STUDYING NEUROGENESIS IN CEPHALOPODS: WHY AND HOW?

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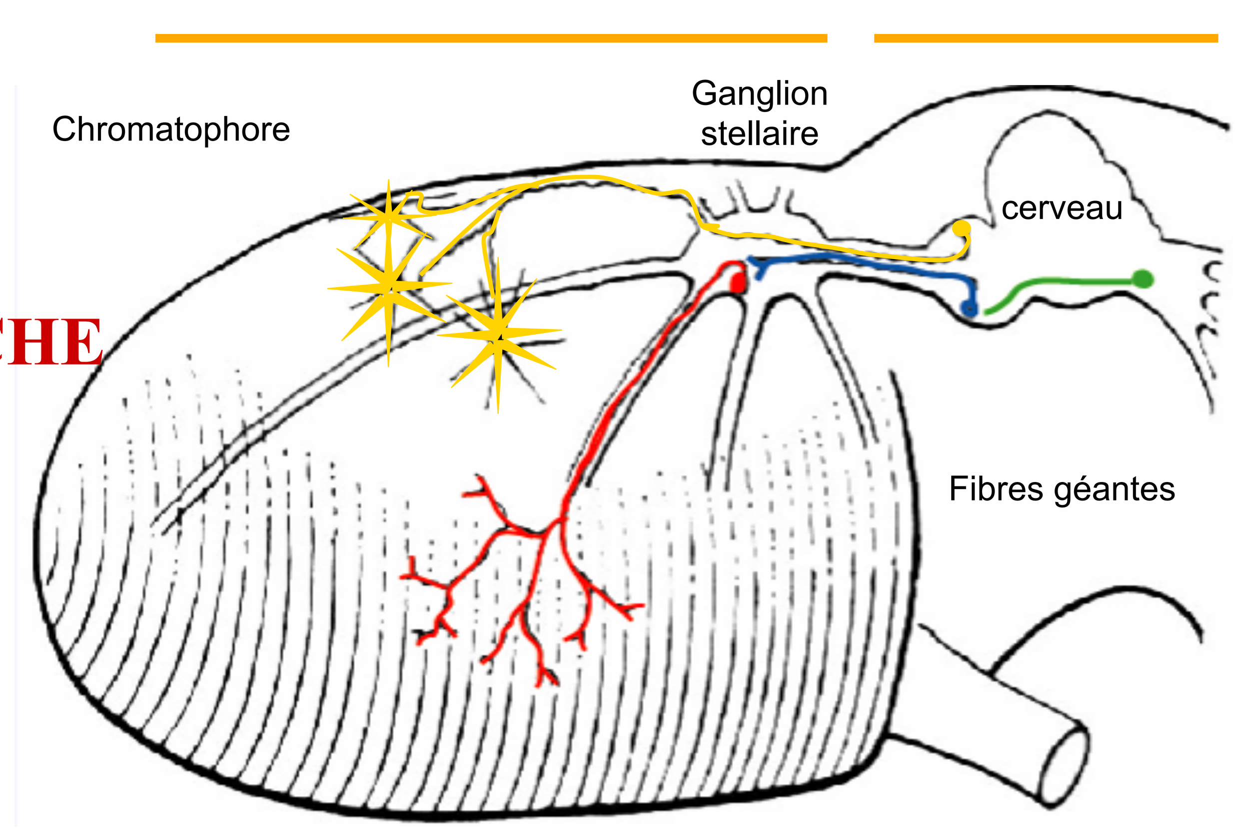
Baratte Sébastien, Sandra Navet, Aude Andouche & Laure BONNAUD

Equipe « Neurogenèse des Céphalopodes ».Muséum National d'Hisoire Naturelle, DMPA, BOME UMR CNRS 5178 baratte@mnhn.fr

The nervous system of cephalopods exhibits numerous sensorial and structural innovations among molluscs both in central and peripheral nervous system: a brain made of fused ganglia and two voluminous optic lobes, two stellate ganglia, many giant fibres and chromatophore systems, nervously controlled. They show evolutionary grades of the peripheral nervous system in relation with a wide range of adaptations to different life style. Their diversity in morphology attests a high flexibility and adaptability and makes them a relevant biological material for evolutionary studies. Nevertheless, neither their development nor the mechanisms that could have led to the evolutionary emergence of these derived traits have been studied. Among mollusca, choosing a model with derived states of characters is informative about the mechanisms that appeared during evolution to generate such morphological novelties. Few lophotrochozoan possess as many convergences with vertebrates as cephalopods and they are used as a comparative model for vertebrates. Intense research efforts have been directed to understand physiological function of the brain and giant axons but comparatively nothing is known about the molecular pathways underlying their development. For example the process of the neural bilaterality establisment remains unknown in these species without neural cord.

