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## History of Neurology The curious synalgia of Henri Gourdan de Fromentel (1858–1914)



neurologique

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#### ABSTRACT

In 1883, Henri Gourdan de Fromentel defended his thesis on an original topic that has not really been studied since. He examined the simultaneous perception of pain in two distinct and distant, but homolateral, areas of the body following a single stimulation on himself. In the discussion he compared his synalgia with other types of synaesthesia that did not involve pain and concluded that it was likely to be of central nervous system origin. After a brief account of Fromentel's life, this article discusses his thesis and a book on the subject he published five years later in the light of current understanding of the phenomenon and the proximity of synalgia and allachaesthesia.

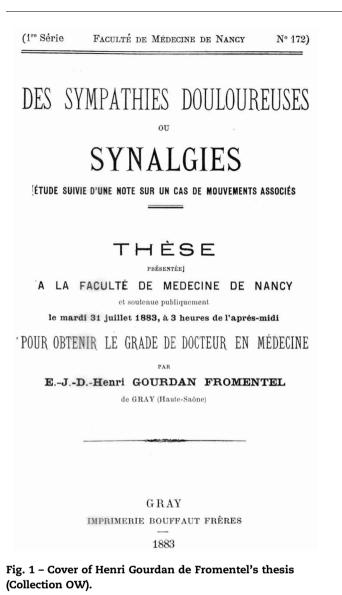
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Henri Gourdan de Fromentel (1858–1914) defended his doctoral thesis in medicine on 31 July 1883 (Fig. 1) at the medical school in Nancy. Henri Beaunis (1830–1921), the Professor of Physiology, presided over the jury. Fromentel's subject was highly original as was his decision to write it in the first person: *Des sympathies douloureuses ou synalgies* (pain sympathy or synalgia) [1]. To emphasise the family nature of this symptom, he noted that his father, Louis Gourdan de Fromentel (1824–1901), a physician remembered also for his paleontological research, experienced symptoms identical to his own. Fromentel like his father before him became a family doctor in the village of Gray in northeastern France, which had

E-mail address: walusinski@baillement.com. https://doi.org/10.1016/j.neurol.2021.05.003 0035-3787/© 2021 Published by Elsevier Masson SAS. around four hundred inhabitants at the time. Mobilised at the age of 56 in August 1914 Henri Gourdan de Fromentel died on the front shortly thereafter, having obtained the rank of auxiliary physician (second battalion of the 73rd infantry regiment).

#### 1. 1883 doctoral thesis: Synalgia

In his 68-pages thesis, Fromentel tried to describe the nature of a curious symptom of pain occurring not only at the site of the initial stimulus but simultaneously in a second remote



unstimulated site. He coined the term "synalgia" to describe this phenomenon, whereas in 1866, Alfred Vulpian (1826-1887) had used the term "synaesthesia", from the Greek sun, union (meaning together), and aisthesis, sensitivity (meaning sensation): "Production of a double sensation arising from one stimulus originating in a circumscribed sensory area. One of the sensations is perceived at the site of the stimulus; the other involves an area that is more or less distant from the first and has not undergone any direct stimulation" [2]. Synalgia is specific for pain, whereas Vulpian's synaesthesia applies to all types of cutaneous sensibility. The word "synaesthesia" carries today a more or less different meaning describing an experience in which stimulation in one sensory or cognitive stream leads to associated experiences in a second, unstimulated stream. For example, in grapheme-colour synaesthesia, a certain grapheme induces a specific colour ("the numeral 1 is red"). The most prevalent form involves colour as the concurrent (e.g. grapheme-colour, smell-colour, touch-colour, taste-colour), but there are rarer types like touch-taste or sound-touch [3].

