



Professor Stanisław Wolfarth, Ph.D., M.D.
(1933–2007)

OBITUARY

Biography of Professor Stanisław Wolfarth, an excellent scientist and honorable man, is a history of a man, who despite very difficult beginning of his career, achieved great success in his life being a self-made man. He accomplished this owing to his talent and hard work, and most of all, to strong character and passion for knowledge.

Professor Stanisław Wolfarth, Ph.D., M.D. was born on February 10th, 1933 in Gostyń, a small town in the Poznańskie region, in which his father was a starost (the chief executive official of the district). He was 6 years old when World War II broke out, and this was the last time when he saw his father, who left home in September 1939 to join defenders of Warsaw from Nazi Germany. His father never returned home again, and later it came out that he died in the concentration camp in Oświęcim in 1942.

During the occupation of Poland, young Wolfarth was taught at home by a priest, harbored by his mother, and after the end of WWII, in a secondary school in Gostyń. However, he did not graduate from this school, since his mother was harassed by communistic administration as so-called “private enterpriser”

(she tried to manage a private café after the war) and was unable to support him. His living circumstances constrained him to start working when he was 16 years old. At the beginning, he worked as a waiter, clerk, cafeteria manager, then he was called up to the army, and as a “uncertain element”, he was assigned to the famous Labor Battalion in the “Piaś” mine, where he had been working for 2 years. After he was released from service in the army, he started working again, now as an electrician and senior packer. In 1956, he was granted a secondary-school certificate from the Jan Sobieski Second Secondary School after he successfully passed the examination as a candidate from outside the school. Then, he commenced studies at the Faculty of Medicine of the Medical Academy in Kraków, from where he graduated in 1963 and was granted a certificate of general practitioner.

Immediately after graduation, he started scientific work, first as a volunteer then as a postgraduate student at, formerly, the Department of Pharmacology, Polish Academy of Sciences (later transformed into Institute), where he was working until 2006, i.e. 43 years. There he prepared his doctor’s thesis entitled

“The effects of 3,4,5-trimethoxybenzyl alcohol esters on the central nervous system” under the guidance of Professor Józef Hano and dissertation qualifying for associate professorship “Experimental basis of the therapy of Parkinson’s disease and the cholinergic-dopaminergic equilibrium in the basal ganglia”. Since, at that time, the Institute of Pharmacology, PAS was not authorized to grant scientific degrees, he presented both theses at the Institute of Immunology and Experimental Therapy in Wrocław. Doctor’s degree was conferred on him in 1969 whereas he was promoted to an Associate Professor level in 1977. He was granted a professor’s and full professor’s rank in 1989 and 1995, respectively.

While he was engaged in scientific work, he was receiving training as a medical doctor at the 3rd Clinic of Internal Diseases under supervision of Professor Julian Aleksandrowicz and at the Clinic of Psychiatry, Medical Academy in Kraków under the guidance of an eminent professor of psychiatry Antoni Kępiński.

In the period between 1970–1971, he was granted a stipend from French government to visit the Department of Neuro-Psychopharmacology INSERM, where he joined the team of Professor Boissier, and his studies focused on the extrapyramidal system. At that time, he also paid short visits to the Department of Experimental Neuropathology in Lyon to Professor Jouvret, the most notable European specialist in the studies of sleep, and to the Department of Neurophysiology (CNRS) to Professor Naquet, a famous expert in the field of electroencephalographic seizure activity and epilepsy, in Marseilles.

After return to Poland in 1971, he was appointed by the head of the Department of Pharmacology, Professor Hano, to be the acting head of the Laboratory of Neuropharmacology. He had remained at that position in that laboratory, later transformed into Department, unceasingly until 2003, when he retired, i.e. for 32 years!

Studies into functioning of the basal ganglia and their role in development of Parkinson’s disease, which he initiated during his visit to France, became a passion of his life. He instilled this passion into his disciples and, thus, this is still the leading research program at the Department of Neuro-Psychopharmacology.

The turn of the 1970s is the period just after discovery of the role of dopamine in Parkinson’s disease. At that time, investigations focused on the contribution of dopaminergic-cholinergic imbalance to the de-

velopment of Parkinson’s disease. Professor Wolfarth wholeheartedly joined this research direction demonstrating significance of this balance not only in the striatum, as expected earlier, but also in the substantia nigra. These studies, which became basis for his dissertation qualifying for associate professorship, showed that clinical relationships termed dopaminergic-cholinergic balance were a resultant of interactions of complex neuronal systems located in many brain structures, like the substantia nigra, striatum, thalamus and cerebral cortex. These were groundbreaking investigations, whose results were corroborated by an array of later studies. Professor Wolfarth was awarded first time the Prize of the Scientific Secretary of PAS in 1977 for examination of significance of the nigrostriatal pathway in the regulation of the striatum.