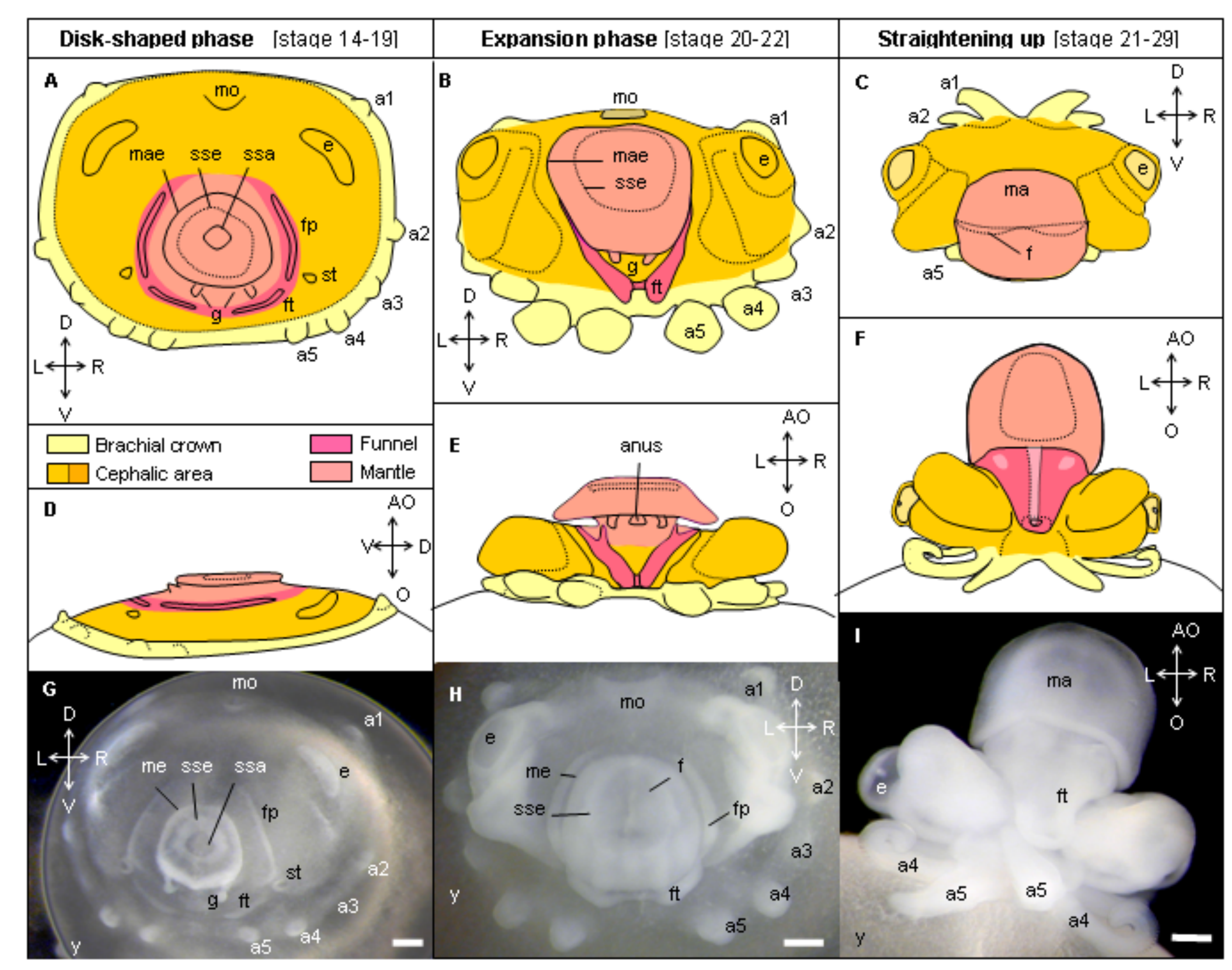
NERVOUS SYSTEM AND DEVELOPMENT

MOCHE



Cephalopods present a direct development (no veliger stage as the other molluscs), which is advantageous because the organisation of the juvenile is not modified by metamorphosis. The development of the adult organs can be followed from juvenile to adults without any change or endocrine perturbation.

Within cephalopods, *Sepia officinalis* shows "intermediate" states of characters for its peripheral nervous system (giant fibres and chromatophores) and is the most studied for the central nervous system physiology. The nervous system is established before hatching but changes occur from juvenile to "adult" in the relative proportion of the brain parts.

