History of Neurology

Samuel Alexander Kinnier Wilson. Wilson’s disease, Queen Square and neurology

Samuel Alexander Kinnier Wilson. La maladie de Wilson, Queen Square et la neurologie

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Abstract

This historical article describes the life and work of the British physician Samuel Alexander Kinnier Wilson (1878–1937), who was one of the world’s greatest neurologists of the first half of the 20th century. Early in his career, Wilson spent one year in Paris in 1903 where he learned from Pierre-Marie at Bicêtre Hospital. He subsequently retained uninterrupted links with French neurology. He also visited in Leipzig the German anatomist Paul Flechsig. In 1904, Wilson returned to London, where he worked for the rest of his life at the National Hospital for the Paralysed and Epileptic (later the National Hospital for Nervous Diseases, and today the National Hospital for Neurology and Neurosurgery) in Queen Square, and also at Kings’ College Hospital. He wrote on ‘the old motor system and the new’, on disorders of motility and muscle tone, on the epilepsies, on aphasia, apraxia, tics, and pathologic laughing and crying, and most importantly on Wilson’s disease. The other objective of our paper is to commemorate the centenary of Wilson’s most important work published in 1912 in Brain, and also in Revue Neurologique, on an illness newly recognized and characterized by him entitled “Progressive lenticular degeneration, a familial nervous disease associated with liver cirrhosis”. He analyzed 12 clinical cases, four of whom he followed himself, but also four cases previously published by others and a further two that he considered in retrospect had the same disease as he was describing. The pathological profile combined necrotic damage in the lenticular nuclei of the brain and hepatic cirrhosis. This major original work is summarized and discussed in the present paper. Wilson not only...
Maladie de Wilson
Mouvements anormaux
Dégénérescence hépatolenticulaire
delineated what was later called hepato-lenticular degeneration and Wilson’s disease, but also introduced for the first time the terms extrapyramidal syndrome and extrapyramidal system, stressing the role of the basal ganglia in motility. The present historical work emphasizes the special contributions made by Wilson to the study of movement disorders, including akinnesia and bradykinesia in Parkinson’s disease, and their relation to basal ganglia pathology.

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RÉSUMÉ

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1. Introduction

Wilson’s disease is a rare inherited metabolic illness due to copper accumulation which damages the liver and the brain, particularly the basal ganglia, and is eminently treatable by copper elimination using chelators, but fatal if left undiagnosed and untreated. It took a long time to delineate this disease and to develop modern diagnosis and therapies. This historical article describes the life and work of Dr. Samuel Alexander Kinnier Wilson, who identified this disease. Wilson was one of the world’s greatest neurologists of the first half of the 20th century. He worked at the National Hospital for the Paralysed and Epileptic (later the National Hospital for Nervous Diseases, and today the National Hospital for Neurology and Neurosurgery) in Queen Square, and later also at Kings’ College Hospital, in London, United Kingdom. Another objective is to commemorate the centenary of his most important work published in Brain in 1912 on progressive lenticular degeneration, an illness newly recognized and characterized by him (although in retrospect, other cases of the same disease had previously been described under different labels), and later named Wilson’s disease. Finally, we emphasize the special contributions made by Wilson to the study of Parkinson’s disease and other movement disorders, and their relation to basal ganglia pathology.

