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Angelo Mosso: a holistic approach to muscular fatigue

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ABSTRACT

Angelo Mosso (1846-1910) was an Italian physiologist who significantly contributed to the development of all fields of modern physiology. Mosso believed that "with the graphical method the palpitation of the heart, the breathlessness of the breath, the tremor of the muscles, the velocity of the blood, the word, the perception they leave of themselves are indelible traces". Mosso's main aim was to exactly measure man's muscular work. In this way Mosso had constructed an instrument that could exactly measure the workman's muscle mechanics. He called this instrument the ergograph which means work recorder. He was a fervent promoter of the pedagogic importance of physical exercise and training in the psychophysical development of adolescents. For Mosso fatigue and training represented the basis of sports, and in the speech delivered at the Olympic games in Roma in 1905 he declared: "In muscle resistance to fatigue lies most of the future richness of our Country". Indeed, he wrote: "I believe that pedagogy, just like medicine, is an art and it serves to help nature". Importantly, Mosso tried to join philosophical and psychological studies with biological studies. This holistic approach is now commonly adopted in cognitive neuroscience, and it is resurging in exercise physiology. This "maestro" is a shining example of a great scientist, and his legacy will continue across future generations.

Key words

History of Physiology • Mosso • Fatigue

"A science is not understood until
its history is known"
Auguste Comte

The International Society for the History of Neuroscience, the Scuola Normale di Pisa, the History of Science Museum in Florence, and the universities of Ferrara, Pavia, and Paris have decided to organize a conference called "From Carlo Matteucci to Giuseppe Moruzzi: two centuries of European Physiology". Professors Cesira Batini, Marco Piccolino, Jean Gael Barbara, Michel Meulders and Nicholas J. Wade all wanted to stay at Villa Corliano in Pisa in order not to forget the past but be stronger and in the hope that the scientific spirit might be shared with future generations. Angelo Mosso was a physiologist at the University of Turin who strongly influenced the historical development of Physiology in both Italy and internationally (Di Giulio et al., 2006). New scientific scenarios appeared in his historic times, and the ideas of Mosso reappear with unmistakable topical interest.

Angelo Mosso was born in Turin on the 30 May 1846 and grew up in Chieri near Turin during the years following the unification of Italy (1861). In 1864 he enrolled in the Faculty of Medicine and before he graduated, he taught Natural Sciences in Chieri High School. He graduated Magna cum Laude in Medicine and Surgery on the 25 July 1870 presenting a thesis in physiology on the

