Langley, John Newport

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John Newport Langley (1852-1925)

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John Newport Langley was born in Newbury, Berkshire, UK on 10 November 1852, the second son of John Langley a private school teacher. He was educated first at home and then at Exeter Grammar School before entering St John's College, Cambridge in 1871. His initial studies were in mathematics and history with a plan to enter the civil service in Britain or India. In his second year he was influenced by the biology lectures of Michael Foster (1836-1901) and changed his course to the natural sciences graduating with first class honours in 1875. In 1876 he became an associate to Foster in his physiology laboratory and by 1878 he received the MA and Fellowship of Trinity College (Sheehan, 1936). Langley's career at Cambridge extended over 50 years in which he made seminal discoveries on the functional organization of the autonomic nervous system and also taught a generation of students including Henry Dale, Charles Sherrington and Thomas Elliott (Finger, 1994).

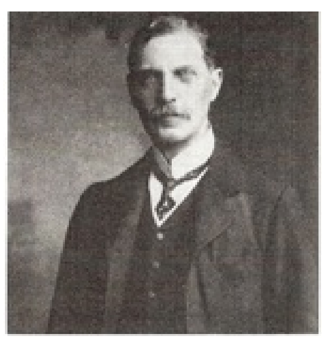

Figure 1: John Newport Langley

In 1878 Foster was elected to the House of Commons and moved to London. His choice of successor was Langley, who took over the responsibility of his laboratory and teaching at Cambridge. In 1900, Langley was appointed professor and in 1903 he succeeded Foster in the chair. At the young age of 31 he was elected to a fellowship of the Royal Society and became its vice-president in 1904.

Langley's research career could be divided into two periods. His initial studies from 1875 to 1890 were directed at the processes of glandular secretion, whilst the second period concerned work on the structure and function of the vegetative (autonomic) nervous system. He coined the term 'autonomic' nervous system and made seminal discoveries on the function of the sympathetic and parasympathetic components (Langley, 1898). In addition, his work laid the foundation for humoral neurotransmission and his concept of 'receptor substances' was foundational to the receptor theory of neurophysiology and neuropharmacology. His experimental work included 170 publications, an extraordinary number for that era, with many published in the *Journal of Physiology*.

The first experiments in Langley's laboratory were on the action of the extract of jaborandi (pilocarpine) on the heart which had been initially studied by Foster (Langley, 1875). Stanley Ringer had given a sample of pilocarpine to Foster who passed it on to Langley. He found that pilocarpine produced significant slowing of the heart when injected intravenously in animal experiments. He deduced that the effect could be the consequence of the pilocarpine acting on inhibitory fibres in the vagus nerve to the heart. The response was not abolished by the prior administration of curare which was believed to paralyse nerve endings. As a consequence he concluded that pilocarpine acted more peripherally than the vagus nerve endings.

Langley's emphasis shifted from the heart to the salivary glands when he discovered that pilocarpine stimulated abundant salivation from the salivary glands (Langley, 1876). His work moved from frog heart to mammalian glands with the secretory changes examined in a series of experiments over 15 years. His findings on the effect of pilocarpine on secretory processes were at odds with Rudolf Heiderhan, who proposed that in the course of secretion the glandular cells become more granulated. Langley, however, found that secretory granules are accumulated in the resting gland and in the process of secretion are released from the cells. In his meticulous studies he distinguished between the 'loaded' and 'exhausted' states of the gland. He showed also that in the salivary gland of the dog, the secretion induced by pilocarpine could be abolished by prior injection of atropine or stopped by atropine if administered subsequently. Thus he was able to conclude that "the secretion or absence of secretion is dependent on the relative quantity of the two poisons present, just as in the standstill or beat of the heart" (Langley, 1905).

The work on the salivary glands formed the basis to his subsequent studies on the functions of other nerves. Working with Langley at Cambridge was Henry Gaskell, who established that the vegetative nervous system was composed of two antagonistic systems that were located in three regions, cranial, thoracic and sacral. His studies in the central nervous system established that this system was not completely independent (Gaskell, 1886).

The nicotinic property of ganglion blocking was discovered by Langley and Dickinson in 1889 and it proved to be a valuable analytic tool in investigating the sympathetic nervous system (Langley and Dickenson, 1889). By blocking ganglia it was possible to distinguish nerve fibres ending in ganglia with those passing through to an end organ. Utilizing nicotine, Langley was able to analyse all of the ganglionic system and determine for each ganglion its system of conducting fibres. He was able to elucidate that only one nerve cell was involved in the sympathetic nervous system from its central link to effector organ and that the cell body is located in the ganglion. As such each ganglion represents a form of switching station and the efferent sympathetic nerves were either 'preganglionic' or 'postganglionic'. In the 1890s, Langley and Sherrington established the distribution of the sympathetic fibres innervating the skin and their relationship with sensory fibres of the associated spinal nerves.

Langley's studies on the antagonistic effect of nicotine and curare led him to speculate on the mechanisms involved. He believed that this mutual antagonism could be understood as a process of competition between nicotine and curare for some 'receptor substance' in the end organ or smooth muscle which may itself be a chemical compound (Langley, 1905). With respect to the action of the chemical on muscle preparation, it may also be due to its action on a receptor substance. This concept was taken up by others, notably Dale and Loewi with respect to chemical synaptic transmission.

The term 'autonomic' nervous system was coined by Langley in his 1898 paper in the *Journal of Physiology*: "I propose the term 'autonomic nervous system' for the sympathetic system and the allied nervous system of the cranial and sacral nerves and for the local nervous system of the gut" (Langley, 1898). Autonomic nervous system replaced 'vegetative' nervous system of Johann Christian Bell and Francois Xavier Bichat's 'ganglionic' nervous system. Langley retained Winslow's term 'sympathetic' nervous system for the division which had its cell bodies in the lateral horns of the thoracic and lumbar spinal cord. For the cranial and sacral divisions which were involved with visceral innervation he applied the term 'parasympathetic'.

In 1894 Langley became editor and took over financial control of the Journal of Physiology. The journal established by Foster had achieved a high reputation but struggled with financial debts. Langley was an active editor who was meticulous in style and often re-wrote submissions for clarity and precision. His own research was summarised in his most substantial scientific work, The Autonomic Nervous System, published in 1921. The terminology established by Langley is now part of the neurological vocabulary and his pioneering discoveries have been foundational to our understanding of this system.

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Selected Quotations

1. "I propose the term 'autonomic nervous system' for the sympathetic system and allied nervous system of the cranial and sacral nerves, and for the local nervous system of the gut" (Langley, 1889). Quoted in the Oxford English Dictionary, the origin of autonomic derived from autonomy, independent, functioning independently of the will.

2. "When I wanted to describe the results of these studies, I did not find an appropriate term for this part of the nervous system, with which I was dealing. All former terms were used at different times with different meanings. Therefore I called the entire system the 'autonomic nervous system'. By this I meant a 'local' autonomy. The word autonomy indicates without doubt a much greater degree of independence of the central nervous system, than it is in reality, with the possible exception of innervation of the gastrointestinal canal, but I think that for novel concepts in science it is also necessary to introduce new terms, even if those terms would not represent a precise description of the subjects" (Langley, 1921).

3. In the debate about the neurone theory over the old concept of a continuous network of nerve cells and fibres, Langley kept an open mind, "because the facts cannot be expressed in terms of both theories without extraordinary verbiage" Langley, 1901).

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