Journal of Biology

BioMed Central

Minireview

Neuronal remodeling on the evolutionary timescale

Ithai Rabinowitch and William Schafer

Address: MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 0QH, UK. Email: wschafer@mrc-lmb.cam.ac.uk

Published: 15 December 2008

Journal of Biology 2008, **7**:37 (doi:10.1186/jbiol102)

The electronic version of this article is the complete one and can be found online at http://jbiol.com/content/7/10/37

Abstract

Despite its remarkable capacity to undergo change at timescales ranging from a fraction of a second to a lifetime, there are many aspects of the nervous system that can be modified only at the enormously longer evolutionary timescale. A new study in *BMC Biology* using nematodes illustrates such evolutionary neuronal remodeling.

One of the hallmarks of the nervous system is its exceptional capacity to remodel itself through a huge variety of complex mechanisms occurring at multiple timescales. Within an individual's lifetime, parameters such as synaptic efficacy, membrane excitability and micro-morphology can undergo major changes during development or as a consequence of learning and memory. Over the much longer evolutionary timescale, more fundamental remodeling can take place across species: the number of neurons can be significantly modified, the gross anatomy can be reorganized and the specializations of particular neurons and neuronal circuits can be substantially altered. Given the fundamental importance of behavior to an organism's survival and reproduction, understanding the mechanisms by which evolutionary changes in brain circuitry modify behavior is a major challenge in evolutionary biology.

Nematodes offer unique advantages for exploring neuronal remodeling at the evolutionary timescale. They have relatively simple nervous systems, typically consisting of around 300 neurons, and ample information exists on the phylogenetic relationships among nematode species. In addition, a complete connectivity map is available for the widely used model nematode *Caenorhabditis elegans* [1], and a significant and increasing body of information exists about the functional properties of particular neurons in this organism. Perhaps most unusually, nematode nervous systems are exceptionally stereotyped in their anatomy, even across wide evolutionary distances. Not only is neuron number remarkably consistent across diverse nematode species; even the arrangement and anatomy of individual neurons shows extensive conservation [2,3]. Remarkably, the counterpart of an individual *C. elegans* neuron can typically be identified in other nematodes to which *C. elegans* is quite distantly related. Thus, evolutionary changes in nervous system function appear to occur within a consistent and well defined anatomical framework: all nematode nervous systems seem to make use of the same complement of cells in the same overall pattern of organization. The problem of understanding behavioral evolution therefore reduces to a much simpler, tractable question: how do changes in the functional properties of particular neurons lead to behavioral differences between species?

A new paper in *BMC Biology* by Srinivasan *et al*. [4] explores these questions in the nociceptive circuits that mediate avoidance of noxious stimuli. Nematodes contain polymodal sensory organs called amphids, which contain ciliated neurons of varying morphologies. The anatomy and sensory specialization of many of these neurons are remarkably similar across nematode species [2,5]. In *C. elegans*, the sensory modalities of the amphid neurons have been assessed by cell ablation studies. Seven amphid neurons extend cilia directly into the amphid channel and

