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Decorrelation of sensory-evoked neuronal responses in rat barrel cortex during postnatal development

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ABSTRACT

The ability to detect and discriminate sensory stimuli greatly improves with age. To better understand the neural basis of perceptual development, we studied the postnatal development of sensory responses in cortical neurons. Specifically, we analyzed neuronal responses to single-whisker deflections in the posteromedial barrel subfield (PMBSF) of the rat primary somatosensory cortex. Responses of PMBSF neurons showed a long onset latency and duration in the first postnatal week, but became fast and transient over the next few weeks. Trial-by-trial variations of single neuron responses did not change systematically with age, whereas the covariation of responses across trials between neurons (noise correlation) was high on postnatal day 5–6 (P5–6), and gradually decreased with age to near zero by P30–31. Computational analyses showed that pooled responses of multiple neurons became more reliable across stimulus trials with age. The period over which these changes occurred corresponds to the period when rats develop a full set of exploratory whisking behavior. We suggest that reduced noise correlation across a population of neurons, in addition to sharpening the temporal characteristics of single neuron responses, may help improve behavioral performance.

1. Introduction

In humans and many animal species, the ability to detect and discriminate sensory inputs greatly improves with age (Aslin et al., 1981; Atkinson, 2002). This improvement is supported by the development of peripheral sensory organs, and neurons/circuits in the central nervous system. Spike responses of individual neurons are immature in infant animals. As animals grow older and accumulate sensory experiences, the sensitivity and selectivity of the single neuron responses for the temporal and spatial properties of the sensory inputs acquire mature characteristics (Walsh and Romand, 1992; Knudsen, 2002; Kiorpes and Movshon, 2004). This development accounts for some, but not all, aspects of behavioral improvement (Kiorpes and Movshon, 2004). To better understand the neural basis of perceptual development, it is necessary to expand the analyses to include an assessment of the developmental changes in the sensory coding in a neuronal ensemble.

The activity of single cortical neurons varies across repeated presentations of an identical stimulus (Werner and Mountcastle, 1963; Tolhurst et al., 1983). This variation makes single neurons unreliable estimators of sensory stimuli. The neural representation of sensory stimuli is generally based on a population of neurons. The reliability of population coding is determined by the response variations of individual neurons and the correlation of the trial-by-trial fluctuations in their responses, or "noise correlation" (Abbott and Dayan, 1999; Averbeck et al., 2006). In particular, as noise correlation between neurons with similar stimulus preferences approaches zero, coding the sensory stimuli by the population responses becomes more reliable (Zohary et al., 1994; Shadlen et al., 1996). Although noise correlation may change during development, which then affects the perceptual and behavioral abilities of developing animals, to our knowledge this change has not been systematically studied.

We investigated this problem by studying neurons in the posteromedial barrel subfield (PMBSF) of the rat somatosensory cortex. Rats explore their environment by moving their whiskers to locate and discriminate objects. The behavior and behavioral responses to whisker stimuli emerge in the second postnatal week and continue to develop up to the adult stage (Welker, 1964; Grant et al., 2012). Individual PMBSF neurons respond to whisker deflections with a low probability (Simons, 1978). To encode whisker

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deflection occurrences reliably, the activities of multiple neurons should be used (Jadhav et al., 2009).

Previous studies examined developmental changes of responses of single PMBSF neurons (Armstrong-James, 1975; Stern et al., 2001; Borgdorff et al., 2007; Shoykhet and Simons, 2008). In the present study, we examined how responses of both single neurons and neuronal populations with a shared principal whisker develop by performing multiple single-unit recordings of whisker-evoked activity in an ensemble of neurons arranged along a column. We demonstrate that during the second and third postnatal weeks, single neuron responses become shorter in latency and duration, and that noise correlation observed in 1-week old rats reduces to near zero by postnatal day 30–31. Simulation of population responses shows that the reduction improves the reliability of the responses. We suggest that the improved coding at the levels of both single neurons and a population of neurons contributes to the better behavioral performance in older animals.

