Press Release from National Tsing Hua University
For information, please contact
Alice Yu, Division of Public Affairs
iryu@mx.nthu.edu.tw
+886-3-516-2372

Taiwanese scientists discover shunting mechanism to direct information flow in the complex brain networks

腦科學重大突破—清華大學發現神經訊號在複雜腦神經網路中如何轉軌

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A research group led by Professor Ann-Shyn Chiang of National Tsing Hua University in Taiwan has discovered a shunting mechanism for gating information flow in parallel neural circuits. Using FlyCircuit, a virtual fly brain database containing thousands of single neurons, Chiang's team predicted and validated neural circuits relaying olfactory information to higher brain centers in the *Drosophila* brain.

They found that odor information takes specific pathways in the brain, depending on concentration context in order to orchestrate locomotion behavior.

"*A grand challenge in neuroscience is to understand how the internal brain circuits represent external world and eventually result in memory underlying learning and behaviors. To this end, understanding how the information flows and turns in the complex brain networks has great and fundamental implication in not only biomedicine but also neuro-inspired engineering*," exclaimed by Chiang.

The finding was reported in the 2013/6/14 issue of Science.

Neuroscientists have long realized the value of using animals to model and understand how the billions of neurons in the human brain function. The brain of the adult *Drosophila*, commonly known as fruit fly, contains only approximately 100,000 neurons and uses the same set of neurotransmitters such as acetylcholine, GABA, glutamate, dopamine, serotonin, histamine, octopamine, and tyramine. While significantly different in gross anatomy, both insect and mammalian brains are composed of neural circuits with a cohort of shared gene products governing normal function of sensory modalities and complex behavior. A sophisticated genetic tool box, simple brain circuits for intricate behaviors, and complete genomics and proteomics information make *Drosophila* an ideal model system for studying basic mechanisms underlying brain operation.

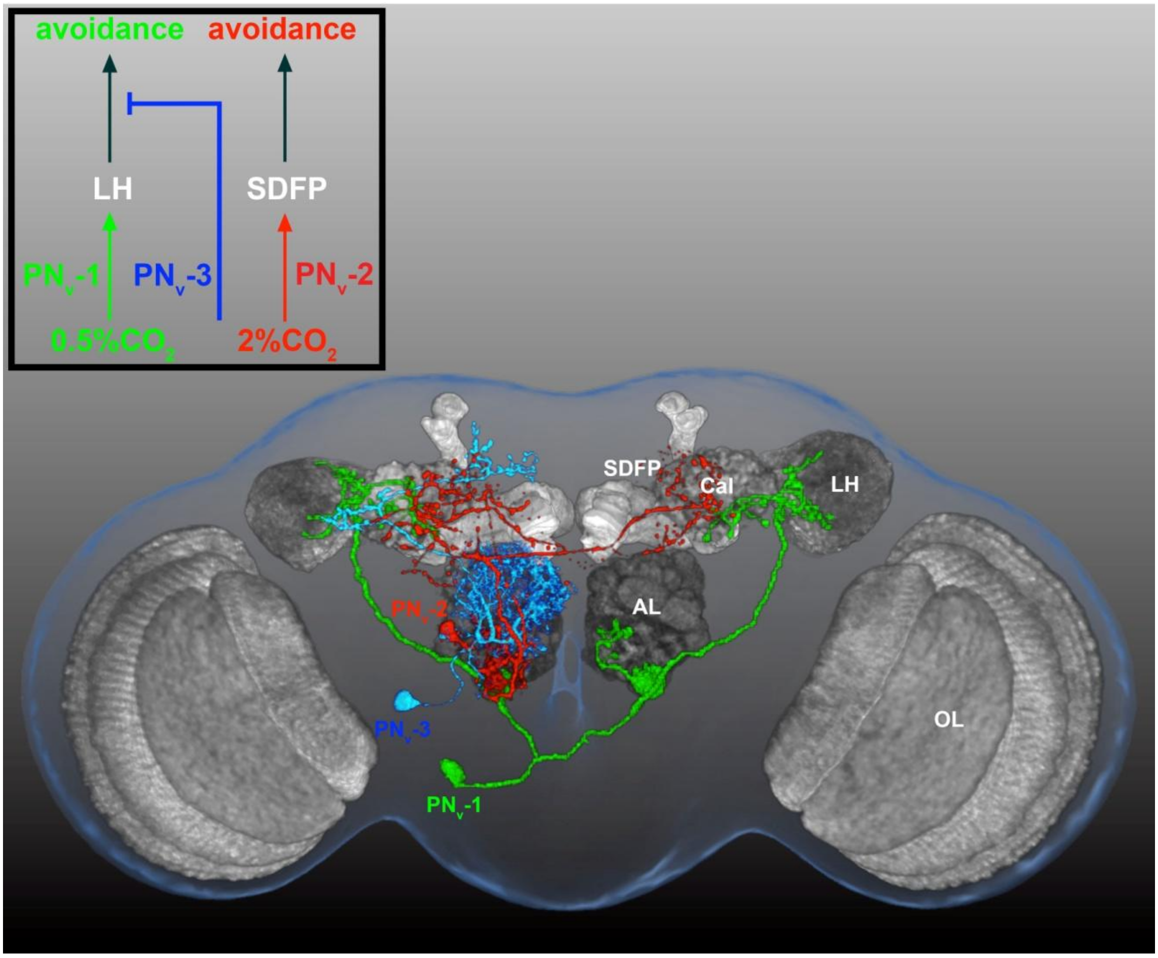
Humans are often attracted to certain smells at low concentrations but repelled by the same scents if they become too strong. Each odorant is detected by specific receptor neurons that relay information to particular brain regions. How the brain interprets the same sense in differing context remains unclear; however, research carried out by Chiang's team on the *Drosophila* brain sheds light on this question.

