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Carlo Matteucci, Giuseppe Moruzzi and stimulation of the senses: a visual appreciation

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ABSTRACT

The senses were stimulated electrically before speculations of the involvement of electricity in nerve transmission received experimental support; it provided a novel means of defining the functions of the senses. Electrical stimulation was used by Charles Bell and Johannes Müller as a source of evidence for the doctrine of specific nerve energies because it resulted in the same sensations produced by natural or mechanical stimuli. The basis for understanding nerve transmission was provided by Luigi Galvani and Alesssandro Volta and elaborated by Carlo Matteucci and Emil du Bois-Reymond, both of whom maintained an interest in the senses. A century later, Giuseppe Moruzzi demonstrated how incoming sensory signals can be modulated by the reticular system.

Key words

Matteucci • Moruzzi • Nerve impulses • Reticular system • Senses

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

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Fig. 1. - Upper, Villa di Corliano with superimposed portraits of Matteucci on the left and Moruzzi on the right. Lower left, *Matteucci's eye*; the diagram of the eye is derived from his book, the title page of which is shown in Fig. 3. Lower right, *Moruzzi's ascending reticular system*. Moruzzi and Magoun described the reticular system in 1949 and the diagram in which Moruzzi's portrait is embedded is derived from a figure used by Magoun (© Nicholas Wade).

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 jirk 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

