
Sigmund Freud, MD: Forgotten Contributions to Neurology, Neuropathology, and Anesthesia

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Abstract

Dr. Sigmund Freud began his professional career as a neurologist and clinical investigator. While his contributions to psychoanalytic theory account for his worldwide renown, it is his early work in the neurosciences that Freud hoped would bring him the professional respect he desired. Today his contributions to neurology, neuropathology, and anesthesia are all but forgotten. In fact, many students and clinicians in the neurosciences are not even aware that Freud's initial scientific work was instrumental in allowing for the major discoveries of his time. In fact, Dr. Sigmund Freud made several notable contributions to the fields of neurology, neuropathology, and anesthesia; contributions that have long since been forgotten despite their pivotal role in launching the discoveries of other scientists. It is these forgotten contributions that best demonstrate Freud's scientific and research capabilities - particularly his ability to observe and describe a variety of disease processes.

INTRODUCTION

Freud became interested in the neurosciences early in his career as a physician and researcher. Prior to beginning work on his theory of psychoanalysis, Freud (under the tutelage of great thinkers like Charcot and Maynert) made several contributions to the field of neurology and completed four large texts on several topics of interest to neurologists, neuropathologists, and anesthesiologists during the early years of his career. His primary contributions include, but are not limited to, the following investigations and research papers regarding the following topics that will be described briefly in this article:

1. Freud initiated his work in neurology with basic science research into the phylogenetic association between the central nervous system of lower vertebrates and humans. [1,2,3]
2. Using Crayfish, Freud demonstrated that nerve fibers emerge from a web-like substance in the neurons and that the structure is always fibrillary. [15]
3. Freud introduced the use of gold chloride to stain nerve tissues. [4]
4. Freud published three important papers describing the structure and function of the medulla oblongata and the connection between the posterior columns

of the spinal cord, the acoustic nerve, and the cerebellum.

5. Freud wrote the first analytical and scientific summary of research on cocaine and was the first investigator to predict its potential use as a local anesthetic. [5,6]
6. Freud also wrote four major texts describing neurological disorders including a work entitled, *Aphasia: A Critical Study*, published in 1891. [7,8] His second book, co-authored with Oscar Rie, was a monograph entitled *Clinical Study on the Unilateral Cerebral Paralysis of Children* also published in 1891. [9,10] In addition, Freud published a third text in 1893
7. entitled *On the Knowledge About Cerebral Diplegias of the Childhood Age (In Connection with Little's Disease)*. [9,10] Freud's work in the area of cerebral paralysis culminated in 1897 when he published his final work in neurology entitled, *Infantile Cerebral Paralysis*. [11]

Figure 1

Copy of Sigmund Freud's Birth Certificate. Published with permission of Sigmund Freud Copyrights, LLC/ Paterson Marsh Ltd.



FREUD'S EARLY PROFESSIONAL YEARS

Born in the town of Freiberg, in what is now Czecko-Slovakia, on May 6, 1856, Sigismund Schlomo Freud, the father of psychoanalytic theory, was to become one of the most prominent, if not controversial, personalities of the 20th century. [12] Born with an innate curiosity to understand the world around him, Freud excelled in his studies throughout childhood. As all young students tend to do, Freud explored several possible career choices, including law, before settling on a career in Medicine.

In 1873, Freud enrolled at the University of Vienna, the prominent University of the City where he had lived since the age of four when his family moved to Austria. Freud experienced immediate disappointment during his early days at the University as he was exposed, not for the first or last time, to anti-Semitic sentiment. In his autobiography, Freud reports [13]:

These first impressions at the University, however, had one consequence that was afterward to prove important; for at an early age I was made familiar with the fate of being in the Opposition and of being put under the ban of the 'compact majority.' The foundations were thus laid for a certain degree of independence of judgement. (PP 7)

Independence of judgement and thinking is exactly what Sigmund Freud developed in those early years at the university as he worked in the company of great thinkers like Ernst Brucke, Ernst von Fleischl-Marxow, Christian Theodor Billroth, Oscar Hertwig, Carl von Rokitansky, Willem Einthoven, Carl Koller, and many others. It was during these early years that Dr. Freud developed his keen skills of observation and study - skills that Freud would later

put to good use in his investigation of a variety of neurological disorders, prior to conceptualizing his own unique vision of the human psyche. It was these early years, in fact, that laid the foundation for Freud's theoretical description of the inner workings of the human mind and his development of the theory of psychoanalysis.

