

# Supplementary file

## SEARCH STRATEGY FOR THE HISTORICAL NOTE

We performed a systematized search on October 17, 2020 with the term “Juliano Moreira” in PubMed, which resulted in 3 articles, although only one of them had been fully reviewed. The same search was performed in LILACS with 76 retrieved results; several of these were used to write this review. Additionally, we searched on Google Scholar, performed a manual search in citation references, lists of reviewed articles, and reviewed books, and theses on Moreira’s life. The majority of the references used in our note and **Supplementary file** are secondary sources except for his major works in Neurology in which the primary sources were reviewed and mentioned in detail.

## JULIANO MOREIRA’S CONTRIBUTION TO THE FIELD OF NEUROLOGY

### *Contribution to the field of Neurology whilst in Bahia*

Juliano Moreira first demonstrated his inclination towards the field of Neuropsychiatry in his doctoral thesis<sup>1</sup>. In his inaugural work, Moreira identified a gap in the study of syphilis related to the causes that made the disease malignant and early in most of the cases found in the literature and observed during his education. On the etiological agent of syphilis, namely “syphilis-microbe” (which would only be discovered 14 years later), he analyzed works by great scientists of the microbial revolution such as Pasteur, Neisser, Koch and Klebs, prioritizing the qualitative aspects of the presumed agent and highlighting its relationship with the host<sup>2</sup>. Moreira refuted the widespread notion at that time that syphilis was more prone to transmission and malignancy in the tropics due to climate and racial factors<sup>3</sup>.

Moreira also contributed to the Neurological field with his writings and role at *Gazeta Médica da Bahia* (GMB), one of Brazil’s first scientific medical journals. From 1893, he published several articles in this journal on syphilis and its neurological consequences, among other nervous diseases<sup>4</sup>. Moreira has detailed the role of the pharynx in syphilis by describing two patients with syphilis and pharyngeal spasm triggered by the ingestion of liquids, leading to a patient’s death in one of the cases. He also mentioned similar cases of syphilis patients with convulsive and repetitive swallowing movements lasting several minutes described by Jean Martin Charcot and Oppenheim<sup>5</sup>. In 1902, Moreira wrote in GMB about myoclonic epilepsy, stressing the familial aspects

of the condition and reviewing the cases of Unverricht, in Estonia (later known as Unverricht-Lundborg disease), and others. Moreira wrote about the early onset of the condition, describing aspects relating to the neurological examination of patients and spells<sup>6</sup>. In the same year, he wrote about sleeping sickness, commenting on this and other tropical diseases not typically found in Brazil. Moreira refuted the reports of this disease on black Brazilian workers and detailed the clinical and pathological aspects of the condition, making considerations about its causal agent and its origins in Africa, based on studies resulting from a Portuguese mission to “Prince’s Island” in São Tomé and Príncipe, and Angola<sup>7</sup>. Notably, Juliano Moreira became editor of GMB in 1896 and editor-in-chief in 1901<sup>4</sup>.

In 1896, Moreira applied for a substitute lecturer position in the Nervous and Mental Illness Department recruitment process with a seminal thesis entitled “Arsenic Dyskinesia”, in which he described the alterations of arsenic poisoning, focusing on its neurological manifestations<sup>8</sup>. The term dyskinesia, which is currently applied to hyperkinetic movement disorders (mainly chorea), was adopted by Moreira to refer to general motor function alterations. The condition he was describing has been mentioned in the medical literature since the thirteenth century, but it was more comprehensively described in the mid nineteenth century, being named arsenic paralysis or paraplegia. Moreira did not agree with that term on the grounds that patients could present a much broader motor clinical picture than just paralysis. Moreira described eight cases of arsenic poisoning, four of them related to a single accidental poisoning with arsenic acid and the other four by iatrogenic ingestion, three by chronic use of Fowler’s liquor (1% potassium arsenite) for a variety of conditions and one by chronic use of Boudin’s arsenic granules for tuberculosis treatment. It is worth mentioning that the golden age of arsenic compounds as therapeutic agents occurred around the turn of the twentieth century. With very broad indications, these substances were widely prescribed as tonics and fortifiers that appeased nebulous conditions<sup>9</sup>. One of the main applications of arsenic compounds in their various formulations was the treatment of syphilis, which is possibly one of the reasons why Moreira’s thesis topic was chosen, given his experience with the condition and the side effects of its treatments. Moreira proceeded to perform a detailed description of the neurological examination of those cases, in which there were marked sensory and motor changes and, in some cases, cognitive symptoms. He also operated detailed electrodiagnostic characterization with Faradic and Galvanic explorations. Moreira reviewed ninety other acute and chronic cases of arsenic poisoning from the literature. In his review,

