

## Physiology of the senses—a prominent area of science in Uppsala at the end of the nineteenth century

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The first volume of *Uppsala Läkareförenings Förhandlingar (Proceedings of the Uppsala Medical Society)* in 1865–1866 contains a report from a lecture given by the newly appointed professor of physiology, Frithiof Holmgren, with the title ‘A method to make objective the effect of light on the retina’ (1). Neither Holmgren nor his listeners at that time understood that he had made a discovery of great scientific value. He had shown for the first time that impressions from a sense organ are transmitted to the brain through electrical impulses. Instead of the subjective perception, an objective registration of impulses between the sensitive organ and the brain was possible. Its importance for the understanding of the function of all sense organs cannot be overestimated.

Fifteen years earlier, Holmgren’s great teacher, Emil Du Bois-Reymond, had shown that when a nerve is stimulated electrically, the electric impulse is transmitted along the nerve. The same phenomenon appeared after a physiological stimulation of the nerve as an index of the activity, and it was called the action potential current. Another of Holmgren’s teachers, Herman von Helmholtz, was the first to measure the velocity of the current.

Holmgren had worked in Du Bois-Reymond’s laboratory in Berlin in 1863–1864. When he returned to Uppsala, he thought it would be possible to register impulses between the cornea and the optical nerve when the retina was exposed to light. For that purpose, he used eyes from frogs. In order to be able to register the weak currents he needed a very sensitive galvanometer. The best he could find at that time was Wiedemann’s mirror bussol (*bussola* is Italian for ‘compass’). He registered the current between an electrode on the cornea and another on the optical nerve and found that the eye responded with a current both when the light was shut on and off. Holmgren thought that he had registered what he had intended to do, but the nerve had very little to do with the phenomenon. The apparatus (Figure 1) was too insensitive to register the rapid, weak currents on the nerve sheath. It took him several years to understand what he had found.

When Holmgren continued his studies, he moved the electrodes against each other in different diameters of the eye bulb and understood that the potential had nothing to do with the optical nerve, but could emanate only from the retina. He published his new findings in Swedish five years later (2), but they became internationally known only when they were printed in a German paper edited by his friend Willy Kühne, who had succeeded Herman von Helmholtz as professor of physiology in Heidelberg (3).

Already in his first publication Holmgren had discussed the possibility of studying the effect of coloured light on the retinal current. He thought, in analogy with the auditory organ, that oscillations with different wave-lengths should give different deviations on the galvanometer, but he did not proceed on these projects. The reason for that may have been that the galvanometers of that time were too insensitive and laborious. With the development of



Figure 1. The equipment Holmgren used when he detected the retina current. The apparatus belongs to the Museum of Medical History in Uppsala.

modern electronic equipment, electroretinography has today become a valuable tool in the diagnosis of eye diseases in humans and animals.

Problems with colour vision were to occupy most of Holmgren's thoughts during the rest of his life and made him much more known among the general public than the scientifically more important work on the retinal current. The problems with perception of colours could not be solved with the electro-physiological methods he had used earlier, but required experiments on human beings.

Only once did he return to problems related to the current. The anatomist Heinrich Müller had found orange and red pigments (rhodopsin or visual purple) in the retina, and it had been proposed that these were important for the formation of pictures on the retina. Kühne had shown that the pigments were rapidly bleached by light and regenerated rapidly in darkness.

Holmgren's aim was to elucidate the relationship between the pigments and the electrical current. After experiments with eyes from frogs and rabbits, he found that the visual purple and the retinal current are independent of each other. He even drew the conclusion that the visual purple is of no importance for the vision at all, a too rash deduction (4). Studies with modern electro-physiological techniques have made it evident that reactions when light is shut on and off are indispensable for visual discrimination. The outlines of the visual objects are brought into relief, i.e. enhanced, when the eye is moved with small oscillations and when rhodopsin rapidly is bleached and reactivated. Rhodopsin is also necessary for adaptation to darkness and bright light.

### Colour-blindness

In 1867, a new physiological laboratory was built after a donation from Anders Fredrik Regnell (5). For the first time, physiology had got a place of its own. Six rooms and sufficient equipment were now available, which proved to be necessary. In the next decades Holmgren had to examine several hundreds of individuals for colour-blindness for his studies of its occurrence in the population.

During a year from August 1869 to August 1870, Holmgren worked in Heidelberg under the guidance of one of the greatest physiologists ever, Herman von Helmholtz. Among his many interests, Helmholtz studied colour-blindness.

