

FOOD DIGESTION IN IVAN PETROVICH PAVLOV STUDIES ON 115 ANNIVERSARY OF HIS NOBEL PRIZE AND PRESENT AVENUES

Stanisław Berger¹, Krystyna Rejman¹

¹Faculty of Human Nutrition and Consumer Sciences, Warsaw University of Life Sciences WULS-SGGW, Nowoursynowska 159c, 02-776 Warsaw, Poland

ABSTRACT

Story of *Pavlov's* studies on food digestion including his Nobel Prize in 1904 are presented. Some new ideas and concepts are also viewed based on 3th International Conference on Food Digestion held in Wageningen (the Netherlands) in 2014.

Key words: *food digestion, fistulas, saliva, gastric juice, pancreatic juice, intestinal juice, conditioned and non-conditioned biological reflexes, enzymes*

STRESZCZENIE

Przedstawiono historię badań *Pawłowa* nad trawieniem żywności, w tym jego Nagrodę Nobla w 1904 roku. Dokonano przeglądu niektórych nowych idei i koncepcji na podstawie 3. Międzynarodowej Konferencji na temat Trawienia Żywności, która odbyła się w Wageningen (Holandia) w 2014 r.

Słowa kluczowe: *trawienie żywności, przetoki, ślina, sok żołądkowy, sok trzustkowy, sok jelitowy, warunkowe i bezwarunkowe odruchy biologiczne, enzymy*

INTRODUCTION

Food digestion is prerequisite process for its further utilization by human body. Consumed food products containing proteins, fats and carbohydrates, must be split into amino acids, fatty acids, glycerol or fatty acids, and monosaccharides before dietary tract can absorb these nutrients into blood or lymphatic circulation for further metabolism. Catalytic activities of various enzymes and emulsifiers provide crucial mechanisms starting with ca. 6.8 pH in the mouth through 1.0 pH in the stomach and 7.0 in duodenum up to 8.0 pH in the rest of the intestines [3].

The knowledge of food digestibility is very useful in the final evaluation of all nutrients bioavailability to our body. Therefore respective digestion coefficients both in humans and especially animals are used both in health and diseases. It is also important that undigested fragments (e.g. fibre) of food and “waste” products are eliminated this way through the gastrointestinal tract. Also age and/or diseases related changes in this tract are often linked with xerostomia, dysphagia, atrophic gastritis or achlorhydria. Often changes of sensory perception are also linked (usually decreasing) with age having the risk of nutrient deficiency or digestibility due achlorhydria, liver and pancreas diseases or lactose intolerance.

STUDIES OF IVAN PETROVICH PAVLOV ON FOOD DIGESTION PROCESS

It seems to be very surprising that in the famous and interesting book “A History of Nutrition” by *Elmer Verner McCollum* [6] there is a chapter (12 pages) on “Ideas about food utilization derived from studies on digestion” no single sentence is devoted to *I.P. Pavlov's* studies. As a matter of fact this scientist was never mentioned in the whole book containing index of circa one thousand names. Similarly in “A Textbook of General Physiology” by *Mitchell* [7] there is a nice chapter on digestion (41 pages) but no studies related to *I.P. Pavlov* are mentioned in the literature list, however his name was quoted several times in the text.

Therefore the authors of this paper considered that the 115 anniversary of awarding *Ivan Petrovich Pavlov* (Figure 1) the Nobel Prize in Physiology or Medicine 1904 is a right opportunity to present his studies.

As seen from the Table 1, *I.P. Pavlov* was born in the priest family in Ryazan (Russia) in 1849 and obtained education at a cleric seminary. In these times the interest in life sciences scientific literature grew very quickly in Russia. For the first time Pavlov read about digestion and saw the digestive tract schema in

Corresponding author: Krystyna Rejman, Faculty of Human Nutrition and Consumer Sciences, Warsaw University of Life Sciences WULS-SGGW, Nowoursynowska 159c, 02-776 Warsaw, Poland

an English philosopher *G.E. Lewes* book “Physiology of Common Life”, published in Russian in 1861-62. He was also deeply influenced by the study of great Russian physiologist *Ivan M. Sechenov* (1829-1905)

on brain reflexes, published in 1863. To pursue his interest *Pavlov* enrolled in 1870 at St. Petersburg University, in Faculty of Mathematics and Physics, the Department of Natural Science.

