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CHARLES SHERRINGTON – THE SYNAPSE FROM ANTIQUITY TO ACTUAL STATUS

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ABSTRACT

This paper aim is to discuss and clarify about the way we perceived the functionality of the synapse since 4th century BC up to modern times and actual status. The discussions over the way synapses work began over 2400 years ago and it all started from the simple question of how the locomotive system works and how do the muscles contract. The first who discussed about this concept was Plato during the 4th century BC. We are discussing about René Descartes (1596-1650) depiction of a clear view in the book entitled "De Homine" (1662) over the view of the brain and the innervation of the body. In modern times, the word "synapse" was coined for the first time in Michael Foster's 7th Edition "Textbook of Physiology" of 1897 , for which Sherrington wrote 3 chapters. He proposed his former Professor to introduce the word "synapse" which comes from Greek and means "conjunction". For this discovery, Charles Sherrington and Edgar Douglas Adrian were awarded the Nobel Prize in Physiology or Medicine in 1932.

INTRODUCTION

Charles Scott Sherrington (1857-1952) was a well-known English neurophysiologist, histologist, bacteriologist, and pathologist (Figure 1). Besides, he and Edgar Douglas Adrian worked together in order to discover the functions of the neurons which act as a vast network that control the human reflexes. This breakthrough ensured them the popularity across the entire medical community and above all, they were awarded The Nobel Prize in Physiology or Medicine in 1932 (1).

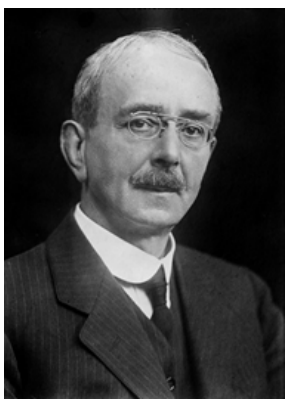

Figure 1. Charles Scott Sherrington (1857-1952)

Sir Charles Scott Sherrington was born on 27th of November 1857 in a district of London called Islington. His father, James Norton Sherrington, died when Sherrington was just a child and later on his mother married doctor Caleb Rose of Ipswich, who played an important role in persuading Sherrington to follow a medical career. Therefore, he began his studies at Royal College of Surgeons of England "—"(2).

Then, he continued his studies in September 1876 at St Thomas' Hospital, a place which gave him the opportunity to carry on studying at Gonville and Caius College, Cambridge. There, he was a first-rate student and he preferred learning physiology, which was taught at that time by Sir Michael Foster, considered the "Father of British Physiology" and who would become a key person for the researches of Charles Sherrington (3).

Later on, he became Membership of the Royal College of Surgeons on 4th of August 1884 and during the next year he acquired the degreed of Bachelor of Medicine and Surgery from Cambridge.

The history of the synapse

The synapses represent the most specialized interaction of the neural cells, because they represent the way of transmitting information from a neuron to another and in the end the impulse reaches the effector through both electrical and chemical paths. However, even if today the synapse represents one of the most important theories of the way the nervous system works, a clear description of the synapse was not coined until 1897, when Charles Sherrington came up with the name "synapse" (4).

The discussions over the way synapses work began over 2400 years ago and it all started from the simple question of how the locomotive system works and how do the muscles contract. The first who discussed about this concept was Plato during the 4th century BC (5).

At that time, it was considered that there was a special bonding between the psyche and the body. The psyche represents the soul which was thought to be composed of multiple spherical particles, most of them concentrated in the brain. According to the writings of Plato in the book entitled "Timaeus", the bonding between the soul and the body takes place in the cranial and spinal cavities, which we consider today the marrow and the brain (6).

600 years away from the theory of Plato regarding the bonding of soul and the body, Galen, a Greek physician,

together with his students, thought that the pneuma which represents the necessary air for the normal functioning of the vital organs becomes "vital pneuma" when it reaches the bronchioles.

Beginning from the lungs, the vital pneuma travels through the arteries to the brain where it becomes "psychic pneuma". It was thought that this type of air would flow through the nerves of the brain and spinal cord to the muscles, inducing the contraction(7).

