

THE ANIMATED MIND OF GABRIELLE LÉVY

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"Sa vie fut un exemple de labeur, de courage, d'énergie, de ténacité, tendus vers ce seul but, cette seule raison: le travail et le devoir à accomplir"¹
[Her life was an example of labor, of courage, of energy, of perseverance, directed at that single target, that single reason: the work and the duty to fulfill]

These are words, used by Gustave Roussy, days after the early death at age 48, in 1934, of his colleague Gabrielle Lévy. Eighteen years previously they had written their joint paper on seven cases of a particular familial disease that became known as Roussy-Lévy disease.² In the same *in memoriam* he added "And I have to say that in our collaboration, in which my name was often mentioned with hers, it was almost always her first idea and the largest part was done by her". Who was this Gabrielle Lévy and what did she achieve during her short life?

Gabrielle Lévy

Gabrielle Charlotte Lévy was born on January 11th, 1886 in Paris.^{*1,3} Her father was Emile Gustave Lévy (1844-1912; from Colmar in the Alsace region, working in the textile branch), who had married Mina Marie Lang (1851-1903; from Durmenach, also in the Alsace) in 1869. They had five children (including four boys), the youngest of whom was Gabrielle. At first she was interested in the arts, music in particular. Although not losing that interest, she chose to study medicine and became a pupil of the well-known Paris neurologist Pierre Marie and his pupils (Meige, Foix, Souques, Crouzon, Laurent, Roussy and others), who had been professor of anatomic-pathology since 1907 and succeeded Dejerine at the chair of neurology ('maladies du système nerveux'; that had been created for Jean-Martin Charcot in 1882). She started her *externat* in Paris in 1911. Between 1912 and 1915 she worked successively at the surgical department of the Pitié hospital, Hôpital Beaujon (prof. Oulmont), Hôpital des Enfants-Malades (prof. Marfan) and again at Hôpital de la Pitié (prof. Enrique). In 1915 she became *externe en premier* of Pierre Marie, one of Charcot's well-known pupils, at the Salpêtrière (1915-1918) and subsequently she did her internship between 1918 and 1919. She was an appreciated student and terms that were passed on from this period include "excellente externe, très satisfaisant, zélée et active" [excellent extern, very satisfying, diligent and active].



Fig. 1. Gabrielle Charlotte Lévy (1886-1934; courtesy Dominique Weil)

Gabrielle Lévy declined a proposal of marriage from an ophthalmologist.[†] As was not rare in those days, the reason for this was that she did not wish to abandon her professional activities to devote herself entirely to family life.

^{*} Biographical information was obtained from the obituaries written by Gustave Roussy in *La Presse Médicale*, an anonymous obituary in the *Journal of Mental and Nervous Diseases* and from a descendant, Dominique Weil, of the Lévy family.

[†] Several of Gabrielle Lévy's still living family members were acquainted to the pertinent ophthalmologist.

Still working with Pierre Marie, she had several functions at the Salpêtrière, including chief of his laboratory (1920-1922) and assistant at the pathology department (1923-1926). In 1925 she became associated physician at the Paul-Brousse hospital[‡] that had opened in 1913. Here Gustave Roussy was head of the hospital and opened the first French oncologic consultation center for out-patients in 1919. Lévy became full attending physician not long before death in 1934. She suffered from a severe disease of the nervous system,[§] which she diagnosed herself.

Lévy's thesis on encephalitis lethargica (EL)

In April 1917, the Austrian physician Constantin von Economo presented seven cases (including two with autopsy) of a strange epidemic that seized Europe during the 1916-7 winter, at a meeting of the Vienna Society for Psychiatry and Neurology. '*Since Christmas, we have had the opportunity to observe a series of cases at the psychiatric clinic that do not fit any of our usual diagnoses. Nevertheless, they show a similarity in type of onset and symptomatology that forces one to group them into one clinical picture. We are dealing with a kind of sleeping sickness, so to speak, having an unusually prolonged course.*' The disease began abruptly in some patients and in others insidiously, like influenza. Following the initial phase, the patients developed behavioral changes, cranial nerve palsies, motor disorders and variable grades of lethargy. The seven patients presented by Von Economo had a persistent, intractable stupor in common. Although some were only mildly affected, others became stuporous. In the following years it became pandemic, affecting about five million people, of which a third did not survive the acute phase. It left thousands of patients, suffering from post-encephalitic syndromes, that sometimes appeared after a latent period of years, in nursing homes.^{**}

Von Economo distinguished three forms of EL,^{††} including a) a somnolent-ophthalmoplegic form, in which patient suffered from a prodrome of malaise, chills, fever, and nasal catarrh, followed by meningism, somnolence, delirium, ophthalmoplegia and oculogyric crises; this type of EL often resulted in stupor, coma and death; b) a hyperkinetic type, with a flu-like prodrome, followed by motor agitation and behavioral symptoms. Myoclonia, chorea, tics, and athetosis were often observed. Moreover other forms of hyperactivity, such as continuous jerking, rolling, whistling and fidgeting were observed. Anxiety, hypomania, violent outbursts, and delirium with visual hallucinations were the usual mental symptoms. The psychomotor agitation was worse at night and resulted in 'sleep inversion' (sleeplessness at night and hypersomnia by day); c) an amyotatic-akinetic form, with the same prodrome, followed by rigidity, propulsion or retropulsion, bradykinesia, and sometimes tremor; depression and mutism were the most frequent mental symptoms.^{4,5} Von Economo published a monograph on EL in 1929.⁶

