

60 Years of Sleep Medicine at the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague

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The Sleep Centre of the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague was founded by that renowned Czechoslovak neurologist Bedřich Roth. B. Roth was born in 1919 in Slovakia where he also spent his young years. After the outbreak of World War II, he fled to Switzerland to start his medical studies there which he subsequently completed in Paris. On his return to post-war Czechoslovakia, he started his medical career first at the hospital of Hradec Králové, from where he soon moved on to the Department of Neurology in Prague's Kateřinská Street, then headed by Professor Kamil Henner. That was where he spent years working as a physician, teacher and scientist until his death in 1989. Bedřich Roth was not only an experienced neurologist but also one of the first Czechoslovak electroencephalography specialists, and it was exactly his notable skills in electroencephalography that facilitated his establishment in the field of research into sleep disorders. His professional interest in sleep dates back to the late 1940s. It was as early as 1951 that he made his first recordings of sleep at Henner's department of neurology and that – as a man of vision – he started developing a sleep laboratory as one of the world's first. His first monograph on narcolepsy appeared in 1957. In the 1960s, Bedřich Roth established co-operation with prominent colleagues abroad, in particular with Rechtschaffen (USA), Passouant (France), Koella (Switzerland), with a group of specialists of the then rising sleep centre at Stanford University, California, and with a number of others. It was also during the 1960s that he developed his own classification of sleep stages, a system which remained in use until the end of the 1980s, mainly in Czechoslovakia of the time. In those days, Bedřich Roth had accumulated a great deal of experience of narcolepsy and idiopathic hypersomnia because he was an excellent clinician and because his cohort of patients was then the largest anywhere in the world. He was the first to describe idiopathic hypersomnia. In Chicago in 1968, he took part – as one of the eight authors – in the drafting of "A manual of standardised terminology, techniques and scoring system for sleep stages of human subjects", which is still in use as a basic rule. In the 1970s, notwithstanding considerable restriction of opportunities for travel and suppression of independent research work, Bedřich Roth continued his study of narcolepsy and idiopathic hypersomnia. He took a share in the foundation of the European Sleep Research Society (ESRS), a medical organisation officially founded at its first Congress in Basel in 1972. It was about then that he became friends with Roger Broughton of Ottawa; their cooperation then gave rise to a number of scientific publications and to the third monograph on narcolepsy and hypersomnia. In the 1980s, our group with Bedřich Roth in charge, in cooperation with the Max Planck Institute of Munich, had a share in the first research into narcolepsy relative to the HLA system. In the field of sleep research and sleep medicine, Bedřich Roth is on record for training a number of followers, in particular the authors of the present article. Following a protracted disease, Bedřich Roth died close before the end of the communist rule in 1989.

As already mentioned above, Bedřich Roth was the first in the then Czechoslovakia to launch a systematic study of sleep disorders. Unfortunately, owing to the adversities of the political and economic situation and also due to absolutely no support from the health-care bodies of the day, further development of his sleep laboratory was halted in terms of material provisions – in marked contrast to the situation in all the major already established or subsequently launched centres of sleep research in the western countries. That was why, after the period of communist socialism came to an end, the sleep research laboratory founded by Bedřich Roth had to start practically from scratch money-wise.

Soon after the change of regime, a modern sleep laboratory slowly started coming into existence at the Department of Neurology, thanks – among other things – to the fact that S. Nevšimalová and K. Šonka, still in their teacher's last year of life, were able to learn about modern sleep medicine during their long-term study visits abroad (S. Nevšimalová at Professor Broughton's in Ottawa, K. Šonka at Professor Billiard's in Montpellier).

The material situation of the sleep laboratory took a rather long time to improve, thanks mainly to grants. The first achievement consisted in the addition of a time synchronised video recorder and pulse oxymetry to the original adapted analogue 8-channel EEG apparatus Bioscript. Multiple sleep latency testing (MSLT) was introduced in the mid 1990s. In 1992 the department acquired a four-channel system for limited polygraphy – MESAM 4 – for routine investigation of snorers with suspected sleep apnoea. In 1994, sleep apnoea started being treated with the method of continuous positive airway pressure (CPAP), first with manual pressure titration during nocturnal polysomnography. In those days, thanks to the courtesy of the company Lékařská elektronika, the laboratory had the use of a Respisomnograf, one of the first digital polysomnographs.

