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# How we came to understand the neuromuscular junction

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Interest in the mechanism of the neuromuscular junction began with studies of the South American arrow poison, curare. Claude Bernard proved that curare acts at the neuromuscular junction in 1855.

Thomas Willis (known for the Circle of Willis) published the first recognizable case report of myasthenia gravis but it was not until the end of the 19th century that Friedrich Jolly (1884) named the disease *Myasthenia Gravis Pseudoparalytica.* He also showed a decremental response of the muscle to repetitive nerve stimulation.

In 1916 acetylcholine was discovered and proved to be a neurotransmitter in 1921 by Otto Loewi. With her breadth of knowledge and clinical acumen, Mary Broadfoot Walker (1930) noted the similarity between curare poisoning and myasthenia gravis. Curare poisoning could be reversed with physostigmine and, she discovered, so could myasthenia.

In the latter half of the 20th century the quantal nature of ACh release from the neuromuscular junction became understood and the steps following the arrival of a nerve impulse, particularly the importance of calcium ions. On the clinical front, new therapies based on anti-cholinergic drugs and a recognition of myasthenia as an autoimmune disease improved the lot of patients.

Meanwhile laboratory studies, aided by the discovery of bungarotoxin, showed the detailed architecture of the neuromuscular junction and the structure of the acetylcholine receptors. We still need to know more about how these structures are brought together and renewed or repaired.

Clinicians recognized that some cases of ‘myasthenia gravis’ did not respond to treatment and MUSK deficient myasthenia became known as well as congenital myasthenias. The molecular genetics of these conditions is being described.

Eric Stalberg studied the motor unit and developed single fibre EMG, the most important investigation for disorders of the NMJ. Single fibre EMG has been applied in in Sri Lanka to krait envenomed patients and those with intermediate syndrome of organophosphorus poisoning. The method and results will be briefly reviewed.