

Historical note**Brunner's missing 'Aha experience' delayed progress in diabetes research by 200 years**Fritz S. Keck¹, Leonidas H. Duntas²¹Westkuestenkrankenhaus Heide, Germany, ²Evgenidion Hospital, Athens University School of Medicine, Athens, Greece**ABSTRACT**

In 1889, the pancreatectomy performed on a dog by Joseph von Mehring and Oskar Minkowski led to the discovery of the pancreatic origin of diabetes disease. Already 200 years before, Johann Conrad Brunner had successfully performed eight pancreatectomies on dogs and had precisely described the symptoms of polyphagia, polyuria, and polydipsia. He did not, however, recognize the association with the diabetes disease and thus missed an opportunity to accelerate the course of diabetes research by 200 years.

Key words: Aha experience, Diabetes mellitus, Dogs, Gestalt psychology, Pancreatectomy

“Ευρεκα! Ευρεκα!”
Archimedes of Syracuse

INTRODUCTION

The contribution of Joseph von Mehring (1845-1908) and of Oskar Minkowski (1858-1931) to the discovery of the pancreatic origin of the diabetes disease is well known.¹ Less known is the fact that 200 years earlier, Johann Conrad Brunner (1653-1727) had used exactly the same experimental paradigm without, however, identifying the interrelation of the findings or the connection to the human disease, namely diabetes.² The difference in intellectual out-

come will be explained in terms of the psychological Gestalt theory as introduced by Max Wertheimer (1880-1943), Wolfgang Kohler (1887-1967), and Kurt Koffka (1886-1941).³

Since Galen's days (129-199), the origin of diabetes mellitus, although not designated as being 'unknown' (Morgagni, 1682-1771), was usually assigned to malfunctioning of the kidneys or, as in the case of Claude Bernard (1813-1878), attributed to a disorder of the nervous system. In 1889, Minkowski, following a discussion with Mehring with regard to the role of the pancreas on fat digestion, removed the pancreatic gland in a dog. Subsequently, in an argument with the lab assistant regarding the presence of the dog's urine on the laboratory floor, Minkowski realized that the dog he had operated on was urinating repeatedly. He examined the urine on the floor and found in it a sugar content of more than 10%. Glucosuria, polyuria, polydipsia, polyphagia, and weight loss following pancreatectomy had already been described

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in von Mehring's and Minkowski's first paper.¹ In subsequent experiments with pancreatectomized dogs, Minkowski confirmed that glucosuria always followed the operative procedure used by him.⁴ The theory of 'pancreatic diabetes', a term first employed by Lancereaux in 1877 for the rapid onset form of diabetes,⁵ was most compellingly established.

Neither researcher was aware of the experimental data on pancreatectomy produced by Johann Conrad Brunner (1653-1727), whose name is also nowadays known by the designation of 'glandulae duodenales'. Brunner studied medicine at the University of Strasbourg, where he wrote his doctoral thesis in 1672, and then pursued his education in anatomy in Paris with especial focus on anatomy of the pancreas. After additional studies in Oxford and in London, where he met Thomas Willis^{6,7} (1621-1675), he worked as a practitioner at Diessenhofen from 1676 on. Even during this time, however, he continued his investigations into the pancreatic gland in animals as well as in human corpses. He discussed his results with the members of the so-called Schaffhausen medical school, a group of medical doctors, among them being the famous pathologists Johann Jacob Wepfer (1620-1695), his father-in-law, and Johann Conrad Peyer (1653-1712), who described the Peyer's plaques of the small intestine.

In 1686, Brunner took up the newly instituted third medical chair for anatomy at the University of Heidelberg and became one of the most famous physicians of the closing years of the 17th century. For his medical and scientific activities, Brunner constrained himself to the use of logic, rationalism, and empiricism, thereby rejecting traditional natural philosophy and turning to experimental physiology. In 1683, he published his seven pancreatectomies performed since 1673 in his book 'Experimenta nova circa pancreas',⁸ in which he meticulously described his technique. From the two parts of dog pancreas, he removed the bigger one (pars caudalis) surgically, while leaving the smaller part (pars duodenalis) because of unfavourable surgical field. He, however, ligated its excretory duct and, in addition, interrupted the duct surgically. Brunner's highly praised manual dexterity,⁷ long before any knowledge concerning antisepsis and anaesthesia was available, was so ex-

ceptional that, even today,^{9,10} people have difficulty in believing that he was able to achieve such remarkable scientific results.

