Dispatch

Behavioral Plasticity: A Nose For Every Season

A recent study in *Caenorhabditis elegans* identifies the dynamic expression of a single odorant receptor as a molecular mechanism for context-dependent modulation of olfactory preferences and food prioritization.

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In an ever-changing environment, animals need to reversibly and dynamically adapt their behavior to meet their specific needs and challenges in each context. In recent years there has been a renewed interest in the mechanisms regulating context-dependent modulation of behavior [1]. While the focus has been on the role of neuromodulators and how they alter neural circuit properties to provide behavioral plasticity [2], less is known about the molecular effectors of behavioral decisions. In this issue of *Current Biology*, Ryan *et al.* [3] identify the dynamic expression of an odorant receptor as the common molecular mechanism by which three dimensions of internal state — gender, developmental stage and nutritional status — regulate the olfactory preferences linked to changes in behavioral prioritization in *Caenorhabditis elegans*.

Sexual reproduction in animals imposes differences in parental investment including gamete production, mate choice and parental care. In *C. elegans*, too, priorities are influenced by differences in reproductive needs. *C. elegans* males must find mates (i.e., hermaphrodites) to reproduce, whereas hermaphrodites, which are essentially sperm-carrying modified females, can **(Au: OK?)** reproduce by self-fertilization. Accordingly, the male devotes most of his exploration to find a mate, whereas the hermaphrodite explores mostly in search of food.

With a combination of cell-specific genetic manipulations and cleverly designed behavioral assays, Ryan *et al.* [3] find that adult males chemotax less efficiently than hermaphrodites towards food. Food desensitization allows males to leave food patches depleted of mates and explore other territories in search of mates, thus increasing evolutionary fitness. Furthermore, the authors show that one underlying molecular mechanism for sex-specific differences in food attraction is the expression of a single olfactory receptor gene. Adult males have reduced or absent expression of the diacetyl receptor ODR-10 in the gender-shared chemosensory neuron AWA.

But the findings of Ryan *et al.* do not end here. Behavioral priorities are not only different between sexes; priorities also change over time in individuals **(Au: OK?)**. Surely, not many of us would choose to invest money on a retirement plan at 18, or throw money at the bar in a nightclub every Friday night at 80. Similarly, *C. elegans* males do not always prioritize sex over food. Ryan *et al*. show that sexually immature males at the third larval (L3) stage chemotax towards food as efficiently as hermaphrodites and this too is correlated with high levels of *odr-10* expression in the AWA neurons of L3 males [3]. Previous experience is also an important determinant of priorities. Starvation causes males to prioritize food over sex [4,5], and this again is dependent on *odr-10* expression being switched on upon starvation [3]. So, dynamic expression of one olfactory receptor underlies the changes in food attraction associated with the different priorities set up by sex, age and hunger (Figure 1).

That expression of a single chemoreceptor has such profound impact on food attraction is a novel and unexpected finding. Diacetyl is only one of the many metabolites produced by bacteria that *C. elegans* feed upon. This indicates that *odr-10* may recognize other food-related compounds, or that diacetyl is the major cue by which *C. elegans* recognizes *Escherichia coli*. Also uncommon (although not unique [6]) is to find changes in behavioral prioritization executed through dynamic regulation of odorant receptor gene expression. Indeed, modulation of synaptic strength and/or neuronal excitability is the mechanism most often reported for context-dependent behavioral plasticity [7–10]. These changes in circuit properties are often regulated by the action of neuromodulators released in a context-specific manner [9,11]. Although not addressed in the Ryan *et al*. paper, an intriguing possibility is that *odr-10* dynamic expression is under the regulation of neuromodulators signaling through the insulin receptor DAF-2 during starvation, or the nuclear hormone receptor DAF-12 during sexual maturity. Both *daf-2* and *daf-12* are important regulators of male behavioral prioritization [5,12].

The male's reproductive needs impose exploration in search of mates as a behavioral priority in many contexts [5]. In mate-deprived adult males, sex-specific neurons and gender-shared neurons modulated by the neuropeptide PDF generate a state of arousal for mate searching [13,14]. In turn, dynamic expression of *odr-10* in

AWA provides the male with the ability to orient his chemosensory function to find either mates or food according to his priorities in each context [3]. That different sets of genes and neurons regulate each specific component of a behavioral sequence dedicated to reproduction reflects the apparently pervasive modularity of behavior [15]. Indeed, analysis of the function and connectivity of the *C. elegans* male posterior nervous system has identified specific circuit modules dedicated to each step of the mating sequence [16,17].