In 1802, Thomas Young had postulated the existence of three types of photoreceptors (now known as cone cells) in the eye, each of which was sensitive to a particular range of visible light. Helmholtz developed the theory further in the 1850s. According to the Young-Helmholtz theory of colour vision, there are three receptors in the retina that are responsible for the perception of colour. One receptor is sensitive to the colour red, another to green, and a third to blue (or violet). These three colours can then be combined to form any visible colour of the spectrum. Light stimulating all the types of cones is perceived as white. Helmholtz was conscious that the three-colour theory not could be proven anatomically. He therefore tried to bridge the gap between the microscopic picture of the retina and the physiological analyses of colour vision. Helmholtz divided the retina in three chromatic zones, which had different distributions of cones and rods. During his stay in Heidelberg, Holmgren took part in the practical experiments on these zones. He had his vision field examined with a perimeter by the

Russian ophthalmologist Mikhail Mikhailowitsch Woinow. It turned out that he had a small defect in the red-blind middle zone. The central zone merged over to the peripheral zone directly at this spot. The interpretation was that such variations of the colour vision may occur normally (6).

When Holmgren had returned to Uppsala, he published a series of studies on the subject (7). He also made an appeal to the medical profession in Sweden to report to him all cases of colour-blindness they had detected. In that way he got access to the greatest statistical material of colour-blindness at the time (32,165 men and 7,119 women) and found that 3.23% of males and 0.26% of females in Sweden were colour-blind. He also noted that colour-blindness was hereditary and was inherited from the mother's side (8). Once, Holmgren had the opportunity to examine two colour-blind sisters, but he did not mention if their parents had impaired colour vision (9).

The chromosomes and the connection with the X chromosome were unknown at that time. Red-green colour-blindness is passed from mother to son on the X chromosome, which is known as the sex chromosome because it also determines sex. Females have two X chromosomes and males one X and one Y chromosome. The faulty gene for colour-blindness is found only on the X chromosome. So, for a male to be colour-blind the faulty gene only has to appear on his single X chromosome. For a female to be colour-blind it must be present on both of her X chromosomes. If a woman has only one colour-blind gene she is known as a carrier, but she will not be colour-blind herself. When she has a child she will give one of her X chromosomes to the child. If she gives the X chromosome with the faulty gene to her son, he will be colour-blind, but if he receives the 'good' chromosome he will not be colour-blind.

The lack of knowledge about the causes of colour-blindness explains why Holmgren devoted himself to two laborious studies we now know to have been futile. In one, he tested a statement in a German book *Grundzüge der physiologischen Optik* by Herman Aubert that colour-blind persons had a shorter distance between the pupils of their eyes. Holmgren constructed a special apparatus for the study and then tested 100 colour-blind individuals and 100 without any colour vision deficiency. He concluded that the distance between the pupils had no correlation to colour-blindness (10).

In May 1880 Frithiof Holmgren proclaimed a reward of 2,000 Swedish crowns to those who put at his disposal for investigation a person with a complete, inborn colour-blindness on one eye and a normal colour vision on the other (11). The prize had been put at his disposal by a person whose name not was given. It corresponds to over 100,000 crowns today. In several papers he later reported a few cases of alleged one-sided colour-blindness, but in no case had those individuals been examined earlier in life. Thus, the deficient colour vision may have been due to a retinal disease in one eye.

There were several different methods for testing colour-blindness before Holmgren's time. Most often colour vision deficiency was reported simply by subjective descriptions of what the test person saw. In 1837 August Seebeck used a more advanced technique. He used a set of more than 300 coloured papers and let people match or find a colour closely related to a sample colour. This type of colour vision test abandoned the naming of colours, which differs a lot between persons.

Holmgren adapted this kind of test by using skeins of wool instead of coloured papers. The examined person had to match one piece of wool to the samples in a box. There were light and dark shades to confuse the person. The advantage to all other methods was that it was simple, rapid, and inexpensive. An examination took less than a minute, compared with about an hour with the old methods. The Holmgren wool test was widely used and even commercially available more than 100 years later (12).

In the night of 15 November 1875 a railway accident occurred in Lagerlunda near the Bankeberg station in Ostrogothia. Nine people were killed, among them the engineer, the oiler, and the firemen. If only death and injury were considered, the Lagerlunda incident was not remarkable. Every year more than 1,000 people were killed in England in railway accidents during the 1870s. One reason that contributed most to the national and international horror of the disaster was a sketch by the later famous artist Carl Larsson, then part time illustrator for *Ny Illustrerad Tidning*. The sketch was reproduced by a woodcut procedure and published in many newspapers around the world (Figure 2).

During the ensuing trial, only the stationmaster at Bankeberg was found guilty and sentenced to jail. The court's decision was met with criticism, and it was commonly thought that he had been made a scapegoat by the management. According to a recent review of the event, there were a lot of circumstances pointing at several broken regulations by higher-placed persons in the railway company (13).

