(1999). A eukaryotic protein, NOP-1, binds retinal to form an archaeal rhodopsin-like photochemically reactive pigment. Biochemistry *38*, 14138–14145.
8. Borkovich, K.A., Alex, L.A., Yarden, O., Freitag, M., Turner, G.E., Read, N.D., Seiler, S., Bell-Pedersen, D., Paietta, J., Plesofsky, N., *et al.* (2004). Lessons from the genome sequence of *Neurospora crassa*: tracing the path from genomic blueprint to multicellular organism. Microbiol. Mol. Biol. Rev. *68*, 1–108.
9. Saranak, J., and Foster, K.W. (1997). Rhodopsin guides fungal phototaxis. Nature *387*, 465–466.
10. Waschuk, S.A., Bezerra, A.G., Jr., Shi, L., and Brown, L.S. (2005). *Leptosphaeria* rhodopsin: bacteriorhodopsin-like proton pump from a eukaryote. Proc. Natl. Acad. Sci. USA *102*, 6879–6883.
11. Idnurm, A., and Heitman, J. (2005). Light controls growth and development via a conserved pathway in the fungal kingdom. PLoS Biol. *3*, e95.
12. Brook, P.J. (1969). Stimulation of ascospore release in *Venturia inaequalis* by far red light. Nature *222*, 390–392.
13. Calpouzos, L., and Chang, H.-S. (1971). Fungus spore germination inhibited by blue and far-red radiation. Plant Physiol. *47*, 729–730.
14. Klein, R.M., and Klein, D.T. (1962). Interaction of ionizing and visible radiation in mutation induction in *Neurospora crassa*. Am. J. Bot. *49*, 870–874.
15. Mooney, J.L., and Yager, L.N. (1990). Light is required for condiation in *Aspergillus nidulans.* Genes Dev. *4*, 1473–1482.
16. Kircher, S., Gil, P., Kozma-Bognár, L., Fejes, E., Speth, V., Husselstein-Muller, T., Bauer, D., Ádám, E., Schäfer, E., and Nagy, F. (2002). Nucleocytoplasmic partitioning of the plant photoreceptors phytochrome A, B, C, D, and E is regulated differentially by light and exhibits a diurnal rhythm. Plant Cell *14*, 1541–1555.
17. Busch, S., Eckert, S.E., Krappmann, S., and Braus, G.H. (2003). The COP9 signalosome is an essential regulator of development in the filamentous fungus *Aspergillus nidulans.* Mol. Microbiol. *49*, 717–730.
18. Seo, H.-S., Watanabe, E., Tokutomi, S., Nagatani, A., and Chua, N.-H. (2004). Photoreceptor ubiquitination by COP1 E3 ligase desensitizes phytochrome A signaling. Genes Dev. *18*, 617–622.
19. Magliano, T.M.A., Botto, J.F., Godoy, A.V., Symonds, V.V., Lloyd, A.M., and Casal, J.J. (2005). New Arabidopsis recombinant inbred lines (Landsberg *erecta* x Nossen) reveal natural variation in phytochrome-mediated responses. Plant Physiol. *138*, 1126–1135.
20. Yager, L.N., Lee, H.-O., Nagle, D.L., and Zimmerman, J.E. (1998). Analysis of *fluG* mutations that affect light-dependent conidiation in *Aspergillus nidulans.* Genetics *149*, 1777–1786.

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Neuroscience: Comraderie and Nostalgia in Nematodes

Two recent papers on social rearing and olfactory imprinting show that early developmental experiences can lead to long-lasting changes in behaviour of the model nematode *Caenorhabditis elegans*.

Cori Bargmann

To what extent is the nervous system organized by genetic templates, and to what extent is it reorganized by experience? Since Hubel and Wiesel [1] showed that closing one eye leads to rewiring of eye-specific columns in the visual cortex, physiologists and anatomists have explored the relationship between sensory activity and wiring. A similar question about early experience has been asked by ethologists since Lorenz [2] in their studies of imprinting, a process in which sensory experiences early in development lead to long-lasting changes in an animal's behavior. The most familiar example of imprinting may be the olfactory imprint that allows adult salmon to return to the river in which they were spawned.

