invest Ophthalmol* 1975; **14**:468–469.
19. Stryker M, Blakemore C. Saccadic and disjunctive eye movements in cats. *Vision Res* 1972; **12**:2005–2013.
20. Latour PL. Visual Threshold during eye movements. *Vision Res* 1962; **2**:261–262.
21. Beeler GW. Visual threshold changes resulting from spontaneous saccadic eye movements. *Vision Res* 1967; **7**:769–775.