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John P. McGovern Award Lectureship

LEONARDO DA VINCI AND THE SEARCH FOR THE SOUL

by

Rolando F. Del Maestro, MD, PhD, FRCS(C), FACS, DABNS
William Feindel Emeritus Professor in Neuro-Oncology
Department of Neurology and Neurosurgery, McGill University

John P. McGovern, M.D.

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On the cover - The John P. McGovern Award Lectureship commemorative medal which is presented to each annual lecturer.

The 30th John P. McGovern Award Lecture

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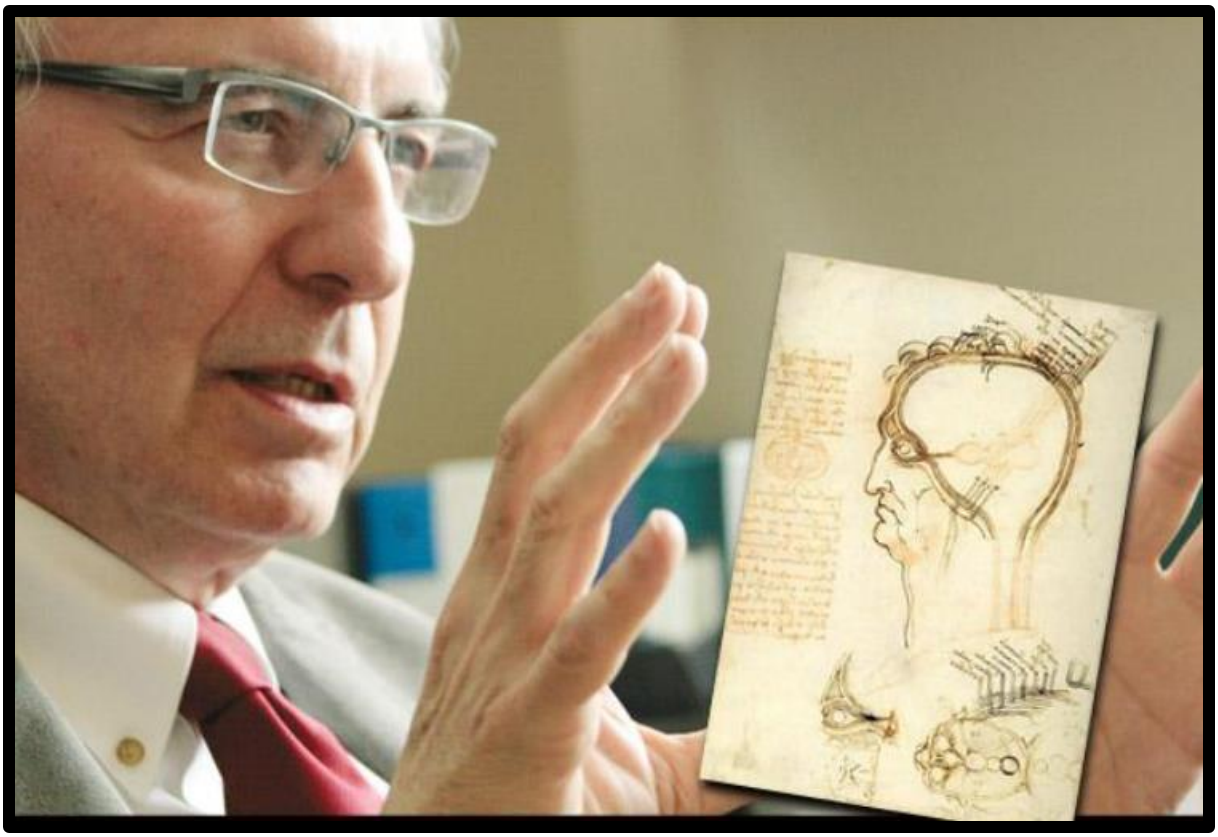


Dr. Del Maestro is the William Feindel Professor Emeritus in Neuro-Oncology at McGill University, Montreal, Canada. As the Director of the Neurosurgery Simulation Research and Training Centre at the Montreal Neurological Institute and Hospital at McGill University, his research is focused on developing and accessing virtual reality surgical simulation using the NeuroTouch platform working in cooperation with the National Research Council of Canada and multiple national and international research groups. http://neurosim.mcgill.ca/

Along with his wife Pam and Steve Northey, he co-founded the Brain Tumour Foundation of Canada in 1982. This organization is a dynamic cross Canada organization fostering excellence in brain tumour patient care, patient support and research funding. His other interests include Leonardo da Vinci and the History of Medicine. He is the Chairperson of the Standing Committee of the Osler Library of the History of Medicine at McGill and one of its Board of Curators. Dr. Del Maestro has one of the largest private collections of materials related to Leonardo Da Vinci. Using this material he has curated a number of exhibitions related to Leonardo's art and anatomical interests as well as an exhibition on the History of Neuro-Oncology at the Osler Library at McGill University and Montreal's Leonardo da Vinci Centre. www.delmaestro.org/rolando His latest book entitled A Relationship Etched in Time: Leonardo da Vinci, The Earl of Arundel and Wenceslaus Hollar will be published by the McGill-Queens Press.

First I would like to thank Pamela Miller for her very gracious introduction. Second I think we should acknowledge Pamela Miller for her marvelous stewardship of the William Osler Library of the History of Medicine at McGill University as its History of Medicine Librarian for the last 15 years.

I would also like to thank the Board of the American Osler Society for giving me the opportunity to present the John P. McGovern Award Lectureship. As well I extend my heartfelt thanks to Dr. Herbert M. Swick, President of the American Osler Society for his kindness and Renee Ziemer for making all my interactions with the American Osler Society Office such a pleasure.

What a man leaves after him are the dreams that his name inspires and the works that make his name a symbol of admiration.

Paul Valery (1871-1945), a French poet, used these words to describe Leonardo da Vinci. They are also more than appropriate to outline the accomplishments of Dr. John P. McGovern. There is a certain poetry to all human endeavor. Each of us by our words, songs, music and actions, and especially our work, adds to the poetic tapestry of human existence.

To the poetry of Medicine: Dr. McGovern contributed a number of poems.
To the poetry of Multiple Institutions: The Osler Library of the History of Medicine at McGill which I know best. Dr. McGovern contributed numerous volumes.
To the poetry of the World: Dr. McGovern contributed whole libraries.

Introduction

The concept of the soul has always been associated with a mysterious component linked to the reason and purpose of our individual human existence and has challenged human collective intellect from the dawn of recorded time. One useful definition of the soul is that it is the essential component of our intellectual life and passions and its major role is to interpret our existence.[1] Humans have always been interested in the question of the exact anatomical site of the soul. Questions as to whether the soul was located within the human body or in some non-human location have been vigorously debated. Early civilizations, including the Egyptians, Mesopotamians and Hebrews, believed that the heart was the essential organ that contained this elusive entity.[2] Some Greek philosophers were strong supporters of the heart (cardiocentric) while others supported the brain (cephalocentric) as the organ of the mind and thus the location of the soul. Theologians have speculated on the location of the soul either linked or not associated with the human body. At the time of the Renaissance this controversy was still very alive. The purposes of this presentation are to explore some of the sources of this ancient question, Leonardo's integration of the contemporary and ancient knowledge base related to the location and functions of the soul which culminated in his own personal 'search for the soul' and some modern concepts of the location of intellectual function.

In Egyptian writings such as the *Ebers* papyrus (dating from the Eighteenth dynasty, sixteenth century B.C.) the heart plays a central role in controlling both one's physical and emotional functions:

The actions of the arms and the movements of the legs the motions of every other part of the body are done according to the orders of the heart that has conceived them.[3]

It is the heart that draws from the senses every judgment and the tongue that pronounces that which the heart has thought.[3]

In Egyptian mythology, at the time of one's death, all organs were removed from the body except for the heart since it permanently recorded an individual's accumulated good and evil deeds. This allowed a judgment to take place after the death of each individual which involved the 'weighing of the feather'. The heart was weighed against a special feather and if that individual's heart weighed less than the feather (unburdened by evil deeds) then that individual's spirit would live for eternity. However, if that person's heart was 'heavy with sin' and therefore weighed more than the feather that individual's heart would be consumed by 'Ammit' and that spirit eliminated from the ashes of time.[4] In the *Papyrus of Ani* (The Egyptian book of the Dead, Fig. 1) it is written:

Thus says Thoth, judge of truth, to the Great Ennead which in the presence of Osiris: Hear the word of the very truth. I have judged the heart of the deceased, and his soul stands as a witness to him. His deeds are righteous in the great balance, and no sin has been found in him. He did not diminish the offerings in the temple, he did not destroy what had been made, he did not go about with deceitful speech while he was on earth.[4]

The concept of linking the judgment of one's heart (i.e. good or bad deeds) to an eternal existence after death would profoundly influence the Western concepts of intellectual function, religion and philosophy.

Figure 1 *The Egyptian book of the Dead. The Papyrus of Ani*, Egypt, 19th Dynasty.

The Egyptians believed that the heart was their seat of physical, emotional and intellectual life. The heart of Ani represented as a hieroglyph of a mammalian heart is depicted weighted against a feather, the symbol of *Maat*, which represents 'Truth, Rightful Order'. An unbalanced and less then proper life resulted in a heavy heart which weighed more than the feather and thus the multifaceted beast Ammit 'she who swallows the dead' seen on the far right of the scene, was more than happy to end your existence.

A Greek speaking population colonized the islands and mainland along the Aegean Sea about 1000 years before the birth of Christ. The development of an easy to learn, write and understand language allowed the thoughts of these individuals to spread throughout the western world. Ionian philosophers such as Thales (flourished circa 580 B.C.) believed that the *cosmos* (Greek word for universe) could be understood by the human mind. His prediction of the solar eclipse that took place in 585 B.C. confirmed how human knowledge could be used to understand the world. Thales also believed that some human experiences, such as the actions of a magnet, could not be explained by information that was appreciated by our senses. Although a close relationship between the outer cosmos and the inner personal cosmos existed, they all required explanations.[5] Leucippus (first half of the 5th century B.C.) and his student Democritus who flourished circa 420 B.C were involved in developing the Atomic School.[6] They proposed that the soul was like breath and since breath was material it must be composed of atoms. Many of the words that are used to conceptualize the meaning of the soul have some relationship to the words used for breath (anima, spiritus, and psyche). In the Democritean *corpus* all objects in the cosmos were composed of atoms. Since they believed that the soul was a component of the cosmos it must obey the laws of a physical universe and thus there can be no 'First Unmoved Mover'. Therefore, since one's soul belongs to the physical universe it must have a physical location and that location is the human body. The Democritean *corpus* localized the soul in all the different parts of the human body. The concept that the soul was in some way chained to individual human anatomy was very difficult for the Aristotelians and Christians to accept and this discredited the Leucippus-Democritean atomic hypothesis for more than two millennia.

In Raffaello Sanzio's *The School of Athens*, Leonardo was depicted as Plato carrying a volume of the *Timaeus* – one of Plato's best known works (Fig. 2).[7]

Figure 2 Detail from *The School of Athens* 1509-1510 by Raffaello Sanzio.

Leonardo da Vinci is depicted as Plato who can be identified carrying his book called the *Timaeus*. Leonardo can be identified both by his well-known appearance and the symbolic gesture of his pointing to the heavens; a common element in Leonardo paintings. Walking beside Plato is another individual identified as Aristotle since he is carrying his work called *Ethics*. Controversy exists as to which painter this represents. My interpretation is that Raphael would have placed the two most famous living painters in this portal and thus the individual depicted to the right of Leonardo Da Vinci may be his representation of Michelangelo Buonarroti although this is not the common interpretation. Fresco, Stanza della Segnatura, Vatican Museums, Vatican City.