2. Materials and Methods

2.1. Animal preparation

Sprague-Dawley rats of either sex, reared in litters with their mother in a cage, were used. All surgical, experimental, and animal care protocols were approved by the Animal Experiment Committee of Osaka University and conform to the National Institutes of Health Guide for the Care and Use of Laboratory Animals. General experimental procedures were similar to those described previously (Kimura et al., 2010).

Neuronal recordings were performed in 32 rats at P5–31 (day of birth, P0) under urethane anesthesia (1.2–1.8 g/kg intra-peritoneal injection; Fig. 1A and B). If spontaneous body movements were observed, additional urethane was administered. Local anesthesia (lidocaine) was administered subcutaneously to surgical sites. A metal plate with a center hole for electrode penetration was attached to the exposed skull with glue and dental cement (Fig. 1A), and was held by a custom-manufactured holder. Through the hole, craniotomy and duratomy were performed over the PMBSF on the right hemisphere. After inserting an electrode, the exposed cortex was covered with 1–2% agar to prevent drying. Throughout the experiments, body temperature was maintained at 37 °C with a thermostatically controlled heating pad. An electrocardiogram was used to continuously monitor the anesthetic state.

2.2. Electrophysiological recording and histology

We performed extracellular unit recordings using a single shaft electrode with 16 recording probes arranged linearly and spaced 50 μm apart (width, 123 μm at its shaft; thickness, 15 μm; surface area of a single probe, 413 μm^2; catalog # a1×16-3mm50-413, NeuroNexus Tech., Ann Arbor, MI; Fig. 1C). We inserted an electrode perpendicularly to the cortical surface using a microdrive. All recording probes were in the cortex and spanned 750 μm below the pial surface, corresponding to layers 2–5 (Fig. 1C). After the electrode stopped slipping in the cortex, recording session of 200 or 800 trials was started. Voltage signals were amplified (× 10,000), band-pass filtered (0.5–3 kHz), digitized (16 bit, 20 kHz) and archived (Fig. 1D).

After the recording was completed, electrolytic lesions were made by passing anodal current through two probes. The rats were then overdosed with pentobarbital sodium, and transcardially perfused with 4% paraformaldehyde. The brain was removed, infiltrated with sucrose for cryoprotection, flash-frozen in optimal cutting temperature medium, and sectioned at 80 μm in the coronal plane. Lesions, which appeared as cell-sparse zones in Nissl-stained sections (Fig. 1C), were successfully identified in all samples. Histological reconstruction showed that the electrode penetrations were made perpendicularly to the cortical surface as intended, and that the sampled neurons were located between layers 2 and 5 (see Table 1 for the number of stimulus-responsive neurons in each layer and each age group). We did not attempt to determine by cytochrome oxidase staining whether the sampled neurons were located in barrel columns or in septa between barrels, because the recording diameter of each probe was estimated to be more than 100 μm. The distance corresponds to the interval between three successive recording probes, and spikes derived from a single neuron were often recorded at three successive probes (Fig. 1D).

