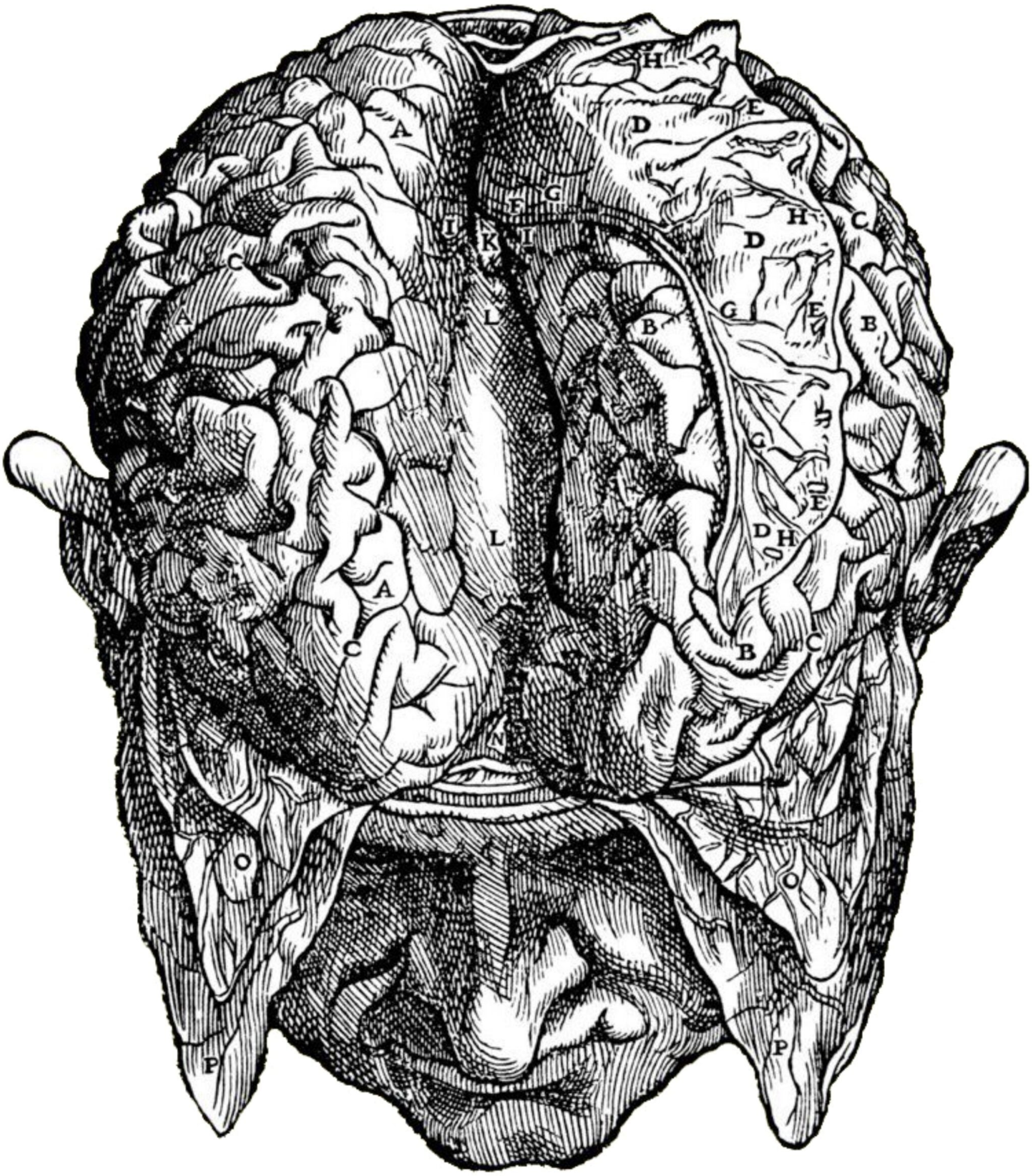
Looking at the Human Brain: from Vesalius to the Present

Andreas Vesalius (1514-1564) published his *De Humani Corporis Fabrica* (On the Fabric of the Human Body) in 1543 (O'Malley, 1964). This book, based on dissections of human cadavers, provided illustrations of the human brain that were both anatomically correct and esthetically pleasing. The scientists that followed Vesalius expanded on our knowledge, and produced their own representations of the human brain. This essay traces the evolution of these pictures.

The View from Above

One of Vesalius' most striking illustrations shows the head of a man with the top of his skull (calvarium) removed (Catani & Sandrone, 2015, p 220). The cerebral meninges (membranes) – composed of the dura mater (tough mother, P in the illustration) and the arachnoid mater (spidery mother, O) – were cut in the midline and then folded down over the edge of the skull. The cerebral hemispheres (A and B) were spread apart and the falx cerebri (cerebral sickle, D) was pulled up and folded over the left hemisphere. This revealed the corpus callosum (tough body, L) connecting the two hemispheres. At the base of the falx cerebri was a large vein later known as the inferior sagittal sinus (F, G).



In 1656, Vesalius' illustration served as a model for Rembrandt's representation of the brain in *The Anatomy Lesson of Dr Deyman.* The original painting portrayed the professor and his students in much the same way as the earlier painting *The Anatomy Lesson of Dr Nicolaes Tulp* (1632). After the painting was damaged by fire in 1723, all that remains are the hands of the professor as he dissects the meninges, his assistant holding the calvarium, and the cadaver of the recently executed thief, Joris Fonteyn, also known as “Black Jan:”

Anne Carson wrote a brief prose poem about the painting in her *Short Talks* (1992):*

> A winter so cold that, walking on the Breestraat and you passed from sun to shadow, you could feel the difference run down your skull like water. It was the hunger winter of 1656 when Black Jan took up with a whore named Elsje Ottje and for a time they prospered. But one icy January day Black Jan was observed robbing a cloth merchant’s house. He ran, fell, knifed a man and was hanged on the twenty-seventh of January. How he fared then is no doubt known to you: the cold weather permitted Dr. Deyman to turn the true eye of medicine on Black Jan for three days. One wonders if Elsje ever saw Rembrandt’s painting, which shows her love thief in

