Introduction

Giuseppe Moruzzi (1910-1986, Fig. 1) was born one hundred years ago, and this significant anniversary has been marked by a conference held in Villa di Corliano, San Giuliano Terme (Fig. 1) from 22-26 June, 2010. It also celebrated the distinguished physiologist Carlo Matteucci (1811-1868, Fig. 1) and the full title of the meeting was “From Carlo Matteucci to Giuseppe Moruzzi: two centuries of European physiology”. Matteucci lived in the Villa for several years (1850-1854), and he would travel by train to the University of Pisa to conduct his research and to deliver his lectures.

Stimulating the senses

Both Matteucci and Moruzzi derived insights into the operation of the nervous system from studies of the senses. Indeed, the senses have provided an avenue to understanding the brain and its functions since antiquity. However, sources of stimulation then available were limited: students could report on their experiences when stimulated naturally, and they could relate them to their body parts. Additional inferences could be drawn from disease or injury. Recourse was frequently made to philosophy, usually linking the senses to the elements – fire, earth, water, and air – which permeated perception. The situation regarding the senses and the nervous system was radically revised in the nineteenth century, with developments in physics, anatomy, and physiology. Sources of stimulation could be specified and controlled more precisely, and among these was electricity.

In 1752, Johann Georg Sulzer (1720-1779) described the taste produced by placing different metals in the mouth. When silver was placed on one side...
of the tongue and lead on the other, he reported a sour or alkaline taste which was interpreted as due to the mechanical vibrations the metals induced. The effects were pursued more systematically by Alessandro Volta (1745-1827; 1793, 1800) and Richard Fowler (1763-1793), both of whom extended the senses to which electricity was applied. Much has been written about Volta’s self-administered shocks (see Piccolino, 2003) but less attention has been directed to Fowler’s similar studies. Volta found that very small currents could be experienced by the tip of the tongue, which was in fact more sensitive than the extant physical devices for measurement. Fowler, on the other hand, explored the
senses in what could be considered as heroic self experiments (see Jacyna, 1999). Fowler commenced his studies of the senses after reading Volta’s report (although neither cited Sulzer’s anecdotal observation). Rather than placing different metals on and beneath the tongue, as Sulzer and Volta had done, he applied electrical discharges and noted the differences in the sensations produced by the two procedures: “Both, indeed, are subacid, but as unlike to each other, as the taste of vinegar is to that of diluted vitriolic acid” (Fowler, 1793, p. 82). He found that the sensations were strongest when the tongue was at normal temperature, and that reducing its sensitivity chemically also diminished the sensation. The effects of stimulating the eyes were much more intense than those of taste and smell: flashes of light appeared at the onset and offset of currents applied to the region around the eyes. The flashes were distinguished from the long known effects of pressing on the eye, as no increase in pressure was involved. Even more intense sensations were generated with zinc and gold than with tin-foil and silver. Attempting to stimulate the optic nerve itself “by insinuating a rod of silver, as far as possible, up my nose, and thus arming this nasal branch, I could, by bringing the silver into contact with a piece of zinc, placed upon my tongue, pass this new influence up the course of the nerve, and thus produce the flash in the eye. The experiment answered my most sanguine expectation. The flash, in this way produced, is, I think, if any thing, stronger than when the ball of the eye itself is armed” (pp. 87-88). He used the technique to demonstrate that the pupil constricted upon stimulation.

In contrast to the many experiments involving stimulation of the eyes, that of the ears was not repeated due to its distinctly unpleasant consequences: “On placing different metals in the meatus auditorius externus of both my ears, and establishing an insulated metallic communication between them, I felt, or fancied that I felt, a disagreeable jerk of my head. The metals used were a silver probe, a roll of tin-foil, and a common brass conductor belonging to an electrical machine. On withdrawing them from my ears, I experienced a feeling similar to that which one has after emerging from under water” (Fowler, 1793, p. 85). Volta also reported a jerk to his head when applying a current between his ears: “At the moment the circuit was completed I felt a shaking in the head” (1800, p. 427). The shaking did not last long and when the current was continued he experienced sound and then noise. Both Fowler and Volta found the sensations so disagreeable and considered them potentially dangerous that they did not wish to repeat them. It is likely that the jerking or shaking of the head was a consequence of stimulating the vestibular system, although very little was then known about its functions (Wade, 2003).

