

## **M. Bulletti <sup>1</sup>, The Advance of the Geometric Structure of the Brain (GSB) and the Optogenetic Rehabilitation in the Coma**

**1. Background.** The first conception of the Geometric Structure of the Brain was found out by the author in March 1983. **2. Aim.** The discovery has occurred during the rehabilitation of coma patients with spastic quadriplegia caused by different pathologic etiologies. **3-4. Method and Results.** The technique consists in light stimulations with eight 3V torches, one with white light and seven with the solar spectrum colors, in a rigorous bio-feedback, with reactions that followed the sequential order of the Cartesian coordinates x, y, z. The technique has been applied only to coma patients. Here it is presented the first case completely rehabilitated in 6 months and presently normal: an 11 years old boy in a second grade (GCS) coma affected by hydrocephalus surgery after-effects, with severe neural suffering, spastic tetraparesis with hypertone and hyperflexia and the insertion of a cannula for the tracheotomy in situ. CT showed, amongst other things: ventricular dilatation, on the left side, presence of a hypodense collection, apparently hypertensive, in the frontoparietal lobe and another hypodense collection in the right parietal lobe. **5. Discussion.** The study and the monitoring of the 3 phases of the rehabilitation could unveil cerebral aspects still unknown in optogenetics and explain inherited dynamics of brain's plasticity which obligate an accurate study, to this day neglected.

### **0.1. Introduction**

After the publication on April 2014, in Science, of the article by Karl Deisseroth et al. *Structure-guided transformation of a channelrhodopsin into a light-activated chloride channel*, are evidents the optogenetics studies from basic biology to the mammalian<sup>2</sup>. In my sperimental investigation are obtains incredibles results but in the human, results that want be placed in the light with a proper research. As a consequence we have considered worthwhile to publish this work of ours, which is a study of human experimentation. In this article, Methods, Results and Discussion are presented in a

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<sup>1</sup> Psychotherapist, Via Francesco Alunni Pierucci, 33 -06132- Perugia (ITALY), mail: info@mariobulletti.it, phone number: +39.075.517.0599, mobile: +39.348.8243663.

<sup>2</sup> A. Berndt - S.Y. Lee - C. Ramakrishnan - K. Deisseroth, *Structure-guided transformation of a channelrhodopsin into a light-activated chloride channel*, in Science, April 2014, 344 (6182): 420-4.

synchro-diachronic series in order to provide the reader with a more functional and direct reading that occur so gradually recovering from the asperities of contextualization.

We are presenting an original research about the first discovers of the GSB. In the future we would like to use this technique to rehabilitate patients who have the same situation. At the same time, the computation of the sequence of the optogenetic stimulations which shape the technique can be used as a digital paradigm for the regulation of a computerized system that reproduces the functioning of the human brain.

The medical reports of the last two computerized tomographies (CTs), before A. Leonardo's hospitalization, showed: 'Ventricular dilatation. Catheter in situ on the level of the right occipital horn. Presence of drill holes at the level of the right parietal bone, due to a previous treatment for a bilateral subdural haematoma. On the left side, presence of a hypodense collection, apparently hypertensive, in the front-parietal lobe. Another hypodense collection in the right parietal lobe. The report of the current examination is similar to the one of the previous tests (11368); there is also a significant ventricular dilatation here; the hypodense collection is still in the left front-parietal and on the right parietal areas.

According to Glasgow Coma Scale (GCS), the clinical test showed the following responses in Leonardo: Eyes 2: 'opens eyes in response to painful stimuli', Verbal 1: 'makes no sounds', Motor 3: 'abnormal flexion to painful stimuli (decorticate response)'. Therefore, with a total of 6 points out of 15, the patient was in a coma of second grade in a scale from 1 to 5, in which the lowest grades mean the most serious illness. As a result, the clinical examination also showed a spastic tetraparesis with hypertone and hyperflexia, and the insertion of a cannula for the tracheotomy in situ. Once the effectiveness of this rehabilitating technique was satisfactorily proved, the same technique was repeated in the neurochirurgical clinic and in the intensive-care unit (ICU) of the Regional Hospital of Perugia (Italy). There were 21 patients treated: seventeen had different traumatical pathologies of the brain, one patient with non-traumatic etiology, that's to say, a haemorrhage of the cerebral trunk and three who were transferred to another hospital before fulfilling a ten-days treatment. The 18 treated patients experienced a very fast total rehabilitation: from 6 months of Leonardo's case to three years of the patient who had suffered a haemorrhage of the cerebral trunk. With a certain frequency, the rehabilitation time was proportionally related to the seriousness of the illness. When the experimental work finished, we also did a regular medical supervision of some patients for a long time. There was a computer technician, a nurse, a truck

driver, a university teacher of Maths and a farmer. After 25 years, they had an absolutely normal psycho-physical situation and a good social integration.