Holmgren suspected that the engineer had been colour-blind, but he had lost his life. On 15 July 1876, Holmgren gave an account of his method of screening with the wool test at a Nordic medical congress in Gothenburg. The assembled physicians resolved that it was necessary to investigate the occurrence of colour-



Figure 2. Medal engraved in 1964 in commemoration of the 100th anniversary of Holmgren's detection of the retina current by the Royal Swedish Academy of Sciences. Sculptor Leo Holmgren. On the medal is engraved '*Luci retinam electrice respondere primus demonstravit*', i.e. 'He was the first who demonstrated that retina responded on light with an electric current'. Uppsala University Coin Cabinet.

blindness among the staff of the railways. Holmgren also wrote a letter to the management of *Statens Järnvägar* (Swedish State Railways); they were, however, sceptical: If colour-blindness really existed, it could not, at any rate, be amongst their employees, or it would undoubtedly have been noticed. They had had a lot of possibilities to prove their ability to distinguish signals.

But Holmgren got permission to test all employed by the railroad between Uppsala and Gävle. Among the 266 tested, he found 13 that were colour-blind. He also got permission to perform a demonstration before the board of *Statens Järnvägar*, which took place on 13 October 1876 in Uppsala.

In a dark room, the members of the board were sitting on one side of the room. At each end of the room, Holmgren had stationed one red-blind and one green-blind conductor, each with a signal lantern. They were instructed that when one signalled to the other, the second should respond with the same signal. The general director of *Statens Järnvägar* was to order what signal to show. He chose ready, i.e. white. The first conductor showed red to which the second responded with green. In the silence that followed, Holmgren said: 'Gentlemen, now that we have seen this, it is clear that if any accident occurs as a result of colour-blindness, there is no doubt about where the responsibility lies'.

Three days later, *Statens Järnvägar* issued an order requiring all railroad physicians to screen for colour deficiency with Holmgren's method. His article 'Colour-blindness in its relation to accidents by rail and sea' was translated to French, English, German, Russian, and Italian and was referred to in Danish, Polish, and Spanish publications (14). As a consequence of this, the laboratory in Regnellianum was visited by numerous scientists from near and far.

What neither the colour-blind conductors nor the members of the board knew was that Holmgren had manipulated the lanterns. He knew that colour-blind persons were accustomed to judge colours by their luminosities and had placed coloured glass of different thickness in the lanterns. In a paper two years later, he reported on a method to make a correct diagnosis on a person who simulates colour-blindness or is trying to conceal his handicap, but he did not mention that he had used this trick in front of the railway board (15). The secret was revealed only after his death in a footnote in the obituary written by his successor as professor, Hjalmar Öhrvall (16).

Politically, Holmgren was liberal, and his wife Ann-Margret Tersmeden was a member of the radical student association *Verdandi* and a member of its editorial board. Thus, it is worth noting that Holmgren, although he stressed that a colour-blind person could not get a position in a railway company, he cared about those already working as engineers or in other positions where perfect colour vision was needed. In his paper, he elaborated at length about the problems of discharging people with long, immaculate service on the grounds that they had an inborn error. He suggested some sort of compensation or that they should be transferred to new posts, where colour-blindness was no hindrance.

Gustaf Göthlin, professor of physiology in Uppsala 1918–1939, found that some persons had a weak colour sense in spite of normal results with Holmgren's wool test. A person having normal vision will need a particular intensity ratio of red, green, and blue primary colours to see white; he is a normal trichromate. Some individuals, however, need more of one of the primary colours than the other two; these are anomalous trichromates. With a double spectroscopic method devised by Göthlin, these persons could be found (17). His method, however, was too complicated, and in 1934 pseudo-isochromatic pictures were introduced for the testing in Sweden and most other countries. Holmgren's wool method had then been used for 58 years.

In the 1880s, Holmgren became more interested in the theoretical aspects of colour vision. He was an ardent believer in the Young–Helmholtz theory, but there were other competing theories. The best known was proposed



by the German physiologist Ewald Hering. He disagreed with Young and Helmholtz that colours are based on three primary colours: red, green, and purple (or blue). He instead believed that colour vision is based on a system of colour opponency. In this model colours are perceived through receptors sensitive to three couples of opposing colours: red–green, yellow–blue and white–black. His colour concept gave rise to mostly fruitless controversies, because it appeared to be incompatible with the theory put forward by Young and Helmholtz. Holmgren defended the Young–Helmholtz theory in a sometimes very excited debate (18). It must be said, however, that Helmholtz himself took a much more active part in the dispute.

In a lecture in honour of Gustaf Göthlin when he retired from the chair of physiology in 1939, Ragnar Granit (1900–1991), professor of neurophysiology at the Karolinska institute and Nobel Prize laureate in 1967, presented a method to register impulses from single nerve fibres of the retina with microelectrodes. He used glass tubes with silver cores pulled out to fine tips and applied them directly onto the retina of frogs. The experiments were carried out under micro-illumination. The spectral lights were reflected internally from the silver-coated glass rods. When the light spot and the microelectrode were adjusted relative to one another in order to obtain a precise response, the distance between the two tips was such that only the optic nerve fibres themselves could be considered as sources of the spikes obtained (19).