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growth of the bones under the supervision of Prof. Jakop Moleschott. In August 1873 he joined the Physiology Laboratory of Moritz-Schiff (1823-1896) in Florence where he stayed for two years followed by another important two-year period at the Institute of Physiology in Leipzig in Germany under the direction of Carl Friedrich Wilhelm Ludwig (1816-1895) where he studied respiratory gasses and the graphic recording of respiration. Luigi Luciani (1840-1919) preceded Angelo Mosso at the same Institute, studying for two years in 1872 and 1873. Several tracings obtained using a kymograph were given to Mosso by Ludwig, and Mosso then began to record the volumes of the limbs using the manometer of Ludwig. Mosso went to Berlin in 1875 to meet E. Du Bois Reymond (1818-1896) and E. Brucke (1819-1892) who had been students of J. Muller (1801-1858). Brucke taught and was Professor of the Physiology of Freud (1856-1939). Angelo Mosso felt that "using the graphic method the heart rate, breathlessness, muscle tremor, velocity of blood flow, words, and perception all leave an indelible trace". Before returning to Italy, he stayed in Paris for several months where he got to know the French experts Claude Bernard (1813-1878), Charles Edouard Brown-Sequard (1818-1894), and Antoine Ranvier (1835-1922). Mosso became a friend of Etienne-Jules Marey (1830-1904), a leading expert in graphic recordings and photographic techniques who had a strong influence on the career of Mosso. Marey was a friend of Claude Bernard and the artist Degas. Degas got the idea for his sculpture of the ballerina from the physiological studies of movement made by Marey and the first one was sculptured precisely for the Institute of Physiology in Paris. In 1875 Mosso was appointed Professor of Pharmacology in Turin and at the age of 33 replaced Moleshott to become Full Professor of Physiology in Rome. As a result of not getting this job, Moleschott's assistant Dr. Rubini had to move to the chair of Pharmacology. The eclectic Mosso combined his social and scientific interests with a love for work and the physiology of man "to heighten the refinement of the soul in the strength of the body". Being enthusiastic, optimistic, and permeated by the positivist culture of the times, he built up a great school of Physiology in Turin. He was awarded the Royal Prize of the *Accademia dei Lincei* in 1879 and became a member in 1882. In the first lecture he gave on the university course, Mosso said: "The evolution of mechanics is reducing man's muscular work, which in saving strength, improves the abundance and effectiveness of intellectual work" and furthermore how "mechanical machines" could increase the intellectual needs of individuals because they reduced the amount of time devoted to physical work. Gabriele D'Annunzio, the poet from the Abruzzo region of Italy, wrote in "A Party for Science": "Let's learn about the method of physiology so that the art will also produce healthier fruit". D'Annunzio had already shown his interest in the work of scientists in his first novel *Il Piacere* (Pleasure) published in 1889 so much so that in the days of his youth the only lecture he diligently attended at the University of "La Sapienza" in Rome was that of Physiology. The relationship between D'Annunzio and Mosso became so close that D'Annunzio developed a passion for physiology. D'Annunzio wrote: "Physiology is not a science that has exhausted all its possibilities... but develops every day. It is consolidating…and is destined to absorb the arts of other sciences". Mosso and D'Annunzio shared the same publisher, Treves, and the marriage of Mosso to Maria Treves meant he could consolidate his links with the Publisher.

Mosso played a role in the reorganization of the academic world. At that time Humbold taught in Bologna, and Moleshott became director of the Institute of Physiology in Turin in 1861. In the twenty-five years under the direction of Mosso, the Institute of Physiology in Turin saw the arrival of a great many renowned researchers such as Warren Lombard (1857-1939), Sherrington (1857-1952), Wood, Harley, Rosenthal, Ferrier (1843-1928), Richet, Von Frey (1852-1932), Cushing (1869-1939), and Tunnecliffe.

Mosso developed an interest in the brain that led him to study "the physical basis of the mental functions" correlating cerebral circulation with mental physiology connected to the distribution of blood in the brain. The plethysmograph tracings showing the hematic redistribution between arms, feet, and brain demonstrated to Mosso that "the brain becomes redder during emotions". Mosso attempted to combine philosophy and psychology with biology. He taught various Italian psychologists such as A. Gemelli and M. Ponzo. Mosso played a part in the difference between the organic and inorganic world disappearing through the entry of physics and physiology into psychology. He promoted experimental psychology by setting up the first three chairs of Physiological Psychology, the first was in Turin followed by Naples and Rome. In this job application process Mosso was part of the job selection committee with his colleagues Golgi, Morselli, Tanzi, and Aducco. The winner of the chair at Turin was Federico Kiesow (1858-1940) who had been assistant to Wund in Leipzig and had initially moved to Italy to be assistant in Physiology in Turin with responsibility for Psychology (Sinatra, 2000). Mosso tried to get physiology and physics to converge with the psychological, and in the "Study of the Physiology of the unhealthy" he asserted that pathology might be combined with physiological research. Mosso preferred to work directly on people rather than stimulate muscles removed from the bodies of animals, correlating the motor phenomena with physical, intellectual, and emotional activity. In the "Fear" in which he used the plethysmograph to measure changes in the volumes of organs, he described the physical correlates of fear. Lombroso himself confirmed the hypotheses of Mosso by applying new techniques to the study of the anthropology of criminals.