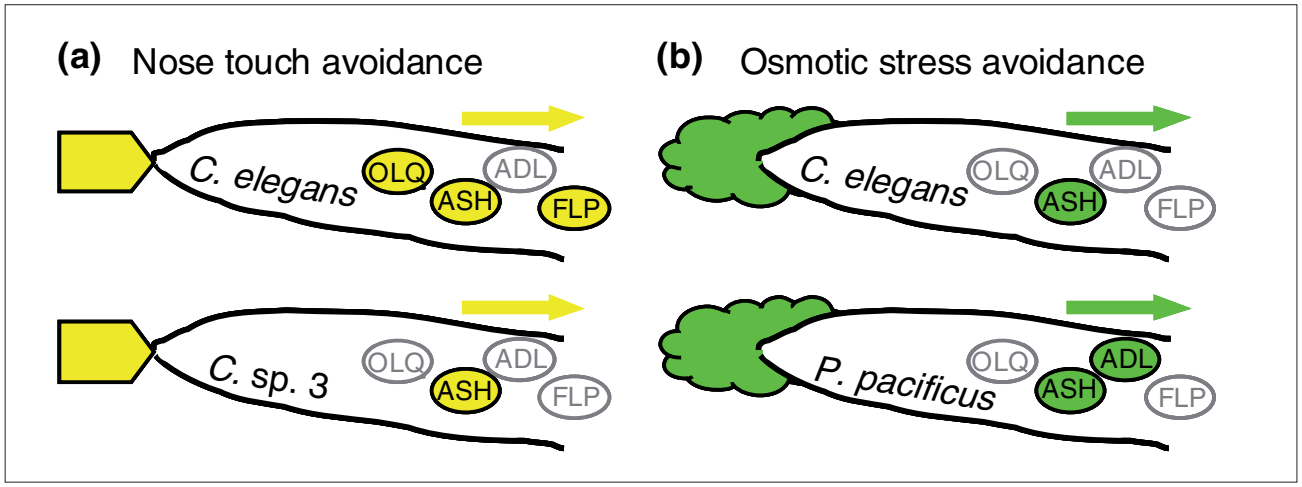

Figure 1
Evolutionary neuronal remodeling between nematode strains. **(a)** In *C. elegans* three sets of neurons, ASH, FLP and OLQ, mediate aversion to light mechanical stimulation of the nose (top). The same response was found to require ASH alone in *C.* sp. 3 (bottom). **(b)** In *C. elegans*, only the ASH neurons are necessary for sensing high osmotic stress (top). This response was sensed in *P. pacificus* by the ADL neurons in addition to the ASH neurons (bottom). Arrows indicate the direction of the response.

are specialized for tasting soluble attractants or repellents, three form wing-like cilia at the edge of the channel and are specialized for olfaction, and one so-called finger cell projects its cilium into the cuticle and appears to be thermosensory. One neuron, ASH, is unusual in that it has the morphology of a taste neuron, but is polymodal in its response properties: ASH is a major neuron for detection of both soluble and volatile repellents, as well as aversive touch and osmotic stimuli. In other nematodes, similar classes of neurons are observed, but fine inter-species differences in anatomy, such as the number of sensory processes stemming from each neuron [2,5], as well as variation in the responses of particular homologous neurons to a specific stimulus, have been reported [6].

Effect of neuronal ablation on response to noxious stimuli

In their new study published in *BMC Biology* Srinivasan *et al.* [4] systematically compared the neural circuits involved in detecting noxious stimuli in six different nematode strains. To characterize these circuits, they determined which single-cell ablations affected avoidance of particular stimuli. For example, nematodes of all species tested showed strong avoidance of the odorant 1-octanol. In this case, all strains showed similar ablation phenotypes: killing ASH strongly impaired octanol avoidance, whereas ablation of other amphid neurons had no significant effect. Likewise, light mechanical stimulation of the nose produced comparable avoidance responses in all species, although habituation was much faster in one species, *Cruznema tripartitum*. However, whereas three neuron types, ASH, FLP and OLQ, affect nose touch avoidance in *C. elegans*, in a different species (*Caenorhabditis* sp. 3) only ASH is important (Figure 1a). A similar but opposite effect was observed for osmotic avoidance, which in *C. elegans* is mediated solely by ASH, but was found to involve the ADL and ASH neurons in *Pristionchus pacificus* (Figure 1b). Surprisingly, *P. pacificus* was one of several species tested that responded more weakly to the high osmotic stimulus despite the extra neurons in its circuit. A clustering analysis based on the avoidance responses of the various species in the study revealed not only examples of correlation between behavioral similarities and phylogenetic proximity, but also cases of greater behavioral differences between closely related species than between more distantly related ones. Thus, evolutionary remodeling of these sensory circuits might occur readily in response to natural selection.

What do ablation results tell us about how nociceptive circuits have been remodeled during nematode evolution? One possibility is that particular neurons might alter or even lose functionality in the course of evolution. One should be cautious, however, as the components of a neural circuit are not necessarily limited to those neurons whose ablation early in development impairs the circuit's function. During development, an ablated animal can sometimes compensate for a missing neuron, for example by reorganizing the remaining neurons in the circuit. Moreover, recent examples demonstrate that it can be easier for a circuit to

compensate for a missing neuron than for an inactive one, even when the neuron's function is absent throughout development [7,8]. Ablation studies can be said to define the group of neurons whose functions are most critical for a given behavior. Thus, if ablation of a neuron no longer affects the function of a particular circuit, this might not indicate a change in the overall function of the neuron, but might indicate its importance or dispensability for the circuit.

