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Brief history of transcranial direct current stimulation (tDCS): from electric fishes to microcontrollers

Electrical stimulation to treat medical conditions is not a new therapy; it has been used to treat diseases for centuries. The first electricity sources used for electrical stimulation were produced by animal electricity. Antique Egyptians knew about the electrical proprieties of Nile catfish, but it is unclear if (and how) they experimented with them for clinical purposes. The first reported evidence of electrical stimulation arrives some centuries later in antique Greece times, when Plato and Aristotle described the ability of the torpedo fish to generate curative effects by its electric discharges (Althaus, 1873; Rockwell, 1896; Harris, 1908).

The first evidence of transcranial stimulation in history comes in Roman Empire times, when Scribonius Largus (the physician of the Roman Emperor Tiberius Claudius Nero Caesar) described how placing a live torpedo fish over the scalp could relieve headache in a patient (Scribonius Largus, 1529). Perhaps the first person known to have been cured by torpedo fish electricity was Anthero, a freed slave of Tiberius Caesar, who suffered *gutta* (probably gout) (Cambridge, 1977). In the late 11th century, the Muslim physician in Persia, Ibn-Sidah also suggested the use of torpedo fishes to treat epilepsy (Priori, 2003), placing the live catfish on the brows of the patients (Delbourgo, 2006). The use of electric fish stimulation also spread to Africa, where Jesuit missionaries in early modern Abyssinia (Ethiopia) reported that locals used catfishes as a method of expelling 'Devils out of the human body' (Delbourgo, 2006). Fish electricity was maybe the most popular type of electrical stimulation for more than 10 centuries though it is not clear how the effects were measured.

In 1660 the German scientist Otto von Guericke invented the first electrostatic generator (Comroe & Dripps, 1976), a frictional crank-controlled machine. This device could be considered the first stimulator device and its variations were used later by scientists like the Italian anatomist Leopoldo Marco Antonio Caldani in 1756 to stimulate muscles in sheep and frogs (Caldani, 1760). The Middlesex Hospital (England) was probably the first hospital to purchase an electrostatic machine in 1767 (Cambridge, 1977).

In 1745 Ewald Georg von Kleist invented the Leyden jar, the first capacitor in history (Keithley, 1999). This device could store electric charge produced from an electrostatic generator. Experimenters, like Anton de Haen in 1755 (Priestley, 1767) and Benjamin Franklin in 1757 (Franklin, 1757), were able to combine electrostatic generators and the Leyden jar for therapeutic electrification (McWhirter *et al.* 2015).

In 1773 the anatomist and physiologist John Hunter studied the torpedo fish thoroughly. These investigations were undertaken at the request of John Walsh, who showed that the 'shocks' produced by the torpedo fish were caused by the generation of electricity (Walsh, 1773). These kind of animals or fishes have an electric organ that, on brain command, generate a three-dimensional dipole field around their bodies, discharging single-cycle pulses from below 1 Hz to about 65 Hz at rest (Hopkins, 2009). Electric fish electricity is not direct current (DC); nevertheless it is the first reported kind of stimulation in history.

Unlike fish electricity and electrostatic electricity, DC is the flow of electrical charge that does not vary with time, generating a constant signal (Belove & Drossman, 1976). The birth of the DC generator was in the 1st century BC with the so-called Baghdad battery, attributed to the ancient Persian civilization (Scrosati, 2011), but other references attribute the invention to the Parthians, calling it the Parthian galvanic cell (Keyser, 1993). This invention remained forgotten until the 20th century, when the archeologist Wilhelm Köning discovered it in Iraq and it was possibly used for medical purposes. In the 18th century Luigi Galvani invented a DC battery (galvanic battery) and his nephew, Giovanni Aldini, was one of the first persons to utilize DC for clinical applications. Aldini's most detailed account of DC clinical treatment concerns Luigi Lanzarini, a 27-year-old farmer suffering from melancholy madness (major depression), who had been committed to Santo Orsola Hospital, in Bologna, Italy on 17 May 1801, but first assessing the effects of galvanic currents on his own head (Fitzgerald, 2014). The patient's mood progressively improved so that Lazarini was apparently completely cured several weeks after the beginning of the treatment (Parent, 2004).