René Descartes (1596-1650) was the one who dismantled all the theories regarding the psyche which was thought to be involved in muscle contractions and reflexes. He stated that dead bodies lose the heat due to the disintegration of the organs, responsible for producing the heat and contradicted the old the theories regarding the psyche as the vital energy needed by the body in order to live.

Descartes also played an important role in neuroanatomy, since his drawings presented in the book entitled "De Homine" (1662) (8) depicted a clear view of the brain and innervation of the entire body. Moreover, in this book there is also presented the nociceptive flexion reflex, which represents the main self-defence system of the human beings. Therefore, René Descartes was the first one to bring out the idea of a complex network of nerves that have their origins in the brain and marrow and innervates the entire body in order to control both the motor and sensitive aspects of the body (Figure 2.).

Nonetheless, the 18th century represented a key point in the evolution of the idea of synapse which paved the way for the future discovery made by Charles Sherrington. Personalities such as Luigi Galvani (1737-1798) who demonstrated by mistake that the muscle contraction is the result of an electrical stimulation since one of his collaborators accidentally touch the muscle of a frog with a lancet that was electrically charged, producing therefore a muscle twitch and Herman Boerhaave (1668-1738) who depicted schematically for the first time the neuromuscular junction(5).

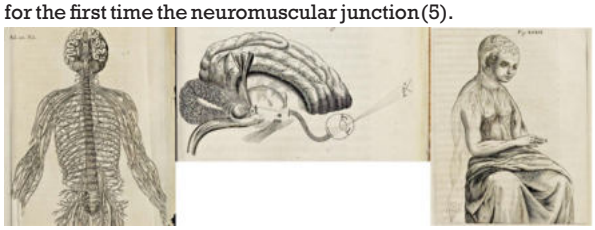

Figure 2. Drawings made by René Descartes, in the book entitled "De Homine" (1662), presenting the fairly advanced neuroanatomy knowledge during the 17th century(8).

Charles Sherrington and the discovery of the synapse

During the end of the 19th century and the beginning of the 20th century, the entire medical community started to make statements regarding the neurons and their way of functioning.

In 1873, thanks to the new staining technique invented by Camilo Golgi, known as "black reaction", the neurons could be observed with a greater degree of detail. He proposed "The reticular theory", which stated that the entire nervous system acts as an independent organ, with a single continuous neural network(9). It represented the utmost discovery of that time concerning the nervous system.

However, it was not completely true. 4 years later, in 1887, Santiago Ramón y Cajal demonstrated that the brain and the marrow are composed of multiple cells, with independent metabolism and aspect. Together, these cells which were given the name "neurons" by Wilhelm von Waldeyer constitute one of the most diversified and complex organs of the body, called the nervous system(9).

After Cajal's discovery, more and more neuroanatomists started to investigate the fascinating cell called neuron. Therefore, here lays the names origin of the neuron parts, axon, dendrites and cell body.

Thanks to them and many other anatomists of that era, the "Neuron Theory" was formulated and since the idea of interconnected neurons was clear, the future explorations focused on discovering what happens between 2 nerve cells. How do they send and receive information from the central nervous system and from the peripheral sensory receptors?

During the late 19th century, Sherrington was studying the method by which the spinal reflexes work. He used the anatomical basis discovered by Ramon y Cajal, in order to generalise a physiological concept concerning the neural transmission. His experiments were meant to demonstrate the way the impulse from the sensory neuron goes through dendrites and cell body in order to be continued by a motor neuron to the muscle.

The question that aroused was concerning that junction and it was clear at that time for Sherrington that it plays an important role in transmission of the information from a neuron to another. Therefore, he coined the name "synapse" to ease the scientific discussions about the space between the free-end of a neuron axon and another's dendrites.

This new word appeared for the first time in Michael Foster's 7th Edition "Textbook of Physiology" of 1897 (4), for which Sherrington wrote 3 chapters. He proposed his former Professor to introduce the word "synapse" which comes from Greek and means "conjunction".

