EXPLORING THE MIND WITH A MICROSCOPE: FREUD'S BEGINNINGS IN NEUROBIOLOGY

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Abstract: Sigmund Freud (1856-1939), the acknowledged founder of psychoanalysis, started his research career as a promising neurobiologist. This article presents an overview of his early articles in neuroanatomy and a literature update regarding the awareness of Freud's origins in neurobiology. In all, Freud invested a decade studying animal histology, cell biology and basic neuroscience before turning to human neuropsychiatric disorders. Through his histological studies, Freud provided coherent evidence supporting the neuron doctrine and suggesting that the protoplasm consists of a contractile fibrillary network, the present-day cytoskeleton. Freud also documented movements of nucleoli in neurons, a phenomenon presently referred to as nuclear rotation. In certain instances, Freud's observations antedate later views by more than half a century and are important to our understanding of neuronal structure and intracellular motility.

Key words: Freud, History of neuroscience, Neurohistology, Neuron theory.

INTRODUCTION

Whether one may agree (Edelman, 1992; Gabbard, 2004; Kandel, 2002) or disagree (Eissler, 1995; McCrone, 2004; Tallis, 1996) with Sigmund Freud's propositions on the functioning of the mental apparatus, it is a common admission that psychoanalytic theory has had a considerable impact on twentieth century scientific, intellectual and cultural thought. Freud as a psychologist is viewed as one of the greatest explorers of the human mind that ever lived (Gay, 1988; Panek, 2004).

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On the occasion of celebrating the sesquicentennial anniversary of Freud's birth (May 6, 1856), the present study retraces his early research career in neurobiology. Freud's first skips in science happened during his medical school years at the University of Vienna. Beginning in 1875 as a sophomore medical student, until 1885, the year he went to Paris to study clinical neurology at *La Salpêtrière* under the world-famous Jean-Martin Charcot (1825-1893), Freud explored the histological structure of nerve cells in fish and crustacea, subsequently focusing on human neuroanatomy and neuropathology.

Much of the neurohistological work took place in the Institute of Physiology at the University of Vienna headed by Ernst Wilhelm von Brücke (1819-1892), after whom the ciliary muscle in the eye, Brücke's muscle, is named. Carl Ludwig Brücke (1816-1895), Hermann von Helmholtz (1821-1894), and Emil du Bois-Reymond (1818-1896) dominate the history of physiology in the second half of the nineteenth century, finally delivering this science from all traces of speculation and mysterious forces ("vitalismus"); only physical concepts and the quantification of all processes count.

Freud had been exposed to Darwinian theory through the teachings of Solomon Stricker (1834-1898), his Professor of Histology (Stricker, 1872), and Carl Claus (1835-1899), his Professor of Zoology and Comparative Anatomy at the University of Vienna (Freud, Freud, & Grubrich-Simitis, 1978; Ritvo, 1990). He worked diligently at the Physiology Institute from 1876 to 1881 (the year of his graduation). Nevertheless, there was scant livelihood in it, and, as Brücke candidly informed him, no future[1]. Freud, who was contemplating marriage, reluctantly went into clinical medicine, specializing in what we could now call Neurology and Psychiatry (Freud et al., 1978). By then, based on his anatomical observations, Freud had published 14 original articles, some of them pioneering contributions to neuroscience, which gained him wide recognition among the neurohistological, neuroanatomical and neuropathological circles.

Freud's contributions to neurobiology touch upon five cellular domains: (1) The emanation of nerve fibers from nerve cell somata (Freud, 1877b, 1878); (2) The emergence of the concept of cytoskeleton (Freud, 1882); (3) The movement of nucleoli in nerve cells (Freud, 1882; Henneguy, 1896); (4) The role of the nerve cell as a unit in the nervous system (Freud, 1884c), and (5) The existence of 'contact barriers' between nerve cells (Freud 1895/1966). These issues have been thoroughly covered in the literature (Bernfeld, 1949, 1951; Brito, 2002; Brun, 1936; Frixione, 2003; Gray, 1948, 1951; Jelliffe, 1937; Kandel, 1979, 1981, 2002; Pearce,

1. Brücke's two assistant professors were only ten years older than Freud, and unlike Freud, not Jewish.

1996, 2003; Solms, 1993, 1996, 1998, 2004; Sulloway, 1979; Triarhou & del Cerro, 1985, 1986, 1987a, 1987b).

FREUD'S WORKS IN BASIC NEUROSCIENCE

The first study carried out by Freud was, interestingly enough, on the microscopic structure of the eel testis, then known as Syrski's organ (Freud, 1877a). One should not attribute any "Freudian" connotation to the choice of topic, as it had been assigned to the young student by his mentor, Professor Carl Claus. Freud conducted his experiments on 400 specimens in two visits, during 1875 and 1876, to the Zoological Station in [then Austrian] Trieste, supported by travel grants from the Austrian Ministry of Education.