FREUD'S INITIAL WORK IN THE FIELD OF NEUROLOGY

After the initial shock of university life wore off, Freud found peace in the laboratory of Ernst Brucke. As Freud describes in his autobiography [13], "in Ernst Brucke's physiological laboratory, I found rest and satisfaction... Brucke gave me a problem to work out in the histology of the nervous system; I succeeded in solving it to his satisfaction and in carrying the work further on my own account" (pp. 8). The work referred to be Freud in his autobiography includes his earliest publications in neurology and neuropathology - studies regarding the histologic features of the nervous system of certain species of fish.

In the physiological laboratory of Ernst Brucke, where he worked on and off between 1876 and 1882, Freud carried out several experiments and published three original papers. [1,2,3] His first original paper describes the histologic structure of a lobe-shaped organ of the eel. [3] While this was Freud's first written work in the field of neuropathology, because of the delay associated with the review process required of scientific manuscripts, it was his second publication in the year 1877. In his first publication [2], (actually the second written article), *Über den Ursprung der hinteren Nervenwurzeln im Rückenmark von Amnocoetes (Petromyzon Planeri)*, ("On the origin of the posterior nerve roots in the spinal cord of Amnocoetes"), Dr. Freud demonstrated that certain undifferentiated cells in the spinal cord of fish (the dorsal gray matter) represented the origin of the sensory root fibers that later evolved to form the posterior root ganglions. Freud persevered in his research and continued to describe the histologic anatomy of the fish spinal column and the origin of the dorsal root ganglion and nerve root in his third publication in 1878. [3]

While these papers described only lower vertebrates, Freud's histologic work in these early studies taught him the basic skills necessary to work with human tissue. In a letter to Wilhelm Knopfmacher dated August 8, 1878 [14], Freud expressed his pride in these first publications when he wrote:

I am also sending you herewith my collected works, not my complete ones as I have reason to suspect, for I am awaiting

the correction of a third, and a fourth and fifth keep appearing in my prescient mind, which is startled by them like Macbeth by the ghosts of the English kings: "What! Will the line stretch out to the crack of doom?"

During these holidays I have moved into another laboratory, where I am preparing myself for my real profession: "flaying of animals or torturing of human beings," and I find myself more and more in favor of the former. (PP 6-7)

These early works formed the cornerstone for the neuropathological investigations that would follow in which Dr. Freud produced a detailed description of the medulla oblongata tracing the interconnections between its fibrillary nerve tracts and the cerebellum of the human central nervous system. Dr. Freud's papers on this topic would become the first detailed description of these important neurological pathways.

FREUD AND NEUROPATHOLOGY: A STUDY OF THE MEDULLA OBLONGATA

Following his early publications in basic neuroscience research, Freud began his work in clinical neurology. Freud's first publication in clinical medicine was prompted by a recommendation from his friend, mentor, and colleague, Ernst Brucke, who advised him to pursue research in clinical medicine where his talents could be more readily recognized by other colleagues. According to Dr. Brucke, there was no recognition in academia, and without recognition, there could not exist intellectual or financial freedom. Freud listened carefully to his mentor and friend, and took Dr. Brucke's advice to heart, becoming increasingly involved and interested in clinical medicine during his middle years at the university.

Freud's first clinical publication in neurology, a detailed case report of cerebral hemorrhage in a patient with scurvy, demonstrates quite well the care with which Freud observed every detail of the disease process. He could hardly contain his excitement and wrote an account of his first clinical case presentation to his future wife, Martha Bernays, on January 18, 1884 [14] in which he recalled:

Today at last I started working on nervous disorders; I hope I have found the material for my first small clinical publication. [15] For yesterday a poor tailor's apprentice arrived with scurvy, the well-known disease in which ecchymosis appears in all organs. Apart from some apathy, he didn't show any visible symptoms. Early this morning he was quite unconscious, which suggested a cerebral

hemorrhage. So I went to see him again before luncheon and found a number of interesting symptoms from which could be deduced the locality of the hemorrhage (always our chief concern in brain disorders). So I sat beside him all the afternoon and observed the interesting and most variable development of the illness till seven o'clock, when symmetrical paralysis appeared, with the result that until his death at 8 P.M. nothing escaped my notice. The publication of this case is justified by several interesting and instructive phenomena, indeed it is imperative, especially if the autopsy tomorrow yields some satisfactory conclusions and confirmation of my diagnosis, which is based on localization. Now I need the Primarius' consent to publish, which I hope he won't refuse; I intend to keep at him. (pp. 91-92)

