A novel neuronal glutamate biosynthetic pathway mediating enhancement of learning and memory by UV light

With the support by the National Natural Science Foundation of China, National Key R&D Program of China, and the Chinese Academy of Sciences, the research team led by Prof. Xiong Wei (熊伟) and Prof. Huang GuangMing from the University of Science and Technology of China revealed a molecular mechanism of how moderate sunlight exposure improves the learning and memory, by using single-cell mass spectrometry (MS) and multiple biological techniques. This finding was recently published in *Cell* (2018, 173: 1716—1727).

It has been well known that exposure to moderate amounts of sunlight not only boosts our physical state due to stimulating the biosynthesis of vitamin D, but also changes our mood, cognition, and learning behaviors. However, the molecular and cellular mechanism responsible for such neurobehavioral changes caused by skin exposure to sunlight remains to be fully elucidated, due to lack of appropriate techniques for the sensitive and accurate measurement of intracellular metabolites.

Prof. Xiong and Prof. Huang's groups have developed the single-cell metabolite profiling method, which can interrogate the intracellular composition of neurons. In brief, a pipette, typically used for whole-cell patch clamp, is utilized to aspirate the cytoplasm of a single neuron, which can be subsequently analyzed by nano-electrospray mass spectrometry (*PNAS*, 2017, 114: 2586—2591).

Using this approach in combination with multiple biological techniques, the researchers demonstrated that moderate exposure to UVB radiation elevated the level of urocanic acid (UCA) in the blood, which in turn crossed the blood-brain barrier and entered neurons. Then they found that UVB exposure significantly increased the intracellular glutamate level through a novel intracellular metabolic pathway from UCA to glutamate (GLU) in these neurons.

Next the elevated GLU levels within neurons resulted in more GLU packaging into synaptic vesicles and more GLU release from synapses, thus activating the glutamatergic neural circuits in hippocampus and motor cortex which improved the mouse related behavioral performance such as motor learning and object recognition memory. The finding of this novel GLU metabolic pathway in the brain is vital for our further understanding of the mechanism of sunlight exposure-induced neurobehavioral changes and related brain disorders, since GLU plays multiple critical physiological roles in protein biosynthesis, energy metabolism and excitatory neurotransmission in the brain.

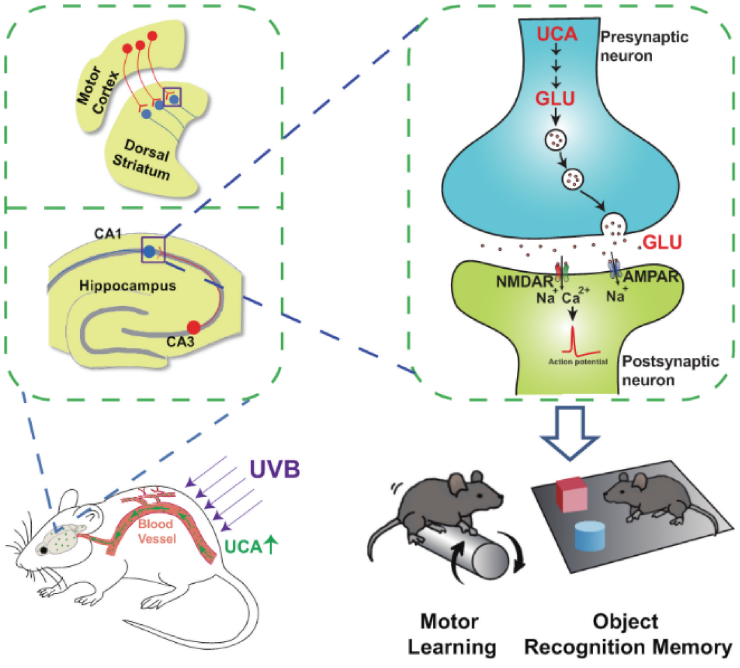

Figure Moderate UV exposure improves motor learning and object recognition memory by activating the UCA-GLU metabolic pathway in the brain.