論文の内容の要旨

Identification of a neural circuit controlling locomotion speed by regulating the phase delay between the movement of head and tail in Drosophila larvae

(ショウジョウバエ幼虫において頭尾の位相差の調節による運動速度制御を担う神経回路機構の解明)

氏　名:　劉 英濤（リュウ　イントウ）

LIU, Yingtao

Locomotion speed is essential for animals' survival. To achieve the desired speed, animals regulate the locomotor cycle called stride by its duration and amplitude in terrestrial animals. It has been widely observed in terrestrial animals that a stride can be separated into two phases: a "variable phase" and an "invariable phase" in terms of their duration. The duration of the "variable phase" is mainly varied with speed while the duration of the "invariable phase" remains almost unchanged (e.g., in pedestrian animals, the duration of the stance phase varies primarily with changing speeds, while the duration of the swing phase is not much varied). However, how the central nervous system generates the variable motor output is less understood. This gap is due to the basic technical difficulty in recording and manipulating the component neurons in most animals. In this thesis, I investigated the neural mechanisms to modulate the motor output for the desired speed using

Drosophila melanogaster larvae, a model animal with powerful genetic tools to target and manipulate the central neurons.

Larvae move by peristalsis, a type of movement widely used by legless animals defined as a sequential wave-like movement from one end to the other. Though the tools for neuroscience study have been well established in *Drosophila* larvae, it remains not well understood how the movement dynamics are changed with speed. This study aims: (1) to identify the kinematic parameters varied with speeds and the key muscular groups; (2) to identify the neural circuit that modulates the speed-dependent rhythm.

First, I analyzed the kinematics in larval locomotion to reveal the key parameters adapted to locomotion speed. I defined a stride as the period between consecutive unhooking moments and then divided each stride into two phases: the first portion named tail lag phase is a period from unhooking to the initiation of the peristaltic wave, and the second portion named wave phase is a period from the initiation of the wave to unhooking. I found that the tail lag and the wave duration vary differently with the speeds and the tail lag varies more. To reveal the muscular mechanism to control the tail lag, I analyzed the dynamics of muscle contraction during locomotion. As a result, a group of muscles perpendicular to the crawling direction, the lateral transverse muscles (LTM), were identified to contract together before a forward wave is initiated, with the relaxation of these muscles coinciding with the start of the wave. The greater the duration of the contraction of the LTM, the more the tail lags the initiation of the wave.

Next, I investigated the upstream central mechanisms and found that the interneurons A26f and A31c have significant functional roles in regulating the activity of LTM and the locomotion speed. A26f neurons, which are GABAergic premotor neurons providing most output to LTM, are coactivated across the segments of the ventral nerve cord at the initiation of the fictive forward locomotion to inhibit the LTM. A31c neurons, which are GABAergic second-order premotor neurons

presynaptic with A26f neurons locally, burst synchronously at an earlier phase of the initiation of the fictive forward locomotion and are activated again when the wave-like pattern is initiated. Using perturbational analysis by optogenetic tools, I revealed that A31c and A26 neurons are required to regulate the activity of LTM during peristalsis. A31c neurons upregulate the contraction of LTM while A26f neurons downregulate. Furthermore, A26f neurons play a significant function in regulating the appropriate tail lag as well as the locomotion speed.

In summary, this study revealed that: (1) by analyzing the kinematics of peristalsis and dividing a stride into tail lag phase and wave phase, the tail lag varies more with speed than the wave duration varies, (2) by analyzing the muscular contraction pattern, the lateral transverse muscular group contract together during the tail lag and their duration of contraction naturally depends on the tail lag thus the speed, and (3) by analyzing the upstream neural circuit, A31c-A26f system modulates the inhibitory input to LTM to regulate the tail lag and thereby the speed. These results suggest that *Drosophila* larvae use a speed control strategy shared in the animal kingdom that the duration is adjusted preferably in one phase but less in the other. The LTM is similar to the extensor muscles in pedestrian animals regarding their adaption to the variation of the “variable phase” (stance phase/tail lag phase). Because of the basic similarity in the structure of the kinematics and the adaption of muscular activity underlying the speed control in the animal kingdom, the revealed central mechanism that the modulation of inhibitory output regulates the duration of the “variable phase” may be generally identical across animals. Further work may be required to target and analyze the descending neuronal pathways to unravel the higher central mechanism of speed control, which is difficult to be accessed in most animals. In addition, as the co-contraction of transverse muscles and their role in speed regulation is first reported, this work advances the understanding of the mechanism behind the peristaltic movement.