Mosso was not only concerned with Physiology but also combined these studies with pedagogy, and in fact wrote: "I believe Pedagogy, like Medicine, is an art and serves in helping nature". In *Mens Sana in corpore sano* he suggested education should integrate physical education and study. His commitment to physical exercise in schools was great. In fact, in support of the idea of returning to the traditional Greco-Roman open-air games to improve physical performance.

His friendship with the scientist and politician Quintino Sella who founded the Italian Alpine Club contributed to the studies Mosso made of the effects of altitude and mountaineering on fatigue experienced by climbers. In 1882 he started the *The Italian Biology Archive*. Then he published *La Paura* (Fear) in 1884, followed by *La Fatica* (Fatigue) in 1891, and *The Physiology of Man on the Alps* in 1897. At the first International Congress of Physiology held in Basle in September 1889, Mosso demonstrated muscular fatigue by using the ergometer. The fifth International Congress of Physiology in Turin (17 to 21 September 1901) had Mosso as its president and among those taking part were Helmholtz, Brucke, Ludwig, Du Bois Reymond, Foster, Marey, Lucani, Magnus Blix, Zunt, Flechsig, and Golgi.

Mosso became rector of the University of Turin for the 1899-1900 academic year, and four years later became Senator of the Kingdom thereby being able to translate many of his own ideas into laws of the State (Losano, 1996). One idea of Mosso was made into reality with the help of the King, the Department of Education and Science and the Italian Alpine Club when in July 1904 work began at 2901 meters above sea level on the Col D'Olen to develop a busy biological, medical, meteorological, and geophysical research station, which was inaugurated in August 1907 (Herlitzka, 1937; Di Giulio, 1993). During the seventh International Congress of Physiology in Brussels in 1904, Mosso presented the "Monte Rosa Physiology Laboratory" and its work on muscle fatigue. It was decided on that occasion to dedicate the "Col d'Olen" building to Angelo Mosso as a promoter of and reference for Alpine Physiology. Many physiologists including John West, Sukhamay Lahiri, and Jim Milledge visited the Monte Rosa laboratory on the centenary of the Capanna Margherita (4559 m a.s.l.) in August 1993. In June 2000 a fire caused by lightening destroyed the building on the "Col d'Olen". Since then, a series of recovery projects have brought teaching and research structures back into being again.

In the last few years of his life, Mosso changed his field of interest and concentrated on anthropometric studies, dedicating his scientific curiosity to the "origins of Mediterranean civilization" and began excavating in Crete in 1907. He also took part in excavations in Sicily at Tarquinia, in Apulia at Molfetta, Terlizzi, Manfredonia, and Bisceglie discovering necropolises, dolmens, and collecting ceramics. Thanks to his friendship with D'Annunzio, his passion for archeology took Mosso to the Abruzzo where he developed his final archaeological studies in the Province of Teramo, as mentioned by Luigi Luciani in his commemorative address "only one piece of information is missing, that concerning the last excavations carried out in the Valle della Vibrata. Death has hit our illustrious colleague in the days just when he was preparing himself to account for the fruit of his latest archaeological campaign".

After the sudden death of Angelo Mosso, the material found in the various sepulchers was collected together after 1930 by Ugo Rellini in a prehistoric section in the Museum of Ancona, which included "The oldest ceramic painted in Italy".

Angelo Mosso died on the 24 November 1910 at 64 years of age. He was consistent, strong-willed, and hard working, committed to the spiritual and physical well-being of the population. With the passing away of Mosso in 1910 "the golden half-century of Turinese medicine" that began with the arrival of Moleschott in 1861 came to an end. There have been many criticisms but Mosso was a product of his time with so many interests as to be a polymath. Generally speaking the "hypercritical critics" are those who have done little in their lives and are very judgmental. In contrast, the city of Chieri dedicated a school and a piazza in memory of Physiologist and Archaeologist Angelo Mosso 1846-1910.