Till the end of the 1970s, anatomical connections of the basal ganglia got much better recognized. GABA was revealed to be a neurotransmitter in many of them. Investigations into the role of GABAergic transmission in manifestation of parkinsonian symptoms became the new focal point of Professor Wolfarth’s research. In 1975, he was awarded first time a stipend from the Max Planck Society for studies at the Institute of Experimental Medicine in Göttingen joining the team of Professor Sontag, who at that time was engaged in studies on spinal regulation of reflex activity of skeletal muscles. The Polish visiting scientist proposed to study the effect of brain structures on this activity. This was facetiously named the research on the effect of that what was occurring above the tie on functioning of that what was located below. During his stay in Göttingen, Professor Wolfarth demonstrated that nigral neurons modulated by GABA controlled activity of muscle fibers, while the thalamic GABA-ceptive neurons played a crucial role in initiation of movements. Moreover, he discovered a relationship between nigral cholinergic and GABAergic system in transmitting neuronal impulses *via* nigrostriatal projection (which was a continuation of his research qualifying for associate professorship), and the presence of sequential arrangement of GABAergic neurons transmitting patterns of catalepsy (as a model of parkinsonian akinesia), muscle rigidity, asymmetric behavior and others. He continued to explore these issues in Krakow, and the initial bilateral cooperation was extended by Professor Alexander Cools’ team from the Catholic University in Nijmegen, The Netherlands. In total, Professor Wolfarth spent over 2 years

in Göttingen and Nijmegen, and his cooperation with Professor Sontag had been continued for about 9 years. Professor Wolfarth was again awarded The Prize of Scientific Secretary of PAS in 1980 for demonstration of functional diversity of the substantia nigra and contribution of GABA and acetylcholine to transmission of stimuli via nigrostriatal pathway.

The 1980s are the period marked with studies on the role of GABAergic transmission in other structures of the basal ganglia, like globus pallidus, zona incerta and lateral hypothalamus in extrapyramidal disturbances. These issues were the subject of the next doctor's theses supervised by Professor Wolfarth, that were prepared by presently Professor Ossowska and Associate Professor Wardas. The studies showed, *inter alia*, that GABAergic transmission in the zona incerta and lateral hypothalamus was significantly implicated in parkinsonian akinesia. This was a pioneer discovery, because these structures were earlier attributed a regulatory function in the endocrine system. For a series of articles about the role of new central GABAergic pathways implicated in pathogenic mechanisms of Parkinson's disease, the team headed by Professor Wolfarth was awarded The Prize of VI Department of Medical Sciences in 1989.

One of the primary symptoms of parkinsonism is muscle rigidity. To be able to investigate these symptoms in animal models, in the mid eighties, Professor Wolfarth initiated in the Department of Neuro-Psychopharmacology the construction of a prototypic device for objective measurement of passive muscular resistance of rat's hind paw induced by its passive movements. The measuring technique was designed to resemble measurements of muscular tone in patients of the Clinic. Development of this apparatus was the subject of doctor's thesis of Dr. Kolasiewicz, prepared under the guidance of Professor Wolfarth. This device was later modified many times and was used for development of animal models of parkinsonian muscle rigidity, which facilitated the search for new drugs efficiently alleviating this symptom of Parkinson's disease. Mechanograph is still a crucial piece of equipment in the Department of Neuro-Psychopharmacology and is the only apparatus of this type used in laboratory practice worldwide.

Within the last 15 years, Professor Wolfarth was actively engaged in two main research programs. The first was focused on the search for new antiparkinsonian drugs among substances influencing glutamate receptors – initially ionotropic and then metabotropic.

The second research direction involved investigation of the effect of aging on motor functions and development of Parkinson's disease. At the beginning, it was shown that NMDA receptor blockage by compounds binding to ion channel of this receptor and to modulatory glycine site reduced muscle rigidity of parkinsonian type in rats. Unfortunately, this research and experiments in many other research centers indicated that NMDA receptor antagonists can be expected to produce a number of serious undesirable side effects, that limit introduction of these compounds into clinical practice. Metabotropic glutamate receptors proved to be more interesting. Studies conducted jointly with the Department of Neurobiology, Institute of Pharmacology, demonstrated that the blockage of postsynaptic group I receptors or stimulation of group II and III mGluRs alleviated both muscle rigidity and akinesia (catalepsy) in rats. The paper published in 1998 that dealt with inhibitory effect of compound LY374500 on muscle rigidity was the first report postulating potential use of metabotropic receptor ligands in Parkinson's disease.