Later, Granit found further experimental support of the trichromate theory of Young and Helmholtz (20). His pupil, the Finnish-Swedish-Venezuelan neurophysicist Gunnar Svaetichin found experimental support for the opponent theory of Hering (21). It is now clear that the two colour concepts can be reconciled with one another. Nowadays, we know that the human being possesses three types of receptors, which are combined in three opponent channels as proposed by Hering. Thus, both Hering and Helmholtz were right. Frithiof Holmgren, always very keen on applied physiology, would have been pleased if he had lived to see this development.

As a young medical student the future professor of physiology at the Karolinska institute, Jöns Johansson, was Holmgren's amanuensis in physiology. Holmgren inspired him to study the colour sense in the area just around the blind spot. In an investigation on his own right eye, Johansson found that the perception of red and green ceases gradually towards the macula until a complete colour-blindness occurs, just as in the periphery of the retina (22).

In a later report, Holmgren stated that Johansson's colour vision was not quite normal, which is why he repeated his investigation of the conditions around the blind spot in his own eyes. He confirmed Johansson's finding but extended it to a scotoma he had had in the central part of his right eye since 1880. He found that colour-blindness appeared around the scotoma, just as around the blind spot. He stated that in any part of the vision field near a blind area, normal colour vision does not cease instantly, but there is a gradual transition through a red-blind zone before total colour-blindness develops (23).

The scotoma gave him a partial macropsy, a defect of vision in which objects appear to be larger than their actual size. Towards the end of his life, he tried to determine the nature of this scotoma. In order to do so, he measured the enlargement by comparing the size of a sheet of paper, as seen by the right eye with the size seen by his healthy left eye. He calculated the enlargement to be 2.5 times vertically and 1.14 times horizontally. He also tried to determine the size of the scotoma through an examination with a perimeter, but was not satisfied with the results. He wrote: 'a more accurate information about the scotoma can only be accomplished through a direct microscopic examination of the eye. I have thus donated the eye to my colleague professor J. A. Hammar'.

On 14 August 1897, when Holmgren died, it became evident that it was not legal to take out the eye immediately, but only after 24 hours. His widow Ann-Margret then said: 'Had Frithiof known this, he would certainly have tried to get exemption from the law'; now it was too late.

After 24 hours a post-mortem examination was performed and the right eye removed and examined. The post-mortem decomposition prevented a detailed microscopic examination, but some old haemorrhages close to the central fovea were found. The results from the examination were printed in *Proceedings of the Upsala Medical Society*, the same journal where his greatest scientific discovery had been published 32 years before (24).

Holmgren was not the only person at this time to donate an organ to science. Many neuroscientists thought that it was possible to find a correlation between the size and configuration of the brain and the person's intelligence and character. The famous scientists Gustaf Retzius, Sonja Kovalevsky, and Salomon Eberhard Henschen had their brains examined. Holmgren's own pupil, Magnus Blix, donated his brain to his friend Magnus Fürst, professor of anatomy in Lund. The result of the investigation was published 14 years later in a publication in honour of the 250th anniversary of the foundation of the University of Lund (25).

Holmgren was the first professor of physiology in Uppsala (Figure 3). He put his stamp on the department and his pupils, many of whom were to continue his research in various fields of physiology of the senses.



Figure 3. The railway collision in Lagerlunda. A sketch by Carl Larsson in *Ny Illustrerad Tidning*, 20 November 1875.

### The specific nerve energies of the skin

#### *Magnus Blix*

Magnus Blix was the first of Holmgren's pupils to make his own scientific career. He had been an assistant in physiology since 1872 and demonstrator since 1882 until 1885, when he was appointed professor of physiology in Lund.

Ever since antiquity, sense organs had been considered as a kind of entrances, into which the impressions from objects in the surrounding world penetrated along the nerves and were integrated into what was called *sensorium*.

The law of specific nerve energies, first proposed by Johannes Müller in 1826, rather states that the nature of perception is defined by the pathway over which the sensory information is carried. Therefore, differences in perception of seeing, hearing, and touch are not caused by differences in the stimuli themselves but by the different nervous structures that these stimuli excite. For example, pressing on the eye elicits sensations of flashes of light because the neurons in the retina send a signal to the occipital lobe. Despite the sensory input being mechanical, the experience is visual.

The previous conception was that all perceptions could be provoked from every spot on the skin, which was not in accordance with Müller's law. Blix thought that, by applying a localized excitation, it should be possible to register different local responses from the nervous end organs in the skin. He thus applied a weak faradic current with a thin metal point. The current evoked distinct sensations of warm or cold on the skin surface. In his most famous work Blix demonstrated the existence of specific end organs in the skin for the different perceptions of touch, cold, and warmth (26). He showed that there were different end organs for different sensations and called them cold, warmth, and pressure points. In order to study them, he constructed a simple but ingenious piece of equipment (Figure 4).

