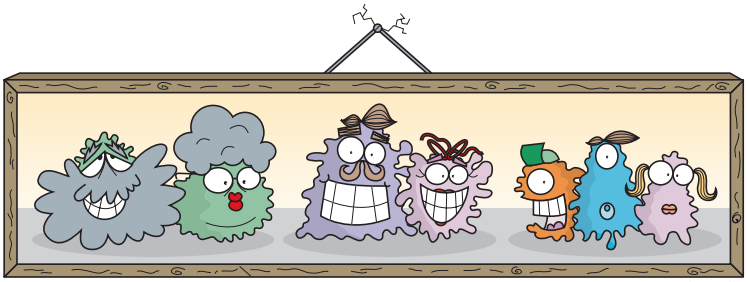
EVOLUTION

Keeping it in the family



Neil Smith

The origins of the complex aspects of the vertebrate nervous system have not been studied in the evolutionary context of increased molecular complexity at the synapse. Grant and colleagues have now compared proteins of the postsynaptic density (PSD) across 19 species from yeast to vertebrates. They concluded that the origins of the modern brain can be traced back to unicellular organisms, and that the increased molecular complexity in vertebrates contributed to the anatomical specialization of the brain and the diversification of the behavioural repertoire.

Grant and colleagues examined the molecular composition of the PSD in 19 species of different complexity, using genomic, proteomic and expression profiling. Initially they compared the overall number of orthologues (genes with a common ancestor that are found in different species) across the selected species. Of the 650 postsynaptic mouse genes that they investigated, 45% were represented in invertebrates and 25% were represented in yeast. This indicates that the origin of a significant proportion of the proteins that are found in the PSD precedes the development of a nervous system.

The authors then grouped the orthologues into functional classes and analysed the rate of expansion (the increase in number) and diversification of each class. Proteins that are involved in general cell-biological processes, such as protein synthesis, were termed 'downstream components', whereas proteins with specific synaptic functionality, such as neurotransmitter receptors, were termed 'upstream components'. It emerged that those classes of proteins considered to be upstream components have expanded at a much higher rate in the evolution towards vertebrates than downstream components.

If the complexity of the nervous system is mirrored in the molecular complexity of the synapse, the molecular composition of the invertebrate synapse should be simpler than the vertebrate one. The authors investigated this hypothesis by comparing the postsynaptic proteins that are found in *Drosophila melanogaster* to those that are found in yeast and mice. Most downstream components of the postsynaptic proteome of *D. melanogaster* were present in yeast, whereas upstream components showed significant expansion in the fly. By comparison, 60% of mouse orthologues were present in *D. melanogaster*, but only 25% of these were upstream components. Comparing upstream components of the fly and the mouse, the absolute number of proteins in each functional protein class was significantly higher in the mouse; however, the proportion of each class in the two species' entire postsynaptic proteome was the same. This indicates that all functional classes of proteins that contribute to postsynaptic function were established in invertebrates, and that proteome expansion from invertebrates to vertebrates is due to gene-family expansion rather than *de novo* generation of proteins.

Finally, the authors investigated the extent to which expansion of the postsynaptic proteome can be correlated to the anatomical regionalization of the brain that is found in higher vertebrates. They compared expression profiles of 150 postsynaptic proteins in 22 different regions of the mouse brain. Indeed, although most proteins are expressed in all regions, proteins that evolved only recently showed a much higher variation of expression than proteins that evolved earlier.

This analysis of the postsynaptic proteome has shed new light on the evolution of the nervous system. Future work could attempt to reconstruct the evolution of the molecular mechanisms of synaptic transmission. Certainly, taking evolutionary information into account when dissecting complex aspects of the vertebrate nervous system is a novel and, as demonstrated in the publication, valid approach.

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ORIGINAL RESEARCH PAPER Emes, R. D. *et al.* Evolutionary expansion and anatomical specialization of synapse proteome complexity. *Nature Neurosci.* **11**, 799–806 (2008)