In 1876, Adolphe Gubler (1821–1879) used the expression "douleurs répercutées" (reflected pain) to describe the phenomenon reported by Fromentel: "What can rightfully be called pain echoes, caused by spontaneous or provoked pain and which reverberate at a distance in parts that are connected via the central nervous system with the part that is the point of departure of the stimulus" [4] He added another point: "A pain provoked in a given area will only echo in one other area which is often at a significant distance" Fromentel bore witness to this statement in his own experience: "When I scratched certain areas of my skin with my fingernails, I felt a pricking, pinching, shooting pain at points far from the irritated point This pain was sometimes so sharp that I was reluctant to stimulate the little bumps [hypertrophied, inflamed pilosebaceous follicles] on the back of my shoulders for fear that I would feel, with each scratch, a very painful shooting pain around my waist in the lumbar area" (Fig. 2). He noted that the sensations were always on the same side Fromentel used the word "sympathie" to represent a descriptive and explanatory mechanism. In accordance with Louis Bourgey, the earliest mention of "sympathie" in medical literature is to be found in a book of the Hippocratic collection: "all parts of the body are in sympathy; the body is an organism" [5]: "The sympathetic shooting pain is often more intense than at the stimulated point and persists for a few seconds after the initial discomfort has stopped" Fromentel also used another neologism that Gubler had coined: "echo pain" He noted that repeating the stimulation at the initial point abolished the echoed perception When the initial pain involved touching an area of acne, he observed that when scarring of the inflamed area developed it was no longer possible to trigger synalgia After studying the phenomenon in several dozen of people, Fromentel asserted that "synalgia is a stable phenomenon in the same person and across subjects" and that stimulation of pain at a specific point always triggered the echogenic pain at the same point Fromentel classified the areas of referred pain as upper and lower depending on whether they were above or below the initial stimulus He asserted that, very exceptionally, "mixed synalgia" occurred; that is, one excitation could correspond to two echo points of pain, one above and one below the initially stimulated area.

He added diagrams to his thesis representing the trigger and echo zones (Fig. 2). There were also about ten pages of tables summarising the implicated nervous branches. Fromentel called on his readers to share their experiences if they had the same sensations so that he could add further detail to his descriptions, noting that the areas he had indicated were not "definitively established". He concluded his thesis by referring to his pathophysiological theory concerning synalgia, described at the end of this paper.

Mathias Duval (1844–1907) invited Fromentel to present his personal case to the French Society of Biology on 05 January 1884. Duval's explanation of the phenomenon described by Fromentel mainly involved the cortex, where "the excitation appears to be propagated from one cerebral centre to another nearby centre" [6]. He dreamed of one day having "a geographical map of the projection of peripheral points on the cerebral cortex"! In response, Auguste Ollivier (1833–1894) added: "It would be very useful to know the exact topography

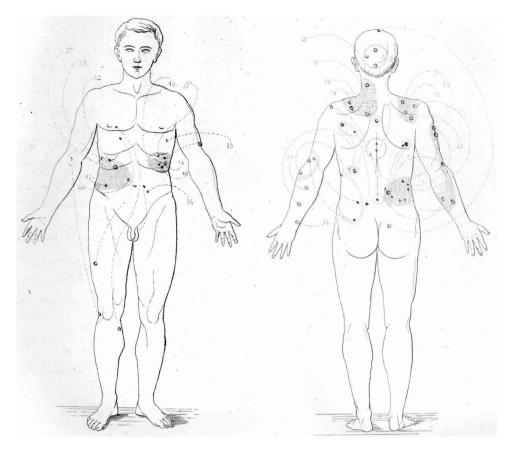


Fig. 2 – Diagrams illustrating Henri Gourdan's 1883 thesis (Collection OW).

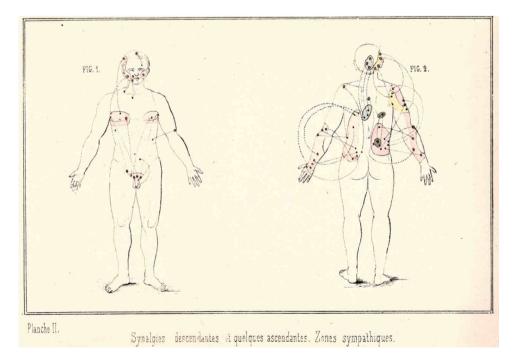


Fig. 3 - One of the three illustrations in Henri Gourdan Fromentel's 1888 book (Collection OW).

of all parts of the body to see how excitation causes either movements or sensory impressions in an area at a greater or lesser distance". Antoine-Auguste Pierret (1845–1920), a pupil of Jean-Martin Charcot (1825–1893), wrote a report on Fromentel's thesis in the journal Lyon médical: "Synalgia is essentially a variety of synaesthesia, a more general term that refers to an unspecified double sensation perceived at two distinct points of the body more or less distant from each other and as the result of excitation of only one of these points. Thus, synaesthesia can be considered the genus and synalgia the species" [7].