This book was to have a significant influence on anatomical thought throughout the Middle Ages and the Renaissance.[8] Leonardo was aware of this work and one of his sources was Albert of Saxony's *Quaestiones*: a book present in his personal library.[9] Plato believed in a dualism between the soul and the body along with the immortality of the soul. In the *Timaeus,* he divided the soul into three essential components or 'parts'. The most important of these 'parts' was located in the head, the rational'part' (intellectual soul). The secondary centers in his model were in the chest and heart as the courageous or spirited 'parts' (sensitive soul) and the appetitive "part" (vegetative soul) was located in the upper abdomen (the liver).[10] In the *Phaedo*, Plato commented:

Is the growth of animals the result of some decay which the hot and cold principle contracts, as some have said? Is the blood the element with which we think, or the air, or the fire? Or perhaps nothing of the kind-but the brain may be the originating power of the perceptions of hearing and sight and smell, and memory and opinion may come from them and science may be based on memory and opinion when they have attained fixity.[11]

Plato's concept that mental process occurred by an organized sequence including three dynamic processes: 1) information obtained from external sensations through our sense organs, 2) this information is then integrated resulting in reasoning, 3) memory is then stored to be retrieved at a future time to further reinforce and amplify intellectual function. The *Corpus Hipporaticum* which was composed by a number of writers (ca. 430-350 B.C.) also supported the brain as the essential modulator of bodily functions. In their book concerning epilepsy called *On the Sacred Disease.* These authors write:

It is thus with regards to the disease called sacred; it appears to me to be nowise more divine nor more sacred than other diseases, but has a natural cause from which it originates like other affections...the brain is the cause of this affection, as it is of other great diseases.[12]

This is amplified more fully when these authors comment further that:

Men ought to know that from nothing else but the brain comes joys, delights, laughter and sports, sorrow, griefs, despondency, and lamentations. And by this, in a special manner, we acquire wisdom and knowledge…in these ways l am of the opinion that the brain exercises the greatest power in the man.[13]

Thus a number of influential early Greek thinkers and medical writers outlined their opinions that the brain was the location of the soul. The most famous student of Plato, Aristotle (384-322 B.C.), carrying his work *Ethics* is depicted as Michelangelo Buonarroti (1475-1564) in Raffaello Sanzio's painting *The School of Athens*, tipped the scales to the cardiocentric view. Leonardo owned a number of volumes by Aristotle including those entitled *Problems* and *Propositione* and commentaries on him in Albert of Saxony's (ca. 1320-1390) *Questiones in Aristotelis libros De coelo et mundo* and quoted him in his notebooks on numerous occasions.[14] Aristotle was a very careful investigator having dissected 49 species of animals ranging from sea urchins to elephants.[15] He had a particular interest in the embryological development of animals even commenting that he had dissected a 40 day old human fetus.[16] During his studies on the development of the chick embryo Aristotle stated that:

Generation from the egg proceeds in an identical manner with all birds…the heart appears like a speck of blood in the white of the egg. This point beats and moves as though endowed with life.[17]

His observation that the heart, one's 'speck of blood' appeared very early in chick embryonic development, possibly along with his studies on human fetuses, reinforced his view that the heart must be our most crucial organ. Aristotle's idea related to the brain was that it functioned as an organ to cool the heart and the vascular system throughout the body. This concept can be appreciated based on his inability to locate blood vessels on the brain surface of animals he studied (possibly the fish or reptilian species he assessed).[18] Aristotle's syntheses of his investigations on the brain includes:

The brain in all animals is bloodless, devoid of veins, and naturally cold to the touch; in the great majority of animals it has a small hollow in its center (ventricles)… From the eye there go three ducts to the brain: the largest and medium-sized to the cerebellum, the least to the brain itself: and the least is one situated nearest the nostril.[18]

The fact that the brain was cold and insensitive to his touch as compared to the warm and beating heart helped to confirm his cardiac location for the functions of the soul.[18] Aristotle was the first author to describe the presence of a series of cavities in the brain that are called the cerebral ventricles. These structures were to play a substantial role in the anatomical location of the soul to the investigators who were to follow him. In his book, *De Anima, (On the Soul),* Aristotle introduced the word '*Sensus communis*'. He used the word to represent the part of human psyche which receives and organizes sensory information from our various sense organs integrating these inputs into an intelligent and coherent representation.[19] This book, along with his many other contributions, disseminated his views concerning the function and cardiac location of the human soul. This cardiocentric concept of the human soul's location that was further outlined by the Stoics and Epicureans dominated Western philosophy for over two thousand years.[20]

In the famous medical school of Alexandria, Herophilus (flourished circa 290 B.C.) and Erasistratus (flourished circa 280 B.C.) believed that the brain was the seat of the soul. Herophilus, expanding on Plato's concept of three components of mental function located these in the ventricles of the human brain. The ventricle system, since its discovery, had been divided into four separate components. Herophilus placed the soul in the fourth ventricle and animal spirits (intellectual and motor function) in the brain itself.[21]

Galen of Pergamum (circa A.D. 130-200) was trained in a number of medical schools, including that at Alexandria and was influenced both by the *Corpus Hippocraticum* and the philosophy and biology of Aristotle. Galen did believe in the tripartite nature of the soul as proposed by Plato but commented:

But if it is immortal, as Plato wants, he would of done well to tell us why it should be separated [sc. From the body] when the brain is excessively cooled, or overheated, dried or moistened…For death occurs, according to Plato, when the soul is separated from the body. I would very much like to learn from Plato himself, if only he was alive, why a massive loss of blood, or a draught of hemlock, or a raging fever, should separate it. But he is no longer with us, and none of my Platonist teachers ever gave me any reason why the soul should be separated from the body as a result of the things l have mentioned.[22]

Galen firmly demonstrated experimentally that the brain and not the heart was the seat of motion and sensation. As the surgeon to the gladiators he had experience with spinal cord injuries and he carried out a series of experiments to demonstrate that:

When a nerve is cut, pinched, contused or tied by a ligature…all motion and sensitivity is suspended…So great is the power [descending] through the nerve from its great source above [i.e. the brain]… For whatever is above the section [of the nerve] and continuous with the brain, this still will preserve the activity [coming] from its [cerebral] source; but what is lower will be unable to exercise sensation or motion.[23]

He made no attempt to localize specific functions to specific brain regions. He felt that the brain functions were located in the brain substance rather than in the ventricular system.

The Medieval World

The dissolution of the Roman Empire resulted in termination of anatomical investigations into the position of the soul. Theologians such as St. Augustine (flourished circa A.D. 354-430) and Nemesius, Bishop of Emesa (flourished circa A.D. 390) began to integrate Greek scientific and theoretical concepts of cerebral function into a system compatible with the Christian faith. These authors fused the ideas of Plato, Aristotle and Herophilus into an encompassing system which allows anatomical concepts to be integrated fully into what has been called the 'cell doctrine'. [24] This theoretical system localized the mind within cerebral ventricles which had been discovered by Aristotle and infused with purpose by Herophilus. Plato's concept of three orderly sequences of brain function allowed the ventricular system anatomy to fit well into this theoretical approach. Anatomically the two lateral ventricles represented the first cell to which sensory information flowed and Aristotle's word '*Sensus communis'* was applied to its function. The next cavity in anatomical terms was the third ventricle and was considered to be involved with reasoning (second cell). The anatomical fourth ventricle in the posterior part of the brain was associated with memory (third cell). In early manuscripts the ventricles were divided into little cells. These were labeled by means of balloons and strings that led back into segments of the head. The posterior component of the first cell or anterior component of the second cell was felt to be involved in *imaginative* (imagination) and *fantasia* (fantasy). The second cell was the seat for reasoning. A number of different words were used for this including *aestimativa* (judgment), *cognitive* (thought) and *ratio* (reason). In the third cell representing the posterior portion of the brain, *memorativa* (memory) resided. A number of different words were employed by multiple commentators to outline this concept but the basic philosophical and anatomical representation of three specific areas within the brain remained relatively constant.[25] This model of brain function superimposed on the ventricular anatomy of the brain contained the integration of both theological and anatomical medieval thinking. This concept was reproduced in many different manuscripts.[26]

Influence of books in Leonardo's Library in his Search for the "S*enso Comune*"

Multiple notebooks (libretti) were employed by Leonardo to collect information, outline his thoughts and draw conclusions. In these small volumes he outlined the books he had purchased, books he was reading, had borrowed and were translated by friends. Leonardo outlined his library holdings in two extensive lists present in his manuscripts. In 1494 he listed forty items (Codex Atlanticus 210 r) and thirty one reappear in his 1504 Madrid Codex. In Leonardo's Madrid Codex II on folio 2 verso and 3 recto is outlined in mirror script from right to left books present in his library.[27] Leonardo listed one hundred and sixteen items which outline the extensive range of books in his possession. This list does not outline the many books that Leonardo had access to. The scientific knowledge that Leonardo acquired was rooted in the careful assessment of the anatomical, medical, surgical and dietary volumes present in his library. Albertus Magnus (1193-1280), a

Dominican monk, produced a number of works in which he commented on and paraphrased the work of Aristotle along with some original observations. Two of Albertus Magnus' major works *Filosofia d'Alberto Magno* and *Secreti d'Alberto Magno* were in Leonardo's library. Albertus Magnus had an early conception of what was necessary to carry out experimental investigations. Through the writings of Albert Magnus Leonardo became aware of the anatomical ideas of Aristotle and these concepts were an important influence on Leonardo's anatomical explorations in his search for the location of the soul. Another volume in Leonardo's library the *Liber phisionomiae* by Michael Scotus (1175-1234) who further developed Aristotle's concept of physiognomy derived from the Greek *physis* (nature) and *gromon* (judge) is of interest related to Leonardo's concepts of beauty and ugliness.[29] Owning a copy (*fassciculu medicine-latino)* and having access to other copies of Mondino's *Anothomia* in Ketham's *Fasiculus Medicinae* initially published in 1491 but only containing Mondino's dissection manual in the 1493 Italian edition and latter editions, significantly advanced Leonardo's personal attempt to locate the *senso comune*.[30] Mondino De'Luzzi (ca.1275-1326) is considered the 'restorer of anatomy' because his anatomical thesis, which was written in 1316 at the University of Bologna, could be employed as a practical dissection manual. Mondino's *Anatomia* initially published in 1476 was used by generations of physicians, anatomists and painters including Leonardo da Vinci to carry out anatomical dissections. He was pivotal in beginning the study of the human body and all anatomical studies that have followed were deeply rooted in his overall structure.

Leonardo's Search for the 'S*enso Comune'*

Leonardo's investigations into the anatomy of the central nervous system (brain, cranial nerves and spinal cord) can be divided into three phases. In his first Milanese period (1485-1489) Leonardo predominantly for artistic purposes, initiated investigations focused on deciphering the physiology of vision and perspective and involved a series of animal experiments. This initial phase allowed Leonardo to both integrate and visually reconstruct information that he had obtained from a number of printed sources. In the second phase, after 1489, Leonardo had access to the Italian edition of the anatomical thesis of Mondino and a number of human skulls.[31] The third phase involved investigations conducted between 1508 and 1514 in which Leonardo concentrated his neurological studies on cerebral anatomy and in particular the brain's ventricular system. His studies associated with proportions of the human body along with his explorations of light and perspective were all designed to aid him in the depiction of three-dimensional reality in two-dimensional painting. The depiction of how the eye and nervous system related to a visual image and how this impacted on the human mind continued to challenge his intellect.

Phase 1: Early Experimental Concepts

In this initial phase of his anatomical conceptualization he appeared to have attempted to outline, in visual three dimensional drawing formats, information that he had been able to obtain from a number of written sources supplemented by initial experimental results. He used a very similar reconstructive method to outline the anatomical details of reproductive anatomy that had been taken from Plato's *Timaeus* (K/P 36r). In 1490 the first pictorial representation of the 'cell doctrine' in a published volume was a woodcut contained in the *Philosophia Pauperum* by Albertus Magnus. This book was initially published in 1480(?) but without this diagram. The first illustrated medical book, Ketham's *Fasiculus Medicinae* was published in 1491 and the Latin copy published in 1491 that was in Leonardo's library contained a woodcut of the 'cell doctrine'. However, these woodcut illustrations could not have been incorporated into his knowledge base at the time of these initial drawings of the 1485-1489 time period. Figures in volumes like The *Margarita philosophica* an encyclopedia of all the

sciences edited by Gregor Reisch (c. 1467-1525) was written in 1496 and published in 1503. This volume contained a number of anatomical illustrations including one of the 'cell doctrine' which outlined the medieval concept as seen in the 1504 edition and provided individuals like Leonardo with careful visual constructs which they could further exploit (Fig 3).[31]

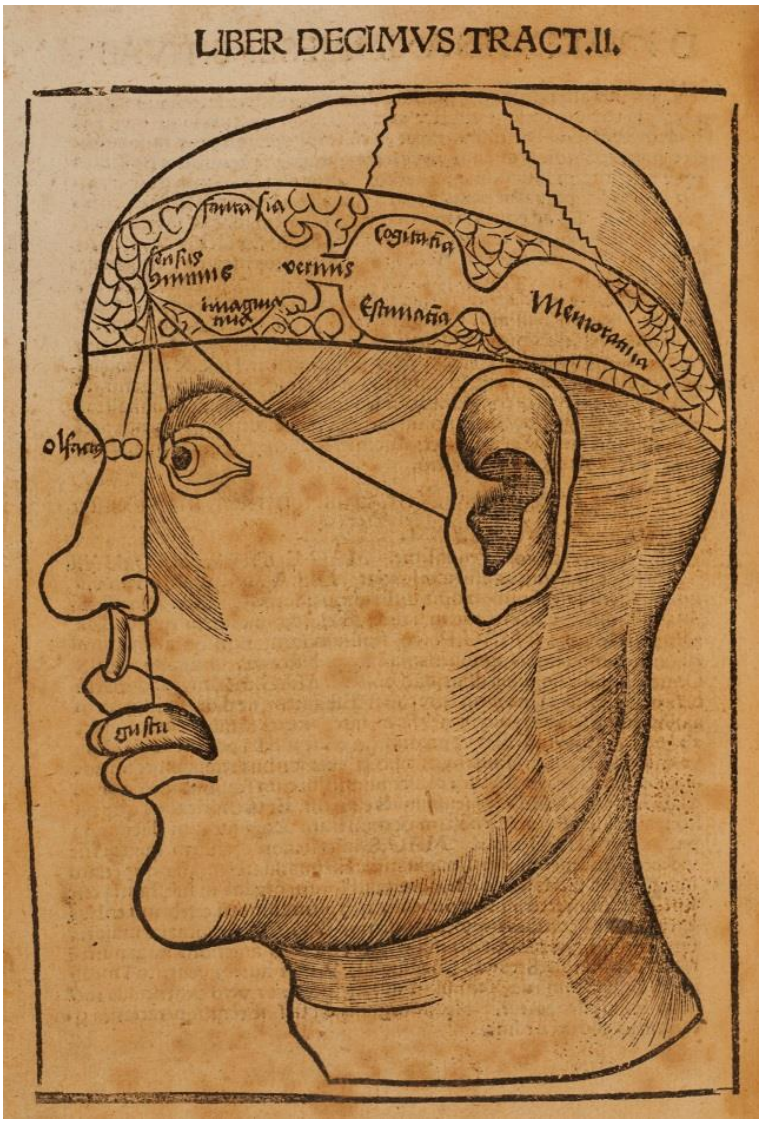


Figure 3 *Margarita philosophica* edited by Gregor Reisch, ed II, Freiburg, 1504, Illustration from Liber X.

