Title: Homeostatic structural plasticity of neuronal connectivity in response to external stimulation: A combined study using computer simulations and *in vivo* experiments

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Thesis summary [English]
Pyramidal neurons are highly plastic units of neural circuits. Under basal conditions, axonal boutons and dendritic spines continually form or break synapses. External perturbations further accelerate such changes. Hebb's rule,``fire together, wire together", was first proposed to explain the observed synaptic plasticity. However, accumulating evidence suggests neurons homeostatically control their neural activity. The conventional solution in computer simulations is combining Hebb's rule with other homeostatic mechanisms to stabilize network dynamics. A recent model of homeostatic structural plasticity (HSP), which includes structural changes and negative feedback control of neural activity, preserves network stability and meanwhile presents similar properties as Hebb's rule. This thesis explores the feasibility of using this model to explain the plasticity induced by external stimulations and pinpoints its time scale. We build our knowledge step by step with computer simulations and mouse experiments. We first showed in a numeric study transcranial direct current stimulation (tDCS) perturbed the neural activity and triggered a cell assembly formation. We then investigated the time course of homeostatic structural plasticity in mouse pyramidal neurons after chronic optogenetic activation in the anterior cingulate cortex (ACC). We observed that when the neural activity returned to baseline, the dendritic spine morphology and synaptic proteins showed biphasic modulation within 48 hours after the last stimulation session, roughly as predicted by the HSP model. In the last numeric study, we showed that the modulatory effects of tDCS on learning substantially depend on the interaction between the cell assemblies, respectively induced by learning and tDCS. Altogether, this thesis characterized the responses of homeostatic structural plasticity to external stimulation with computational modeling and revealed its time course with mouse experiments. Besides, our numerical studies provided a framework to explain the inconsistent results observed in tDCS human experiments. Our mouse experiments also hinted at the relationship among the ACC neural activity, synaptic plasticity, and depressive-like behaviors.

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