STROKE *A Curse or a Catalyst for Learning*

Raktim Roy

STROKE is one of the deadliest conditions, with about 12 million new cases in 2021 since 1990. It has been estimated that 1 in 4 adults over 25 years of age will experience a stroke in their lifetime. But how can one define a stroke? To understand this life-threatening condition, one must first understand the human brain. Only by fully understanding the fundamental workings of the brain can we really find novel strategies to prevent and/or cure stroke.

The brain is the most unique organ in the whole body. The fundamental unit of the brain is a neuron. Neurons are generally considered "terminally differentiated" cells, i.e., they won't divide to form new neurons. Whatever neurons a person is born with will stay with them till their lifetime. There are an estimated 100 billion neurons in the human brain. Together, the neurons of the brain and spinal cord comprise the nervous system, which is the body's communication system. This system works by receiving a sensory signal (for example, touching a hot surface), processing the signal, and producing an appropriate voluntary motor response (for example, removing the hand). All this beautiful coordination is achieved due to the unique properties of neurons.

A typical neuron consists of 3 parts — a cell body or soma that houses the nucleus, dendrites that receive sensory signals, and an axon that transmits the signal. When a neuron wants to communicate, it fires an electrical pulse known as an action potential that races down the axon, much like a spark travelling along a wire. At the axon's end lies a small gap called a synapse, where the electrical signal is transformed into a chemical message. Molecules called neurotransmitters leap across this gap and bind to the next neuron, passing the message along. In this way, billions of neurons exchange information every second, forming the intricate communication network that allows us to think, move, and feel. This entire process leads to something called "neuronal plasticity", which refers to the brain's exceptional ability to change and reorganise in response to learning. The fundamental process of neuronal plasticity is why we can learn and remember myriad experiences throughout our lifetime. Interestingly, this is also the process that is heavily relied upon for recovery from stroke, which I will discuss in more detail later.

Neurons, like any other cell types in the body, require a constant supply of resources and removal of waste products to function properly. This is achieved via blood vessels — arteries and veins. The arteries provide oxygenated blood and nutrients to the neurons, while the veins act as a drainage system, removing deoxygenated blood and other waste products. A stroke occurs when a blood vessel ruptures (hemorrhagic stroke) or when the blood supply to the brain is interrupted (ischemic stroke). The result is the death of neurons and, therefore, loss of brain function(s). Since neurons require a constant supply of oxygen and nutrients, an interruption in the blood flow or rupture of blood vessels will lead to the instant death of neurons in that specific brain region.

An ischemic stroke occurs when an artery gets blocked, often due to blood clots, and a hemorrhagic stroke occurs when either an artery or a vein ruptures, thereby leading to blood leakage in the brain. Normally, the major cause of stroke is high blood pressure. High blood pressure damages the artery wall, which leads to the formation of blood clots, which in turn can cause ischemic stroke. Also, high blood pressure weakens blood vessels that can easily rupture, leading to hemorrhagic stroke. However, in recent times, there have been numerous non-traditional causes of stroke that have been identified. For example, genetics has been shown to play a significant role in determining an individual's susceptibility to stroke. People with a family history of stroke — especially when multiple first-degree relatives are affected or when stroke occurs at a younger age — have a substantially higher lifetime risk compared to those without such a history. This does not mean that a stroke is inevitable, but it indicates a higher inherited predisposition that may interact with other risk factors such as a sedentary lifestyle and hypertension. Genetics can contribute to stroke risk in two main ways — in a small subset of individuals, rare single-gene disorders — such as CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) or COL4A1 mutations — can directly lead to stroke. However, in the majority of cases, risk arises from the combined effect of multiple common genetic variants, each exerting a modest influence. These variants can increase stroke susceptibility indirectly by promoting conditions like high blood pressure or diabetes, or directly by affecting biological pathways involved in lipid metabolism, thrombosis, vascular integrity, or inflammation. Recently, another non-traditional cause of stroke that has been identified is COVID-19. Studies have shown that the initial strain of COVID virus can lead to excessive blood clotting (hypercoagulability) that can increase the chances of ischemic stroke. A majority of the people who have suffered COVID-19 reported experiencing a stroke post-COVID-19 infection. As a result, stroke research is now one of the most emerging research topics in the field of neuroscience and medicine.

Stroke recovery has emerged as a major focus area within the domain of stroke research. As mentioned previously, neuronal plasticity is one of the mechanisms that