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REVIEW ARTICLE

Vision and the Nobel Prize

A visão e Prêmio Nobel

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ABSTRACT | The Nobel Prize is the world's foremost honor for scientific advances in medicine and other areas. Founded by Alfred Nobel, the prizes have been awarded annually since 1901. We reviewed the literature on persons who have won or competed for this prize in subjects related to vision and ophthalmology. The topics were divided into vision physiology, diagnostic and therapeutic methods, disease mechanism, and miscellaneous categories. Allvar Gullstrand is the only ophthalmologist to win a Nobel Prize; he is also the only one to receive it for work in ophthalmology. Other ophthalmologists that have been nominated were Hjalmar Schiötz (tonometer), Karl Koller (topical anesthesia), and Jules Gonin (retinal detachment). Other scientists have won the prize for eye-related research: Ragnar Granit, Haldan Hartline and George Wald (chemistry and physiology of vision), and David Hubel and Torsten Wiesel (processing in the visual system). Peter Medawar is the only person born in Brazil to have won the Nobel Prize.

Keywords: Nobel Prize; Ophthalmology; Vision; Laureates; Physiology

RESUMO | O Prêmio Nobel é a principal honraria do mundo para avanços científicos em medicina e outras áreas. Fundada por Alfred Nobel, os prêmios são concedidos anualmente desde 1901. Revisamos a literatura sobre pessoas que ganharam ou competiram por esse prêmio em assuntos relacionados à visão e oftalmologia. Os tópicos foram divididos em fisiologia da visão, métodos diagnósticos e terapêuticos, mecanismo de doenças e variados. Allvar Gullstrand não é o único oftalmologista a ganhar um Nobel, porém é o único a recebê-lo por contribuições na oftalmologia. Outros oftalmologistas foram nomeados: Hjalmar Schiötz (tonometro), Karl Koller (anestesia tópica) e Jules Gonin (descolamento da retina). Outros cientistas ganharam o prêmio com pesquisas relacionadas à visão: Ragnar Granit, Haldan Hartline e George Wald (química e fisiologia da visão); David Hubel e Torsten Wiesel (processamento no sistema visual). Peter Medawar é a única pessoa que nasceu no Brasil a ganhar o prêmio.

Descritores: Prêmio Nobel; Oftalmologia; Visão; Laureados; Fisiologia

INTRODUCTION

The Nobel Prize is the world's foremost honor in recognition of cultural and/or scientific advances for activities related to chemistry, physics, physiology or medicine, literature, economics, and peace. Every year, in October, candidates who have done work of great value for the good of humanity in these areas are chosen to receive the prize in December 10, the birthday of the creator of the award, Alfred Nobel.

The history of the prize begins with Alfred Nobel, the inventor of dynamite. After experiencing displeasure for the death and destruction caused by his invention, Nobel proposed creation of an award that would honor those who, in the future, would serve the good of humanity. He left his fortune of SEK 32 million for the creation of an institute to administer the prize, the Nobel Foundation. The first award ceremony took place in 1901 at the Royal Conservatory of Stockholm[1]. These awards are given annually by the Royal Academy of Sciences of Sweden, Swedish Academy, Norwegian Nobel Committee, and Karolinska Institute to individuals and organizations that have contributed exceptionally in the above areas[2].

Considering the scarcity of specific literature on this important topic in the history of ophthalmology, we reviewed the scientific literature on people who won or competed for the Nobel Prize in Medicine or Physiology, and also the prizes in other areas related to ophthalmology, such as physics.

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TOPICS

Only one individual who practiced ophthalmology for a significant period has ever received a Nobel Prize. This was Allvar Gullstrand, a Swede who was awarded the Nobel Prize in Physiology or Medicine in 1911. Although Gullstrand often is said to be the only Nobel laureate who was an ophthalmologist, this is incorrect. Fritz Pregl, an Austrian ophthalmologist who deserted the eye for analytical chemistry, received the Nobel Prize in Chemistry in 1923. Walter Hess, a Swiss ophthalmologist and physiologist, was awarded the Nobel Prize in Physiology or Medicine in 1949 for his work on autonomic control by the hypothalamus. Therefore, although Gullstrand is not the only ophthalmologist to win a Nobel Prize, he is to date the only ophthalmologist who has been given a Nobel Prize for work in ophthalmology[3].

