Women in Neuroscience: A Short Time Travel

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Glossary

Aphasia Alteration in language production and/or comprehension due to brain injury.

Gender bias Unequal treatment or perceptions of individuals based on their socially constructed gender roles.

Intellectual ability The ability to think or act in a goal-directed way, to create new connections between elements, and to solve problems in new situations.

Nobel Prize Annual international award established by Alfred Nobel and bestowed since 1901 for outstanding achievements in physics, chemistry, physiology or medicine, literature and for work in peace.

Spanish Neurological School The school founded by Santiago Ramón y Cajal in 1902 in Madrid which, also through the numerous prominent disciples, made an extraordinary contribution to understanding the structure of the nervous system.

Introduction

The shaded side of the history of neuroscience shows how women took part to the development of this modern interdisciplinary field from the beginning, despite the plain hurdles in accessing higher education.

Their contribution, acknowledged and sometimes awarded by the scientific community of the time, has been forgotten and in some cases actively removed so as to leave only faint traces in the reference handbooks and academic student textbooks. This scarce presence led to the thesis that women were not inclined to scientific research, and above all they would remain focused on their predisposed role: the care of husband, children, older people. Embarking on a scientific path would have prevented women from stay at home and take care of the family. Furthermore, science required the intellectual abilities of which women were believed to be lacking and it is not necessary to go far back in the years to hear echoes of this belief in university classrooms and lecture halls.

"Women are so grossly under-represented in modern science because, for most of history, they have been treated as intellectual inferiors and deliberately excluded from it" wrote Angela Saini in her book Inferior (Saini, 2017), which encouraged international awareness campaigns on gender discrimination in the scientific world. As for women inferiority, the story begins with Charles Darwin who explained his thesis in the book The Descent of Man and summarized his thought in the correspondence with Caroline Kennard, to whom he wrote in 1881: "I certainly think that women though generally superior to men [in] moral qualities are inferior intellectually, and there seems to me to be a great difficulty from the laws of inheritance, (if I understand these laws rightly) in their becoming the intellectual equals of man" (Saini, 2017). The thesis then found fertile ground in the following decades and became increasingly structured in the academic and general communities. Still today, some maintain that the small proportion of women in major international scientific awards (Nobel Prizes, Fields Medals, etc.) can be explained with the supposed female lower aptitude for abstraction, mathematics, and physics.

Female Nobel laureates are not lacking but they are very few indeed. Between 1901 and 2019, the Nobel Prizes were awarded to 21 women (Marie Curie received it in Physics in 1903 and in Chemistry in 1911) out of 615 scientists. However, cases of women who have been denied the recognition they deserved have emerged in recent years. Lise Meitner, Marguerite Vogt, and more recently Jocelyn Bell Burnell are just a few examples of women who made essential contributions to discoveries that led to Nobel Prizes awarded to their male colleagues.

The impact of removing women from science is still evident today in the small number of celebrations dedicated to the pioneer women of neuroscience, in the limited access to the top positions of departments and laboratories, as well as to the highest academic positions.

Scientific errors, cultural barriers, and gender segregation have led to this removal. Gender bias and discrimination prove to be very effective in leaving women's innovation potential unexpressed through horizontal and vertical segregation (Chiofalo and Metitieri, 2019).

In the next four sections we will illustrate the condition of women in neuroscience through a temporal dimension: recovering the stories of some representative women neuroscientists from the past; referring to the transition from sources sought in the hidden historical archives to the autobiographies accessible online; summarizing the current situation of women in neuroscience; and, finally, tracing the unknowns of the future that with the COVID-19 pandemic are likely to cancel the slightest changes made to diversity in the last few years.

The Past: Five Forgotten Pioneer Women of Neuroscience

Until the early 1900s, it was widely believed that the lower physical strength of women than men implied similar mental weakness and a more delicate nervous system. In the 19th century, different fields in brain research highlighted that sexual differences were reflected in exaggerated gender distinctions: from biology to psychology, to phrenology and evolutionary theory, the scientists claimed that women had fewer intellectual abilities than men (Houghtaling, 2008). Moreover, being at the mercy of their hormones, it was said, women were thought to be emotionally unstable and unable to make decisions. In medicine, this belief justified the idea that women could not reach high standards in their studies and was the excuse with which they were prevented from accessing post-graduate specialization courses and hospital traineeships, which in France remained exclusive to men until 1881 (Digby, 1996). Despite social and cultural barriers, some women managed to enter the academic world, a world for men only, and there to find their place. Among these are five pioneer women of neuroscience born in the late 1800s who produced seminal works in the first half of the last century.