Fowler’s observations were amplified in a letter to him from John Robison (1739-1805; 1793). Electrical stimulation was applied to an open wound and also to a tooth cavity: “I made a piece of zinc having a sharp point, projecting from its end. I applied this point to a hole in a tooth, which has sometimes ached a little, and applied the silver in an extensive surface to the inside of the cheek. When the metals were brought into contact, I felt a very smart and painful twitch in the tooth, perfectly resembling a twitch of the tooth ack” (p. 172). In his endeavours to increase the intensity of stimulation, Robinson came close to making a battery: “I had a number of pieces of zinc made of the size of a shilling, and made them up into a rouleau, with as many shillings. I find that this alternation, in some circumstances, increases considerably the irritation, and expect, on some such principle, to produce a still greater increase” (p. 173).

Applying electrical discharges (galvanic stimulation) to the tongue, Johann Wilhelm Ritter (1776-1810) provided experimental support for warmth and cold as sensory qualities. His first reports regarding warm and cold were in 1801: “Another contrast in sensation is that between warm and cold… if one brings into contact a zinc pole on the tongue and silver on the gums, that on the tongue feels very clearly warm, but it feels cold with silver in the same arrangement” (p. 458). Thus, stimulation by the positive pole produced the sensation of warmth, whereas the negative pole resulted in experiencing cold. Slightly earlier in the same year, Christoph Heinrich Pfaff (1773-1852; 1801) had described the sensation of coldness when he applied a current to his finger. Ritter (1805) extended the studies on temperature sensitivity on the tongue as well as the finger; he found that the sensation could vary according to the intensity and duration of the current. His general conclusion was that: “one must consider the sense of temperature (for warmth and cold) as essentially different from
the common sense, and as a special sense” (p. 10). Galvanic stimulation resulted in a short shock as well as the particular sensation. In the case of temperature sensitivity, Ritter reported that the shock remained constant even when the sensation changed from warm to cold. Rather than merely speculating that warmth and cold are separate sensory qualities, Ritter afforded experimental evidence for this via his studies of galvanic stimulation.

The manner in which the nerves themselves worked was hinted at by Luigi Galvani (1737-1798, Fig. 2) when he made a case for ‘animal electricity’ (Galvani, 1791). He applied a discharge from a Leyden jar to the exposed crural nerve or muscle of an isolated frog’s leg and it twitched. More significantly, the muscle twitched in the absence of an external discharge if it was connected to another excited nerve or to metal. Galvani suggested that this
was due to a special type of electrical fluid that accumulates in the muscles of animals (see Bresadola, 1998; Piccolino, 1997, 2000, 2012 [this issue]). Volta (Fig. 2) maintained that animal tissue was not necessary for a current to pass, and that Galvani’s experiments were flawed. As noted above, Volta had interests in the effects of electrical discharges on the senses; he carried out studies of galvanic light figures in the 1790s, and also found that intermittent stimulation produced longer lasting effects than constant stimulation. In his letter describing the pile or battery, Volta (1800) described how he applied electrical stimulation to the eyes, ears, nose, and tongue. He connected the wires from a battery between the mouth and conjunctiva of the eye, which resulted in the experience of light, even in a dark room. Moreover, he noted that the visual sensation was associated with the onset and offset of the current, and a continuous impression of light could be produced by rapid alternation of polarity.

Volta’s (1800) pile did much to hasten experimental studies of the senses. Electricity was a common stimulus that could be applied to different sensory organs, inducing different sensations. The link between energy and sense organs was forged soon thereafter. Charles Bell (1774-1842; Fig. 2) is noted for discovering that the anterior spinal nerve roots carry motor nerves (see Cranefield, 1974). His principal concern, however, was in specifying the senses and their nerve pathways to the brain. His experiments were described in a privately published pamphlet which also related stimulation to specific senses (Bell, 1811). In the context of vision, Bell was able to demonstrate that light was experienced with the application of electricity to the eye: “If light, pressure, galvanism, or electricity produce vision, we must conclude that the idea in the mind is the result of an action excited in the eye or in the brain, not any thing received, though caused by an impression from without. The operations of the mind are confined not by the limited nature of things created, but by the limited number of our organs of sense” (1811, p. 12).