2. Samuel Alexander Kinnier Wilson, the neurologist

Samuel Alexander Kinnier Wilson (1878–1937) (Fig. 1) was born in New Jersey, USA, from an Irish-Scottish family. Due to the early death of his father, he went to Scotland as a youth where he was brought up and educated (Ashworth and Jellinek, 2001; Critchley, 1937, 1938; Gordon, 1937; Haymaker, 1953; Hoogenraad, 2001; Kennedy, 1937; Westerman, 1993; Wilson, 1938). After qualifying in medicine in Edinburgh in 1902, Wilson worked at the Royal Edinburgh Infirmary under Sir Byron Bramwell (1847–1931) who inspired him to study neurology. In 1903, he went to Paris and worked under Pierre-Marie (1853–1940) at Bicêtre Hospital (Ashworth and Jellinek, 2001; Critchley, 1938; Haymaker, 1953; Hoogenraad, 2001; Kennedy, 1937; Westerman, 1993). His one year stay in Paris was for Wilson a great opportunity to meet other French neurologists who became lifelong colleagues and friends. These included among others Joseph Babinski (1857–1932), Louis Eduard Octave Crouzon (1874–1938), Jean Lhermitte (1877–1959), Achille Alexandre Souques (1860–1944), Charles Foix (1882–1927), Henry Meige (1866–1940) and particularly Georges Guillaume (1876–1961), who had a remarkable academic career in Paris at the same time as Wilson did in London (Critchley, 1988). Wilson published several papers in French
Fig. 1 – Photograph of Dr. Kinnier Wilson taken by Dr. Foster Kennedy.

Fig. 2 – Recommendation letter from Pr. Pierre-Marie in 1904 when Kinnier Wilson returned to London and made an application as house physician in Queen Square. (Image courtesy of the Queen Square Library, archive and museum. Copyright National Hospital for Neurology & Neurosurgery).

neurological journals in 1904 (Crouzon and Wilson, 1904; Léri and Wilson, 1904a, 1904b; Wilson, 1904a, 1904b) and also later in the 1910s and 1920s. His fellowship in Paris had a great influence in his subsequent career during which he had uninterrupted links with French neurology. Wilson also visited in Leipzig the German anatomist Paul Flechsig (1847–1929).

In 1904, Wilson returned to the United Kingdom with a warm letter of recommendation from Pierre-Marie (Fig. 2). He began his work in London at the National Hospital, Queen Square, where he remained for all his life and became one of the most brilliant and renowned specialists in neurology in the world (Ashworth and Jellinek, 2001; Critchley, 1988; Haymaker, 1953; Hoogenraad, 2001; Kennedy, 1937; Westermak, 1993). In his early career as house physician (1904–8), and registrar (1908–12), he was fortunate to learn from Hughlings Jackson (1835–1911) who had retired but still attended the hospital from time to time and asked residents to show him patients of special interest (Purdon Martin, 1975). Jackson inspired Wilson and was a physician he constantly admired (Critchley, 1988; Reynolds, 2005). One of Wilson’s young colleagues at that time and later close friend was the American neurologist Foster Kennedy (1884–1952) who was a fellow resident at Queen Square before returning to New York City (Critchley, 1988; Kennedy, 1937; Wilson, 1988). Prior to 1918, British neurologists were still general physicians who took a particular interest in diseases of the nervous system, but after the first World War, specialized posts were established, with Wilson being appointed lecturer in Neurology at King’s College Hospital, thus becoming the first ‘pure neurologist’ in the United Kingdom (Ashworth and Jellinek, 2001; Critchley, 1988; Hoogenraad, 2001; Munk’s Roll, 1955). During the 1920s and 1930s, he was, with Gordon Holmes (1876–1965), one of the leading figures in Queen Square (Ashworth and Jellinek, 2001; Critchley, 1988; Hoogenraad, 2001). Wilson had an encyclopedic knowledge, and was fluent in French and German, thus covering not only the English but also the French and the German neurological literature. He published extensively. His thesis and paper on progressive lenticular degeneration were in fact early contributions, published when he was only a registrar, and made him famous as a young physician a long time before his appointment as a full physician at Queen Square in 1925 and senior neurologist at King’s College Hospital in 1928. He wrote on ‘the old motor system and the new’ (see below the comments on the extrapyramidal system) (Wilson, 1924), on disorders of mobility and motor tone, on the epilepsies, on aphasia, apraxia, tics, and pathologic laughing and crying (Critchley, 1988; Haymaker, 1953). Wilson was the founder, in 1920, and editor-in-chief of a new journal called Journal of Neurology and Psychopathology (Wilson, 1920). The journal was later named Journal of Neurology and Psychiatry in 1938, then Journal of Neurology, Neurosurgery and Psychiatry in 1944. His unfinished 2-volume textbook Neurology was published in 1940, three years after his death (Wilson, 1940), and edited by Dr Alexander Ninian Bruce, an Edinburgh neurologist who was also Wilson’s brother-in-law. This was one of the greatest works ever written for the discipline of neurology after the classical handbook of the German physician Hermann Oppenheim (1858–1919) (first edition in 1884, seventh and last edition after his death in 1923).
(Oppenheim, 1884; Critchley, 1988; Haymaker, 1953), earlier of the British pioneer in neurology, Sir William Richard Gowers (1845–1915) (Gowers, 1886–1888) and in French medical literature, the two important reference books published in the 1910s by Pierre-Marie and by Jules Dejerine (1849–1917) (Dejerine, 1914; Marie et al., 1911).

