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Manasseina, Pavlov and the Russian School

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Next year we'll celebrate the 170th anniversary of the birth of Maria Mikhailovna Manasseina-Korkunova (1843 – 1903), also known as Marie von Manassein and Marie de Manacéine, a pioneer experimental somnologist. Manasseina published articles in Russian, French and German, and she is sometimes mistakenly referred to as a French or German male scientist. Maria Manasseina worked as a physiologist in St. Petersburg from 1872, performing studies in dog puppies with prolonged deprivation of sleep using forced walking and handling. She came to the conclusion that the main effects originate in the brain itself and are very different from that associated with 20 – 25 days of starvation. Manasseina concluded that sleep is more important for an organism than food, and rejected “the strange opinion regarding sleep as a useless, stupid and even noxious habit”. In 1892, Manasseina published a sizeable hardcover volume entitled “Sleep as one third of human life, or physiology, pathology, hygiene and psychology of sleep”. Its revised and significantly expanded version was later published in English (1897) and Swedish. According to Manasseina, “scientists who regarded sleep as a cessation or diastole of cerebral activity are mistaken, for during sleep the brain as a whole does not sleep at all, it does not stay idle entirely, but only those parts of it which constitute an anatomic substrate of consciousness are under the process of sleeping”. “Sleep is a time for the rest of our consciousness”, she wrote. This book on sleep was the best known of all Manasseina’s works and positive reviews were published in “Philosophical Reviews” and “Science” in 1898.



Photo 1. Maria Manasseina (1860ties) and her original book

Manasseina presented her results at the International Congress of Medicine in Rome (1894). Her works had a tremendous impact on sleep science. In 1896 two American psychologists, G. T. V. Patrick and J. A. Gilbert, clearly inspired by Manasseina’s pioneer work, performed the first study of sleep deprivation in humans, and in 1898 three Italian investigators, L. Daddi, G. Tarozzi and C. Agostini, also inspired by her studies, performed more detailed investigation of sleep deprivation in dogs. Later, at the beginning of the 20th century, the Japanese scientist K. Ishimori and the

French scientist H. Piéron, independently made the first attempts to explore the accumulation of sleep substances (“hypnotoxins”) in a sleep-deprived organism and their transmission to non-deprived animals (donor-recipient transfusions). Being influenced by Manasseina’s work, both researchers referred to her book and followed Manasseina’s method of sleep deprivation in their experiments, also on dogs (see Kovalzon, 2009, for the references).

It is well known that the great Pavlov was very much interested in sleep problems, considering sleep as the key to his theory of higher nervous activity. Everyone knows his definition of sleep as a “spreading cortical inhibition”. After the discovery of paradoxical (REM, dreaming) sleep, it seemed that Pavlovian theory had become hopelessly obsolete in this respect. Indeed, the idea of the creation of the “physiology of dreaming” could not come to his mind. However, if we take into account slow wave (NREM, orthodoxic) sleep, “sleep in general”, and recall some recent discoveries, such as the strong activation of inhibitory neurons and the release of their mediators – GABA, galanin, adenosine, starting in local hypothalamic areas and gradually spreading through the neocortex; or the extreme hyperpolarization of thalamo-cortical neuronal network which, being alternated with brief depolarization periods, predominates during this state, we can hardly come to the conclusion that this fully intuitive idea of Ivan Pavlov about sleep was completely wrong.



Photo 2. Ivan Pavlov (1849 – 1936)

At the end of his long life, in 1935, Pavlov wrote: “It is clear that our diurnal working is nothing but a sum of irritations that is the cause of a correspondent sum of exhaustion and when this sum of exhaustion comes to the end it induces automatically, by internal humoral way, the inhibitory state followed by sleep”. This formulation could be regarded as prophetic – it actually sounds quite contemporary.

Russian-originated scientists and their ideas have certainly played an important role in history of sleep science. It would be sufficient to remember that Nathaniel Kleitman (1895 – 1999) was born in, and graduated from a secondary school in, Kishinev, Russia (now in the Republic of Moldova). Russian was his native language, and it was a paper of the Russian authors M. P. Denisova and N. L. Figurin “Periodic events in children sleep” (1926) which became the starting point for the revolutionary discovery of REM sleep in 1953 (Dement, 2001).

