Guillain-Barré Syndrome Study

By Kitty C3

Guillain-Barré Syndrome affects the peripheral neurones. It often starts with a tingling in the hands and feet, but can spread, causing paralysis of arm and leg muscles and the muscles that controls breathing. In some cases this can be fatal.

In the early 1990s in rural China every summer many children would be hospitalised with breathing difficulties, an event that had not yet been associated with GBS. Research revealed that the paralysis was brought on by an autoimmune cross-reaction. The children had contracted food poisoning from contaminated water and their immune systems were fighting not only bacteria, but also their own peripheral nervous systems.

To understand GBS, first we need to understand the peripheral nervous system. Neuromuscular junctions are the synaptic connection between the terminal end of a motor neurone and muscles. They are the sites where action potential is transmitted from nerve to muscle. They ensure that the signals from the brain are communicated to the muscles that control movement. Peripheral nerves contain axons that are extensions of the lower motor neurones. The cell bodies of these neurones are in the spinal cord, which is part of the central nervous system (CNS).

It is important for the impulses sent by the brain, via the spinal cord and peripheral nerves, to reach this meeting point and allow communication with the muscles. Many conditions can interrupt the impulses at any stage along the pathway (see figure 1).

A neuromuscular junction is a vulnerable site. It is not protected by the blood-nerve barrier that surrounds the CNS, leaving it exposed to substances circulating in the blood. This allows toxins and viruses to exploit this vulnerability, as they can enter the nervous system by latching onto the terminal membrane of a motor neurone, where they are taken up by endocytosis. Botulinum toxin enters via a motor neurone terminal membrane and inhibits neurotransmitter release, preventing impulse transmission across the synaptic cleft to the muscle, resulting in muscular paralysis. As well as circulating factors that come form outside the body, a neuromuscular junction is vulnerable to autoimmune attack by circulating antibodies generated by the body itself. Myasthenia gravis is when antibodies destroy acetylcholine receptors on the postsynaptic muscle cell membrane, preventing the depolarisation and activation of the muscle cells. In GBS it is the presynaptic motor neurone terminal that is affected by autoimmune antibody attacks.

Many cases of GBS had come after a recent infection. The most common is Campylobacter jejuni, the bacterium that causes food poisoning. The bacteria are covered by glycolipids called lipooligosaccharides, which share a striking structural similarity to glycolipids called gangliosides, which cover our neurones. In GBS patients the immune system mounts an adaptive antibody response against the infective pathogen. However, the adaptive antibodies also cross-react with gangliosides on the surface membranes of motor neurones.

An important trigger of GBS is calcium ions. This is caused by complement. This is when antibodies bind to gangliosides at the motor neurone terminal and activates complement, which forms a pore in the membrane, allowing calcium ions into the axons (see figure 2). Calcium ions activate the protease enzyme calpain, which breaks down axon proteins (see figure 2). Nerve terminals then are broken down (see figure 3).

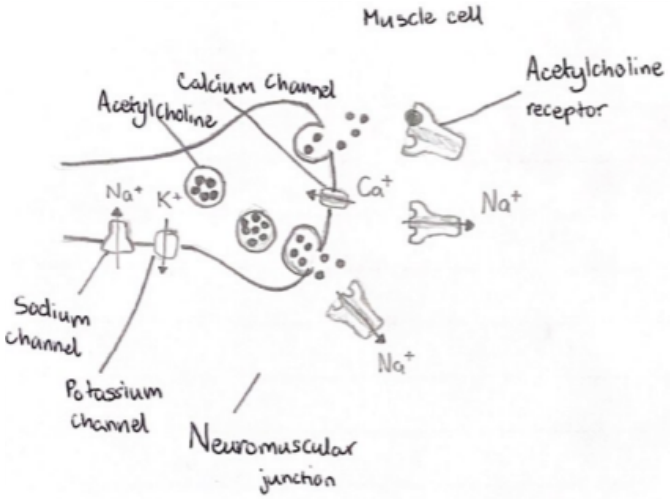

Figure 1

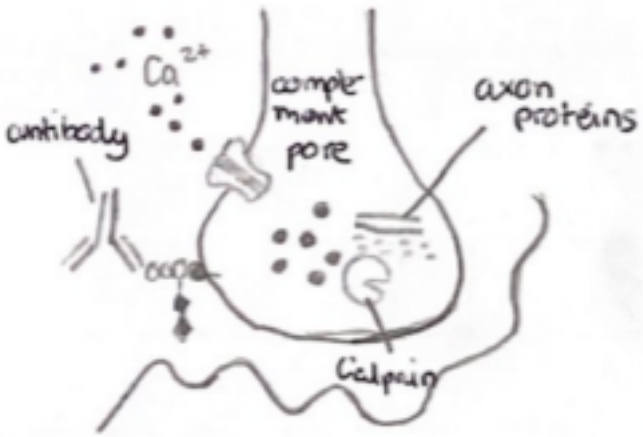

Figure 2

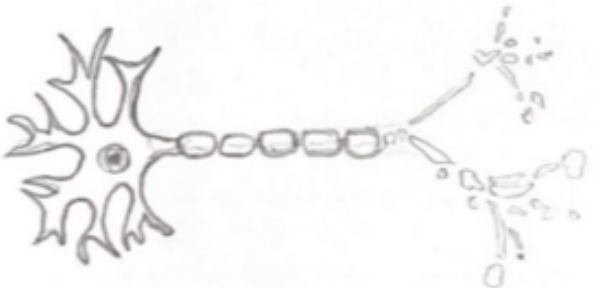

Figure 3