Entitled, Ein Fall von Hirnblutung mit indirekten basalen Herdsymptomen bei Skorbut [15], Freud hoped that his professors and colleagues at the university would take notice of his acumen after this first clinical publication.

Following the apparent success of his first clinical publication, Freud began work on a method to stain nerve fibers in order to pursue further neuropathological study of the interconnections between the medulla oblongata and the cerebellum. His novel histologic staining technique for this purpose appeared in May, 1884 in the journal, *Brain: A Journal of Neurology*. [4] In this article, Freud described a new technique, using gold chloride, to stain nerve fibers for better visualization of the microscopic and histologic anatomy of the nervous system, a method that Freud would later use to visualize the intricate connections between the cerebellum and the medulla oblongata. [4] An excerpt of Dr. Freud's article published in 1884 with a description of the technique follows [4]:

Pieces of the organ are hardened in bichromate of potash, or in Erlicki's fluid (2 1/2 parts of bichromate of potash and 1/2 of sulphate of copper to 100 parts of water), and the process of hardening is finished by placing the specimen in alcohol; thin sections are cut by means of a microtome and washed in distilled water. The washed sections are brought into an aqueous solution of chloride of gold (1 to 100) to which is added half or an equal volume of strong alcohol. This mixture is to be preferred to the simple aqueous solution of chloride of gold, which has been hitherto used in staining preparations; the sections are to remain in it from 3 to 5 hours... By this method the fibres are made to show in a pink, deep purple, blue or even black colour, and are brought

distinctly into view, while the grey substance, vessels and neuroglia, lost in the slightly tinged background, are not obtruded upon the attention of the observer. A good many fine fibres, which cannot be revealed by carmine, and were not known until the methods of Exner and Weigert came into use, are seen scattered everywhere throughout the white and grey substance. (pp. 86-88)

Immediately following publication of his new staining technique, Freud published a neuropathological and neuroanatomical description of the neurofibrillary tracts interconnecting the cerebellum and the brain stem, in particular the medulla oblongata. Dr. Freud was the first to describe and trace the course of the spinocerebellar white matter tracts from the lateral portion of the spinal cord to the cerebellum. Dr. Freud also described a method for determining the origin of nerve fibers. In fact, in his lecture, *The Structure of the Elements of the Nervous System*, [16] Freud theorized that the nervous system was composed of fibrillary structures. In fact, Dr. Freud came close to being the first person to describe the neuron theory of the central nervous system. His landmark articles detailing the anatomical structure of the medulla oblongata and the histological structure of the nervous system were instrumental in opening the door for the breakthrough work that would be performed by other investigators in later years; work that would lead to the development of a unified theory of cerebral structure.

Freud's work in the field of neurohistology was monumental and provided the scientific community with the basic foundation necessary to carry out further investigations that would inexorably lead to a unified theory of the structure of the nervous system. Dr. Freud's new staining technique with gold chloride provided a method to view the microscopic world of the neuron and trace the interconnections between different areas of the nervous system. Even though his work was instrumental in assuring that future scientists would be able to carry out the crucial investigations necessary for the development of the "neuron doctrine," when H. W. G. Waldeyer published his groundbreaking monograph in which he first coined the term "neuron," [17] Dr. Freud's investigations in the area were all but ignored. It would be a few more years before the Spaniard, Santiago Ramon y Cajal (1852-1934), using Camillo Golgi's (1843-1926) refined staining technique, would describe the synaptic cleft present between nerve fibers and the neuron; and many more years still, for the neuron doctrine to gain widespread recognition and acceptance following the vigorous defense of its

principals by Dr. Ramon y Cajal before the international community (versus the prevailing "reticular theory" proposed and defended by Dr. Golgi). [18,19,20] As Ernest Jones's, Freud's first biographer, wrote [21], "It was not the only time that Freud narrowly missed world fame in early life through not daring to pursue his thoughts to their logical -- and not far-off -- conclusion."