Other ophthalmologists have been nominated, but not selected, for the Nobel Prize in Physiology or Medicine. Hjalmar Schiötz was considered for his tonometer, as was Karl Koller for his discovery of topical anesthesia in the eye. Jules Gonin nearly received the award for his innovations in retinal detachment surgery. The Nobel Prize has been awarded to other scientists whose work concerns the function of the eye. In 1967, Ragnar Granit, Haldan Keffer Hartline, and George Wald were designees for their contributions to our understanding of the chemistry and physiology of vision. In 1981, David Hubel and Torsten Wiesel were recipients for their work on information processing in the visual system[4]. Peter Brian Medawar is worth mentioning as the only person born in Brazil to win a Nobel Prize. For his research on corneas with the theory of acquired immunological tolerance, he shared the Nobel Prize in Physiology or Medicine in 1960 with Sir Frank Macfarlane Burnet[5].

For didactic purposes, we divided this review into topics related to the physiology of vision, diagnostic and therapeutic methods, mechanisms of disease, and miscellaneous categories (some laureates whose research has some relation to ophthalmology).

Physiology of vision

Ragnar Granit, Haldan Keffer Hartline, and George Wald (WON)

The 1967 Nobel Prize in Physiology or Medicine was awarded jointly to Ragnar Granit, Haldan Keffer Hartline, and George Wald "for their discoveries concerning the primary physiological and chemical visual processes in the eye."

Ragnar Granit was born in Helsinki, Finland. He used microelectrodes to measure nerve impulses. He showed that light on the retina elicits excitatory and inhibitory signals as measured in the optic nerves; the sum of these effects helps to produce images perceived by the brain. Granit also worked on development of the electroretinogram (ERG), with which he and his colleagues studied the basic principles of color vision. The ERG remains a major investigative tool in clinical and research studies in ophthalmology.

A New Yorker, George Wald, studied the chemistry of the retina and found that rhodopsin is made up of opsin, a protein, and retinal, an aldehyde of vitamin A. He then showed that light causes breakdown of the rhodopsin molecule, with darkness reversing the process. From these findings, Wald postulated that night blindness was due to vitamin A deficiency. In the 1950s, Wald and colleagues isolated other retinal pigments related to vitamin A and demonstrated their role in color vision and color blindness.

Born in Bloomsburg, Pennsylvania, and educated at Johns Hopkins University, Haldan Keffer Hartline began studying impulse transmission in the well-differentiated optic nerve fibers of horseshoe crabs. He discovered that signal rates are proportional to the intensity of light falling on the photoreceptors, and that in the visual system of the frog, the nerve fibers are activated according to the type of light, brightness, and object movement. Hartline also elucidated the mechanisms of signal processing in the retina, night vision, and the recognition of patterns and motion by the retina.

Although many of the theories of Granit, Wald, and Hartline have changed, the research methods they developed and the basic concepts they advanced were crucial for the growth of cognitive neuroscience and neuro-ophthalmology[6].

David H. Hubel and Torsten Wiesel (WON)

Torsten Nils Wiesel, a Swedish neurophysiologist, together with David Hunter Hubel, a Canadian neurophysiologist, received the 1981 Nobel Prize in Physiology or Medicine for their discoveries concerning information processing in the visual system. The prize was shared with Roger W. Sperry for his independent research on the cerebral hemispheres[7].

The work of Hubel and Wiesel was a quantum step in our understanding of the visual system[8]. Their work it provided fundamental insight into information processing in the visual system and laid the foundation for

the field of visual neuroscience. They had many achievements, including, but not limited to, the discovery of orientation selectivity in visual cortex neurons and characterization of the columnar organization of visual cortex through their discovery of orientation columns and ocular-dominance columns[9]. They received the Nobel Prize for two major contributions: their work on development of the visual system, which involved a description of ocular dominance columns in the 1960s and 1970s, and their work establishing a foundation for visual neurophysiology, describing how signals from the eye are processed by visual parcels in the neocortex to generate edge, motion, stereoscopic depth, and color detectors, which are building blocks of the visual scene. By depriving kittens of the use of one eye, they showed that columns in the primary visual cortex receiving input from the other eye take over the areas that normally would receive input from the deprived eye. This has important implications for the understanding of deprivation amblyopia. These kittens also did not develop areas receiving input from both eyes, a feature needed for binocular vision. Hubel and Wiesel's experiments showed that ocular dominance develops irreversibly early in childhood. These studies opened the door for the understanding and treatment of childhood cataracts and strabismus[10].