Peyer was one of those who contested his conclusions on the function of the pancreatic gland. In response, Brunner once more performed a pancreatectomy on a dog on Oct. 6th 1685, subsequently describing his surgical procedure and the dog's postoperative course in the precise language of a daily medical report.² It is obvious from the description that Brunner clearly identified the signs of striking polyuria, polydipsia, and polyphagia. From his report it can be concluded that the diabetic clinical signs induced by the operational procedure were transitory. This phenomenon can be attributed to transient posttraumatic functional damage of the remaining pancreatic part.¹¹ Over the long term, this part of the pancreas was capable of sustaining glucose homeostasis, since ligating of the pancreatic duct causes atrophy in the pancreatic exocrine cells, with only transitory damage to the endocrine cells.¹² Indeed, half a year later, Brunner discovered through a 'second look operation' in the same dog – the dog meanwhile having given every sign of being as vigorous as ever before – the remnants of the left ligated part of the pancreas shrunken to the size of half a finger. Thus, Brunner was the first to induce transient pancreatic diabetes mellitus, without however perceiving this fact.

The Gestalt theory, introduced at the beginning of the 20th century, made important contributions to the analysis of mental processes in perception and problem solving. According to the Gestalt theory, people behave in the ways they do based on how they perceive the environment rather than on what the environment actually is. Learners sometimes experience a moment in which the various components of their task or problem come together in ways that significantly advance their understanding, thus emerging as a new Gestalt. This moment of insight when, in terms of the Gestalt theory, comprehension takes place between two entities, is called the 'aha experience', a term introduced by K. Buehler.¹³ These moments sometimes induce a positive feeling in the learner. The classical example of an 'aha experience' is the story of Archimedes of Syracuse (287-212 BC), who discovered the principle of buoyancy when, on entering

his bathtub and spilling part of the water, he suddenly acquired a new insight into what was happening so that, as the legend goes, he ran naked through the streets shouting "Eureka" (I have found it!).

When comparing Brunner's and Minkowski's work, it becomes evident that their experimental settings correspond most closely. Both researchers had developed interest in the exocrine function of the pancreas, Brunner for the purpose of studying its interaction with the bile juice and Minkowski to investigate the extent to which it was involved in cleaving fat into free fatty acids. They used a similar pathophysiological paradigm: both found the clinical signs of polydipsia, polyphagia, and polyuria, but only one made the intellectual synthesis.

In comparing the personal data of the two researchers, they do not essentially differ regarding age at which they first published their results, intellectual faculties, or manual dexterities, as judged by others.^{6,7,10} What does make a difference, however, are scientific education and intellectual setting. After his doctoral thesis, Brunner had built up a considerable reputation as co-worker of outstanding anatomists, such as Josef Gichard Duverney (1648-1730) in Paris.^{1,11,12} He reported his pancreatectomies to the 'Schaffhausen medical school' in which, among others, famous pathologists like Johann Jacob Wepfer and Johann Conrad Peyer participated. Minkowski had previously worked on metabolic questions during his Koenigsberg period.^{8,14} During his time in Strasburg, when metabolic research was being performed at several university institutes, von Mehring had motivated him through the challenge of a fat-metabolic question to perform the pancreatectomy, and his chief, B. Naunyn, was the most prominent diabetologist of the time.

DISCUSSION

Since the time of Aretaios the Cappadocian (81-138 A.D.), polyuria, polydipsia, and weight loss were known to be symptoms of the diabetic disease.¹⁵ Thomas Willis added the sweetness of the diabetic urine to the list of characteristic symptoms.¹⁶ Since chemical methods for sugar urine examination were not in use at the time, Brunner would have tasted the dog's urine, if he had suspected diabetes inducing the

symptoms that occurred after pancreatectomy. Urine tasting, however, belonged in those days to common medical examination procedures.

As outlined above, both researchers were interested in scientific issues regarding digestion and were certainly prepared for postoperative problems arising from this field. Minkowski, however, needed but the observation of one single symptom of diabetes, namely polyuria, for a new Gestalt to emerge in his consciousness out of the elements perceived after pancreatectomy. It can therefore be assumed that Minkowski's diabetologic experiences and scientific environment induced this intuitive insight. Given that Brunner was not so close to diabetologic thinking and practice, he was not 'equipped' with this special kind of attitude. Had he been, he could well have accelerated the course of diabetes research by 200 years.

The paradigm illustrates once more the validity of cross talking between experimental and clinical scientists in accelerating the application of basic scientific progress in the treatment of human disease.

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