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RESPONSE PROPERTIES OF LOCAL FIELD POTENTIALS AND MULTIUNIT ACTIVITY IN THE MOUSE VISUAL CORTEX

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Abstract—Extracellular local field potentials (LFPs) and multiunit activity (MUA) reflect the spatially integrated activity of multiple neurons in a given cortical structure. In the cat and primate visual cortices, these signals exhibit selectivity for visual stimulus features, such as orientation, direction of motion or spatial frequency. In the mouse visual cortex, a model which has been increasingly used in visual neuroscience, the visual stimulus selectivity of population signals has not been examined in detail. We recorded LFPs and MUA using multielectrode arrays and two derived measures, the high-pass filtered continuous MUA and the bipolar first spatial derivative of the LFP, in the visual cortex of isoflurane-anesthetized C57Bl/6 mice. We analyzed the onset latency and characterized the receptive fields in addition to the direction, orientation, and spatial and temporal frequency preferences of these signals. Population signals exhibited onset latencies as short as ~30 ms and possessed receptive fields as large as ~38° with MUA receptive fields smaller than those of LFPs. All four population signals exhibited similar spatial frequency preferences (~0.1 cycles per degree) and temporal frequency preferences (~1 cycle per second). However, for all population signals, spatial and frequency tunings were broad and orientation and direction of motion preferences were absent. The characterization of the visual stimulus selectivity of LFPs and MUA in the mouse visual cortex should provide information regarding their usability in characterizing stimulus properties and disclose possible limitations.

Key words: visual cortex, mouse, LFP, multiunit activity, receptive fields, stimulus selectivity.

INTRODUCTION

In recent years, the mouse visual cortex has become increasingly used as a model in visual neuroscience, mainly because of the availability of advanced transgenic technology in mice. Although mice are not primarily visual animals, individual neurons in the mouse visual cortex exhibit properties similar to those of neurons in the visual cortex of cats and primates (Hübener, 2003). The mouse visual cortex possesses a smooth retinotopic organization to produce a topographic representation of the visual field (Schuett et al., 2002; Kalatsky and Stryker, 2003; Wang and Burkhalter, 2007). Furthermore, single-cell recordings have revealed that all receptive field types that have been described in cats and primates are also present in mice (Dräger, 1975; Mangini and Pearlman, 1980; Métin et al., 1988). Individual neurons in the mouse visual cortex exhibit specific tuning to the orientation of bars or gratings, in addition to distinct spatial and temporal tuning preferences (Niell and Stryker, 2008; Gao et al., 2010; Andermann et al., 2011). However, cellular functional imaging revealed that the preferred orientation and spatial characteristics of individual neighboring cells are randomly distributed in a salt-and-pepper fashion (Ohki et al., 2005; Ohki and Reid, 2007; Andermann et al., 2011). In contrast, the visual cortex of cats or primates displays a columnar organization, in which tuning features for orientation or spatial selectivity are organized into functional columns (Hubel and Wiesel, 1968; Hubel et al., 1978, 1977; Tootell et al., 1981).

The organization of the functional properties of individual cells influences the stimulus selectivity of population signals such as the local field potential (LFP) and multiunit activity (MUA). In cats and primates, the LFP and MUA exhibit stimulus selectivity and specific tuning preferences (Frien et al., 2000; Siegel and König, 2003; Lashgari et al., 2012). In the mouse visual cortex, stimulus selectivity of these signals has not been examined in detail, and it is not clear how the underlying functional organization of individual neurons in the mouse visual cortex reflects these modes of population activity. Because population signals reflect the cumulative activity of a given cortical volume, the spatial organization and functional properties of each constituent cell affect the response properties of the

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Abbreviations: ANOVA, analysis of variance; cpd, cycles per degree; cps, cycles per second; cMUA, continuous multiunit activity; CRT, cathode ray tube; DI, direction index; dLFP, derivative of the LFP; HSD, honestly significant difference; LFP, local field potential; MUA, multiunit activity; OI, orientation index; SD, standard deviation; SE, standard error.

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population signal. Because population-based measures recorded with multielectrode arrays are often used for functional characterization of the cortex, it is of interest to determine how the heterogeneous functional organization of the mouse visual cortex affects these population signals.

To address these questions, we examined the visual stimulus selectivity of population signals in the mouse visual cortex. We characterized the onset latency, receptive field size and spatial, temporal, orientation and direction tuning, and we compared the LFP responses to the MUA and also to two derived signals, the continuous high-pass filtered MUA (cMUA) and the bipolar first spatial derivative of the LFP (dLFP). Because these signals presumably differ with respect to their extent of spatial integration of neuronal activity, we were also interested in determining the disparity in visual stimulus selectivity between these different population signals.