Table 1. *Ivan Petrovich Pavlov's* life – main events and achievements

	Event	Place	Date	Remarks
1.	Birth	Ryazan, Russia	14.IX.1849	Or 26.IX.1849
2.	Study at University of Saint Petersburg	St. Petersburg, Russia	1870-1875	Outstanding degree – Candidate of Natural Science
3.	Study and work at Academy of Medical Surgery, Veterinary Institute and Military Medical Academy (MMA)	St. Petersburg, Russia	1876-1879	Gold medal award for his research work in physiology at MMA
4.	Cooperation with famous clinician S.P. Botkin at MMA	St. Petersburg, Russia	1880-1883	Doctor's thesis: The centrifugal nerves of the heart (1883)
5.	Study with prof. Rudolf Heidenhain and prof. Carl Ludwig	Breslau and Leipzig, Germany	1884-1886	Food digestion in dogs – Heidenhain or Pavlov pouch
6.	Offers from University of Saint Petersburg, Tomsk University, University of Warsaw	St. Petersburg, Tomsk, Warsaw, Russia	1887-1889	No appointments
7.	Professor of pharmacology at the MMA	St. Petersburg, Russia	1890-1896	Chairmen of Physiological Department, up to 1896
8.	Director of the Department of Physiology, Institute of Experimental Medicine	Russia/Soviet Union	1897-1936	Most important center of physiological research
9.	Chairmanship of Physiology at the MMA	Russia/Soviet Union	1895-1925	
10.	Member of the Russian Academy of Sciences	St. Petersburg, Russia/Soviet Union	1901* 1907**	*correspondent member ** academician
11.	The NOBEL PRIZE in Physiology or Medicine	Oslo, Norway	10 Dec 1904	“In recognition of his work on the physiology of digestion through which knowledge on vital aspects of the subject has been transformed and enlarged”
12.	Doctor Honoris Causa of Cambridge University	Cambridge, UK	19 July 1912	Story of artificial dog filled with fistulas from students
13.	Copley Medal of The Royal Society	London, UK	1915	On the ground of his investigations in the physiology of digestion and of the higher centres of the nervous system
14.	Order of the Legion of Honour	Medical Academy of Paris	1915	
15.	President of the XVth International Physiological Congress	Leningrad and Moscow, Soviet Union	9-17 Aug 1935	Monument of the Dog
16.	Passed away	Leningrad, Soviet Union	27 Feb 1936	

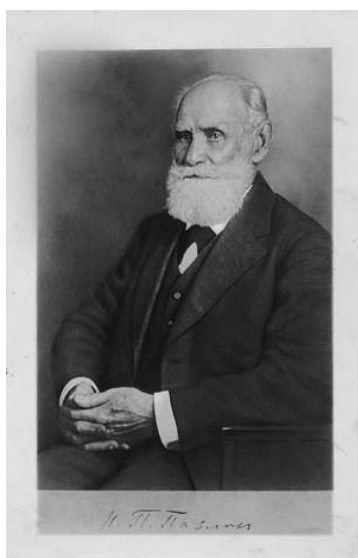


Figure 1. Portrait of *Ivan Petrovich Pavlov*
Source: <http://www.iemrams.spb.ru:8100/english/pav-photo.htm>

In 1875 *Pavlov* graduated from the University winning a gold medal for the first learned treatise on the physiology of the pancreatic nerves, developed in collaboration with *M.I. Afanasyev* (another student). *Pavlov* decided to continue studies in animal physiology and proceeded to the Academy of Medical Surgery (later Military Medical Academy) in St. Petersburg. He studied at professor *Ilia Cion* (1842-1912) and *Sergius Botkin* (1832-1880) laboratories and has learnt how to perform surgery operations.