Maria Manasseina and the Foundation of Sleep Science

Maria Mikhailovna Manasseina (1843–1903) was one of the first women to graduate in medicine in Europe (Kovalzon, 2009). She published important contributions to biochemistry, physiology, and sleep deprivation. She discovered that the negative effects of prolonged sleep deprivation originated in the brain and demonstrated that sleep is more important than food for the preservation of life (Bentivoglio and Grassi-Zucconi, 1997). Manasseina published the first comprehensive handbook on sleep in 1889, in Russian. The book was then translated in English (de Manacéïne, 1897) and widely distributed in Europe, becoming the sleep encyclopedia, a reference book in those times. Manasseina stated that sleep represents a definite state of brain activity which is different from the absence of activity, as it was commonly seen at the time: a remarkable intuition, considering that the objective recording of brain electrical activity through the electroencephalogram would have been introduced after more than 20 years. Before studying sleep, Manasseina worked at the Polytechnic University of Vienna, where she had the opportunity to study the alcoholic fermentation process by discovering that it is due to specific components that can be isolated from yeast cells (she called them "unorganized enzymes") rather than the living yeast per se (Lagnado, 1992). The same results were replicated by Eduard Buchner after 25 years and, although he was aware of Manasseina's work, he did not even mention her in his publications. Buchner was awarded the Nobel Prize in Chemistry in 1907 for this discovery and Manasseina's name obliterated.

Laura Forster and Manuela Serra at the Spanish School of Neurohistology

Laura Forster and Manuela Serra were the first two women working at the Spanish Neurological School of Santiago Ramon y Cajal in Madrid (Giné et al., 2019). Although almost all Cajal's collaborators were men, Forster and Serra appeared on the official list of school members drawn up by Cajal in 1922, on the occasion of the Echegaray medal reception by the Royal Spanish National Academy of Physics, Exact and Natural Sciences (Giné et al., 2019).

Laura Elizabeth Forster (1858–1917) was born and initially studied in Australia. She moved to England after the death of her father, and, in 1887, she entered the University of Bern in Switzerland as a medical student and graduated in 1894. She remained working at the Institute of Pathology for the next six years and devoted her research to the study of muscle spindle fibers. Returning to the United Kingdom, she settled in Oxford and attended the Physiological Laboratory under the supervision of Gustav Mann. There, she published a scientific paper on the histology of the lymph nodes of a patient suffering from tuberculosis. To gain more mastery in neurohistological techniques, Forster went to Madrid in 1911, in the Cajal laboratory, where she stayed a few months. Her research focused on the degeneration of nerve fibers after a traumatic lesion of the spinal cord in birds, to compare its effects with what was observed in the previous studies on mammals conducted by Cajal and others. Forster was the first to apply the neurofibrillary techniques to birds and her findings were published in August 1911 in a long scientific paper written in Spanish and elegantly illustrated by six drawings in the style of the Cajal school. Cajal cited Forster's work in his laboratory at least three times. Laura Forster's scientific career ended in 1912 when at the outbreak of the First Balkan War, she enlisted as a nurse, since women could not serve as doctors on the war front. She also served at the outbreak of the First World War.

Biographical information regarding Manuela Serra is scarce, as reported by Giné et al. (2019). Despite being neither a doctor nor a senior researcher, Manuela Serra conducted her studies on the intracellular fibrils of ependymal cells and astrocytes in the spinal cord of the frog and published a paper in the Cajal laboratory's journal in 1921. In this publication, illustrated by ten drawings, Serra reported for the first time the presence of microglia, which she called "mesoglia", in the white matter.

The women neuroscientists in the Cajal school were admitted as independent researchers or collaborators, a role not as prominent as that of female scientists in other countries, despite their outstanding findings and their relevance for the development of neuroscience.

