Robert Bentley Todd’s Contribution to Cell Theory and The Neuron Doctrine

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Robert Bentley Todd, who is best remembered for “Todd’s paralysis,” made many more important contributions to neurology and neuroscience, including the concept of brain electricity and electrical discharges in epilepsy. He was also a pioneering microscopist and we here review his neurohistological studies and his contributions to the application of Schwann’s (1839) cell theory to the nervous system and the later neuron doctrine, as described in his textbook The Descriptive and Physiological Anatomy of the Brain, Spinal Cord and Ganglions (Todd, 1845), his Cyclopaedia of Anatomy and Physiology (1847) and his joint textbook with William Bowman The Physiological Anatomy and Physiology of Man (1845). Writing in the mid-1840s, Todd acknowledged that the “vesicles” he observed corresponded to the earlier descriptions of “globules” or “kugeln” by Valentin and which Schwann first interpreted as cell bodies. Todd was among the first to recognize that nerve cell bodies were in continuity with axons (“axis cylinders”), sometimes associated with “the white substance of Schwann” (“tubular” fibers), or sometimes without (“gelatinous” fibers). He also described continuous nerve cell branching processes, later called dendrites. He was the first to recognize the insulating properties of Schwann’s “white substance” (myelin) to facilitate conduction. Influenced by his contemporary, Faraday, Todd was also the first to develop the functional concept of dynamic polarization (“nervous polarity”) to explain nerve cell conduction.

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Robert Bentley Todd and the Nervous System

Robert Bentley Todd, FRS (1809–1860) is best remembered today for his descriptions of postictal paralysis that bears his name (Binder, 2004), but this was a small part of his many contributions to neurology and neuroscience (Reynolds, 2005a). Todd was an Irishman who trained in medicine in Dublin where his father was Professor of Anatomy and Surgery at the Royal College of Surgeons. He was a scientific clinician who in 1836 was appointed to the Chair of Physiology and Morbid Anatomy at King’s College in London where he also became the leading physician at King’s College Hospital, which he founded in 1842 and where his statue was erected in 1861 (Figure 1).
Figure 1. Statue of Robert Bentley Todd outside King’s College Hospital that he founded. Originally (1861) the statue stood in the lobby of the second King’s College Hospital in Portugal Street, close to King’s College in The Strand. When the third King’s College Hospital was opened on Denmark Hill, South London, in 1913, the statue was placed outside the hospital where it has remained.
Todd made several contributions to general medicine (Reynolds, 2003), but his main interest was always in the nervous system. He was the first to identify the functions of the posterior columns of the spinal cord and, on this basis, he was able to separate spinal ataxia from spinal paraplegia before Romberg, Russell Reynolds, or Duchenne. Gowers (1888) credits Todd with the first exact account of locomotor ataxy or tabes dorsalis. Todd also first recognized that certain poisons, such as lead, initially attacked the nervous system by advancing along the peripheral nerves to the nervous centers. His studies of paralysis advanced the whole clinical and pathological field, cerebral, spinal, and hysterical, as well as identifying postictal paralysis (Todd, 1854). He also distinguished the “irritating” (epileptic) from the “paralyzing” phenomena of cerebral lesions that we now associate with the later but similar concepts of Hughlings Jackson who used the words “discharging” and “destroying” (Reynolds, 2005a). Perhaps Todd’s greatest achievement, influenced by his contact with Michael Faraday (1791–1867), was to apply the new knowledge of the polar forces of electricity and magnetism to the brain and to first develop the concept of electrical discharges in epilepsy, a generation ahead of Jackson’s chemical discharges (Reynolds, 2004, 2007).

Todd was also a pioneering microscopist and, assisted by his colleague, William Bowman (1816–1892), turned his attention to the largely uncharted and difficult field of the microscopic anatomy and physiology of the nervous system. In this article, we examine Todd’s neurohistological observations published in the 1840s in his textbook (Todd, 1845), his Cyclopaedia (Todd, 1847; see Figure 2), and his joint work in humans with William Bowman (Todd & Bowman, 1845; see Figure 3). He made significant contributions to the application of Schwann’s (1839, 1847) cell theory to the nervous system and to the foundations of the later “neuron doctrine.” Like much of Todd’s neurological work these neurohistological achievements have been overlooked by subsequent generations.

**Todd’s Neurohistological Observations**

Todd undertook his microscopic studies in the late 1830s and early 1840s at a time when very little was known of the microanatomy of the nervous system. At the macroscopic level, it was known that there were centers of nervous action composed of grey and white nervous matter intimately connected with nerves that appeared to conduct to and from them (Todd, 1845, p. 1). The two forms of nervous matter could be further distinguished into vesicular and fibrous, the former grey or ceneritious in color and granular in texture, the latter white and mostly composed of tubular fibers (Todd & Bowman, 1845, p. 205).