Diagnostic and therapeutic methods

Allvar Gullstrand (WON)

Born in Landskrona, Sweden, Gullstrand was a professor at the University of Uppsala from 1894 to 1927. He applied the methods of physics and mathematics to the study of optical images and refraction of light in the eyes, discovering intracapsular mechanisms through which visual accommodation is processed. He described the dioptric system of the human eye with unprecedented precision and invented and designed far-reaching ophthalmic instruments. Today, Gullstrand is best known as the inventor of the slit lamp. He combined a slit with a microscope made by the Zeiss Optical Works in Germany, creating the instrument that is used by all ophthalmologists today. He was recognized for making the most significant contribution to the understanding of the eye as a refractive organ after the pioneering work of Hermann von Helmholtz, a German physician and physiologist who invented the ophthalmoscope in 1850[11].

Gullstrand is the only individual who received and declined a Nobel Prize. (Rarely has a Nobel Prize been declined.) In 1910 and 1911, Gullstrand was nominated for the Nobel Prize in Physics. In 1911, the Nobel Committee for Physics, of which he was a member, suggested that he receive the prize. At the same time, the Nobel Committee for Physiology or Medicine was considering him for their prize. Gullstrand declined the Nobel Prize in Physics in favor of the Nobel Prize in Physiology or Medicine[12].

Despite all his intelligence, Gullstrand had a strong personality that had a negative impact on his career. As a member of the Royal Swedish Academy of Sciences, he served on the Nobel Physics Committee. While serving on the committee, he used his position to block Albert Einstein from receiving a Nobel Prize in Physics for his theory of relativity, which Gullstrand believed to be wrong. He wrote two harsh opinions against giving the prize to Einstein in 1921 and 1922[13].

Hjalmar Schiøtz and Carl Koller (NOMINATED)

A Norwegian professor of ophthalmology, Hjalmar Schiøtz, described the first simple and generally reliable tonometer designed to measure intraocular pressure (IOP). Since 1905, his instrument has become the standard for measuring IOP, and it remains useful for measurements at the bedside and in the operating room. It also earned him a nomination for a Nobel Prize. Placing a Schiøtz tonometer on the eye requires topical anesthesia. Credit for discovering topical anesthesia belongs to Carl Koller, who introduced cocaine as a local anesthetic for eye surgery. Koller, an Austrian ophthalmologist who began his medical career as a surgeon at the Vienna General Hospital and was a colleague of Sigmund Freud, would have won a Nobel Prize if the award had been created by that time. Previously, pressure-measuring devices were placed on the eyelids or awkwardly on the scleral conjunctiva without the benefit of anesthesia-a procedure undoubtedly associated with marked squeezing of the eyelids and apprehension on the part of the patient and physician, which markedly limited the reliability of the measurements. Schiøtz's invention deserves a moment of reflection, since it has influenced the frequency with which IOP is measured and has emphasized the importance of IOP in managing glaucoma. Such an acknowledgment also provides us an opportunity to consider if we are any closer to Schiøtz's goal of developing a reliable and accurate instrument to measure IOP[14].

Disease mechanisms

Jules Gonin (NOMINATED)

Before the turn of the 20th century, eyes with retinal detachment were considered doomed. At this time, surgical treatment of retinal detachment still was in its infancy, and the surgical success rates were less than 5%. From 1902 to 1921, Jules Gonin almost single-handedly changed the landscape of retinal detachment surgery. He recognized that the retinal break was the cause-and not the consequence, as was largely believed at the time-of the retinal detachment, and that treatment must at all costs accomplish closure of the break by cauterization. He named the procedure *ignipuncture*, as he cauterized the retina through the sclera with a very hot, pointed instrument. Despite rigorously detailed clinical observations and increasing success rates, his discovery was not accepted readily and sometimes was openly opposed by a large part of the ophthalmic establishment. Not until 1929 did he receive worldwide acclaim at the International Ophthalmological Congress in Amsterdam for his surgical technique. His legacy lives on in the eye hospital in Lausanne that bears his name and in the Gonin Medal awarded by the International Council of Ophthalmology every 4 yr for the highest achievement in ophthalmology[14].