As Freud himself boasted in his autobiography [12]:

In the course of the following years, while I continued to work as a junior physician, I published a number of clinical observations upon organic diseases of the nervous system. I gradually became familiar with the ground; I was able to localize the site of a lesion in the medulla oblongata so accurately that the pathological anatomist had no further information to add; I was the first person in Vienna to send a case for autopsy with a diagnosis of polyneuritis acuta.

The fame of my diagnosis and of their post-mortem confirmation brought me an influx of American physicians, to whom I lectured upon the patients in my department in a sort of podgin-English. I understood nothing about the neuroses. On one occasion I introduced to my audience a neurotic suffering from persistent headache as a case of chronic localized meningitis; they quite rightly rose in revolt against me, and my premature activities as a teacher came to an end. By way of excuse I may add that this happened at a time when greater authorities than myself in Vienna were in the habit of diagnosing neurasthenia as cerebral tumour.

In the spring of 1885 I was appointed Lecturer on Neuropathology on the ground of my histological and clinical publications. (pp. 10)

ALMOST FAMOUS... AGAIN: SIGMUND FREUD AND COCAINE

At the time he was completing his work on the neuropathology of the medulla oblongata, Dr. Freud became interested in a novel alkaloid known as cocaine and began working on a comprehensive, scientific review of the therapeutic benefits of cocaine. He described his interest regarding the therapeutic benefits of cocaine in a letter to his fiancée, Martha Bernays, written from Vienna on Saturday, April 21, 1884, [14] in which he reported:

I am also toying with a project and a hope which I will tell you about; perhaps nothing will come of this, either. It is a therapeutic experiment. I have been reading about cocaine, the effective ingredient of coca leaves, which some Indian

tribes chew in order to make themselves resistant to privation and fatigue. A German has tested this stuff on soldiers and reported that it has really rendered them strong and capable of endurance. I have now ordered some of it and for obvious reasons am going to try it out on cases of heart disease, then on nervous exhaustion, particularly in the awful condition following withdrawal of morphine (as in the case of Dr. Fleischl). There may be any number of people experimenting on it already; perhaps it won't work. But I am certainly going to try it and, as you know, if one tries something often enough and goes on wanting it, one day it may succeed. (13, pp. 107-108)

Figure 2

Prescription for Cocaine, circa 1884. Published with permission of Sigmund Freud Copyrights, LLC/ Paterson Marsh Ltd.



Freud had begun to author a comprehensive literature review of the physiological effects of cocaine in order to delineate potential therapeutic uses. Freud's work on cocaine culminated in a publication of his work on cocaine in *Zentralblatt für die gesamte Therapie* in 1884. As Freud wrote to Martha again on June 19, 1884, in yet another letter from Vienna [14]:

Coca wasn't finished till last night; the first half has already been corrected today; it will be 1-1/2 sheets long; the few gulden I have earned by it I had to subtract from my pupil, whom I sent away yesterday and today. (pp. 113)

In this first article describing the therapeutic uses of cocaine [5, 6], Freud described the history of the drug's use by residents native to South America and then proceeded to trace the migration of cocaine to the European continent. Freud then continued by illustrating in detail the experimental evidence of the physiologic effects of cocaine on animals as well as healthy human subjects, himself among them. (It was not uncommon at the time to experiment with pharmacological agents on oneself.) Freud describes the effects of cocaine on his person in this publication [6]:

A few minutes after taking cocaine, one experiences a

sudden exhilaration and feeling of lightness. One feels a certain furriness on the lips and palate, followed by a feeling of warmth in the same areas; if one now drinks cold water, it feels warm on the lips and cold in the throat. On other occasions the predominant feeling is a rather pleasant coolness in the mouth and throat. (pp. 58)

Following a summary of the physiological effects of cocaine, Freud proceeded to review the potential therapeutic uses of the alkaloid via extensive review of experimental evidence available at the time. These therapeutic properties included the stimulant effect of the drug, its therapeutic use in digestive disorders of the stomach, its use in cachexia, its use in the treatment of morphine and alcohol addiction, its use in asthma, its use as an aphrodisiac, and finally, its potential use as a local anesthetic. In fact, Freud's paper was the first to describe the potential anesthetic properties of cocaine. As Freud wrote in this publication [6]:

