

Kamen Usunoff and His Scientific Contribution to Neuroscience: Scientific Rite of Passage

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The current paper summarises the outstanding scientific contribution made by Professor Kamen Usunoff to the neuroscience and neuroanatomy. He contributed fundamentally to our knowledge of the (1941-2009) nervous system. He was one of the important anatomists that achieved remarkable success in brain research by understanding pathogenesis of neurodegenerative diseases. Some data about his scientific and academic career are also provided. Professor Usunoff is highly recognised as a leading scientist and teacher who has made significant contribution to the development of the Bulgarian morphological school.

Key words: neuroscience, basal ganglia, amygdala, pain

Introduction

A rite of passage marks an important stage after a person's death to place its definitive scientific identity. The young Bulgarian scientists hardly remember or know of Kamen Usunoff's scientific inheritance. Therefore, let's start with some remarkable moments in his life (don't expect a chronological overview). Kamen participated in a scientific exchange between Leiden's Neuroanatomy and Sofia's Anatomy (Prof. Wladimir Ovtsharoff) instigated by both governments, but without financial support in 1990. The 3th October is "Leidens Ontzet" (Leiden's relief (1574) of the Spanish occupation of Holland during 16th and 17th century). Walking back from the lab, we were stopped by the 3th October festival procession. In front of us an open trailer with women dressed as Wrens (Woman's Royal Navy Service) singing Second World War songs. To my surprise Kamen knew the songs by heart, he knew them all, the consequence of the free post-war time in Bulgaria? His memory of the songs was incomprehensibly good. Bulgarian radio refused to let Kamen participate any longer in the game "guess the song". He always won.

Kamen went with his father to London. His father, a well-known psychiatrist, was invited due to his excellent studies on alcoholic encephalopathies (a real pestilence around 1940-1955). Kamen noticed the underhand sniggering of his father's colleagues due to his bad English. Because of this he achieved excellent English by self-study.

During his military time in communist Bulgaria, Kamen had to do sports as all people in the military had to. He chose wrestling and boxing. His technique caused him to become a Bulgarian military wrestling champion. Although he had the possibility to participate in the international wrestling arena, it never happened.

Kamen started his medical studies in 1961 in Sofia and finished in 1967 and then became a member of the Anatomical Department of the Medical University, Sofia, in the same year. His further specialisation in 1972 occurred in Germany in Frankfurt am Main in the department of Prof. Dr Rolf Hassler (1914-1984; head of the Max Planck Institute), known for his substantia nigra studies and stereotactic treatment of Parkinson patients. A remnant of that time was Kamen's strong support of Hassler's subdivision of the human substantia nigra [14].