Augusta Dejerine-Klumpke, an Exceptional Neurologist and Neuroanatomist

Augusta Marie Dejerine-Klumpke (1859–1927) was born in the United States to German parents. She spoke English, German and French, and knowing these languages was a considerable advantage to access scientific literature, since, during the first decades of the 20th century, many scientists still wrote in their native language. Only after the Second World War English became the main language of science. In 1882, following the published work of the German neurologist Wilhelm Heinrich Erb, which described the clinical signs following the injury of the brachial plexus (Bogousslavsky, 2005), Dejerine-Klumpke characterized the paralysis of the lower brachial plexus, that was named after her Klumpke's palsy. During the First World War, together with her daughter Yvonne, she treated soldiers with spinal cord injuries, and founded a professional rehabilitation center near Fontainebleau, thanks to donations from family and friends (Schurch and Dollfus, 1998).

Dejerine-Klumpke contributed significantly, with her husband Jules Dejerine (1849–1917), to the two-volume Anatomie des centres nerveux [Anatomy of the Central Nervous System] (Dejerine, 1895, 1901), one of the most significant works in the field of neurology. In 1908, she took part in the 3-day scientific meeting of the French Society of Neurology in Paris, during which a dispute took place between Jules Dejerine and Pierre Marie, Charcot's most important pupil. The first supported a differential classification of aphasias, while the second claimed the existence of only one type of aphasia (Wernicke's aphasia). For Pierre Marie, Broca's aphasia consisted of adding anarthria to Wernicke's aphasia, and its neuroanatomical basis was to be localized in the "quadrilateral space" which included the basal ganglia and internal capsule. Augusta Dejerine-Klumpke, through neuroanatomical data, proved that Marie's assumptions were incorrect due to the fact that a lesion within the quadrangle is capable of causing aphasia only if it affects the anterior, upper and external parts of the area, thus sectioning the third frontal convolution foot and cap devoted to language skills (Lecours and Caplan, 1984). After Jules Dejerine's death, Pierre Marie took over the chair of clinical neurology and fired Augusta, asking her to free the laboratory from all Dejerines' documents and personal effects. Dejerine-Klumpke, then, together with her daughter, created the "Fondation Dejerine" to collect all their clinical and research works in a museum and a laboratory.

The Foundation collection is currently located in the basement of the Sorbonne University in Paris under the management of the library. In her career, Augusta Dejerine-Klumpke received many prizes and awards: The Anatomy prize for free teaching in 1878–1879, the Godard prize of the Academy of Medicine in 1886, the silver medal from the Faculty of Medicine in Paris, the Lallemand prize of the prestigious Académie des Sciences for her doctoral thesis in 1890, a first Legion of honor for her scientific studies in 1913, and a second in 1921 with the rank of Officer for her strong commitment in the care of wounded soldiers during the First World War. She was the first woman to become president of the French Society of Neurology in 1914 (Berhoune et al., 2014).

Cécile Vogt: Neuroscience to Dismantle Cultural and Political Discrimination

Augustine Marie Cécile Mugnier Vogt (1875–1962) was one of the first women admitted to medical school in Paris. She studied under the neurologist Pierre Marie and his research team at the Bicêtre Hospital and graduated in 1900 with a dissertation in neuroanatomy. In Paris, Cécile met Oskar Vogt (1870–1959), who worked for some time in the laboratory of Augusta and Jules Dejerine at La Salpêtrière Hospital. After getting married, they settled in Germany, Berlin, and at the Neurobiological Laboratory (*Neurobiologische Laboratorium)*, the Vogts began a long and productive scientific collaboration that would lead them to landmark discoveries in the field of neuroanatomy and neuropathology. In 1914, Oskar and Cécile Vogt started to work at the new Kaiser Wilhelm Institute for Brain Research (KWI), in Berlin, which later became the Max Planck Institute for Brain Research, as appointed director and head of the anatomy department, respectively.

Cécile Vogt's work on the morphology of the nervous system contributed to a new understanding of the interactions between the different regions of the brain. She conducted systematic clinical-anatomical research and published important studies on the myeloarchitectonic organization of the thalamus, on the pathology of the corpus striatum, and the cytoarchitecture of the cerebral cortex (Klatzo, 2002; Vogt and Vogt, 1919). In her first work on thalamus myeloarchitecture, she identified several thalamic nuclei and their connections. It was a pioneering work for the modern understanding of the thalamus' physiology. Cécile Vogt was among the very few scientists in Europe, together with Sherrington in the United Kingdom, to use cortical electrical stimulation. She countered, also through her research, the pervasive prejudice that women were intellectually inferior to men. In the 1920s, Vogt explicitly stated that her research did not support the hypothesis of a difference between male and female brains (Akkermans, 2018).