By putting the fine cone on the skin and marking with different colours the sensations he or his assistant Andersson perceived when the cone was cold, warm, or just pressed on the skin, Blix could map the areas for the different sensations. He found that they very rarely coincide. He wrote, however, that sensations of warmth and cold sometimes could be evoked from the same spot, a view Torsten Thunberg later confirmed. Blix's research was not well known internationally until it was published in German in 1884. Independently of each other, Alfred Goldscheider, professor at the University of Berlin in 1884, and Henry Donaldson, in 1885 at Johns Hopkins University, reported that the skin was not continuously sensitive, but instead, had specific loci for specific tactual senses.

Blix also tried to demonstrate separate trigger points for pain, but writes: 'If there are such points, other methods are needed in order to prove them'. This was done in 1894 when Max von Frey, professor of physiology in Würzburg and Zürich, proposed that pain is an independent tactile quality, together with touch, heat, and cold.

Hjalmar Öhrvall, Holmgren's successor as professor of physiology in Uppsala, characterized Blix's findings in the following exuberant words: 'Since Olof Rudbeck in 1650 detected the lymphatic vessels, the Swedish physiology has not made such an important scientific discovery as the discovery of the cold-, warm-, and pressure points, one of the most important within the physiology of the senses. It has already given inspiration to several other scientists' (27).

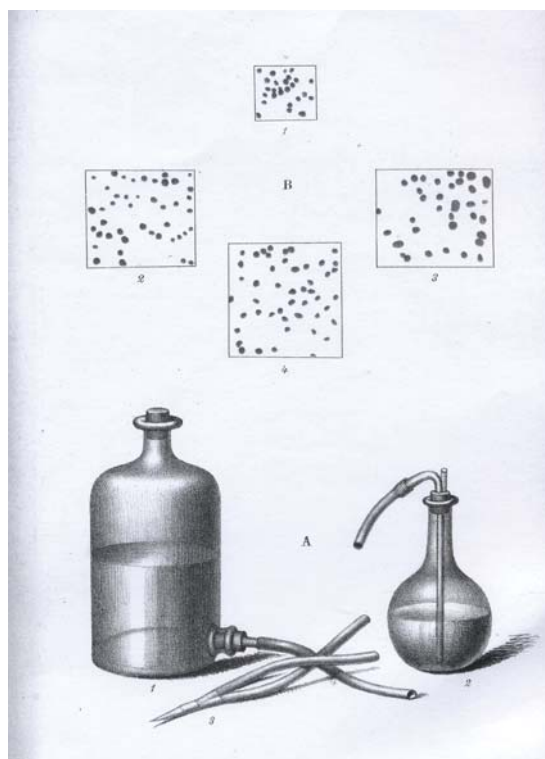


Figure 4. Equipment constructed by Magnus Blix to define the three different sense points. A: 1, a bottle with cold water; 2, a retort with hot water; 3, a hollow electroplate cone. B: cold and warmth points on 1, the dorsal side of Blix's hand; 2, his wrist; 3, his elbow; and 4, dorsal side of J. H. Andersson's left hand.

Blix proved the universality of Müller's law of specific nerve energies, and the idea that a nerve fibre could propagate impulses of different kinds was forever abandoned.

When Blix became professor of Lund, he did not pursue his investigations of the punctuate sensitivity of the skin, but devoted the rest of his life to the study of muscular physiology.

#### *Torsten Thunberg*

One of the scientists inspired by Holmgren and Blix was Torsten Thunberg, successor to Blix as professor of physiology in Lund in 1905. He continued the studies of the senses of the skin. In order to determine the threshold of the sensitivity for warmth and cold, he constructed a series of silver plates with an area of  $2 \text{ cm}^2$  and a weight between 2 and 500 mg. The plates were glued to a cylinder of cork in order to make them easier to handle. Silver was chosen because of its high warm conduction. The warm capacity of the silver plates correlated with their thickness. When a plate of a certain temperature and mass was applied to the skin, it deprived the skin of warmth. Thunberg could by such means estimate the minimum perceptible stimulus (28).

With the equipment that Thunberg had constructed (Figure 5) he also investigated the simultaneous occurrence of the sensation of warmth and cold. He set up two separate spiral brass tubes that were connected by rubber tubes to retorts with warm and cold water. The coils of the tubes were interlocked as shown to the left in the figure; a modern Thunberg grill is shown to the right.