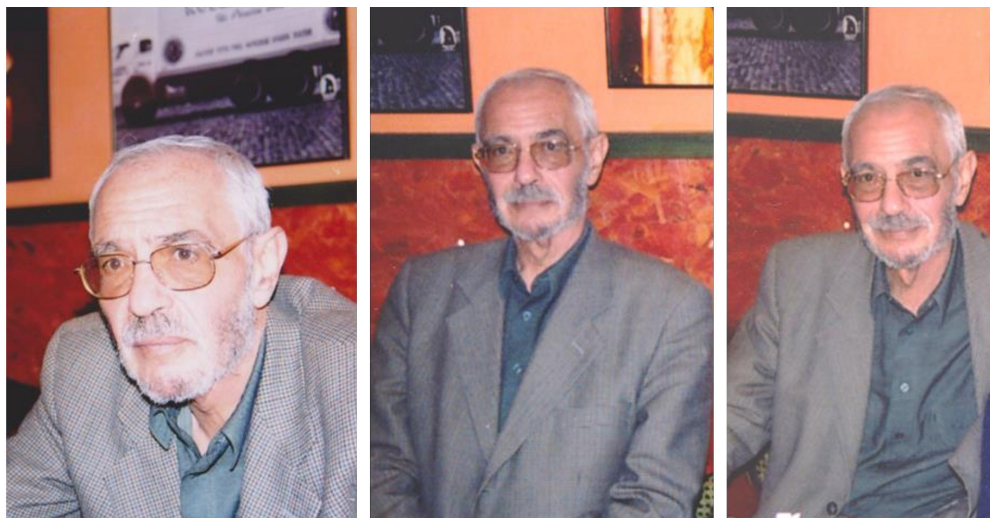


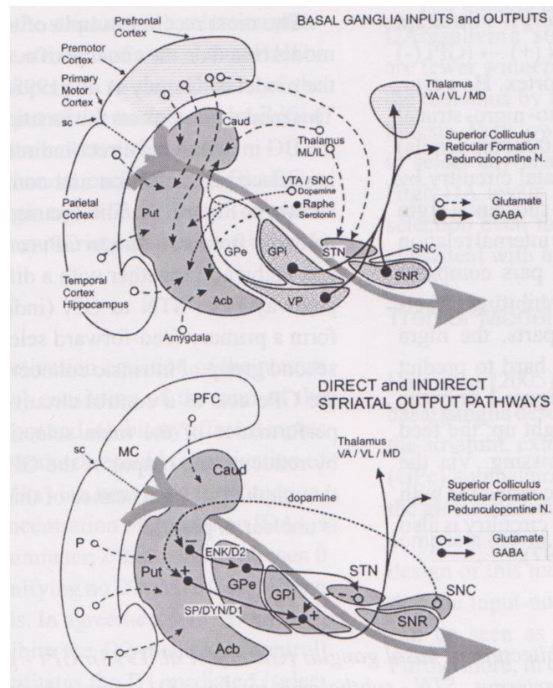
Fig. 1. Kamen Usunoff, “remember his piercing glance during straight forward discussion. Personally he was tough at the outside, but soft and very friendly in the inside” (photos 15-04-2005 and Chaldakov’s obituary citation, 2010) [1].

Kamen Usunoff’s Achievements in Neuroscience and Neuroanatomy

Kamen’s interest was mainly putamen, globus pallidus, substantia nigra and the subthalamic nucleus (**Fig. 2**, basal ganglia and related nuclei). He contributed to all aspects of the basal ganglia, although other brain areas, such as the amygdala, were also frequently researched. His thesis (1990) concerned: “Cytoarchitectural, ultrastructural, and histochemical characterization of the substantia nigra”; it appeared in six volumes and only parts have been published in international journals [12]. Due to the Hassler time he had an incredible overview of all neurological related diseases.

Hidden in a large article on “Neuromelanin in the human brain” [4 also 19, 20], you will find descriptions of idiopathic Parkinson’s disease, Parkinson-plus

Fig. 2. Neuroanatomical schemes for basal ganglia input and output and the direct and indirect striatal output pathways, which were Kamen Usunoff's main research areas (courtesy H. J. Groenewegen, see Groenewegen and Van Dongen, 2008) [3].



syndromes (supranuclear palsy, dementia complex, cortico-basal degeneration, multiple system atrophy, and Pick's disease to name a few) and secondary parkinsonian syndromes. Notice has been given to etiology and pathogenesis of Parkinson's disease that treats topics, now in the midst of our attention: genetics, environment, cascade of multiple deleterious factors, role of iron, glutamate excitotoxicity, role of calcium, mitochondria, glia cells and necrosis. One has to read the text carefully and, often underestimated, you will find unexpected ideas on these diseases, ready for research. An effective network kept him up to date, also due to the students he had trained in neuroscience.

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Kamen cooperated also with Andreas Wree, head of the Anatomy department in Rostock. Together they published in 2003 an overview on the pedunculo-pontine tegmental nucleus (a hardly known article) [13]. It was a forward-looking publication. The bulk of articles on this nucleus have been published between 2010-2023. It also contributed to the publication and thesis of Marcel Lourens (University Twente, 2009, 2011, 2013) [6, 7, 8] concerning the pedunculo-pontine nucleus as an alternative target for deep brain stimulation and added to the opening towards more computational modelling of this nucleus [8, 13, 22].