Original as his first study was, and important as his subsequent studies on cell motility were (Triarhou & del Cerro, 1987b), the basic science contributions of Freud that have better survived to our days were those on the structure of the nerve cells (Triarhou & del Cerro, 1985). Those contributions have been highly regarded by established researchers at the time and incorporated into the neuroscientific literature, including citations by Santiago Ramón y Cajal (1852-1934), the father of modern neurobiology[2], in his classic book *Textura del sistema nervioso del hombre y de los vertebrados* (Ramón y Cajal, 1897-1904) along with those of Nansen[3] (1861-1930) who apparently knew Freud (Fodstad, Kondziolka, & de Lotbiniere, 2000).

Freud conducted his histological studies on the nervous system of the lamprey (Petromyzon) (see Figure 1) and the river crayfish. In the legends of his histological drawings in the resulting publications in the Proceedings of the Imperial Academy of Sciences (Freud, 1877b, 1878, 1882), Freud gives technical information on the optical components used for his observations. Clearly, Freud, and Brücke's laboratory had a strong preference for the optics produced by Edmund Hartnack[4] (1826-1891).

2. Santiago Ramón y Cajal whose *Textura del sistema nervioso del hombre y de los vertebrados* (Ramón y Cajal, 1897-1904) is considered the cornerstone of modern neurobiology (Andres-Barquin, 2001; DeFelipe, 2002; Sotelo, 2003), and who shared the 1906 Nobel Prize in physiology or medicine with Camillo Golgi (1844-1926) for their investigations of the structure of the nervous system.

3. Fridtjof Nansen is another key protagonist who produced important groundwork supporting the individuality of nerve cells as structural and functional units of the nervous system. He was also an Arctic explorer, humanitarian, and winner of the 1922 Nobel Prize in peace.

4. This was a well-placed trust for Hartnack as an innovator (Bradbury, 1967) whose instruments are highly regarded by microscope historians (Moe, 2004). In 1857, Georges Oberhäuser (1798-1868), an uncle of Hartnack, went into partnership with his nephew in Paris to form the fine

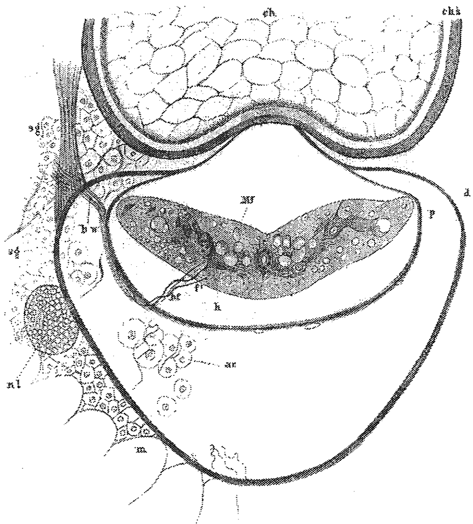

Figure 1. Freud's drawing of the lamprey spinal cord, from his first study on the petromyzon (Freud, 1877b).

Freud further worked out some new methods for dissecting and staining nervous tissue specimens (Freud, 1879, 1884a, 1884b), and summarized his histological findings in a review (Freud, 1884c) on the structural elements of the nervous system (Figure 2a and 2b).

Through his neurohistological studies, Freud became one of the early protagonists of the neuron doctrine (Koppe, 1983; Rueda Franco, 2001; Shepherd, 1991). Waldeyer (1891), working at the First Anatomical Institute in Berlin, coined the term "neuron" (first appearing in Homer's Iliad, cf. Ochs, 2004) and popularized the neuron doctrine. Meanwhile, the subject had received substantial contributions from anatomists including Forel, Gowers, His, Kölliker, Nissl, and van Gehuchten (McHenry, 1969; Meyer, 1971; Ramón y Cajal, 1907; Shepherd, 1991).

instrument-making firm Oberhäuser & Hartnack. Hartnack assumed sole control of the firm in 1860. Ten years later, as a result of the Franco-Prussian war, Hartnack moved to Potsdam, leaving the Paris firm division Hartnack & Prazmowski to his partner Adam Prazmowski (1821-1888), a Polish professor of Mathematics and Astronomy who had previously worked at the Warsaw Observatory. Hartnack is credited with the first use of water-immersion lenses in the commercial production of microscopes and the adoption of the substage condenser in his later instruments. Microscopes by Hartnack, contemporary with the one that allowed Freud to observe nerve cells in the laboratory and to reach his fundamental histological conclusions, can be found in several microscope collections (Purtle, 1974; Turner, 1989).