he commenced by drawing inferences related to the state regulation of arsenic usage by different countries and suggesting that its ease of access by people would have consequences for the frequency of poisoning cases. Moreira gave a detailed description of the sensory findings of the condition (tactile, thermal sensitivity, pain, and visual system), describing tremors and athetoid movements that he attributed as secondary to peripheral nerve injuries. Moreira described the pattern of distal muscular atrophy and its speed of progression with the involvement of proximal muscle groups only later on in the progression of the disease. He also documented behavioral changes and amnesia associated with the condition. Another possible reason for the choice of his thesis topic is that arsenic poisoning can lead to neurological, psychiatric and dermatological symptomatology, thus combining his main medical fields of interest. Regarding dermatological features of arsenic poisoning, Moreira described changes in skin coloration pigmentations similar to those seen in Addison's disease but sparing mucous membranes. Additionally, he made considerations about the dermatological lesion aspects in non-white individuals, mentioning that these lesions tend to have differences of hue proportional to the color of the affected tegument<sup>8</sup>. In his theses, Moreira proposed a classification for arsenic poisoning, parsing the condition into multiple phases with defined prognosis and duration of symptoms. After performing a detailed review of the literature on the anatomopathological findings of arsenic poisoning in humans and on toxicological experiments in animals, he reported his own toxicological animal model experiments in dogs, cats and guinea pigs, depicting marked changes at the level of peripheral nerves. Possibly, such studies were only feasible considering his recent experiences as a topographic anatomy preparer at the Medical School of Bahia. Moreira concluded his thesis establishing considerations about the pathophysiology of the condition, stating that peripheral polyneuritis was the major neurological presentation, and that muscle findings would be secondary to denervation due to peripheral nerves or anterior horn damage by arsenic poisoning. He finishes his work discussing the condition diagnosis in light of the limitations of toxicological tests at that time and highlighting the role of the cutaneous signs for the diagnostic hypothesis<sup>8</sup>.

### **Contribution to the field of Neurology whilst in Rio de Janeiro**

As previously mentioned, some authors have historically considered that the practice of neurology began in Brazil at the NHI, which was directed by Moreira from 1903 to 1930<sup>3,10,11</sup>. During this period, the hospital underwent a series of renovations focused on improving patient care along with the creation of new pavilions for disparate conditions, including specific areas for children (Bourneville Pavilion) and for patients with epilepsy, as well as the Institute of

Neurosyphilis, later transformed into a psychiatric hospital, the Philippe Pinel Institute<sup>12</sup>. Of note, Bourneville Pavilion-School is considered the first Brazilian institution that provided mental health care to infants with intellectual disability. It was inaugurated by the pediatrician Fernandes Figueira who was also part of the medical staff in a brand new specialty at NHI during Moreira's administration<sup>13</sup>. The Pavilion-School, offering a gymnasium, courses for co-education of boys and girls, appropriate beds and a geometric garden, was built to improve the NHI organization and to provide adults and children with separate living spaces. The proposal was to offer specialized treatment for infants based on Bourneville's method, aiming to "adjust" these children to social patterns, to increase their literacy and to teach them an occupation<sup>13,14</sup>. Besides this, the Observation Pavilion was created in 1893 and has since remained under the directorship of a professor of Clinical Psychiatry and Nervous Diseases from the Medical School of Rio de Janeiro, and not by the director of the Hospice. Antônio Austregésilo was appointed to the NHI in 1904 as the person in charge for the Observation Pavilion<sup>12</sup>.