3. The description of Wilson’s disease

The present historical article is an opportunity to celebrate the centenary of the description by Wilson in 1912 of the disease that was later named after him “Wilson’s disease” (Wilson, 1912a). His major breakthroughs in the elucidation of progressive lenticular degeneration are summarised and commented upon below.

As recently quoted in a historical note in Brain (Compston, 2009), the definition by Wilson of this new disease in his 1912 Brain article (Fig. 3) was as follows: “Progressive lenticular degeneration may be defined as a disease which occurs in young people, which is often familial but not congenital or hereditary; it is essentially and chiefly a disease of the extrapyramidal motor system, and is characterized by involuntary movements, usually of the nature of tremor, dysarthria, dysphagia, muscular weakness, spasticity, and contractures with progressive emaciation; with these may be associated emotionalism and certain symptoms of a mental nature. It is progressive, and, after a longer or shorter period, fatal. Pathologically it is characterized predominantly by bilateral degeneration of the lenticular nucleus, and in addition cirrhosis of the liver is constantly found, the latter morbid condition rarely, if ever, giving rise to symptoms during the life of the patient.”

This major publication was preceded by Wilson’s thesis, submitted for the degree of MD at the University of Edinburgh in July 1911, for which a gold medal was awarded. He wrote, in 215 printed pages, the longest paper ever published in Brain. He encountered four cases (two of whom were siblings), making the diagnosis at post-mortem in three, and in life in the last case who was still alive when his Brain paper was written; he acknowledged that the literature already contained six previous reports of this disease published under varying labels (Gowers, 1906; Ormerod, 1890; Homén, 1890, 1892), and added two other previously unpublished cases. All these 12 observations are presented in Table 1. H1 to H6 are the earlier published historical cases that Wilson considered in retrospect had the same disease as he was describing.

Table 1 – Main clinical features of the 12 patients with progressive lenticular degeneration reported in Wilson’s 1912 Brain article. These include his personal cases and also previously published cases and unpublished observations from other authors. For the purposes of this review, cases are numbered in a different manner to that in the paper.

