Exploring the Role of Frazzled in Drosophila Neural Circuit Assembly and Foraging Behavior

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The mushroom body (MB) is an intelligence center of the Drosophila brain. It plays essential roles in many aspects of behavior, including learning and memory, motivation, courtship, and sleep. The function of MB requires a precisely wired neural circuit. However, the molecular mechanisms regulating the assembly of the circuit remains unclear. To understand the mechanisms, I focus on the PPL1- $\alpha'2\alpha^2$ neurons in MB's neural circuits. PPL1- $\alpha'2\alpha^2$ is a type of dopaminergic neuron specifically projecting neurites to the $\alpha'2$ and α^2 zones of the MB. Its neurotransmission is known to mediate food-seeking behavior in hungry flies. To explore the molecular machinery underpinning PPL1- $\alpha'2\alpha^2$ neurite targeting, I adopted the GAL4-UAS system to express RNAi against candidate genes that are potentially involved in neurite guidance in PPL1- $\alpha'2\alpha^2$ neurons. Among these genes, knockdown of frazzled caused a significant innervation loss in the α^2 and $\alpha'2$ zone of MB. I then examined the impact of frazzled overexpression on neurite guidance in other MB neurons. Interestingly, this manipulation misdirected the neurites towards the α^2 and $\alpha'2$ zone in some neurons, but had no obvious effect in others. These results suggest that the effect of frazzled neurite guidance is context-dependent. Finally, I found that abnormal neurite targeting of PPL1- $\alpha'2\alpha^2$ neurons under frazzled knockdown did not affect food-seeking behavior in hungry flies, suggesting the MB neural circuit is flexible and can adapt to developmental errors. An exciting future research direction is to understand how the MB circuit detects and compensates for the miswiring of PPL1- $\alpha'2\alpha^2$ neurons.

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