When Thunberg applied his coil to the skin, he made an unexpected observation. Innocuous warm and cool coils that were spatially interlaced produced a painful burning sensation. He could not wholly explain his finding. His first hypothesis was that the warm and cold nerve endings were situated at different depths from the skin surface, but he dismissed this idea. Instead he speculated on some sort of direct and indirect nerve stimulation. The *nerve endings* were thought to be extra sensitive to weak thermal stimulation, but were reacting with a long latency. With *direct nerve* stimulation, the latency time disappeared. Simultaneous stimulation on both these manners entailed the painful sensation (29,30).

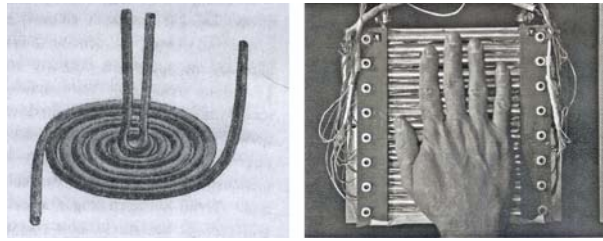


Figure 5. Thunberg's brass coils from 1894 (left) and a modern Thunberg's grill (right), in which fifteen 1-cm-wide silver bars are set about 3 mm apart. Alternate (even- and odd-numbered) bars can be heated or chilled independently.

Thunberg's discovery was not fully understood during his lifetime and was forgotten for many years, but it has now been re-evaluated. It provides an interesting model of integrative mechanisms in the nervous system, supposed to be relevant in explaining the hypersensitivity found in chronic pain of unclear etiology. It is now called the Thunberg (or thermal) grill illusion, or just the Thunberg illusion.

It has been suggested that the thermal grill illusion could be of clinical relevance, casting light on mechanisms involved in neuropathic pain including cold-allodynia. The occurrence of cold-allodynia may also be related to the pathological processes involved in chronic wide-spread pain and is, for instance, common in fibromyalgia (31).

The illusion is created by an interlaced grill of warm (e.g. 40°C) and cool (20°C) bars. When someone's hand presses against the grill, he or she experiences the illusion of burning heat. But if the person presses against only a cool bar, only coolness is experienced; if the person presses against only a warm bar, only warmth is experienced.

### Hjalmar Öhrvall

Hjalmar Öhrvall had been an amanuensis at the physiological laboratory, and when he had defended his doctoral thesis in 1889 he became a demonstrator. In 1899, he succeeded Holmgren as professor.

In his thesis (32), Öhrvall first discussed how taste should be defined. According to older opinions, there were about 10 different tastes. Linné, for example, mentioned 11 in *Sapor medicamentorum*. His basis of division was the use of medicaments (33). At the end of the nineteenth century, however, physiologists had agreed on just four tastes: salt, sweet, sour, and bitter.

Öhrvall translated some of Helmholtz's books into Swedish and was an ardent supporter of his theory of modality, which states that there are various types of sensation, such as vision, hearing, smell, temperature, pressure, and taste. Within each sense, there are differences in quality, such as red, blue, yellow, etc., for vision, and low and high pitch for sound. When two colours are put together, for example blue and green, they create a new, yellow, and when two simple tones are put together they create a complex tone.

Taste was different. A mixture of salt and sweet did not create a new taste, but still tasted both salt and sweet. Accordingly, taste should not be considered as a single modality with four qualities, but as four different senses without any merging between them.

Öhrvall was inspired by Blix's method of stimulating separate end-points in the skin when he proved that there were separate points for the different qualities of sense.

The existence of the taste buds had independently been discovered by Gustav Schwalbe and Christian Lovén in 1867. Öhrvall decided to use Blix's method in order to investigate if there were different taste buds for the taste of salt, sweet, sour, and bitter. He used a concave mirror, which gave a sufficient magnification so that he could distinguish the different buds on his own tongue (Figure 6). Solutions of the tested substances were applied to the different buds with a fine brush.

Öhrvall found that in the papillae fungiformis at the tip of the tongue, of the 91 sensitive to acid, only 12 papillae were sensitive exclusively to acid. And whereas 79 were sensitive to sweet, only three papillae were sensitive to just sweet. No papillae responded only to bitter, although 71 responded to bitter and another taste solution. He excluded the results obtained with salt, because the sensations elicited were not distinct enough. His conclusion was that there were different end organs for the different taste perceptions. These end organs are present in different combinations on the tongue (32).

Öhrvall did not pursue his studies of the sense of taste, but almost 50 years later, his doctoral thesis was reported in detail in Emil von Skramlik's comprehensive textbook *Psychophysiologie der Tastsinne*.



