



**Dr. Gert Schulze, M.D.
(1941–2013)**

In memoriam

Dr. Gert Schulze was born in Dresden. He studied human medicine at the Free University of Berlin in West Berlin, graduating with a doctorate on June 23rd 1972 with a thesis entitled “Investigations on the impact of 6-aminonicotinamide upon monoaminergic mechanisms in the rat brain and body temperature of rats”. His advisor was Professor Helmut Coper who had been appointed founding director of the Institute of Neuropsychopharmacology by the Free University in 1967. As the first research associate of Coper’s team, Gert Schulze established the working group Geriatric Neuropharmacology. The starting point of the group was the observation that aged patients may react in a paradoxical way to antipsychotic medication. Dr. Schulze begun his scientific work by studying body functions that reacted in an age-dependent manner in response to treatment with antipsychotic drugs. The motor function of adult and aged rats was chosen as the initial model. Later, he focused on the model of body temperature, challenging the adult and aged rats with very low and extremely high environmental tem-

peratures. His central conclusion from these studies was that in aged individuals the capacities of compensation mechanisms were impaired and therefore were no longer able to cope with such extreme challenges. These mechanisms are not specific for thermoregulation alone but are composed of multiple brain functions with the common task to compensate for a failing body function to restore an appropriate equilibrium. This was a highly novel and important outcome as it was in contrast to earlier views and opened up a new avenue of research.

Dr. Gert Schulze supervised several medical students while conducting experiments as part of his studies in geriatric neuropharmacology. They all graduated successfully with a medical degree from the Free University. For several decades he was involved in teaching medical students in basic pharmacology both at the Free University and later at the Charité. The long lasting collaboration with Polish colleagues was one aspect of his research that was particularly close to his heart.

Dr. Gert Schulze first met with Polish scientists in 1987 when Prof. Stanisław Wolfarth, at that time the head of the Department of Neuro-Psychopharmacology of the Institute of Pharmacology, Polish Academy of Sciences (PAS) in Kraków, paid a visit to the Institute of Neuropsychopharmacology at the Free University of Berlin at the invitation of Prof. Helmut Coper. The main research topic of the Department of Neuro-Psychopharmacology in Kraków was related to searching for pathomechanisms of Parkinson's disease based on animal models of this disease. Since the progression of Parkinson's disease depends on aging processes, it was logical for the teams to establish a scientific cooperation.

A primary symptom of Parkinson's disease is muscle rigidity. In order to quantify severity of this symptom in a rat model of this disease, an apparatus, called mechanograph was constructed in the Institute of Pharmacology in Kraków in the 1980s. The mechanograph measured muscle resistance of the hind limb of the rat in response to passive flexion and extension in the ankle joint. Experiments with the use of the mechanograph were designed to model a clinical method of assessment of muscle rigidity in patients. In 1988 Prof. Wolfarth came to Berlin by car bringing with him the mechanograph with the aim of measuring muscle tone in old rats. At that time, the Institute in West Berlin had a number of very valuable female rats which were 3 or more years old. Such old rats can be very rarely encountered in laboratories worldwide due to a very high price. That visit sparked a close cooperation between Dr. Schulze and Prof. Wolfarth's group.

Joint research in the following years (1990–2000) concentrating mostly on the analysis of the mechanisms of muscle tone in rats were headed by Prof. Helmut Coper and Prof. Stanisław Wolfarth and financially supported by 3 DFG grants, 2 BMBF grants and statutory funds of the Free University of Berlin on the German side and by statutory funds of the Institute of Pharmacology PAS in Kraków and partially by The State Committee for Scientific Research (KBN). Dr. Gert Schulze was the German principal investigator in all these projects. During this cooperation, the mechanographic device was modified and prototypic force sensors were replaced by newer ones while new software allowed not only for a more precise measurement of muscle tone but also for a concomitant analysis of electromyographic activity of flexors and extensors of the rat's hind limb in the ankle joint. Works on the construction of this device and on de-

veloping software that could control its function had been performed by a whole research team of which Dr. Schulze was an important member, thanks to his interest in technical issues and information technologies. Three copies of the device were constructed and one of them was used in Berlin.

The device, called mechano-electro-myograph was used for studies on the relationship between the electromyographically measured reflex response and muscle tone, performed in Berlin and in Kraków. The investigations indeed demonstrated the dependence between muscle tone and long-latency supraspinal reflex response of gastrocnemius muscle in young male and female rats. Then, similar measurements were performed in old female rats. Our bilateral cooperation was extended when the project was joined by the research group of Prof. Irena Hausmanowa-Petrusewicz and Prof. Anna Kamińska from the Mirosław Mossakowski Institute of Experimental and Clinical Medicine PAS and the Clinic of Neurology of Medical Academy in Warszawa, who were experienced in electromyography and investigation of skeletal muscle morphology. This trilateral cooperation helped to obtain electromyographic and morphological evidences of the features of chronic denervation of the hind limb muscles in old rats. In addition, muscle stiffness in the hind limbs was documented in those rats which was not dependent on reflex response but was associated with deposition of non-elastic connective tissue in the muscles. Moreover, the studies showed that, in opposite to muscle stiffness in old rats, rigidity observed in animal models of Parkinson's disease (after 6-OHDA, haloperidol or fluphenazine administration) is the result of excessive reflex response of muscles. Models of the rigidity of parkinsonian type in rats were used to examine potential antiparkinsonian drugs, including ligands of NMDA receptor complex.