A similar sentiment, voiced with primary reference to the nerves and their pathways, was written a few decades earlier by John Hunter (1728-1793; 1786). The examples he gave to support this contention were the referred sensations arising after damage or amputation. The seeds of this idea can be found in antiquity, although it was based on philosophical rather than physiological speculation. The doctrine of specific nerve energies, as it became called, was given further support by Johannes Müller (1801-1858; Fig. 2), in a monograph on comparative physiology and on eye movements (Müller, 1826) and it was amplified in his influential handbook of human physiology (Müller, 1838). Although the doctrine was framed in terms of differences between the senses, it was used increasingly to determine qualitative distinctions within them (see Finger and Wade, 2002). Müller used the effects of electricity on the senses to support his doctrine: “The stimulus of electricity may serve as a second example, of a uniform cause giving rise in different nerves of sense to different sensations” (1843, p. 1063). The first example was mechanical stimulation.

The action of nerves on muscles led first Matteucci (Fig. 3) and later Emil du Bois-Reymond (1818-1896; Fig. 3) to propose the ways in which nerves propagate impulses (Finger and Piccolino, 2011). Experimental evidence of action potentials was to await technological advances in recording and amplifying small electrical signals; this was provided by Adrian (1928) who was able to amplify the signals from a single isolated nerve fibre (Finger, 2000). When recordings of nerve impulses could be made from individual cells in the visual pathway their adequate stimuli could be determined. Adrian coined the term ‘receptive field’ to refer to this, and it was applied to other senses, too.

**Carlo Matteucci and Giuseppe Moruzzi**

Matteucci was born in Forli and studied in Bologna, Paris, Florence and Ravenna. He was appointed professor of physics at the University of Pisa in 1840. The scientific ideas that excited him most were those based on the studies of Galvani and Volta. Matteucci extended the experiments of Galvani on animal electricity and he provided the experimental basis for understanding how nerve impulses are propagated (see Finger and Piccolino, 2011). The importance of Matteucci’s research was noted throughout Europe, and his papers were translated into several languages. An indication of the esteem in which he was held was the award of the Copley Medal by the
STIMULATING SENSES 23

Fig. 3. - Upper left, Matteucci’s frogs in which his portrait is combined with two of his diagrams showing the stacked nerve-muscle preparations (his galvanoscopic frogs) and the arrangements of frog’s legs on a board. Upper right, Du Bois-Reymond’s nerves with his diagram of nerve propagation derived from the final part of his treatise on animal electricity (Du Bois-Reymond, 1884). Lower left, Matteucci’s Traité in which his portrait is accompanied by the title page of his book describing his experiments. Lower right, Matteucci’s Memoir showing the first page of his paper published in the Philosophical Transactions of the Royal Society. It was delivered, in his absence, by Michael Faraday (© Nicholas Wade).
Royal Society of London in 1844. He also wrote several books; the title page of his *Traité* is shown in Fig. 3; this has been described as the most important work on animal electricity after Galvani (Finger and Piccolino, 2011). Matteucci had been in correspondence with Michael Faraday (1791-1867) since 1833 and Matteucci’s first memoir to the Royal Society (Fig. 3) was communicated by Faraday. Moruzzi not only collected historical books and journals but he also wrote on the history of science (see Meulders, Piccolino and Wade, 2010). One of his works was a biography of Matteucci, who was acknowledged as a major figure in the history of European neuroscience (Moruzzi, 1964, 1996). Moruzzi followed in the line of Matteucci by studying neurophysiology, but with more sophisticated equipment than was available to Matteucci. Moruzzi was born in Campagnola Emilia and was educated in the schools and University of Parma, obtaining a degree in medicine. His love of books was cultivated by his family and their libraries, and he remained devoted to literature as well as science throughout his life. Moruzzi was a historian of science as well as an excellent experimenter. As the Professor of Human Physiology at the University of Pisa, appointed in 1949, he built up a library that housed not only the current periodicals but also back issues of important journals (Fig. 4). The *Istituto di Fisiologia* in Via San Zeno became a storehouse of history as well as a powerhouse of experimental research, and Moruzzi was happy when reading the journals in his library. His early interests were recording from the brain, either by means of the electroencephalogram (EEG) or from single nerve cells. He commenced his EEG research with Frederic Bremer in Brussels, and two recordings from this collaboration are shown in Fig. 4. Following the period in Bremer’s laboratory, Moruzzi went to Cambridge to work with Edgar Adrian (Fig. 5). He encountered quite a different way of approaching experimental problems in Adrian’s laboratory: there was no detailed programme of planned experiments, rather happy accidents were seized upon and followed through. It was in this way that Moruzzi and Adrian made some of the first recordings from single nerve cells in the brain. In both Brussels and Cambridge, Moruzzi was supported by grants from the Rockefeller Foundation.