The international restaurant chain manageress was the only case of a complete social integration, who died of a cause external to the haemorrhage of the cerebral trunk.

This optogenetical technique has often been repeated by other specialists, always with higher results than expected.

At this moment, the author can state that the technique has had so positive results because he followed the correct itinerary prefigured by the Cartesian co-ordinates  $x$ ,  $y$ ,  $z$ . These co-ordinates are orthogonal exactly as the axis of the GSB described by Wedeen et al. (Wedeen et al 2012)<sup>3</sup>. Besides, according to the author's research, which has not been discovered up to now, the spastic tetraplegia of the patients disappeared when the optogenetic stimulation connected their responses positively in the vertical axis  $z$  of the Cartesian co-ordinates. The same patients started recovering their mental functions.

## **0.2. An Introduction to the Optogenetic Technique 'Leonardo' by Mario Bulletti**

The light stimulations were done in a dark room, using eight 3-volt torches. The first one emitted a white light and the other ones emitted a colored light with films which reproduced the seven colors of the rainbow in the following order: red, orange, yellow, green, light blue, indigo and violet. The light stimulation had a response from the patients in coma when it beat on the front-back axis of the Cartesian axis  $x$ . At the beginning there were only responses in this axis. There weren't any responses in the horizontal Cartesian axis  $y$ , or in the vertical Cartesian axis  $z$  of the homonymous co-ordinates. As the time passed, it was checked with every patient, that everyone responded to the light stimulations only in this compulsory sequence  $x$ ,  $y$ ,  $z$ . Afterwards, when there was a response to the first phase of beating stimulation, the stimulation with permanent light could go on. It's relevant to say that the stimulation was in a dynamic relation to the positive responses from the patients. The dynamics was consequently organized according to a compulsory feedback managed

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<sup>3</sup> V.J. Wedeen - D.L. Rosene - R. Wang - G. Dai - F. Mortazavi - P. Hagmann - J.H. Kaas, W.I. Tseng, *The Geometric Structure of the Brain Fiber Pathways* (2012) Science 30; 335 (6076): 1628-34.

by the patient. The course followed this pattern: a) stimulation, b) acceptance of the stimuli, c) response to the stimuli, d) extinction of the response to the stimuli, e) a new stimulation with a different color, f) acceptance of the procedure of the new stimuli and repetition of the successive previous steps. The objective of the method used in every sequence was to avoid therapeutical insistence on an already strong traumatized person. This empirical investigation demonstrated that the acceptance of the stimuli improved the response when they were graded and adapted to the patients' possibilities.

In short, the author followed a method of a graded and progressive stimulation in the patients. He always considered the patient as a subject with its own personality, that is, as a psycho-physical hendiadys and not only as a mere passive object. This was true in Leonardo's case and in the other 17 treated patients (Bulletti 2004)<sup>4</sup>, (Bulletti 2010)<sup>5</sup>.

At present, the dynamics is clear because the activated technique followed the pattern of the three orthogonal axes, that's to say, the GSB discovered by the author in March 1983 and confirmed by Wedeen et al. in March 2012.

That's useful to remember that in 1982, the year when the investigation of this optogenetic stimulation started, there was a precise contraindication (Rappaport 1982)<sup>6</sup>. This contraindication warned about the adverse effect of the light stimulation in patients with intracranial pressure, as it was in the A. Leonardo's case of the unbalanced hydrocephalus, who was completely rehabilitated by the author. This positive result shows that the preceding techniques of the Optogenetic Rehabilitation in coma were not carried out in the proper way. On the contrary, the technique used by the author revealed the correct GSB function.

### 0.3. More explanations about 'Leonardo' technique

In the empirical confirmed praxis when a patient diminished its response to a color with an eye, which was stimulated at first, the other eye was stimulated in a second place with the same color. When the response of the second eye extinguished, he was shown another color stimulating the first

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<sup>4</sup> M. Bulletti, *La genesi della violenza in Occidente*. Volumnia, Perugia, 2004.

<sup>5</sup> M. Bulletti, *La completa riabilitazione con una semplice tecnica di stimolazioni luminose di un adolescente di 11 anni, affetto da una grave sofferenza cerebrale*, in Circolo di Corrispondenza della Quatuor Coronati, 2010, pp. 105-203.

