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Review

The acquisition of myelin: An evolutionary perspective

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ABSTRACT

It has been postulated that the emergence of vertebrates was made possible by the acquisition of neural crest cells, which then led to the development of evolutionarily advantageous complex head structures (Gans and Northcutt, 1983). In this regard the contribution of one important neural crest derivative—the peripheral myelin sheath—to the success of the vertebrates has to be pointed out. Without this structure, the vertebrates, as we know them, simply could not exist. After briefly reviewing the major functions of the myelin sheath we will ask and provide tentative answers to the following three questions: when during evolution has myelin first appeared? Where has myelin initially appeared: in the CNS or in the PNS? Was it necessary to acquire a new cell type to form a myelin sheath? Careful examination of fossils lead us to conclude that myelin was acquired 425 MY ago by placoderms, the earliest hinge-jaw fishes. I argue that the acquisition of myelin during evolution has been a necessary prerequisite to permit gigantism of gnathostome species, including the sauropods. I propose that this acquisition occurred simultaneously in the PNS and CNS and that myelin forming cells are the descendants of ensheathing glia, already present in invertebrates, that have adapted their potential to synthesize large amount of membrane in response to axonal requirements.

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1. Functions of the myelin sheath

Myelin has three major functions. Chronologically it was first described as a way to protect naked axons. It is Remak who first reported, in 1838, the co-existence in peripheral nerves of two types of fibers, some being wrapped by a thick sheath (Remak, 1839). When in 1854 Virchow proposed to name myelin this sheath wrapped around axons (Virchow, 1854) this was at the time when the first communication cable was laid under the sea between France and England (1850) followed by the first transatlantic cable between Ireland and Newfoundland (1858). The heart of the cable was made of seven wires (axons) of copper, enrobed (wrapped) by three layers of gutta-percha (the myelin) to protect the copper wires. As Virchow wrote: "The medullary sheath serves as an isolating mass, which confines the electricity within the nerve itself and allows its discharge to take place only at the non-medullated extremities of the fibers." Later, Ranvier extended the comparison to transatlantic cables: "Electrical wires immersed in a conductive medium need to be protected from this medium by a non-conductive sheath; it is on this principle that transatlantic cables are built." (Ranvier, 1878).

The second major function of myelin sheath is to accelerate the speed of conduction of nerve influx. There are only two ways transmission of action potential can be accelerated: increase the diameter of the axon and/or wrap the axon with a myelin sheath (Rushton, 1951). In most species (vertebrate and invertebrate) the axon diameter averages between 0.3 and 30 μm. As a consequence, action potentials along non-myelinated invertebrate axons propagate at about 1 m/s or less for an axon of about 10 μm in diameter. This is sufficient, however, for routine conduction within the framework of animals of relatively small size (between 0.1 and 30 cm). Among invertebrates only the cephalopods (squid, octopus) have larger axons, but this large size is generally limited to those neurons involved in the rapid escape response. By increasing the diameter of key axons up to 1 mm or more, cephalopods have increased action potential speed, and so have been able to evolve a larger body size. In vertebrates, the entire CNS is confined into the skull (brain) and the vertebrae (spinal cord) rigid bony structures, which impose a physical constraint preventing the increase in axon diameter. It has been calculated that, in human, to maintain a speed of conduction of 50 m/s, solely by increasing the diameter of axons, the spinal cord would reach a diameter of 1meter! Acquisition of the myelin sheath, by maintaining the axon diameter below 10–15 μm, permits to keep, in human, the width of spinal cord to a maximum of 6–7 cm. Plotting the speed of conduction against the axon diameter in non-myelinated and myelinated fibers shows that myelination is favored when the axon diameter is superior to 1 μm (Rasminsky, 1971; Koles and Rasminsky, 1972; Moore et al., 1978).

The third function of the myelin sheath has been illustrated only recently (Fünfschilling et al., 2012; Lee et al., 2012a, 2012b). These authors have suggested that myelin-forming cells provide nutrient and support the integrity of axons. In this respect it has to be reminded that body size is again an issue. Indeed, length of axons are easily 1000 to 10,000 times higher than neuronal cell body. Transport along axons can be either fast or slow. Traffic of vesicles along the axons is relatively rapid, varying between 2 and 17 mm/h. In contrast soluble molecules move slowly at a maximum of 300 μm/h. Therefore, for a human motoneuron, which axon can easily be 1 m in length, it will take between 3 and 20 days for proteins trafficking using the fast moving vesicular cargoes. In contrast, for nutrients, such as glucose or lactate, transport from the neuronal cell body will take in the average 200 days to reach the neuro-muscular junction! Neurons are highly vulnerable to energy deprivation. Myelin forming-cells, have therefore a crucial role for axon function and survival by transferring energy metabolites (namely lactate) from their cell bodies to axons through monocarboxylate transporter (Morrison et al., 2013). It is likely that this transfer of lactate from oligodendrocytes to axons takes place at the paranodal loops of myelin wraps.

A key consequence of the acquisition of myelination has been the possibility to increase body size. In an interesting paper, Sander and Clauss (2008) proposed a set of factors that contributed to the evolution of massive body size in sauropods. These authors suggested that « the unique gigantism of sauropods was made possible by a combination of phylogenetic heritage (lack of mastication, egg-laying) and a cascade of evolutionary innovations (high growth rate, avian-style respiratory system, and a flexible metabolic rate". Surprisingly, a critical factor omitted from these authors' analysis was the introduction of the myelin sheath. Imagine a Diplodocus 40 m in length bitten in the tail by a predator. Clearly, if Diplodocus had not been myelinated, nerve impulse along fibers whose diameters could without myelin ensheathment only support an extremely slow rate of conduction (~1 m/s), a full 40 s would have been required for action potentials to ascend the length of this giant sauropod to its brain, and another 40 s for the return signal to the tail muscles-completely incompatible with fast reaction times necessary for escape. However, the same signal, traversing the same diameter myelinated axon, would make the 80 m round trip at a speed of 100 m/s and reach the tail musculature in only 800 ms. Large predatory dinosaurs such as