In 1838, the botanist, Matthias Jakob Schleiden (1804–1881) suggested that the structural elements of plants are composed of cells or their products. The following year the zoologist, Theodore Schwann (1810–1882), who knew Schleiden, published an identical hypothesis for animal tissues:

> The development of the proposition, that there exists one general principle for the formation of all organic productions, and that this principle is the formation of cells, as well as the conclusions which may be drawn from this proposition, may be comprised under the term cell-theory, using it in its more extended signification, whilst in a more limited sense by theory of the cells we understand whatever may be inferred from this proposition with respect to the powers from which these phenomena result (Schwann, 1839, translated into English 1847).
Figure 2. Frontispiece of the third volume of *The Cyclopaedia of Anatomy and Physiology* that was published in five volumes; all edited by Todd between 1835 and 1859. Volume three, which was published in 1847, contains the section on the nervous system and was written entirely by Todd.
Figure 3. Frontispiece of Todd and Bowman’s textbook on *The Physiological Anatomy and Physiology of Man*, Volume one, which includes the section on the nervous system, was published in 1845.
There have been several reviews of the many neurohistological studies of the nineteenth century that culminated in the so-called “neuron doctrine,” that is, the application of Schwann’s universal cell theory to the complex microstructure of the nervous system (Brazier, 1988; Clarke & O’Malley, 1996; Jacobson, 1993; Jones, 1994; Meyer, 1971; Shepherd, 1991; Van der Loos, 1967). None of them refer to Todd’s studies. It is widely accepted that Jan Purkinje (1837) and his student in Breslau, Gabriel Valentin (1836), were the first to identify structures in the nervous system that they called “kugeln” or “globules,” which in retrospect were cell bodies. Schwann published his cell theory 3 years later, in 1839, and it was he who recognized the significance of Purkinje’s and Valentin’s observations and first applied his own cell theory to the nervous system.

Writing in 1845 before Schwann’s 1839 book had been translated into English in 1847, Todd clearly was aware of and accepted Schwann’s cell theory: “The essential elements of the grey nervous matter are ‘vesicles’ or cells, containing nuclei and nucleoli. They have also been called nerve or ganglion ‘globules’” (Todd & Bowman, 1845, p. 212; Todd, 1845, p. 64). Furthermore, “In the perfect nerve-vesicle, the cell form of primitive development is persistent. We have the nucleolus and nucleus (cytoblast) and the cell; and, according to Schwann, the only change which the full-grown cell exhibits consists in an increase of size and in development of the pigmeny granules within” (Todd, 1845, pp. 69–70).

Todd acknowledges that the “vesicles” or cells that he is describing are similar to the “globules” described by Valentin. At that time, however, Valentin and Purkinje did not consider the “fibers” they observed were connected to the globules. Todd described several kinds of vesicles and their processes from different areas of grey matter including peripheral ganglia and cortex (Figure 4). One particular form of nerve vesicle “is characterised by one or more tail-like processes extended from it and to such nerve vesicles we may apply the term caudate — sometimes there is but a single process from a vesicle; or there may be two, proceeding from opposite sides; or there may be several, extending in various directions — in point of structure, the caudate processes are exceedingly delicate, and finely granular, like the interior of the vesicle, with which they distinctly seem to be continuous” (Figure 5) (Todd & Bowman, 1845, p. 213).

Todd distinguished two types of nerve fibers: “tubular” and “gelatinous.” Tubular fibers are “infinitely more numerous” and are responsible for the white appearance of white matter. There is an external tubular membrane, “an homogenous and probably elastic tissue of extreme delicacy analogous to the sarcolemma of striped muscles” (Todd & Bowman, 1845, p. 208). Within this membrane, on each side, are two thicker lines that mark the outer and inner limits of an inner layer of different composition that is known as the “white substance of Schwann.” Within this is a transparent material occupying the axis of the nerve that Todd refers to as the “axis cylinder,” a term probably first used by Purkinje. The much less numerous “gelatinous” fibers to which Todd refers were devoid of any white substance of Schwann (Figure 6) (Todd & Bowman, 1845, p. 209).

