Introduction

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Introduction to 'Homology and convergence in nervous system evolution'

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The origin of brains and central nervous systems (CNSs) is thought to have occurred before the Palaeozoic era 540 Ma. Yet in the absence of tangible evidence, there has been continued debate whether today's brains and nervous systems derive from one ancestral origin or whether similarities among them are due to convergent evolution. With the advent of molecular developmental genetics and genomics, it has become clear that homology is a concept that applies not only to morphologies, but also to genes, developmental processes, as well as to behaviours. Comparative studies in phyla ranging from annelids and arthropods to mammals are providing evidence that corresponding developmental genetic mechanisms act not only in dorso–ventral and anterior–posterior axis specification but also in segmentation, neurogenesis, axogenesis and eye/photoreceptor cell formation that appear to be conserved throughout the animal kingdom. These data are supported by recent studies which identified Mid-Cambrian fossils with preserved soft body parts that present segmental arrangements in brains typical of modern arthropods, and similarly organized brain centres and circuits across phyla that may reflect genealogical correspondence and control similar behavioural manifestations. Moreover, congruence between genetic and geological fossil records support the notion that by the 'Cambrian explosion' arthropods and chordates shared similarities in brain and nervous system organization. However, these similarities are strikingly absent in several sister- and outgroups of arthropods and chordates which raises several questions, foremost among them: what kind of natural laws and mechanisms underlie the convergent evolution of such similarities? And, vice versa: what are the selection pressures and genetic mechanisms underlying the possible loss or reduction of brains and CNSs in multiple lineages during the course of evolution? These questions were addressed at a Royal Society meeting to discuss homology and convergence in nervous system evolution. By integrating knowledge ranging from evolutionary theory and palaeontology to comparative developmental genetics and phylogenomics, the meeting covered disparities in nervous system origins as well as correspondences of neural circuit organization and behaviours, all of which allow evidence-based debates for and against the proposition that the nervous systems and brains of animals might derive from a common ancestor.

1. Emergence, convergence and correspondences

Among the huge diversity of extant species, the existence of what appear to be many different kinds of brains and central nervous systems (CNSs) provides not one but numerous conundrums. One is the possibility, discussed in this issue, that neurons may have evolved twice independently, and thus that nervous systems would have separate origins [1]. Such possibilities emphasize an intriguing landscape of questions and hypotheses punctuated by enormous gaps, in which our knowledge is still profoundly deficient. We still are not able to determine whether circuits and pathways in what we define as a brain in one taxon share common ancestry with circuits and pathways in the brains of distantly related taxa. Which taxa can be experimentally shown to exhibit commonality both at

the morphological and genetic levels that would lead to claims of genealogical correspondence? Which taxa might be comprehensively excluded from such commonality? For example, the recent discovery that the unique organization of the octopus CNS is a reflection of this taxon's unique genomic organization, including the observation that Hox genes play a conserved role in the development of rostral regions of the brain, would seem to define the CNS of cephalopod molluscs as wholly distinct from all other taxa [2]. Yet even the nervous systems of cephalopods are likely to be extreme examples of evolved divergence from a far simpler ladder-like arrangement, such as those found in present-day aculiferan molluscs where colinearity of Hox gene expression during development is comparable to that in annelids, arthropods and deuterostomes [3], the nervous systems of which are linearly ganglionated.

In more general terms, in suggesting homology of brain and nervous system organization across phyla, one would have to admit that many taxa would have acquired evolved reduction, loss or radical modification of ancestral neural arrangements. The likelihood of such events can be observed in extant species, for example in tunicates, whose chordate-like larvae are subject to extensive rearrangements during metamorphosis to form sessile adults [4]. These events entail regression of parts of the CNS that are regulated by ERK/JNK signalling and the complement cascade [5–7]. Thus, evolved loss, reduction or radical modification of the CNS can occur during ontogeny of a species, and could thus have occurred multiple times during the evolution of the nervous system. A case in point is the selective advantage obtained by late developmental atrophy in cavefish of the eyes and optic tecta, conserving what would normally consume 17% of the resting metabolism of the brain, as it does in related surface fish [8]. However, favouring convergent evolution of the CNS would seem to be more comfortable because no other explanation could seem to account for the observed disparity among extant nervous systems [9]. Yet, opposite views have also been held, in one form or another, since the middle of the nineteenth century when early investigators were struck by similarities of brain organization in arthropods, vertebrates and worms.