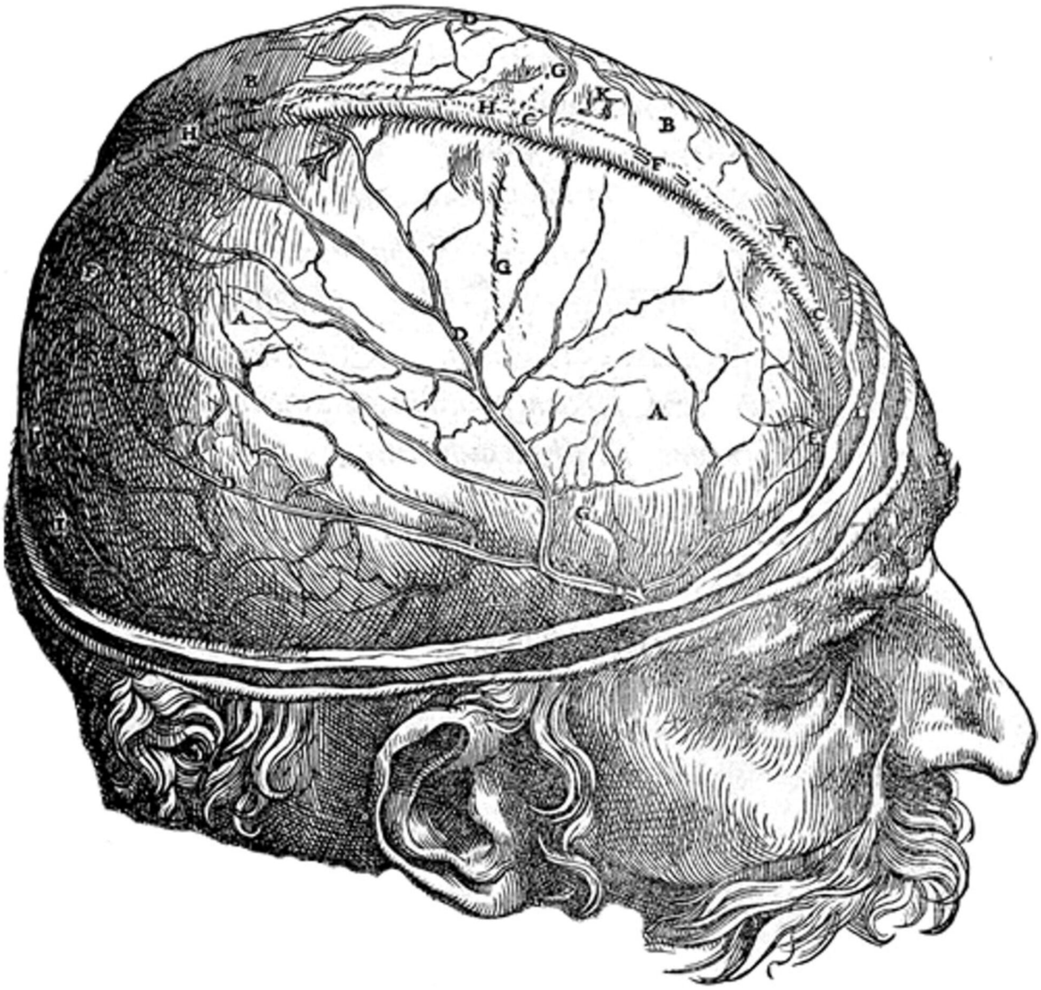
> violent frontal foreshortening, so that his pure soles seem almost to touch the chopped-open cerebrum. Cut and cut deep to find the source of the problem, Dr. Deyman is saying as he parts the brain to either side like hair. Sadness comes groping out of it.

Carson uses two striking images: the transition from sun to shadow like water on the skull, and the parting of the brain like hair. She also remarks on the foreshortening – Rembrandt was using Mantegna's *Lamentation of the Dead Christ* (1480) as a model. And she sadly links the soles of the feet to the soul of Black Jan, recently released from his cerebrum.

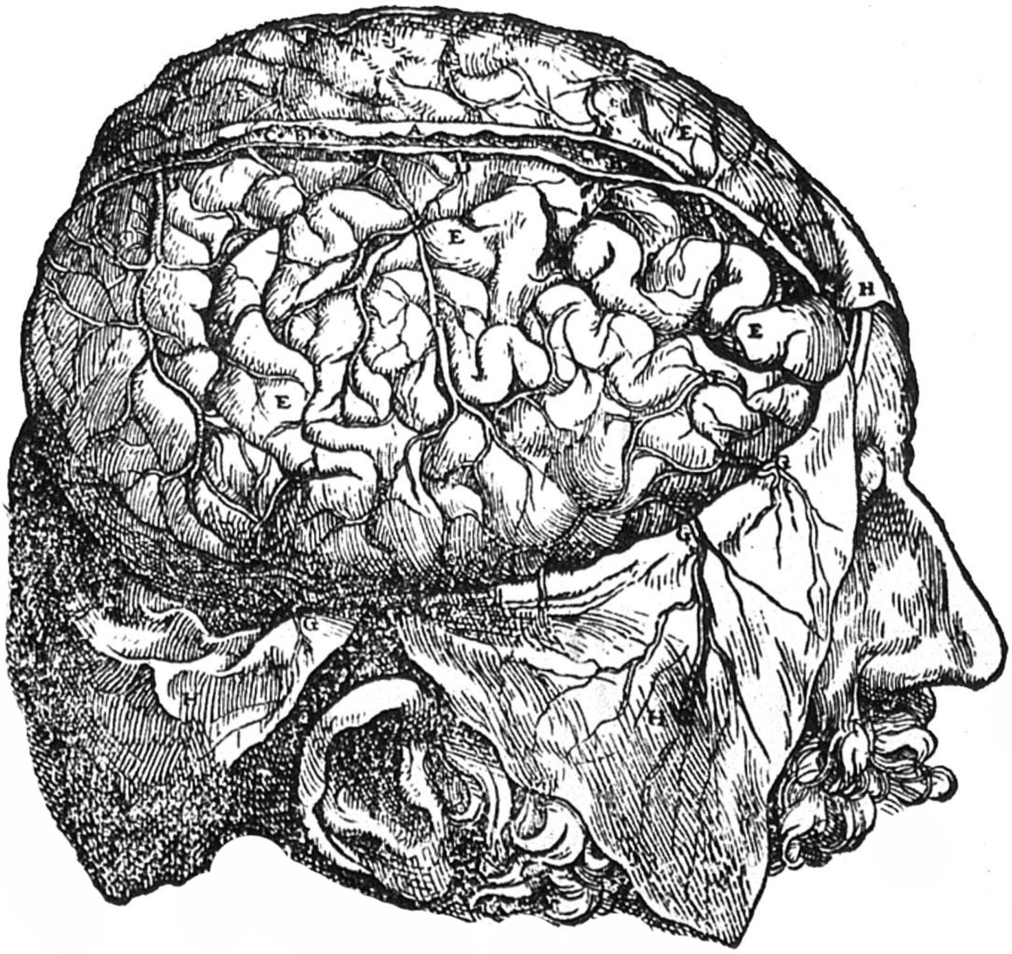
In a series of engravings to illustrate the brain (1802), Charles Bell produced a delicately colored view of the brain and meninges (available from the Wellcome website) very similar to that of Vesalius. The dura mater (B) is folded away. The arachnoid mater is preserved over the left hemisphere. The arachnoid mater (D) from the right hemisphere is folded over the left hemisphere. Bell identified anterior middle and posterior lobes (H, I, K) in the right hemisphere but these were not clearly demarcated. Deep in the cerebral fissure can be seen the corpus callosum (L) and the anterior cerebral artery (M).

