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THE TEMPORAL–SPATIAL DYNAMICS OF FEATURE MAPS DURING MONOCULAR DEPRIVATION REVEALED BY CHRONIC IMAGING AND SELF-ORGANIZATION MODEL SIMULATION

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Abstract—Experiments on the adult visual cortex of cats, ferrets and monkeys have revealed organized spatial relationships between multiple feature maps which can also be reproduced by the Kohonen and elastic net self-organization models. However, attempts to apply these models to simulate the temporal kinetics of monocular deprivation (MD) during the critical period, and their effects on the spatial arrangement of feature maps, have led to conflicting results. In this study, we performed MD and chronic imaging in the ferret visual cortex during the critical period of ocular dominance (OD) plasticity. We also used the Kohonen model to simulate the effects of MD on OD and orientation map development. Both the experiments and simulations demonstrated two general parameter-insensitive findings. Specifically, our first finding demonstrated that the OD index shift resulting from MD, and its subsequent recovery during binocular vision (BV), were both nonlinear, with a significantly stronger shift occurring during the initial period. Meanwhile, spatial reorganization of feature maps led to globally unchanged but locally shifted map patterns. In detail, we found that the periodicity of OD and orientation maps remained unchanged during, and after, deprivation. Relationships between OD and orientation maps remained similar but were significantly weakened due to OD border shifts. These results indicate that orthogonal gradient relationships between maps may be preset and are only mildly modifiable during the critical period. The Kohonen model was able to reproduce these experimental results, hence its role is further extended to the description of cortical feature map dynamics during development.

Key words: Ocular dominance map, Orientation map, Monocular deprivation, Optical imaging, Simulation.

INTRODUCTION

Computational models can play an invaluable role in quantitatively exploring brain function, which depends upon the complex, rapidly changing interactions that occur between billions of neurons. In past years, the use of computational models has considerably deepened our understanding on cortical map formation and organization in the primary visual cortex (Kohonen, 1982; Durbin and Mitchison, 1990; Goodhill and Willshaw, 1990; Obermayer et al., 1990; Miller and MacKay, 1994; Miller, 1996; reviewed in Swindale, 1996; Chklovskii and Koulakov, 2004; Carreira-Perpiñán et al., 2005; Goodhill, 2007). Recently, the self-organization model based on the Kohonen algorithm not only simulated the precise spatial organization pattern between multiple feature maps, but also generated a series of quantitative predictions that were later successfully confirmed in adult animals (Yu et al., 2005; Farley et al., 2007; reviewed in Goodhill, 2007). While this model reliably predicts feature map patterns in mature, relatively static visual cortex, whether the same model can be used to accurately predict the temporal and spatial dynamics during rapid functional re-organization of a highly plastic developing nervous system, remains unknown.

Ocular dominance (OD) plasticity presents a well-suited paradigm for exploring this question. In the critical period, altered visual input, such as monocular deprivation (MD), can shift the response of neurons in the primary visual cortex to become more attuned to input from the non-deprived eye. As a result, the deprived eye-associated cortical regions shrink rapidly (Wiesel and Hubel, 1963; Hubel and Wiesel, 1970). However, the exact temporal kinetic and spatial dynamics which occur during MD remain unclear and controversial. Temporally, several studies have indicated that a few hours of binocular vision (BV) can restore the loss of function elicited by long-term MD, suggesting recovery may have different kinetics compared to MD (Krahe et al., 2005; Schwarzkopf et al., 2007; Mitchell and Sengpiel, 2009). However, other studies, which were based on firing rate, intrinsic signal and dendritic spine turnover, have demonstrated that the MD effect can also be rapid within a few hours (Mioche and Singer, 1989; Trachtenberg et al., 2000; Yu et al., 2011). Spatially, orientation selectivity is believed to form independent of the OD index, as MD does not influence the spatial layout of orientation maps in the reverse suture (RS) experiments (Kim and

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Abbreviations: 2D, two-dimensional; BV, binocular vision; MD, monocular deprivation; OD, ocular dominance; RS, reverse suture.

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Bonhoeffer, 1994; Gödecke et al., 1997). However, monocular enucleation of ferrets at birth suggests that removal of the OD map affects the layout of other feature maps, including the orientation map (Farley et al., 2007); simulations based on dimension reduction models have led to similar conclusions (Swindale, 2004; Carreira-Perpiñán et al., 2005).

Another fundamental question is whether the layout of feature maps is inherited or established after birth. The OD map does re-organize dramatically after MD during the critical period, suggesting the key role of visual experience. However, the OD map pattern seems to be already formed before the critical period (Horton and Hocking, 1996; Crowley and Katz, 1999, 2000). Similarly, without common binocular visual experience, the orientation map of the left eye develops to be identical to the one of the right eye (Kim and Bonhoeffer, 1994; Gödecke et al., 1997). Beyond the divergence on single feature maps, how the interactions between different feature maps change upon MD remains unknown. In normal adult visual cortex, different feature maps have been simulation-predicted and experiment-confirmed to be inter-related (Blasdel and Salama, 1986; Bartfeld and Grinvald, 1992; Hubener et al., 1997; Crair et al., 1997a; Müller et al., 2000; Yu et al., 2005). This relationship helps to achieve the optimal coverage and continuity of various features in 2D cortical space (Swindale et al., 2000). However, when MD significantly reshapes the layout of the OD map, will the spatial principle between the OD and other feature maps be preserved? How and when are they established and modified?