It is of no surprise that Pierre Marie and Gabrielle Lévy became interested in research of EL and published rare syndromes arising from this disease. Her first paper co-authored by Pierre Marie, on ten cases of movement disorders associated with EL, already appeared the year following Von Economo's first paper.⁷ Prior to her thesis on EL, at least 14 of Lévy's papers published in that period deal with EL or post-encephalitic syndromes.^{8,9,10,11,12,13,14,15,16,17,18,19,20} Pierre Marie was first author of most of these papers. Many of these deal with movement disorders in EL, including postencephalitic parkinsonism (PEP). In one of these papers they described movement disorders in 49 patients with EL. Four patients were mentioned in more detail with choreic movements, bradykinetic oscillations (slow rhythmic movements of the proximal limbs in particular), myoclonus, parkinsonism, rarely isolated tremor (of the face), and localized facial movements (tongue-face-masticatory or ocular).¹² In another paper they described involuntary movements in the lingual-facial-masticatory muscles.¹³ Yet another paper also dealt with such movements, but included facial pain.^{14,15} Two years later they again published on features of EL, notably respiratory problems and insomnia.^{16,17}

[‡] Named after Paul Brousse, a French physician and socialist politician

[§] In her own family, it was repeatedly said that she died from the disease that she was studying.

^{**} Readers may remember that some survivors with postencephalitic parkinsonism were treated by levodopa when it became available in the late 1960s. Oliver Sacks treated patients at Beth Abraham (New York) and often observed spectacular results. His book on this period is well known *Awakenings*.

^{††} At last 28 types of EL have been described; see Vilensky's book (ref. no. 23).

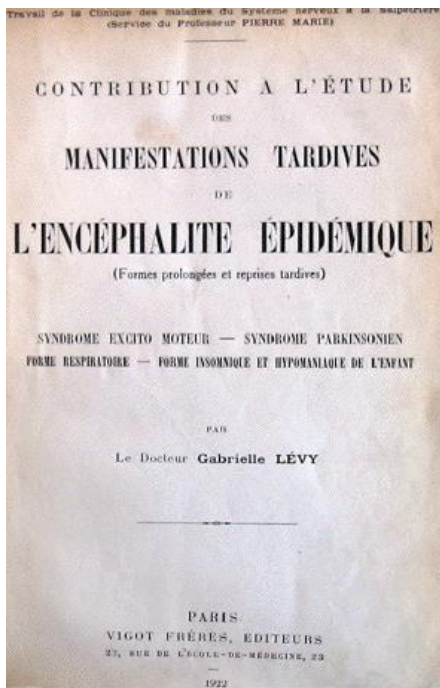


Fig. 2. Title page of Lévy's 1922 thesis

Considering the titles of her journal papers, it is most probably that the material from these papers was used for Lévy's thesis *Contribution à l'étude des manifestations tardives de l'encéphalite épidémique* [Contribution to the study of the late manifestations of epidemic encephalitis] that was published in 1922.²¹

The 314-page book provides an extensive description of post-encephalitic syndromes in three parts: I) clinical aspect (excito-motor syndrome, parkinsonian syndrome, other neurological manifestations, other general disorders, including respiratory and sleep problems, lasting mental changes, pediatric manifestations and prognostic aspects; II) pathologic-anatomical aspects of four cases; and III) descriptions of 68 (comprising 110 pages) of the 129 case studies that were used for thesis. The majority of the cases was aged between 10 and 50 years.

The most important of the manifestations, in order of importance, were considered the parkinsonian syndrome (which was most frequent, 70 cases, with a tendency to become chronic), the excito-motor syndrome, the insomnia and hypomania syndrome in children and the respiratory syndrome. The prognosis of these late syndromes was unfavorable.



Fig. 3a. From Lévy's thesis (p.51): 'Typical aspect of the parkinsonian syndrome with fixed features'; 3b. Jeanne V. (9 year-old; p.100); start of 'plicature' [folding] in the course of a parkinsonian syndrome; 3c. Parkinsonian syndrome in a 12 year-old child.



FIG. 21. — Début de plicature, au cours d'un syndrome parkinsonien. (Obs. 49)



FIG. 35. — Syndrome parkinsonien chez enfant de 12 ans. (Obs. 47).

Lévy concluded that the parkinsonian syndrome after EL resembled Parkinson's disease with respect to rigidity and tremor, but differed from it with respect to the predominance of the rigidity vs the tremor, the extreme

slowness, the predominant cervico-facial localization of the signs, important salivation and the frequency of retropulsion in PEP (p.287).

The thesis included four cases, in whom pathologic anatomy was performed.