The soil nematode *Caenorhabditis elegans* is known for a dramatic response to early developmental experience. At the end of its first larval stage, each animal integrates three sensory inputs — a pheromone, chemical cues from food, and temperature—to decide whether to become a feeding third-stage larva or a developmentally arrested dauer larva, which has a distinct morphology, physiology, and behavior [3]. The dauer decision can be viewed as an extreme form of experience-dependent plasticity, and it shows clearly that the sensory nervous system has powerful access to the nematode's biology. But to what extent is the dauer decision a special case? Does the simple nematode nervous system, composed of just 302 neurons, have the flexibility to remodel itself in response to other sensory information?

Rankin and colleagues [4] addressed this question using a biologically relevant source of sensory information: the presence of conspecific individuals. They compared animals raised in isolation on a bacterial lawn to animals raised in colonies of 30 to 40 animals. At this density, dauer larvae do not form, food is in vast excess, and the small nematodes spend most of their time alone, occasionally encountering another individual.

There are strains of *C. elegans* that aggregate on lawns, but the strain used in this experiment is solitary, and the animals appear to pay little attention to each other. But appearances can be deceiving. In fact, the animals raised in small colonies were strikingly different from isolate-reared animals as adults. Group-reared animals had a much stronger avoidance response to mechanical stimuli than animals raised in isolation. Colony growth also accelerated the rate of development, so that animals grew larger and reached the adult stage about 4 hours earlier (at ~70 hours of development) than isolated animals.

An increase in mechanical stimulation in colonies, presumably because of collisions between animals, may explain the stronger avoidance behavior of group-reared animals. A brief, intense mechanical stimulation increased the avoidance responses of isolated animals almost to the level seen after group rearing, but did not change the behavior of group-reared animals. The AMPA-type glutamate receptor GLR-1, which has a relatively minor role in mechanosensation per se, is required for this effect. GLR-1 is prominently expressed on, and affects the activity of, the giant interneurons known as ‘command neurons’ which stimulate forward and backward movement in *C. elegans.* Remarkably, a tagged GLR-1 receptor transgene is expressed at higher levels in the axons of group-reared animals, providing a molecular correlate of their altered avoidance responses [4]. Most of the GLR-1 receptors are not associated with mechanosensory synapses, so this molecular change reveals an overall change in the interneurons and not just a strengthening of mechanosensation.

Mechanical stimuli did not rescue the effects of isolation on development and body size, although mechanosensory neurons play a role in the response. Chemosensory inputs are known to regulate body size, so a colony may provide both chemical and mechanical cues to the animals [5]. Earlier clues had suggested that *C. elegans* was aware of other animals even when grown at moderate densities; the pheromone that regulates dauer larva formation affects the expression of chemosensory receptors at levels below those that cause dauer development [6,7]. Perhaps body size, like dauer larva formation, involves the integration of different kinds of sensory information. A plausible target pathway for integration is the TGF-β pathway that regulates the polyploidization of somatic tissues and therefore the overall size of the nematode [4,8].

What is the underlying explanation for the effect of solitary rearing? One possibility is that the isolated animals are deprived of neuronal activity that helps organize development [4]. An alternative possibility, suggested by game theory, is that competition between individuals in a colony drives them to grow bigger and faster. Little is known about the natural history of *C. elegans,* but recent papers [9] have begun to explore its distribution in the soil. Nematodes are apparently dispersed enough that many animals may develop in isolation from other individuals.

A different view of the behavioral plasticity of *C. elegans* is provided in a paper by Remy and Hobert [10]. They used pure odors to show that exposure to attractive odors in the first larval stage leads to an increased preference for those odors in adults. This increased preference, or olfactory imprinting, requires that the odors be presented with food, a result observed in several *C. elegans* learning protocols. Even when multiple odors are detected by the same class of sensory neuron, the effect of olfactory imprinting is odor-specific. These experiments broaden the idea of developmental flexibility in *C. elegans* by showing that different experiences can lead to specific behavioral outcomes. Not all odors can be imprinted, however, revealing a limit to the flexibility of the system. So far, the effect of odor exposure was only seen in a sensory neuron whose complex odorant receptor expression pattern is regulated by sensory input and input from synapses [11]. Perhaps these sensory pathways are the substrate for modification by early experience, or perhaps downstream receptors on interneurons are altered [10].