This work [3] extends and provides ethological relevance to the previous finding by the Portman lab that males and hermaphrodites have different olfactory preferences [18]. In a chemotaxis choice assay between pyrazine and diacetyl, males preferentially travel towards a pyrazine source whereas hermaphrodites navigate towards diacetyl. Employing novel sex-reversal manipulations in specific subsets of cells, Lee *et al.* showed that sexually dimorphic olfactory preference is established by the sex-determination pathway, and that this pathway acted cell-autonomously within the nervous system [18]. In their current paper [3], the authors further show that the sex determination pathway establishes olfactory dimorphism by regulating the expression of the diacetyl receptor in the olfactory neuron AWA so that ODR-10 is ON in hermaphrodites and OFF in adult males. In both vertebrates and invertebrates, sexual dimorphism is frequently represented by such quantitative differences (i.e., the same cell populations are present in both genders but there are molecular differences within these cells in each gender). However, in most instances [19,20] it is difficult to establish with certainty whether a cell population is indeed the same in both sexes or whether sex-specific neurons exist within the population.

The findings from Ryan *et al.* underscore the beauty and power of working in an organism with such a stereotyped and exceptionally well-described anatomy as *C. elegans* when it comes to rigorous analysis of development, circuits and behavior.

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Figure 1. Dynamic expression of a single odorant receptor provides plasticity in food attraction and behavioral prioritization in *C. elegans*.

Diagram depicts a dorsal view of the *C. elegans* head and the AWA chemosensory neuron bilateral pair. Inset shows the ciliated sensory ending of the AWA neuron at the tip of the nose. Expression of the diacetyl receptor ODR-10 (green) increases food-related responses in hermaphrodites and immature or starved males, all of which prioritize food over sex. Down-regulation of the ODR-10 chemoreceptor expression (grey) decreases food attraction in adult males, which prioritize sex over food.

In Brief

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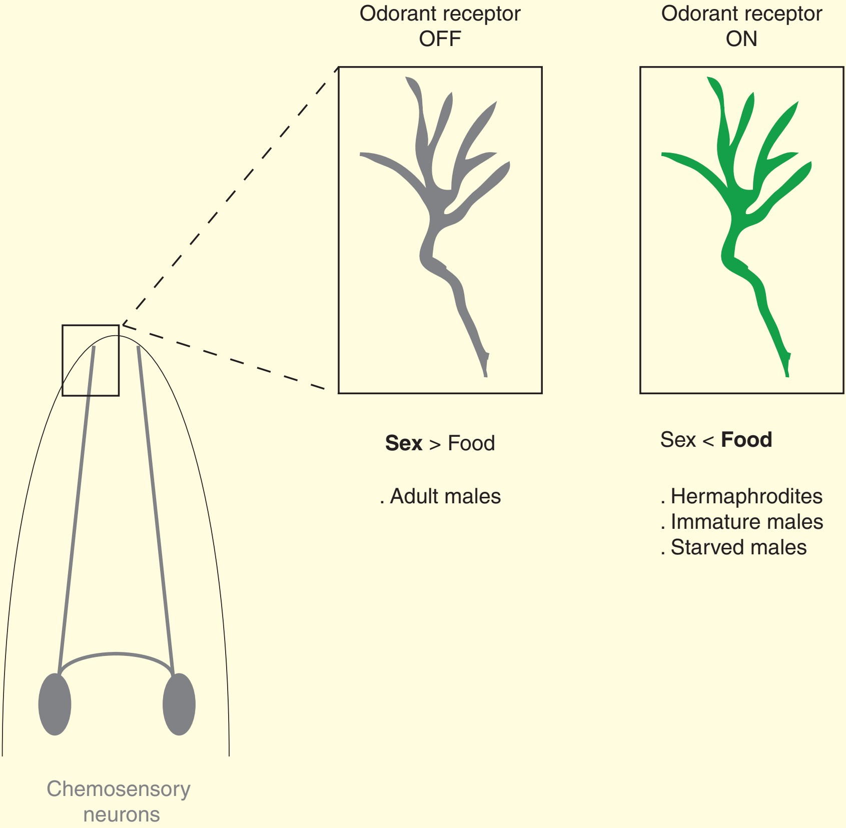

Odorant receptor
OFF
Odorant receptor
ON
Sex > Food
. Adult males
Sex < **Food**
. Hermaphrodites
. Immature males
. Starved males
Chemosensory
neurons