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A Rewarding View on the Mouse Visual Cortex. Effects of Associative Learning and Cortical State on Early Visual Processing in the Brain

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A REWARDING VIEW ON THE MOUSE VISUAL CORTEX

Effects of associative learning and cortical state on early visual processing in the brain

The central goal of the thesis is to contribute to a better understanding of how the daily routines of seeing, experiencing and learning affect the neural circuits of the very senses that are used to perform these functions in the first place. The introduction (chapter 1) describes what is already known about how neurons in the visual cortex process inputs from the eyes and subsequently can be modulated by, for instance, internal state and attention, and can also incorporate long-term changes as a result of learning. The experimental work in the thesis aimed to provide evidence for reward related plasticity in V1, and further insights into the mechanisms that the visual cortex employs to improve stimulus representations, either as a consequence of cortical state or learning.

Chapter 2: Selective reward effects in V1 assemblies

The first experimental chapter focused on the question of how learning a visual stimulus-reward association changes stimulus specific circuits in the visual cortex. In a video-screen equipped conditioning chamber, mice learned that the presentation of an oriented moving grating predicted the delivery of a food-pellet, while presentation of gratings having an orthogonal orientation was never followed by reward. After these animals reliably expressed the learned association in their behavior, orientation tuning of large sets of cells in the primary visual cortex was assessed using *in vivo* two-photon calcium imaging under anesthetized conditions. Neurons in V1 that had a preferred orientation similar to the conditioned orientation, showed overall broader tuning curves as well as increased selectivity for stimulus direction. These effects were, at least in part, related to increased amplitudes of responses to the rewarded stimulus orientation, as compared to the unrewarded stimulus. In addition, cells with a tuning preference for the reward-associated orientation were more likely to be neighbors in the two-dimensional imaging field of view, suggesting a non-uniform effect of reward-related plasticity in the visual cortex. The primary conclusion of this study was that stimulus-reward learning selectively changes response properties in stimulus specific sets of neurons, already at the level of the primary visual cortex.

Chapter 3: Conditioning refines spatial coding in V1

The next chapter addressed the question of whether primary sensory cortical representations optimize their response properties and organization to support detection and/or discrimination of behaviorally relevant stimuli. Mice were exposed to a behavioral setting in which the location (up or down) of a small square patch of moving grating was indicative of reward delivery. The orientation and other features of the moving grating were held constant for the two different outcome conditions. The spatial mapping of the visual field in V1 restricted the reward association to a single region of cortex, while the non-rewarded region and non-trained stimulus orientations could be used to study effects of visual conditioning and exposure. Mesoscale intrinsic optical signal imaging under light anesthesia showed that cortical representations for trained stimuli in the rewarded and non-rewarded locations were spatially more segregated after conditioning, as compared to before. Small populations of calcium-imaged V1 neurons located at the border between the two stimulus representations discriminated the conditioned stimuli better, compared to untrained control orientations. The improved population coding for the conditioned stimuli was reflected in specific differences in tuning curves as well as in the correlation structure of responses to the trained stimuli. This study indicated that learning a stimulus-reward association improves the discriminability of the rewarded from non-rewarded stimuli, affecting cortical representations at the level of single-cell tuning curves, population correlation structure and mesoscopic spatial organizations.

Chapter 4: Anesthesia impairs direction coding in mouse V1

The last chapter revolved around the question of how a change in brain state, i.e. the difference between wakefulness and being under anesthesia, alters activity patterns of neurons in the primary visual cortex that emerge spontaneously and in response to visual stimuli. Using two-photon calcium imaging, a set of V1 neurons was imaged while the mouse was awake and subsequently revisited after the mouse was anesthetized (or in reversed order). Activity patterns of randomly selected pairs of cells were much more strongly correlated under anesthesia. This was especially apparent in the low frequency domain, suggesting that cells entrained their activity patterns to a single dominant rhythm or input rather than responding in a more individualistic fashion. Interestingly, the way neurons were tuned to stimulus orientation was not affected, but selectivity for stimulus direction was reduced. This loss in selectivity could not be attributed to overall reductions in response amplitudes, or to increased correlations in activity patterns of pairs of cells. The reduction in selectivity was rather explained by an increase in response amplitude to the null direction of the cells. The overall conclusion was that spontaneous and stimulus-selective activity patterns of primary visual cortex neurons are shaped by processes that can change between brain states and do not only reflect a straightforward linear integration of converging synaptic connectivity.

In the discussion (chapter 5) the experimental results of the thesis are combined and supplemented with other experimental and theoretical work, to illustrate how the present results may advance our conception of the function of the visual cortex. In summary, the experimental chapters and previous work indicate that neurons in the visual cortex can be acutely modulated by internal state, but can also incorporate long-term changes as a result of learning. To put the results in a broader context, we can make the assumption that the ability to adapt the function of the neural circuits of vision has the aim of improving the representation of visual stimuli in such a way that it benefits the organism. Under this assumption, the changes observed in chapter 2 and 3 suggest that learning of a stimulus-reward association can lead to changes in the visual cortex that may improve detection, salience, generalization, pattern completion and/or discrimination of these stimuli. Moreover, visual cortex activity between awake and anesthetized animals differs with respect to the amount of visual detail that the response patterns represent, and thus suggests that awake visual processing incorporates more complex network interactions as compared to anesthesia. If one needs to remember one single message from reading this thesis, it would have to be that the functioning of the primary visual cortex in the mouse is dynamic, depends on the state of the animal, and may adapt, if needed, to optimally process the specific environment that is being experienced.