A NEW HISTOLOGICAL METHOD FOR THE STUDY OF NERVE-TRACTS IN THE BRAIN AND SPINAL CHORD.

BY DR. SIGM. FREUD,

Assistant Physician to the Vienna General Hospital.

IN the course of my studies on the structure and development of the medulla oblongata I succeeded in working out the following method, which will be found a powerful aid in tracing the course of fibres in the central nervous system of the adult and the embryo.

Pieces of the organ are hardened in bichromate of potash, or in *Erlicki's* fluid (2½ parts of bichromate of potash and ½ 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

Figure 2a. Freud's technical paper in Brain (Freud, 1884b).

Die Structur der Elemente des Nervensytems.

Von

Dr. Sigm. Freud,

Secundararzt im allgemeinen Krankenhause.

(Nach einem im psychiatrischen Vereine gehaltenen Vortrag.)

Sehr bald, nachdem Nervenzelle und Nervenfaser als die wesentlichen Bestandtheile des Nervensystems erkannt worden waren, begannen die Bemühungen, die feinere Structur dieser beiden Elemente aufzuklären, wobei die Hoffnung von Einfluss war, aus der erkannten Structur Schlüsse auf die physiologische Dignität derselben ziehen zu können. Es ist bekanntlich nicht gelungen, nach einer dieser beiden Richtungen befriedigenden Aufschluss und Einigung zu erzielen: dem einen Autor gilt die Nervenzelle als körnig, dem anderen als fibrillär; die Nervenfaser oder deren wesentlicher Bestandtheil, der Achsencylinder, dem einen als ein Fibrillenbündel, dem andern als eine Flüssigkeitssäule, und dem entsprechend wird die Nervenzelle hier als der eigentliche Herd der Nerventhätigkeit gewürdigt, dort zur Bedeutung eines Kernes der Schwann'schen Scheide degradirt.

Da ich nun glaube, dass in meiner Untersuchung „Ueber den Bau der Nervenfasern und Nervenzellen beim Flusskrebs"[1] eine wohl begründete Lösung des uns beschäftigenden Problems gegeben ist, will ich mir erlauben, den Inhalt derselben an dieser Stelle vorzubringen. Vorher muss ich es aber rechtfertigen, dass ich den Flusskrebs zum Object meiner Untersuchung gewählt, oder dass ich den

Figure 2b. Freud's review on the structural elements of the nervous system (Freud, 1884c).

FREUD'S WORKS IN CLINICAL NEUROSCIENCE

After his graduation from medical school, Freud worked in the Institute of Brain Anatomy headed by Theodor Meynert (1833-1892), his Professor of Psychiatry[5]. Freud published three works, based on the Weigert stain of incompletely myelinated human fetuses, on the connections of the superior olivary nuclei (Freud, 1885), on the origin and the course of the acoustic (eighth cranial) nerve (Freud, 1886), and on the anatomical relations of the restiform body in the medulla oblongata (Darkschewitz & Freud, 1886). These studies (Figure 3a and 3b), their precedence, and their caveats, have been discussed in detail by Wiest and Baloh (2002).

2. Zur Kenntniss der Olivenzwischenschicht.

Von Dr. Sigm. Freud in Wien.

Aus einer Untersuchung über den Faserverlauf in der Oblongata des menschlichen Foetus, welche ich in Professor Meynert's Laboratorium mit Hülfe der Weigert'schen Hämatoxylintinction durchgeführt habe, sei hier Einiges über die Olivenzwischenschicht (beim Foetus von 5—6 Lunarmonaten) mitgetheilt. Vorauszuschicken ist eine gedrängte Darstellung des Acusticusursprungs, weil dieser Nerv derzeit das Bild beherrscht, und auch die in Rede stehende Fasermasse an ihn anknüpft.

Die Acusticuswurzeln bilden eine continuirliche, von aussen und unten

Figure 3a. Freud's paper on the interolivary tract (Freud, 1885).

I. Originalmittheilungen.

Ueber die Beziehung des Strickkörpers zum Hinterstrang und Hinterstrangskern nebst Bemerkungen über zwei Felder der Oblongata.

Von Dr. L. Darkschewitsch (Moskau) und Dr. Sigm. Freud, Privatdocent (Wien).

Die Ansichten der Hirnanatomen über den Zusammenhang zwischen Strickkörper oder unterem Kleinhirnschenkel und den Hintersträngen des Rückenmarks

Figure 3b. Freud's paper on the restiform body (Darkschewitsch & Freud, 1886).

