RESEARCH HIGHLIGHT

A Shared Neural Node for Multiple Innate Behaviors in *Drosophila*

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The nervous system orchestrates diverse behaviors such as reproduction, sleep, feeding, and aggression, and selects a single behavior for execution at any given time. This requires neural mechanisms for behavioral selection sensitive to both internal physiological states and external environmental conditions. For example, hungry animals bias their selection towards the acquisition and ingestion of food, and away from other behaviors. Despite its tremendous biological importance, as well as substantial progress on the neuronal control of individual behaviors, how neural circuits underlying individual behaviors interact to ensure proper behavioral selection remains poorly understood.

Drosophila melanogaster, like other animals, engages in multiple innate behaviors such as sleep, feeding, fighting, and sexual behaviors. The molecular and neuronal mechanisms of these individual behaviors have been intensively studied for decades [1–3], making them ideal for exploring the neural mechanisms underlying crosstalk among innate behaviors. There are at least two main questions to be elucidated in this regard: (1) how neural substrates governing individual behaviors communicate with each other, and (2) whether a common neural substrate mediates these innate behaviors?

Recently, Zhang *et al.* describe a subset of male-specific interneurons, P1 neurons, that act as a shared neural node to regulate sleep, courtship, and feeding in a hierarchical manner [4]. P1 neurons express both the male-specific Fruitless (Fru^M) and Doublesex (Dsx^M)

proteins, which are crucial for male sexual development and behavior [5]. In females that do not express Fru^M and express the female-specific Dsx^F protein instead, P1 neurons undergo programmed cell death [5]. It has been shown that P1 neurons integrate chemosensory information from potential mates and initiate male courtship [1, 5–7]. However, more and more recent studies indicate that P1 neurons not only regulate male sexual behaviors, but also directly or indirectly control many other innate behaviors [4, 8–10].

First, P1 neurons co-regulate fighting and sex. While increased activity of P1 neurons promotes male courtship towards female flies, when two such males encounter each other, they fight more. One study proposed that different subsets of P1 neurons regulate fighting and courting separately, as they identified subsets of *fru*- and *dsx*-positive P1 neurons responsible for courtship, and *fru*-negative, *dsx*-positive P1 neurons for aggression [9]. Another study showed that activation of the same sets of P1 neurons regulates courtship and aggression in a threshold-dependent manner, as optogenetic activation of P1 neurons promotes aggression at a threshold below that required for wing extension, a key step in courtship behavior [8].

Second, P1 neurons regulate sex and sleep in an activity-dependent manner. Chen *et al.* found that mild activation of P1 neurons promotes wakefulness but does not induce wing extension, and only a higher level of P1 activation is able to induce wing extension (courtship). They also found that P1 neurons act on wake-promoting DN1 neurons to regulate sleep, which, by negative feedback, inhibits P1 activity such that sleepy males reduce their courtship towards females [10].

To reveal how P1 neurons may regulate sex and other behaviors, Zhang *et al.* identified five independent P1

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driver lines, aiming to sub-divide P1 neurons and further dissect their functions in different innate behaviors. The five driver lines (P1^a–P1^e) labeled from 9 to 23 P1 neurons per hemisphere (20%–50% of all P1 neurons); however, there is still insufficient evidence whether they are distinct from each other. Zhang *et al.* used a range of temperatures from 25.5 to 32 °C to activate the warmth-activated cation channel dTRPA1 that was artificially expressed in P1^a–P1^e neurons, and found that mild activation of all P1 subsets consistently promoted wakefulness, but did not induce wing extension or affect feeding upon starvation; higher activation of P1 neurons (*e.g.* at 30 °C) labeled by four of the five P1 drivers was sufficient to induce courtship, further confirming that P1 neurons regulate sleep and courtship in an activity-dependent manner. Interestingly, the authors found that only higher activation of P1^e that labeled ~23 pairs of P1 neurons suppressed feeding by starved males, while activation of P1 neurons labeled by the other four drivers (9–12 P1 neurons by P1^a–P1^d) at 30 °C or 32 °C was not able to affect feeding behavior. The authors showed that feeding suppression by activating P1^e neurons was not due to increased locomotion, and proposed that higher activation of a larger number of P1 neurons, or activation of specific P1 neurons included in P1^e but not other P1 drivers, is responsible for suppressing feeding behavior. Thus, this study, together with other findings, reveals P1 neurons as a common neural node that mediates sleep, courtship, fighting, and feeding behaviors.

P1 neurons are located in the very center of the fly brain and integrate multiple sensory cues and past social experiences as well as sleep needs, thus P1 neurons may act as an internal arousal center that interacts with environmental cues to modulate arousal-related behaviors including sleep, sex, and fighting. Note that P1 neurons cross-talk with neurons that have a more direct role in regulating sleep and aggression, but more detailed studies on how P1^e neurons interact with the feeding circuit are needed to support a role of P1 neurons as a shared circuit node. There are nearly 50 pairs of P1 neurons in the male fly brain, and only half of them were studied. Do P1 neurons regulate behaviors other than sleep, courtship, aggression, and feeding? In the future, better tools for sub-

dividing P1 populations and driver lines targeting small and distinct subsets of P1 neurons would be helpful to address these questions.

P1 neurons act as a shared neural node for multiple innate behaviors but are male-specific. Why is such an important circuit node only present in males and not females? One possibility is that there are also counterpart neurons (*e.g.* pC1 neurons) that act as a shared neural node for multiple innate behaviors in females; this awaits future studies. Nevertheless, sexual dimorphism occurs in all these innate behaviors at least partially or simply due to the male-specific P1 neurons.

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