

Japan-U.S. Brain Research Cooperation Program  
Group Joint Study Project Program FY2014 - FY20\_\_; Report

Field: 2

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2. Project Title:

Converging effects on network formation of distinct forms of spike timing-dependent plasticities onto L2/3 pyramidal neurons in the barrel cortex.

3. Japanese Group

Names, Titles and Affiliations of Principal Researcher and Collaborating Research Members

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4. U.S. Group

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5. Research Period, from/to (mm/dd/yyyy) and total number of years.

From 1 Apl. 2013 To 31 Mar. 2015 ( 2 Years)

6. Abstract, Results, and Research Significance (300 words):

Despite evidence that coordinated patterns of neuronal activities affect the organization of neural circuits, how activity is translated into long-term structural changes in connection remains obscure. In the current study, we report alteration and interaction of spike timing-dependent plasticity (STDP) underlies reorganization of neural network. The formation and refinement of topographical projection of thalamocortical axons (TCAs) is an activity dependent process. TCAs reach near the pia surface through cortical plate (CP) around P2-4, then retract and confined below L2/3-L4 border later. We found TCA to L2/3 synapses showed t-LTD in neonates, but its magnitude decreased gradually, and the STDP switched from t-LTP to t-LTD after P7-8. The t-LTD was mediated by type 1 cannabinoid receptors (CB1R), located at TCA terminals. As L4-L2/3 synapses exhibit t-LTP until P13-15, two opposite forms of STDP converge onto L2/3 for one week during development. We found that the converging STDP caused heterosynaptic plasticity: the induction of t-LTD at TCA-L2/3 automatically generated potentiation at L4-L2/3 synapses. Moreover, we found that t-LTD leads to a retraction of TCA projection. Administration of CB1R agonists, including  $\Delta^9$ -tetrahydrocannabinol caused substantial retraction of TCA. Consistent with this, individual thalamocortical axons, which are confined below L4-L2/3 border at

P12, exhibited exuberant innervation in L2/3 in CB1R knockouts. These findings indicate that developmental switch and interaction of STDP plays an important role in shaping neural network.

7. Other (Research-related concerns, particular points of note):

\*Please attach any reference materials as necessary.