Leonardo's conceptualization of the cerebral location of the soul was based on information gleamed from these types of illustrations. Three cerebral cells communicating with each other are depicted around the skull dome. The anterior ventricle (made up of the two anatomical lateral ventricles) is called Sensus communis, fantasia, imaginativa, the intermediate one Cogitativa, Estimativa, and Memorativa is outlined in the third ventricle. Four lines travel to the anterior ventricle from the anterior border of external ear, the roof of the nasal cavity Olfact(o?), the pupilla, and the dorsum of the tongue Gust(o? indicating how sensory information flows to the sensus communis in this model.

Private Collection Dr. Rolando Del Maestro.

Research conducted by Leonardo in 1485-1487 provides critical insights into his personal exploration – his search for the soul the '*senso comune.*' This experiment is outlined in the upper left on a sheet of blue paper in a silverpoint drawing (K/P 1r) in the first anatomical series of Leonardo drawings (1485-1487) that are presently available to us (Fig 4). This vivisection investigation drawn at a 45º to the right which involved the 'pithing of a frog' resulting in the destruction of the upper spinal cord and medulla oblongata allows us to analyze Leonardo's conceptual reasoning. His thinking and methods allow us to gain an appreciation for how he experimentally attempted to solve the problem as to the position of the soul. Leonardo, having a copy of Livy (59 BC-AD17) in his library, outlined this initial critical information in a note he made in one of his manuscripts, Paris MS. B, f 9r. He states:

The *scalpro* (spike) was a sharpened iron used to prick and control elephants. Livy In the Seventh Book of the Carthaginian War, says that many more elephants were killed by their own governors than by the enemy. For when these beasts got enraged with them the governor with a mighty blow thrust the sharp *scalpro* between the ears where the neck joins the spinal column: and this was the most rapid death that could be given to so huge a beast.[32]

On the same page Leonardo draws his conception of a '*scalpro*' along with a series of other warfare instruments. This information was derived from Robert Valturio's book called *De Re Militari.*[32] He must have been aware and concurred with the writings of Plato's *Timaeus* and also the Hippocratic authors since he wrote the word '*generative power*' (in normal writing) on the spinal cord itself. These sources outlined that the origin of sperm was from the brain. Leonardo describes this crucial experiment in these words in his usual right to left backward writing on the left side of his drawing:

The frog retains life for some hours when deprived of its head and heart and all its bowels. And if you puncture the said nerve [spinal medulla] it immediately twitches and dies. All nerves of animals derive from here [spinal cord]. When this is pricked, the animal dies at once. (K/P 1r)

All words on the right of this drawing are in normal writing. Leonardo wrote '*sense of touch*' on the two cord-like structures located alongside the spinal cord which are the paired vertebral arteries coursing through the transverse foramen of the cervical vertebrae. He may not have visualized blood present in these very small vessels in the frog and therefore considered them solid structures. The words '*cause of movement*', '*origin of nerves*' and '*transit of animal powers*' are all outlined on his sheet with lines to the vertebral arteries. It is interesting that in this experiment Leonardo wrote his own conclusions in his customary right to left backward writing while on the spinal cord and the right side of the drawing he would outline the words used in normal writing. One could speculate that in this particular case Leonardo was using Italian words and/or translating Latin words directly from written sources available to him and then copied and/or translated these words directly onto this drawing.

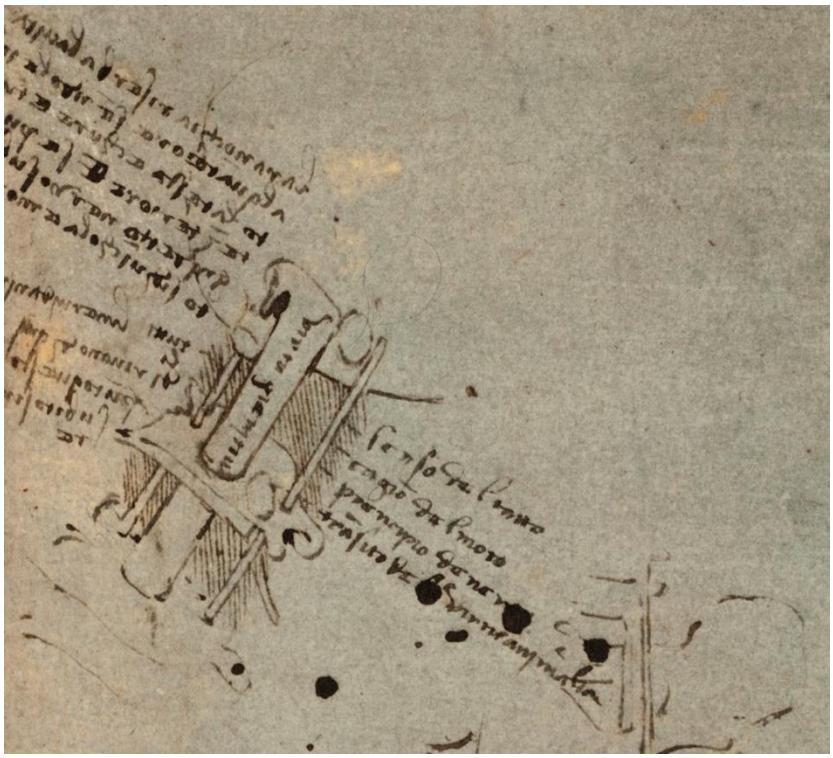


Figure 4 Leonardo da Vinci, *The Pithing of the Frog,* Detail from K/P 1r (ca. 1485-1487)

This is an exploded view of the base of the skull and first cervical vertebrae of a frog showing the foramen magnum, the spinal cord and the vertebral arteries laterally. Leonardo labeled the spinal cord with the words '*generative power*' demonstrating his dependence on Plato's *Timaeus* and the Hippocratic canon in normal left to right writing. Leonardo's laboratory notes written from right to left with his left hand comment on the results of these experiments on puncture of the spinal medulla on the left side of the drawing. While on the right side pointing to the vertebral artery '*sense of touch*' '*cause of movement*', '*origin of nerves*' and '*transit of animal powers*' is written normally from left to right.

The opposite side of this sheet is a cornucopia of Leonardo's anatomical explorations also involving a number of other vivisection experiments including another dissection of the foramen magnum region. Leonardo may have returned to this page later in his life since in writing from this time period he writes:

Frog instantly dies when its spinal medulla [medulla oblongata] is perforated. And previously it lived without head, without heart or any interior organs, or intestines or skin. Here therefore, it appears, lies the foundation of movement and life. (K/P 1v)

To Leonardo's mind the experiment was definitive and dealt with the crucial question concerning the location of the soul. The location, based on his experimental studies, must be the brain. Twenty years later in 1508 outlining his list of subjects to be discussed in the *Book on Anatomy* he must have remembered this initial experiment and also extrapolated the information from his experiences associated with war and human disease. Leonardo comments:

What the soul is. Of nature which is necessary makes the vital and actual instruments of suitable and necessary shapes and positions. How necessary is the companion of nature. Represent from whence comes the semen. Whence the urine. Whence the milk. How nourishment proceeds to distribute itself through the veins. Whence comes intoxication. Whence vomiting. Whence gravel and stone. Whence colic. Whence dreaming. Whence frenzy by reason of sickness. Why it is that compressing the arteries a man falls asleep. Why it is that a prick on the neck may cause a man to drop dead.[33]

The conceptual methodology Leonardo employed used to carry out his scientific exploration is evident when one reconstructs this critical experiment. The location of the place in the body to be pithed came from information that he had abstracted from Livy's account, the instrument was fashioned after the description of Robert Valturio and the expected result from Livy's narrative. Since the frog is much smaller Leonardo needed to modify his experiment taking into account a very different experimental animal and designed the appropriate '*scalpio*.' Leonardo needed to complete an initial series of studies to understand the anatomy of the frog's foramen magnum and cranial base along with the upper cervical cord. Even today utilizing an operating microscope this is a difficult dissection. The removal of the animal's head, heart and internal organs had to be both conceptualized and appropriately carried out.

On the verso of this sheet a series of studies assessing the base of skull, cervical vertebrae along with the brachial plexus of the dog suggesting that the initial frog experiments led him to test other hypotheses concerning the anatomy of the nervous system (K/P 1v). A series of other drawings on this sheet demonstrate his attempt to project onto drawings of the human arm anatomical information of the brachial plexus and nerves of the upper arm gleaned from his animal experiments (Fig 5).

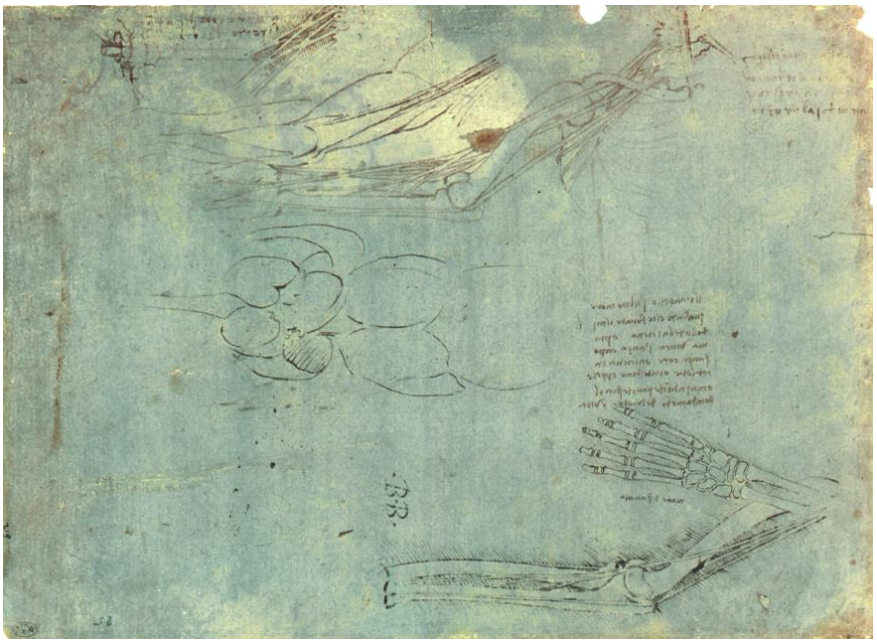


Figure 5 Leonardo da Vinci, *Studies on Base of Skull, Cervical Vertebrae and Brachial Plexus of the Dog* K/P 1 v (ca. 1489).

The initial frog experiments may have led Leonardo to test his observations in further experiments. The most interesting of these experiments may have related to the damaging of the dog brachial plexus. Leonardo also attempted to project his knowledge gained through the dissection of the dog brachial plexus in a series of studies seen on this sheet.

Leonardo must have been impressed by the results of his experiment as he carefully recorded the information on both sides of the sheet where he outlined the exploded drawing of the frog's anatomy. The results of this initial experiment appear to have triggered a series of follow up studies recorded on the same sheet. He may have carried out other experiments on damaging the brachial plexus in the dog since he comments on K/P 1v:

'The dog [or the arm] will be lost whichever of these [nerves] is punctured.'