Kamen's Rostock cooperation was also based on his earlier amygdala studies and has been directed to this nucleus and its surrounding area. Orexinergic and nitric-oxid synthase distribution, efferent projections of the medial amygdala, parabrachial nucleus projections and amygdala-trigeminal projections, showed his immunological and connectivity interest of this nucleus of "fear and threat" [15, 17]. Next to these studies, the Rostock connection extended to pain research. Together with Propatiloff, Schmitt and Andreas Wree a monograph "Functional neuroanatomy of pain" appeared (2006) [18].

Those who think that Kamen's interests belonged exclusively to neuroscience have to be disappointed. As a real anatomist he worked together with several scientists in the department. For example, with Krassimira Michailova he studied serosal membranes. Michailova published a series of articles from 1988 on till 2006, on stomata, milky spots, transport through serosal membranes, its secretory functions and healing and regeneration of these serosal membranes under the guidance of the former head of the department Vasil Vassilev (1928-2020). The milky spots attracted Kamen's special

neuroanatomical attention because bundles of thin unmyelinated or myelinated fibers are occasionally present in the vicinity of the milky spot vessels [10]. If you have ever worked with serosal membranes one appreciates Michailova's electron microscopic pictures that are of a high quality. This cooperation produced a monograph [11] exclusively on serosal membranes of nearly all organs.

Jaap Schoen, a Dutch neurologist, who worked on the human brain at the Leiden Department of Neuroanatomy under WJC Verhaart and J Voogd, left, by his sudden death, an enormous amount of human series on brain damage, prepared with Nauta and Fink Heimer silver impregnations. Kamen, during his visits at the Leiden department, started organising the results that brought a monograph on the human trigeminal nucleus in the series of *Advances in Anatomy, Embryology and Cell Biology*. Subdivisions of the human descending trigeminus and the small trigeminal related nuclei all are given attention [16], resulting in citations in the large neuroanatomical handbooks. The human mesencephalic part of the trigeminal system was larger than anticipated in other publications. Its nearly hundred citations for a well-known human brain area, of which one should expect that everything is known, shows its importance. Incidentally trigeminal studies centered also in the rest of Bulgaria performed by Nikolai Lazarov [4, 5] and sometimes co-supported by Kamen Usunoff. The human trigeminal study posed two questions: are interneurons present in the trigeminal motor nucleus and is the cortical input mono-synaptically transferred to the trigeminal motor neurons? Its clinical consequences are clear.

In 1998 the first National congress of the Bulgarian Society for Neuroscience took place. Over 80 abstracts were present in the congress booklet. In it a series of foreign participations and of course a large in-put by Wladimir Ovtcharoff, Kamen Usunoff and Nikolai Lazarov, showing the strong activity and high quality of the Bulgarian neuroscientists, not least by Kamen's contributions.



Fig. 3. The Bulgarian neuroanatomist crew (Nikolai Lazarov, Enrico Marani, Wladimir Ovtcharoff and Kamen Usunoff) at the appointment of E.Marani's professorship in Neurophysiology (1998) at the Twente University. Kamen Usunoff at the Leiden groups outing. He was a very good story teller. The 5th December photos of Kamen with Saint Nicolas are renounced of!

In 1998 a cooperative project also started between Leiden Neuroanatomy, Sofia Anatomy and Twente's department of Biomedical Signals and Systems (**Fig. 3**). The project originated from the deep brain stimulation of the subthalamic nucleus in Parkinson's disease. The two monographs (Part I Marani et al., 2008 and Part II T. Heida et al, 2008, both together with Kamen Usunoff) [2, 9] on subthalamic's development,

topography, connections modelling and simulation of activity reached their targets: Springer sold over 5000 monographs in 2017. Since several species beside Man are used in studies on deep brain stimulation, the topography of rat, cat and baboon were included [19, 20, 21]. These distributions of the subthalamic nucleus originated from Kamen's thesis (Fig. 4). His critical reading of the neuroanatomical text increased its quality enormously and to our surprise Kamen was not unknown with subthalamic nucleus physiological activity. Note in Fig. 4 Kamen's topographic naming, while normally one encircles areas in its abstracts of figures, Kamen had an inborn overview and memory of its sections, look for example at the thalamus.