The neurohistorians referred to above (Brazier, 1988; Clarke & O’Malley, 1996; Jacobson, 1993; Jones, 1994; Meyer, 1971; Shepherd, 1991; Van Der Loos, 1967) credit Robert Remak (1815–1865), also writing in the early 1840s (Remak, 1841, 1844), with the first evidence of the direct connection of the axis cylinder (axon) with the cell body, although this was not particularly convincing until 1844 when he was able to show that each anterior horn cell of the spinal cord was continuous with one ventral root fiber. Remak also distinguished “tubular” (myelinated) from “gelatinous” (nonmyelinated) fibers but referred to the former as “organic” and the latter as “primitive” fibers, respectively. Within the “organic” (Todd’s “tubular”) fibers, Remak refers to the axis cylinder as a “flattened band.”
In the early 1840s, therefore, Todd and Remak were coming to similar conclusions about the continuity of the axon with the cell bodies; although they used different terminology and, in Todd’s case, expressed a similar view about all the cell processes (Figure 5). Both recognized the distinction between myelinated and unmyelinated fibers with Todd specifically referring to the “white substance of Schwann.” Todd adds:

It is a conjecture by no means devoid of probability, that the processes of the caudate vesicle may, after passing some way, become invested by the tubular membrane and by the white substance of Schwann (Todd & Bowman 1845, p. 225).

As will be discussed in more detail later, Todd also recognized the importance of the white substance of Schwann as a form of “insulation” for the axis cylinder to enhance its functional role in “nervous polarity.”
Figure 5. a. A large caudate nerve vesicle (cell) with diverging and branching processes (from Todd & Bowman, 1845). Some processes, b, are seen to pass off into extremely minute filaments. These seem to bear a very close resemblance to the central part of a tubular fibre, c, which is prolonged some way beyond the broken edge of its tubular membrane and white substance, d. At e, are some small nerve-vesicles, stellate in form, doubtless from numerous processes given off from them: f, several extremely small nerve-tubes, some of which are varicose. This figure exhibits the great variety of size of the vesicles and tubes. a. is from the posterior horn of the gray matter of the spinal marrow and is magnified only 120 times, while the vesicles and tubes at e, from the gray matter of the lower end of the cord, are magnified 300 times. d. is also from the spinal marrow and is magnified 200 times.

As is clear from Figure 5, Todd has identified what today we would call “dendrites,” a concept that was developed by Deiters 20 years later in 1865, but who continued to call them “protoplasmic processes” until the term “dendrites” was later introduced by His in 1889.

Todd noted that in most areas of grey matter the vesicles mingled with tubular fibers and with gelatinous branching processes (fibers). He was deeply interested in the precise connections between the vesicles and the various fibers but all he could observe with his techniques at that time was the relation of nerve fibers to nerve vesicles in the centers was most intimate, and that the latter were rarely met without one or more of the former in immediate connection with them (Todd & Bowman, 1845, p. 215).

Todd emphasized the limits to present knowledge when he stated that

It is in vain, in the present state of our knowledge, to speculate upon the use of these caudate processes. Do they constitute a bond of union between the nerve vesicles and certain nerve-tubes? Or are they commissural fibres serving to connect the grey substance of different portions of the nervous system? Until a more extended research has made us better acquainted with peculiarities of these vesicles in various localities, it would be premature to offer any conjecture concerning their precise relation to the other elements of the nervous centres (Todd, 1845, p. 67).

The Neuron Doctrine

The above questions occupied the minds of numerous neuroscientists for the whole of the second half of the nineteenth century and were not resolved until after Golgi developed his famous silver impregnation staining technique in 1873. Even then the debate
Figure 6. Tubular and gelatinous nerve fibres (from Todd and Bowman 1845). A. Diagram of tubular fibre of a spinal nerve. a. Axis cylinder. b. Inner border of white substance. c.c. Outer border of white substance. d.d. Tubular membrane. B. Tubular fibres; e, in a natural state, showing the parts as in A. f. The white substance and axis cylinder interrupted by pressure, while the tubular membrane remains. g. The same, with varicosities. h. Various appearances of the white substance and axis cylinder forced out of the tubular membrane by pressure. i. Broken end of a tubular fibre, with the white substance closed over it. k. Lateral bulging of white substance and axis cylinder from pressure. l. The same more complete. g. Varicose fibres of various sizes, from the cerebellum. C. Gelatinous fibres from the solar plexus, treated with acetic acid to exhibit their cell nuclei. B and C magnified 320 times.
continued between advocates, supported by Golgi, of the network theory (reticularism) of axons and their branches in direct continuity with each other or what became known as “the neuron doctrine,” of the nerve cell as the elementary unit of the nervous system, that is, the neuron as the embryological, structural, functional, and trophic unit of the nervous system. The word “neuron” was introduced by Wilhelm Waldeyer in 1891 in his review of the neurohistological literature, especially the work of His, Forel, and Cajal. However the verification of the “neuron doctrine” really depended on the more extensive work of Cajal (1894, 1907), utilizing Golgi’s technique, reinforced by the concept of the “synapse,” developed by Sherrington in 1897. When Golgi and Cajal jointly received the Nobel Prize for Medicine in 1906, Golgi attributed the neuron doctrine to Cajal but personally continued to favor the network/reticular theory (Golgi, 1907).