The View from the Side

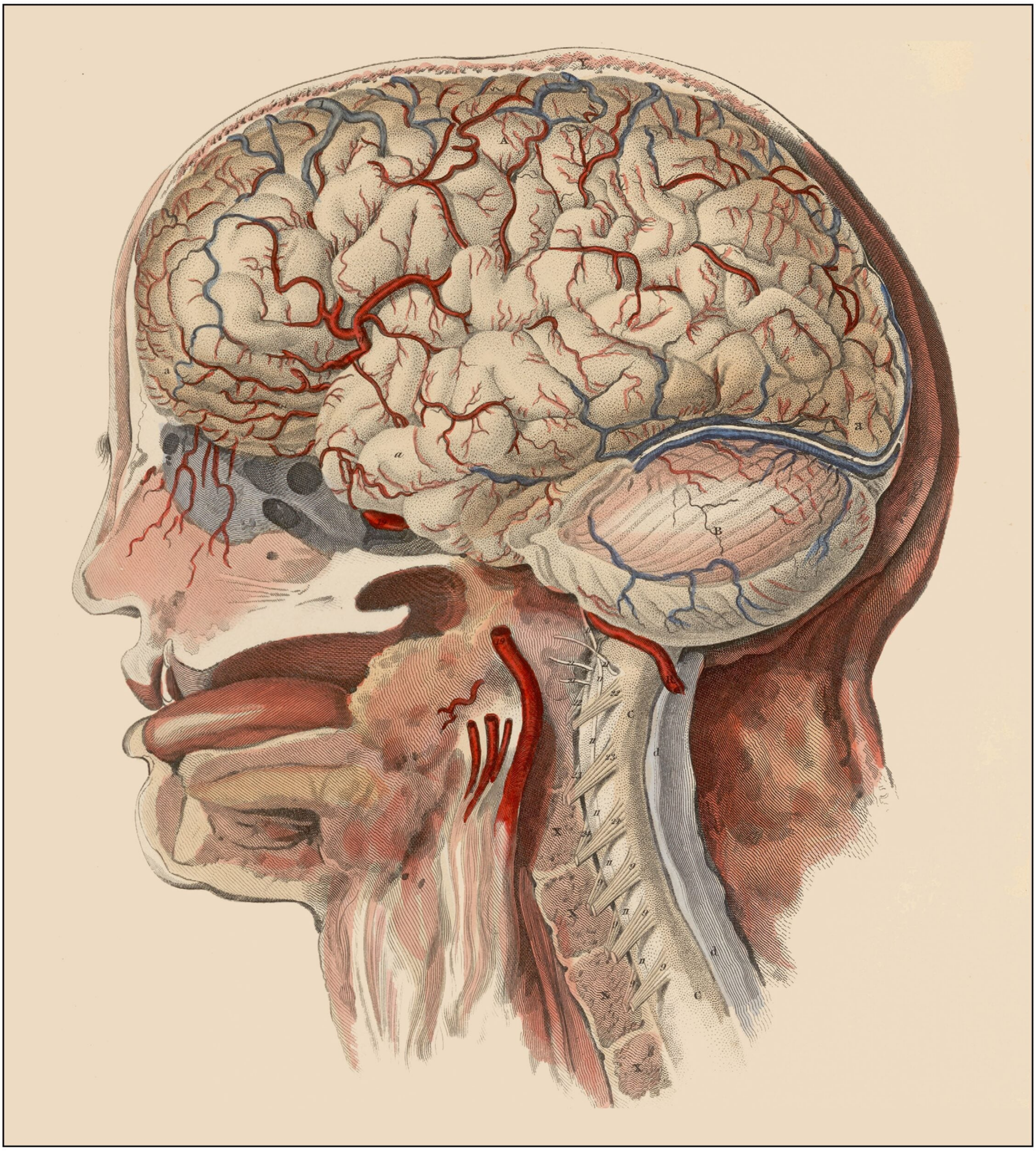
The first illustration of the brain in Vesalius’ book shows the dura mater looks viewed from the side once the skull has been removed. Of note are the superior sagittal sinus (C), and the paired blood vessels (D) that we now know as the middle meningeal artery and vein. This was before William Harvey’s 1628 differentiation of the arteries and veins



The dura was cut through and both dura and arachnoid mater werefolded down over the edge of the skull to reveal the underlying brain. Vesalius made no effort to delineate the cerebral surface accurately. The cerebral gyri are reminiscent of the random coils of the small intestine.