The scenario for the appearance of "Fatigue"

Fatigue by Mosso was published by Treves in 1891 and had a double identity: firstly, social commitment and secondly, popularizing scientific findings. Mosso dedicated this book to "Ugo Kronecker, Professor of Physiology at the University of Berne, with the gratitude of a disciple and the affection of a friend". *Fatigue* was a great success from its initial publication and it enjoyed a good seven reprintings up to 1936. The book was read around the world, being translated into German in 1892, Russian in 1893, French in 1894, and English in 1904.

This was a book that affected doctors, politicians, sociologists, entrepreneurs, scholars, and revolutionaries because it confronted scientific, cultural, sociopolitical, medico-psychiatric, and pedagogic themes and ideas. Its dissemination during the second half of the nineteenth century, a period in which *social development* was subject to scientific research, especially that the perception of the "riches of the community of workers" and of "laboring work" was considered to be cardinal in the development of a new industrial society (Nani, 2001). At that time the Kingdom of Italy was an agricultural country with serious problems: poverty, high infant mortality, health crises, and diseases such as tuberculosis, pellagra, and malaria. He initiated "Psychotechnics", the interaction between science and factory for laborers and miners, becoming the basis for a set of work ethics. Explaining physical exhaustion and neurasthenia of the workers was a sort of physiology of daily life in the relationship between hours of work and fatigue, forming the basis of a *Physiology of Work* through the coming together of several disciplines, especially Hygiene, which gave rise to modern *Medicine of Work.*

Training and fatigue were the basis of sport for Mosso. In his speech to the Olympic Games held in Rome in 1905, he suggested that in muscle resistance to fatigue lies most of the future riches of our country and how physical exercise and training should have a pedagogic value in the psychophysical development of young people. As "defender of sport" Angelo Mosso founded the *Scuola di Ginnastica Medica* (Medical Gymnasium School) in 1897 and in 1898 promoted the first National Congress of Physical Education for which he proposed the "First Football Championship". His idea of writing a popular tract on physiology was then forgotten among his new interest in physical education, games, and in research into fatigue and physical exhaustion: "the children strongly feel the impulse that drives them into movement" needing to avoid fatigue of the brain, especially needing to avoid sitting down for too long when at school. Due to their shared respect for young people, Mosso became a very close friend of Edmondo De Amicis, the author of *Libro Cuore* (The Heart Book).

Many mentors contributed the birth of ideas in Mosso at the time: Prof. Schiff who he stayed with in Florence, and Helmoltz, Muller, Virkow, Moleshott, and Ludwig. Using his kymograph stylus to record vital phenomena graphically, Ludwig changed international physiology in 1846. Helmoltz used the kymograph to study the muscles of the frog and, using progressive methods, Mosso managed to measure the temperature, variations in the arterial pulse, and respiratory activity in marching soldiers, and so the relationship between exercise and science grew ever closer.

Fatigue

Mosso aimed to measure mechanical work carried out by man accurately. The first chapter of his book entitled *Fatigue* begins with an analysis of the migration of African birds (quails, swallows, cranes, and storks) and the extreme degree of fatigue (tiredness) they exhibited after nine hours flight. Furthermore, Mosso presented a study of military pigeons that reached Sardinia from Rome in five hours. These methods were very similar to the interests of Marey who in studying movement found analogies between birds and the human arm. Mosso set up a station of homing pigeons in his laboratory that he studied for twelve years. His experiments showed that from the sixth year of life, the stamina of the pigeons in flight decreased, therefore sensing that ageing caused a reduction in the maximum consumption of oxygen and fatigue resistance. He also described the decline of physical capacity and intellectual ability in man with ageing: "The elderly are obliged to slow down and above all not use willpower to force themselves". As such Mosso was the precursor of modern gerontological studies of sarcopenia in the elderly.

It was Marey who made the use of graphic methods in Medicine popular, differentiating the "latent excitation time" between the electrical excitation and the contraction. As a supporter of mechanical recording, Mosso wrote: "the graphic method reproduced the minute details of movement and shows us phenomena that would otherwise remain unknown and confused".

