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Thalamostriatal system controlling learning and behavioral flexibility

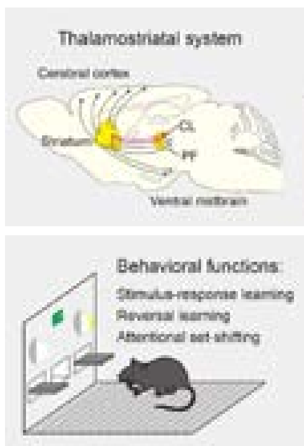
Kazuto Kobayashi
Fukushima Medical University, Japan

Selection of appropriate motor actions and flexible switching of those actions in response to environments are essential for survival and maintenance of individuals and species. The striatum, a key structure in the basal ganglia circuit, plays important roles in the coordination of instrumental motor actions and behavioral flexibility. The intralaminar thalamic nuclei provide the major sources of thalamostriatal inputs and contain multiple nuclear groups, including the central lateral nucleus (CL) and parafascicular nucleus (PF). However, little is known about behavioral roles of these pathways originating from the CL and PF

Methodology: The behavioral functions were addressed by using the selective neural pathway targeting. A lentiviral vector for highly efficient retrograde gene transfer encoding a receptor for a recombinant immunotoxin was injected into the striatum, and then immunotoxin solution was injected into the CL or PF, resulting in selective elimination of thalamostriatal pathway from each nucleus. The functions were also studied by chemogenetic suppression of specific neural pathways.

Findings: Elimination of the CL thalamostriatal pathway resulted in impaired response selection and lengthening of response time in the performance phase of sensory discrimination with no impact on the behaviors in the acquisition phase and disturbed the reversal and attentional set-shifting of learned responses. Chemogenetic suppression of CL-derived pathway supported the importance of these neurons in reversal learning and set-shifting. In contrast, eliminating PF thalamostriatal pathway impaired mainly the acquisition phase of sensory discrimination, affecting transiently the response selection in the performance phase.

Conclusion and Significance: Two thalamostriatal pathways have essential but distinct roles in the acquisition and performance phases of stimulus-response learning, suggesting a functional shift of neural circuit during learning processes. In addition, the CL thalamostriatal system plays a key role in behavioral flexibility in response to changes in the choice or strategy, suggesting the main contribution of this pathway in the control of basal ganglia circuit linked to the prefrontal cortex.



Biography

Kazuto Kobayashi has his expertise in genetic manipulation of neural circuits by using transgenic and viral vector technologies. He has studied the neural mechanisms of motor control and learning through basal ganglia circuitry in rodents. In particular, his group developed a novel technology for conditional cell targeting with a recombinant immunotoxin (Kobayashi et al., 1995), and further a technology for selective neural pathway targeting by combing this immunotoxin targeting with a viral vector system for highly efficient retrograde gene transfer (Kato et al., 2011). He is interested in understanding the neural mechanisms on how cortico-basal ganglia-thalamic network controls action selection and behavioural flexibility in rodent and non-human primate model (common marmosets) brains.

kazuto@fmu.ac.jp