As from the early 1990s, close cooperation was in progress with other Hospital and Medical Faculty Departments; first with the ENT Department, with the 3rd Department of Medicine, with the Department of Psychiatry and the 1st Department of Tuberculosis and Respiratory Diseases, later on also with the Department of Stomatology and subsequently with the 2nd Department of Medicine. In 1996, MESAM 4 was replaced by two eight-channel devices POLYMESAM. A major turning point in the history of the sleep laboratory came with the acquisition of a modern digital 16-channel video polysomnograph BrainLab. The Department of Neurology, then headed by Prof. Jiří Tichý, MD., acquired it from the Municipality of Prague thanks to kind help from Prof. Laštovka, MD., in 1997. From that moment on, the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague, can boast running a full-scale sleep laboratory.

The salient point in the recent history of the sleep laboratory came in the year 2000 when Prof. S. Nevšimalová, MD., was in charge of the Department. The laboratory moved to new premises in the northern wing of the Department's

main building (former X-ray ward) where it had use of two separate rooms for patients undergoing videopolysomnography or videoelectroencephalography, a central operation room, record evaluation room and sanitary facilities for patients and for the staff. At that time, the technical facilities were upgraded from grant-based funds by the addition of another recording unit, a central server and an independent evaluation unit supplied by the same manufacturer as the previous polysomnograph to form an integrated operating network for polysomnography, and videoelectroencephalography. Called Monitoring Unit, the sleep laboratory, together with its outpatient unit, soon acquired the status of a Centre for Sleep and Wake Disorders (“The Centre”). More technicians were recruited as the Monitoring Unit continued working round the clock, seven days in a week. The Monitoring Unit also began applying long-term videoelectroencephalography to patients with diagnosed and/or suspected epileptic involvement. In 2006, the Department’s paediatric division acquired another polysomnograph made by the same manufacturer and linked to the network. The latest expansion occurred in the year 2010 with Prof. E. Růžička, MD., as head of the Department, when one three-bed room was added to the laboratory and the record evaluation room moved to a place in the southern wing of the building. At the same time, the Monitoring Unit was made an independent ward of the Department. The former record evaluation room began to serve clinical investigation of hospitalised patients and routine medical paperwork with scope for the addition of another polysomnography bed. Consequently, the Monitoring Unit now has use of 4 BrainLab PSG recording units (with one unfortunately as a standby only) and four computers equipped with licensed analysis BrainLab software. The Monitoring Unit also has at its disposal a number of modern technological devices for limited polygraphy, several self-adjusting CPAP and Bilevel positive airway pressure (BiPAP) systems and a set for adaptive servoventilation. The laboratory is staffed with five technicians working in a shift-work regimen, and two on daytime shifts. Outpatient service is provided as part of the Department’s outpatient ward.

All the above listed organisational changes gradually helped to step up the Monitoring Unit’s activities from sporadic afternoon recording sessions and from exceptional nocturnal recordings during Prof. Roth’s lifetime up to the present everyday diagnostic and therapeutic hospitalisations of a number of patients. The Centre now takes diagnostic and mostly also therapeutic care of patients with all kinds of sleep and waking disorders. (A certain limitation pertains to the group of insomnias because the Centre is not primarily aimed at such pathologies and cannot offer psychotherapy, the basic therapeutic procedure in such cases.)

Many of the Department’s physicians have either worked at or at least taken part in the work of the sleep laboratory and, of late, the Monitoring Unit. We have to mention namely colleagues (chronological order) M. Pretl, R. Hofmannová, S. Dostálová, P. Frimmelová, K. Blažejová-Švejsová, D. Hořínek, P. Bušek, M. Jakoubková-Klementová, P. Hnídková-Šourková, J. Vaňková-Bušková,

I. Štěpánová-Příhodová, E. Maurovich Horvat, D. Kemlink, J. Kelemen, J. Volná, J. Vávrová, T. Roučková-Vorlová, J. Piško, L. Plchová and Z. Šrůtková who helped in daily routine medical work and scientific activities of the Centre in the past 20 years. Of late, most of the young neurologists of the sleep group have been able to take advantage of short-term or longer-term stays abroad (Gent, Göttingen, Ingolstadt, Milano, Montpellier, Munich, Lyon, Paris, Regensburg, Rome, Troina, Zurich and other cities). Studies in sleep disorders have provided the ground for the defence of four post-graduate doctoral theses in the discipline of Neurosciences, five Candidate of Sciences theses in neurology, three Doctor of Sciences theses, two habilitation thesis in neurology and two professorships in the field of neurology. In the past two decades, assistance from the Sleep Laboratory and later from the Centre have helped to materialise three research plans of the Ministry of Education, Youth and Sports, six grants under the aegis of the Grant Agency of the Ministry of Health, three grants of the Charles University Grant Agency, two grant projects of the Grant Agency of the Czech Republic, two grants of the Ministry of Education, Youth and Sports “Kontakt”, one grant of the Ministry of Transport, an international 6. RP EU ENRAH grant and an international PHEA (“nEUroped”) grant project. Completed grants received very good rating.