In his book *Fatigue*, Mosso proceeds to analyze the origin of muscle strength, starting with the notes of Helmoholtz on the relationships between heat, work, and energy transformations. This is the context in which he studied the effects of anemia on the muscle and on the brain, and at the same time studied the effect of the emotions on cerebral circulation in an attempt to "scientify psychology" relating everything to the material functions of the organism. The case of "Signor Bertino" who presented with a two cm wide aperture in the frontal region remains a special case. Mosso covered it using gutta-percha. He placed a glass tube inside the aperture connected to a plastic tube so as to transmit the movements of the brain to a hydrosphygmomanometer

Mosso built an instrument that could measure the mechanical work performed by the human muscle accurately and gave it the name "ergograph" which means *work recorder.* The ergograph records the isotonic contractions and the transcription of muscle work into mechanical work using the flexor muscle of the middle finger. Up until then graphs of fatigue only described the maximum degree of isometric muscle tension while the ergograph was composed of two parts, one that held a hand approximately 50 cm long and 17 cm wide and the other that transcribed the isotonic contractions. The problem lay in isolating the work of the muscle, fixing the hand using two brass tubes with internal diameters between 18 and 22 mm depending on the size of the finger belonging to the person being studied. The index and annular fingers of the right hand were introduced into the two tubes while the middle phalanx of the middle finger was inserted into a leather ring connected to a cord made of gut similar to that used to make cello strings. At the end of this cord was a 3-4 kg weight that was attached via a pulley so that the stylus could record the degree of flexion of the middle finger on a rotating cylinder following the rhythm of a simple pendulum or metronome. The smoked paper turned slowly following a clock and graphically recorded the various fatigue profiles of the experimental subjects placed in the same conditions of weight and rhythm. After 45 muscle contractions there was a slow decline until the sudden cessation of the contraction itself, "through the ergograms the ergograph provided us with the written evidence of the more detailed characteristics of an individual and how some resist work and others suddenly stop, that is to say, the way in which we get fatigued".

Study of ergometry made it possible to deduce individual laws of fatigue and construct "occupational guidance", the "vocational psychology" for the new generations so as to direct the young according to their own particular characteristics, attitudes, inclinations, and temperament into manual or intellectual work: "just as some find a short walk tiring, others do 100 km without a break. Some get drunk on a glass of wine and a cup of coffee prevents them from sleeping the whole night. In resisting work some men suddenly feel tired and stop, others use their strength a little at a time". The start of human classification was based on the anthropometric characteristics to condition the career choices made by the young.

Mosso devised a plethysmograph to measure and graphically transcribe the changes in volumes that occur in the organs of the human body as a result of the pulsations and flow of blood. He modified a great many instruments of the time such and the pneumograph and the hydrosphygmograph, he designed a *bed scale* to measure changes in the distribution of blood between the cephalic and podalic parts of the body. Furthermore, he modified the ponometer to obtain graphs of nervous effort that increased fatigue. He constructed the "myotonometer" to measure muscle tonicity in which the subject sat with their legs suspended with their feet lower than their heels, measuring the angle formed between the sole of the foot and the vertical line of the leg, setting the tension of the tricep muscle by progressively applying heavier weights. Sometimes Professor Mosso took his students and assistants to horse riding schools and stables to study the relationship between the pace of the quadripeds and their respiratory rhythm in response to physical exercise or to see rowers in their boathouse to study fatigue in the oarsmen. Any place could become an experimental laboratory including the slaughterhouse where it was possible to record the thermal graph of the bovine liver after death, and the scholastic classroom to record the temperature of a lecturer after the pressure and agitation of a lecture, or of marching soldiers.

Using the ergograph and stimulating the muscle with direct current without the person using their will i.e. independent of volition, he was able to distinguish a central and a peripheral psychic fatigue corresponding to the transformation of chemical energy in the fiber during mechanical work. Central fatigue, purely nervous and relating to the will, is an internal sensation that disappears by degrees: "it is not the will nor the nerves but the muscle that is fatigued following intense work by the brain".