The Nobel Prize Committee considered giving the award to Gonin. A questionnaire on Gonin's work was sent to several ophthalmic authorities around the world[15]. All replied favorably, with one exception, the prominent Alfred Vogt, who was famous for his gift of observation and an enormous working capacity, and as one of the three describers of Vogt-Koyanagi-Harada disease, and also for his aggressive nature[16]. Vogt quite wrongly and groundlessly cast doubt on Gonin's priority in discovering this first consistently successful operation for retinal detachment. This unfortunate decision persuaded the Nobel Committee to postpone their decision on Gonin's work for a year. This has become one of the more glaring omissions of the Nobel Prize. It is very likely that the prize would have been conferred on Gonin the next year, since the reasons for the opposition against him receiving the prize were unsubstantiated. Gonin nearly received the award for his innovations in retinal detachment surgery, but his premature death prevented him from doing so[17].

Peter Brian Medawar (WON)

Although he was not an ophthalmologist, Peter Brian Medawar is worth mentioning as the only person born in Brazil to have won a Nobel Prize. He was born in Petrópolis, Rio de Janeiro, and was a naturalized British citizen. He spent his early years in Brazil and later studied biology and zoology at Magdalen College, Oxford. In 1947, he was a senior lecturer in zoology at Birmingham University; 2 yr later, he was elected a Fellow of the Royal Society. Sir Peter Medawar is best remembered for developing the theory of acquired immunological tolerance, thus laying the foundation for successful organ and tissue transplantation. He described the cornea as an immune-privileged tissue and the anterior chamber as an immune-privileged site. In 1960, he shared the Nobel Prize in Physiology or Medicine with Sir Frank Macfarlane Burnet[18]. When he became an adult, he received a scholarship from the British Government. He requested the intervention of his godfather, Salgado Filho, the Minister of Aeronautics, to obtain exemption from compulsory military service in Brazil. Unfortunately, his request was not granted. As a result, he lost his Brazilian citizenship, and his Brazilian nationality was never tied to the laureate[19].

Miscellaneous

Albert A. Michelson was the first American scientist to be awarded a Nobel Prize (Physics, 1907) for his optical precision instruments and the spectroscopic and metrological investigations performed with their aid[20]. A Michelson interferometer, one of the devices that he developed in his lifelong quest to measure the speed of light experimentally, was a key element of time domain optical coherence tomography, which was described first in 1991[21].

Lasers are used frequently in ophthalmic practice. In 1953, a group led by Townes at Bell Laboratories and the Russian team of Basov and Prokhorov nearly simultaneously developed the microwave amplification by stimulated emission of radiation, in which microwave emission can be amplified greatly and well collimated, and for which they received the 1964 Nobel Prize in Physics[22]. Arthur Leonard Schawlow won the Nobel Prize in Physics in 1981 for his contribution to the development of laser spectroscopy[23].

The Nobel Prize in Physics in 2005 was divided; half was awarded to Roy J. Glauber "for his contribution to the quantum theory of optical coherence" and the other half was awarded jointly to John L. Hall and Theodor W. Hänsch "for their contributions to the development of laser-based precision spectroscopy, including the optical frequency comb technique"[24].

In 2015, the Nobel Prize in Physiology or Medicine was awarded to two scientists who helped defeat river blindness. William C. Campbell and Satoshi Ōmura won the prize for their discoveries that helped stop blinding parasitic infections around the world. The drug ivermectin, which the two men helped discover, drastically cut the transmission rate of river blindness. River blindness, or onchocerciasis, is caused by a roundworm parasite found in swiftly moving water in rivers and streams. For many years, the disease haunted parts of Central and South America, sub-Saharan Africa, and South Asia. According to the World Health Organization, an estimated 18 million people are infected and 270,000 are blinded by the parasite. Without treatment, approximately half of all those infected will become blind[25].

COMMENT

Given the complexity of the eye and its optical pathways as well as its therapies, the study of the visual sciences is a broad field of investigation and research. Knowledge of these award-winning scientists, many of whose findings remain part of our daily eye practice, is critical to assessing the importance of scientific research for current and future generations of ophthalmologists.

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