The novelty of Leonardo's experiment is evident by the fact that it does not appear to have been repeated until reported by Alexander Stuart (1673-1742) in 1738, 249 years later (Fig. 6).[34]

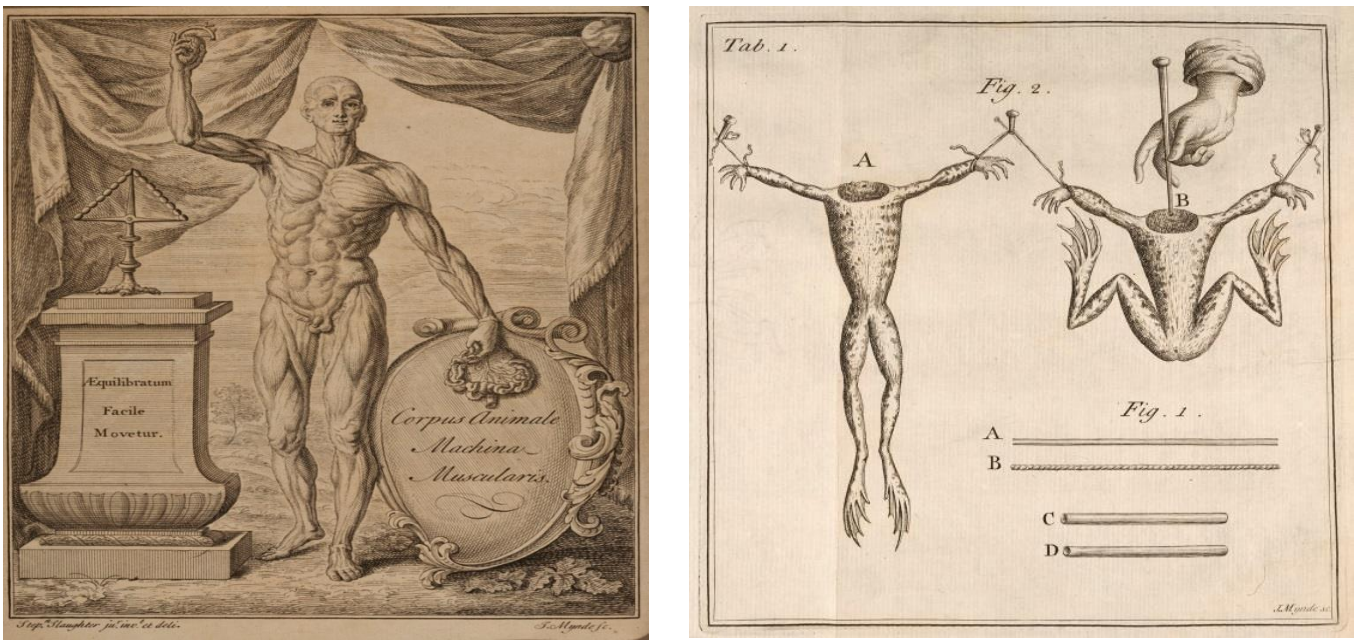


Figure 6 Alexander Stuart (1673-1742), *Dissertatio De Structura et Motu Mufculari*, London, Excudit Samuel Richardson, 1738.

> Alexander Stuart was a Scottish natural philosopher and physician whose principal concern was demonstrating that a strict hydraulic iatro-mechanism was the best theory to account for muscular motion. In this volume which demonstrated his theory (Additional title, left) he used a decapitated frog (right), which is illustrated in this work for the first time since Leonardo's experiment.
>
> Private Collection Dr. Rolando Del Maestro.

These initial studies by Leonardo localize the soul to the brain. He then used information abstracted from multiple sources to perform a three dimensional synthesis of his experimental research. Three drawings from approximately 1487, clustered around 14 others on K/P 4r outline his attempt at synthesis. In the central drawing the optic nerves do not begin at the back of the globes but are projected into them, they then course backwards to the optic chiasm continuing as one tube into the anterior cavity (Fig. 7). This anterior cavity (ventricle) is labeled *'imprensiva'*. The olfactory and auditory nerves course towards the middle ventricle labeled as the '*senso comune'* and a third and posterior ventricle contains the word '*memoria'*. Leonardo has made an attempt to outline this information in a more three-dimensional representation in the two flanking drawings.

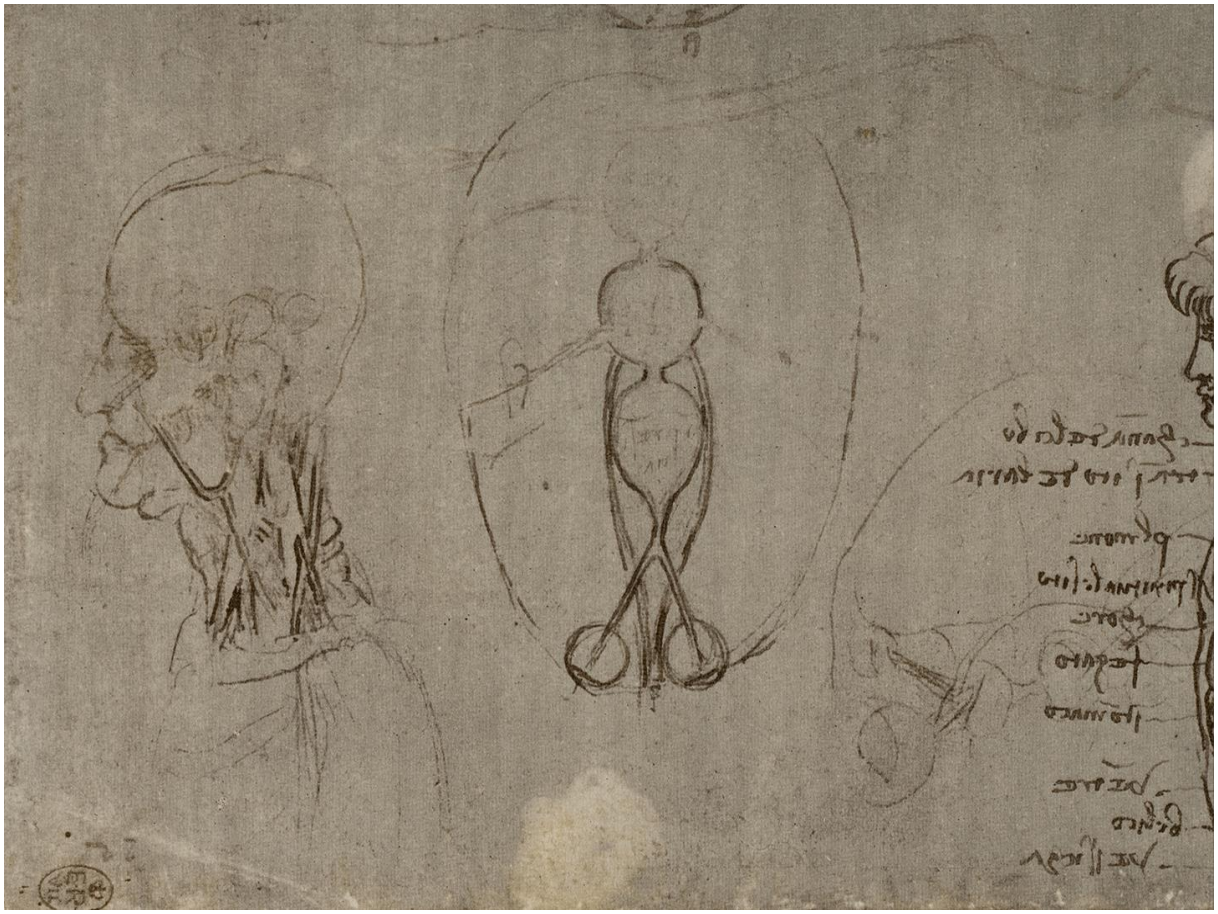


Figure 7 Leonardo da Vinci, *Drawing of the Cell Doctrine of Cerebral Localization*. Detail from K/P 4r (ca. 1487).

> Among the 14 drawings on this sheet are three that demonstrate Leonardo's concept of the senso comune. Leonardo made a modification in the medieval version of this doctrine into a new schema that he visually projected. In the central figure the optic nerves start in the orbits and project to the anterior cavity which he labeled 'imprensivo'. The olfactory and auditory nerves course toward the middle cavity labeled 'senso comune'. The third cavity is labeled 'memoria'.
>
>

Under ultraviolet light in a similar drawing (K/P 6r) we can see that Leonardo has labeled the anterior ventricle '*intelletto'* (intellect) and '*imprensiva'*. The middle ventricle is labeled '*volonta'* (will) and '*senso comune'* and the posterior ventricle is labeled '*memoria'* (memory). Leonardo has reordered the standard medieval concept of the cell doctrine. He associated intellect with the ventricle towards which the optic nerves run. '*Imprensiva'* is a term used only by Leonardo and this suggests the concept of a sensory information center having a direct effect on intellect. Leonardo's '*Volonta'* or will (voluntary motion action) has a place in the middle ventricle. Therefore it would appear that Leonardo's conceptualization is that sensation is integrated and action arises from the middle ventricle, the '*senso comune'*. This entity is therefore influenced by intellectual input from both the anterior ventricle and previous stored information from the third ventricle.

In a synthesis of this information written in about 1490 Leonardo says:

The Common Sense, is that which judges of things offered to it by the other sense. The ancient speculators have concluded that that part of man which constitutes his judgement is caused by a central organ to which the other five senses refer everything by means of impressibility; and to this centre they have given the name Common Sense. And they say that this Sense is situated in the center of the head between Sensation and Memory. And this name of Common Sense is given to it solely because it is the common judge of all the other five senses *i.e.* Seeing, Hearing, Touch, Taste and Smell. This Common Sense is acted upon by means of Sensation which is placed as a medium between it and the senses. Sensation is acted upon by means of the images of things presented to it by the external instruments…Surrounding things transmit their images to the senses and the senses transfer them to the Common Sense, and by it they are stamped upon by memory and are more or less retained according to the or force of impression. That sense is most rapid in its function which is nearest to the sensitive medium and the eye, being the highest is the chief of the others.[35]

It would be perfectly in keeping with Leonardo, the painter, and obsessed with the visual world to place the optic nerves going directly to the ventricle concerned with intellect. He comments:

The eye, which is called the window of the soul, is the chief means whereby the understanding may most fully and abundantly appreciate the infinite works of nature; and the ear is the second, inasmuch as it acquires its importance from the fact that it hears the things which the eye has seen.[36]

Explaining his reasons for the priority of the eye Leonardo says:

Since the eye is the window of the soul, the latter is always in fear of being deprived of it, to such an extent that when anything moves in front of it which causes a man sudden fear, he does not use his hands to protect his heart, which supplies life to the head where dwells the lord of the senses, nor his hearing, nor sense of smell or taste; but the affrighted sense immediately not contented with shutting the eyes and pressing their lids together with the utmost force, causes him to turn suddenly in the opposite direction; and not as yet feeling secure he covers them with one hand and stretches out the other to form a screen against the object of his fear.[37]

An advanced conceptualization of the layers of the scalp (dura) along with the location of the three rounded communicating ventricles in K/P 32r has been dated from c.1490 to 1493-94 (Fig. 8).[38] This drawing is a further synthesis involving Leonardo's concept of the theories of Avicienna (Latinate form of Ibn-Sīnā flourished ca. 980), Albertus Magnus, Mondino and the French surgeon, Guy de Chauliac (ca. 1300-1360).[38] He uses the analogy of the layers of an onion to explain the successive layers of the scalp and brain coverings which also had been used by these authors. In a notebook from the period, the Codex Forster III, Leonardo paraphrased the work of Guy de Chauliac from a book known to be present in his library *(Guidone in Cerusia).* [38,39] The frontal sinus here outlined in sagittal reconstruction for the first time depicts Leonardo's discovery of this structure. A transverse view of the brain and surrounding skull opened, tilted backward and incorporating the orbits, optic nerves and auditory nerves again demonstrates Leonardo's attempt at three dimensional synthesis as can be seen in the lower left drawing.

Figure 8 Leonardo da Vinci, *Sagittal and Horizontal Sections of the Human Head with Layers of the Head compared with an Onion*. K/P 32r (ca. 1490).

On this page Leonardo outlined in a sagittal and transverse plane the 'cell doctrine' concept. The brain cavity is depicted as an empty space with three balloon-like expansions connected to the eye by dura-like coverings connecting with the posterior component of the eye. Using the onion analogy Leonardo comments on the layers of the scalp, eye and brain coverings. The eye is shown in sagittal section with the traditional spherical lens and the frontal sinus for the first time.