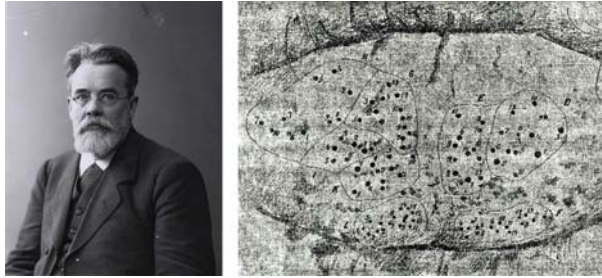


Figure 6. Hjalmar Öhrvall and the tip of his tongue magnified twice. The picture is drawn according to a photograph and shows the position and relative size of the papillae fungiformis referred to in his thesis. (UUB, Kart- och bildenheten, ID 7255).

### *Sydney Alrutz and the perception of heat*

Sydney Alrutz had quite another background than the other scientists working at the department of physiology in Regnellianum. His father was the owner of an iron export company in Stockholm, and when Sydney had passed his high school examination in 1886 it was taken for granted that he would join the family business. During the following years he studied iron melting and passed *Falu Bergsskola* in 1888. But he became more interested in philosophy and theosophy. In July 1891 he was the Swedish delegate at the first annual convention in London of the Theosophical Society of Europe.

In 1892, Alrutz attended lectures in philosophy in Uppsala and at the same time followed courses in physiology, anatomy, and histology at the faculty of medicine. Both Frithiof Holmgren and Hjalmar Öhrvall welcomed him, and he started to participate in the physiological experiments of the senses of the skin.

In Alrutz's first publication, he did not merely repeat Blix's studies from 1882 of the law of the specific energies of the nerves, but could also convincingly show that the criticism against Blix's findings was inaccurate and based on faulty techniques (34). In a following paper 'On the sensation "hot"' (35) he used a series of thin silver plates of different thickness designed by Thunberg to test the thermal sensations released by cold and hot stimulus. He described a perception called *heat*, a quality to be distinguished from *warm*.

At that time, Alrutz was just a student at the faculty of science, but he wanted to pass the examination for *filosofie licentiat*. According to the rules, the examination must comprise three subjects; two of them were theoretical and practical philosophy. As a third subject, Alrutz wanted to include physiology, but that belonged to the faculty of medicine. He had to apply to His Majesty the King for an exemption from the rules. His application was supported both by the two professors of philosophy and by the faculty of medicine. He argued for a combination of philosophy and physiology because he thought psychologists needed insight in the functions of the human body and the physiologists needed knowledge about the mind. His application got a forceful support from the faculty of medicine and was approved by the King (36).

In 1900 Alrutz passed his degree as a licentiate, and in 1901 he defended his thesis 'Investigations into the sense of pain' (37) and became a *docent* the same year. In 1902, he established a psychological laboratory in two rooms at the bottom floor of Regnellianum. It was used for courses in which 530 participants took part during the years 1902–1908. Later, regular laboratory courses started, and in all of them he was supported by Öhrvall and the other physiologists.

After some years, however, Alrutz's theosophical interests took over, and he started studies of occult phenomena such as telepathy and clairvoyance. Through what he called *nerve radiation*, he argued that he could affect a person at a distance by moving his hand upwards or downwards over the body without touching him. He called these movements *passing*. Upward passes increased the sensitivity and downward passes decreased it (Figure 7). Alrutz performed numerous experiments – mainly with a single participant and himself as the experimenter – in order to eliminate alternative explanations such as telepathic phenomena or suggestion. His assumption was that information could be transferred over distance, and that this transference could not be explained within the framework of ordinary physical laws. His main study person was Karl Wennersten, a bicycle repairer, who had consulted him because of nervousness.

All these activities must have appeared strange to the rational scientist Öhrvall, but it is difficult to find official statements from him on what he thought about the line of research going on in the two rooms at Regnellianum. Öhrvall seems to have reacted only once. In April 1905, Alrutz gave a lecture at the association Minerva, whose



Figure 7. Sydney Alrutz and Karl Wennersten during an experiment on 27 April 1913. According to the figure text in '*Till nervsystemets dynamic*', Alrutz is doing downward passes with both hands at the same time. Photographer: Östling, Uppsala.

goal was to promote co-operation between practitioners from different disciplines. He talked about 'The phenomenon of table-turning and its explanation'. The newspaper *Dagens Nyheter* then received an anonymous letter under the heading 'The occult science in Uppsala'. According to the letter, Öhrvall had been present, and he stated that he was not familiar with the literature within the field, but if the occult science was true, many of the findings of modern natural sciences were wrong. He also pointed out that if the forces Alrutz talked about were true, it would be difficult to do chemical analyses and would even destroy the confidence in provision and poultry dealers, when they, in spite of legally hallmarked weights, could make unlawful profit because of the peculiar psychical force. The letter pointed out that Öhrvall's opinion was that Alrutz's lecture was ridiculous and puerile.

In a reply Alrutz protested vehemently against the content of the letter and that his 1½ hour long lecture only was related in a few lines. Professor Öhrvall's short contribution to the discussion, on the other hand, was related almost completely, but he did not write that Öhrvall was quoted incorrectly. This statement of Alrutz indicates that Öhrvall in fact was very critical (38).