<table>
<thead>
<tr>
<th>Case</th>
<th>Name/Sex</th>
<th>Age at onset (years)</th>
<th>Survival (mo or yrs)</th>
<th>Brain pathology</th>
<th>Liver pathology</th>
<th>Consultant &amp; years of onset &amp; death</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1</td>
<td>Sydney Moor /M</td>
<td>10</td>
<td>5.5 mo</td>
<td>“normal” (macro only)</td>
<td>cirrhosis</td>
<td>W. Gowers 1886–1886</td>
</tr>
<tr>
<td>H2</td>
<td>Charlotte Moor /F</td>
<td>15</td>
<td>14 mo</td>
<td>“normal”</td>
<td>cirrhosis</td>
<td>W. Gowers 1887 /8</td>
</tr>
<tr>
<td>W5</td>
<td>Samuel Moor /M</td>
<td>10</td>
<td>4.5 yrs</td>
<td>no p/m</td>
<td>no p/m</td>
<td>W. Gowers 1874 –9</td>
</tr>
<tr>
<td>H3</td>
<td>Walter William S/M</td>
<td>10</td>
<td>7–8 mo</td>
<td>lentiform</td>
<td>cirrhosis</td>
<td>J.A. Ormerod 1889–90</td>
</tr>
<tr>
<td>H4</td>
<td>Alfred K’/M</td>
<td>20</td>
<td>3 1/2 yrs</td>
<td>lentiform</td>
<td>cirrhosis</td>
<td>E.A. Homén 1886–90</td>
</tr>
<tr>
<td>H5</td>
<td>Wilhelm K’/M</td>
<td>12</td>
<td>7 yrs</td>
<td>lentiform</td>
<td>cirrhosis</td>
<td>E.A. Homén 1882–9</td>
</tr>
<tr>
<td>H6</td>
<td>Anna K’/F</td>
<td>20</td>
<td>6 yrs</td>
<td>lentiform</td>
<td>cirrhosis</td>
<td>E.A. Homén 1882–8</td>
</tr>
<tr>
<td>W1</td>
<td>Sylvia Tylor /F</td>
<td>25</td>
<td>4 yrs &amp; 2 mo</td>
<td>lentiform</td>
<td>cirrhosis</td>
<td>D. Ferrier 1904–8</td>
</tr>
<tr>
<td>W2</td>
<td>DP’/F</td>
<td>17</td>
<td>2 yrs &amp; 8 mo</td>
<td>lentiform</td>
<td>cirrhosis</td>
<td>D. Ferrier 1904–7</td>
</tr>
<tr>
<td>W3</td>
<td>EP’/M</td>
<td>19</td>
<td>3 yrs</td>
<td>lentiform</td>
<td>cirrhosis</td>
<td>D. Ferrier 1907–10</td>
</tr>
<tr>
<td>W4</td>
<td>Charlotte Tolputt /F</td>
<td>18</td>
<td>still living; 22 mo</td>
<td>still living</td>
<td>still living</td>
<td>H. Tooth 1910–</td>
</tr>
<tr>
<td>W6</td>
<td>Christopher Johnson /M</td>
<td>11</td>
<td>2yrs</td>
<td>no p/m</td>
<td>no p/m ascites &amp; oedema</td>
<td>J.A. Ormerod 1887–9</td>
</tr>
</tbody>
</table>

mo: months; yrs: years; no/pm: no post-mortem examination; lentiform: lentiform nuclei lesions; H4: Homén’s case 2; H5: his case 3; H6: his case 1.

a Still living in 1911 with 18 months of follow-up; transient jaundice aged 21.
b Psychotic troubles onset when aged 17.
c Jaundice onset when aged 13.
d Sibs.
e Sibs.
f Sibs.
The four personal cases looked after in life by Wilson are numbered W1–W4; the first three died before the paper was submitted, and Wilson conducted the autopsy in all three. He had travelled from London to the sanatorium at Chebres, near Lausanne, Switzerland, to do a follow-up visit on WP (W3) in June 1910, and did the autopsy in September 1910, 27 hours after death. “As the body had been kept in the open air, the sanatorium being at a considerable altitude and the nights very cold, it was in an excellent state of preservation”.

W5 and W6 (W5 being the third affected sibling of the Moor family containing H1 and H2) are two further cases, hitherto unpublished, from the late 19th Century who Wilson did not see, but again considered had “his” disease. In his 1940 textbook, Wilson noted that since his original 1912 publication, he had personally seen nine more (making a total of 13), of which only five had been briefly recorded (Wilson, 1940).

Survival from neurological onset in the 11 deceased cases ranged from five and a half months to seven years (mean 38 months), and age at onset in the 12 cases ranged from 10 to 25 (mean 15.6) years.