Mosso correlated the rhythm, time, and weight it takes for fatigue to develop, calculating the load with which the maximum effect is obtained in the same conditions. He established how every individual presents a typical fatigue graph under both voluntary and electrical muscle stimulation. The circumstances that influenced the line on the ergograph related to atmospheric pressure, temperature, time of day, and also to the nutritional state of the subject and whether or not he or she were jejunum. Mosso correlated diet and the administration of foodstuffs with the ability of the muscle to carry out work. In particular, he identified how sugar may restore muscle capacity diminished by work. He studied the effect of the seasons on fatigue and the emotions at various ages, the action of intellectual fatigue on muscle fatigue, and the increase in strength as a result of training. He described the training effect of doubling muscle strength and the effect of muscle fatigue on muscles directly stimulated by electrical current without an act of will. Furthermore, he studied the correlation between manual and intellectual work, the extreme ease with which the brain gets tired, and how cerebral superwork may influence physical fatigue and vice versa, stating: "I noted that my muscle fatigue made me pay less and less attention until I paid none at all and it weakened the memory to the point where I could no longer remember it". In addition, Mosso demonstrated the relationship between attention and resistance to tiredness and how excessive muscular effort inhibits the ability to think so that he proposed the rationalization of physical education in schools. He studied the effects of fatigue on visual acuity, the perception of colors, and one's own ability: "fatigue produces an excitement that generates the mistake of believing yourself to be stronger than you are". Practice and habit make us more resistant to cerebral and muscle fatigue as Mosso confirmed: "I have seen extremely robust soldiers sweat with a large pen in their hands… cerebral work for those who are not used to it results in more tiring work for the muscles. There are well built and robust people for the development of muscle strength who are incapable of any intellectual work whatsoever".

In revisiting the studies of Lavoiseir and Spallanzani, Mosso not so much researched into the causes of fatigue from the point of view of lack of oxygen but from that of the production of toxic substances such as carbonic acid, showing how muscle fatigue as a process might be chemical in nature. He noted how washing the muscle of frogs directly with physiological solution eliminated the tiredness, probably by removing "an X factor" of a typically chemical nature. The concept of fatigue as poisoning had already been mentioned by the physiologists Pfűgler and Zuntz. These consumption products of muscle activity act as toxic substances causing tiredness and muscle exhaustion. Mosso carried out an experiment on a blood sample taken from a dog that was anesthetized and tired after tetanic stimulation and injecting it in another dog induced the respiratory and cardiac symptoms of fatigue. Elimination of CO_2 and reduction of lactic acid form the basis of changes in respiratory frequency and even at that time Du Bois-Reymond had already demonstrated how the fatigued muscle would be acidic while a rested muscle would be alkaline.

The progressive reduction in excitability and attitude to work during fatigue is described by Mosso in the laws of *muscle exhaustion*:

1) Muscle fatigue should be considered as a peripheral phenomenon that is independent of the will but at the same time there is in a holistic relationship between energy in the nervous centers and fatigue.
2) Fatigue should be considered as a form of "poisoning " due to the production of waste material that blood flow and respiration tend to remove.
3) The presence of carbonic and lactic acid impedes and reduces muscle contraction.
4) Fatigue reduces muscle sensitivity and the general sensitivity of the body.
5) Fatigue represents the "alarm signal" for muscles, the trigger point to clean up the "dross" and to recover the loss of energy immediately during strenuous contractions.

In other words, the differences between physical and intellectual work disappear. Mosso stated: "there is only one fatigue, the nervous […] even muscle fatigue is fundamentally fatigue from exhaustion of the nervous system".

