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SYNAPTIC PLASTICITY

Balancing firing rates *in vivo*

Homeostatic plasticity mechanisms have been proposed to maintain neuronal firing rates within an optimum range and thus counteract the potentially destabilizing effects of activity-dependent plasticity. This stabilization of neuronal firing has only been demonstrated *in vitro*; however, two new papers now provide evidence of such homeostatic plasticity in the cortex of awake rodents.

Manipulations that reduce or enhance sensory input to the cortex can be used to examine homeostatic responses. In their study, Hengen *et al.* used a well-established monocular visual deprivation (MD) paradigm, in which one eyelid is sutured, to reduce sensory drive to the visual cortex (V1) of freely behaving rats. Keck *et al.* reduced input to V1 more drastically by carrying out bilateral retinal lesions to eliminate all input resulting from retinal activity in mice.

Hengen *et al.* used a chronically-implanted multielectrode array to record the firing of V1 neurons receiving input from the sutured eye. Analysis of the recordings enabled them to separate the responses of regular spiking (RS) neurons (putative pyramidal cells) from those of putative fast-spiking (FS) interneurons. They revealed decreased firing in FS and RS neurons within 1 day and 2 days of MD, respectively, followed by a rebound to baseline levels by 2 and 6 days post-MD, respectively.

Similarly, Keck *et al.* — using two-photon imaging to measure neuronal activity in mice expressing a genetically-encoded calcium indicator — revealed a decrease in neuronal activity in V1 6 hours after the lesion and an increase back to the levels of controls by 24 hours. Thus, both studies found evidence of a homeostatic restoration of firing rate following altered sensory input.

Changes in behavioural state can modulate cortical firing patterns, but their effects on homeostatic plasticity mechanisms are unknown. Surprisingly, Hengen *et al.* found that average firing rates and the restoration of firing after sensory deprivation were similar in sleeping and awake states, suggesting that homeostatic plasticity mechanisms operate across different behavioural states.

Synaptic scaling, in which the strengths of all of the synapses of a neuron are 'scaled' up or down by the insertion or removal of AMPA receptors (AMPARs) is a key homeostatic plasticity mechanism. In both studies, the amplitude of miniature excitatory post-synaptic currents recorded in brain slices collected at various time points after sensory deprivation increased on a timescale that corresponded to the measured restoration of activity levels *in vivo*, suggesting that synaptic scaling was taking place. Changes in dendritic spine size are known to reflect alterations in synaptic strength and AMPAR number, suggesting that they may also reflect synaptic scaling. Indeed, Keck *et al.* observed an increase in the size of V1 neuron dendritic spines 24 hours after retinal lesion.

These studies provide the first evidence of homeostatic mechanisms regulating neuronal firing in awake animals *in vivo* and suggest that synaptic scaling contributes to this process. Furthermore, these studies raise the interesting possibility that disruptions in homeostatic plasticity could contribute to disease states characterized by activity imbalances in the brain.

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ORIGINAL RESEARCH PAPERS Keck, T. *et al.* Synaptic scaling and homeostatic plasticity in the mouse visual cortex in vivo. *Neuron* **80**, 327–334 (2013) | Hengen, K. B. *et al.* Firing rate homeostasis in visual cortex of freely behaving rodents. *Neuron* **80**, 335–342 (2013)

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