The Department of Neurology sleep centre has, in the past years, been in close contact with many research centres abroad – Stanford University, California, departments of neurology or sleep medicine in Montpellier, Leiden, Treysa-Schwalmstadt, Regensburg, Edinburgh, Košice, with the Institute of Human Genetics (Technische Universität München), Max Planck Institute, München and others; the Centre is a member of the European Narcolepsy Network and the European Sleep Apnoea Database (ESADA). As for the Czech Republic-based cooperating centres, the Institute of Physiology, Academy of Sciences of the Czech Republic (Prof. Illnerová, Dr. Sumová) and the Institute of Hematology and Blood Transfusion (Dr. Dobrovolná) deserve special mention.

The Sleep Centre owes its international renown to its founder – Bedřich Roth, himself the author of many publications and speaker at many congresses abroad where his papers were invariably seen as milestones of sleep medicine. Thus, Web of Science refers to a total of 78 original sleep focused publications by authors from the sleep group of the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague. While before the end of the 1990s, only isolated publications appeared annually, the number of impacted original publications rose to some five or six from the year 2001 on – to reach as many as ten original articles in the year 2009 (Figure 1). Similarly, the citation rate of sleep-related works by authors from the Department of Neurology has been rising steadily since 2001 and continues growing unabated (Figure 2). According to the Web of Science, to the date of March 1st 2011, the most frequently cited study by members of the sleep group of the Department of Neurology was: “A mutation in a case of early onset narcolepsy and a generalized

absence of hypocretin peptides in human narcoleptic brains” by Peyron C., Faraco J., Rogers W., Ripley B., Overeem S., Charnay Y., Nevsimalova S., Aldrich M., Reynolds D., Albin R., Li R., Hungs M., Pedrazzoli M., Padigaru M., Kucherlapati M., Fan J., Maki R., Lammers G. J., Bouras C., Kucherlapati R., Nishino S., Mignot E. in *Nat. Med.* 2000, 6: 991–917 (a total of 709 citations). As for the most frequently cited work with a researcher from the Department of Neurology topping the list of authors: “PTPRD (protein tyrosine phosphatase receptor type delta) is

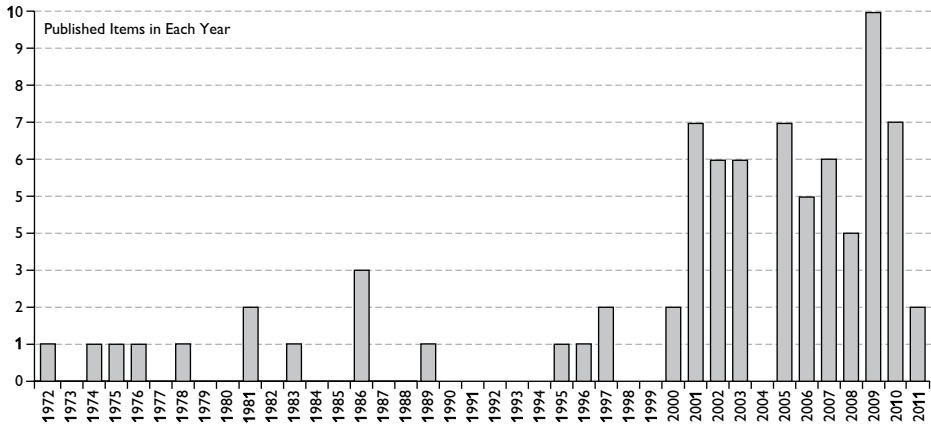


Figure 1 – Annual number of original scientific articles focused on sleep published in journals with impact factor by members of the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague (Web of Science, March 1, 2011).