An image analysis system (MCID, St. Catharines, Ontario, Canada) purchased by the Free University of Berlin within the framework of one of the German-Polish grants supported by DFG was used jointly with Dr. Schulze to perform the autoradiographic studies of NMDA, AMPA and D2 receptor levels in the rat brain which demonstrated the age-dependent loss of these receptors. The paper co-authored by Dr. Schulze was awarded the prize for the best article published in Polish Journal of Pharmacology in 1997, while the series of publications entitled „Different mechanisms of muscle rigidity in Parkinson's disease and during

aging: Data from animal models” was given the award of the Department of Medical Sciences, Polish Academy of Sciences in 1999.

In addition, an attempt was made to answer the question whether receptor changes observed in the brain were implicated in the development of motor and cognitive deficits in old rats. In order to examine the latter disturbances, rats' performance in complex behavioral tasks in the T-maze was examined. The maze was invented and constructed in Berlin in the 1980-ties with the contribution of Dr. Schulze. It was composed of six T-shaped intersections where the animal's change of location was registered by means of infrared sensors, connected to PC for analysis of a number of behavioral parameters. All programs analyzing mechanographic, electromyographic and maze studies generated a vast body of data and they had to be systematized before their correlation with biochemical data was possible. To achieve that goal, Dr. Schulze chose factor analysis with the promax rotation. The factor analysis is used to reduce variables by grouping the highly intercorrelated experimental data into common sets i.e., factors. Afterward, in order to discover significant relations between these factors, a canonical correlation analysis was used. The effect was worth the huge and laborious work performed by Dr. Schulze. He showed that both motor deficits measured mechano-electro-myographically and disturbances of motor and cognitive functions recorded in the T-maze test in aging were dependent on the loss of NMDA but not AMPA or D2 receptors. After the grant expired, on the initiative of Dr Schulze, the image analysis system was first lent and then donated by the Free University of Berlin to the Institute of Pharmacology PAS in Kraków where it had been used till 2011.

Since 2001, joint Polish-German grants were headed by Prof. Hans Rommelspacher on the German side and on the Polish side first by Prof. Stanisław Wolfarth and since 2003 by Prof. Krystyna Ossowska who succeeded Prof. Wolfarth as the head of the Department of Neuro-Psychopharmacology, Institute of Pharmacology PAS. These projects were funded by BMBF and KBN and focused on pathomechanisms of Parkinson's disease and on searching for neuroprotective therapies. The studies were conducted both *in vitro* and *in vivo* on rats. Papers published jointly with Dr. Schulze demonstrated also neurotoxic action of certain endogenous tetrahydroisoquinoline and β -carboline derivatives and the pesticide paraquat on dopa-

minergic neurons. Administration of these substances in rats allowed for development of new animal models of Parkinson's disease.

After retirement, Dr. Schulze continued the cooperation with the Institute of Pharmacology PAS. He regularly visited Kraków because he wanted to get again a breath of the atmosphere of a laboratory and to feel needed. On his initiative, the Institute of Pharmacology was given precise actometers (cages for measurement of motility of rats equipped with 16×16 infrared beams located on X and Y axes) as a gift from Berlin. These cages were designed by Dr. Schulze and Dr. J. Wolffgramm and manufactured by GERB Elektronik GmbH in Berlin in the 1980s. However, both control and data analysis software were based on the old operating system DOS while commands and manuals were written in German. In order to make work of Polish colleagues easier, Dr. Schulze generously translated all materials into English and succeeded in transferring the software into Windows environment, finally, he also helped to implement the use of those devices in the Institute of Pharmacology. In the last years, he also actively participated in research conducted in the Department of Neuro-Psychopharmacology. He helped with data analysis and discussion, edition of manuscripts and gave valuable advises to Polish colleagues to solve many scientific and administrative problems.

For more than 20 years, the above-described cooperation of the Institute of Neuro-Psychopharmacology in Berlin with Polish pharmacologists had been close and very vivid. The laboratory in Berlin was visited by a dozen or so scientists from Kraków and Warszawa, who always were very pleased to come there thanks to a warm and friendly atmosphere. On the other hand, Dr. Schulze regularly visited Kraków (in total about 50 times) and together with Polish colleagues participated in symposia and congresses. Sixteen original papers, cited 187 times were published jointly. The last paper appeared in *Brain Research* in 2012.

Remembering Dr. Schulze, one cannot leave his personality unmentioned, as it was vital for his relations with Polish colleagues. He was a well-mannered, gentle and modest person. For these reasons, he was well-liked and highly regarded and his every visit to Kraków was awaited with joy. For Polish pharmacologists, he was much more than only a foreign partner, he became an integral part of their team. Private contacts after hours in Berlin and Kraków, shared

tours, visits to museums, listening to concerts and operas and long-hour talks on different topics allowed to get a better reciprocal knowledge of cultures and to learn how to understand the mentality of both nations. We, his former colleagues, grieve for a highly valued friend. We will always remember him as a good and reliable man who helped us considerably on our way through the highs and lows of our laboratories during decades together.

He will remain in our memories as a fascinating, wise man with a warm smile, a lover of Thomas Mann, Franz Schubert and Richard Wagner.

*Professor Helmut Coper
Professor Krystyna Ossowska
Professor Hans Rommelspacher*