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GLIAL AND NEURONAL CELLULAR COMPOSITION, BIOLOGY AND PHYSIOLOGY

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The brain has the unique ability to affect so many things from movement to emotion to cognitive abilities. It can, together with life events, transform a person into an artist, a priest, a scientist, or a teacher. To achieve any goal, all of our body systems need to collaborate with one other. It is the brain that controls and co-ordinates the activity of all in response to environmental cues and demands with the assistance of all of the nervous system. Each and every demand is detected by our senses and messages are judged by merit, which in turn, directs particular responses. Taken together, our nervous system is concerned about sensory input and motor output. Sensory nerves collect information about the body's internal and external environment and convey it to the central nervous system (CNS). Motor nerves carry instructions on what to do. Let me describe it with an example. When we feel hungry, our internal environment generates a sensory input that provides us the awareness of hunger. Then sensory input from the external environment provides us the information on how to obtain food. Consequently, motor output is generated in the external environment to get and swallow food. Then motor activity in the internal environment assists us with the food intake to the extent until we get the nod from our sensory input from the internal environment that enough food has been consumed.

This input and output business is simply dictated by a group of cells forming the basis of the supercomputing system of the brain – called neurons. This particular group of cells forces us to revere brain as an elite organ. It is the “neuron doctrine” of Professor Cajal that contributed to the basic understanding of the organization of the CNS. As nobody in this world is unable to survive alone, neurons are also not an exception from this universal rule. Therefore, there are other cells in the CNS, called glial cells (Figure 1). Glial cells have diverse functions that are necessary for the proper development and function of the complex nervous system. The growing number of links between glial malfunction and human disease has generated great interest in glial cell biology.

Axons are surrounded by while matter coating called myelin that consists of a layer of proteins packed between two layers of lipids. This myelin coating enables axons to conduct impulses between the brain and other parts of the body. Myelin is synthesized by specialized cells – oligodendrocytes in the CNS and Schwann cells in the peripheral nervous system

(PNS). Although the composition of CNS and PNS myelins are not same, they are assigned for the same function - to promote efficient transmission of a nerve impulse along the axon. Schwann cells have an intimate association with axons and each Schwann cell forms myelin around a single axon, and lines up along the axon to define a single internode. On the other hand, one oligodendrocyte extends several processes and can myelinate upto 1 to 40 axons with distinct internodes. In addition to myelination, Schwann cells are able to migrate and phagocytose debris from the PNS. However, oligodendrocytes do not have such activity.

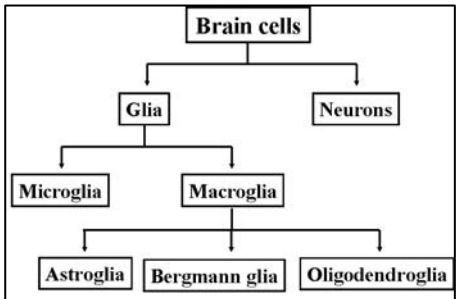

Figure 1. Classification of brain cells

The major cells in the CNS are astrocytes that are believed to support the entire structure of the microenvironment (Liedtke et al., 1996) together with endothelial cell lining. In addition to structural support, astrocytes have many other important functions, such as food supply, water balance, ion homeostasis, regulation of neurotransmitters, detoxification of ammonia, organizing information network, and release of neuropeptides and neurotrophins. Because neurotrophins support the growth of neurons and astrocytes are the major producer of neurotrophins in the CNS, these cells also play an important role in neurogenesis. The other important cell type is microglia, the resident macrophages in the CNS. As happens in other organs, cells in the CNS also undergo natural cell death. Then microglia keep the CNS microenvironment clean by scavenging these dead cell bodies. In addition, when immune responses are generated within the CNS or from outside the CNS, microglia, being the primary CNS immune cells, receive and pass on that response to other cells (Carson 2002; Rock et al., 2004). Under physiological condition, the immune response usually ends up with a logical conclusion leading to the development of a better neuroimmune system. Another less characterized glial cell type is Bergmann glia that are composed of unipolar protoplasmic astrocytes in the cerebellar cortex. These are associated with granule cells in the developing cerebellum and with Purkinje cells in the adult cerebellum.

As part of our life, we experience stress, trauma, infection, injury etc and come in contact with various toxic substances. Although brain is separated from the rest of our body by a well-defined blood-brain barrier, brain perceives and faces each of these challenges (Figure 2). Therefore, after these insults, the injured brain cell usually tries to either die or survive. When an injured cell dies, the death process usually becomes associated with increased production of proinflammatory molecules, decreased production of anti-inflammatory molecules, increase in T-helper 1 (Th1) response, decreased production of growth factors, increased expression of death genes (e.g. bad, bax), decreased expression of survival genes (e.g. bcl_2, X-IAP, survivin), and over-activation of tumor suppressor genes (e.g. p53). On the other hand, during the survival of an injured cell, opposite phenomena are observed (Figure 2). If the survival process is accompanied by a very high Th2 response, huge production of growth factors, abnormal cell growth, and mutation of tumor suppressor genes, the injured cell may like to live as a cancerous cell. Although everybody is receiving some kind of insults or injuries, everybody does not get the disease because in healthy human beings, there is a proper balance between cell death and cell survival. When this invaluable balance is lost, we see the disease (Figure 2). Although there are four major cell types in the CNS, under neuroinflammatory and neurodegenerative stress conditions, only neurons and oligodendroglia succumb to cell death. On the other hand, astroglia and microglia do not die but undergo activation and gliosis under the same condition. Although glial activation is not always bad, when activated glia are forced to