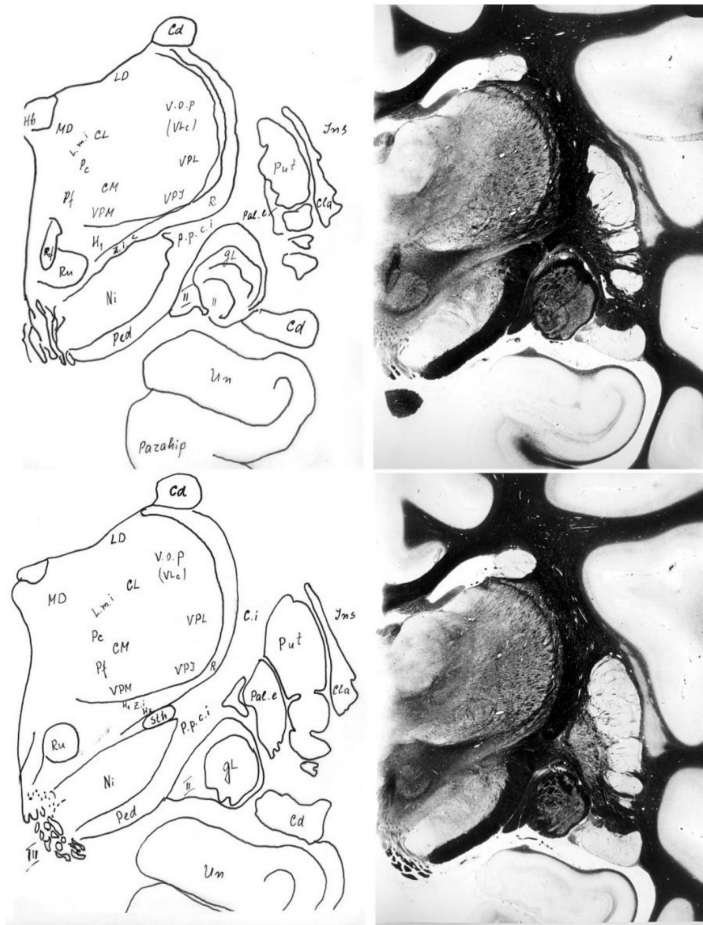


Fig. 4. Figures from Kamen's thesis and Fig. 11, in The Subthalamic nucleus part I: Transverse Waelcke and Nissl sections of the baboon's mesencephalon. Main abbreviations: cd , nucleus caudatus; ci , capsula interna; cla , claustrum; H , H1 , H2 , fields of Forel; Ni , Nic , Nir , substantia nigra, pars compacta, pars reticulata; pale , pali , globus pallidus externus and internus, respectively; ppci , pars peduncularis of the capsula interna; put , putamen; Ru , nucleus ruber; STH , nucleus subthalamicus; TcTT(R) , tractus corticotegmentothalamicus (Rinviki); VPM , VPI and VPL , nucleus ventralis posterior, intermediate and lateralis thalami; Zi , zona incerta; II , optic tract [12].

You cannot do research without assistance. At the lab the analytical women and men are of the utmost importance, as the digital supporters are (both often underestimated). Whether in Leiden, Twente or Sofia his friendly character with co-operators made working for Kamen a nice job. He sometimes had to support sad members and he was always there for them. Could he be serious on the work quality, you bet.

Kamen Usunoff contributed fundamentally to our knowledge of the nervous system (six monographs have been published, besides over 115 publications, with nearly 1600 citations and 5000 reads). Not only by his results, but also by his scientific personality, which still is expressed in a series of students he educated and who are widespread over the world. To those who worked with Kamen, his friendly, but sometimes strict attitude, showed his involvement in you.

“The past is gone, invisible, but in various aspects still with us”, which also holds for Kamen Usunoff’s scientific contributions.

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