Felix Dujardin, for example, publishing in 1850, argued that the folds of the honeybee's mushroom bodies correspond to the gyri and sulci of the human cerebral cortex, ascribing to both the properties of sociality and industriousness [10]. Guiseppe Bellonci in 1883 dedicated papers to the structural correspondences shared by the glomerular organization of olfactory centres in *Squilla mantis*, a stomatopod crustacean, a freshwater eel and a cricket [11]. A century later, functional and circuit correspondences among olfactory systems were argued to be universal across most phyla [12]. In the early 1890s, Gustav Retzius, the great Swedish biologist, in his privately published journal *Biologische Untersuchungen* made explicit his view that the neuronal organization of the ventral cord of annelids and crustaceans correspond in detail. Furthermore, his Golgi study of the dorsal cord of the hagfish *Myxine glutinosa* reveals his fascination in similarities of ganglionic organization [13–15]. Fridtjof Nansen's discovery that nerve cells were discrete elements, not part of a syncytium, also distinguished monopolarity versus bipolarity of invertebrate and vertebrate nerve cells [16,17]. Today, studies on ctenophores go much further in suggesting not different morphologies but two wholly separate origins of the neuron [1].

Fascination in, and questions about, the origins of nervous systems are today no less enthralling than they were over a hundred years ago. Such has been the prime motivation for the Royal Society for sponsoring two meetings to debate the origin and evolution of nervous systems. The results of these two events are now published, one referring to the 'Origin and evolution of the nervous system' published in volume 370 of *Philosophical Transactions B* [18], and the second 'Homology and convergence in nervous system evolution' in this companion issue that presents a variety of topics centred around whether what we know about the evolutionary emergence of neurons, sensory systems and circuits might assist in resolving questions about nervous system origins.

2. Organization and contributions to this issue

The first contribution to this issue is by Budd & Jackson [19], who consider origins: the origins in the Early Cambrian; and the earliest fossil evidence for bilaterian radiation that occurred after the beginning of the Cambrian, about 541 Ma. This time was preceded by an about 9–19 Myr period in the Late Ediacaran during which detectable trace burrows suggest the presence of organisms able to express extremely simple avoidance-like behaviours. The earliest Cambrian trace fossil *Treptichnus pedum*, which already indicates an appreciable elaboration of behaviour compared to Ediacaran evidence [20], denotes the beginning of the Cambrian's Terreneuvian series which, as proposed by Budd & Jackson, saw the appearance of characteristically U-shaped tubes that are best ascribed to trace fossils of sessile stem group lophotrochozoans. While the preponderance of this fauna may explain the rarity of traces ascribable to deuterostomes or spiralians, it also suggests that such sessile taxa are likely to have given rise to modern lineages of errant lophotrochozoans with homologous neural attributes.

If the earliest animals moved and were able to actively respond to stimuli, then they must have been equipped with sensory-motor organization. The second article in this issue is by Brunet & Arendt [21], who theorize how such circuits might have originated in unicellular eukaryotes with the first action potentials appearing with the evolution of sensory cilia, whereby potentials generated in cilia would spread through the cell, itself a motile unit. In the first multicellular organisms, these would have provided systems of mechanoreceptive cells, from which evolved true neurons and muscles. The implications are that metazoan origins would have been concomitant with the origin of nervous systems.

In the following article [22], Eisthen & Theis emphasize the degree to which environmental and symbiotic microbes play a central role in the physiology of the CNS. The suggestion is that such interactions, which today command the attention of biomedical researchers, may have archaic origins to the extent that microbes once played a crucial role in the evolution of neural systems by driving the evolution of epithelial–microbial interactions leading to internalization of specialized conducting cells, which assumed the role of proto-neurons. The authors suggest that throughout metazoan evolution, microbes likely played a role in the evolution of cellular communication, defences and relevant sensory systems.

Already posed in the Introduction is the question whether neurons and nervous system evolved just once, or more than once. This is discussed in detail by Moroz & Kohn [1], the

focus here being on Ctenophora, semi-transparent marine predators known as comb jellies. Their nervous systems are proposed by the authors to be uniquely distinct from the nervous systems of Cnidaria and all bilateria. The authors' conclusions are based on the unique genomic properties of the ctenophore nervous system, which suggest that it evolved independently, as did its preponderance of peptide signalling coupled with the absence of transmitter substance that characterize other metazoan nervous systems. The authors explain their view of neurons as a functional category of cells. By proposing that neurons have evolved several times independently they refute the notion that neurons are homologous across phyla and suggest that their synaptic structures have likewise evolved several times.