Cocaine and its salts have a marked anesthetizing effect when brought in contact with the skin and mucous membrane in concentrated solution; this property suggests its occasional use as a local anesthetic, especially in connection with affections of the mucous membrane. According to Collin [22], Ch. Fauvel strongly recommends cocaine for treating diseases of the pharynx, describing it as "le tenseur par excellence des cordes vocales." Indeed, the anesthetizing properties of cocaine should make it suitable for a good many further applications. (pp. 73)

Unfortunately, despite his astute observations regarding the therapeutic benefits of cocaine, particularly as they refer to the drug's local anesthetic properties, Freud did not perform the necessary experiments to confirm these hypotheses himself, an essential element of the scientific process. [23] Instead, Freud confessed his conviction in these hypotheses to a colleague, Dr. Königstein, in whom he placed a charge to carry out the necessary experiments in his absence. Unfortunately, Königstein never followed through with Freud's request and allowed the project to sit untouched on the sidelines.

At the same time, however, one of Freud's medical school friends, Dr. Carl Koller, himself an aspiring ophthalmologist, was actively searching for a compound with local anesthetic properties to utilize during ocular surgery. He became interested in the compound that Freud had been studying, alkaloid of cocaine, after Freud discussed his work with him and allowed Koller to review his manuscript *Über Coca*. As a result of his conversations with

Sigmund Freud, Carl Koller developed a solution of cocaine and demonstrated conclusively that it could be used to anesthetize the eye. [24, 25] Yet again, Sigmund Freud had missed an important opportunity to gain worldwide recognition as a clinician and researcher. He describes his regret at not having taken decisive action with respect to this discovery in his autobiographical sketch [13]:

I may here go back a little and explain how it was the fault of my fiancée that I was not already famous at an early age. A side interest, though it was a deep one, had led me in 1884 to obtain from Merck some of what was then the little-known alkaloid cocaine and to study its physiological action. While I was in the middle of this work, an opportunity arose for making a journey to visit my fiancée, from whom I had been parted for two years. I hastily wound up my investigations of cocaine and contented myself in my book on the subject with prophesying that further uses for it would soon be found... When I returned from my holiday I found that not he [Konigstein], but another of my friends, Carl Koller (now in New York), whom I had also spoken to about cocaine, had made the decisive experiments upon animals' eyes and had demonstrated them at the Ophthalmological Congress at Heidelberg. Koller is therefore rightly regarded as the discoverer of local anaesthesia by cocaine, which has become so important in minor surgery; but I bore my fiancée no grudge for her interruption of my work. (pp. 13)

Even so, Freud's role in the discovery of the first local anesthetic, cocaine, cannot, and should not, be overlooked. [23]

DR. FREUD: EXPERT IN THE FIELD OF CHILDHOOD PARALYSIS

In addition to his work on the therapeutic properties of cocaine, Freud also developed an interest in other areas of neurology and neurobiology. In particular, Freud became interested in clinical neurology on the advice of Ernst Brucke. As a result of Dr. Brucke's advice, during the early years of his career, Freud's scientific interest gradually shifted from basic science work to clinical investigation and practice. In time, this shift led him down the path towards the development of his landmark theories on the human mind and the birth of psychoanalytic theory. For the time being, however, Dr. Freud remained content with his pursuits in clinical neurology.

Freud's first purely clinical work evolved from his experience with victims of stroke in whom aphasia was common. These clinical observations naturally led him to

perform an in depth study of aphasia. Following extensive research into the available evidence on the phenomenon of aphasia, Freud wrote and published a landmark manuscript on aphasia, his first book-length manuscript. [7,8] In this book, Freud reviews, in great detail, the experimental evidence and the multitudinous clinical descriptions of the varying forms of aphasia and their clinical presentation. In addition, Dr. Freud attempts to debunk the theory that all aphasia can be localized to two or three primary anatomical structures and begins his personal quest for a more unified theory of the mind. The book entitled, *On Aphasia: A Critical Study*, was published in 1891 [7], and remains a classic in neurology to this day. In *On Aphasia*, Freud reviews the evidentiary data available during this period of time regarding the different forms of aphasia, both expressive and receptive in nature. [8] As was the case with his earlier publication, *Über Coca*, Freud's manuscript on the topic of aphasia was well researched and describes the evidence available to clinicians at the time of its writing.