In 1905, two years after being appointed as the head of NHI, Moreira wrote about reforming assistance to epileptics, suggesting the creation of colonies. In this very interesting historical text, Moreira argued that assistance to epileptics in Brazil, marked by social exclusion and by the association at that time with criminality, could be improved with the creation of specific agricultural colonies for epileptics. Moreira reviewed international experiences, describing the creation and effectiveness of these colonies in Germany. He mentioned that in the middle of 1905, the Bielefeld colony in Westphalia was home to around 3,000 epileptics, reporting full recoveries in one sixth of hospitalized epileptics and improvements in another 40%. Moreira explained that pastor Boldeschwingh's positive experiences in the Bielefeld colony led to the foundation of other similar institutions; however, he regretted that only with the help of religious charity public authorities have reached such essential results. Moreira reported on similar experiments with colonies for epileptics in Switzerland, Russia, Spain and Belgium. He highlighted the role of the creation of epileptic colonies in England as a contributing factor in the emergence of associations dealing with epilepsy, such as the National Society for the Employment of Epileptics founded in 1893 in England and, later, the role of Craig Colony in the USA, which was founded to "secure the human curative, scientific and economical care and treatment of epileptics" and gave rise to the American Association for the Study of Epilepsy. Moreira ends his paper suggesting that the president of Brazil and its interior minister consider the beneficial example of other countries in order to encourage the development of initiatives to take care of epileptics in Brazil<sup>15</sup>.

In 1907, Moreira and Carlos Penafiel wrote about dementia paralytica in Brazil, providing NHI data. From 1889 to 1904 they reported the admission of 9,609 “insane” individuals, of which 266 (2.76%) were general paralytics, a much lower relative frequency than that reported in various European countries, ranging from 5% in Switzerland to 44% in some French series. Subsequently, Moreira and Penafiel documented the incidence of the disease in tropical countries, which was rare in Java and Georgetown, and had no case descriptions in Zanzibar. Conversely, there were also no cases in Iceland, a cold climate country. Therefore, the authors considered that climate was not influencing the frequency of the disease. As with his undergraduate thesis, Moreira considered that comorbidities should be responsible for the disease severity in dementia paralytica, reporting similar frequencies among Brazilians and foreigners at the NHI. Interestingly, the authors provided data on relative frequencies of general paralytics among the population suffering mental health problems in São Paulo (3.87% among Brazilians and 8.3% among foreigners) as well as others in Rio de Janeiro (1.6 to 6.2%, but reporting a selection bias for the higher percentages) and Rio Grande do Sul (1.46%). The authors also made considerations about racial aspects on disease severity, refuting any relation of it as a factor of worst prognosis, analysing NHI and data from other countries<sup>16</sup>.