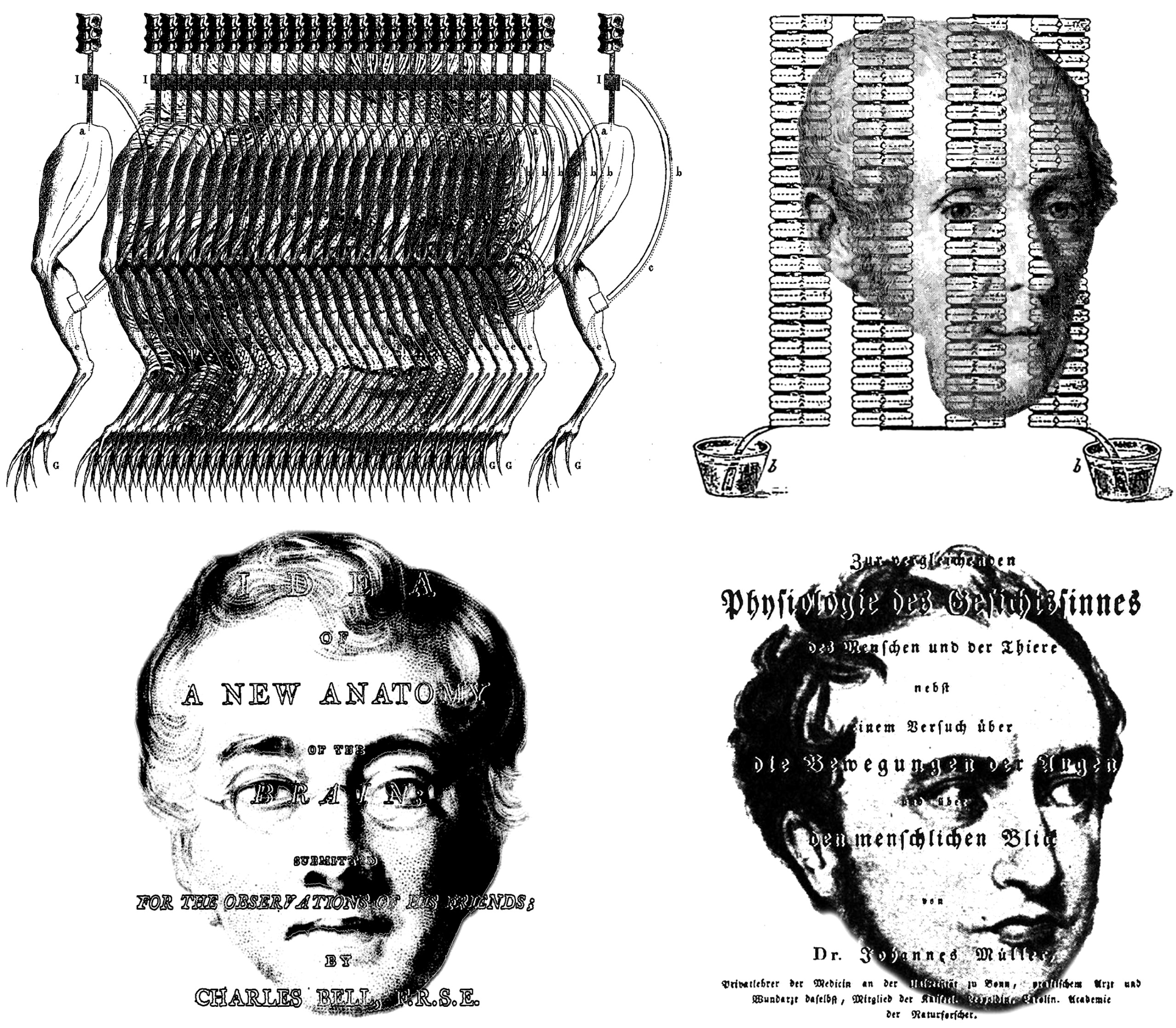


Fig. 2. - Upper left, *Galvani's frogs*, in which Luigi Galvani's portrait is combined with multiple images of his frog preparation. Upper right, *Volta's battery* shows a portrait of Alessandro Volta together with the stacked metal columns of his battery. Lower left, *Bell's Idea* shows Charles Bell and the title page of his privately published *Idea*, only 100 copies of which were printed. Lower right, *Müller's Vision* contains a portrait of Johannes Müller with the title page of his book on the physiology of vision and movements of the eyes; his initial description of the doctrine of specific nerve energies was given in this book (© Nicholas Wade).

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.

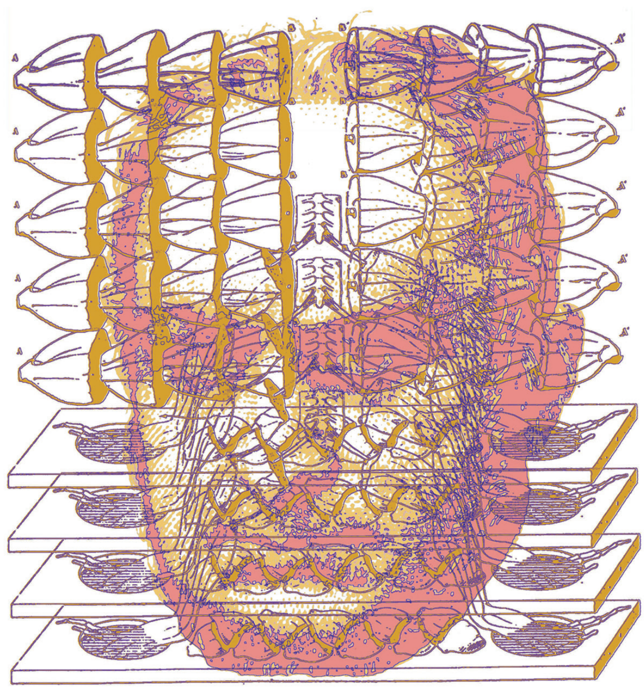
Volta's (1800) pile did much to hasten experimental studies of the senses. Electricity was a common stimulus that could be applied to different sensory organs, inducing different sensations. The link between energy and sense organs was forged soon thereafter. Charles Bell (1774-1842; Fig. 2) is noted 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).

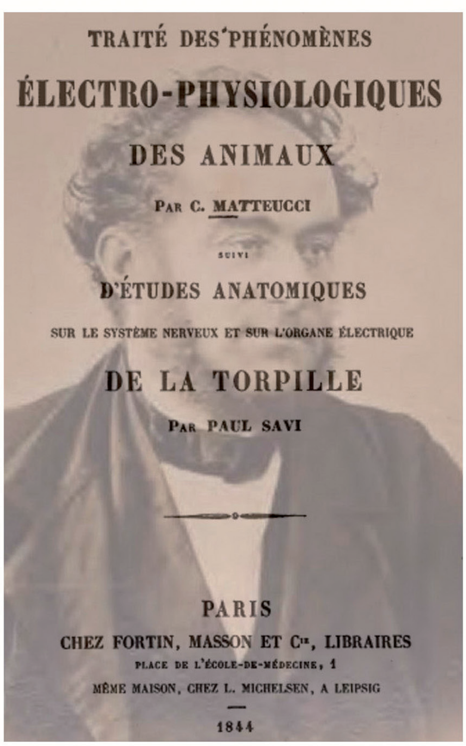
A similar sentiment, voiced with primary reference to the nerves and their pathways, was written a few decades earlier by John Hunter (1728-1793; 1786). The examples he gave to support this contention were the referred sensations arising after damage or amputation. The seeds of this idea can be found 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