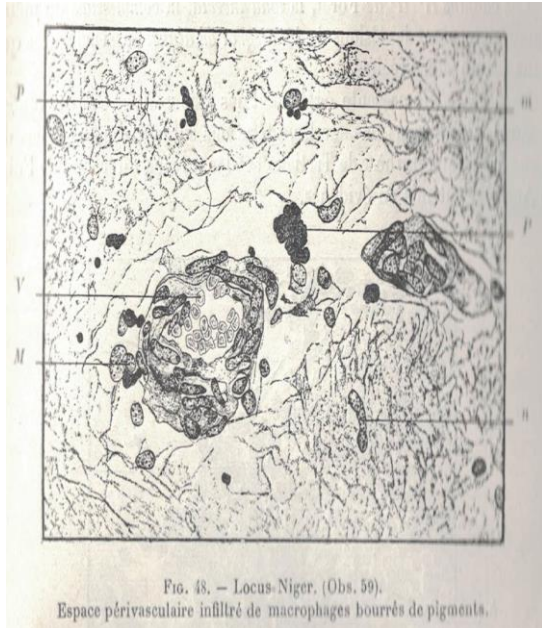


Fig. 4 Locus niger [probably substantia nigra]; perivascular space infiltrated by pigment filled macrophages

The book was reviewed in the journal *Revue Neurologique* in 1923 by E. Feindel, who opined that it was rich in new facts and original ideas. She mainly observed cases with a prolonged duration. The prolonged forms (a) and late manifestations (b) of the disease 'constitute the most fearful threat of the disease'. Facts suggested that the 'continuation of the virus', as was believed at the time, explains the late manifestations in most cases, although this had not been proved yet. A third form (c) is mentioned, notably the first manifestation of encephalitis, in which the acute phase passed completely unnoticed.

Three years after her thesis, a new edition was published as a book *Les manifestations tardive de l'encéphalite épidémique* [The late manifestations of epidemic encephalitis] with a preface by Pierre Marie.²² An extensive review on EL was published in 2011 and another is expected soon.^{23,24}

The eponymous publication - Roussy-Lévy syndrome

The best known paper, leading to eponymous celebrity, Lévy wrote, was the one with her colleague Gustave Roussy (1874-1948). Roussy, 12 years her senior and of Huguenot descent, was born in Switzerland (Vevey).^{25,26} Following his medical study at Geneva, he went to Paris, where he worked with Pierre Marie and Joseph-Jules Dejerine (who was also born in Switzerland).



Fig. 5. Gustave Roussy in 1929 (age 55)

He wrote his thesis on the thalamic syndrome (or Dejerine-Roussy syndrome) in 1907,²⁷ publishing a paper with Dejerine on this subject in the *Revue Neurologique* in 1906.²⁸ Following French naturalization, he became professor of pathology in 1910 and head of Paul Brousse Hospital (1913). Following WWI, during which he served at the Army Neurological Centre (of the VIIth region at Besançon)²⁹ - collaborating in several books on the "psychonévroses de guerre" [war psychoneurosis]-,³⁰ he became full professor of pathology in 1925. Although he did important neurological work, his main merit is his fight against cancer (the Gustave Roussy Institute at Villejuif became a famous cancer centre). Roussy and Lévy wrote their joint paper on 7 patients with hereditary areflexic dystasia, the Roussy-Lévy syndrome, in 1926.² The first sentence of their paper reads as 'Nous avons eu l'occasion d'observer sept cas d'une maladie familiale dont la symptomatologie nous a paru singulière, et non encore décrite' [We have had the occasion to observe seven cases of a familial disease, of which the symptomatology appeared remarkable, and not yet described]. They admitted that the disease resembles Friedreich's disease with respect to the clubfoot and areflexia, and possibly Charcot-Marie's amyotrophy, 'although the amyotrophic phenomena are exceptional in our patients'. The first patient 'Me Berthe Pli... âgé de 25 ans, vient consulter à l'hospice Paul-Brousse en septembre 1925' [mrs. Berthe Pli... age 25 years, comes for a consultation at the Paul-Brousse hospice in Septembre 1925]. She and her two children as well as other family members had troubles at walking.

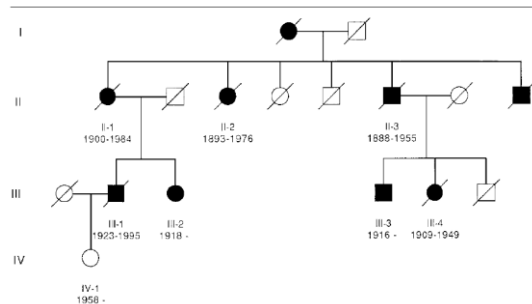
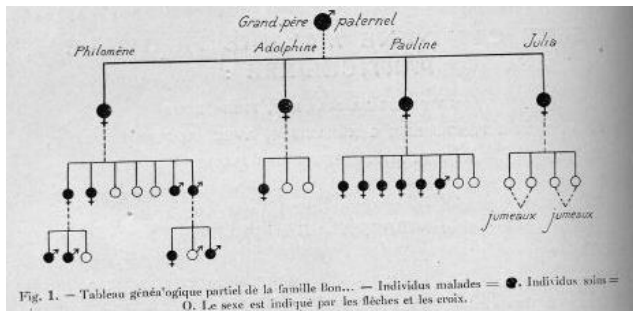


Fig.6a. Pedigree from original 1926 paper by Roussy & Lévy and the same family (6b) as published in 1999. Berthe Pli... is the 1st most left patient in the 3rd generation (6a) and II-1 in 6b. Obviously there is an error in the 4th generation (6a) as she had a boy and a girl, as is rightly indicated in 6b.