### **Other contributions to the field of Neurology: lumbar puncture and clinical pathology laboratories**

Moreira is considered to be the first physician to ever perform a lumbar puncture for diagnostic purposes in Salvador<sup>17</sup>. Later, he installed a clinical laboratory at the NHI in Rio de Janeiro, establishing diagnostic routines including lumbar punctures along with cytological exams of cerebrospinal fluid in cases of Tabes Dorsalis, paralytic dementia, cerebral syphilis and various forms of meningitis<sup>3,11</sup>. The implementation of the laboratory facilities addressed Moreira’s desire to articulate the work of psychiatrists with the experimentalism and organicism of German medicine. Thus, as Dunningham pointed out, from 1906 onward “lumbar punctures started to be practiced regularly, and cytological examinations of the cerebrospinal fluid supported and clarified diagnoses”. The dissemination of the works of the German doctor August von Wassermann served as a stimulus for “the studies of serology of syphilis, with Artur Moses’ excellent contribution, at the Instituto de Manguinhos”. Nonne’s four reactions (so named in reference to the neurologist Max Nonne), widely used in the laboratories of Brazilian psychiatric institutions, came to encompass not only Wassermann’s reaction in blood and blood cerebrospinal fluid, but also “pleocytosis” and “high albumin levels” in the cerebrospinal fluid, hence contributing to the improvement of the diagnosis of syphilis<sup>18</sup>.

## **FOUNDATION OF SCIENTIFIC JOURNALS, MEDICAL SOCIETIES AND LEAGUES**

Another important contribution of Juliano Moreira to Brazilian medicine in general and to the Neurology field in particular was the creation in 1905, with his colleague Afrânio Peixoto, of the journal “Arquivos Brasileiros de Psiquiatria, Neurologia e Ciências Afins”, the first Brazilian publication to specialize in Neuropsychiatry. In 1908, the journal changed its name to “Arquivos Brasileiros de Psiquiatria, Neurologia e Medicina Legal” following the foundation of the Brazilian Society of Neurology, Psychiatry and Legal Medicine (BSNPLM), in 1907, of which Moreira was the director until his death in 1933<sup>18</sup>. In 1915, in order to reinforce the publication’s commitment to the fields of Neurology and Forensic Medicine, the editors highlighted the three areas of knowledge on the cover of the magazine alongside their respective heads: in psychiatry, Juliano Moreira; in neurology, Antônio Austregésilo; and in legal medicine, Afrânio Peixoto. In 1919, the journal again changed its name, this time to “Arquivos Brasileiros de Neuroiatria e Psiquiatria”<sup>14</sup>. During its five decades of existence, the journal had an extensive influence and was fundamental to the promotion of modern Neurology in Brazil.

It should be noted that despite having a similar name, the journal “Arquivos de Neuro-Psiquiatria”, founded in 1943 under the initiative of Oswaldo Lange from the medical schools of Universidade de São Paulo and Escola Paulista de Medicina<sup>19</sup>, has no direct connection with the above-mentioned journals. “Arquivos de Neuro-Psiquiatria” has been edited by the Brazilian Academy of Neurology since 1970, suggesting an increasing influence of São Paulo’s school in Brazilian Neurology over the years.

Moreira also participated as one of the first members of the International League Against Epilepsy (ILAE), being one of the 46 persons present in Budapest in 1909 at the specific meeting in which the league was founded<sup>20</sup>. Moreira was elected full member of the National Academy of Medicine of Brazil in 1903, acting as its vice-president from 1922 until 1923, and from 1925 until 1933<sup>21</sup>. In May 1916, Moreira was one of the founders of the Brazilian Academy of Sciences (ABC), in the words of Afrânio Peixoto, “giving his light, authority and prestige to that academy”. In 1917, Moreira became vice-president of ABC until 1926 when he became its president (1926-1929). Moreira received Albert Einstein in Brazil in 1925, while vice-president of ABC, performing an opening speech on the influences of the Theory of Relativity in other areas of knowledge, especially in biology. Einstein visited the NHI and had lunch with Moreira and his German wife, Augusta Emma Peck, eating *vatapa*, a typical dish from Bahia. Einstein, who was implacable in his diary notes, was very impressed about Moreira<sup>21</sup> (Figure 2).