#### 2. Les synalgies et les synesthésies (1888)

After these encouragements, Fromentel set out to "add some new facts" to his research, disseminate his ideas more widely, and bring it to a broader public by publishing a 186-page book on synalgia in 1888. Duval flattered and encouraged him by writing, "Your observations may result in marvellous inductions on the probable interconnections between cerebral centres". The first chapters used the clinical argumentation from his thesis, only adding marginal data of little interest.

He sometimes had difficulty objectively determining the precise area of the echoed pain. However, his self-experimentation raised the possibility that there was a back-and-forth transmission between the two areas and stimulation in the area of the referred pain could sometimes induce pain in the site of between the two areas (Fig. 3). Fromentel had consulted many old medical books and realised that descriptions related to synalgia were very rare. He discussed at some length the writings of Robert Whytt (1714–1766) on forms of sympathy [8]. But the conclusion of his long review of these sources was that no cases reported by any author were similar to his own. He regretted that the future Nobel prizewinner Charles Richet (1850–1935) only devoted a short section to synaesthesia in his thesis defended on 23 January 1877, entitled "Recherches expérimentales et cliniques sur la sensibilité" (Experimental and clinical research on sensitivity) [9], where Vulpian had presided over the jury. Richet wrote: "The most interesting phenomena, rightfully called synaesthesia, are nothing other than irradiations with a remote effect. Among the various types of synaesthesia, there are both normal and pathological forms. The cause of the latter appears to be hyperaesthesia of the spinal cord. Among the normal forms, one of the most common is the painful sensation felt in the teeth when a sharp, strident sound is heard. Pathological synaesthesia is more frequent and easier to explain" [9]. Although the dental pain/strident noise example can be understood as a clinical type of synaesthesia, Richet provides no examples similar to Fromentel's descriptions of synalgia. Fromentel concluded his historical and bibliographical chapter by citing Gubler as the only author to have reported what he had observed in his own body.

#### Synalgia compared to allochiria, allachaesthesia, synaesthesalgia

The living organism receives information about the external environment and its changes through a certain number of sensitivities. Some of that give rise to a phenomenon of consciousness that is referred as sensation, which can be described by words. Sensation can also have an affective aspect, denominated as pleasure or displeasure, an important determinant of behavior. The sensation of pain is associated with displeasure, possibly anticipated with onset of anxiety [10]. Numerous pain phenomena, or phenomena associated with pain, have been written about for centuries. A review will show us how they differ or not from synalgia.

In his lesson on 21 July 1864, for the course of physiology at the Museum of Natural History, Vulpian used the term "sympathy" in the following example reminiscent of Whytt: "Mechanical irritation of the external auditory canal gives rise to a peculiar sensation, a tickling in the throat that causes fits of coughing" [2]. When the ear is cleaned using tubing and a bulb to remove wax build-up, water passing though the external auditory canal triggers coughing in many people. The auricular branch of the vagus is responsible for this phenomenon known as Arnold nerve reflex, which are different from Fromentel's synalgia.

In 1877, in his clinical lessons, Sigismond Jaccoud (1830-1913) stated "Apophysal points, arthralgia, and all types of socalled kinaesthetic pain or associated pain, characterised by the fact that the sensation experienced is not at the site of the actual lesion and is felt at a distance from it; for example, the pain in the right shoulder in liver disease, arthralgia in the knee in cases of coxalgia, and pruritis in the nostrils in cases of intestinal worms" [11,12]. These phenomena, well known to clinicians, enable them to recognise rupture in tubal pregnancies by pain in the right shoulder, coxarthrosis by gonalgia, and so forth. Are these examples of irradiation or synalgia? Irradiation is defined as a single process along a continuum whereas in synalgia, there are two distinct localisations separated by a certain distance. Already in 1835, John Hunter (1728-1793) in his "Lectures on the Principles of Surgery" was the first to give an explanation for this type of mistaken perception. He hypothesized that nerves could converge in the body or connect in the brain in such a way as to create a misrepresentation of the localization of the referred pain: "an account for delusion of sensation in ourselves" [13,14].