**Reticular system**

The reticular system was always associated with the names of Moruzzi and Magoun, who discovered its function in 1949. Just as Moruzzi’s research was becoming known throughout the scientific world, war was declared. He heard about the impending conflict while he was attending a conference in Copenhagen, and returned to Italy with a heavy heart. The war period was an unhappy one for Moruzzi, but he managed to continue his research under difficult circumstances, and was able to extend them when hostilities ceased. Subsequently, this research stood him in good stead to seek opportunities farther afield. He went to work with Horace Magoun at Northwestern University, Chicago, and it was there that the discoveries concerning the ascending reticular system were made (Fig. 5). It was on the basis of the international acclaim accorded to this discovery that Moruzzi was invited to become Professor of Human Physiology in the Medical Faculty at the University of Pisa. He accepted this invitation despite the fact that he had received many other offers to stay in the USA. In Pisa, he continued working on the reticular system and gradually built up a physiological institute of world standing. Students and scientists from many countries came to work in it, and some of them were present at the conference held in Villa di Corliano, as were colleagues from Pisa. They expressed their gratitude for having had the opportunity to work with this distinguished scientist. I did not have such an opportunity: I only knew of his research from afar. Accordingly, my tributes to him are graphical rather than personal. Homage is also accorded to Matteucci who laid the foundations from which Moruzzi could build his system.

**Conclusion**

Knowledge about sensory function has been advanced by electrical stimulation. This stimulus was applied to a range of senses before the nature of nerve transmission was appreciated. Matteucci provided a platform from which others could explore communication between nerves and muscles and Moruzzi was able to show how the reticular system could regulate the manner in which the brain responded to stimulation of the senses.
Fig. 4. - Upper left, Moruzzi’s Istituto; Moruzzi’s as a young man together with a recent photograph of the Instituto di Fisiologia, via S Zeno, Pisa. Upper right, Moruzzi’s library; a portrait of the Professor with a recent photograph of books from his library in the Instituto. Lower left and right, images from Moruzzi’s early physiological research: left, Moruzzi’s facilitation; his facial features are hidden in one of his tracings demonstrating neural inhibition; right, Moruzzi and Bremer; Moruzzi as a young man is shown in recordings published with Bremer in 1938 (© Nicholas Wade).
Fig. 5. - Upper, Adrian and Moruzzi in the title page of their article on recording from single nerve fibres in the brain. Lower, Wakefulness and sleep. Moruzzi and Magoun are shown in the title page of their article describing the reticular formation, which controls sensitivity to stimulation and is involved in the cycles of wakefulness and sleep (© Nicholas Wade).
Acknowledgement

I am most grateful to Marco Piccolino for stimulating discussions about Matteucci and Moruzzi as well as on the senses.

References


Fowler R. Experiments and Observations Relative to the Influence Lately Discovered by M. Galvani and Commonly Called Animal Electricity. Edinburgh, Duncan, Hill, Robertson & Berry, and Mudie, 1793.

Galvani L. De viribus electricitatis in motu musculari. De Bononiensi Scientiarum et Artium Instituto atque Academia Commentarii, 7: 363-418, 1791.


Matteucci C. Traité des Phénomènes Électro-Physiologistes des Animaux Suivi d'Études Anatomiques sur le Système Nerveux et sur l’Or-