## PSYCHIATRIST, NEUROLOGIST OR NEUROPSYCHIATRIST? PROFOUND INFLUENCES OF MOREIRA IN THE FUTURE OF NEUROLOGY IN BRAZIL

Writing in GMB in 1901, Moreira lamented the manner in which the XIII Congress of Medicine in Paris<sup>22</sup> was organized, with separate sections of psychiatry and neurology. He highlighted the dissatisfaction with this separation by several delegates, evidenced in the speech of the general secretary of the Neurology section, Pierre Marie, who said: “the members of the Neurology section meeting at the Sorbonne send cordial greetings to the Psychiatry section... and hope that the two sections working in parallel with the same spirit of devotion to science contribute effectively for the advancement of our knowledge in everything that concerns the normal and pathological nervous system”<sup>22</sup>.

Only later on, at the BSNPLM in 1926, did Moreira resolve that the sections of Psychiatry and Neurology of the society should occur separately<sup>23</sup>, with the Psychiatry section under the coordination of Henrique Roxo, and the Neurology section under the coordination of Antônio Austregésilo who, at that point, was vice-president of the society, but with both sections under the presidency of Moreira himself. In the period of 1926 to 1931, there was an increase in Austregésilo's influence on the destinies of the BSNPLM and, in 1933, after

Moreira's death, Antônio Austregésilo was elected president of BSNPLM<sup>23</sup>.

## OTHER NOTES

Moreira also wrote biographic notes, one of them about Jean-Martin Charcot, in 1925<sup>24</sup>. Identifying somewhat with him, Moreira highlighted that Charcot, together with his disciples, founded several journals, and had filled the position of the chair of pathological anatomy. In Moreira's biographical note of Charcot, he chose not to refer to him as the founder of modern neurology, preferring instead to state that Charcot established and developed the best school of this specialty, being responsible for multiplying the number of neurologists in Paris, France, Europe, and the Americas<sup>24</sup>. Likewise, Juliano Moreira had a great influence in psychiatry and neurology in Brazil, and the father of modern Brazilian neurology, Antônio Austregésilo, worked under the direction of Moreira at NHI, participating in societies, academies, and journals alongside Moreira. Therefore, if not the founder of scientific neuropsychiatry, he is definitely one of the most important influencers for the establishment and development of Clinical Psychiatry and Neurology in Brazil.