Among the 12 cases in the paper, 11 had died, nine of whom had autopsies, revealing cirrhosis in all 9, and reporting lentiform lesions in seven (the other two had macroscopic examination only). There were 3 sets of affected siblings accounting for 8 of the 12 cases, the remaining four having no similarly affected relatives. Perhaps the one important point whose significance was not fully grasped by Wilson was the genetic aspect. Thus in his paper he wrote: “The disease is familial, in the sense that frequently more than one member of a family is affected, but is not hereditary”. Although both dominant and recessive inheritance in peas and bees had been described in 1860 by Gregor Mendel (1822–1884), human genetics trailed long behind, the term genetics being coined for the first time by William Bateson (1861–1926) in 1906. Wilson may have simply been implying that there was no evidence of dominant inheritance. In 1916, Sir Byron Bramwell, the former Wilson’s teacher as recalled above, presented a familial series of cirrhosis of the liver in 4 sibs, with rapid fatal outcome and no apparent neurological signs. He suspected a relationship to cases of progressive lentiform degeneration and suggested a genetic origin for Wilson’s disease (Bramwell, 1916). Evidence for recessive inheritance of Wilson’s disease was later published in 1921 by Hall, who was also the first to apply the term hepato-lenticular degeneration (Boudin and Pépin, 1959; Hall, 1921), yet even in 1937, Wilson in his textbook (Wilson, 1940) wrote: “Paucity of information hardly justifies the statement . . . that the disease is inherited as a Mendelian recessive”. Yet “I was struck long ago by the curious fact that the families seem to be large”, which of course increased the chances of producing affected sibling pairs.

Although Wilson wrote in his 1912 paper that “This hepatic cirrhosis does not reveal itself by any symptoms during life, nevertheless it is always found after death”, this is often not the case, but one should recall that imaging and biochemical assessments of liver dysfunction were not available in 1912. Moreover, Wilson himself recorded jaundice preceding the neurological presentation by 4 and 5 years in his own cases W1 and W2. His case W3 presented with psychiatric disturbance two years before neurological onset.

Wilson did not mention the Kayser-Fleischer ring in his 1912 Brain paper. In his 1940 textbook he wrote: “The ring was first described by Kayser (Kayser, 1902) in a case diagnosed as multiple sclerosis, and to Fleischer (Fleischer, 1903, 1912) is due the credit of realising its significance in relation to his “Hitherto unknown disease with nervous symptoms and cirrhosis”. In 1933, Wilson wrote: “I have seen the ring only three times”, and in the same abstract Paton was quoted as saying “Probably most (Royal Society of Medicine Ophthalmic Section members) have heard of it, but few have seen it” (Wilson, 1934).

4. Discussion

4.1. Wilson’s disease

Wilson’s 1912 articles on progressive lenticular degeneration deserve several additional commentaries.

First, even though the extensive description of Wilson’s disease was printed in Brain in its March 1912 issue, additional short versions were published the same year in two other journals. One was printed in The Lancet in its April 27th issue (Wilson, 1912b). The other one was an earlier report in the February 1912 issue of Revue Neurologique (Wilson, 1912c): Fig. 4. Indeed, thanks to his close links with French neurology, Wilson orally presented his work in French on 25th January 1912 at the Paris Neurological Society, with the following title: “Dégénération lenticulaire progressive. Maladie nerveuse familiale associée à la cirrhose du foie”, i.e. in English “Progressive lenticular degeneration, a familial nervous disease associated with liver cirrhosis”. The 1912 Revue Neurologique Wilson article is presented in its entirety in the present issue of the journal. Wilson’s description of “his disease” was rapidly recognized in the international neurological circles due to its publication not only in English and French journals but also in German neurological books (Wilson, 1914). Later, in 1921, Pierre-Marie invited twenty prestigious scientists in Paris to give a lecture at the Faculty of Medicine (Marie, 1922). Wilson was one of them and his talk in French was entitled: “Sur quelques questions de pathogénie, de diagnostic, et de physiologie pathologique, à propos de la dégénérescence lenticulaire progressive” (i.e. in English: “On some pathogenic, diagnostic and patho-physiological issues related to progressive lenticular degeneration”). He stated that the degeneration cannot exist without liver cirrhosis and evokes a toxic origin, possibly manganese.