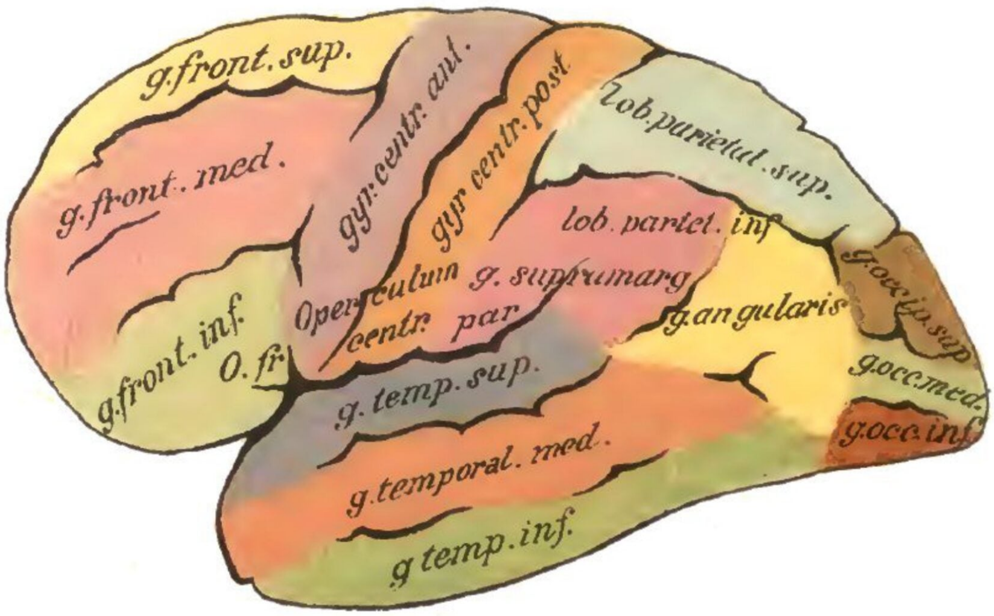


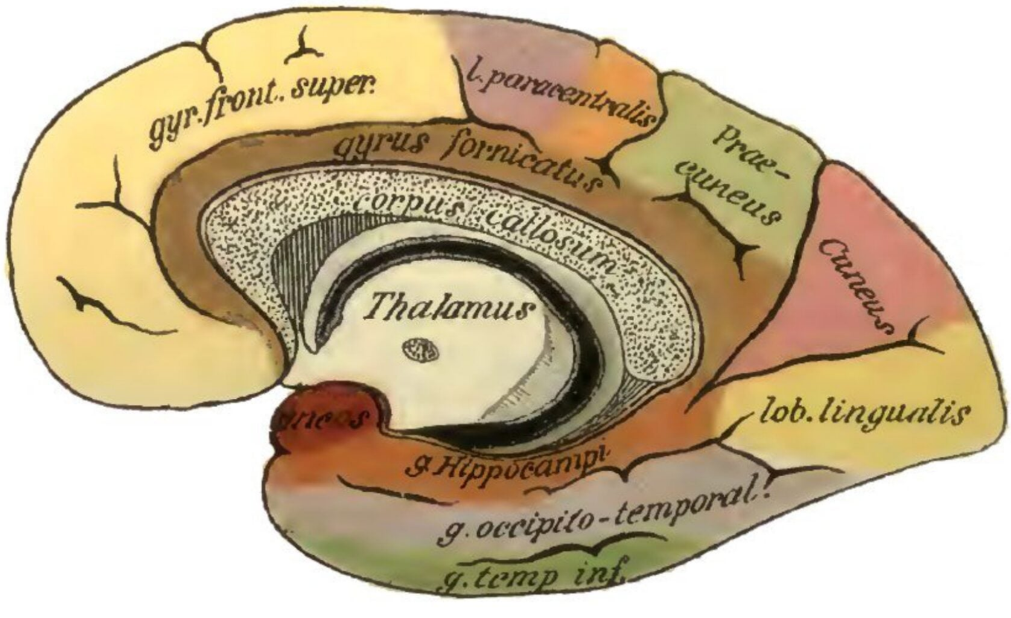
It was not really until the 19^{th} Century that more realistic depictions of the cerebral gyri and sulci became available. The following illustration is from a series of beautiful hand-colored etchings produced by the surgeon John Lizars and his father Daniel Lizars in about 1825. The cerebrum and the cerebellum are well represented, together with their arteries and veins (with their red and blue colors accentuated). However, the orientation of the brainstem and its connections to the spinal cord are quite distorted.