In the "Spinal cord (physiology)" chapter of the Dictionnaire encyclopédique des Sciences médicales of Amédée Dechambre (1812-1886) published in 1874, Vulpian wrote a section on synaesthesia: "The more or less direct anatomical connections that exist in the spinal cord between the receptive centres and the centres where peripheral impressions are transformed explain a fact that may occur in good health, but especially in the morbid state, namely the production of double sensations stemming from an impression originating in a circumscribed sensory area. One of these sensations is perceived to be linked to this area as its starting point; the other involves an area that is more or less distant from the first and that has not undergone any direct stimulation" [11]. Vulpian gave the example of pain in the shoulder in diaphragmatic pleura inflammations but did not present any cases of the type described by Fromentel. In 1893, Henry Head (1861–1940) put forward an explanation, establishing and mapping the segmental relationship underlying the dermatomal rule, i.e. a pain arising in disordered viscus, when referred to a point (region) on the body surface, is felt in an area of the skin of the same embryonal segmental origin as the diseased viscus. Head, him too, spoke of referred pain [15]. Louis Antoine Ranvier (1835–1922), was fascinated by the discovery of the ramifications of the axon, made by Camillo Golgi (1843–1926) in 1873, using "the black reaction". Behind, Ranvier proposed an ingenious theory of referred pain in his *Traité technique d'histologie* [16]. He suggested that the nerve fibers originating from the irritated area and those coming from the region to which the sensation is referred converge on the same axon, and thus the same cell body, causing the spatial dislocation of sensation [17]. This theory was never proved and seems inadequate to explain Fromentel's synalgia.

The Austrian neurologist Heinrich Obersteiner (1847–1922) introduced, in 1882, the term "sensory allochiria" from the Greek allos (other) + chiria cheir (hand), to describe clinical cases he observed and to denote a confusion of sides: the patient responds to stimuli presented to one side of their body as if the stimuli had been presented at the opposite side. Allochiria is observed nowadays mainly in the context of neglect, which is usually due to a lesion affecting the right parietal lobe i.e. stroke, parieto-occipital tumors, or myelopathies (tabes dorsalis, multiple slerosis) and occasionally hysteria [18]. The majority of allochiria's cases are related to the tactile sense, including sensory modalities of pain but allochiric responses have been also described as visual or auditory allochiria. Allochiria can occur in relation to any or every segment of the body but it may be restricted only to one part of the body [19]. In the same order of ideas, the British neurologist Thomas Grainger Stewart (1877–1957) coined, in 1894, the term allachaesthesia from the Greek allache (elsewhere) + alsthanesthal (to notice, to perceive), (ie, allesthesia, allochaesthesia, alloesthesia, or atopognosis) to denote horizontal or diagonal displacements of localization for touch confined to the ipsilateral side of the body. Allachaesthesia refers to a mislocation of tactile sensations, to a location other than the one that is actually being touched. Actually, allochiria is considered a variant or a subset of the class allachaesthesia [20]. Fromentel's synalgia can be seen as a condition phenomenologically related to pain's allachaesthesia.