Martinez and colleagues [23] debate similar questions about origins, here with reference to the nervous system of Xenacoelomorpha, an equivocal clade comprising three acoelomate groups, the nervous systems of which range from simple to well-ordered networks, the latter associate with an anterior condensation of neurons that relate to apical sensory organs. The authors propose that by studying Xenacoelomorpha both at the genomic level and with regard to nervous system organization, it should be possible to determine whether within this group, and thus by extension to other evolutionary trajectories, brains can, and indeed may have evolved several times independently.

Considerations about the origin of sensory organs are crucial to an understanding of brain evolution. Among sensory systems, the origin of eyes has dominated discussions and theories about what selection pressures have driven eye evolution; from the first appearance of photosensitive receptors to the appearance of single lens eyes and compound eyes and their underlying circuits. In their paper, Randel & Jékely [24] discuss the origin of the simplest eyes and the function that such an innovation might have served. The proposal is that dynamic phototaxis, a helical propulsive movement, could have arisen as an early light-driven behaviour mediated by paired eyespots appropriately wired by a simple sensory-motor circuit. With reference to connectomics of larval eyes of the annelid *Platynereis dumerilii*, the authors provide a scenario for the evolutionary transition from a non-visual sensory system to one that is visual and from thence to the evolution of image-forming eyes.

Similar to the evolution of photosensitive cells, the emergence of mechanosensory and sensory-motor neurons likely played a crucial and selective role in nervous system evolution, especially for the formation of neural circuits underlying goal-directed behaviour. A case in point is made by Galliot and co-workers [25] using Hydra, a genus of Cnidaria, that are characterized by a simple nerve net that interconnects sensory photoreceptors and touch-sensitive mechanosensory and sensory-motor neurons located in their body wall and tentacles. The latter neurons continuously differentiate from interstitial stem cells but perturbation of this mode of adult neurogenesis results in cell-type-specific alterations of gene expression. Wenger *et al.* [25] determine transcriptome data which reveal that epitheliomuscular cells switch on expression of genes encoding proteins involved in neurogenesis and neurotransmission typical for sensory neurons. The authors suggest that ancestral multi-functional epithelial cells in basal metazoans possessed proto-neuronal functions which progressively diversified into more specialized cells during evolution.

Divergent evolution of certain clades within Metazoa is epitomized by the arthropod radiation, a diversification that has provided at any time since (and including) the 'Cambrian Explosion' the most species-rich phylum. In her review, Angelika Stollewerk demonstrates that clear variation in neurogenesis may have supported such divergence despite the fact that a subset of conserved genes is known to underlie neurogenesis in all Metazoa [26]. Here, the author compares arthropod neurogenesis to demonstrate how variations of function and regulation of neural genes could have facilitated divergent evolution of developmental neurogenesis in this phylum, using examples from its major representatives.

Divergence of body plans underlies the next paper in this series by Nick Holland [27], who provides a comprehensive overview of the various scenarios, both historical and current, that have attempted to explain the origin of the vertebrate nervous system from an invertebrate predecessor. Ideas about how the transformation from invertebrate-to-vertebrate might have occurred are discussed with special reference to two theories, one originating historically from Anton Dohrn's nerve cord inversion theory [28], the other from William Bateson [29], who suggested that the chordate ancestor was vermiform and unsegmented, exemplified by the acorn worm *Balanoglossus*. According to Bateson this species showed clear evidence of a condensed nervous system during development. Bateson's work was published in 1884. Today, *Balanoglossus* is viewed as a key for investigating deep ancestry of the vertebrate CNS as this taxon possesses a diffuse nervous system expressing many 'proneural' genes involved in patterning the chordate brain and spinal cord [30]. In his article, Holland demonstrates the many difficulties inherent in deciding which of the two theories is the more plausible and suggests strategies and their attendant requirements for further resolving this.

Since the 1990s, numerous papers have appeared arguing from evidence that specific attributes of the brains of vertebrate and arthropods share similarities that can best be interpreted as homologous. In their comparisons of arthropod and vertebrate brains, Wolff & Strausfeld [31] identify numerous structural, molecular and genetic characters that are shared by the vertebrate hippocampus and the arthropod mushroom bodies. The correspondences include a neuronal ground pattern that defines these forebrain structures and their ancestral relationships with the olfactory system. Proteins that have been shown in flies and mice to be crucial for memory acquisition denote these centres and, in addition, reveal mushroom body-like structures in annelids, nemerteans and polyclad flatworms. That these proteins define discrete brains in certain acoels emphasizes the question whether such circuits might have originated very early in bilaterian evolution.

