

EVOLUTIONARY DEVELOPMENTAL BIOLOGY

More than one way to a central nervous system

Have the molecular mechanisms that are linked to the developmental organization of centralized nervous systems evolved once or multiple times? Evidence from nine animal species points to the latter.

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Animal nervous systems come in many shapes and sizes, ranging from a handful of neurons to large, complex brains. A key question has been whether the centralized nervous systems found in many bilaterally symmetrical animals (bilaterians), which include vertebrates and insects, share a common evolutionary origin, or evolved more than once. At a superficial level, both flies and vertebrates boast a brain connected to a single nerve cord that extends into the trunk. In addition, molecular data indicate that key regulatory genes are deployed similarly during nervous-system development in vertebrates, flies¹ and another bilaterian, a segmented worm (an annelid)². These similarities have been interpreted as evidence for evolutionary conservation of an ancient bilaterian developmental program for centralized nervous systems. But in a paper online in *Nature*, Martín-Durán and colleagues³ provide evidence for the independent evolution of such nervous systems.

The evolutionary steps between a nerve net and the elaborate centralized nervous systems of bilaterians have been an area of active interest for more than a century⁴. In the mid-1980s, our ability to study this process received a boost, thanks to the discovery of a large family of genes that encode transcription factors containing a DNA-binding homeobox domain⁵. It emerged that members of this homeobox-gene family, including the Hox complex, are expressed in the same order along the head-to-tail (anterior–posterior) axis during development in many distantly related bilaterians, including flies and vertebrates⁵. It was later shown that a signalling pathway governed by genes that encode bone morphogenetic proteins (BMPs) is needed to establish the dorsal–ventral (back-to-belly) body axis in diverse bilaterians⁶.

Given these insights, it was not surprising to find that a suite of homeobox genes is also expressed in strikingly similar patterns along

the dorsal–ventral axis of the developing nervous systems of vertebrates and fruit flies¹. Along this axis, staggered homeobox-gene expression correlates with the development of specific neuron types in different regions. The discovery that these genes are also expressed along the dorsal–ventral nervous-system axis in *Platynereis dumerilii* (an annelid distantly related to flies and vertebrates) was seen as evidence that bilaterian nerve cords are evolutionarily conserved².

Advances in phylogenetic methods for analysing evolutionary relationships, coupled with broader sampling across the evolutionary tree, have altered our understanding of animal relationships. In 2016, a phylogenetic

analysis identified an assemblage of small, bilaterally symmetrical, simple worms, collectively referred to as xenacoelomorphs, as the sister group to the rest of the bilaterians (nephrozoans)⁷. Because xenacoelomorphs are the closest living relatives to the nephrozoans (Fig. 1), comparisons between these two groups can help researchers to infer traits present in the last common ancestor of all bilaterians.

Xenacoelomorphs display diverse nervous-system arrangements. Some have only a nerve net, like the closest relatives of bilaterians, the cnidarians (jellyfish and sea anemones). Others also have one or more nerve cords that are located dorsally, ventrally or at multiple positions along the dorsal–ventral axis. Martín-Durán and colleagues investigated the expression of patterning genes in four xenacoelomorph species. They found that, although the expression of BMP and anterior–posterior homeobox genes in these species was consistent with patterns seen in other bilaterians, the expression of the dorsal–ventral homeobox genes in the nervous system was not.

Martín-Durán *et al.* next investigated dorsal–ventral patterning in the nephrozoans. For this work, they extended their analysis of dorsal–ventral homeobox genes to five species within the Spiralia, a large but

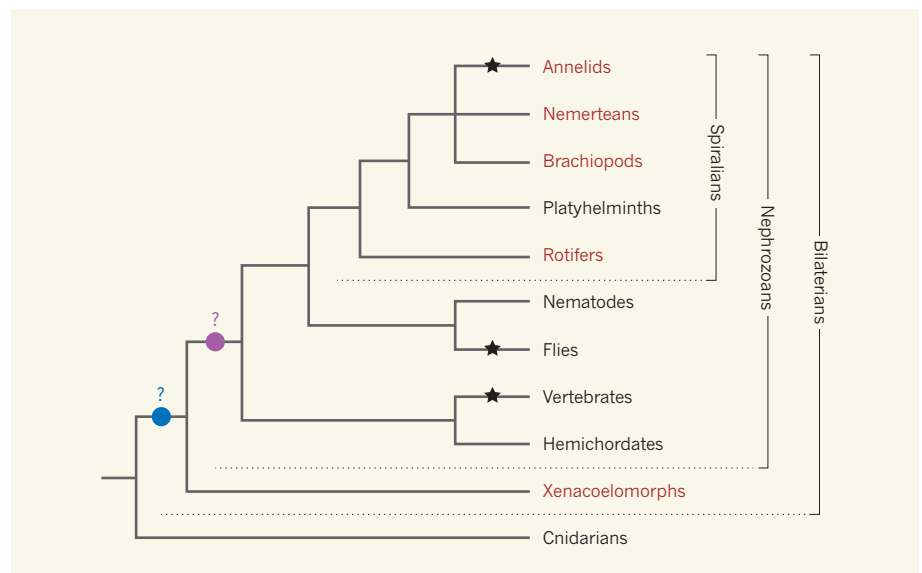


Figure 1 | Evolution of animal nervous systems. The bilaterians (animals that show bilateral symmetry) consist of nephrozoans and a sister group, xenacoelomorphs. Many nephrozoans and xenacoelomorphs have centralized nervous systems, unlike their closest relatives, cnidarians, which feature a simple nerve net. A suite of homeobox genes is expressed (stars) along the back-to-belly axis of the central nervous systems of vertebrates, flies and a segmented worm (an annelid), and it has been posited that this is an evolutionarily conserved gene-expression pattern guiding the development of a centralized nervous system that originated from a common bilaterian (blue circle) or nephrozoan (purple circle) ancestor. However, Martín-Durán *et al.*³ did not find this pattern in nine bilaterian species — five spirilians and four xenacoelomorphs (red text). Their data strengthen the case that the developmental and morphological similarities between bilaterian centralized nervous systems are the result of independent evolutionary events that converged on similar outcomes.