Finally, in 1915, Achille Souques (1860-1944) added new observations to those collected by Pierre Marie (1853-1940) and Chiriachitza Athanassio-Bénisty (1885–1938) [21] in relation to soldiers with partial severance of the median nerve and coined the word "synaesthesalgia" or "algic synaesthesia" to describe their pain: "If an object brushes against any point on the surface of the skin, this causes an algic synaesthesia in the injured hand. Furthermore, the subject does not extend what is happening in one hand to the other. He perceives and perfectly localises tactile excitation in the healthy hand and clearly distinguishes it from the sensation produced simultaneously in the injured hand. The term 'synalgia' is not more appropriate; the pricking of the skin of the healthy hand does not have any abnormal effect in the paralysed hand" [22]. It can be seen as a form of synchiria, during which a stimulus applied to one side of the body is felt on both sides. Most often, these soldiers were suffering from what is now known as causalgia or reflex sympathetic dystrophy, actually called complex regional pain syndrome, caused by a functional disorder of the autonomic nervous system. Alfred Cayla (18911983) added three other similar observations in 1917 and concluded that "synaesthesia is only found in causalgia", described by Silas Weir-Mitchell (1829–1914) during the American Civil War [23,24]. As Souques noted none of these observations shed light on Fromentel's synalgia,

#### 4. Pathophysiological explanations

Fromentel presented four pathophysiological theories to explain synalgia. He rejected the theory of peripheral anastomosis of the sensory nerves, finding it contrary to known anatomical observations, because his perceptions did not correspond to the various recognised nerve plexuses that could be routes of communication. The German physiologist Johannes Müller (1801–1858) seems to have been the first to try to understand the neurological basis of referred pain. Fromentel credited him for the notion, which underpinned the second and third theories. In his 1845 Manuel de physiologie [25], Müller referred to associated sensations and suggested two explanations. The first involved a mixture of sensations at the dorsal root ganglion, the second involved a referral of the sensation perceived at various points along the spinal cord. Müller acknowledged the totally hypothetical nature of his suggestions, which did not specifically address pain but rather tactile sensations in general. Fromentel rejected these hypotheses after discussing them at length in his book. These sections now appear incoherent, due to the limited understanding of the physiology of nervous transmission at the time of his writing, and because of a lack of detailed knowledge on the anatomy of the various sensory pathways.

Fromentel was clearly unaware of the description of allochiria by Obersteiner. Fromentel believed synalgia originated in the cortex with initial sensation being diffused by contiguity or by association fibres to nearby perceptive centres receiving sensations from other areas of the body: "Sensory irradiations always occur between neighbouring, contiguous centres, connected by means of cellular extensions". Unaware of later localisation knowledge, including the homunculus of Wilder Penfield (1891–1976), he assumed that "the perceptive centre of cutaneous impressions in the upper limb is juxtaposed to two similar centres of the head and lower limb, making them contiguous to the centre of the trunk". He went on to review the work on cerebral localisations of David Ferrier (1843-1928) and Hermann Munk (1839-1912), suggesting that the study of synalgia could help better understand the functional anatomy of the cerebral cortex. This implied a specific pain centre, which had yet to be precisely localised.

At the end of his book, Fromentel established a parallel between "the sympathies of mobility or synkinesias and the sympathies of sensitivity". In this context, he discussed a case of "pseudochromaesthesia" or synopsia that he related to the "association of ideas and cross sensitivity" without addressing their resemblance with synalgia.

#### 5. Current thinking

Synaesthesia, trans-sense synaesthesia more precisely, is a phenomenon that interests psychologists more than physicians and has been a particularly popular subject for research in the last 20 years [26]. Émile Littré (1801–1881) defined it as follows: "Production of two or more sensations under the influence of a single impression; one of the sensations can be linked to the exact point of excitation, whereas the others occur in areas more or less distant from the initial point" [27]. In 2020, Serge Nicolas proposed that synaesthesia was "a mental phenomenon where the objective stimulation of a sensory or cognitive pathway leads to subjective involuntary experiences in a second sensory or cognitive pathway" [26]. According to Nicolas, more than seventy different types of synaesthesia have been identified, but he considered the most interesting types to be coloured hearing or chromaesthesia and grapheme-colour synaesthesia, which around 4% of the normal population experience at some stage of their lives.

In synaesthesia, two different but simultaneous sensory perceptions are associated, one automatically producing the other. Fromentel only described a single sensation localised to two sites, at a distance from each other, and induced by a single stimulation. The current anatomofunctional knowledge can help us to understand Fromentel's perceptions.