Studying the CNS of species belonging to less familiar taxa is an absolute requirement for gaining information about the diversity of brain evolution. The contribution by Hejnol and co-workers [32] describes the organization of the nervous system in the larva of the penis worm, a member of Priapulida. Priapulida is recognized as an ecdysozoan that is little different from fossil priapulids from Early [33] and Mid-Cambrian Lagerstätten [34], in which traces of a nervous system with ganglion-like arrangements have been identified [35]. Here the authors describe the larval a nervous system using a palette of antisera raised against cytoskeletal proteins and neuropeptides to resolve the early development of a circumstomodeal

condensation of neurons leading to a single ventral nerve confluent with a caudal ganglion. It is suggested that studies of such early developmental stages may provide a window on the early evolution of the ecdysozoan CNS.

Drawing from a wealth of studies of circuits that mediate rhythmically patterned motor actions, particularly in gastropod molluscs, Paul Katz [36] shows that comparative studies reveal a common Leitmotif: that of divergent evolution of behaviours resulting from evolutionary modifications of homologous underlying circuits. The author also shows that whereas major rewiring of an ancestral circuit leads to corresponding changes of behaviour, in some instances divergence of wiring has arisen without any observable behavioural alteration. Moreover, where corresponding rhythmic behaviours are known to have evolved convergently, the neural circuits for such homoplasic behaviours are obviously different. The summed results of Katz's research suggest that one cannot assume simplistic assumptions about the behavioural consequences of convergent evolution of circuits nor assume that homologous neural components necessarily underlie homologous behaviours.

An altogether different level of behavioural analysis tackles questions about neurological constituents that contribute to the evolution of intelligence [37]. The authors of this contribution emphasize that it is not simply brain size that should be taken into consideration; indeed, such consideration can be misleading. Rather, intelligence relates to the volume of cortex, the packing of its neurons and high conduction velocities enabling rapid sensory integration and synthesis. These features define in common the brains of corvids and primates, both taxa that display high levels of intelligence as defined by introspective problem-solving.

It is claimed that the extraordinary evolution of intelligence in hominids, which sets them apart from all other species, is one coordinate in an evolutionary matrix representing advanced cognitive behaviours, distinguishing vertebrates from most invertebrates with the exception of some cephalopod molluscs and, possibly, stomatopod crustaceans and some hymenopteran insects. In his article, Seth Grant [38] makes the case for this distinction in our own species due to the expansion of the synaptic proteome and the consequent diversity of synapses, a diversity suggested to specifically relate to the evolution of unique human cognitive attributes.

The finale of this special issue is written by Michael Ghiselin, the foremost exponent of the concepts and ideas underlying what is meant by Darwinian evolution [39]. Ghiselin's article reminds us how important it is to use terms correctly, because each holds a unique meaning and thus value in discussions about evolution, whether it is about brains or, for example, the evolutionary diversification of nudibranch molluscs. An understanding of some homology, meaning a correspondence of parts due to common ancestry, is a lynchpin in evolutionary considerations yet the term is easily used with abandon and thus incorrectly applied, even to convergence. This final essay is one that every evolutionist should keep in the back of her or his mind when trying to communicate our ideas in a language that is understood by scientist and layman alike.

3. Some concluding remarks

It has been argued that the evolution of the nervous system, its centralization and the emergence of a brain and mind are inevitable events in the course of evolution [40,41]. While this may sound like a heretical and misplaced reprise of teleology, the proposition does indeed question previous attempts to find basic rules of organization in '*what unites form rather than divides it*' [41]. Homology and convergence are two conceptual frameworks for discussing correspondences and to identify genealogical order amongst the many different types of nervous systems that characterize extant species across large phylogenetic distances. Both the concepts of homology and convergence can be united for a common aim: that of identifying the '*geometry of life*' [41] whose algorithms, if uncovered, would enable an explanation for the many similarities observed, for example, between the brains of arthropods and chordates and the stunning differences exemplified by the brains of cephalopods. In other words: what might be the laws of nature that can lead to nervous system centralization and the formation of brains, or their evolved reduction and loss several times during the course of evolution? In one–now historical–search for such a "geometry of life," D'Arcy Thompson's thesis 'On growth and form' [42] identified correlations between biological forms and mechanical phenomena. Yet, while such correlations have found some mechanistic footings (e.g. [43,44]), they are however insufficient to grasp key aspects of brain functionality such as mediating allocentric memory, goal-directed behaviours and voluntariness [45,46], which themselves are driving forces of evolution. It is becoming clear that more than genes, genomes and morphologies are needed to elucidate the origin and evolution of the nervous system, although a start has been made.

Guest Editor profiles

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