These new papers [4,10] show that the normal flow of sensory information can wield a subtle, and specific, sculpting influence on stable properties of the *C. elegans* nervous system. They provide a physiological context for understanding the observation that large-scale disruptions of neuronal activity give rise to a variety of morphological and molecular changes in *C. elegans* neurons [12–15].

Paradoxically, the extreme stereotypy of *C. elegans* development and behavior are what allowed the observations of behavioral flexibility to be made. It would not have been possible to see the relatively subtle changes caused by odor exposure or group rearing if the variation between normal individuals had been great. The ability to raise dozens or hundreds of genetically identical individuals in the same sensory environment provides exceptional opportunities to tease apart the effects of genotype and experience at high resolution.

References

1. Hubel, D.H., and Wiesel, T.N. (2004). Brain And Visual Perception: The Story of a 25-year Collaboration. (Oxford University Press).
2. Lorenz, K. (1981). The foundations of ethology. (Springer).
3. Golden, J.W., and Riddle, D.L. (1984). The *Caenorhabditis elegans* dauer larva: developmental effects of pheromone, food, and temperature. Dev. Biol. *102*, 368–378.
4. Rose, J.K., Sangha, S., Rai, S., Norman, K.R., and Rankin, C.H. (2005). Decreased sensory stimulation reduces behavioral responding, retards development, and alters neuronal connectivity in *Caenorhabditis elegans.* J. Neurosci. *25*, 7159–7168.
5. Fujiwara, M., Sengupta, P., and McIntire, S.L. (2002). Regulation of body size and behavioral state of *C. elegans* by sensory perception and the EGL-4 cGMP-dependent protein kinase. Neuron *36*, 1091–1102.
6. Peckol, E.L., Troemel, E.R., and Bargmann, C.I. (2001). Sensory experience and sensory activity regulate chemosensory receptor gene expression in *Caenorhabditis elegans.* Proc. Natl. Acad. Sci. USA *98*, 11032–11038.
7. Nolan, K.M., Sarafi-Reinach, T.R., Horne, J.G., Saffer, A.M., and Sengupta, P. (2002). The DAF-7 TGF-beta signaling pathway regulates chemosensory receptor gene expression in *C. elegans.* Genes Dev. *16*, 3061–3073.
8. Flemming, A.J., Shen, Z.Z., Cunha, A., Emmons, S.W., and Leroi, A.M. (2000). Somatic polyploidization and cellular proliferation drive body size evolution in nematodes. Proc. Natl. Acad. Sci. USA *97*, 5285–5290.
9. Barriere, A., and Felix, M.A. (2005). High local genetic diversity and low outcrossing rate in *Caenorhabditis elegans* natural populations. Curr. Biol. *15*, 1176–1178.
10. Remy, J.J., and Hobert, O. (2005). An interneuronal chemoreceptor required for olfactory imprinting in *C. elegans.* Science *309*, 787–790.
11. Troemel, E.R., Sagasti, A., and Bargmann, C.I. (1999). Lateral signaling mediated by axon contact and calcium entry regulates asymmetric odorant receptor expression in *C. elegans.* Cell *99*, 387–398.
12. Peckol, E.L., Zallen, J.A., Yarrow, J.C., and Bargmann, C.I. (1999). Sensory activity affects sensory axon development in *C. elegans.* Development *126*, 1891–1902.
13. Zhao, H., and Nonet, M.L. (2000). A retrograde signal is involved in activity-dependent remodeling at a *C. elegans* neuromuscular junction. Development *127*, 1253–1266.
14. Loria, P.M., Duke, A., Rand, J.B., and Hobert, O. (2003). Two neuronal, nuclear-localized RNA binding proteins involved in synaptic transmission. Curr. Biol. *13*, 1317–1323.
15. Grunwald, M.E., Mellem, J.E., Strutz, N., Maricq, A.V., and Kaplan, J.M. (2004). Clathrin-mediated endocytosis is required for compensatory regulation of GLR-1 glutamate receptors after activity blockade. Proc. Natl. Acad. Sci. USA *101*, 3190–3195.

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