In the tenth chapter Mosso described the relationship between attention, human intelligence, and fatigue. He studied the subjective sensation of fatigue by applying the psychophysical studies of Fechner on sensitivity thresholds. We only have one word to describe fatigue but fatigue is the result of a subjective internal sensation, sometimes vague, undecipherable, and not easily quantified. When fatigue exceeds certain limits, whether as intellectual or muscle fatigue, it produces changes in the mood of the individual. Mosso also studied how attention could be strictly connected to motor phenomena. Moreover, he proved that inability to concentrate was caused by muscle fatigue and vice versa. Consequently, muscle fatigue in Alpine climbers resulted in all concentration being lost as well as memory loss, with Mosso stating "I have been to the top of Monte Rosa twice and I cannot remember anything of what I saw from the summit. It seems that in poisoning the blood with the products of fatigue, thought and memory become more difficult". In fact, fatigue influenced the reaction time to a stimulus comparable to the effects of cocaine or alcohol. The question was how much could we work without getting tired? "Virgil, Pascal, and Leopardi who seemed to be physically underdeveloped were wonderful with their brains".

Using the ergograph in the mountain, Mosso demonstrated the differences in the tracings of the same individuals recorded in Turin and then in the mountains. He proved the precocious occurrence of muscle fatigue with altitude. These studies were then used as a basis for discovering that the maximum consumption of oxygen decreases with age. He used the ergometer to observe himself when he was 64 years old in order to study acclimatization to altitude during aging and muscle fatigue.

Mosso investigated the fatigue of lectures and examinations: "there are professors who are averse to presenting themselves in front of many students. Some are shy and confused at first, some suffer nausea and are sick just before the lesson, others shake, visual acuity deteriorates".

Mosso noted a considerable decrease in muscle strength after two hours of examination and demonstrated that the initial 53 muscle contractions decreased to 12 contractions, an effect that continued even two hours after the lecture as if there had been no recovery.

Talking of teaching, he stated: "there are also professors who improvise, abandon the terrain in the manuals, and those who listen to them feel your emotion […] These are the hours that make you feel younger in which you feel the sacred fire of the school, in which you can be certain no tract, no book can substitute or equal its educational effectiveness. A lot of people know that after intensive intellectual work, you feel uncertain in your arm and leg movements, and Mosso confirmed this idea: "fatigue of the brain decreases muscle strength".

The description of periodic breathing at altitude by Mosso also correlated high altitude hypoxia with carbon monoxide poisoning. He studied the relationships between apnea and acapnia, the latter being a term that he himself coined. He demonstrated the increased presence of periodic breathing in children and the elderly when they are asleep and how this disappears with inhalation of CO_2 and not O_2. Furthermore, he demonstrated how altitude sickness (mountain sickness) might be more serious during sleep since less CO_2 is produced during the night due to muscle inactivity. Furthermore, he proposed supplying balloonists (aeronauts) with compressed oxygen containing 8% CO_2. He studied the relations between carbon monoxide intoxication and mountain sickness, and felt that mountain sickness occurs due to a lack of carbon dioxide (acapnia), and not because oxygen availability decreases, a conviction that caused arguments with Paul Bert. Mosso had an iron decompression chamber constructed within his laboratory so he and his colleagues could be subjects as they studied the process of air rarefaction. His daughter Mimi Mosso described that his father reached more than 8000 m of altitude in the chamber (Mosso Mimì, 1935).

Twenty-three letters by Mosso to his mentor Moleschott are preserved in the Archiginnasio of Bologna. In one of these, written at the time of the publication of the book *Fatigue*, Mosso says; "I am happy that you are my teacher and that my mind has been unlocked under the breath of your words […] If my writings manage to make a contribution because they keep the attention of the public on the great ideas of physiology alive and might continue the tradition of your school, I will be the happiest of your followers".

In the hope that the scientific spirit of Angelo Mosso may be shared by future generations, I would like to conclude by reporting one of his on regarding didactics found in his book Fatigue: "The new ideas and concepts expressed by you at that time, by the voice you heard in the lecture hall, will discuss new horizons in the minds of the young who listen to you, and they will endure in some of them as an affectionate memory for all of their lives, and it will raise the hope in you that glory will perhaps shine from one of these young minds, for which you aspired in vain".

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