

Myelination, development and Multiple Sclerosis

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The relationship between brain development and behavior in infants and young children are of great interest to developmental psychologists. Myelin and myelination of the axons effect the development of the human brain. The developmental process of myelination and the adult regeneration process of remyelination share the common objective of covering an axon with a myelin sheath. The underdeveloped myelin or the demyelination of the axons has significant effects for those with these neurological disorders. Discussed is the myelination process, reasons for under-myelination, demyelination, and how the destruction of myelin in Multiple Sclerosis patients along with possible remyelination techniques.

The closure of the neural tube on the 28th day of fetal gestation begins the development of the brain and spinal cord (“Developmental Anatomy,” 2011). Neural organization and myelination starts in the third trimester. The myelination process does not end at, but continues well after birth (“Developmental Anatomy,” 2011). In fact, general brain development takes another 10-12 years to complete (“Myelination in Development,” 2011). At birth, almost all the neurons have been created and the brain is about 25% of the adult brain weight. However, the brain continues to grow and develop and by age 2, the brain is about eighty percent of the adult size. By age 3, the brain has increase dramatically in size and features billions of cells and trillions of synapses. Each of these synapses are pathways for brain and body functions (Carmody, Dunn, Boddie-Willis, DeMarco and Lewis, 2004).

The white color of the “white matter” of the brain is produced by myelin. Myelin is the fatty, white sheaths formed by oligodendrocytes that wrap around axons (Giedd and Rapoport, 2010).

Cognitive, motor and sensory development requires the structural maturation of individual brain regions and their connecting pathways. As the synapses are structure of the brain matures the neurological impulses become smooth and the flow of information is integrated across the many brain regions that have also developed. The speed of information transmission is an important developmental

factor depends not only on the junctions between nerve cells, known as synapses, but also on the structural properties of the neuron connecting fibers, known as axons (“Myelination in Development,” 2011). Critical axon structural properties include their diameters and the thickness of the special insulation (myelin) around many fibers. Large groups of myelinated axons, which connect various regions in the brain, appear visibly as "white matter" (“Myelination in Development,” 2011). Axons connecting the major pathways in the human brain, such as those of the corpus callosum (which connects the two halves of the brain), continue to develop throughout childhood and adolescence (Stiles and Jernigan, 2010).

To better understand nerve impulses, in terms of physics, the neuron axon behaves similar to an electrical transmission line with a transverse electrical wave, voltage conduction and a high capacity. The diameter of an axon is important for impulse velocity: the larger the diameter, the greater the velocity of transmission. The myelin sheath that surrounds certain types of axons is like an electrical insulation and it increases the pulse velocity over that of a bare axon of the same diameter. Myelination is therefore a major characteristic of neural circuits. (“Myelination in Development,” 2011).

Myelination begins in the in the brain and brainstem and then continues to progress to other nerves throughout the body. The shortest axons are the first to myelinate, followed by those of the upper extremities and the trunk of the body, with the lower extremities (having the longest axons) being last. This is completed at about 24 months of age, correlating with the pattern of head-to-toe developmental milestones (Volpe, 2008).

The authors of a 1998 study report the analysis reveals age-related increases in white-matter density. These findings suggest provide evidence for a gradual maturation, during late childhood and adolescence, of fiber pathways presumably supporting motor and speech functions (“Myelination in Development”, 2011). Regions of the brain that help with the function of motor skills and senses are

developed and myelinated first. Language regions are the last parts of the brain to develop and myelinate (Aslin and Schlagger, 2006).

Many psychiatric disorders (in both children and adults) have long been thought as a reflection of subtle abnormalities in brain development (Giedd and Rapoport, 2010). Neurological disorders are, however, not linked directly to the initial development of the brain, but the maintenance of the myelin sheaths and the neural axons. Age related development may be linked to the expression of genes that affect myelination (Piaton, 2010). A study of the genes related to Alzheimer's disease, for example, shows certain attributes begin to develop in the fetal stages, but not fully expressed until late adulthood (Giedd and Rapoport, 2010).

Children with movement coordination difficulties also have difficulties in "executive cognitive function tasks that require inhibition, task switching and working memory" (Pangelinan, Zhang, VanMeter, Clark, Hatfield, Haufler, 2010). Those with neurological disorders, such as Multiple Sclerosis show these same difficulties. These difficulties may be connected with the inability of the MS axons to remyelinate. In MS, the central nervous system demyelination is, as in others, often followed by spontaneous repair (Piaton, Gould and Lubetzki, 2010). However, the extent of this myelin repair differs from those without MS, ranging from loss of axonal connectivity to full repair. The remyelination process is disrupted and structured organization of the axons are effected (Piaton, et.al, 2010).

Typically, remyelination is spontaneous and creates nerve conduction; it also creates a protection against future damage or breakdown of the myelin sheath (Riekmann and Smith, 2001). However, in MS patients, the remyelination is spontaneous but is insufficient to repair damage in demyelinated plaques in most cases, thus leaving areas of plaque buildup in the CNS (Piaton, et.al, 2010). Only axons with a diameter larger than 0.2 micrometers are ever myelinated and the larger the diameter, the more wraps of myelin the axon will have (Piaton, et.al, 2010). Therefore, the spinal cord has largest amount of myelin

sheathing in the CNS, followed by the connections between the cerebellum and the two hemispheres of the brain (Bruce, Zhao and Franklin, 2010).

Chronic demyelination predisposes axons to degenerate. This is an irreversible occurrence that is thought to be a major cause of progressive functional decline (Coman, Barbin, Charles, Zalc and Lubetzki, 2005). Spontaneous remyelination of MS lesions may occur, but is often insufficient after a few years due to disease evolution (Coman, et.al, 2005). The slow expansion of demyelinated areas of the CNS and the incomplete remyelination in the spinal cord correlates with a higher disease-related disability (Bramow, Frischer, Lassmann, Koch-Henriksen, Lucchinetti, Sorensen and Laursen, 2010). Although, the causes of incomplete remyelination in MS is unknown, the basic understanding of the steps of demyelination and remyelination is becoming more clear (Bramow, et.al, 2010).

The reason for choosing this topic was to better understand the development of the central nervous system, progression of Multiple Sclerosis and review some of the studies being conducted on these subjects. My wife and sister are both affected by MS. However, their symptoms are varied. My sister has very few exacerbations, where my wife has at least two or three each year, with one being severe. I know of many others with the disease and each of their experiences are different. This intrigues me to the point that I have read many studies on the disease and I continue to look at the newest information for more details on such a puzzling disease. Though I have little understanding of the cause of MS, as I have studied the topic of brain development with a focus on MS, I have gained a better appreciation for the central nervous systems attempts to correct the effects of the debilitating disease of MS.

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