We hypothesized that simulation-guided depictions of OD plasticity would help to elucidate these issues. Then we utilized *in vivo* animal experimental data to help test the validity of the predictions generated by our self-organization model. Specifically, in our experimental setup, we performed repeated chronic *in vivo* imaging of the OD and orientation maps of visual cortex in young ferrets during the critical period. We examined how MD and recovery by BV exposure affected the temporal and spatial dynamics of multiple maps. The time-lapse experimental data collected from the same piece of cortex enabled detailed analysis and direct comparisons of observed temporal and spatial modifications to our simulations. Overall, we found that most of the controversies described above were reconciled well in our model. And importantly, these model-based predictions were quantitatively confirmed by experimental results.

EXPERIMENTAL PROCEDURES

Computational model

We used a self-organization model based on the Kohonen algorithm (Kohonen, 1982), as modified by Obermayer et al. (1990, 1992) to simulate the mapping of response features across the cortex. Each stimulus is represented as a multicomponent vector, $\mathbf{V}_s = (x_s, y_s, q_s\cos(2\varphi_s), q_s\sin(2\varphi_s), z_s, f_s)$, in a multi-dimensional feature space. Here, x and y correspond to the azimuth and elevation retinotopic position, respectively; q is orientation selectivity; φ is orientation preference; z is OD; and f is spatial frequency preference. The feature x ranges from $(0, X)$, y from $(0, Y)$, q from $(0, Q)$, φ from $(0, \pi)$, z from $(-Z, Z)$, and f from (0, F). The stimuli are mapped onto a cortical surface, which is represented as a two-dimensional (2D) grid of $N \times N$ cortical points. Each cortical point $r = (i, j)$ has preferred features (i.e., a "receptive field") defined as $\mathbf{W}_r = (x_r, y_r, q_r\cos(2\varphi_r), q_r\sin(2\varphi_r), z_r, f_r)$. At the beginning of the simulation, the maps are initialized as $x_r = i$, $y_r = j$, $q_r = Q/2$, $\varphi_r = \text{rand} \times \pi$, $z_r = 0$, and $f_r = F/2$. The maps are formed through iterations (usually around $1–2 \times 10^6$) of three steps. For each iteration, (1) a stimulus $\mathbf{V}_s$ is chosen randomly from the complete feature space, assuming a uniform distribution of each feature. (2) The cortical point $\mathbf{r}_c = (i_c, j_c)$, whose preferred features are closest to those of the stimulus, is identified as the "winner". The closeness of the feature is measured with the Euclidian distance between the vectors $|\mathbf{V}_s - \mathbf{W}_r|^2$. (3) The preferred features of the cortical points are updated according to the equation $\Delta\mathbf{W}_r = \alpha h(r)(\mathbf{V}_s - \mathbf{W}_r)$. Here, α is the learning rate, r is the cortical distance between a given cortical point (i, j) and the winner $\mathbf{r}_c$, and $h(r) = \exp(-r^2/\sigma^2)$ is the neighborhood function. The neighborhood function restricts the changes in receptive fields to those cortical points near the winner (in cortical distance).

The following parameters were used for the simulations: $N = 513$, $\sigma = 5$, $\alpha = 0.02$ (or arbitrary functions to simulate the critical period, see later description), $X = \rho N$, $Y = N$, $Q = 40$, $Z = 30$, and $F = 60$ (elevation to azimuth magnification ratio of the retinotopic map and was chosen as four in ferret, Yu et al., 2005). The maps for further analyzing did not include the boundary regions (50 pixels of each edge were excluded). Rectangle regions (similar size to the experimental data) of the model cortex were cropped for display purpose. The feature maps could be formed and the relationships between the maps persisted for a range of simulation parameters (Q from 30 to 50, Z or F from 50 to 80, and σ from 5.0 to 5.5), whereas the degree or strength of these relationships systematically varied within these ranges (see Fig. 7A–F).

To simulate the MD, we changed the OD range of the stimulus space. The range of z was cut in half, $(0, Z)$ instead of $(-Z, Z)$, to simulate the absence of input from the deprived eye. The deprivation window was usually set to 1×10^6 iterations (or 2×10^6 to achieve a saturation effect, which is analogous to several days of MD in experiments). For ordinary simulations, the parameter changes usually started after 2×10^6 iterations, at which time the feature maps were fully developed, since MD took place after OD map was well formed in the cortex in the animal experiments (Crair et al., 1997a). The start time could be changed according to different purposes, and the effect was examined. After MD, BV was achieved by setting the z range of the stimulus space back to $(-Z, Z)$, without any other modifications on specific parameters. For RS simulation, the range of z was taken as $(-Z, 0)$.

To simulate the critical period, the learning rate α was set by the logistic function [$\alpha(t) = 0.02/(1 + e^{t-4.5\times10^6})$],