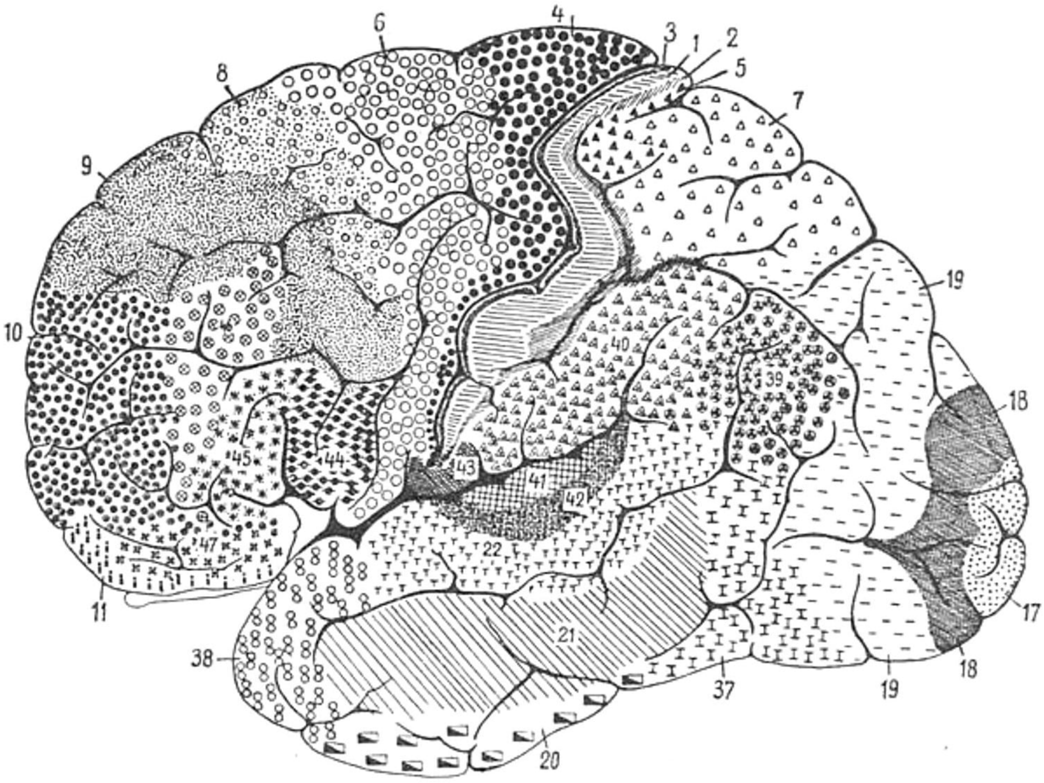
It was not until late in the 19^{th} Century, as physiologists began to study the localization of function, that images distinguished the different gyri of the cerebrum. The following illustration is from the atlas of Christfried Jakob (1895). The gyrus fornicatus (arched), now known as the cingulate (girdle) gyrus, is an important part of the limbic system which mediates visceral sensation, emotion and memory.

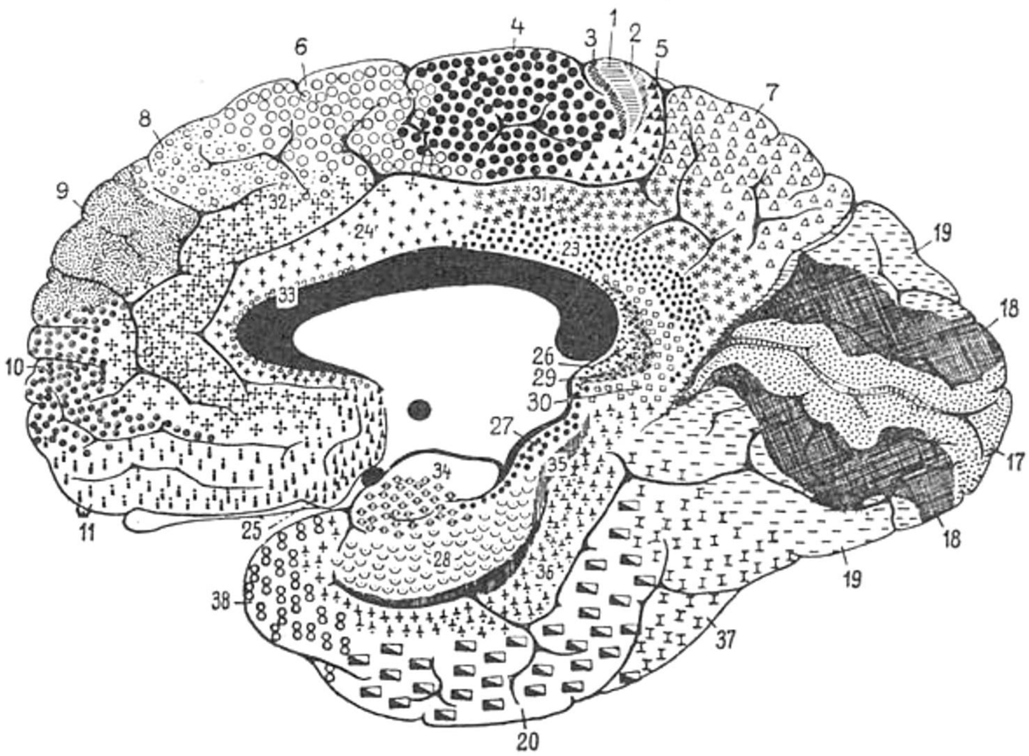
The word fornication (extramarital sex) derives from ancient brothels, which often provided vaulted or arched chambers for their clients.





In 1909 the German anatomist Korbinian Brodmann further differentiated the cerebral cortex into 52 regions based on microscopic analysis of the cortical structure (Brodmann, 1909, p 131)