Cécile and Oskar Vogt worked also with Korbinian Brodmann, and they were recognized as "key figures in establishing modern brain research" (Klatzo, 2002). In the years following 1933, they became the target of inspections and accusations by the National Socialists and were forced to leave the KWI. From 1937 they moved to Neustadt in the Black Forest and continued to work in their privately funded Institut für Hirnforschung und Allgemeine Biologie (Institute for Brain Research and General Biology). Cécile Vogt had a very productive scientific career for over 60 years, despite the two World Wars and the very tough social and economic situation in Germany. Before they met, Cécile had given birth to a girl, Claire, whom Oskar adopted once married. They had two other daughters: Marthe and Marguerite.

We are in the presence of an entire and unique family of scientists, and remarkable women, since Claire (1838–1978) conducted and published research about pediatric neurology in Paris, and was a pioneer in child neuropsychiatry (Poirier and Poirier, 2020); Marthe (1903–2003) was a leading neurophysiologist and pharmacologist, conducted, in the United Kingdom, pioneering research on neuropharmacology for the treatment of mental illness, and was elected a Fellow of the Royal Society (Wright, 2003); and Marguerite (1913–2007) was an outstanding cancer biologist and virologist, worked at the California Institute of Technology (Caltech), in Pasadena, United States, with Renato Dulbecco, and they were the first researchers to observe that polio virus formed plaques in tissue culture (Rubin, 2017). Vogt and Dulbecco founded the field of molecular virology. Despite her high reputation in the scientific community, Marguerite Vogt never received major awards and honors and was not bothered by the fact that Dulbecco received many awards for their joint work (including the Nobel Prize in 1975) (Wunderlich, 2013). In his Nobel Lecture, Renato Dulbecco acknowledged the assistance of many researchers but forgot the name of Marguerite Vogt, despite the inclusion of five of their joint publications in the reference section.

From Archives to Autobiographies

Many other names can be listed, among those sought in the historical archives or brought to light by historians. The crossed paths between Augusta Dejerine Klumpke and Cécile Vogt were recounted at the 2019 Annual History of Neuroscience meeting in Paris, dedicated for the first time to pioneer women in medicine and neuroscience. That event revealed, among others, the lives and careers of the Italian anatomist Anna Morandi Manzolini (1714–1774); two French neurologists from La Salpetrière, Chiriachitza Athanassio-Benisty (1885–1938) and Gabrielle Lévy (1886–1934); and the Nobel laureate Rita Levi Montalcini (1909–2012). The meeting was also attended by Nicole Le Douarin, pioneer of microbiology, who is also the author of a fascinating chapter in The History of Neuroscience in Autobiography, Volume 7 (Le Douarin, 2012).

Volume 2 of this collection includes the Autobiography of Brenda Milner (Milner, 1998) "the renowned neuroscientist who changed our understanding of brain and behavior" (Watkins and Klein, 2018). Milner was recently celebrated on occasion of her 100th birthday, the July 15, 2018, with a ceremony and a series of conferences at the Montreal Neurological Institute. She continues to conduct research and to support "troops" of scientists from all over the world (Watkins and Klein, 2018). For her discovery of multiple brain systems for memory she was awarded the Kavli prize in 2014 with John O'Keefe and Marcus Raichle. The awards ceremony was captured in a very representative image in which Brenda Milner was the only woman to stand out with her blue dress among many white men in black (**Fig. 1**): the non-diversity in science at its peak. Although unintentionally, Brenda Milner continues to be a role model for several generations of women neuroscientists as well as for young students who want to pursue a scientific career. Her work has also become popular through a comic book and the children's book Good Night Stories for Rebel Girls 2 (Watkins and Klein, 2018).

The place reserved for women in neuroscience is well illustrated in the indices of the ten volumes of the above-mentioned collection The History of Neuroscience in Autobiography, published by the Society for Neuroscience (SfN) from 1996 to 2018: 17.5 out of 143 essays are authored by distinguished women neuroscientists, corresponding to about 12% of all chapters by seniors, singles or couples.

The Present: From Admitting the Gender Gap to Initiatives to Reduce It

In recent years many initiatives have been launched to move toward gender diversity in the field of neuroscience.

Society for Neuroscience provides opportunities to empower women scientists and increase awareness for gender bias, through the Women in Neuroscience initiative (WIN), created in 1980. WIN is an international organization that aims at promoting professional advancement and facilitating communication between women working in neuroscience (Haak, 2002).