Second, there were other recorded cases considered at the time and later to be possible earlier examples of the same disease (Boudin and Pépin, 1959). Thus, in 1883, Carl Westphal (1833–1890) had described two cases of what he called “pseudosclerosis”, but brain pathology was normal and there was no cirrhosis (Westphal, 1883). Adolf Strümpell (1853–1925) in 1898–9 had described three further cases of “pseudosclerosis”, but at autopsy the lentiform nucleus was normal in all three (Strümpell, 1898, 1899); one had cirrhosis (so possibly Wilson’s disease) but also syphilis, and neither of the other two had cirrhosis. There is also an important two-page addendum to Wilson’s Brain paper, in which he acknowledges that “Within a few days of the publication of
La maladie dont j’ai l’honneur de communiquer à la Société de Neurologie la très courte description, n’est pas précisément nouvelle, puisque les deux premiers cas (concernant la frêre et la sœur) ont été décrits par S. William Gowers, en 1888, sous le titre de “Chorée téniaide”. Deux ans plus tard, Ormerod, en Angleterre, a décrit un troisième cas, et, presque en même temps, Homén, de Helsingfors, a rapporté l’histoire de trois personnes de la même famille (deux frères et une soeur) qui sont mortes de cette affection nerveuse. Mais depuis ce temps-là, c’est-à-dire depuis plus de vingt ans, aucun cas n’en a été publié, à ma connaissance. On peut donc dire, sans crainte d’exagération, que la maladie est restée pour ainsi dire inconnue. Au cours de ces cinq dernières années, j’ai eu l’occasion d’en observer quatre cas, dont trois avec autopsie, et deux familles ; du fait que j’ai pu pratiquer les examens avec les méthodes cliniques et pathologiques modernes, notre connaissance de cette remarquable affection se trouve avoir été largement augmentée.

La “dégénération lenticulaire progressive” est une affection nerveuse très souvent familiale, mais jamais héréditaire ; les sujets sont toujours des jeunes gens dont l’âge varie de 10 à 25 ans. Au point de vue du développement physique et psychique, les enfants sont normaux. Vers l’adolescence eu vers la puberté apparaissent les symptômes, d’une façon ordinairement lente et graduelle, bien que l’affection soit quelquefois aiguë. Les symptômes sont exclusivement nerveux. Ils affectent le système moteur, et surtout les voies motrices extrapyramidales. Les principaux sont les suivants :

**MÉMOIRES ORIGINAUX**

1

DÉGÉNÉRATION LENTICULAIRE PROGRESSIVE
MALADIE NERVEUSE FAMILIALE ASSOCIÉE À LA CIRRHOSIS DU FOIE

(Société de Neurologie de Paris.)

Séance du 25 janvier 1912.

La maladie dont j’ai l’honneur de communiquer à la Société de Neurologie la très courte description, n’est pas précisément nouvelle, puisque les deux premiers cas (concernant la frêre et la sœur) ont été décrits par S. William Gowers, en 1888, sous le titre de “Chorée téniaide”. Deux ans plus tard, Ormerod, en Angleterre, a décrit un troisième cas, et, presque en même temps, Homén, de Helsingfors, a rapporté l’histoire de trois personnes de la même famille (deux frères et une soeur) qui sont mortes de cette affection nerveuse. Mais depuis ce temps-là, c’est-à-dire depuis plus de vingt ans, aucun cas n’en a été publié, à ma connaissance. On peut donc dire, sans crainte d’exagération, que la maladie est restée pour ainsi dire inconnue. Au cours de ces cinq dernières années, j’ai eu l’occasion d’en observer quatre cas, dont trois avec autopsie, et deux familles ; du fait que j’ai pu pratiquer les examens avec les méthodes cliniques et pathologiques modernes, notre connaissance de cette remarquable affection se trouve avoir été largement augmentée.

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**REVUE NEUROLOGIQUE**

this monograph, my attention was drawn to a paper by Völsch on Pseudosclerosis” (Völsch, 1911). At post-mortem, there was... cirrhosis of the liver. The brain was cut... but no abnormality was found. It will be clear to the reader that... notwithstanding the dearth of information, this case, I believe, comes under the category of those which I have described”.