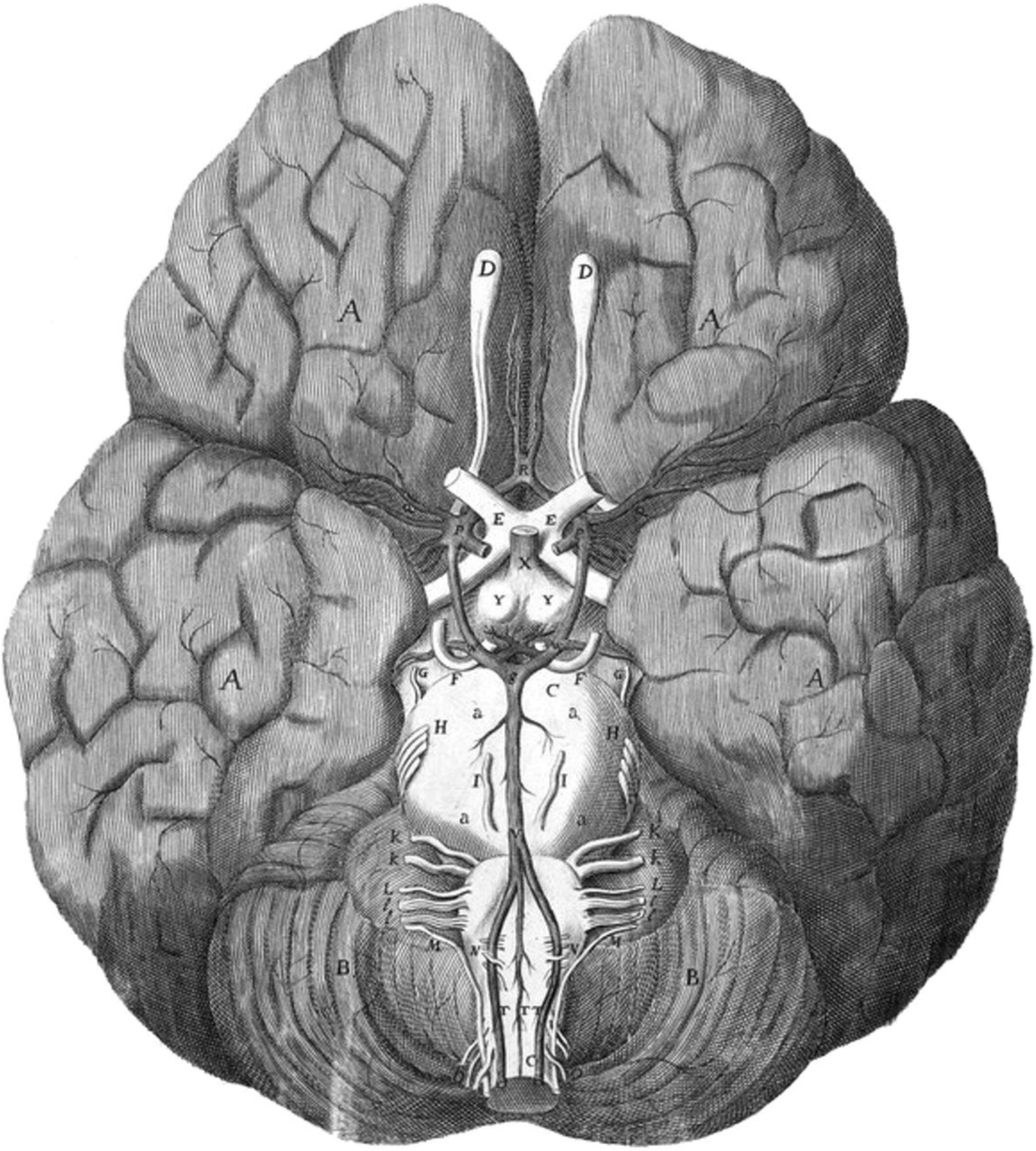




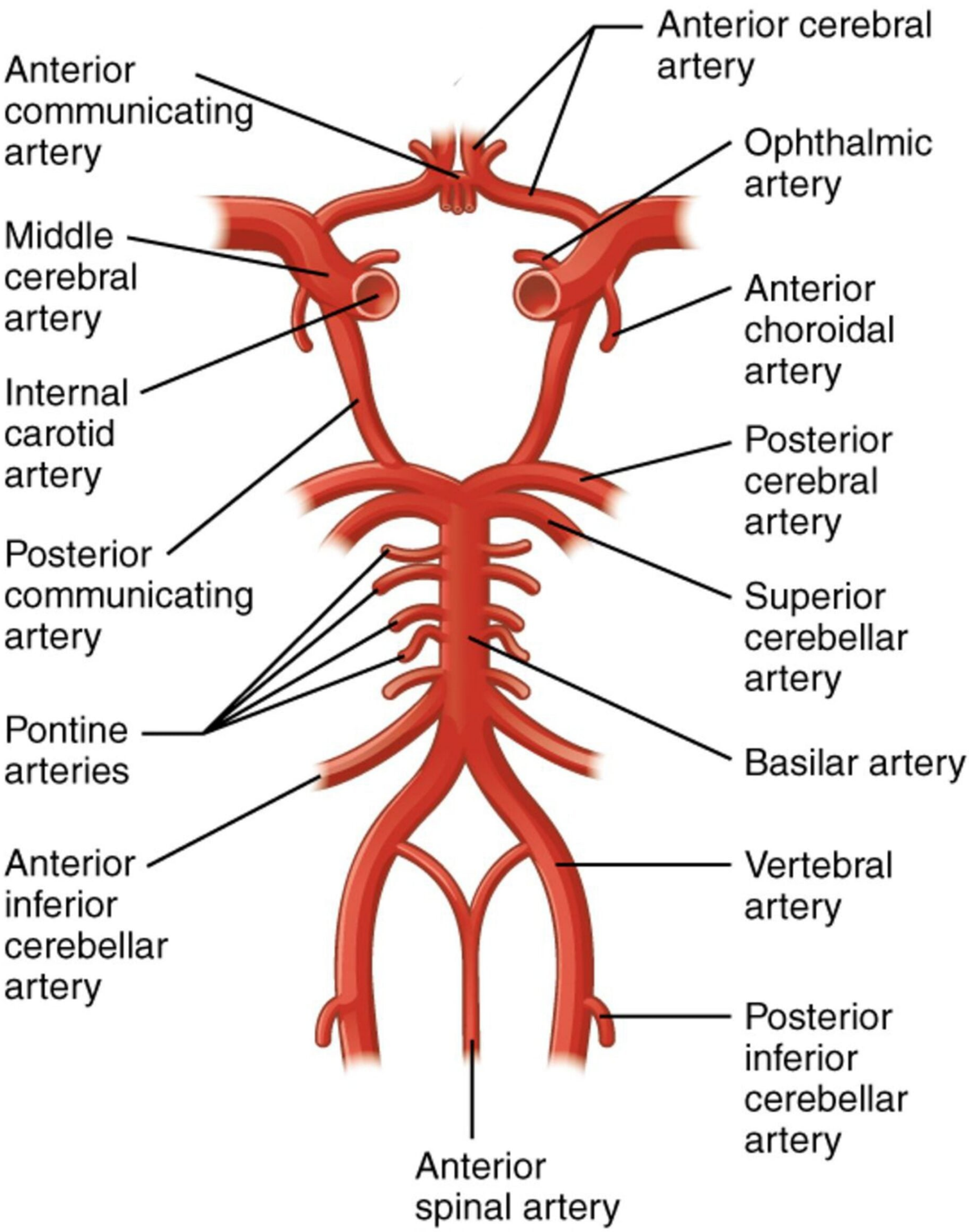
Areas 1, 2, and 3 represent the primary somatosensory cortex on the postcentral gyrus. Area 4 is the primary motor cortex on the precentral gyrus. Area 17 is the primary visual cortex is the primary visual cortex located in and around the calcarine fissure. Areas 41 and 42 are auditory areas located on the superior surface of the temporal lobe. The areas are similar in the brains of other primates. However, area 10 in the frontal lobes and areas 39 and 40 at the temporoparietal junction are particularly important. In the human brain.