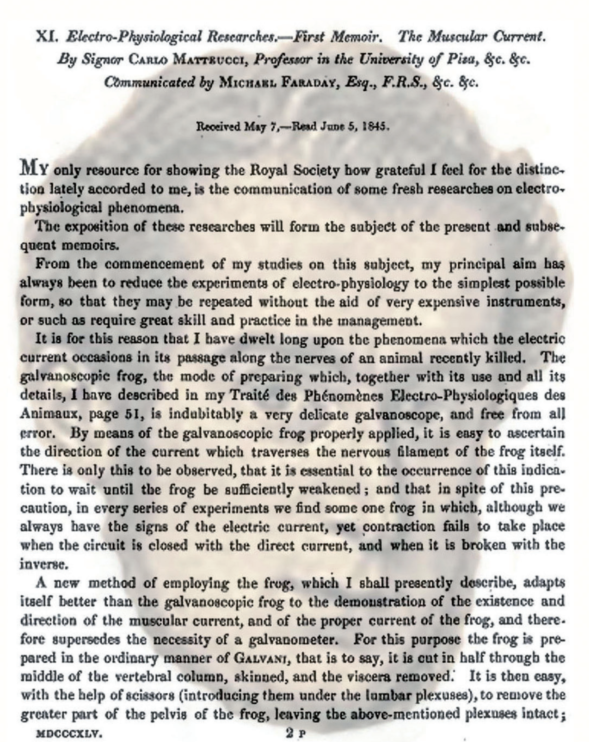
Matteucci was born in Forli and studied in Bologna, Paris, Florence and Ravenna. He was appointed professor of physics at the University of Pisa in 1840. The scientific ideas that excited him most were those based on the studies of Galvani and Volta. Matteucci extended the experiments of Galvani on animal 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





TRAITÉ DES PHÉNOMÈNES
ÉLECTRO-PHYSIOLOGIQUES
DES ANIMAUX
PAR C. MATTEUCCI
SUIVI
D'ÉTUDES ANATOMIQUES
SUR LE SYSTÈME NERVEUX ET SUR L'ORGANE ÉLECTRIQUE
DE LA TORPILLE
PAR PAUL SAVI

PARIS
CHEZ FORTIN, MASSON ET C^IE, LIBRAIRES
PLACE DE L'ÉCOLE-DE-MÉDECINE, 1
MÊME MAISON, CHEZ L. MICHELSEN, A LEIPSIG
1844



XI. *Electro-Physiological Researches.—First Memoir. The Muscular Current. By Signor* CARLO MATTEUCCI, *Professor in the University of Pisa, &c. &c. Communicated by* MICHAEL FARADAY, *Esq., F.R.S., &c. &c.*

Received May 7,—Read June 5, 1845.

MY only resource for showing the Royal Society how grateful I feel for the distinction lately accorded to me, is the communication of some fresh researches on electro-physiological phenomena.

The exposition of these researches will form the subject of the present and subsequent memoirs.

From the commencement of my studies on this subject, my principal aim has always been to reduce the experiments of electro-physiology to the simplest possible form, so that they may be repeated without the aid of very expensive instruments, or such as require great skill and practice in the management.

It is for this reason that I have dwelt long upon the phenomena which the electric current occasions in its passage along the nerves of an animal recently killed. The galvanoscopic frog, the mode of preparing which, together with its use and all its details, I have described in my Traité des Phénomènes Electro-Physiologiques des Animaux, page 51, is indubitably a very delicate galvanoscope, and free from all error. By means of the galvanoscopic frog properly applied, it is easy to ascertain the direction of the current which traverses the nervous filament of the frog itself. There is only this to be observed, that it is essential to the occurrence of this indication to wait until the frog be sufficiently weakened; and that in spite of this precaution, in every series of experiments we find some one frog in which, although we always have the signs of the electric current, yet contraction fails to take place when the circuit is closed with the direct current, and when it is broken with the inverse.

