The Nobel Prize in Physiology or Medicine 1970

Presentation Speech

Presentation Speech by Professor Börje Uvnäs, Member of the Nobel Committee for Physiology or Medicine of the Royal Caroline Institute

Your Majesty, Your Royal Highnesses, Ladies and Gentlemen.

The work for which this year's Nobel Prize in Physiology or Medicine has been awarded has its origin in earlier prize-winning discoveries. It is wellknown that nerve impulses are changes in electrical potential which travel along nerves at high speeds to their terminals where they give rise to new impulses in other nerves or to activity in muscles, glands or other organs of the body. It was long assumed, naturally enough, that the transmission of nerve impulses took place by physical means, in the same way as an electric current passes between two electric cables. However, in the twenties, Henry Dale and Otto Loewi showed that impulse transmission takes place by chemical means. At the nerve ending the impulse releases a biologically-active substance which, in turn, induces electrical activity in the next nerve or the innervated structure. In this way the functional gap between the nerve terminal and the innervated structure is bridged. As with all fundamental discoveries, the discovery of a chemical mediator in nervous transmission led to revolutionary new thinking. Neurochemistry and neuropharmacology developed into rapidly expanding branches of science. A host of new questions arose. How were such highly active transmitter substances synthesized, stored and released? How could they appear, produce their effects and disappear within a fraction of a second, which must happen if chemical mediation was to explain the very fast chain of events taking place in nervous processes. What kind of substances were involved? Each of today's prize winners had made his own special contribution towards solving problems in this field.

Bernhard Katz was specially interested in the electrical events which occur when impulses in motor nerves induce muscle activity by acting at motor end-plates. These special structures in the muscle with condenser-like properties are charged by the nerve impulses and their discharge in turn activates the muscle. Through the discovery of the existence of "miniature end-plate potentials" Katz demonstrated that the messenger substance between the motor nerve and the muscle end-plate, acetylcholine, was released from the nerve terminals in small quanta, small packages if you like.

Ulf von Euler was especially interested in the sympathetic nervous system and early on identified the adrenergic transmitter substance, noradrenaline. Together with a Swedish colleague, the late Nils-Åke Hillarp, he was later able to show that in nerves noradrenaline is synthesized and stored in granules, particles about one ten thousandth of a millimetre in diameter. He has made great contributions to the study of the properties of these nerve granules.

Julius Axelrod has chiefly been interested in the fate of the transmitter substance noradrenaline after it has been released from the nerve terminals. In this connection he has discovered and studied the enzymatic inactivation of the transmitter substance, which occurs by its methylation, but above all he demonstrated the reuptake of noradrenaline by the nerve terminals. The transmitter substance is released in great excess. As soon as the required amount has reached its goal and produced its effect most of the excess is taken up again into the storage sites in the nerve terminals. In other words this is a rapid, effective and economic way of limiting the duration of the effect of the nerve impulse. One might think that the discoveries I have described would be exclusively of theoretical interest. On the contrary, as with all fundamental discoveries, they have led to extensive practical advances with implications in medical fields which to a large extent affect all of us. I will give some examples.

In their religious ceremonies the primitive Mexican Indians sought closer contact with the supernatural powers by intoxicating themselves with mushroom poisons. Our own young people, in their search for increased selfconfidence and social contact, resort to drug taking. In both cases the background to the dreamlike experiences, with their confused and abnormal mental sensations, is the same. It is not a question of mystical forces at work or the invocation of supernatural spirits. The experiences are a result of the disturbing effect of the poisons on the chemical transmission of nerve impulses in the brain.

Our psyches and mental processes are being laid open more and more to chemical manipulation. Psychopharmacology has become a very topical branch of science. Nervous and mental diseases have become accessible to rational treatment with drugs.

New substances for the treatment of high blood pressure and Parkinson's disease are other fruits from the tree of knowledge which has grown from the ever increasing understanding of the mechanisms of chemical transmission. It is my belief that in the near future continued research will lead to new discoveries of importance for the understanding of the intimate nature of mental disease and psychical disturbances. Through these, new ways for their treatment will be opened.

If my vision of the future is fulfilled it will be largely thanks to discoveries of the type which have been made by todays Nobel prizewinners.

Bernhard Katz, Ulf von Euler, Julius Axelrod.

Your fundamental research into the nature of the chemical neurotransmission process has not only enriched our knowledge in theoretical medicine, it has also been of far-reaching importance for the understanding and treatment of nervous disease of peripheral and central origin. Thus, it was fully in agreement with the spirit of Nobel's will when the medical faculty of the Karolinska Institutet awarded you this year's Nobel prize. On behalf of the faculty I have the honour and privilege to congratulate you and to wish you continued success in your future research. I now ask you to step forward to receive your prizes from the hands of His Majesty the King.

From *Nobel Lectures, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972