We found that population signals exhibited stimulus onset latencies as short as ~30 ms and possessed receptive fields as large as ~38°, with MUA receptive fields smaller than those of LFPs. All population signals possessed broadly tuned spatial and temporal frequency preferences with similar acuity thresholds. However, the orientation and direction of motion preferences were absent in these population signals.

EXPERIMENTAL PROCEDURES

Preparation and surgical approach

Sixteen C57Bl/6 mice weighing 20–25 g were used in this study. Anesthesia was induced via intraperitoneal injection of ketamine (100 mg/kg) and xylazine (4 mg/kg). Tracheotomy was performed, and the mice were mechanically ventilated with a 3:1 mixture of O_2 and N_2O. Anesthesia was maintained using isoflurane (1–1.5% during craniotomy). The mice were stabilized in a custom-built head frame. The electrocardiogram (ECG), heart rate, body core temperature and end-tidal CO_2 concentration were continuously monitored. End-tidal CO_2 concentration was monitored using an adapted CO_2 monitor (Capstar-100, CWE Inc., Ardmore, PA, USA) throughout the entire experiment and maintained below 4%. During preparation and surgery, the paw withdrawal reflex, the eyelid reflex, and the presence of whisker movements were monitored, and the anesthetic dose was adjusted as required. All procedures were approved by the Hamburg Administration of Health and Consumer Protection, Germany. Electrodes were positioned such that the topmost site was at the surface of the primary visual cortex. To verify the recording position, electrolytic lesions (15 μA for 15 s) were generated and subsequently identified histologically in three of the animals. Injecting this level of current through the probes may damage the electrode contact, and therefore, we did not use this procedure for all of the animals. Additionally, the silicon probes created injection tracks that were discernible in fixed Nissl-stained sections.

Electrophysiological recording

The right visual cortex was exposed by craniotomy at −3.8 mm posterior and 2.5 mm lateral to the bregma (Paxinos and Franklin, 2004). The dura was left intact, and mineral oil was applied to the cortical surface to prevent dehydration. The reference electrode was a silver-plated wire inserted onto the surface of the frontal cortex under the skull via a second small craniotomy, and it was fixed in place with bone wax and tissue adhesive (Histoacryl, Braun-Aesculap, Tuttlingen, Germany). Sixteen-channel silicon multielectrode arrays (NeuroNexus Technologies, Ann Arbor, MI, USA) were used to record electrophysiological activity throughout all cortical layers. The probe contacts had a surface area of 177 μm^2, were separated vertically by 100 μm and had an impedance of ~1 MΩ at 1 kHz. Under visual inspection, the multielectrode array was aligned orthogonally to the cortical surface and advanced into the brain using a mechanical micromanipulator until the topmost recording site was located at the surface of the cortex. In this manner, the multielectrode array spanned the full depth of the visual cortex (~10 sites). Electrode sites that were positioned in or near the white matter showed a prominent drop in the amplitude of their LFPs. Sites in and below the white matter were excluded from the analysis. Electrode signals were recorded and digitized using an Alpha Omega recording system (Alpha Omega Engineering, Nazareth, Israel). The electrode signals were split into a low-pass filtered (600 Hz) signal sampled at a rate of 3125 Hz and a band-pass filtered (300–5000 Hz) signal with a sampling rate of 25 kHz.

Visual stimulation

Full-field flashes for measurement of visual response latencies were generated using a Stroboscope (Nova Strobe DBX, Monarch Instrument, Amherst, NH, USA). The flash duration was 10–25 μs. The flash rate was 1 Hz for a total of 100 repetitions. The stroboscope was positioned 1.5 m in front of the animal. Structured visual stimuli were generated using Matlab (Mathworks, Natick, MA, USA) with the Psychophysics Toolbox (Brainard, 1997; Pelli, 1997) on a Mac Pro (Apple, Cupertino, CA, USA). Visual stimuli were presented to the contralateral eye with a cathode ray tube (CRT) display (Iiyama Vision Master Pro 451) (refresh rate 100 Hz) with luminance values ranging from 0.2 cd/m^2 (black) to 98 cd/m^2 (white). The screen was positioned at a distance of 28 cm from the animal at a 45° angle. Receptive fields were measured using a sparse-noise method, which consisted of a 10×10 grid of white and black squares flashed at randomly alternating positions on a gray background. Each square encompassed $6° \times 6°$ in the visual field and was presented for 150 ms with 10–20 repetitions for each position. Orientation tunings were measured using static-oriented sinusoidal gratings presented at eight orientations between 0° and 180° with a spatial frequency of 0.1 cycles per degree (cpd). Gratings