Afferent sensory fibers from the receptors follow the peripheral nerves toward the central nervous system (CNS). Close to the spinal cord, the sensory fibers are collected in the dorsal roots and enter the cord. Sensory information reaching the spinal cord through the dorsal roots is further conveyed to higher levels of the CNS. There are two somatosensory pathways, both consisting of the neurons forming a chain from the receptors to the cerebral cortex. The first, the primary sensory neuron, has its cell body in a spinal ganglion. The next, the secondary sensory neuron, has its cell body in the grey matter of the spinal cord. And the third, the tertiary sensory neuron, has its cell body in the thalamus. Both somatosensory pathways are crossed, so that signal from one side of the body are brought to the cerebral hemisphere of the other side. The actual crossing over takes place at different levels of the two pathways. The neurons that conduct signals from different parts of the body are kept separate. Whereas axons conducting from different kinds of receptors lie intermingled in the peripheral nerves and the dorsal roots, they are grouped according to their thickness as soon as they enter the spinal cord. The thick dorsal root fibers (A $\alpha$  and Aß) pass medially, whereas the thin ones (A8 and C) follow a more lateral course into dorsal horn. There, neurons conveying signals related to low-threshold mechanoreceptors and nociceptors (and thermoreceptors) are kept separate in the spinal cord. This segregation is maintained in the pathways that lead from the cord to higher levels.

The medially located, thick dorsal root fibers continue without synaptic interruption rostrally in the dorsal columns without synaptic interruption in the cord. The first synaptic interruption occurs in the dorsal column nuclei, which contain the cell bodies of the secondary neuron in this pathway. The secondary axons cross in the medulla to end in the thalamus on the opposite side, forming the so-called medial lemniscus. From the thalamus, the tertiary neurons send their axons to the primary somatosensory cortex in the post central gyrus. Together, these three links constitute the so-called dorsal column-medial lemniscus pathway. The dorsal column-medial lemniscus pathway conveys perception of touch, pressure, vibration and kinesthesia, and gives the ability to distinguish differently placed and different kinds of stimuli. The central pathway followed by signals conducted in the thin dorsal root fibers make synaptic contacts in the gray matter of the dorsal horn, where most of the secondary sensory neurons of this pathway are located. The axons of the secondary neurons cross to the other side of the spinal cord and form the spinothalamic tract. This tract is important for the perception of pain and temperature, which is consistent with the observation that it transmits information mainly from A $\delta$  and C dorsal root afferent. In the somatosensory cortex, the body is represented somatotopically [28].

Since secondary pain perception in synalgia is precisely localised, only the spinothalamic tract would be implicated. It is possible to hypothesise the existence of aberrant fibres in this tract projecting to two distinct non-contiguous regions of the parietal homunculus to explain the simultaneous perception of two pain localisations arising from a single peripheral stimulation. This proposal is consistent with what Henri Gourdan Fromentel proposed in 1883.

Mirror-touch synaesthesia is a phenomenon in which individuals experience somatosensory sensations when seeing someone else being touched. Mirror neurons were suggested to be the mechanism underlying this type of synaesthesia [29]. Aberrant function of mirror neurons is an unlikely explanation for the synalgia described by Gourdan de Fromentel.

Originally, the term 'diaschisis' was coined by Constantin von Monakow (1853–1930) in 1914 [30] to describe the neurophysiological changes that occur distant to a focal brain lesion. A new type of diaschisis is now defined as the changes of structural and functional connectivity between brain areas distant to the lesion (i.e. connectional diaschisis). As opposed to focal diaschisis, connectional diaschisis, focusing on determined networks, seems to relate more consistently to the clinical findings. Did the concept of functional or connectional diaschisis can explain Fromentel's perception? [31].

When databases such as PUBMED are searched with the term "synalgia", the only results are a few articles on stomatology. Since Fromentel's time, the literature on allachaesthesia appears comparable to his synalgia. Wouldn't it be useful if specialist consultations for treating pain included an investigation to identify such cases so that they could be studied in light of current knowledge?

#### **Statement of ethics**

This work required no approval from an institutional review board and was prepared in accordance with ethical guidelines of the journal.

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