A new method of employing the frog, which I shall presently describe, adapts itself better than the galvanoscopic frog to the demonstration of the existence and direction of the muscular current, and of the proper current of the frog, and therefore supersedes the necessity of a galvanometer. For this purpose the frog is prepared in the ordinary manner of GALVANI, that is to say, it is cut in half through the middle of the vertebral column, skinned, and the viscera removed. It is then easy, with the help of scissors (introducing them under the lumbar plexuses), to remove the greater part of the pelvis of the frog, leaving the above-mentioned plexuses intact;

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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.

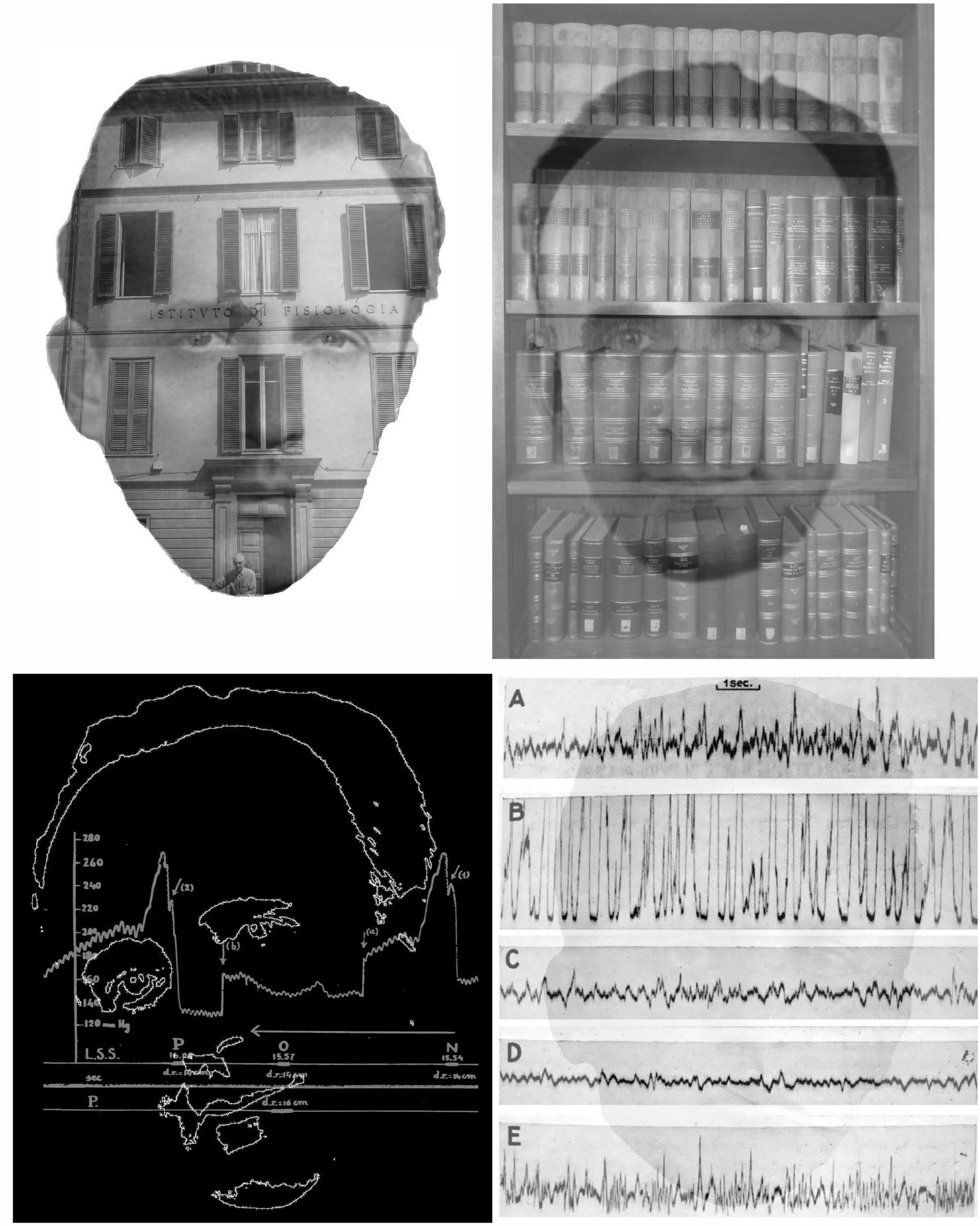

Fig. 4. - Upper left, *Moruzzi's Istituto*; Moruzzi's as a young man together with a recent photograph of the Instituto di Fisiologia, via S Zeno, Pisa. Upper right, *Moruzzi's library*; a portrait of the Professor with a recent photograph of books from his library in the Instituto. Lower left and right, 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).

