Brain-wide mapping of stimulus induced variability quenching reveals modularity of cortical network

Teppei Matsui (tematsui@m.u-tokyo.ac.jp)

Tomonari Murakami (t-mura@m.u-tokyo.ac.jp)

Kenichi Ohki (kohki@m.u-tokyo.ac.jp)

University of Tokyo School of Medicine, 7-3-1 Hongo
Bunkyo-ku, Tokyo 155-0033 Japan

Abstract:

Recent studies have revealed that neurons not directly activated by a given sensory stimulus can nevertheless "respond" to the stimulus by showing reduction of trial-to-trial variability in neural activity ("variability quenching"). Determining the extent of cortical neural circuit that responds to a sensory stimulus is important for understanding how cortical network as a whole process sensory information. Here we used mesoscopic brain activity mapping to find that variability quenching occurred in widespread, bilaterally symmetric, cortical network-module. Each network-module showed variability quenching to particular sensory modality. The network-modules identified by variability quenching closely resembled cortical networks identified by spontaneous activity correlation (a.k.a. resting-state functional connectivity). Thus, although only a subset of neurons is activated, sensory stimulation recruits an entire cortical network-module that share correlated spontaneous activity.

Keywords: mouse brain connectivity and dynamics; mesoscopic imaging; neural network modeling

1. Introduction

What is the fundamental unit of cortical neural circuit that responds to a given sensory stimulus? It has been widely believed that only a sparse subset of neurons should respond to a given sensory stimulus (Olshausen & Field, 1996).

Recently however, this view is being revised. It has been noticed that neurons not activated by the stimulus also "respond" to stimulus by showing reduction in trial-to-trial variability of neural activity (Fig.1A; Churchland et al., 2010). Such a form of response, *i.e.* stimulus-induced variability quenching, is widely observed across different species, cortical areas and regardless of awake or anesthetized conditions. Theoretical studies suggest that variability quenching in a neural population cause reduction of the possible activity patterns of the neural population upon sensory stimulation compared to the spontaneous state (Litwin-Kumar & Doiron, 2012).

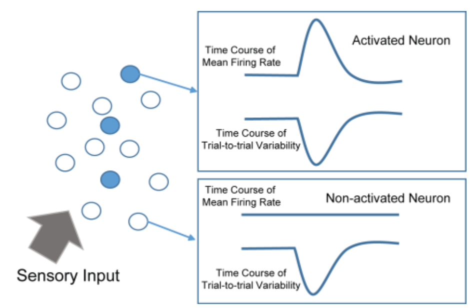

Figure 1: Both activated and non-activated neurons show quenching of trial-to-trial variability.

A critical question is what would be the extent of the neural population that responds to a given stimulus by means of variability quenching. The extent of neural population could be a local circuit consisting of several hundreds of neurons, a cortical area, a network of cortical areas or the entire cortex. In the present study, we investigated this question by using neural activity mapping across multiple spatial scales.

2. Methods

Wide-field calcium imaging using lightly anesthetized wild-type mice injected with adeno-associated virus carrying GCaMP6 or ArchLightD, and transgenic mice expressing GCaMP3 or GCaMP6 in the excitatory neurons. Extracellular electrophysiology was performed in anesthetized wild-type mice using 32-ch linear probe. Visual stimuli were presented using a LCD monitor controlled by Psychopy. Somatosensory stimuli were presented by custom-made piezo stimulator.

3. Results & Discussions

We first examined whether variability quenching could be observed using functional imaging of population neuronal activity. For this purpose, we virally transduced neurons in the mouse visual cortex (V1) expressing GCaMP and monitored population neuronal response to visual stimulation using wide-field imaging (Fig. 2A-B). Over 100 consecutive trials, V1 showed reliable visual responses (Fig. 2C-D). Notably, trial-to-trial variability as quantified by standard deviation across trials yielded sharp decrease in response to the stimulus (Fig. 2E). The same conclusion was supported by voltage imaging with ArchLightD, and extracellular electrophysiology.

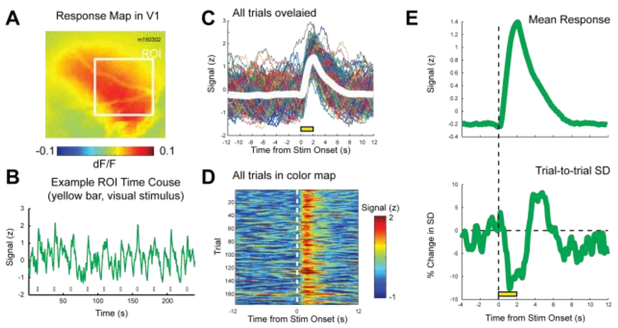

Figure 2: Variability quenching in population activity.

Having confirmed that variability quenching was observable in the population neuronal activity, we next conducted wide-field imaging to assess the extent of the neural population showing variability quenching in the entire dorsal cortex using transgenic mice expressing GCaMP. Repeated presentation of gratings to one eye reliably produced activation in large portions of the contralateral V1 and, as expected, only weakly in the ipsilateral V1 (Fig. 3A). In stark contrast, variability quenching occurred in bilateral V1 at comparable magnitude, but not in the areas outside V1s, such as somatosensory cortex (S1) (Fig.3C, top).

Because visual stimulation induced variability quenching in V1 but not in S1, we wondered if variability quenching occurred in a modality specific way. Experiments with tactile stimulation to unilateral hind limb indeed revealed bilateral variability quenching in S1 but not in V1 (Fig. 3B-C). Overlay of the maps of variability quenching by visual stimulation and somatosensory stimulation revealed that the two maps only had small overlap corroborating the notion that the variability quenching is confined to modality-specific network (Fig. 3D). Notably, the map of variability quenching closely resembled the maps of visual and somatosensory cortical networks as revealed by spontaneous activity correlation (a.k.a. resting-state functional connectivity) (Matsui et al., 2016) (Fig. 3E). Thus, although sensory stimulus activates a small subset of neurons, the cortical network-module responds to the stimulus as a unit. Indeed, unilateral sensory stimulation caused comparable variability quenching in bilateral cortices. Further, similarity with resting-state network suggests that spontaneous activity shared in each module is quenched by modality-matched sensory stimulation.

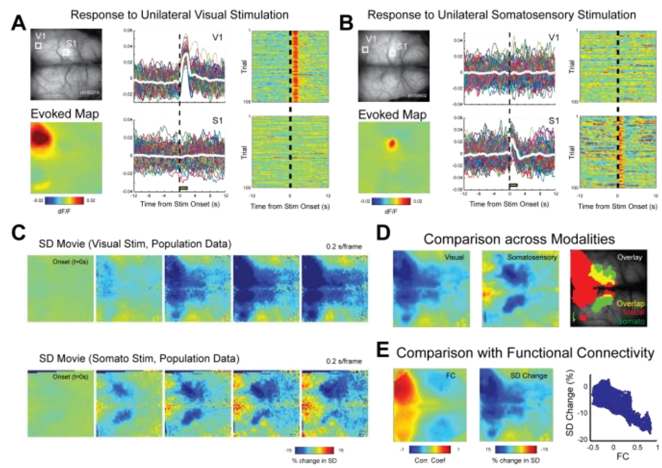

Figure 3: Variability quenching occurred in stimulus-specific cortical network-modules.

Acknowledgments

Grants from Brain/MINDS-AMED, CREST-AMED and SCIP-AMED to K.O., JSPS KAKENHI Grants 25221001 and 25117004 to K.O., 15H06473 and 17K14931 to T. Matsui, and 20153597 to T. Murakami.

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