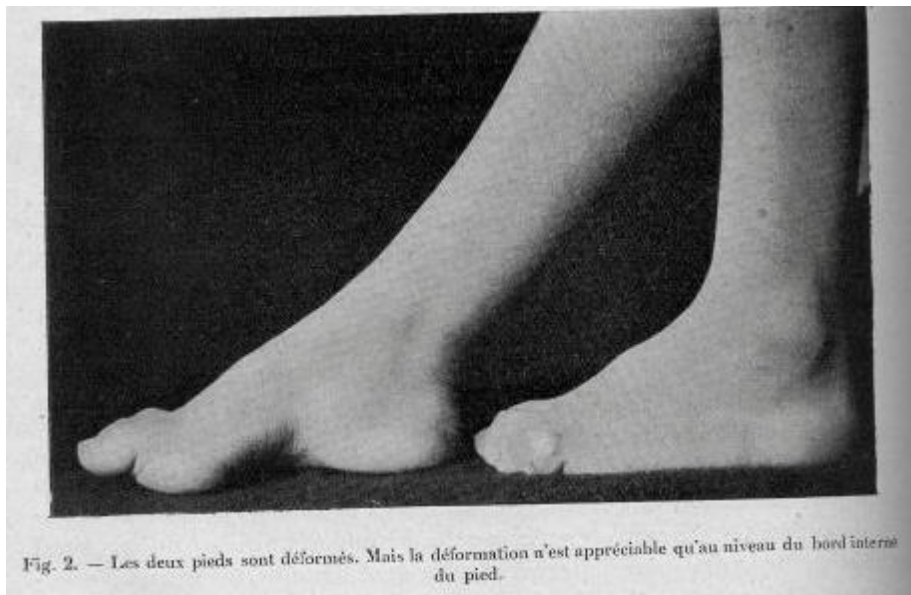


Fig.7. From the original 1926 paper by Roussy & Lévy. [the two feet are deformed. But the deformation is only noticed at the medial side of the foot].

'She has tried to work at a chocolate shop, but she was declined, because she was unable to carry any weight'. She also suffered from clumsiness of the fingers, in particular with sewing and unshelling vegetables. She has had 3 children, one of whom died at age 26 months from pneumonia following whooping cough. At examination she was found to be 'extrêmement gracile' (Fig.8), only 1,44 m and 39 kg, without scoliosis (of course in contrast to Friedreich's disease). She had clubfeet, more pronounced on the right side. Her gait was swaying and unstable, but unlike the gait in cerebellar disease. Muscle strength in the upper extremities was normal except perhaps in the left hand. Movements were executed normally except while handling a needle, for which she needed to stabilize both palms against one another.



Fig.8. Berthe Pli... From original 1926 paper by Roussy & Lévy

'For sewing, she holds her needle with all fingers, pushing the needle through the cloth with considerable difficulty, she trembles ... When she wants to drink, she is trembling too. It concerns a slight, atypical tremor. No tremor at rest'. At the lower extremities the extensor of the hallucis longus was paretic, in particular on the right

side and 'the antero-extern group on the left'. Areflexia was found at all tendon reflexes. No cerebellar signs. Sensory examination was normal 'à tous les modes: tact, piqûre chaud, froid, sens des attitudes, stéréognosies' [for or qualities: touch, hot prick, cold, position sense, stereognosis].

A certain mrs. de Brancas performed the electric examination: 'very remarkable faradic and galvanic hypoexcitability, predominantly at the level of the small extremity muscles'.

EN RÉSUMÉ : Malade de 25 ans, qui présente : du dérochement des jambes et une certaine maladresse des mains, une aréflexie tendineuse généralisée, un pied bot, une démarche légèrement festonnante et un peu de steppage.

Aucun trouble cérébelleux, sauf le petit tremblement intentionnel des mains. Pas d'extension de l'orteil, légère diminution de la force dans certains groupes musculaires.

Pas de troubles de la sensibilité. Pas de nystagmus. Troubles des réactions électriques, sans R. D.

Fig.9. Summary of the first patient [weakness of the legs and a certain clumsiness of the hands, generalized tendon areflexia, clubfoot, a slight swaying gait and some stringhalt. No cerebellar problems, except some intentional tremor of the hands. No extension of the big toe, slight diminution of strength in certain muscle groups. No sensory disorder. No nystagmus. Disordered electrical reactions without RD].