Women neuroscientists are still underrepresented in books, conferences, and various aspects of academic life. Data from the Women in Neuroscience Repository (WiNRepo) show that women: author significantly fewer papers as first or last contributor than men; - are awarded significantly fewer prizes; - and appear significantly less as speakers in departmental seminar series and conferences (Schrouff et al., 2019). WiNRepo is an initiative aimed at increasing the visibility of women in neuroscience, addressing gender bias through proposed solutions at different levels of intervention, and taking responsibility for promoting equal opportunities to new generations of neuroscientists.

Conscious and unconscious gender bias, combined with widespread sexual harassment in both academia and laboratories, can raise barriers that drive young women away from academic careers (National Academy of Science, 2018). Awareness of any gender biases can be increased by getting data periodically. This is the aim of Bias Watch Neuro, an initiative carried out through a Website

Figure 1 KAVLI prize laureates 2014. Courtesy of the Norwegian Academy of Science and Letters http://english.dnva.no/c42030/index.html.

that tracks the gender ratio among speakers in conferences and authors of papers published in key journals, to raise awareness among the organizers and the neuroscientific community.

Under-represion of women in neuroscience also has implications for the general population, biasing the studies in the medical field, where: women's health is understudied, women are less represented in clinical trials, and many neuroimaging studies come from groups of highly educated white subjects. Female invisibility begins in animal studies on brain disorders, which are more likely to be conducted on male animals (Criado Perez, 2019), and comes to the diagnosis of head injury whose outcomes in women are historically attributed to chronic emotional disorders and, therefore, less investigated with neuroradiological tests, compared to men (Casper and O'Donnell, 2020).

Adequate representation of women in neuroscience can improve by acting on institutional, organizational, cultural, and historical levels.

The achievement of women awaits to be recognized and celebrated to strengthen the tradition of women who pursue research or academic paths and offer new generations equal opportunities in the field of neuroscience.

The Future: Women in Neuroscience After the COVID-19 Pandemic

The scenario that will follow the health emergency of the SARS-CoV-2 pandemic could neutralize the small progress made in recent years to promote a greater presence of women and in general a greater diversity in opportunities to study STEM (Science, Technology, Engineering, and Mathematics) disciplines, to devote to scientific research, to pursue an academic career, to take part in conference panels, and to be awarded international prizes.

The closure of schools and universities to control COVID-19 transmission in 188 countries could have a differential impact on high education and job opportunities of women, who provide the majority of informal care at home (Wenham et al., 2020).

The response policies and practices to the indirect impact of outbreaks such as COVID-19 must, therefore, be effective to not perpetuate or exacerbate gender, cultural and socio-economic inequalities in education and professional career.

Although the World Health Organization (WHO) Executive Board recognized the need to include women in the decision-making process for planning outbreak responses (WHO, 2005), there is currently inadequate representation of women on scientific committees and task forces for COVID-19 appointed by national governments.

This makes it uncertain whether long-term investments are made to foster diversity. However, without any targeted intervention, data on publication records, allocated funds, and career advancements over the next two years will show that women in academia who are also engaged in informal home care were disadvantaged in 2020 (Minello, 2020; Viglione, 2020).

Conclusion

Despite visible and invisible social and cultural barriers, women have reached pioneering milestones in neuroscience since the dawn of this modern discipline. The women neuroscientists who conducted their outstanding research in the early 1900s have been almost completely forgotten and, with rare exceptions, there is no trace of their work in science handbooks or university textbooks. Few women neuroscientists have been awarded major international awards, just as the percentage of women in the historical collections of eminent senior neuroscientists that extends to the present day is small. Some initiatives have been undertaken to address gender bias, discrimination, harassment, lack of support for work-life balance, and to increase diversity and equal opportunities in accessing scientific research and academic career advancements.

A cultural change, institutional actions, and the promotion of historical projects are among the needed solutions to increase awareness of bias and barriers, and to continue building a safer, diverse, collaborative, and innovative environment for the whole neuroscientific community.

Building a more inclusive environment is not an enterprise that can be left to individuals, it must be planned through a competent, integrated and widespread decision-making process (Chiofalo and Metitieri, 2019), that is even more important to address in light of the new challenges posed by the COVID-19 pandemic.

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