The View from Below

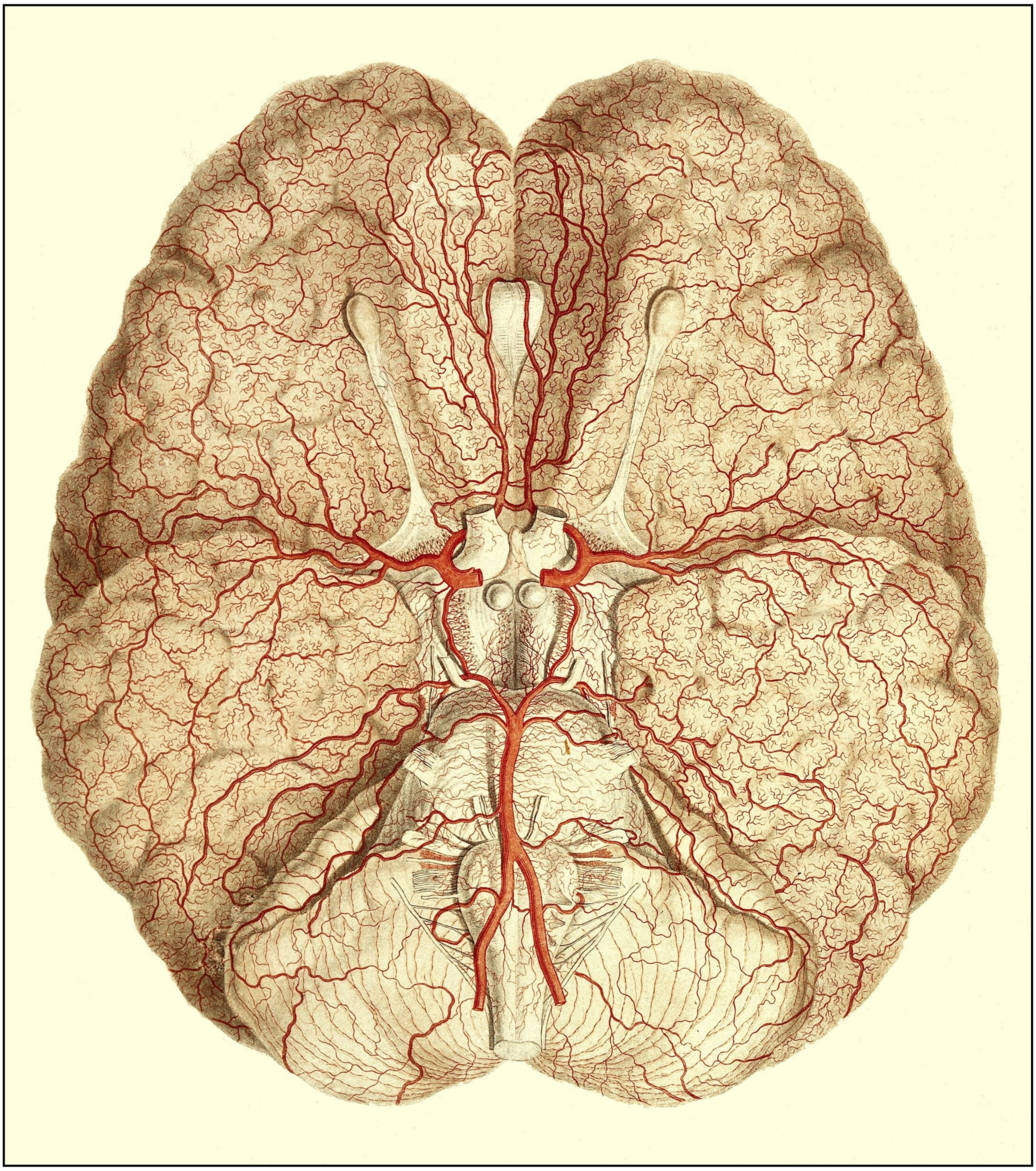
There is an illustration of the human brain viewed from below in Vesalius' book, but it is "still relatively crude and the brain stem in particular is unlife-like" (Clarke & Dewhurst, 1972, p 62). In his *Cerebri Anatome* (1664), Thomas Willis provideded what has become the classical view of the base of the human brain. The original drawing was by Christopher Wren, the architect of St Paul's cathedral (Scatliff & Johnston, 2014).



The drawing clearly demarcates the structures at the top of the brain stem: the olfactory bulb and tract (D), the optic nerve and chiasm (E), the stalk of the pituitary gland (X), and the mammillary bodies (Y). Willis shows cranial nerves of the midbrain: the oculomotor nerve (F), the trochlear nerve (G). The trigeminal nerve (H) is properly located. The lower cranial nerves are not well demarcated. These were not clearly distinguished until the work of Samuel Soemmerring in 1778 (Storey, 2022). One of the most important aspects of Willis’s illustration is that it shows the connections between the arteries supplying the brain: the circle of Willis (illustrated below). His drawing shows the complete circle but the arteries supplying the cerebellum are missing.