IMPULSES IN THE PYRAMIDAL TRACT

By E. D. ADRIAN and G. MORUZZI[1]

From the Physiological Laboratory, Cambridge

(*Received* 28 *July* 1939)

Although it is easy to demonstrate the electrical activity of the brain we are still some way from understanding the full meaning of our records. This is mainly due to the complex structure in which the potential changes occur, though it is true that to simplify the conditions various means have been devised for recording from restricted areas, e.g. by micro-electrodes, multiple leads, etc. In the present work the problem has been approached from a different angle, for we have been chiefly concerned not with the potential waves in the cortex but with the impulses sent down the axons of cortical cells. These have been recorded by leading from the fibres of the pyramidal tract in the medulla: with suitable arrangements it is possible not only to study the composite discharge in many fibres of the tract, but to distinguish the impulses in single conducting units. We have, therefore, a method of determining the activity of the Betz cells in different conditions and we can compare the pyramidal fibre discharge with the potential waves in the motor area. The method has led to several unexpected but illuminating results. In particular it has been found that in the anaesthetized animal there is usually a continued pyramidal discharge which is infra-liminal for the motor nerve cells of the spinal cord, that the cerebral neurones can be made to discharge at extremely high frequencies with certain forms of stimulation, and that such discharges are to be found whenever there is a widespread excitation of epileptiform type.

METHOD

The possibilities of the method were discovered accidentally. It was known that axon potentials could be detected in the white matter of the cortex by an insulated wire electrode [Adrian & Matthews, 1934].

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BRAIN STEM RETICULAR FORMATION AND ACTIVATION OF THE EEG[1]

G. Moruzzi, M.D.[2] and H. W. Magoun, M.D.

Department of Anatomy, Northwestern University Medical School

Transitions from sleep to wakefulness, or from the less extreme states of relaxation and drowsiness to alertness and attention, are all characterized by an apparent breaking up of the synchronization of discharge of elements of the cerebral cortex, an alteration marked in the EEG by the replacement of high-voltage, slow waves with low-voltage fast activity. The magnitude of the electrical change parallels the degree of transition, and that most commonly observed in clinical electroencephalography is a minimal one, consisting of an alpha-wave blockade during attention to visual stimulation. Such activation of the EEG may be produced by any type of afferent stimulus that arouses the subject to alertness, or it may be centrally generated, but the basic processes underlying it, like those involved in waking from sleep, have remained obscure.

Recent experimental findings which may contribute to this subject have stemmed from the observation that EEG changes seemingly identical with those in the physiological arousal reactions can be produced by direct stimulation of the reticular formation of the brain stem. The following account describes such features of the response and its excitable substrate as have been determined, provides an analysis of changes in cortical and thalamic activity associated with it, and explores the relations of this reticular activating system to the arousal reaction to natural stimuli. Alterations produced by acute lesions in this system are presented in a succeeding paper. The effects of chronic lesions within it are under investigation.

METHODS

The experiments were performed in cats under chloralosane anesthesia (35-50 mgm. K. intraperitoneally) or in the "encéphale isolé" of Bremer, prepared under ether, with exposure margins infiltrated with procaine. Ephedrine was administered intravenously immediately after transection of the cord at C 1. At least an hour elapsed after ether was discontinued before work was begun.

Concentric bipolar electrodes, oriented with the Horsley-Clarke technique, were used for stimulation of, or pickup from, the brain stem. Condenser discharges from a Goodwin stimulator were employed routinely. Lesions were made surgically or electrolytically, and their positions, together with those of electrode placements, were verified histologically.

Potentials were recorded with a Grass model III amplifier and inkwriter. Some cortical records were taken directly from the pial surface, but usually as much of the brain case as possible was left intact, and most cortical pickups were between two screw electrodes, 5-10 mm. apart, inserted through burr holes in the calvarium until their tips rested on the dura overlying functional areas. With bipolar leads and by grounding the scalp, stimulus artifacts were negligible. Other technical details are given in the legends.

[1] Aided by a grant from the National Institute of Mental Health, U. S. Public Health Service.
[2] University of Pisa, Italy. Visiting Professor of Neurology, supported by the Rockefeller Foundation.

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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 the 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.

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