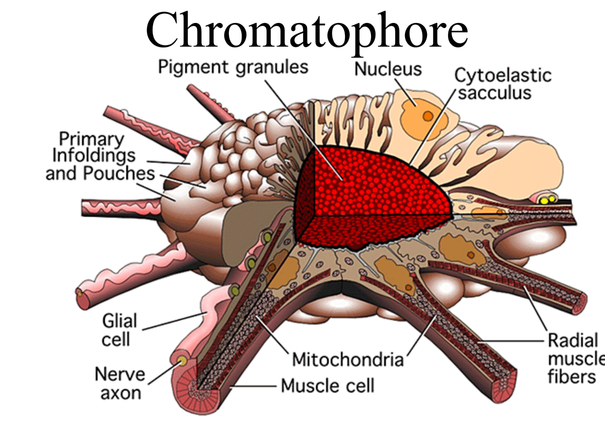


NEURAL INNOVATIONS AND FUNCTIONAL ADAPTATIONS

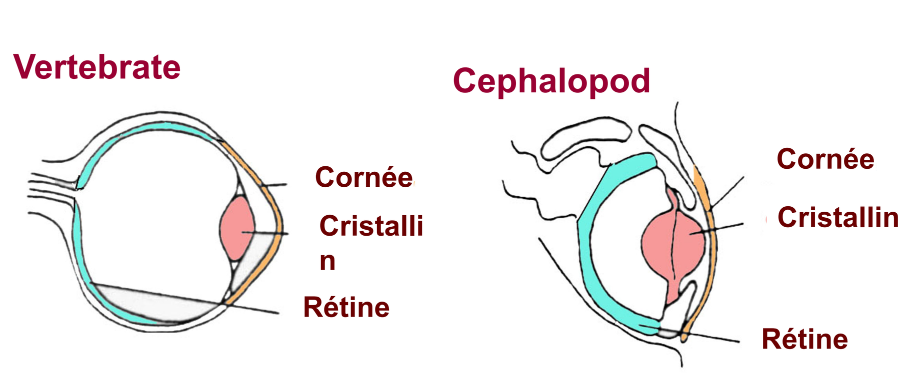
Focus on stellate ganglions, chromatophores and giant axons, three neural novelties
The mechanisms by which the ganglions are formed and are connected with the other nervous structures are informative on the CNS (ganglion) history within Lophotrochozoa. The control of the bilaterality of the chromatophore patterns is meaningful of a specific control of the development of the nerve fibres on each side of the midline within Bilateralia. The processes of formation of giant axons would help to understand the mechanisms by which the fibres are generated from the ganglion and are (or not) fused in a syncitium.
Both the stellate ganglia and the chromatophores set up very early in the development: before stage 25
Evolution of these structures being probably linked to each other, this implies the comparison of representatives of the main groups of cephalopods.

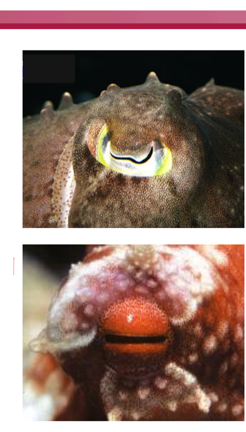
Stellate ganglion

Chromatophore



STRUCTURAL CONVERGENCES AND HOMOLOGOUS GENES





The highly developed nervous system of cephalopods has been an important material for neurocytology, electrophysiology and biophysics. Their Central Nervous System (CNS) has been used as a comparative model to vertebrates (Young, 1971, 1974, 1976; Messenger, 1979; Hochner *et al*., 2003). This convergence allows access to differences or similarities which appeared during evolution in the development of structures with functional equivalence (i.e. analogy).

Among genes known to participate to the nervous system formation in Metazoans few have been identified in the Mollusca yet. We focus on those involved in neurogenesis, especially neuronal determination and specification (*engrailed* and NK family) and axonal growth during embryonic development. We are also interested in genes involved in neuro-endocrine system (POU family).
Our aims are to characterise the genes, to determine their expression patterns and identify their function by extinction (and/or surexpression).

Marquage engrailed/Marquage Pax 6 (ref de notre pub)

engrailed in vertebrates is involved in the delimitation of the different parts of the brain. As expected engrailed is not involved in the formation of cephalopod brain because the brain is formed by the concentration of the mollusc ganglia. But is involved in sensorial structures such as the eye, as Pax6

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By providing a better understanding of the molecular mechanisms underlying the development of cephalopod nervous structures, this project will improve the knowledge of the nervous system evolution among Lophotrochozoans. The nervous peculiarities of cephalopods among molluscs offer a unique opportunity to investigate how genes produce diversity in neural organisation. Beside traditional invertebrate models (*Drosophila*, *C. elegans*) belonging to ecdysozoan, lophotrochozoan models are essential for the comparative study of molecular mechanisms and pattern formation as representative of the bilaterian diversity.