Sherrington noted in Foster's "Textbook of Physiology": "So far as our present knowledge goes, we are led to think that the tip of a twig of the arborescence is not continuous with but merely in contact with the substance of the dendrite or cell-body on which it impinges. Such a special connection of one nerve cell with another might be called a 'synapsis'"(4).

However, Sherrington suggested in the first place another name for the junction between 2 neurons, which would have been "syndesm", as it is presented in a writing to his colleague John Fulton in 1937, but Michael Foster consulted Verrall, a friend of his, in order to conclude that the best name for the junction would be called synapse : "I felt the need of some name to call the junction between nerve-cell and nerve-cell (because that place of junction now entered physiology as carrying functional importance). I wrote him of my difficulty, and my wish to introduce a specific name. I suggested using "syndesm" He consulted his Trinity friend Verrall, the Euripidean scholar, about it, and Verrall suggested 'synapse'"(10).

This represented a key point in demonstrating that the nervous impulse travels unidirectionally through the neuron and the foremost component of a reflex arc is represented by the synapse itself which has an impressive importance in linking the sensory and motor path further determining the muscle contractions.

Nevertheless, the structure of the synapse was totally elucidated during the 20th century due to the discovery of the electron microscope. In 1953, George Emil Palade and Sanford Palay started to work together at the Rockefeller Institute —(11) in order to clarify for the entire medical community that the Cajal's "Neuron Theory" and Sherrington's discovery represented the unquestionable anatomical and physiological way of transmitting the information from one neuron to another.

As a consequence, they could observe using the electron microscope multiple knobs which are called today synaptic vesicles. They were abundant in the presynaptic ending and represented an important landmark for the microscopists,

since they could differentiate the presynaptic and the postsynaptic endings. Moreover, they also discovered that the synaptic membranes were thicker, the vesicles aggregated near the presynaptic ending and most important, they could state precisely that there is a space between the 2 synaptic membranes. They succeeded in continuing the work of both Ramon y Cajal and Sherrington, in order to demonstrate through technology that they were right about the synapse —(11).

Nevertheless, Sherrington did also have important contributions in spinal cord research. Since he was a student, he was influenced by Walter Holbrook Gaskell to study this area of the central nervous system instead of the cerebral cortex (12). First of all, his research was conducted on dogs and later on, he correlated that information with the post-mortem examinations of 2 men.

For the first case, he examined the spinal cord of a 63-year-old man who died due to haemorrhage as it is described "Outside the forepart of the left lenticular nucleus some ochre-coloured clot is seen.". He remarked a degeneration of the spinal nerves' axons due to the haemorrhage located in the motor area(13).

The second case was represented by a 35-year-old man whose death was caused by a chronic inability to walk as well as a severe back pain. He presented "weakness of the lower limbs and shooting-pains, and that a little later he found difficulty in walking in the dark" for almost 2 years. Through this post-mortem examination, Sherrington was able to discover the connection between the antero-lateral tract system and the cerebellum(14).

Another key discovery made by Sherrington is represented by reciprocal inhibition of the muscles. He conducted this research during his years at Oxford and Liverpool and proved that the contraction of a muscle lead to an inhibition of the antagonistic muscle (15). For this discovery, Charles Sherrington and Edgar Douglas Adrian were awarded the Nobel Prize in Physiology or Medicine in 1932 and he presented the entire discovery during a Nobel Lecture on 12th December 1932.

Sherrington also dedicated his studies on researching the muscle spindle which was originally discussed by Wilhelm Kühne (1837-1900) in 1863 (16). However, Sherrington presented through an experiment that once the dorsal ganglion root is removed, 60% of the intact fibres of the muscle are represented by the motor neurons (17). Therefore, he demonstrated that a percent of 40% consists of sensory fibres and as a consequence, the muscle is also a sensory organ.

He did not stop here and continued his studies based on an observation that he made. He noticed that there are 2 different types of motor axons which differed in diameter. Thus, he discovered what we now call □-motor neurons which innervates the muscle spindle and have an important role controlling and limiting the muscle stretch according to the proprioceptive information received by the brain through the sensory root ganglia(12).

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