Phase II: Anatomical Concept Formation

Leonardo must have been dissatisfied with his reliance on other authorities as he began the second phase of his studies of the nervous system in approximately 1489. These investigations were significantly aided by Leonardo's ability to study the human skull. The skull drawings present in Her Majesty Queen Elizabeth II's collection may not represent all of Leonardo's drawings in the skull series. Wenceslaus Hollar (1607-1677) etched at least one other drawing (Fig. 9), which no longer exists, while these skull drawings were in the possession of the Earl of Arundel (1585-1646).[40] This suggests that there could have been other skull drawings which may have given a clearer picture of this intended chapter in Leonardo's book on the human figure. Having human skulls in his possession allowed Leonardo to focus his studies on both the anatomy of the skull and the integration of his interest in the eye, the optic nerves and the *senso comune*.

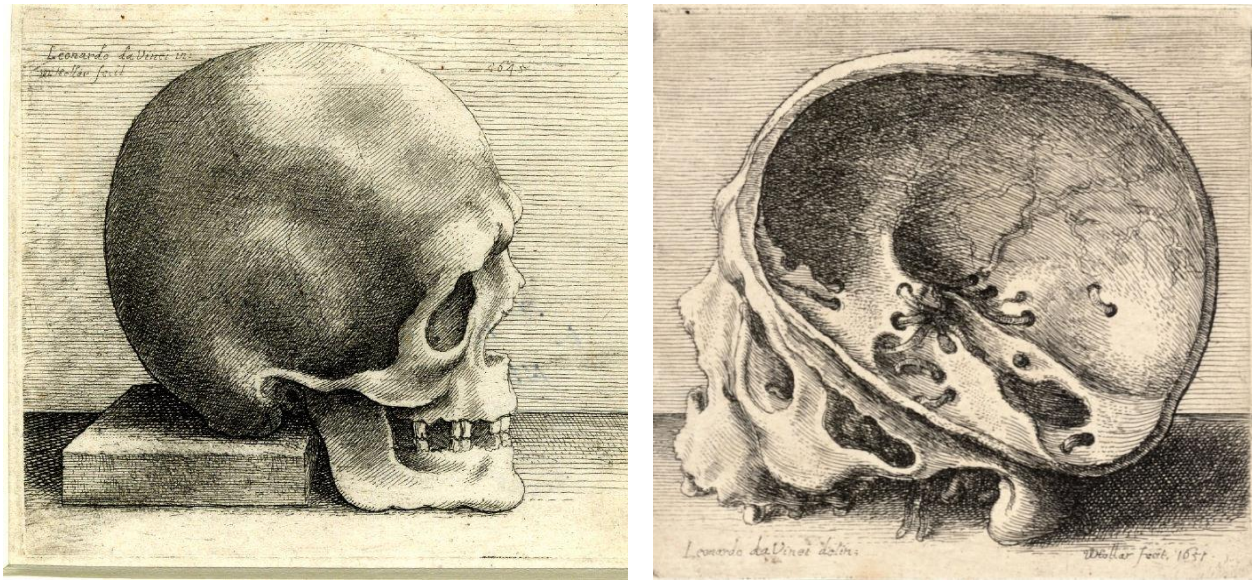


Figure 9 Wenceslaus Hollar, 1607-1677, (after Leonardo Da Vinci) Left: *Profile of a skull* (1645). Right: *Skull with the left lateral skull removed* (1651).

> Wenceslaus Hollar etched this skull profile (left) which is no longer known to exist as a drawing. The skull profile on the right was also etched by Hollar. This etcher did not understand and/or incorporate the anatomical information present in Leonardo's drawing seen in Fig. 12.
>
> Reproduced with permission of the Fischer Library, University of Toronto.

For his rendering of the three-dimensional beauty of the human skull he was critically dependent on the architectural concepts related to the geometrization of terrestrial space. Leonardo possessed a manuscript copy of Francesco di Giorgio Martini's (A.D. 1439-1501) *Trattati di Architetturo* (Treatise on Architecture) and traveled with him to Pavia in 1490.[41] Francesco's concepts of the three-dimensional representation of objects may have been learned from the works of another artisan and architect, Mariano di Jacopo, known as Taccola (1381-ca. 1453). The concept of cutaway and transparency of three-dimensional objects, which allowed the visualization of internal structures without the need for three-dimensional models, appears to have been a method that Taccola used to

render structures inside a solid object. Leonardo also exploited the concept of the exploded view of an object which was initially used by Filippo Brunelleschi (1377-1446).
On the top of the first drawing that inaugurates these skull investigations (K/P 40r) Leonardo wrote 'On the second day of April 1489, book entitled *On the Human Figure'*.

Drawing K/P 40r is the first in a series of drawings one purpose of which it was to localize the '*senso comune'* in three-dimensional space (Fig. 10). Leonardo's drawing outlined the orbital structures and superficial temporal arteries in veins coursing below rather than above the zygomatic arch which may reflect an error due to his dissections of other animal species.

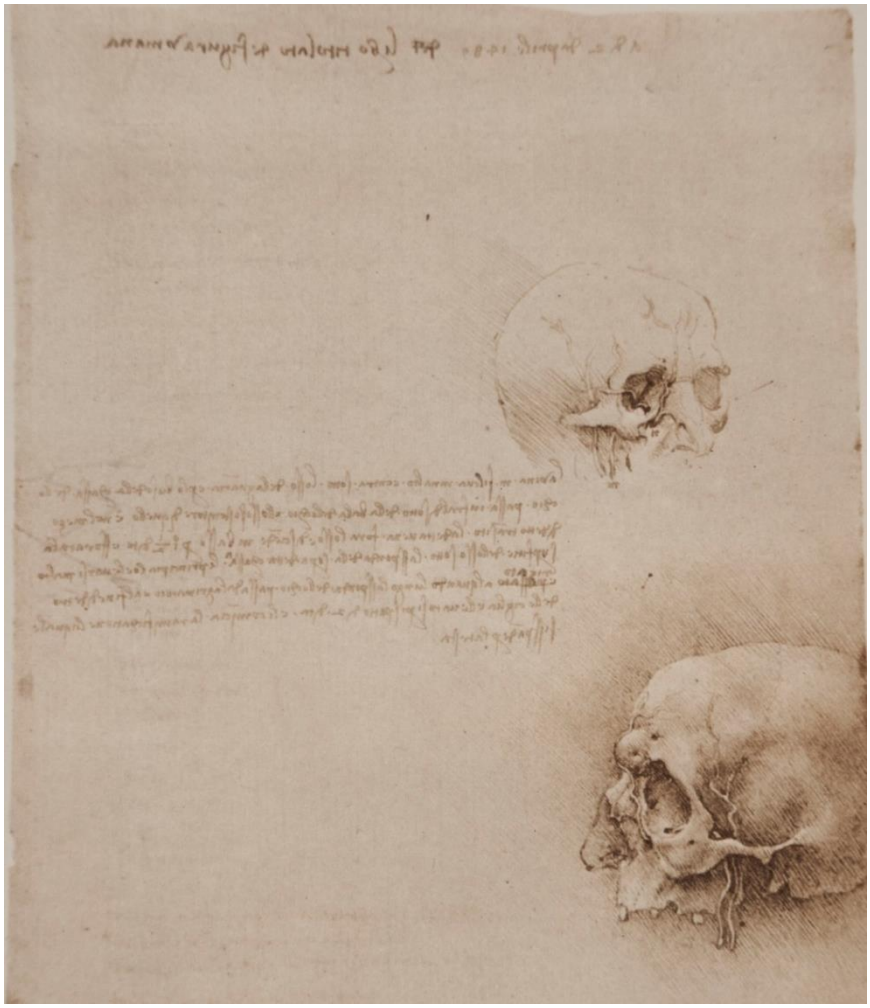


Figure 10 Leonardo da Vinci. *Views of the Skull with Foramen and Blood Vessels.* K/P 40r (ca. 1489).

These drawings are the first presently existent that integrate a series of beautiful skull drawings one purpose of which was to localize the *senso comune* in three-dimensional space. He no longer projected medieval concepts onto his skull drawings but incorrectly drew the superficial temporal vessels coursing under the zygomatic arc. This suggests that he may have been projecting anatomical information from other animal studies onto his human skulls drawings.

In drawing K/P 42v, a frontal view of the skull, Leonardo exploited the cutaway technique to outline the orbit, nose and the anatomy of the sinuses (Fig. 11). His comment below the drawing is enlightening:

The cavity of the eye socket and the cavity of the bone that supports the cheek and that of the nose and mouth are of equal depth and terminate in a perpendicular line below the senso comune.

The recto of this sheet K/P 42r has a carefully constructed drawing in which Leonardo locates the '*senso comune'* in the anterior portion of the third ventricle just above the optic chiasm (Fig.12). It is at the point where two lines meet one dropping down from the junction point of the sagittal and coronal sutures and a glabella-lambda line. Leonardo outlines a number of the cranial nerves at the base of the skull and the superficial middle meningeal artery and vein.

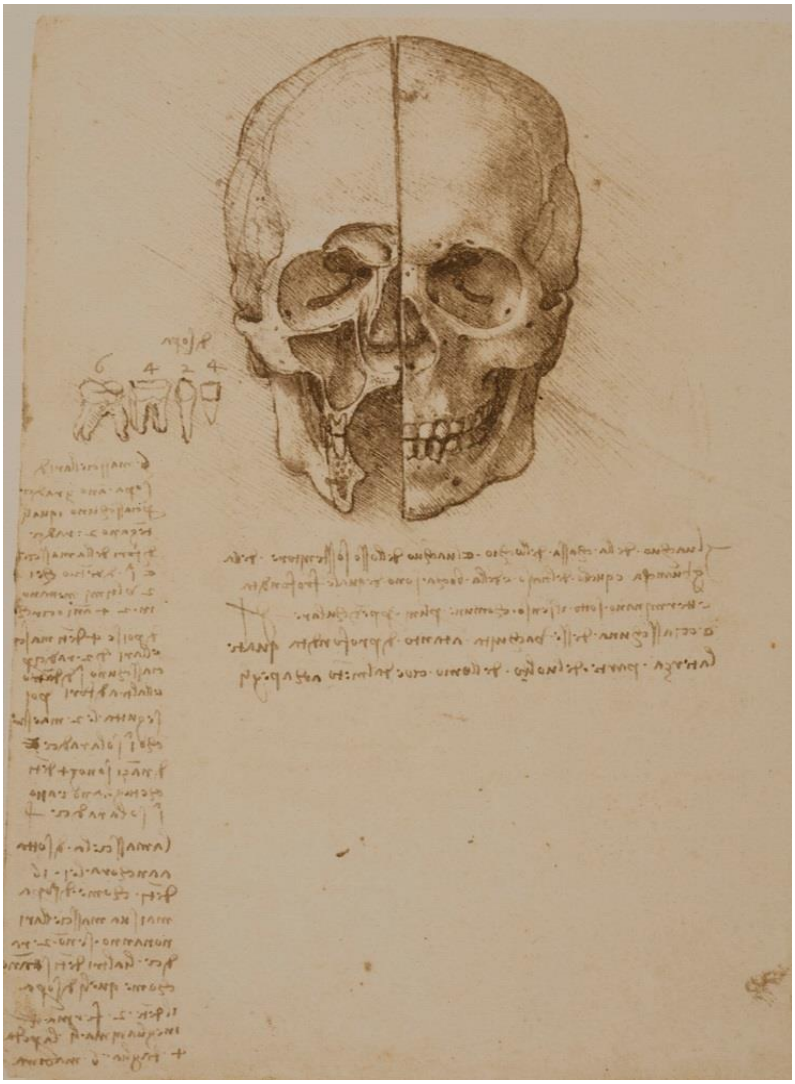
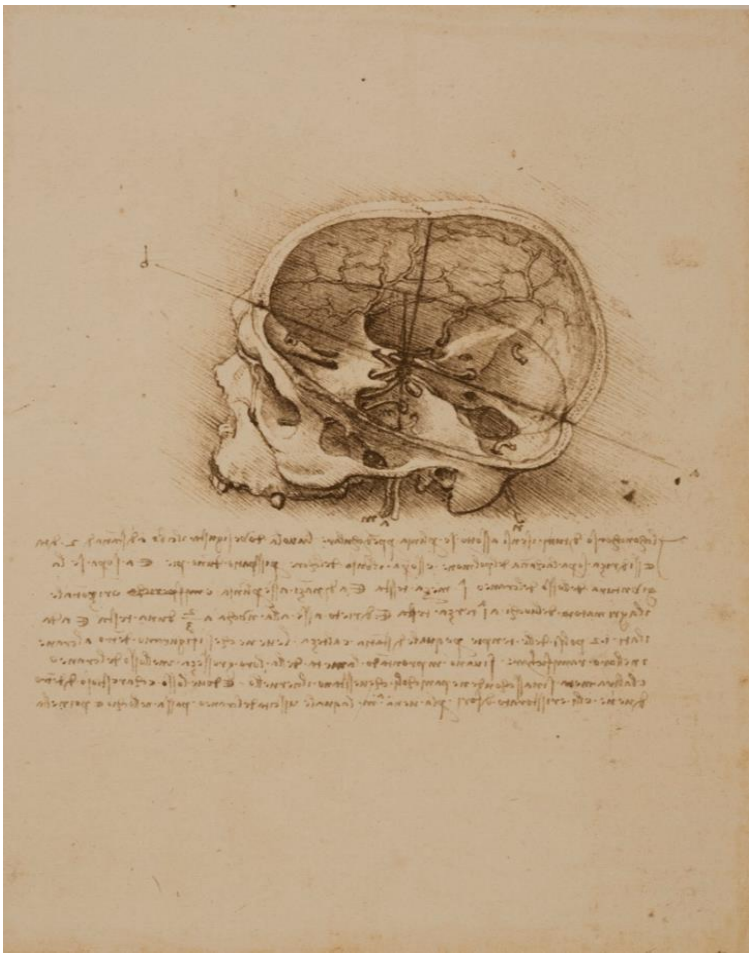


Figure 11 Leonardo da Vinci. *Sectioned and Cutaway Views of the Skull.* K/P 42v (ca. 1489).