The investigations of aging processes were conducted in cooperation with Professor Helmut Coper, Professor Hans Rommelspacher and Dr. Gert Schulze from the Department of Clinical Neurobiology, Clinic of Psychiatry of Free University of Berlin, and with Professor Irena Hausmanowa-Petrusewicz and Associate Professor Anna Kamińska from the Mirosław Mosakowski Institute of Experimental and Clinical Medicine, PAS, and Clinic of Neurology at the Medical Academy in Warsaw. This cooperation started in 1989 and has been continued until the present. Professor Coper's team has been primarily engaged in investigating the cognitive and memory processes. Professor Hausmanowa's research group has worked on neuromuscular pathologies, muscle anatomy and electromyography. The cooperation gave a new insight into aging processes. Mechanographic technique was perfected and its potential was extended by ability to analyze electromyographic activity in rats.

The studies in an animal model demonstrated that despite a relationship between age and development of Parkinson's disease, muscle rigidity in the elderly had completely different physiological basis and depended on other neuronal systems than parkinsonian muscle rigidity. Scientific achievements of Professor Wolfarth in both the above-mentioned fields were highly prized and won him The Prize of VI Depart-

ment of Medical Sciences, PAS, twice in 1997 and 1999.

The publications of Professor Wolfarth encompass about 90 scientific papers, whose vast majority was published in excellent journals with worldwide reach and some 130 conference communications from his studies presented at congresses in Poland, many European countries, Israel and Republic of South Africa. His works are characterized by amazing coherence of research objectives, consistency and up-to-dateness.

Apart from the aforementioned prizes, Professor Wolfarth was also awarded prizes of the Polish Pharmacological Society, European College of Neuropsychopharmacology, and prizes of the Director of the Institute of Pharmacology, PAS, and was honored by Gold Cross of Merit. He organized a number of conferences and symposia in Poland and abroad. He provided training and delivered lectures for different assemblages and in pharmaceutical companies. He was a honorary member of the Polish Neuroscience Society, a member of Polish Pharmacological Society, European Behavioral Pharmacology Society, many-years' member of Scientific Board of the Institute of Pharmacology, PAS, in Kraków and a member of Commission on Aging Biology, the Committee on Human Genetics and Molecular Pathology of the Department of Medical Sciences, Polish Academy of Sciences.

As a boss, Professor Wolfarth was characterized by unusual gentleness and composedness. He was demanding but never *ex cathedra* imposed his opinions upon his subordinates. Instead, he preferred discussions, often setting forth new ideas, helped to identify problems and allowed his co-workers to solve them by themselves. He was loyal to his junior colleagues, promoted them, often stepping aside himself. Thanks to these attributes, he managed to create a school – a team, which is able to continue his work.

Scientific research was not the only form of Professor Wolfarth's activity. He was always a broad-minded person of vivid intelligence, who was interested in many different fields: literature, history, cosmology,

politics. He was endowed with extraordinary easiness of entering into friendly relations with people, while fluent knowledge of three languages: English, French and German allowed him to quickly make friends with foreigners.

In 1980/1981, he was actively engaged in the first Solidarity movement. Then, during the Martial Law, he distributed so-called "forbidden literature" (Konwicki, Andrzejewski, Solzenicyn, Wat or Orwell) among his colleagues pharmacologists, because he had contacts with underground publishers and emigrational societies. He also participated in distribution of aid which, at that time, was coming from abroad to the Archbishopric in Krakow. After the turning point of 1989, he still had been involved in trade-union-related and political endeavors. At the beginning, he participated in activities of the Solidarity Movement's Circle of PAS employees, then he was a member of ROAD, Democratic Union and Freedom Union, that nominated him a candidate for Member of Polish Parliament.

Despite tragic history of his family, he committed himself to establishing friendly Polish-German relations. He conceived the idea of scientific symposium on twenty years' cooperation between Polish and German scientists and was the organizer of this event. The Symposium was held in Zakopane in 1993 and was a great success. Afterwards, professor Wolfarth was an editor of a book containing memoirs of mutual relations written by prominent Polish and German researchers. It should be emphasized that Professor Wolfarth was highly regarded by his German colleagues, many of whom concerned themselves to be his friends.

The above recapitulation does not relate all achievements of Professor Wolfarth. One cannot possibly briefly summarize a human's life, particularly if it was so rich as the life of Professor Wolfarth.

Professor Stanisław Wolfarth passed away in the afternoon 20th November 2007. We shall miss Him very much.

Krystyna Ossowska, Ph.D., M.D.