## REFERENCES

1. Moreira J. Etiologia da syphilis maligna precoce. [Tese de Doutorado]. [Salvador(BA)]: Faculdade de Medicina da Bahia; 1891.
2. Jacobina RR. Nem clima nem raça: a visão médico-social do acadêmico Juliano Moreira sobre a “Sífilis maligna precoce”. Rev Baiana Saúde Pública. 2014;38(2):432-65. <https://doi.org/10.5327/Z0100-0233-2014380200015>
3. Oda AMGR, Piccinini W. Dos males que acompanham o progresso do Brasil: a psiquiatria comparada de Juliano Moreira e colaboradores. Rev Latinoam Psicopatol Fundam. 2005 Oct-Dec;8(4):788-93. <https://doi.org/10.1590/1415-47142005004014>
4. Jacobina RR, Gelman EA. Juliano Moreira e a Gazeta Médica da Bahia. Hist Cienc-Saúde Manguinhos. 2008 Dec;15(4):1077-97.
5. Moreira J. Pharyngismo tabético (nevro-pathologia). Gazeta Médica da Bahia. 1894 Nov;26(5):203-12.
6. Moreira J. O lugar das mioklonias em neuropathologia. Gazeta Médica da Bahia. 1902 Jul;33(7):309-16.
7. Moreira J. Os recentes trabalhos portugueses sobre a molestia do somno. Gazeta Médica da Bahia. 1902 Jan;33(7):317-25.
8. Moreira J. Dyskinesias arsenicaes: nova contribuição e estado actual da questão. [Tese de Concurso para o lugar de Lente Substituto da 12ª seção]. [Salvador(BA)]: Faculdade de Medicina e Farmácia da Bahia; 1896.
9. Gontijo B, Bittencourt F. Arsênio: uma revisão histórica. An Bras Dermatol. 2005 Feb;80(1):91-5. <https://doi.org/10.1590/S0365-05962005000100014>
10. Meira AT, Betini BG, Cardoso F, Gomes MM, Barbosa EG, do Prado RCP et al. First stages towards the establishment of Brazilian neurology faculties. Arq Neuropsiquiatr. 2019 Dec;77(12):888-95. <https://doi.org/10.1590/0004-282X20190147>
11. Nardi AE, Carta MG, Shorter E. The remarkable Juliano Moreira (1872-1933): an Afro-Brazilian psychiatrist, scientist, and humanist in an environment of slavery and racism. Braz J Psychiatry. 2020 Jun 12;00(00). <https://doi.org/10.1590/1516-4446-2020-1097>
12. Gomes MM, Cavalcanti MT. National hospice for the insane and the Brazilian neurology in the beginning of the 20th century. Arq Neuropsiquiatr. 2012 Oct;70(10):823-5. <https://doi.org/10.1590/S0004-282X2012001000013>
13. Silva RP. Medicina, educação e psiquiatria para a infância: o Pavilhão-Escola Bourneville no início do século XX. Rev Latinoam Psicopat Fund. 2009 Mar;12(1):195-208.
14. Facchinetti C, Ribeiro A, Chagas DC, Reis CS. No labirinto das fontes do Hospício Nacional de Alienados. Hist Cienc Saúde-Manguinhos. 2010 Dec;17 Suppl 2:733-68. <https://doi.org/10.1590/S0104-59702010000600031>
15. Moreira J. Assistência aos epiléticos: colônias para eles. Hist Cienc Saúde-Manguinhos. 2010 Dec;17 Suppl 2:572-81. <https://doi.org/10.1590/S0104-59702010000600018>
16. Moreira J, Penafiel A. A contribution to the study of dementia paralytica in Brazil. J Ment Science. 1907;53(223):507-21. <https://doi.org/10.1192/bjp.53.223.507>
17. Dunningham WA. Juliano Moreira: notas sobre a sua vida e obra. Gazeta Médica da Bahia. 2008;78(1):72-5.
18. Facchinetti C, de Muñoz PFN. Emil Kraepelin na ciência psiquiátrica do Rio de Janeiro, 1903-1933. Hist Cienc Saúde-Manguinhos. 2013 Mar;20(1):239-62. <https://doi.org/10.1590/S0104-59702013000100013>
19. Tolosa A, Longo P. Apresentação. Arq Neuropsiquiatr. 1943 Jun;1(1):7-8. <https://doi.org/10.1590/S0004-282X1943000100002>

20. Shorvon S, Weiss G. International league against epilepsy – the first period: 1909-1952. In: Shorvon S, Avanzini G, Meinardi H, Reynolds E, Weiss G, Engle J, et al., editors. International league against epilepsy: 1909 – 2009 a centenary history Simon Shorvon, Giuliano Avanzini, Harry Meinardi, Edward Reynolds, Giselle Weiss, Jerome Engle, Solomon Moshe, and Peter Wolf. Wiley-Blackwell; 2009; p. 1-44.
21. Jacobina, RR. Juliano Moreira da Bahia para o mundo – a formação baiana do intelectual de múltiplos talentos (1872-1902). 1st ed. Salvador: EDUFBA; 2019. 323 p.
22. Moreira J. As secções de psiquiatria e neurologia do XIII Congresso de Medicina de Paris. *Gazeta Médica da Bahia*. 1901 Apr; 32(10):475-86.
23. Cerqueira ECB. A sociedade brasileira de neurologia, psiquiatria e medicina legal: debates sobre ciência e assistência psiquiátrica (1907-1933) [Dissertação de Mestrado]. [Rio de Janeiro(RJ)]: Fundação Oswaldo Cruz, Casa de Oswaldo Cruz; 2014. 234p.
24. Moreira J. “Charcot” academia nacional de medicina: sessão de 28 de maio de 1925. *Bol Acad Nac Med*. 1925;(7):131-8.