Third, although our main objective in the present paper is to highlight Wilson’s 1912 publications on progressive lenticular degeneration, we will briefly recall the main steps by which the role of copper was elucidated in this illness (Walshe, 2006). As mentioned above, remarkable insight of Wilson was his proposal that progressive lenticular degeneration might be caused by a toxin elaborated in the liver, and with a specific action on the lenticular nucleus. This presaged the report by Rumpel in 1913 of excess copper in the liver in a patient dying from what looks like Wilson’s disease (Rumpel, 1913). However, this report was not immediately recognized at that time. Several decades later, the major role of copper was established in 1948 by the finding in Wilson’s disease patients of increased urinary copper by Mandelbrot et al., 1948 and of excess copper in the brain by Cumings at Queen Square in London (Cumings, 1948).

Fourth, one of the major neurological signs depicted in this illness is described by Wilson as spasms or contractures. Spasms, tics, tremor, chorea, rigidité and athetosis were the main clinical terms used to describe movement disorders in the early 20th century. The words dystonia, akinésia and bradykinésia at the time of Wilson’s 1912 Brain paper were not defined or recognized internationally among neurological circles. Indeed, the term dystonia was first introduced by Hermann Oppenheim only a year before Wilson’s Brain paper (and after his thesis) (Oppenheim, 1911). In parallel, as reviewed recently (Krack et al., 1999), the term akinésia was first quoted by German authors, namely Karl Wernicke (1848–1904) in psychiatric patients in 1900, then Karl Kleist (1870–1960) and others in the 1900s and 1910s as a lack of drive in patients with frontal lobe damage, whereas the use of akinésia to refer to delay in initiation of movement in Parkinson’s disease patients was proposed by Friedrich Lewy (1885–1950) in 1923. In France, René Cruchet (1875–1959), one of the pioneers in neurology in Bordeaux, first used the term bradykinésia in 1907 in reference to spasmodic torticollis, and later in 1921 in the context of cases of post-encephalitic parkinsonism characterized by poverty and slowness of movement (Cruchet, 1907; Cruchet, 1921). So the terms dystonia, akinésia and bradykinésia were not available to Wilson in 1912. Later though, in the first of Wilson’s five remarkable Cronian lectures to the Royal College of Physicians of London, published in The Lancet (Wilson, 1925), he discussed “The syndrome of the corpus striatum”, emphasizing that... the cardinal symptomatology may still be summed up in three words: variability in muscle tone (dystonia), the appearance of “involuntary” movements, and the seeming absence of “true paralysis”. Wilson used the terms akinésia and bradykinésia in the same Cronian lecture.

Thus, lacking suitable terms at the time of his 1912 Brain paper, Wilson wrote, under the heading “Spasticity” that “Every one of the series of cases has been characterized by the presence of rigidity or spasticity, which has often reached an extreme degree... in these cases we are dealing with a true hypertonicity of the muscles, involving both synergic and antergic muscles simultaneously”. It is clear that he did not consider this as spasticity in the sense of a pyramidal increase in tone. Indeed, under the heading “Muscular weakness” he was careful to state that one ought not to use the term paralysis: “Paralysis, where motion is concerned, ought to be confined to disease of the pyramidal system... There is no special term to describe this specific motor helplessness resultant on disease of the extrapyramidal motor system”. Wilson clearly considered that most of the spasms and hypertonicity in his patients could not be attributed to pyramidal signs, since there was no Babinski sign, and because anatomical post-mortem examination did not show any damage of the corticospinal tract, in contrast with the marked necrotic lesions found in the lenticular nuclei. To summarize, Wilson’s description and analysis of the motor...
disorder suggest a combination of dystonia, akinesia and extrapyramidal rigidity. Indeed, in order to emphasize his astute observations, Wilson introduced in 1912 for the first time in the literature the terms “extrapyramidal system” to refer to basal ganglia and “extrapyramidal signs” or “extrapyramidal syndrome” to discuss the symptoms and signs associated with basal ganglia pathology. These concepts were later formally expanded and expounded in his Croonian lectures (Wilson, 1925). This new terminology was subsequently largely used in the neurological literature during the 20th century (Kiernan, 2012).