In the cutaway view the internal structures of the face can be seen along with the first depiction of the maxillary sinus. His interest in the eye as 'the window to the soul' is outlined in the care he took in the delineation of the orbital structures. Leonardo's ability to fuse anatomical skill, proportion and architectural perspective is clearly apparent in this creation.

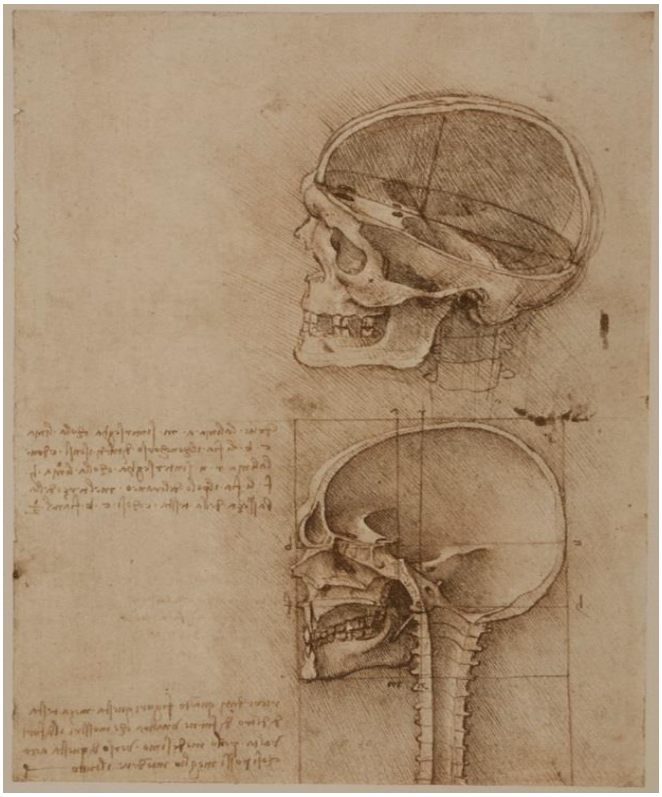


A glabella-lambda line with a perpendicular line dropped from the junction of the coronal and sagittal sutures and a transverse line from the inner aspect of the temporal bones indicates the position of the senso comune in this drawing. The location of this point falls at the anterior portion of the third ventricle. Many of the nerves of the cavernous sinus, middle meningeal vessels branches and the optic chiasm are carefully outlined as are the eight nerves and others converging on the senso comune.

Figure 12 Leonardo da Vinci. *Localization of the senso comune and Anatomical Features of the Skull.* K/P 42r (ca. 1489)

In K/P 43r Leonardo's purpose for these drawings was to more accurately localize the 'se*nso comune'* (Fig.13). To accomplish his goal Leonardo exploited both a cut away direct lateral view in the lower drawing and a representation similar to K/P 42r without nerves and vessels in the upper representation. It is clear that Leonardo utilized concepts of proportion in these drawings since he was carrying out a number of other proportion related studies on animals and the human body at this time.[43]

In the lower more advanced proportional drawing he now labels the lines commenting: 'Where the line am is intersected by the line cd there the meeting of the senses is made.' Leonardo thus outlined his concept that the eye was the 'window of the soul' integrating this into a three dimensional representation of pictorial and architectural space.



The overall purpose of the two drawings on this sheet was to carry out a localization of the *senso comune* in the three-dimensional geometric space within the skull. The projection of both horizontal and vertical lines intersecting at the location of the *senso comune* demonstrate Leonardo's interest and dependence on proportional representation to more accurately localize points in three dimensions. Concerning the lower drawing Leonardo writes "Where the line am is intersected by the line cd there the meeting of the senses is made".

Figure 13 Leonardo da Vinci. *Location of the senso comune*. K/P 43r (ca. 1489).

While conducting these anatomical studies associated with the human skull Leonardo began to conceptualize how the brain worked. In K/P 39r, Leonardo commented on '*How the five senses are servants of the soul':*

The soul appears to reside in the seat of judgment, and the judicial part appears to be in that place where all the senses come together, which is called the 'senso comune', and it is not all of it everywhere in the whole body as many believed, but all in this part. For if it were all in the whole and all in each part it would not have been necessary to make the instruments of the senses converge to one and the same concourse in one place only. On the contrary it would have sufficed for the eye to perform its sensory function on its surface and not transmit by way of the optic nerves the similitude of the things seen to the "senso comune", because the soul for the aforesaid reason, would be able to comprehend them on the surface of the eye…Touch does not finish there (locally); it passes through the perforated nerves and is carried to this 'senso [comune].' Its nerves proceed spreading out into infinite ramifications in the skin which encompasses bodies, limbs and viscera… (the nerves). The perforated cords carry (sensation) command and sensation to the functioning parts….Therefore the joint between bones obeys the tendon, and the tendon the muscle, and the muscle the nerve, and the nerve the "senso comune", and the "senso comune" is the seat of the soul; memory is its store and 'imprensiva' is its standard of reference and the heart is its … [Leonardo leaves this blank]. How the sense gives to the soul and not the soul to the sense, and where the sensory function is missing from the soul, the soul in this life lacks information from the function of that sense, as appears in a mute or one born blind.

Leonardo's drawings localized the '*senso comune'* just above the optic chiasm in the area involving the anterior portion of the third ventricle. In the anterior third ventricle-hypothalamic region there are critical cerebral nuclei which, if damaged, result in significant changes in the way that humans perceive both their inner and outer worlds. Although information is now available related to the multiple functions of the human brain the relationship of how the information that is processed from our senses results in cognitive function continues to be elusive.

Phase III: Integration

Leonardo began the third phase of studies related to the location of the '*senso comune'* in 1508-1509. Applying his skills in sculpture he more accurately outlined the shape of the ventricular system using the ox brain (K/P 104r ca. 1508). Leonardo injected wax into the floor of the third ventricle using a syringe with two vent holes placed in the horns of the lateral ventricles to allow fluid and air escape. After the wax had set he dissected away the brain tissue obtaining a relatively accurate model of the ventricular system (Fig.14). On the lateral projection of the ventricular system one can see that he identified the foramen of Monro which is the connection between the lateral ventricles and the third ventricle along with the aqueduct of Sylvius which connects the third ventricle to the fourth ventricle. Leonardo was able to solve a very complex anatomical problem, the three-dimensional structure of the ventricular system, by using knowledge he had obtained from other artistic disciplines (modeling and bronze sculpture) and applying this information to the problem. This particular experiment may be considered the pinnacle of his brain-related investigations.

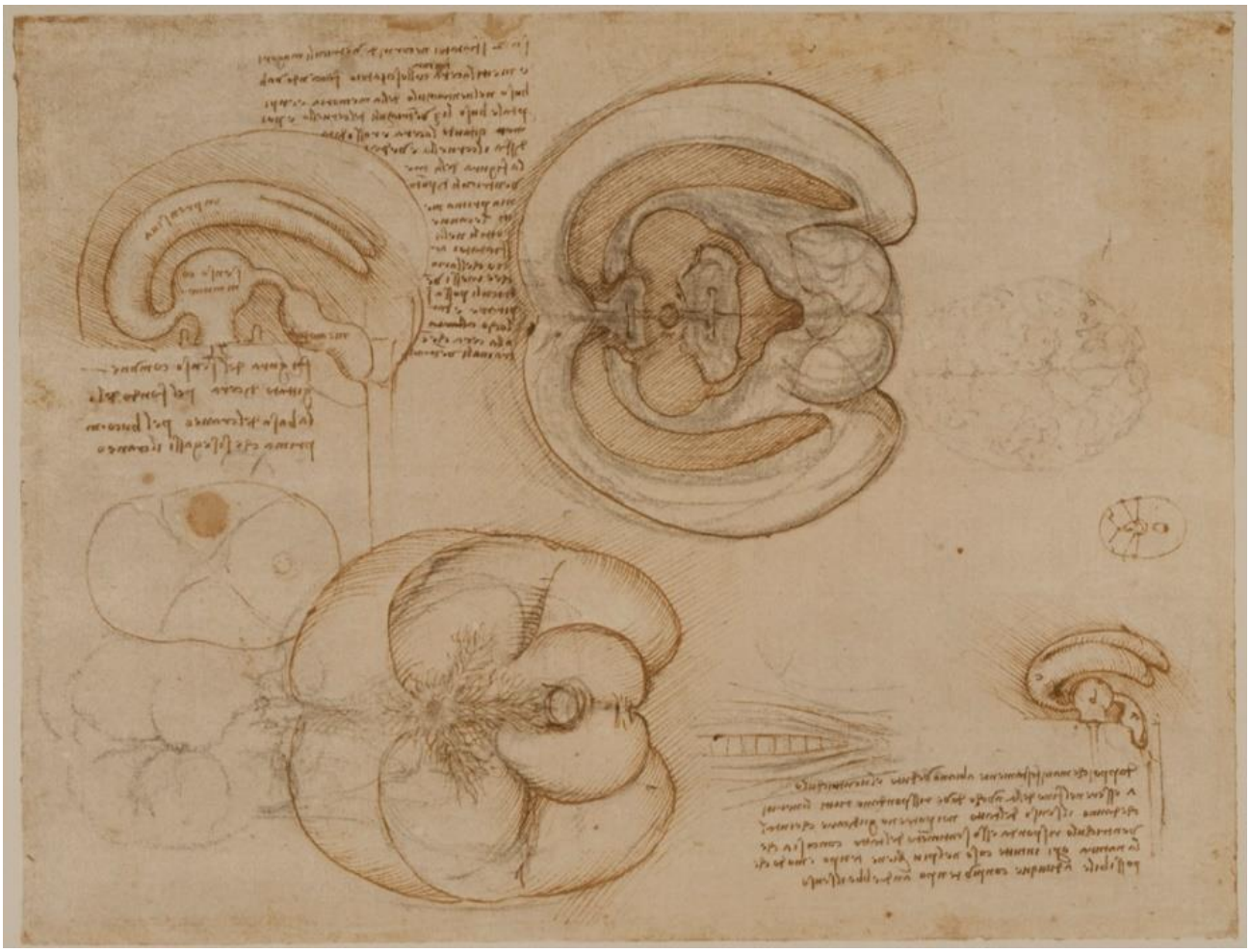


Figure 14 Leonardo da Vinci. *Cerebral Ventricles of the Ox Brain*. K/P 104r (ca 1508).

Leonardo's fusion of artistic and modeling ability combined with the innovations needed to deal with the difficult problem of creating an accurate three-dimensional structural representation of the ventricular system can be appreciated on this sheet of drawings. Leonardo writes: "Make two vent-holes in the horns of the greater ventricles and insert wax with a syringe making a hole in the ventricle of memory and through that hole fill the three ventricles of the brain. Then when the wax has set, dissect off the brain and you will see the shape of the three ventricles exactly. But first put fine tubes in the vent-holes so that air which is in these ventricles is blown out and makes room for the wax to which enters the ventricles." The syringe can be seen inserted into the floor of the third ventricle which has been expanded by the pressure injection in the small drawing on the right. The foramen of Monro linking the lateral ventricles to the third ventricle can be seen, as can the aqueduct of Sylvius and the two lateral and fourth ventricles. In the upper left figure Leonardo adds the words "*imprensiva*" in the lateral ventricles *"senso comune"* in the third ventricle and "*memoria"* in the fourth ventricle. The lower left drawing shows the base of the ox brain and the "*rete mirabile*" while the right upper drawing shows the ventricles from below.