Another recent study comparing feeding behavior in four nematode species [9] provides some insight into how such changes might occur. Nematodes feed by pumping food through a muscular pharynx, which is controlled by the pharyngeal nervous system. Three motor neurons (MC, M3 and M4) appear to have particularly important roles in controlling pharyngeal contraction in all species. However, in one species, *Panagrolaimus* sp. PS1159, a fourth motor neuron, M2 (which has no known function in the other species), has apparently acquired a role in controlling contraction of the pharyngeal isthmus. Likewise, the M4 neuron controls contraction of the pharyngeal isthmus and terminal bulb in most species; in *C. elegans*, however, it appears to have lost the latter function. Interestingly, the mechanism for this change in M4 function appears to involve silencing of M4's terminal bulb synapses during evolution. It is possible that similar types of change might occur in sensory circuits to reconfigure the roles of individual neurons in particular sensory modalities.

Clearly, ablation studies are only a first step in understanding how behavior evolves in nematodes. With modern electron microscopy and computational methods, it should be practical to reconstruct the neuroanatomies of other nematodes at the single-cell level and compare the connectivity patterns with those of *C. elegans*. With the development of transgenesis protocols for other nematode species [10], it will also be possible to use genetically encoded sensors to probe the activity patterns of homologous neural circuits in a range of nematodes. In the near future, there is a real possibility of understanding the detailed genetic and cellular mechanisms by which nematode nervous systems are remodeled during evolution.

References

1. White J, Southgate E, Thomson J, Brenner S: **The structure of the nervous system of the nematode *Caenorhabditis elegans*.** *Phil Trans R Soc Lond* 1986, **314:**1-340.
2. Ashton FT, Li J, Schad GA: **Chemo- and thermosensory neurons: structure and function in animal parasitic nematodes.** *Vet Parasitol* 1999, **84:**297-316.
3. Forbes WM, Ashton FT, Boston R, Zhu X, Schad GA: **Chemoattraction and chemorepulsion of *Strongyloides stercoralis* infective larvae on a sodium chloride gradient is mediated by amphidial neuron pairs ASE and ASH, respectively.** *Vet Parasitol* 2004, **120:**189-198.
4. Srinivasan J, Durak O, Sternberg PW: **Evolution of a polymodal sensory response network.** *BMC Biol* 2008, **6:**52.
5. Bumbarger DJ, Wijeratne S, Carter C, Crum J, Ellisman MH, Baldwin JG: **Three-dimensional reconstruction of the amphid sensilla in the microbial feeding nematode, *Acrobeles complexus* (Nematoda: Rhabditida).** *J Comp Neurol* 2009, **512:**271-281.
6. Ketschek AR, Joseph R, Boston R, Ashton FT, Schad GA: **Amphidial neurons ADL and ASH initiate sodium dodecyl sulphate avoidance responses in the infective larva of the dog hookworm *Anclyostoma caninum*.** *Int J Parasitol* 2004, **34:**1333-1336.
7. Kindt KS, Viswanath V, Macpherson L, Quast K, Hu H, Patapoutian A, Schafer WR: ***Caenorhabditis elegans* TRPA-1 functions in mechanosensation.** *Nat Neurosci* 2007, **10:**568-577.
8. Li W, Feng Z, Sternberg PW, Xu XZ: **A *C. elegans* stretch receptor neuron revealed by a mechanosensitive TRP channel homologue.** *Nature* 2006, **440:**684-687.
9. Chiang JT, Steciuk M, Shtonda B, Avery L: **Evolution of pharyngeal behaviors and neuronal functions in free-living soil nematodes.** *J Exp Biol* 2006, **209:**1859-1873.
10. Li X, Massey HC, Jr., Nolan TJ, Schad GA, Kraus K, Sundaram M, Lok JB: **Successful transgenesis of the parasitic nematode *Strongyloides stercoralis* requires endogenous non-coding control elements.** *Int J Parasitol* 2006, **36**:671-679.