4.2. Wilson’s contribution to the study of movement disorders

The considerable work made by Wilson in delineating “his disease” draws attention to his particular interest in movement disorders and basal ganglia throughout his career (Kiernan, 2012). We will present below several representative examples which illustrate this observation.

To start with, one of Wilson’s early scientific publications was his translation from French to English (Meige and Feindel, 1907) of an important book on tics by two physicians of the Paris neurological school, Henry Meige (1866–1940) and Eugène Louis Clément Feindel (1862–1930) (Meige and Feindel, 1902). This was actually one of the first reference books on movement disorders at the very beginning of the 20th century. Among important topics, Meige and Feindel described in the vein of their master Edouard Brissaud (1852–1909) the “geste antagoniste” (or sensory trick), an important feature in patients with torticollis (today referred as cervical dystonia). Wilson contributed to the rapid recognition and adoption of this sign and term in clinical practice (Poisson et al., 2012). Another indication of Wilson’s primary interest in movement disorders was his long book review in Brain (Wilson, 1907) of an exhaustive treatise on torticollis and other movement disorders of the head and neck published in French by Cruchet (1907).

A few years later, in the early 1910s, Wilson’s description of progressive lenticular degeneration represented a major contribution to the discovery of the role of the basal ganglia in motor disorders, which was hitherto unknown (Wilson, 1924). This was a pivotal paper on this topic together with the pioneering work presented in Germany a year before by Cécile Vogt (1875–1962), who established the relation between athetosis and striatal lesions (Vogt, 1911).

In the late 1910s and early 1920s, the occurrence of the epidemic encephalitis of Von Economo-Cruchet (Cruchet et al., 1917; Von Economo, 1917a, 1917b) led to intense research in neurological schools of Europe and North America on the pathophysiology of post-encephalitic parkinsonism and of Parkinson’s disease. In this area, Wilson had a major influence in providing a better understanding of bradykinesia and akinesia in parkinsonian syndromes as already stressed above (Wilson, 1925) Among other topics, he described increased reaction time in bradykinesia, which overshadowed the parallel work made by the Bordeaux neurological school in France (Cruchet, 1921, 1925; Verger and Cruchet, 1925; Verger and Hesnard, 1922). Much later, in the 1970s–1990s, David Marsden (1938–1998) highlighted the prodigious work of Wilson on the functions of the basal ganglia and especially on the mechanisms of akinesia and bradykinesia (Marsden, 1982).

The particular interest of Wilson in various movement disorders has been emphasized once more very recently by the discovery of a 20-minute silent film he made at Queen Square in the mid-1920’s (Reynolds et al., 2011). This film shows Wilson examining patients with senile tremor, Parkinson’s disease and post-encephalic parkinsonism, hemibalismus, Huntington’s chorea, Sydenham’s chorea, hysterical palsy and tremor, multiple sclerosis and finally progressive lenticular degeneration. Although there were a few other examples of films made by European masters in neurology in the early 20th century, most of them have disappeared. Therefore, Wilson’s films are of great value, and one of the oldest examples from the United Kingdom.

Disclosure of interest

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Appendix A. Supplementary data


REFERENCES


Bramwell B. Familial cirrhosis of the liver: four cases of acute fatal cirrhosis in the same family, the patients being respectively nine, ten, fourteen and fourteen years of age: suggested relationship to Wilson’s progressive degeneration of he lenticular nucleus. Edinburgh Med J 1916;17:90–9.


Leéri Marsden Hoogenraad Marie Mandelbrote Gordon Kayser Haymaker Fleischer Kennedy Marie 934

Cummings JN. The copper and iron content of brain and liver in the normal and in hepatolenticular degeneration. Brain 1948;71:410–5.


Ormerod JA. Cirrhosis of the liver in a boy, with obscure and fatal nervous symptoms. St Bartholomew’s Hosp Rep 1890;26:56–68.