<sup>6</sup> M. Rappaport - K.M. Hall - H.K. Hopkins, *Disability rating scale for severe head trauma: coma to community*, in Arch Phys Med Rehabil, 1982; 63:118-123.

eye with this color and afterwards the second eye. When the response to a color finished, he was shown another color following the succession of the order of rainbow colors, using always the white light at the end. The phenomenon of the diffraction present in the physics of the optics, is reproduced in this way: the white light is divided in the rainbow colors and the sum of these colors reforms the white light. In this way, a technical form was activated on the mathematical operation, so there was 1) a white light - unitary set, 2) colored lights - a divided set, 3) a white light - unitary set.

The described methodology is a continuous synchro-diachronic process, always activated by the patient, even though he is in coma, responding on feedback to every light stimulation. The subject in coma responds watching the light of the torch. That's the response that guides and conditions the sequence of the light stimuli and the direction in the sequential space of the Cartesian co-ordinates. In fact, the Cartesian axis x corresponds to the dorso-ventral axis, the Cartesian axis y corresponds to the medio-lateral axis and the Cartesian axis z corresponds to the rostro-caudal axis by Wedeen et al. The two axial series are both orthogonal and they can be superimposed with little structural differences, which don't modify the base of the orthogonal aspect. Due to the empirical praxis, the author had to follow the compulsory course of the Cartesian sequence, which showed the function of the GSB.

We observed that it was not possible to proceed from the axis x to the axis z because the continuity of the synchro-diachronic process was compulsory. This is the *conditio sine qua non* of the empiric rehabilitation process. It was clear that the stimulation followed the genetic course of the development, according to brain Triune by Paul McLean (MacLean 1973)<sup>7</sup>. It's logical to pay attention to the fact that in each of the three different MacLean brains there was and still there is a particular Cartesian structuration of the brain.

That is useful to say that every light stimulation was accompanied by sound stimulations, in a particular way designed for the mother, the father, relatives and friends to request that the patient followed the light. They did this according to the Cartesian topica where the light was. The relatives of all patients in coma, of Italian ethnicity, also participated in the light stimulation. They signed the informed consent form together with the consent participation in the empirical practice of

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<sup>7</sup> P. D. MacLean, *A triune concept of the brain and behaviour*, University of Toronto Press, 1973.

rehabilitation. It was conformed therefore a methodological practice that began with the case (A) of Leonardo and continued in all those cases with present relatives.

#### **0.4. A brief explanation of the antecedents of optogenetical 'Leonardo' technique**

The author reveals the facts of the discovery of the 'Leonardo' technique. He names this 'Leonardo' technique, because he was his first patient who was treated with this particular technique.

For a clear explanation, the following is stated in the first person. 'On January 18th 1983 it was the first time that I entered the room no 4 of the Regional Hospital of Perugia, managed by Prof. Alessandro Casotto, where Leonardo was. I made his mother this question: "What happened to your son?" She didn't answer to my question but she started crying. Then I realized that little Leonardo increased the breathing pace when he heard his mother's crying. I noticed it when he blew stronger from the cannula of the tracheotomy. I immediately thought that, although the boy was in coma of the second grade of the GCS scale, he was able to communicate with his mother by means of the emotional communication.

During my MAS in psychology at the Université Catholique de Louvain, I had studied the test of the 'Piramide de couleurs' by Pfister<sup>8</sup>, where the colors were associated to the emotions. Little Leonardo wasn't able to activate his *ideative* expression due to his health state. The word *idea* either in classical Greek (*veidon*) or in Latin comes from the word *video*. Then the consonant *v* disappears and becomes *ideo*, synonym of the 'ideative function'. An 'ideative function' as Archimedes' eureka, which is the highest expression of the human psychological creativity. Consequently, as the sight is activated by means of the light, I had the fortunate idea of stimulating little Leonardo with colorful lights. This idea exactly focuses the principles and aims of the optogenetics nowadays. The result was positive, not only with little Leonardo, but with the series of the 18 cases, above mentioned.

Today Leonardo is 42 years old and works regularly as a computer technician. He has an ordinary life and nobody knows that he has had so difficult moments in his life. And this also happens with the other patients who have survived.

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<sup>8</sup> D. Anzieu, *Les méthodes projectives*, Puf, Paris, 1980, p. 190.