During the following years, Alrutz studied the influence of hypnosis on the senses. The results have been summarized in his opus magnum, 'The dynamics of the nervous system' (39). The book comprises 517 pages and has seven appendices.

According to the book, Hjalmar Öhrvall and Gustaf Göthlin, professors of physiology, both took part in the experiments at the physiological laboratory and were sometimes performing the passes themselves. Professor Swedberg, the Nobel Prize winner in chemistry 1926, participated in many séances both at the department of chemistry and in Alrutz's dwelling in Kåbo in the years around 1911–1914. He was even performing passes himself and is quoted as being positive to the séances. Among other prominent professors from the faculty of medicine in Uppsala taking part in Alrutz's séances were Gunnar Forssner, Ragnar Friberger, Johan Wilhelm Hultcrantz, Ivar Thorling, Gustaf Bergmark, August Hammar, and Frey Svensson. Professors Johan Edgren and Frithjof Lennmalm from the Karolinska institute participated in experiments in Stockholm. Alrutz also demonstrated his passing method before the Upsala Medical Society and the Minerva Society.

From the faculty of theology Bror Jonzon, later bishop, and Emmanuel Linderholm, professor of church history, and from the faculty of science the professor of philosophy, Erik Olof Burman, were all present at many occasions and even made passes themselves. Thus, a lot of the leading professors at the university accepted Alrutz's methods and showed a positive interest in his performances; what they really thought is difficult to know as the account is based solely on Alrutz's own statement.

As a medical student, the future chairman of the Swedish medical association and professor of paediatrics at the Karolinska institute, Curt Gyllenswärd, gave an account of an experiment he had carried out on a hysterical patient of the effect of hypnotic passes on the sensibility of the skin and the colour vision. Gyllenswärd concludes: 'As regards the changes of the sensibility brought about by the passes, I must regard these to be caused by some sort of transferred nervous energy'.

As a medical student, Bernhard Jacobowsky, professor of psychiatry in Uppsala 1932–1960, investigated the influence of hypnosis on the perception of red and the stimulation threshold (minimum perceptible) for the sense of light on the same patient. Upwards passes decreased the threshold for the sense of light and the

threshold for red, and the downward passes acted in the opposite direction. His conclusion was that nothing contradicts the hypothesis of Alrutz that the treatments imply the transference of nervous energy from one person to another through some sort of hitherto unknown form of radiation. Both these experiments were performed in the dark-room of the physiological laboratory in 1917.

Alrutz believed very strongly in the effect of passes on nerve radiation and wanted to convince others about its effect. This, perhaps, is why he invited so many prominent men in the scientific community to attend his séances. He tried to convince them empirically through experiments rather than by presenting ideas that could make the phenomenon understandable and lead to testable hypotheses.

Alrutz's contributions in the physiology of the senses are not comparable to the previously mentioned scientists, but he started the psychological laboratory at the department of physiology, which was the first in Sweden. Alrutz's educational programme was also a pioneering achievement in Swedish psychology. In spite of his deviations from established science, Alrutz was an important pioneer for experimental psychology in Sweden. His book 'On the study of mental life on the basis of physiology' from 1899 was a powerful plea for psychology as an independent academic discipline, but a department of psychology was not established until 1948, when the department of education was divided into psychology and education.

#### *E. Louis Backman and the sense of smell*

The last contribution from Uppsala to the physiology of the senses at the turn of the previous century stems from Eugène Louis Backman. Already in 1891, Öhrvall had written about some physical peculiarities of organic compounds with strong scent, but he had not continued this research until late in his time as professor (40). In 1917, the year Öhrvall retired from his chair as professor, Backman published an experimental study where he found that the intensity of a smell is increased when the water solubility of the compound is decreased and is increased with increased lipid solubility. Backman's conclusion was that the ability of the compounds to stimulate the smell sensation must be due to these changes and to the concentrations of them in the peripheral nerve endings for smell (41).

Backman's conclusion is consistent with Ernest Overton's findings some 20 years earlier. Overton investigated the osmotic properties of cells and noticed that the permeability of molecules through membranes is related to the lipid solubility of the compound. This is of fundamental importance for the action of anaesthetic agents (42).

Backman also tested Alrutz's allegation that the patients had a heightened sense of smell during light hypnosis. The experiment subject was first tested for acetic acid and benzaldehyde. Alrutz then made the patient's left side insensible through a downward pass on this side and hypersensible on the right side through an upward pass and applied a light hypnosis. When Backman then tested the patient's ability to smell, he found that the ability to recognize acetic acid had increased twofold and benzaldehyde fivefold as compared with the awake state. It must be stressed, however, that just one, unidentified, test person was examined and that only three different concentrations of the test substances were used, each concentration just once.

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