In 1883 *Pavlov* received there PhD degree on “The centrifugal nerves of the heart”. In the thesis *Pavlov* developed his idea of nervism, using as an example the intensifying nerve of the heart which he had discovered, and furthermore laid down the basic principles on the trophic function of the nervous system. Soon he received a foreign scientific internship in physiology and in the years 1884-1886 continued his research in Germany, in Breslau (Wrocław) in Professor *Rudolf Heidenhain’s* laboratory, then in Leipzig (Lipsk) with Professor *Carl Ludwig* at the Institute of Physiology. Working with these two famous scientists *Pavlov* became acquainted with the functioning of the intestinal organs, including several aspects of food digestion from the mouth to the large intestine (e.g. saliva production or motility of the gastrointestinal tract), including the complex role of the nervous system, as suggested by *R. Heidenhain*. During his stay in Germany, *Pavlov* studied the digestion in dogs using an exteriorized section in the stomach perfecting the technique by overcoming the problem of maintaining the external nerve supply. This section of stomach became known as the *Heidenhain* and/or *Pavlov* pouch (pocket or small stomach). It was very helpful in explaining conditioning and involuntary reflex actions, using implanted fistulas (for collecting stomach

juice). *Pavlov* knew and studied different points along whole the dog digestive tract, particularly stomach, where esophagostomy (Figure 2) was performed. Every day in the morning and the evening (sometimes also in the midday) *Pavlov* collected saliva or stomach juice. He was also using and perfecting an exteriorized section of the stomach improving technique by overcoming the problem of maintaining the external nerve supply.



Figure 2. *Pavlov* experiment: dog with esophagostomy and gastric fistula for collection of “pure” gastric juice during sham feeding (watercolor from the *Pavlov* exhibit at Koltushi)

Source: *Wood J.D.*, The First Nobel Prize for Integrated Systems Physiology: *Ivan Petrovich Pavlov*, 1904. 2004, *Physiology*, 19, 326-330. (<http://physiologyonline.physiology.org/content/nips/19/6/326.full.pdf>)

In 1890, after returning from Germany and unsuccessful applications at universities in St. Petersburg, Tomsk, and Warsaw he was appointed professor of pharmacology at the Military Medical Academy working there 5 years. But in 1895 by invitation of the Institute of Experimental Medicine *Pavlov* has organised and was director of Department of Physiology up to 1925.

In the Institute for over 45 year period *Pavlov* created the most important centre in the physiological studies and research. He developed the surgical method of the long-running experiment with extensive use of fistulas, which enabled the functions of various organs to be observed continuously under relatively normal conditions. With his method he opened the way for new advances in theoretical and practical medicine. He showed that the nervous system played the dominant part in regulating the digestive process, and this discovery is in fact the basis of modern physiology of digestion. In 1897 *Pavlov* published (in Russian) the results of his research in the book entitled “Lectures on the Function of the Principal Digestive Glands” (Figure 3). In recognition of his academic achievements he was elected a corresponding member of the Russian Academy of Sciences in 1901, and then – Academician in 1907.