Two of Berthe's children (Simone, 7 year old and Raymond, 2 year old; III-1 and III-2 in fig. 6b) and her sister Julia Ur... (II-2 in fig. 6b) suffered from the same disease. Raymond walked like 'un petit tabétique' [a small tabetic; at the time this usually indicated a sensory ataxic gait as seen in syphilitic tabes dorsalis].



Fig.10. Raymond standing with his legs widely apart

Following the description of the seven patients, the authors summarized the main signs as being

- a) gait and standing problems
- b) areflexia
- c) clubfoot.

In some family members additional findings included slight clumsiness of the hands, rarely a tendency to atrophy of the palm muscles, disappearance of the cutaneous reflexes and a certain weakness of the sphincters

(involuntary micturition at night and occasionally when laughing). With respect to the differential diagnosis Roussy & Lévy admitted that 'one could indeed suppose that the symptomatology of our patients constitutes an intermediary form of transition ... From that perspective ... Friedreich's disease on one hand and Charcot-Marie's amyotrophy on the other' could be mentioned. However, although pathological-anatomical examination was lacking, at the time they did not doubt to have isolated an individual clinical form. They concluded the paper by writing that even if, in future, the disease would appear to be an aberrant form of a previously classified familial disease, their observation would still be a valuable area of research with respect the evolution and varieties of familial diseases.

Subsequent papers on Roussy-Lévy syndrome and current view

Roussy and Lévy's paper was soon followed by a report from the National Hospital in London by Charles Symonds, who had just returned from a few years' stay in Baltimore and Boston, and his colleague Shaw. They described 'familial claw-foot with absent tendon reflexes' in the same year.³¹ They considered it a 'forme fruste' of Charcot-Marie-Tooth disease. A third pair of authors, Charles R. Rombold and Henry Alsop Riley called it the 'abortive type of Friedreich's disease.'³² Their paper, read in November 1925 at the New York Neurological Society, is of interest. As is clear from the title, they considered the disease an abortive form of Friedreich's disease and described a family with eight patients in three generations suffering from clubfoot, gait disturbance and areflexia of the lower extremities. One of the patients also had Babinski signs. Scoliosis and Romberg's sign were lacking in all patients.

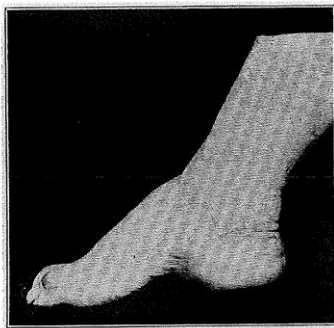


Fig. 2.—The foot of the mother of the entire family, illustrating a typical rigid type of pes cavus with a tendency to the formation of claw-toes.



Fig. 3.—The pes cavus modified by the subastragalar arthrodesis.

Fig. 11. From Rombold's and Riley's 1926 paper

Following the presentation of the eight cases, a discussion evolved between Riley, Bernard Sachs, Smith Ely Jelliffe and Joshua Rosett. In comparison to Friedreich's, the symptomatology as well as the course of the disease were relatively benign. Riley summarized and concluded the discussion as written in the following quotation:

DR. RILEY: I have nothing further to say except that, as Dr. Sachs has pointed out, there are complete transitional forms between all related types of disease, but this does not seem to me to fall exactly into the category of a transitional form. Friedreich's ataxia, as a rule, begins in early adolescence and progresses almost inevitably to a fatal termination as the result of some sort of intercurrent disease after the primary condition has existed for a considerable length of time. This syndrome which we have presented tonight is a Friedreich fragment. It appears as does the typical Friedreich's disease, but comes to a spontaneous cessation after the development of a few symptoms and physical signs; on account of this fact and the paucity of published records, it was considered justifiable to present this family.

Fig. 12. Conclusion from Rombold's and Riley's 1926 paper

In 1934 Roussy and Lévy wrote a new paper on the subject.³³ They again discuss the comparison with Friedreich's disease and Charcot-Marie's amyotrophy: 'Il est indiscutable que la "dystasie aréflexie héréditaire" présente des caractères qui la rapprochent, d'une part à la maladie de Friedreich, d'autre part de l'amyotrophie Charcot-Marie' [It is irrefutable that 'hereditary areflexic dystasia' presents with

characteristics that links it, at one side to Friedreich's disease, on the other side to the amyotrophy of Charcot-Marie]. Roussy, in his *In Memoriam* wrote: 'And it was during the correction of the proofs of a new paper on "Dystasie aréflexique héréditaire" before being published in *Revue Neurologique*, at which she was working, that she was stricken by death in a few hours'.¹ Lapresle reported a follow-up on four of the original seven patients in 1956.³⁴

Today we know the disease may be caused by a heterozygous mutation in the peripheral myelin protein-22 gene (PMP-22 the same gene, in which disorders are found in CMT1A/HMSN-1a and HNPP) or the myelin protein zero gene (MPZ; the same gene is involved in CMT1B). In 1999, a mutation was found in the MPZ-gene of the original family described by Roussy and Lévy.³⁵ The disease usually begins in childhood or infancy with walking problems, clumsiness as well as frequent falls. There are similarities with HMSN-1a (CMT1A) with respect to the *pes cavus*, atrophy and paresis of the limb muscles, areflexia and minor distal sensory loss. It is also a dominant heritable disease. It may be distinguished from HMSN-1a by its postural upper limb tremor and gait ataxia. Electrophysiologically it is characterized by slow nerve conduction. Pathologically by demyelination of nerve fibers with onion bulb formations in nerve biopsy. All patients of the original family described by Roussy and Lévy were able to walk during their seventh decade of life.

