Dissecting our mind based on evolutionary conservation

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The fish brains are anatomically by far more similar to the mammalian brains than people used to think. Taking advantage of this evolutionary conservation and its structural simplicity, we have been studying zebrafish brain to elucidate the mechanism of two aspects of adaptive brain functions, i.e. resolution of social conflict and decision making.

The habenula (Hb) is an evolutionarily conserved diencephalic structure. We discovered that the dorsal and ventral Hb (dHb and vHb) of zebrafish correspond respectively to the medial and lateral regions of mammalian Hb. We have recently found that the two subregions of the dorsal habenula (dHb) in zebrafish antagonistically regulate the outcome of conflict. We now show the evidence that the habenula plays the evolutionarily conserved roles in the resolution of social conflict in mammals.

We also use adult zebrafish as a model animal for the study of decision making in visual-based active avoidance tasks by establishing the closed-loop virtual reality (VR) system for the head-tethered adult zebrafish with the 2-photon calcium imaging system. We have identified two ensembles of neural activities which encode the different aspects of prediction errors between the status represented by the real sensory inputs and the favorable status to achieve to successfully escape from the danger, i.e. visual inputs of the backward moving landscape and the wall color of the goal compartment, and observed that the behaviors are taken so that these errors become minimum. Our results show that the adult zebrafish behaves in decision making based on the behavioral rule called “active inference”, where agents take actions to suppress the prediction errors by trying to make the internal representations of the bottom-up sensory states best match those of the top-down predictions, and have demonstrated the strong conservation of the basic principle of decision making throughout the evolution.

Curriculum Vitae

After taking the MD from the Medical School of Tokyo University, Japan (1983), Hitoshi Okamoto was trained as the molecular geneticist using Drosophila and obtained PhD from Tokyo University (1988), and went abroad to Univ. of Michigan, Ann Arbor, USA to get training on the developmental neurobiology using fish. There, he studied the mechanisms for the axonal pathfinding by the spinal motor neurons toward the pectoral fin in the Japanese Medaka embryo. Back in Japan (1988) at the National Institute for Basic Biology and Keio University, he initiated the study using zebrafish as an independent researcher, and elucidated that a family of transcription factors (Isl1 family) play important roles in the specification of spinal motor neurons. After moving to the Brain Science Institute (BSI) of RIKEN (1997), he performed the large-scale forward mutant screening, and elucidated the mechanisms for the differentiation of the hindbrain motor neurons by analyzing the isolated mutants. In the past ten years, he has been interested in using zebrafish for the study of the neural circuit mechanisms for emotion and decision making by taking advantage of the evolutionary conservation of the brain structures between fish and mammals. Especially, he has elucidated the mechanisms for the asymmetric development of the subregions of the habenula and revealed their critical roles in controlling fear behaviors and in the social conflict resolution for dominance or the submission by using various genetic or optogenetic manipulations. He is currently a deputy director and a senior team leader of BSI and an adjunct professor at Tokyo University, Waseda University and Keio University, and has served as the chair of the Asia-Pacific Regional Committee of the International Brain Research Organization (APRC-IBRO) and the treasurer of the Federation of the Asia-Oceania Neuroscience Societies (FAONS). He was awarded the Tokizane prize by Japanese Neuroscience Society (2014).