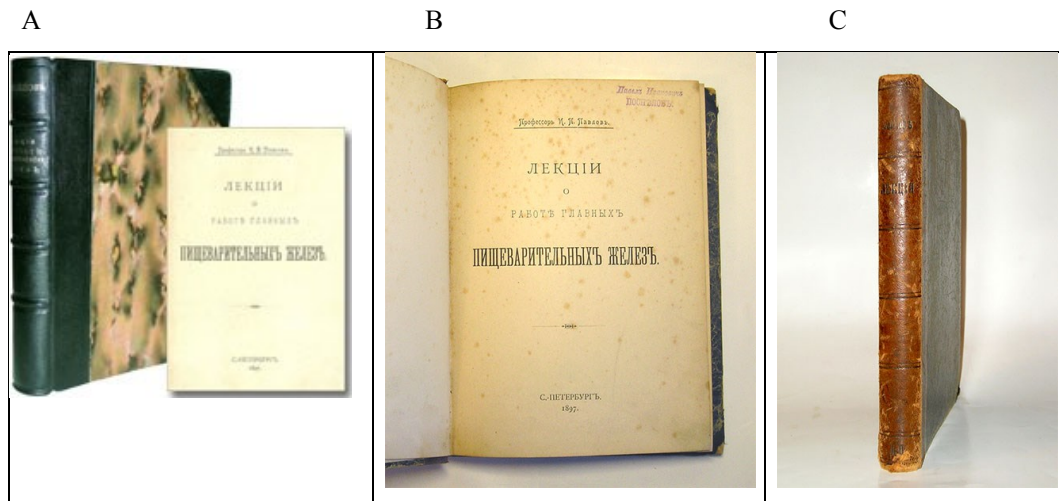


Figure 3. First edition of *I.P. Pavlov's* breakthrough book on digestion, St. Petersburg, 1897; discoveries presented in the book were the base for awarding *I.P. Pavlov* Nobel Prize (the title in Russian: И.П. Павлов. «Лекции о работе главных пищеварительных желез»)

Source A: <http://www.raruss.ru/russian-thought/595-pavlov.html>

Source B-C: <http://knigirossii.narod.ru/html/18/224/1468458.html>

Pavlov research was highly acclaimed in the world and therefore in 1901 he was nominated and in 1904 awarded the Nobel Prize in Physiology and Medicine “in recognition of his work on the physiology of digestion, through which knowledge on vital aspects of the subject has been transformed and enlarged” [12]. *Pavlov's* Nobel Prize was the first ever awarded for integrated systems physiology and the first for a Russian [11]. It is worth noting that in 1904 the Nobel prizes were awarded for the fourth time.

It is interesting to know that *Pavlov* investigated the gastric function of dogs and children by collecting, measuring and analysing juices especially from saliva glands for longer period of time. It was noticed that especially salivation process including psychic secretion and observing also conditioned and unconditioned reflexes e.g. in saliva secretion, which as we know is very much linked with cerebrum activity hormones or some physio-chemical change in the brain [7]. It is worthwhile to note that nervous system is very important in physiology of digestion, as reported by *Pavlov* during presenting his paper on International Congress of Physiologists held in Madrid in 1904. *Pavlov* continued studies on this phenomenon for the next 30 years up to the end of his life.

In 1912 he was given an honorary doctorate at Cambridge University. During the ceremony of nominating him the students participated in the ceremony offered *Pavlov* the pupped dog (a toy) with many fistulas attached. It was taken by professor *Pavlov* with great attention as a very precious present to his laboratory to memorialise this event of his career. The dog was placed among books, diplomas, and many other *Pavlov* souvenirs.

In the following years *Pavlov* received honorary membership of many scientific societies abroad and in 1915, upon the recommendation of the Medical Academy of Paris, was awarded the Order of the Legion of Honour.

Pavlov's achievements have also been highly appreciated by the communist government of the Soviet Union by nominating him as a chairman of the organising committee of the 15th International Physiological Congress which was held in Leningrad and Moscow in 1935. It was *Pavlov's* strong intention to build the monument of the dog as the friend of humanists servicing in science and to be finished just before the Congress (Figure 4).



Figure 4. The Monument to a Dog in the garden of the Institute of Experimental Medicine RAMS, St. Petersburg, on *I.P. Pavlov* initiative installed in 1935 to pay a tribute to the dog's unselfish service to biological science

Source: <http://seaseas.livejournal.com/830261.html>

I.P. Pavlov is recognised as a promoter or creator of the very important and classical now school of physiologists in Russia and the Soviet Union. In the experimental biological station in Koltushi (near St. Petersburg) he introduced a very interesting activity named as “Wednesday Meetings”. It was the possibility to present and discuss his views on present and future scientific activity in the field of many topics, including physiology, among his co-workers since 1921 up to his death in Leningrad on February 27, 1936.

PRESENT STUDIES IN FOOD DIGESTION

After classical discoveries of *I. P. Pavlov* digestion of food was and is studied for many years by several researchers [9]. Recently new avenues in this field are investigated and created. The most current issues on digestion are presented and discussed at the International Conferences on Food Digestion (ICFD). Conferences are organised by INFOGEST, an international network focusing on “Improving Health Properties of Food by Sharing our Knowledge on the Digestive Process”. The specific objectives of the network assign the most important research areas in food digestion which are [8]:

- Comparing the existing digestion models, harmonization the methodologies and suggestion of the guidelines for performing new experiments,
- Validation *in vitro* models towards *in vivo* data in animal and/or human organism,
- Identifying the beneficial/deleterious components that are released in the gut during food digestion,
- Demonstration the effect of these compounds on human health,
- Determining the effect of the matrix structure on the bioavailability of nutrients and bioactive molecules contained in food.