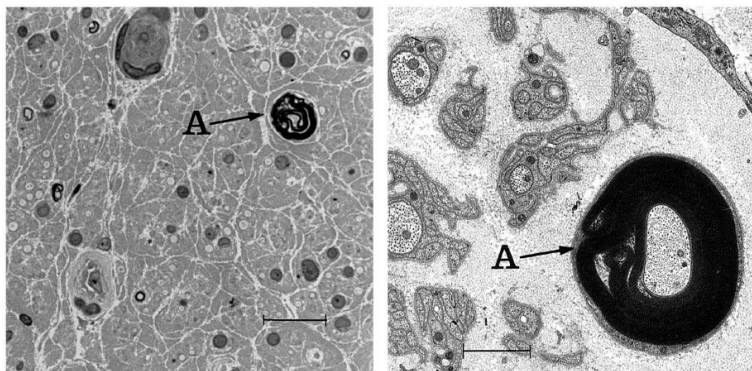


Fig. 13. Sural nerve biopsy of Berthe Pli... as published in 1999 (reduction of density of myelinated fibers; thickened and folded myelin sheath around surviving large fibers).³⁵

Molecular genetic testing identified a previously unknown heterozygous missense point mutation, which yielded an Asn131Lys substitution in the extracellular domain of the myelin protein zero (MPZ). They confirmed, as suggested previously by Yudell, Dyck and Lambert in 1964 and 1965,³⁶ that the Roussy-Lévy family belongs to the CMT1B subtype and has original morphological and genetic features.³⁵ In 1974 PK Thomas, with Calne & Stewart described the overlap between Roussy-Lévy syndrome with CMT1 and Dejerine-Sottas syndrome.³⁷

Other publications by Gabrielle Lévy

Next to the (at least) 14 papers (and thesis) on EL and the papers on the Roussy-Lévy syndrome, Lévy and her colleagues published on several other subjects, discussed in this paragraph. In his *In memoriam* Gustave Roussy mentioned the following areas in which Lévy published.¹

Table 1. Subjects on which Lévy published papers and monographs

With Pierre Marie:

Involuntary movements
 Rhythmic movements
 Extra-pyramidal or cerebellar disorders
 Palilalia

With Antoine Bécèle:

Monograph on the radiology of the nervous system

With Jean Lhermitte:

Phenomena of peduncular hallucinosis and nystagmus of the palate

With Roussy, during the last 10 years:

A series of clinical and anatomical observations on certain rare hereditary diseases

Spasmodic states

Forms of verbal automatism

Peduncular and pontine syndromes

The papers described above and those that follow in this paragraph comprise her bibliography as it was found in several sources, including the bibliography of Gustave Roussy and all papers (and references to papers) by Lévy in the French journal *Revue Neurologique*.

War neurology

In October 1914, the Salpêtrière was transformed into a military neurological center. Following the death of Joseph-Jules Dejerine in February 1917, Pierre Marie became head of the department, but was already guiding several pupils in writing papers and books on war injuries, including Chiriachitza Athanassio-Bénisty (1885–1938), who wrote several books on peripheral nerve injuries. In the preface of one of these Marie wrote: 'La guerre aura été pour nous tous une source inépuisable d'enseignements dans les directions les plus variées. En particuliers les Neurologistes doivent reconnaître qu'ils ont appris bien des choses, dans un domaine ou ils avaient tant à apprendre, celui de la Neurologie de Guerre'.^{38,p.1} [The war will have been an inexhaustible source of teaching material into directions most variable for all of us. Neurologists, in particular, must recognize that they have learned many things in an area where they had much to learn, i.e. the area of the neurology of war].³⁹

At the beginning of her career, Lévy wrote a number of papers on war injuries or particular signs in admitted soldiers, whom she observed with Pierre Marie or with his *chef de clinique* Charles Chatelin.^{40,41,42,43,44}