Leonardo, at this time, was also carrying out experiments related to the optic nerves and nerves associated with the base of the skull as seen in K/P 55r (Fig. 15). He was able after these investigations to carry out a number of hybrid drawings K/P 103r (Fig. 16).

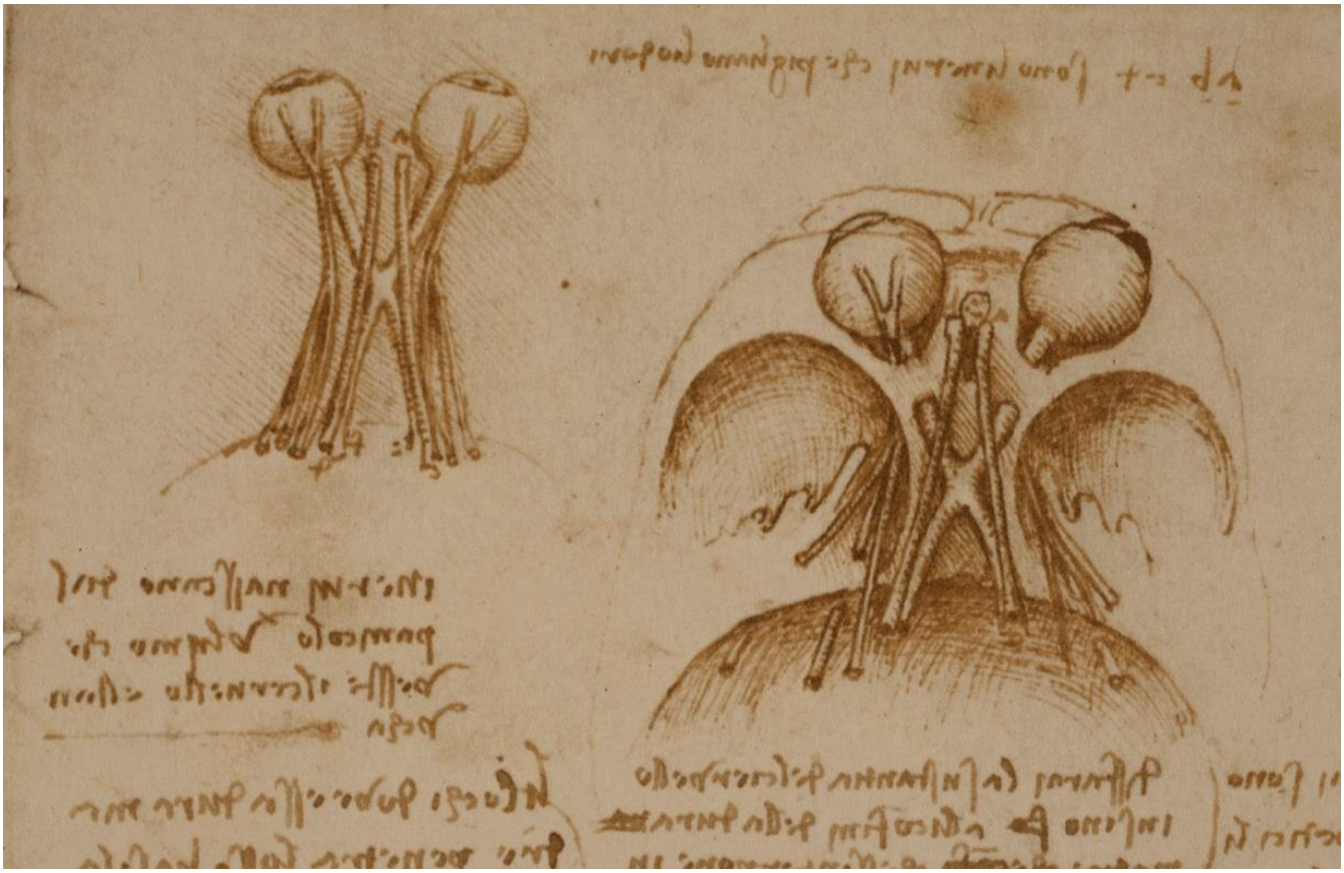


Figure 15 Leonardo da Vinci. *Views of Olfactory and Optic Nerves*. Detail from K/P 55r (ca. 1508).

In these drawings, Leonardo shows one drawing showing the base of the skull and nerves running into the cavernous sinuses (*right*) and a figure in which the skull base is not shown (left). Knowledge acquired from his skull studies is integrated with his better understanding of the course of the cranial nerves. Clearly a great deal of care was used to outline the multiple nerves outlined in these drawings. Describing the technique to prepare the anatomical specimens on this sheet Leonardo says: "Ease away the brain substance from the borders of the dura mater which is interposed between the basilar bone and the brain substance. Then note all the places where the dura mater penetrates the basilar bone with nerves ensheathed in it together with the pia mater. And you will acquire such knowledge with certainty when you diligently raise the pia mater little by little."

Figure 16 Leonardo da Vinci. *Hybrid Drawings Brain and Cranial Nerves*. Detail from K/P 103r (ca. 1508).

These hybrid drawings integrate Leonardo's ventricular structure investigations with his newly acquired knowledge of the skull base and cranial nerves. These drawings convey the complex three-dimensional nature of the brain, cranial nerves and facial structure. Conceptually Leonardo moves from the brain and nerve structures (*left*) adding the ventricular system in the *central* figure and integrating the superimposed facial and bone structures in the drawing on the *right* to provide a more accurate perspectival rendering of the relationships of the various cerebral structures, nerves and facial elements present.

This integrated information from his anatomical studies associated with the ventricular system, his skull studies, and his investigations of the base of the skull and optic nerves allowed the production of quite complex drawings that are on a sheet located at the Kunsammlungen zu Weimar in Weimar, Germany (Fig 17). These drawings not only involve Leonardo's attempt to integrate all his previous studies but demonstrate his ability to use an exploded type of view to visualize the underside of the brain and the skull base in the same diagram. To demonstrate the individual components more accurately Leonardo, in the lower right drawing, has the skull cap rising above the brain which is floating in space rotated so one can see the multiple cranial nerves at the base of the brain. Leonardo was also interested in understanding how the information in the ventricular system could be modulated. The concept of the *'imprensiva'* as a process relay station between the sensory percussion waves was further modified considering the role of the choroid plexus. He commented on 'the muscle call worm' which is situated in the ventricles of the brain and which lengthens and shortens to open and close the passage of the *'imprensiva'* or '*senso comune'* to the memory: (K/P 115r).[38] The choroid plexus ('worm of the brain') in his model functioned not only as a system modulating fluid flow through the foramen of Monro and the aqueduct of Sylvius but was an automatic regulator of flow and therefore communication between the ventricular cavities of the mind.

On this sheet Leonardo integrates his knowledge of cerebral and base of skull anatomy to produce his most complex and accurate drawing of this region. In the lower right figure Leonardo elevates the skull cap, allowing the brain to rotate and float above the skull base. Leonardo thus exploits the technique of displaying the component parts separated in space to outline individual parts more accurately in an architecturally defined type of space. Leonardo writes: "When you make a drawing of the brain join all the nerves which descend from the brain to the perforations made by them in the basilar bone. And this is the true way of showing the true situation of the nerves in their upper parts as well as in their lower parts… and do all this from four aspects"

Reproduced from the Kunstsammlungen zu Weimar, Weimar, Germany.

Figure 17 Leonardo da Vinci. Composite Rendition of the Brain and Cranial Nerves. Weimar verso (ca. 1508).

During this phase of Leonardo's studies, 1508-1514 a vast number of anatomical investigations were carried out encompassing almost all aspects of human anatomy. Of particular interest are Leonardo's drawings of a fetus K/P 198r (ca.1511-1513) in a woman's uterus (Fig.18). One question that concerned him was how the soul of the mother could control her fetus during the pregnancy and in particular how the soul could pass from mother to child. He comments 'One and the same soul governs these two bodies; and the desires, fears and pains are common to this creature as to all other animated parts' (K/P 198r). The synthesis that emerges from his embryological and anatomical studies is summarized in his comments:

Though human ingenuity by various inventions with different instruments yields the same end, it will never devise an invention either more beautiful…than does Nature because in her inventions nothing is lacking and nothing superfluous and she…puts there the soul, the composer of the body, that is the soul of the mother which first composes in the womb the shape of man and in due time awakens the souls which is to be its inhabitant. (K/P 114v)

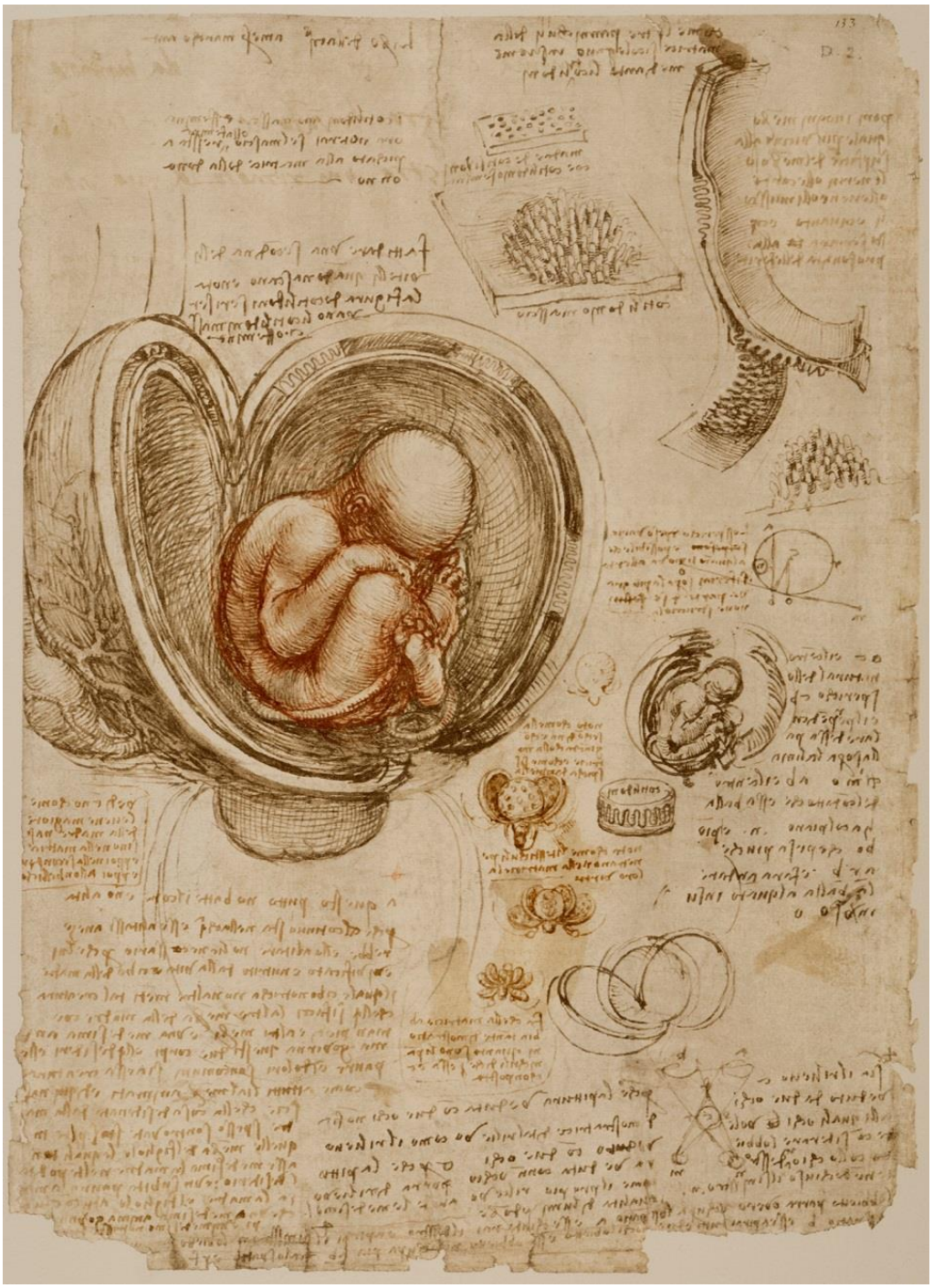


Figure 18 Leonardo da Vinci. Fetus in Utero. K/P 198 (ca. 1511-13).