2.3. Whisker deflection

We identified the "principal" whisker for which deflection evoked the largest responses at a recording site by deflecting whiskers with a hand probe and listening to an audio monitor for voltage signals. All whiskers except for the principal whisker on the left (i.e., contralateral) side of the face were then trimmed. The principal whisker was cut to 10 mm from the base and held with the "V"-shaped tip of the stimulating probe (Fig. 1A). The whisker was deflected in a ramp-and-hold fashion with the probe by using a piezoelectric bimorph actuator (Fuji Ceramics, Fujinomiya, Japan). The resiliency of rat whiskers increases during the first postnatal month. Therefore, in order to deflect the whisker reliably and evoke the maximal responses in PMSBF neurons, we adjusted the location of the stimulating probe along the whisker according to the age of the rat: 2–3 mm (the closest distance possible) from the base at P5–9 and 4–6 mm at all other ages. The tip moved 1.0 mm over 20 ms (mean velocity: 50 mm/s). This speed was high enough to maximize responses in adult rats (Armstrong-James and Fox, 1987). We monitored movement of the stimulus probe tip over time by using a non-contact laser displacement sensor (LK-G85, Keyence, Osaka) and recorded this information for further analysis (16 bit, spatial resolution = 0.5 μm, 20 kHz). In all experiments we observed no unintended vibration ("ringing") of the stimulus probe (Fig. 1D, bottom trace). We defined the onset and offset of deflection as the times when the stimulus probe moved 30 μm away from and back to the resting position, respectively. The duration between the onset and the offset of deflection was 330 ms. The inter-stimulus interval (ISI) was 2 or 10 s. Neurons in rats younger than P13 hardly respond to the second or later whisker deflections with an ISI of 2 s (Armstrong-James, 1975). In such cases, we applied whisker deflections with an ISI of 10 s. The number of trials was 200 or 800 for recordings with 10-s ISI or 2-s ISI, respectively. The total time for a trial thus ranged from 1600 s to 2000 s. For rats older than P13 tested for the two ISIs, we compared the results between the 2-s ISI experiments and the 10-s ISI experiments and found no significant difference.

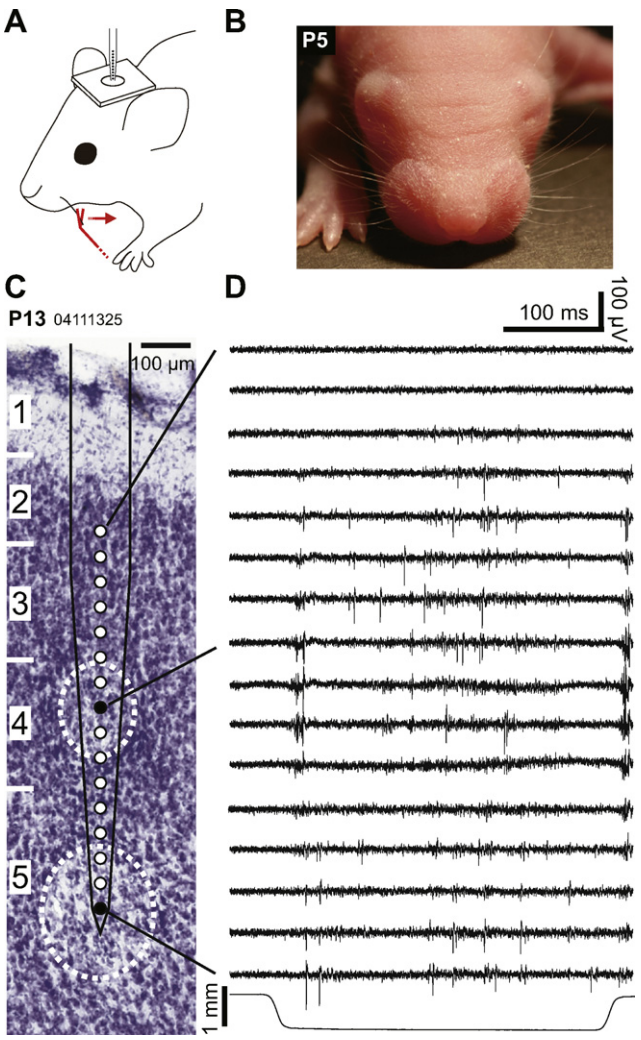

Fig. 1. Extracellular multiple single-unit recordings in the posterior medial barrel subfield (PMBSF) of the primary somatosensory cortex. (A) Schematic diagram of the recording experiment. (B) Photograph of a P5 rat showing its whiskers. (C) Multiple single-unit responses to whisker deflection were recorded using an electrode with 16 vertically arrayed recording probes. All electrode penetrations were aimed perpendicularly to the cortical surface and were histologically verified from electric lesions (made at recording probes denoted as filled circles). Scars (enclosed with white dashes) were visible in the Nissl section. (D) Simultaneously recorded extracellular voltage signals. Eight neurons were isolated from this recording. The bottom trace indicates the position of the whisker stimulus probe (a piezoelectric bimorph actuator) monitored by a laser displacement sensor.