Movement disorders including Palatal myoclonus

Movement disorders is a subject to which Lévy dedicated several papers next the movement disorders that were already mentioned above with respect to EL. One year prior to her work on the eponymous syndrome, she published a paper on rhythmic myoclonus of the palate muscles (or palatal nystagmus).⁴⁵ It was a case presented before the Société de Neurologie in April 1925, of a 72-year old mrs. Joséphine Pr..., who had been admitted two years previously at the ward for senile persons of the Paul Brousse hospital. She had myoclonus not only of the palate, but also of the left eye and diaphragm. Furthermore, she found cerebellar and pyramidal signs. She referred to the work by Foix & Hillemand and by Tinel & Foix. In Lévy's patients, the disorder was supposed to originate from a vascular lesion, given the fact that it began following one or two ictal phenomena. The subject of palatal nystagmus was described in several other or Lévy's papers.^{46,47,48,49} A few years after her first paper, George Guillain and Pierre Mollaret would further describe the syndrome and localize it to a disturbance in the so-called Guillain-Mollaret triangle comprising the dentate nucleus, red nucleus and inferior olivary nucleus.⁵⁰ The history of the syndrome was recently reviewed by John Pearce.⁵¹ Lévy, with her colleagues, published several other papers on athetosis and choreic movement disorders.^{52,53,54,55,56,57,58}

Lhermitte sign

In 1927, Lévy was second author in a paper, in which Jean Lhermitte described his eponymous symptom in multiple sclerosis (MS)-patients.⁵⁹ Lhermitte described his sign in a patient suffering from MS in 1924.⁶⁰ One of the patients gave the following description:

Lorsque je baissais la tête, je ressentais une secousse violente dans la nuque et une douleur ressemblant à celle que produit un courant électrique me parcourait tout le corps, depuis la nuque jusqu'aux pieds, en suivant la colonne vertébrale. [When I bent the head, I felt a violent shock in the neck and a pain like an electric current running through the whole body, from the neck down the vertebral column into the feet].

Lhermitte was not the first physician to write on the subject. The first description originates from Pierre Marie and Charles Chatelin in 1917, who described it in patients with head injury. The occurrence of the sign does not depend on the position of the body. It may be experienced by active as well as by passive flexion of the neck.⁶¹ Joseph Babinski and R. Dubois (1918) reported the phenomenon in patients following neck injury.⁶² However, Bereil and Devic (1918) were the first to mention the phenomenon in MS.⁶³ Supervised by Babinski and Lhermitte, Jean Ribeton published his thesis (1919) on the symptom resulting from neck injury in 13 patients.⁶⁴ However, not until Lhermitte's 1924 paper did the phenomenon become recognized as an important manifestation of MS.⁶⁰ Today, the association with MS still exists - it may be one of the early symptoms - but Lhermitte's sign may occur in a number of other diseases of the cervical spinal cord.⁶⁵

In their 1927 paper three patients were described including the one from 1924. It begins with the question: 'A new symptom of multiple sclerosis! Is it necessary to enrich it with more symptomatology?' They conclude the paper that it may be a useful early symptom, when objective signs are still lacking.

Neuro-oncology

Following the discovery of X-rays by Wilhelm Conrad Röntgen in 1895 and the discovery of natural radioactivity in the first decade of the 20th century by Marie Curie-Sklodowska, under whose direction the first studies with the use of radioactive isotopes were done for cancer, radiation therapy for cancer became a common treatment. After World War I, it became possible to measure the dosage absorbed by the skin.

Becoming associated physician at the Paul-Brousse hospital (1925), where Roussy opened the first French oncologic consultation center for out-patients in 1919, it is of no surprise that Lévy wrote a number of reviews on neuro-oncology. The first paper was co-authored by Roussy and Simone Laborde. Roussy had called Laborde, who became head of the 'curietherapy' laboratory of his cancer center.^{††} Simone Laborde was already interested in medical use of radium before World War I. Following the observation of 5 cases of cerebral glioma, they wrote on radiotherapy of cerebral tumors. The paper was introduced by the words 'Since two years and a half, we have undertaken the treatment by radiotherapy of a certain number of tumors of the nervous system, in the anticancer center of Villejuif'. Patients were referred by Pierre Marie and Henri Bouttier. The paper is accompanied by figures of the pathology.



Fig. 6. — Gliome astrocytaire de la région rolandique. Fragment prélevé par biopsie au cours de l'opération (Obs. 5).

Fig. 14. (transl.) Astrocytic glioma of the rolandic region. Fragment taken by biopsy during surgery (observation 5).

^{††} Her husband Albert Laborde had been a collaborator of Pierre and Marie Curie.

Fibrous tumors were supposed to be radioresistant (often well circumscribed and susceptible to surgery), but tumors of the neuroglia (glioma; often not well circumscribed) were believed to be very radiosensitive (p.142).⁶⁶ The second paper on the subject was written by Lévy as sole author, acknowledging Antoine Bécclère, the French pioneer in radiology (with whom she wrote a chapter in a German radiotherapy book⁶⁷) and Gustave Roussy, her colleague at Paul-Brousse. She described radiotherapy as well as radiodiagnostics of brain tumors, referring to many foreign sources, including German and American papers (for example those by Heuer & Dandy⁶⁸ and Sosman & Putnam⁶⁹).⁷⁰ A year later she and Roussy published a paper on radiotherapy of tumors of the pituitary region.⁷¹ Von Recklinghausen's disease / neurofibromatosis was subject of two subsequent papers.^{72,73}