Aldini's work was the milestone which began the era of DC stimulation for neurological and psychiatric conditions. Later in 1802, Hellwag and Jacobi reported the use of transcranial DC, also reporting the first evidence of phosphenes using DC (Hellwag & Jacobi, 1802; Paulus, 2010). Around 1880 the application of brain stimulation treatments on patients was particularly popular among German psychiatrists, pioneers in electrotherapy, an early tDCS method. Wilhelm Tigges, Rudolph Gottfried Arndt (Steinberg, 2013*a*) and Erb (1883) tried to establish clear rules on the most beneficial application methods and doses in order to investigate which results it may produce and under what circumstances (Steinberg, 2014). The experimental designs with larger groups in electric therapy research protocols were a common factor in this age. For example, Arndt used 12 psychotic patients in his 1870 experiment. Despite being very detailed, Arndt's reports do not provide exact data about the strength of the applied current. Due to controversial reports (some with positive results and others with negative) and the lack of understanding of operating principles, electrotherapy was repeatedly suspected of attaining result through suggestion only (Steinberg, 2013*a*). Many other researchers used DC for the treatment of mental disorders during the 19th century and the early part of the 20th century, but the variation of procedures, unclear descriptions, few qualitative details and the misunderstood effect of polarization led to variable and/or inconclusive results. The use of DC stimulation was abandoned from the 1930s (Steinberg, 2013*b*).

In 1957 DC reappeared in electrosleep therapy and around 1960–1963 electro-anesthesia research incorporated DC bias. In 1964, motivated by animal studies that reported lasting changes in excitability using prolonged scalp DC stimulation, Lippold and Redfearn used 50–500 μA DC currents in 32 healthy subjects, and reported that anodal current induced an increase in alertness, mood and motor activity, whereas cathodal polarization induced quietness and apathy (Lippold & Redfearn, 1964; Guleyupoglu *et al.* 2013). Despite several follow-up research works, from the 1970s DC stimulation was once again abandoned, probably due to the introduction of new psychiatric drugs (Dubljević *et al.* 2014).

It was not until 1998 when the usage of DC was advocated and the modern tDCS was born, when Priori and his colleagues investigated the influence of DC in the brain by testing its effects on cerebral cortex excitability using transcranial magnetic stimulation (Brunoni *et al.* 2012). Characteristics of tDCS, such as the fact that it is non-invasive, mostly well tolerated and its mild adverse effects, have sparked great interest and increase in clinical studies recently (Brunoni *et al.* 2012).

The transcranial DC stimulators have evolved from a simple galvanic battery in the 18th and 19th centuries, passing from vacuum tubes and transistors to microprocessors and microcontroller technologies in the 20th century. Progress in microcontroller technology has enabled electronic and biomedical engineers to build precise tDCS devices with a better control of stimulation parameters (Paulus & Opitz, 2013) at reduced costs. The future tDCS designs will focus on obtaining simple systems by way of reducing size, power consumption, weight and enhanced portability (Kouzani *et al.* 2016).

The tDCS is a promising tool for basic neuroscientists, clinical neurologists and psychiatrists in their quest to causally probe cortical representations of sensorimotor and cognitive functions, to facilitate the treatment of various neuropsychiatric disorders (Schlaug & Renga, 2008) and enhance neurological functions in healthy humans (Dubljević *et al.* 2014). Although tDCS has demonstrated benefits, the scientific community must communicate carefully about their findings, by providing neutral data to the media and public, since the popular media sometimes consider tDCS as a 'miracle device' (Riggall *et al.* 2015). Such sensationalistic news about the benefits of tDCS leads people to self-administer stimulation, as we can see in some Internet do-it-yourself tDCS forums (Wexler, 2015).

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Declaration of Interest

None.

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