Despite the great detriment caused to Russian physiology by the victory of dogmatics (approved by Stalin) at the so-called “Pavlovian session” in 1950, during the post-Stalin period (60ties – 80ties) basic studies of the mechanisms of sleep-

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wake regulation were performed in the Soviet Union on a large scale in dozens of laboratories. Several names are particularly noteworthy: Nikolay Grashchenkov (died 1966) who organized the Laboratory of Nervous and Humoral Regulations at the USSR Academy of Sciences in Moscow; his disciples Aleksandr Vein (died 2003), the founder of sleep medicine and human sleep physiology in Russia, and Lev Latash (died 2002, in the U.S.A.); the living authority Aleksandr Shepoválnikov, the author of the first Russian monograph "Activity of the sleeping brain" (1971) who is actively working as before at the Sechenov Institute of Evolutionary Physiology and Biochemistry, Russian Academy of Sciences, St. Petersburg; three other sleep researchers from the latter city: a known specialist in sleep evolution Ida Karmanova (died 2005) from the same Institute, who published two books in English (Karmanova, 1982; Karmanova, Oganessian, 1999) and a book of poetry "Maski sna" (Masks of sleep), 1991; the late Natalia Moiseeva, a specialist in human sleep EEG from the Institute of Experimental Medicine, Academy of Medical Sciences; the late Nikolay Demin, specialist in sleep biochemistry, from the Pavlov Institute of Physiology, Academy of Sciences; Aleksandr Kogan (died 1989), the chief of the physiology school in Rostov-on-Don; three latter researchers were the authors of an early Russian monograph on sleep (Demin *et al.*, 1978); and Tengiz Oniani (died 2012), the chief of the Georgian sleep school, Tbilisi. The first all-night human sleep recording in Russia was performed in 1968 at the above-mentioned Grashchenkov lab by Nikolay Yakhno (1st Moscow Medical University), Lev Sumskiy (Sklifosovskiy Institute of Emergency Medicine, Moscow) and Vadim Rotenberg (the retired senior lecturer of Tel-Aviv University, Israel) using an old Alvar electroencephalograph. Several international scientific conferences on sleep took place in Leningrad and Tbilisi, and several world known sleep researchers were invited, including Michel Jouvet, Ian Oswald, Ismet Karacan, Wilse Webb and Allan Hobson. As the most important contribution, the discovery of uni-hemispheric slow wave sleep in dolphins by a group of researchers from Severtsov Institute, Russian Academy of Sciences, Moscow, led by Lev Mukhametov should be mentioned, which took place at the beginning of the 1970s. A 35 year experience of the study of dolphin sleep was recently reviewed by Oleg Lyamin *et al.* (2008).

During the 1990s, after the breakdown of the USSR and a disastrous decline in basic science support in Russia, the greater part of fundamental sleep research was discontinued. However, during the 2000s research gradually revived in several labs in Moscow, St. Petersburg and Rostov-on-Don. A new lab for the study of neurobiology of wakefulness and sleep was established at the Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow. This is led by Vladimir Dorokhov, Ph.D., and recently joined the ESRS Consortium of Sleep Labs. The professional organization for somnologists, the somnology section of Pavlovian physiological society (Russian Somnological Society) was founded in 2007, and is led by Vladimir Kovalzon (Severtsov Institute Ecology/Evolution, Russian Academy of Sciences, Moscow), Vladimir Dorokhov (Institute Higher Nervous Activity/Neurophysiology, Russian Academy of Sciences, Moscow) and Yevgeniy Verbitskiy (Southern Scientific Center, Russian Academy of Sciences, Rostov-on-Don). This organization unites mostly experimental and basic human sleep researchers and manages International workshops e.g. "sleep as a window to the world of wakefulness" (supported by IBRO) every second, odd-numbered year. The 6th workshop successfully took place in October 6 – 8, 2011, in Moscow with participation of 65 students from 7 European countries. Also, sleep medicine is greatly developing, several dozens of clinical centers were

created, including more than 20 centers in Moscow, the most important of them led by Alexandr Kalinkin, Mikhail Poluektov, Roman Buzunov, Gennadiy Kovrov and Mikhail Agaltzov. The National Society of Pediatric Sleep Specialists was founded in 2007, and the National Society on Somnology and Sleep Medicine was founded in 2010, both founded and led by Yakov Levin (the 1st State Medical University, Moscow), and units mostly medical doctors. After the sudden death of Prof. Levin on March, 31, 2012, both societies are now chaired by Mikhail Poluektov, M.D. These latter organizations now support conferences entitled "Actual problems of somnology" in the even-numbered years, which were started by Prof. A. Vein in 1998. The 8th Conference will take place in Moscow, November 22 – 23, 2012. Integration of all the societies into the Russian Sleep Federation is now under discussion among the members. A state-of-the-art review of basic somnology was recently presented in Russian (Kovalzon, 2011). So despite all the historical difficulties, Russian somnology is alive and developing in the second decade of the 21st century.



Photo 3. A group of Russian somnologists at the last ESRS Congress in Lisbon, 2010. From left to right: Igor Timofeev (Laval, Québec), Vladimir Dorokhov (Moscow), Ivan Pigarev (Moscow), Roman Yassenkov (Leiden), Vladimir Kovalzon (Moscow).

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