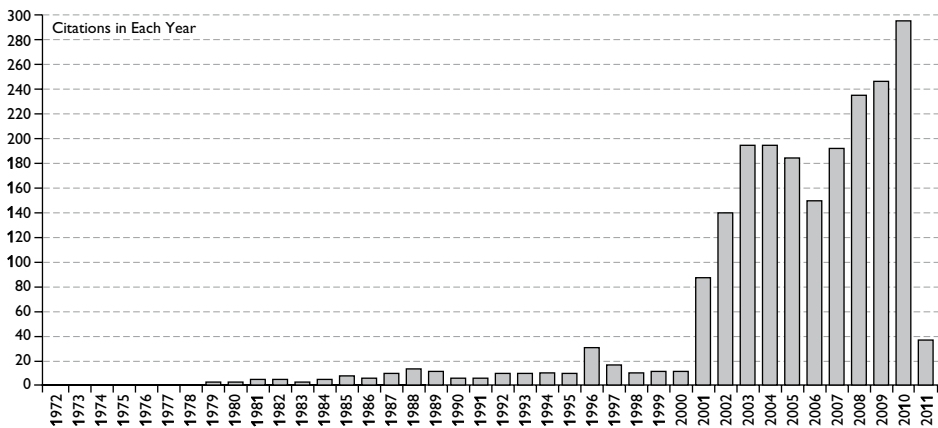


Figure 2 – Annual citation number of articles focused on sleep and published by members of the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague (Web of Science, March 1, 2011).

associated with restless legs syndrome” by Schormair B., Kemlink D., Roeske D., Eckstein G., Xiong L., Lichtner P., Ripke S., Trenkwalder C., Zimprich A., Stiasny-Kolster K., Oertel W., Bachmann C. G., Paulus W., Högl B., Frauscher B., Gschliesser V., Poewe W., Peglau I., Vodicka P., Vavrova J., Sonka K., Nevsimalova S., Montplaisir J., Turecki G., Rouleau G., Gieger C., Illig T., Wichmann H. E., Holsboer F., Müller-Myhsok B., Meitinger T., Winkelmann J. in *Nat. Genet.* 2008, 40: 946–948, scored a total of 34 citations, with the first two authors having contributed an equal part. Next as the most frequently cited work by local authors comes: “Depression in narcolepsy and hypersomnia” by Roth B., Nevsimalova S. in *Schweiz. Arch. Neurol. Neurochir. Psychiatr.* 1975, 116: 291–300 (a total of 31 citations). The Department of Neurology sleep group’s main line of research is what are known as central hypersomnias (narcolepsy, idiopathic hypersomnia and Kleine-Levin syndrome), restless legs syndrome, sleep disordered breathing, sleep disorders associated with other, especially neurological diseases, and circadian rhythm disorders.

In 1991, the Department of Neurology sleep group started holding annual meetings of neurologists specialising in sleep disorders. In this way, the group helped to a great deal promote the foundation of other centres of sleep medicine in the Czech Republic. First, the meetings were just afternoon sessions of papers presented by invited local and international speakers on the premises of the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague, and, towards the end of the 1990s, independent expert events with announced as well as solicited papers (for some time, these were called Prague Sleep Apnoea Symposia). In the year 2001, after a few years of informal meetings and cooperation, M. Moráň, S. Nevšimalová, P. Rambousek, P. Smolík, K. Šonka, M. Trefný, and J. Vyskočilová founded the Czech Society for Sleep Research and Sleep Medicine (ČSVSSM), an interdisciplinary organisation officially resident at the Department of Neurology. The Centre for Sleep and Wake Disorders has provided training for a number of Czech and foreign specialists in the field of sleep medicine.

The ČSVSSM served as the local organiser of the successful 17th Congress of the European Sleep Research Society held in Prague in October 2004. Prague had been chosen to host the event thanks to the reputation of the Department of Neurology Sleep and Wake Disorders Centre and to the efforts of Prof. S. Nevšimalová, who also chaired the local organising committee and who takes most of the credit for the successful course and outcome of that important medical gathering. In the year 2009, the Department – in cooperation with the ČSVSSM and with support from the European Sleep Research Society – organised an international Symposium on narcolepsy and hypersomnia to mark the unattained 90th birthday of Bedřich Roth. Running parallel with the Symposium, an ERS course in excessive daytime sleepiness was taking place.

Taking stock of the 60 years of existence and especially of the past twenty years of the Department’s sleep group justifies undiluted optimism. The Department

succeeded in developing a modern sleep centre of world standard capable of generating scientific output (the most significant of all the post-socialist countries) and training more specialists in this branch of medicine. Our young colleagues find sleep medicine at the Department of Neurology attractive, and the authors of this article are pleased to state that we can be looking forward to further achievements in upholding the heritage of Bedřich Roth.