Freud's subsequent endeavours in clinical neurology and aphasiology go beyond the scope of the present paper, as they are amply covered elsewhere (Delahanty, 1978; Fancher, 2000; Goldblatt, 1992; Greenberg, 1997; Jacyna, 2005; Jellinek, 1993; Kaplan, 1989; Mancia, 2004; Markowitsch, 1986; Miller, 1991a, 1991b; Miller & Katz, 1989), and eloquently dramatized in several novels (Morton, 1979, 1989; Spiel, 1987; Stone, 1971).

5. Meynert is generally credited with promoting a neuroanatomical basis for psychiatric diseases (Meynert, 1884/1968) and as setting the foundations for the cytoarchitectonic study of the human cerebral cortex (Meynert, 1872).

DISCUSSION

One of the first attempts at reconciling Freudian unconscious mental processes with neurophysiology was a speculative hypothesis put forth by Winson (1985), based on the evolution of the dreaming state in mammals. Two entries, on *Aphasia* and on the *Brain*, written by Freud in 1888 for the *Handwörterbuch der gesamte Medizin* (Handbook of General Medicine) that was compiled by Albert Villaret[6] (Solms & Saling, 1990), predate the renowned monograph on aphasia (Freud, 1891, 1891/1953, 1891/1983, 1891/1992) and shed light on historical aspects of the relationship between neurological science and psychoanalysis.

A meeting held at the New York Academy of Sciences in November 1995 (Bilder & LeFever, 1998) examined Freud's "Project" (Freud, 1895/1966) in a neuroscientific perspective. Freud's early scientific works from the "pre-analytic" period are further analyzed in a volume (Guttmann & Scholz-Strasser, 1998), the outcome of a conference organized in Spring 1997 by the Sigmund Freud Society and the Austrian Academy of Sciences. It is argued there that the new language Freud had to create for his system of psychotherapy, after departing from the territories of neurohistology and neurology, followed a similar epistemological approach, which allows current comparisons between his neuroscientific, and his later, psychoanalytic works.

Freud's ideas on hysteria, or sensory conversion disorder, seem to be validated by recent data from fMRI studies: selective alterations in primary sensorimotor cortical (S1) activity have been implicated in subjects with unexplained sensory loss (Ghaffar et al., 2006; Hurwitz & Pritchard, 2006).

Perhaps two other points concerning observations of Freud that pertain to contemporary neuroscience should be mentioned briefly. The first concerns the long-term potentiation of synaptic transmission, a reliable neurophysiological model of learning and memory that consists in the facilitation at the synapse in response to sustained activation. In his "Project", Freud theorized about representing memory at the contact barriers as "a permanent alteration following an event", thus anticipating several crucial physiological properties of long-term potentiation (Centonze et al., 2004; Kandel, 1981).

The other point concerns affective neuroscience (Peper & Markowitsch, 2001), and the pivotal role of Austrian physiologist Siegmund Exner (1846-1926), Freud, and French physician Israel Waynbaum (1862-uncertain), who might all be considered forerunners in that field, having had propounded a neural network theory of emotion that involved a stage of precortical processing, an idea compatible with

6. Published in Stuttgart by Ferdinand Enke (Volume I).

present-day views on the neural substrates and physiological characteristics of emotions.

The resonance of Freud's early scientific work in his later theorizing is striking, and the irruption of Newtonian concepts and causality to the exclusion of all others in physiology undoubtedly stood as a model for Freud's "dynamic" psychiatry (Triarhou, 1989). To quote du Bois-Reymond at the beginning of his career: «Brücke and I, we have sworn to each other to validate the basic truth that in an organism no other forces have any effect than the common physiochemical ones» (Jans Muller, M.D., personal communication, January 1989). Or, to go back all the way to Anaxagoras (500-428 B.C.), «The phenomena are a visible expression of that which is hidden» (Johansen, 1998, p. 73).

The neurobiological background in Freud's thought, and an avant-garde vision of the neurochemical correlates of mental disorders, becomes evident in the following fragment from *The question of lay analysis* (Freud, 1926/1978, p. 54, my translation[7]): «Considering the intimate relationship between the things that we distinguish as bodily and as mental, one may foresee that the day will come, when paths of knowledge and hopefully of influence will open up that will lead from the Biology of organs and from Chemistry to the field of the neuroses.»

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7. «Bei dem innigen Zusammenhang zwischen den Dingen, die wir als körperlich und als seelisch scheiden, darf man vorhersehen, daß der Tag kommen wird, an dem sich Wege der Erkenntnis und hoffentlich auch der Beeinflussung von der Biologie der Organe und von der Chemie zum dem Erscheinungsgebiet der Neurosen eröffnen werden».

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