The Law of Dynamic Polarization

An important aspect of the neuron doctrine developed by Cajal (1894, 1907) is what he and others have called “The Law of Dynamic Polarization.” This law states formally that all dendrites conduct in a cellulipetal and axons in a cellulifugal direction (Jones, 1994). From 1891 onwards, Cajal inserted arrows indicating the direction of nervous conduction in his histological drawings and diagrams (López-Muñoz, Boya & Alamo, 2006).

Although Cajal clarified the direction of transmission, the concept of dynamic polarization undoubtedly belonged to Todd who was influenced by Prochaska’s concept of “Vis nervosa” (Reynolds, 2005b) and especially by the electrical studies of his contemporary in London, Michael Faraday (1791–1867), who in the 1830s and 1840s was developing his concepts of the polar and interchangeable forces of electricity and magnetism (Reynolds, 2004). Todd conceived of nervous polarity generated in nervous centers and compared this with the polar force of voltaic electricity developed in the galvanic battery (Todd & Bowman, 1845, p. 237).

As a result of his histological studies, Todd concluded that the vesicles of the grey matter are extensively connected with nerve fibers. Each fiber is connected with a vesicle and each vesicle is the point of departure of one or several fibers. He, therefore, suggested that each nerve vesicle and its related fibers are a distinct apparatus for the development and transmission of nervous polarity (Todd & Bowman, 1845, p. 237). He develops this concept in more detail as follows:

At these points there is generated constantly and unceasingly a force, which in its nature resembles very closely the galvanic force, or current electricity, as developed in the galvanic battery or the magnetoelectric machine. Adopting the language of the illustrious Faraday, which expresses with clearness and precision the fundamental phenomena of the electric force, we may call the nervous power a polar force, generated in the centres, and propagated by the rapid polarisation of the neighbouring particles in various directions (Todd, 1849).

Remarkably, Todd and Bowman add:

There appears to be a provision for the insulation of the central axis of each nerve fibre in the white substance of Schwann; but there is no such arrangement for insulating the vesicles. In like manner we can insulate the galvanic current by covering the conducting wire with silk, or some other non-conductor (1845, p. 239).
Thus, Todd immediately understood the significance of the white substance of Schwann for facilitating conduction.

Long before Cajal, Todd also considered the possible direction of flow of nervous polarity. He understood that the direction of the conduction was away from the vesicular centers in which it was generated, but how was it conducted to a center from the periphery, for example, by touching a nerve? He pointed out that thermoelectric currents may easily be excited by the influence of heat in a wire or a single metal and inferred that a very slight mechanical or chemical stimulus to a nerve was capable of producing in it that state of polarity that he viewed as the basis for nervous conduction (Todd & Bowman, 1845, p. 240). He also noted that just as the state of polarity induced in a piece of soft iron rendered magnetic by a galvanic current is inferred by its power of attracting iron particles, so the assumption and maintenance of the polar state in a muscular nerve are revealed by the active contraction of certain muscles or a more tonic state of passive contraction (Todd, 1847, p. 720).

It should be added that for many reasons neither Todd nor Faraday regarded nervous polarity as identical to electricity, but they viewed it as another, perhaps higher, polar force also interchangeable with electromagnetism (Reynolds, 2004). It took another century for the ionic basis of Todd’s dynamic polarization, only slightly modified by Cajal, to be clarified by the Nobel Prize-winning studies of Hodgkin and Huxley (1952).

In conclusion, many early microscopists in the 1830s and 1840s contributed to the foundations of the neuron doctrine with their observations of nerve cell bodies (globules, vesicles) and axons (fibers, tubules, axis cylinders) with or without the white substance of Schwann and dendrites/branching processes. Todd’s contributions have, however, been largely overlooked or forgotten, which is surprising for at least two reasons. He was the first to write in the English language in the 1840s on his work. Secondly, Todd is outstanding among these early pioneers because he was a physiologist as well as an anatomist and developed highly original physiological concepts in conjunction with his neurohistological researches, especially his concept of nervous polarity underlying nerve cell function.

References

Reynolds EH (2003): Robert Bentley Todd and the origins of King’s College Hospital. *Guy’s, King’s, St. Thomas’ Gazette* 116: 826–831.