Higher cortical functions

Several papers from Lévy's bibliography deal with what I will categorize as higher cortical functions. These include a paper with Pierre Marie and Gustave Roussy on palilalia, a speech disorder with involuntary repetition of syllables or words. It had been described previously with the term auto-echolalia.^{74,75} Others were on spatial representation in apraxic patients,⁷⁶ cortical sensory disorders,⁷⁷ pseudobulbar speech (in fact not a cortical speech disorder),⁷⁸ several papers on peduncular hallucinosis, including an anatomopathological description.^{§§,79,80,81}

Miscellaneous papers

Next to the subjects described above, Lévy published a number of papers on various subjects, including particular cases of peripheral facial nerve paralysis,⁸² diabetes insipidus following cranial injury,⁸³ and a few other subjects.^{84,85,86,87} Furthermore, Gabrielle Lévy's family has preserved a large number of reprints, many of which are listed among the references, but some are not. I have listed the titles in the appendix. Some are similar to those mentioned the reference list, but published in other journals.

Authorship

Looking at Lévy's bibliography, it is remarkable that she was usually second author. She was only first author in, of course, her thesis (and the subsequent public publication),^{21,22} some of the neuro-oncologic papers,^{70,72,73} and a few miscellaneous papers.^{45,78,82} This may be interpreted by the assumption that she often took care of the pathologic anatomy of the presented patient material, the clinician being first author. Moreover, as appears from her biographical review, she was assistant at the pathology department of the Salpêtrière from 1923 up to 1926 and associated physician at the Paul-Brousse hospital in 1925, perhaps not deserving to be mentioned as first author. Another possibility would be that the male colleague or her superior at the ward was usually the first author. On the other hand, in his *in memoriam*, Roussy admitted, as written above, that in their collaboration, 'in which my name was often mentioned with hers, it was almost always her first idea and the largest part was done by her'. Or was it just by politeness that he had written it?

Disease and early death

A final question to be discussed is by what disease she died? It was already mentioned above that in her family, it was repeatedly said that she died from the disease that she was studying. Was this EL? The EL epidemic disappeared in 1927, although rare cases have been published since then. Or was it from a post-encephalitic syndrome? But there is no indication, at least not from her work that she suffered from a brain disease. On the other hand Roussy wrote about an unexpected death that ended 'a mind that remained intact and lucid, always ready to serve a refined intelligence and a vivid curiosity, while *little by little the disease gradually undermined, in the course of the years*, the creature who instinctively searched to fight against that what weakened her...' (italics by present author). From this we may conclude that although she died suddenly, the disease was chronic and that it was a disease that she had been studying. That probably leaves two possibilities, either a post-encephalitic syndrome or a brain tumor. A remark by Roussy, may indicate the first, perhaps more than the second disease. ' Since her monograph on *Manifestations tardives de l'encéphalite épidémique* that became her inaugural thesis (1922), she

§§ A release phenomenon characterized by vivid, visual images with all the qualities of true sensorial perception. These patients are able to identify the hallucinatory character, unlike in the case of true visual hallucinations.

became an authority on that subject, as well in as in various problems of the physio-pathology of the nervous system that she broached'.¹

In her obituaries it was opined that 'she leaves a name in neurology that she owes to her efforts, to her perseverance and let us say without risk of exaggeration to the passion she had for neuropathology'¹ and that by 'her qualities of intense application and of intelligence brought her to an international position as a neurologist of note, to be ranged with Mme. Dejerine and Mme. Cecile Vogt'.³

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Appendix. Titles of papers (1923-1933), not mentioned in the reference list, of which reprints are preserved by Lévy's family

- Lévy G. Le syndrome excito-moteur tardif de l'encéphalite épidémique. Le Journal Médical français 1923;12: (no. 4, April).
- Marie P, Lévy G. La forme respiratoire de l'encéphalite épidémique. Le Monde Médical de Médecine et de Thérapeutique. 1923 (no.634, November 1st).
- Lévy G, Van Bogaert ML. Recherches sur le rythme respiratoire dans certaines maladies du système nerveux, en particulier chez les pseudo-bulbaires (avec six figures dans le texte). Journal de Neurologie et de Psychiatrie. 1924 (no.5).
- Lévy G. Le traitement des lésions, en particulier des tumeurs, de la région infundibulo-hypophysaire. - Annales de Médecine 1925;18: (no.6, December, 1925).
- Roussy G, Lévy G. Le diabète insipide d'origine traumatique. Annales de Médecine 1925;17: (no.5, may).
- Roussy G, Lévy G. Les troubles d'aspects cérébelleux par lésion corticale. - Collection of papers offered to Edward Flatau, Warsaw, 1929.
- Lévy G. Les formes conscientes de l'automatisme verbal et leurs analogies avec certaines manifestations de l'automatisme comitial (palilalie, écholalie, échopalilalie aphone). La Presse Médicale 1931 (no.73; 12 September).
- Lévy G. Le syndrome parkinsonien de l'encéphalite épidémique. L'Expansion Scientifique Française.
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- Roussy G, Lévy G. Un curieux cas d'aphasie par encéphalopathie de l'enfance (étude comparative de trois observations d'encéphalopathie de l'enfance). Jubilee volume for Marinesco, 1933.

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