**Acknowledgments:** the author dedicates this work to the memory of Prof. A. Casotto who started this research work.

## Corner bibliography

V.J. Wedeen - D.L. Rosene - R. Wang - G. Dai - P. Hagmann - J.H. Kaas - W.I. Tseng, *The geometric structure of the brain fiber pathway*, Science, 2012, 335 (6076); 1628-34. Abstract: The structure of the brain as a product of morphogenesis is difficult to reconcile with the observed complexity of cerebral connectivity. We therefore analyzed relationships of adjacency and crossing between cerebral fiber pathways in four nonhuman primate species and in humans by using diffusion magnetic resonance imaging. The cerebral fiber pathways formed a rectilinear three-dimensional grid continuous with the three principal axes of development. Cortico-cortical pathways formed parallel sheets of interwoven paths in the longitudinal and medio-lateral axes, in which major pathways were local condensations. Cross-species homology was strong and showed emergence of complex gyral connectivity by continuous elaboration of this grid structure. This architecture naturally supports functional spatio-temporal coherence, developmental path-finding, and incremental rewiring with correlated adaptation of structure and function in cerebral plasticity and evolution.

A. Berndt - S.Y. Lee - C. Ramakrishnan - K. Deisseroth, *Structure-guided transformation of a channelrhodopsin into a light-activated chloride channel*, Science, April 2014, 344 (6182): 420-4. Abstract: Using light to silence electrical activity in targeted cells is a major goal of optogenetics. Available optogenetic proteins that directly move ions to achieve silencing are inefficient, pumping only a single ion per photon across the cell membrane rather than allowing many ions per photon to flow through a channel pore. Building on high-resolution crystal-structure analysis, pore vestibule modeling, and structure-guided protein engineering, we designed and characterized a class of channelrhodopsins (originally cation-conducting) converted into chloride-conducting anion channels. These tools enable fast optical inhibition of action potentials and can be engineered to display step-function kinetics for stable inhibition, outlasting light pulses and for orders-of-magnitude-greater light sensitivity of inhibited cells. The resulting family of proteins defines an approach to more physiological, efficient, and sensitive optogenetic inhibition.

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M. Bulletti, *Dalla luce ai palindromi*, in “Hiram, Rivista del Grande Oriente d’Italia”, Roma, Erasmo Editore, n. 4, 2010, pp. 81-102.

### **Short account of the phenomenology and the author**

The phenomenological method applied by the writer, is based on the Socratic maieutics till to the last developments in psychoanalysis, without leaving out the pre-Socratic philosophy. Furthermore is based on biology together with its correlations with physics and the Theoretical basis of the Einstein's theory of relativity, quantum mechanics and the physical information, without losing sight of the connection with the cognitive and Behavioural psychology. This research Landscape has been very visible in the author’s abundant bibliography. In his phenomenological approach, as the physicist declare, it’s clear that our atoms are the same atoms that constitute the physical universe all around us and ourselves with the universe, are governed by the same universal law. For this reason an “ analogical formativity” exists between human and nature, and on its correspondens to the facts, is based the research and the professional method of the writer, adopting the multidisciplinary fenomenological approach . The concept resulting in this matter is the global valuation of the of the human being. In fact, above all, the Phenomenon Identification, in its entirety, it’s the main

purpose that every psychotherapist needs to achieve, to determine that positive transfer that allows the subject who is undergoing analysis to achieve the objective harmonic psychosomatic balance. Instead, the limited and reductionistic view along with the anosognosy, or the Knowledge negation by the intellect, make invisible every phenomenon and most of all, the psychosomatic globality of the human being. This is an obstacle that hides the expression of that synthesis in which the greatest expressions of human ideativity take place, so well-described by the "Archimedean 'eureka'". In concrete terms, the phenomenological method applied by the author crosses rapidly the psychopathological wall by a new formulation of the intellect, and so the psychotherapist becomes like as Mentor in the Mirror of the Soul, and unveils to the subject undergoing analysis factors still unknown. The author, has anticipated by 30 years, some findings that are on the verge of discovery by scientific research. The first one is The invention of an optogenetic method that use Effects of light stimulation at different frequencies for Psychophysical rehabilitation after traumatic brain injury. This technique has preceded, by the way, the discovery of the orthogonal structure of the brain geometry. The second one is the clear evidence of the deep pathology of the Cibele complex, that is the psychological incest between mother and daughter and between mother and son. This complex follows the tracks of the matrilineal mitochondrial biological model. In fact the Cibele complex psychopathology in the most serious forms, causes a Psychosomatic imbalance and behavior disorders, more widely definable as a psychological infibulation in the daughter and a psychological castration in the son. These advances pave the way for research on human and for new questions on the body and soul hendiads or for the neuropsychophysiology of the life of each one.