Htr2c cells control attention

With the support by the National Natural Science Foundation of China, the research team led by Professor Lu YouMing (鲁友明) at Tongji College of Medicine, Huazhong University of Science and Technology, uncovered a novel neural circuitry for control of attention, which was published in *Nature Neuroscience* (2018, 21: 1239—1250).

Pyramidal cells in the CA1 region ($CA1_{PCs}$) form the major output of the hippocampus, a temporal lobe structure crucial for learning and memory in humans, other primates and rodents. $CA1_{PCs}$ are traditionally considered as a homogenous population of excitatory neurons in the brain. This traditional view has been recently challenged by evidence that $CA1_{PCs}$ vary greatly in their gene expression patterns, synaptic connections and physiological properties. Many of these differences are organized along a dorsal-to-ventral axis of the hippocampus. The dorsal $CA1_{PCs}$ receive synaptic inputs mainly from neurons in cortical regions that are required for the encoding and recall of spatial memory.

The ventral $CA1_{PCs}$, based on the gene expression patterns, contain at least three distinct groups of neurons: one expresses a serotonin receptor type-2c gene (Htr2c cells) and the others express transient receptor potential channel-4 (Trpc4 cells) and wolfram syndrome 1 (Wfs1 cells) genes. Trpc4 cells are identified as a component of the storage site of social memory. Wfs1 cells that are located in the superficial CA1 pyramidal cell layer contribute to task performance in spatial navigation. Htr2c cells and their circuits are yet to be studied.

They genetically manipulate a subset of excitatory neurons expressing serotonin receptor type-2c gene (Htr2c) in the ventral CA1 (Htr2c cells). Using genetically-modified virus tracing they find that Htr2c cells establish excitatory synaptic connections directly with a newly identified group of neurons in a mouse brain region that corresponds to the Edinger-Westphal nucleus (EW cells) in humans and monkeys. Targeted silencing of Htr2c cells impairs behavioral performance in a visual detection task that demands attention while preserving multiple functions such as novel object recognition and learning and memory. Attention deficit induced by inhibition of Htr2c cells is recapitulated by genetic inhibition of EW cells and rescued by activation of either EW cells or excitatory synaptic projections from Htr2c cells onto EW cells. This study uncovers a previously-unknown group of excitatory neurons and their circuits for engagement of attention.