In these studies Leonardo places the fetus in the uterus containing the surrounding membranes to complete both an anatomical and conceptual framework of the beginning of life. Leonardo writes of fetal existence: "And breathing is not necessary to it because it is vivified and nourished by the life (vital spirit) and food of the mother… and one and the same soul governs these two bodies"

The Search Broadens…

With the death of Leonardo in 1519, all his notebooks and other materials passed to Francesco Melzi (1491-1570) his favorite pupil who kept them at his villa in Vaprio D'Adda near Milan. During the middle of the 16th century a number of working groups were actively studying and compiling Leonardo's manuscripts.[45] Melzi, working with others compiled the notes for Leonardo's *Treatise on Painting* which was widely circulated in manuscript form before being published in Paris in 1651 in both a French and Italian edition.[46] In approximately 1560, a Milanese painter (possibly Girolamo Figino who flourished in the second half of 16th century), working with Leonardo's original manuscripts at the Villa Melzi, produced a manuscript called *Le Regole del Disegno*.[47] The five books available to us are almost all on the movement and proportions of the human figure. Many individuals saw Leonardo's notebooks and drawings present in Melzi's home. His ideas and drawings were freely copied, used, and plagiarized, but seldom acknowledged. This has made it difficult to trace their influence on subsequent anatomical thought and illustration.[48] Following Leonardo's death, the ventricular localization of brain function was still dogmatically taught in medical schools. Andreas Vesalius (1514–1564) commented:

I have not forgotten how when I was following the philosophical course in the Castle School, easily the leading and most distinguished school of the University of Louvain, in such commentaries on Aristotle's treatise, *On The Soul*, as were read to us by our teacher . . . an illustration was shown us taken from some Philosophic Pearl presenting to our eyes the aforesaid ventricles which each of us studied very carefully as an exercise and added a drawing of it to our notes. We were persuaded that this figure included not only the three ventricles but also, as we were led to believe, it displayed all parts of the head including the brain.[49]

Vesalius correctly realized that Galen and other ancient and medieval authorities had based their descriptions on animal dissections. The performance of his own careful dissections on human material, culminated in the publication of *De Humani Corporis Fabrica* in 1543.[49] Vesalius although denouncing the ventricular localization of brain function advanced no concept to replace it. His work, based on personal dissection experience (as was that of Leonardo), had a profound impact on anatomical thought and illustration. René Descartes (1596–1650) in his book *De Homine* published in 1662 made a complete break from the medieval tradition of the cell doctrine that had been based on Plato's concept of a three-part soul.[50] Descartes localized the soul to the pineal gland, based on his concept that the body was a machine. Because only one soul was needed to run this mechanical body, he dispensed with the others (heart and abdomen). His mechanistic views refocused anatomical investigations into an inquiry of how physical laws could be applied to cerebral and reflex functions. Other anatomists including Thomas Willis (1621–1675) disagreed with Descartes' idea that the pineal gland was the seat of the soul. Willis was an important member of the iatrochemists, a group of researchers who believed that chemical, rather than mechanistic concepts were essential to human function. In his *De Cerebri Anatome*, first published in 1664, Willis still clung to Galenic concepts such as the excretion of animal spirits from the cribiform plate.[51] In this book, he outlined a new concept that in some way the choroid plexus was involved in the absorption of cerebrospinal fluid.[51] In *De Anima Brutorum* published in 1672, Willis proposed that the corpus striatum received all sensory information and was thus the seat of the *senso comune*; the corpus callosum was associated with imagination and the cerebral cortex stored memory.[51] The three-part soul was thus restructured based on a slightly better understanding of brain function. The Cell Doctrine of cerebral function was reworked by investigators like Albert Haller (1708-1777) and Pierre Flourens (1794-1867) who by the weight of their authority and flawed stimulation results would champion an erroneous

concept of equipotentiality of brain function.[52] These ideas would retard progress on the understanding of brain function for almost a century. The careful cortical stimulation experiments reported by Gustav Fritsch (1839-1907) and Edward Hitzig (1837-1927) would begin to redraw the map of localization of cerebral function and the contributions of David Ferrier (1823-1928), Pierre Broca (1824-1880) and Wilder Penfield (1891-1976) would produce a comprehensive understanding of where motor and sensory function were controlled by the cortical tissue of the brain.[52] Penfield concluded that 'the indispensable substratum of consciousness lies outside of the cerebral cortex, probably in the diencephalons.'[53]

Improvements in microscope design and function, which were occurring in parallel with these new brain simulation techniques, allowed researchers a new window into the cellular organization of a variety of tissues including the brain. Gabriel Valentin (1810-1883) showed the first microscopic image of a nerve cell in 1836.[54] The first identified nerve cell in the nervous system was published by Jan Evangelista Purkinje (1787-1869) in 1837.[55] Camillo Golgi (1843-1926), together with Santiago Ramón y Cajal (1852-1934), received the Nobel Prize in Physiology or Medicine in 1906 for their studies of the structure of the nervous system.[56] The studies of Cajal defined the neuron as the structural unit of the nervous system. Further studies by numerous investigators further outlined the neuron doctrine and proposed distinct levels of organization of the nervous system.[56] In this concept each level forms a functional unit which structures the basis of each higher organization plane. These levels include molecules and ions, synapses, microcircuits, dendritic trees, neurons, local circuits, integrated systems and behavioural systems.[56] Thus we have both an appreciation of the complexity of our nervous system and our inadequate understanding of how exactly the brain works to make us what we are.

Leonardo would have very much appreciated our vast armamentarium of experimental, psychological and genetic knowledge. He may have asked a series of provocative questions. These could include: 1) Where does love come from? 2) Where does friendship and caring reside in the brain? 3) Where is that special 'soul' located that allows us to experience not only our consciousness but our humanity? In our present world filled with war, inequality and injustice answers to these important human questions seem very elusive.

Epilogue

Leonardo carried out numerous studies associated with the composition of the human body. These studies were intended not only to help him understand the structure and function of the body but to more accurately understand the mystery of human existence-the human soul. The study of man has always had and will always have an element of mystery. Kenneth Clark writes:

Yet just as Leonardo, in his intellectual pursuit of natural forces, hung on with a kind of inspired tenacity, so in the St. John we feel him pressing closer round the form, penetrating further and further into the mystery, till at last he seems to become a part of it, so that like his contemporaries we no longer think of him as a scientist, a seeker for measurable truth, but as a magician, a man who, from his close familiarity with the processes of nature, has learnt a disturbing secret of creation.[57]

The act of creation of a painting is a critical scientific and intellectual endeavor that only man is able to achieve. Leonardo's investigations related to the pithing of the frog and the studies associated with the three-dimensional representation of the human skull and the position of the soul within that skull and his attempt at synthesis related to the function of the mind all contributed to the knowledge base that aided him in understanding the world around him. The future will involve the utilization of information from advanced anatomical studies, newer methods of molecular biology and the integration of the human genome to provide investigators with further clues as to how the mind is structured to attempt the ultimate goal of understanding itself. Venter et al in a seminal paper published in Science in 2001 concerning the initial elucidation of the human genome comments:

The real challenge of human biology, beyond the task of finding out how genes orchestrate the construction and maintenance of the miraculous mechanism of our bodies, will lie ahead as we seek to explain how our minds have come to organize thought sufficiently well to investigate our own existence.[58]

In this paper almost 30,000 genes were identified many of which still do not have a role in human physiology and/or development. It is certainly possible that some of these genes for which a role has not been found could be related to the development of 'the human soul'. In 2014 the Noble Prize in Physiology or Medicine was awarded to Edvard Moser, his wife May-Britt Moser and John O'Keefe for the discovery of Place and Grid cells.[59] The role of these specialized cells is to outline where we are at any given time and develop a grid system to help us find the right location in our environment for which we are searching. The hippocampus system continuously helps guide and upgrade this system allowing the acquisition of new memory engrams.

In the future my expectation would be that a series of genes guiding the function of dedicated brain cells, which can be continuously modulated by early developmental and life environment that function to help us experience love, friendship and human caring, will be defined. This information will open new doors to our understanding of what makes us truly human. Man will always attempt to further understand the mystery of the mind and how it controls our passions and intellectual functions. Leonardo comments:

What moves you man to abandon your home in town and leave relatives and friends, going into country places over mountains and up valleys, if not the natural beauty of the world.[60]

The search continues…

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Transcriptions, translations, and quotations references:
A series of drawings by Leonardo da Vinci have been used as illustrations. All these can be found in reference 38, Vol. 3. Each drawing is designated by its Keele/Pedretti (K/P) number. All transcriptions of Leonardo's notes on these sheets are taken from the translations provided in Vol. 1 and 2 unless otherwise noted.

John P. McGovern Award Lectureships

1. *Our Lords, The Sick* presented by Albert R. Jonsen, Ph.D., April 12, 1986, in San Francisco, California.

2. *To Humane Medicine: Back Door or Front Door?* presented by Edward J. Huth, M.D., April 29, 1987, in Philadelphia, Pennsylvania.

3. *Medicine and the Comic Spirit* presented by Joanne Trautmann Banks, May 3, 1988, in New Orleans, Louisiana.

4. *The 'Open Arms' Reviving: Can We Rekindle the Osler Flame?* presented by Lord Walton, April 26, 1989, in Birmingham, Alabama.

5. *Rx: Hope* presented by E. A. Vastyan, May 8, 1990, in Baltimore, Maryland.

6. *Osler's Gamble and Ours: The Meanings of Contemporary History* presented by Daniel M. Fox, April 10, 1991, in New Orleans, Louisiana.

7. *From Doctor to Nurse with Love In a Molecular Age* presented by William C. Beck, March 26, 1992, in San Diego, California.

8. *The Heroic Physician In Literature: Can The Tradition Continue?* presented by Anne Hudson Jones, May 12, 1993, in Louisville, Kentucky.

9. "*The Leaven of Science": Osler and Medical Research* presented by David Hamilton, May 10, 1994, in London, England.

10. *A Body of Knowledge: Knowledge of the Body* presented by Sherwin B. Nuland, May 10, 1995, in Pittsburgh, Pennsylvania.

11. *Other People's Bodies: Human Experimentation on the 50th Anniversary of the Nuremberg Code* presented by David J. Rothman, April 25, 1996, in San Francisco, California.

12. *The Coming of Compassion* presented by Roger J. Bulger, April 3, 1997, in Williamsburg, Virginia.

13. *Why We Go Back to Hippocrates* presented by Paul Potter, May 6, 1998, in Toronto, Ontario.

14. *Health Care in the Next Millennium* presented by John D. Stobo, M.D., May 5, 1999, in Montreal, Canada.

15. "*Writ Large": Medical History, Medical Anthropology, and Medicine and Literature* presented by Gert H. Brieger, M.D., Ph.D., May 17, 2000, in Bethesda, Maryland.

16. *Reflections on American Medical Education* presented by Kenneth M. Ludmerer, M.D., April 18, 2001, in Charleston, South Carolina.

17. *John Shaw Billings as a Historian* presented by James H. Cassedy, Ph.D., April 24, 2002, in Kansas City, Kansas.

18. *The Evolution of the Controlled Trial* presented by Sir Richard Doll, May 23, 2003, in Edinburgh, Scotland.

19. *Practising on Principles: Medical Textbooks in 19th Century Britain* presented by W.F. Bynum, M.D., Ph.D., FRCP, April 20, 2004, in Houston, Texas.

20. *Just Call Us Children: The Impact of Tsunamis, AIDS and Conflict on Children* presented by Karen Hein, M.D., April 11, 2005, in Pasadena, California.

21. *A Leg to Stand On: Sir William Osler & Wilder Penfield's Neuroethics* presented by Joseph J. Fins M.D., F.A.C.P., May 2, 2006 in Halifax, Nova Scotia.

22. *Touching Where It Hurts: The Role of Bedside Examination* presented by Abraham Verghese M.D., M.A.C.P DSc (Hon), May 1, 2007, in Montreal Quebec.

23. *Managed Fear: Contemplating Sickness in an Era of Bureaucracy and Chronic Disease* presented by Charles Rosenberg, May 5, 2008, in Boston, Massachusetts.

24. *Is Scholarship Declining in Medical Education?* presented by Patrick A. McKee, M.D., April 21, 2009, in Cleveland, Ohio.

25. *Selling Our Souls: The Commercialization of Medicine and Commodification of Care as Challenges to Professionalism* presented by Nuala P. Kenny, M.D., April 27, 2010, in Rochester, Minnesota.

26. *"The Back Forty":* American Medicine and the Public Interest *Revisited* presented by Rosemary A. Stevens, Ph.D., May 2, 2011, in Philadelphia, Pennsylvania.

27. *"Osler and the Enduring Narrative of Clinical Medicine"* presented by C. David Naylor, M.D., April 23, 2012, in Chapel Hill, North Carolina.

28. *"Louis Pasteur: Exploring His Life in Art"* presented by Bert Hansen, Ph.D., April 8, 2013, in Tucson, Arizona.

29. *"Patients, Their Doctors and the Politics of Medical Professionalism"* presented by Sir Donald Irvine CBE, M.D., FRCGP, FMMedSci, May 12, 2014, in Oxford, England.