The audience of 3rd ICFD heard 27 oral presentations and from this number 4 were given by invited speakers [8]. They focused on methodology issues in digestion research and intestinal microbiome aspects. *Ourania Gouseti* (University of Birmingham, UK) stressed that the area of investigation in digestion has grown lastly significantly aiming to address the design criteria for functional food products, to assess energy density, and protein allergenicity. This resulted in the development of a large number of methodologies varying in the equipment and in the levels and types of chemicals. Current models represent also more complex elements of food digestion, incl. mechanical forces/shear. A new generation of models (e.g. DGM, TIM) is becoming very popular because of their ability to more accurately assess the effect of food matrix in digestion. Dr *Gouseti* team research has demonstrated the potential of food formulation/matrix in modulation

digestion using a chemical engineering approach. The team has developed *in-vitro* and *in-silica* models to study human digestion and nutrient bioaccessibility.

Paul Singh (University of California, Davis, USA) presented novel tools using computational methods and *in vivo* trials to study food digestion. Professor *Singh's* team developed computational models based on average size and shape of a human stomach for understanding the role of physical properties of foods on digestion in the gastrointestinal tract. Viscosity of the digesta was identified as a key physical property: an increase in the viscosity reduced the strength of the fluid motion. During *in vivo* trials with growing pigs physical properties of brown and white rice gastric chyme were quantified to describe the food breakdown during an 8 hours postprandial period. The result of the experiment was that proximal and distal regions of the stomach had different inherent functionalities. On the base of these studies the researchers proposed a new classification system of food breakdown during gastric digestion for future trials on food digestion in a systematic manner.

Hauke Smidt (Wageningen University, The Netherlands) concentrated on identifying gastrointestinal (GI) tract microbes. He stressed that the using of culture-independent approaches is crucial to provide a comprehensive picture of the GI tract microbial functioning. GI tract ecology experiences a revival since the introduction of the approach based on 16S ribosomal RNA (rRNA) and its encoding gene. The culture-independent approaches gave insight into the temporal, spatial and inter-individual microbial diversity in the GI tract. These approaches offer great potential in finding significant correlations between microbiota compositional signatures and the health status of the body. Moreover meta-omics studies and stable isotope probing method allow studying the genetic potential and functional properties of the GI tract microbes. The application of these approaches to understand the role of intestinal microbiota in food components' digestion and health of the host can provide the necessary knowledge for the development of innovative dietary strategies.

Johan Garssen (Utrecht University and Nutricia-research, The Netherlands) started his presentation underling that the development of a healthy intestinal microbiome after birth plays an important role in immune development. Some of non-digestible oligosaccharides transferred through the breastmilk to the child affect the composition and/or activity of the GI tract microbiota leading to health benefits (prebiotic function). The awareness of the importance of these unique carbohydrates in immune-regulation is growing exponentially. The specific non-digestible oligosaccharides scGOS/IcFOS (ratio 9:1) induces a gut microbiome comparable to breastfed infants. Besides these indirect effects on the immune system

via microbiome changes prebiotic oligosaccharides can affect immune cells directly as well. The unique receptors such as lectins/galectins are responsible for these direct immune effects. Clinical trials indicated that scGOS/IcFOS impaired the incidence of infections and allergies, especially in infants and toddlers. However very recent research indicate significant effects on the immune system during HIV infections, cancer and asthma. More multicenter trials and long-term studies are needed in order to validate the uniqueness of non-digestible oligosaccharides in specialised and medical nutrition as well as pharma approaches.