In 1891, the same year that he published *On Aphasia*, Dr. Freud, along with Oscar Rie, published a *Clinical Study on the Unilateral Cerebral Paralysis of Children*, perhaps his most famous non-psychoanalytic manuscript. [9, 10] This manuscript would serve as a precursor to his final book written in the area of neurology towards the end of the century. With this book, Dr. Freud begins his exploration of autistic disorders, known as cerebral paralysis during his lifetime. In cerebral paralysis, Freud found the substrate for a poorly localized neurological disorder that fostered his imagination and solidified his belief that many neurological and psychiatric disorders cannot be firmly localized to a specific area of the cerebral cortex. The foundation was thus set for his broad and speculative theory of psychoanalysis; a theory based on a theoretical construct of the mind that had little correlation with the brain's anatomic pathology.

A shorter text written by Dr. Freud regarding childhood diplegias entitled *On the Knowledge About Cerebral Diplegias of the Childhood Age (In Connection with Little's Disease)*, reflected on research in this area and was published in 1893. [9, 10] This text expanded on his earlier work in the area.

Finally, in 1897 Dr. Freud completed and published his final manuscript in neurology entitled, *Infantile Cerebral Paralysis*. [11] *Infantile Cerebral Paralysis* represented Freud's crowning achievement in the area of childhood cerebral paralysis and childhood cerebral palsy, and

established Freud as a well-respected expert on this topic during his lifetime. In his text, Freud provides, in exhaustive detail, the body of scientific evidence available during his lifetime on the etiology, pathophysiology, nosology, risk factors, and treatment of these disorders of childhood; including an astounding description of Little's disease described by Dr. W. J. Little in his lectures entitled a "Course of Lectures on Deformity of the Human Frame." [26, 27] In this manuscript, Dr. Freud challenged the assertion made by Dr. William John Little that the cause of cerebral palsy is an obstetrical complication of birth resulting in lack of oxygen to the baby's brain. Dr. Freud believed that difficult birth was merely a symptom of the disease itself and not necessarily its cause. [9,10,11] Freud went so far as to pronounce that the association of cerebral palsy with mental retardation, seizures, and sensory disturbances provided evidence that the damage sustained by the brain could only occur during the crucial period of time when the central nervous system was developing within the fetus. While Dr. Little's etiological hypothesis satisfied investigators throughout much of the 20th century, Dr. Freud's observations were finally verified in the 1980's when it was discovered that less than 10% of cerebral palsy cases were actually caused by birth complications leading to anoxic brain injury. [28] It was this final manuscript in neurology, more than any other, that established Freud as a serious investigator and a veritable expert in the field of childhood diplegias.

It was through his observation of children that Freud began to form his hypothesis that the pathology of adulthood, particularly psychiatric disorders, developed during early childhood. For this reason, these early works on childhood cerebral paralysis were crucial to the development of psychoanalytic theory, particularly the important idea that childhood experiences play a crucial role in the formation of adult conscienceness. While his hypotheses were far from accurate on many accounts, his ideas, particularly regarding the existence of childhood sexuality and the subconscious mind, remain important in modern psychiatric thought and theory. Even so, the foundations for these ideas, including the texts described above, have been all but forgotten.

DISCUSSION

A review of Dr. Sigmund Freud's early work within the field of neurology provides historians, biographers, clinicians, and even critics with a unique glimpse of the tremendous observational prowess and meticulous scientific research capability that Freud possessed; skills that would lead him to

postulate a unique, but important, theory of the inner workings of the human mind. While Dr. Freud's early work in the field of neurology is hardly recognized today, it represents an integral part of his research experience, an experience that led him down a path towards historical immortality. In addition, Dr. Freud deserves to be recognized for his important contributions to the development of the neuron theory of the brain (via his neurohistologic staining technique, his early studies on non-vertebrates, and his neuratomical description of the pathways between the brain stem and the cerebellum), and for his contribution to the discovery of local anesthesia (via his description of cocaine's anesthetic properties). His classical work in the field of aphasia and infantile cerebral paralysis remain important to this day.

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