Carbon dioxide generated by stressed flies alerts surrounding flies, causing them to move away. On the other hand, flies in flight are attracted to the CO_2 released by yeast in fermented fruits. How does the same odor produce two opposite behaviors?

Hui-Hao Lin, a graduate student in Chiang's lab, demonstrated that the CO_2 signal detected by specific olfactory sensory neurons is sent to a small spherical region underneath the antennal lobe and then relayed to higher brain centers through multiple parallel pathways. Lin first traced all projection neurons linking between antennal lobe and the brain with a mutated protein that turns into a regular green fluorescent protein after UV irradiation, developed by Tsai-Fung Fu at the National Chi Nan University. Following FlyCircuit analysis, the team predicted that perception of the CO_2 signal involves six brain regions and utilizes three different pathways. Next, in collaboration with Barry Dickson at the Institute of Molecular Pathology in Vienna, they developed a set of specific genetic drivers to manipulate these putative CO_2 pathways. Calcium imaging with GCaMP fluorescent probes showed that all projection neurons connected structurally are functionally responsive to CO_2. Blocking neurotransmission with a temperature sensitive dynamin, a mutant protein stops neurotrnamitter retrieval at high temperature, showed that two independent neural pathways are required for avoidance behavior under low or high concentrations of CO_2, respectively. Interestingly, the third inhibitory GABA-transmitting pathway blocks the low CO_2 pathway when flies are exposed to high levels of CO_2.

To verify this information shunting model, a graduate student Li-An Chu of Chiang's lab developed an optogenetic device that uses an intense blue light to trigger channelrhodopsin induced activation of specific neural pathways. Optogenetic activation of the first and second pathways triggered avoidance behavior, which mimics the stimulation of low and high CO_2 concentrations, respectively. In contrast, these flies did not respond to the activation of the third pathway alone. What is particularly surprising was the discovery that blocking both the second and third pathways under high CO_2 stimulation triggered avoidance behavior via the first pathway.

According to Chiang, "*our finding is the first time to show that there are parallel neuronal pathways for signal processing and mechanisms that allow information shunting in the brain. What remains unknown is whether such a shunting phenomenon occurs in other sensory modalities and how often it is executed as an intermediary step between sensory stimulus and behavioral output in the complex brain networks. It would be truly exciting if such a shunting mechanism, which greatly increases the flexibility of behavioral responses, also occur in the human brain*."



Information routing for fruitfly avoidance behavior. Two distinct neural pathways, PNv-1 (green) and PNv-2 (red), are integral for avoidance behavior in response to low (0.5%) and high (2%) concentrations of carbon dioxide, respectively. While 0.5% activates only PNv-1, 2% triggers PNv-1, PNv-2, and a third class of inhibitory PNv-3 neurons (blue) that blocks the PNv-1 downstream pathway, leaving PNv-2 as the final output. AL, antennal lobe; Cal, calyx; LH, lateral horn; OL, optic lobe; SDFP, superior dorsofrontal protocerebrum.