In the frame of 3rd ICFD many posters were also shown. Among them 4 papers showing the results of the research carried out by *Wiesław Wiczkowski* team at the Institute of Animal Reproduction and Food Research of Polish Academy of Science were presented. The title of these posters were: Bioavailability of anthocyanins from fermented red cabbage; The bioaccessible reducing capacity of buckwheat-enhanced wheat breads estimated by electrochemical method; The Global Antioxidant Response (GAR) of buckwheat-enhanced wheat breads; Buckwheat-enhanced wheat breads ameliorate TNF- α -induced migration in an intestinal cell model (myofibroblasts of colon) [8].

FINAL REMARKS

Ivan Petrovich Pavlov's achievements as a pioneer in nutrition science are recognised in many publications, e.g. *Berger's* chapter entitled "Historia nauki o żywieniu" [History of nutrition science] in *Gawęcki* book (ed.) [1] or *Wood* paper [11].

It should be admitted here that recently some authors are often referring to *Pavlov's* pioneering research on the food digestion physiology. Among them *Clark* in his 15 pages paper [2] adopted the classical origins of *Pavlov's* conditioning. As a matter of fact it was originally introduced to the USA as "the *Pavlov* salivary reflex method" indicating that the term "conditioned" is used to show that the response is "learned".

In the very carefully analysis of *Pavlov* achievements and Nobel Prize Award procedure *Windholz* and *Kuppers* [10] made the statement that his works contributed significantly not only to digestion physiology, but also to the development in the discipline of psychology, and particularly by accepting new methodology and results of the study using conditional reflexes or responses as a paradigm in learning, and the role of the brain of the body interaction with the external environment.

Our paper covers most important activities and scientific achievements of the Nobel Laureate Professor *I.P. Pavlov* as well as some chosen facts of his private life. More information is presented in the very interesting and full of fascinating details book, published in Russian [5] and Polish [4], by great Russian physiologist, professor *Hachatur S. Kosztójanc* (1900-1961). These books are among several vivid publications which were of great help in preparation of this paper.

REFERENCES

1. *Berger S.*: Historia nauki o żywieniu. In: Żywnienie człowieka. Podstawy nauki o żywieniu. (ed.) J. Gawęcki. Wydawnictwo Naukowe PWN, Warszawa, 2010, pp. 22-29 (in Polish).
2. *Clark R.E.*: The Classical Origins of Pavlov's Conditioning. Integrative Physiological & Behavioral Science, 2004, 39, 4, 279-294.
3. *Gawęcki J.*: Trawienie i wchłanianie. In: Żywnienie człowieka. Podstawy nauki o żywieniu. (ed.) J. Gawęcki. Wydawnictwo Naukowe PWN, Warszawa 2010, pp. 88-107 (in Polish).
4. *Kosztójanc Ch.S.*: Opowieść z życia Pawłowa. Książka i Wiedza, Seria II „Nauka i Życie”, Warszawa, 1949, nr 4 (1st edition in Polish).
5. *Kosztójanc Ch.S.*: Rasskaz o Rabotach I.P. Pavlova v Oblasti Phisiologii Pishchevarienija, Izdatielstwo Akademii Nauk SSSR, Leningrad 1950, (4th edition in Russian).
6. *McCullum E.V.*: A History of Nutrition. Houghton Mifflin Company, Boston, University of Kansas, 1957.
7. *Mitchell P.H.*: A Textbook of General Physiology. McGraw-Hill Book Company, Inc., New York (5th Edition), 1956.
8. Proceedings of the 3rd International Conferences on Food Digestion. Wageningen, The Netherlands, March 11-13, 2014.
9. *Thompson J.L., Manore M.M., Vaughan L.A.*: The Science of Nutrition. Pearson Benjamin Cummings, San Francisco 2011, (2nd edition).
10. *Windholz G., Kuppers J.R.*: Pavlov and the Nobel Prize Award. The Pavlovian Journal of Biological Science, 1990, 25, 4 Oct.-Dec., 155-162.
11. *Wood J.D.*: The First Nobel Prize for Integrated Systems Physiology: Ivan Petrovich Pavlov, 1904. *Physiology*, 2004, 19, 326-330.
12. *Ivan Pavlov* – Facts. <https://www.nobelprize.org/prizes/medicine/1904/pavlov/facts/>; [dostęp: 10.05.2017]

Received: 22.10.2017

Accepted: 25.02.2018