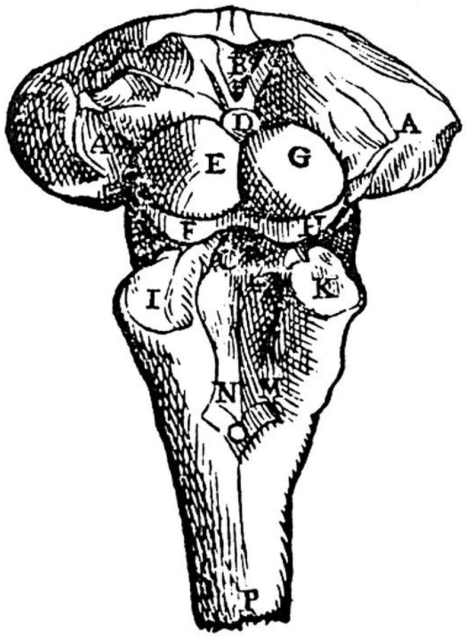


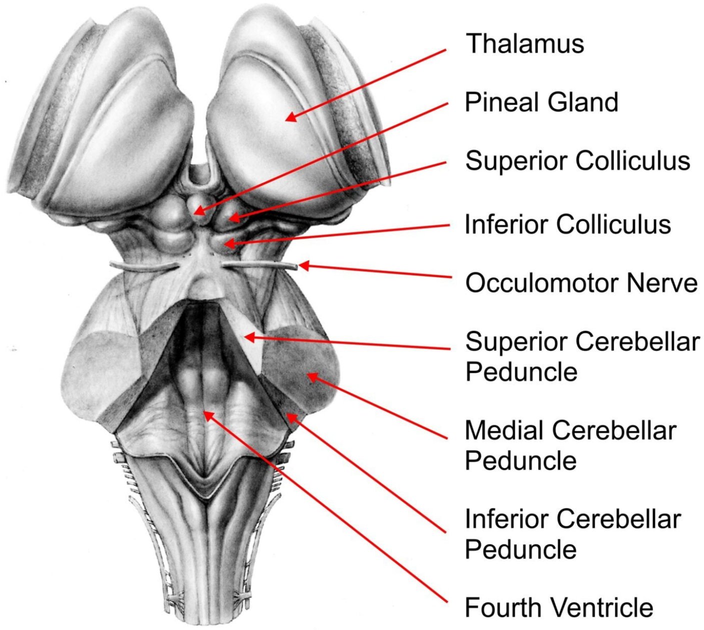
Félix Vicq-d'Azyr produced a more colorful version of the basal brain in 1786 (Plate XIX). The beautiful plates for his book were produced by the engraver Alexandre Briceau. The cerebellar arteries are shown, and the frontal lobes are separated to reveal the corpus callosum:



Views of the Brain Stem

After removing the cerebral hemispheres and the cerebellum, the dorsal aspect of the brainstem becomes visible. Vesalius' drawing of the brain stem is shown below together with a more anatomically correct diagram (derived from Martin, 2012):

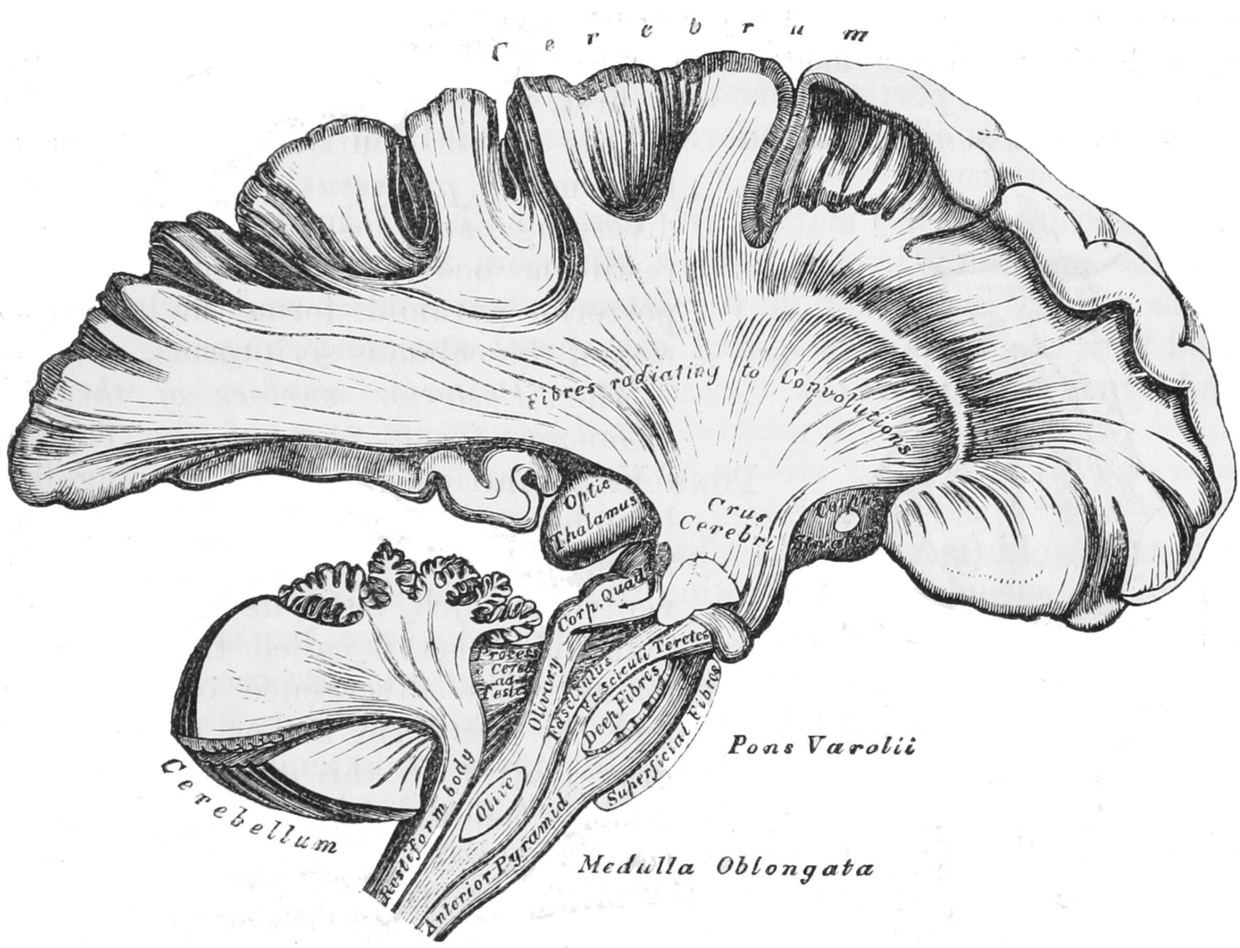


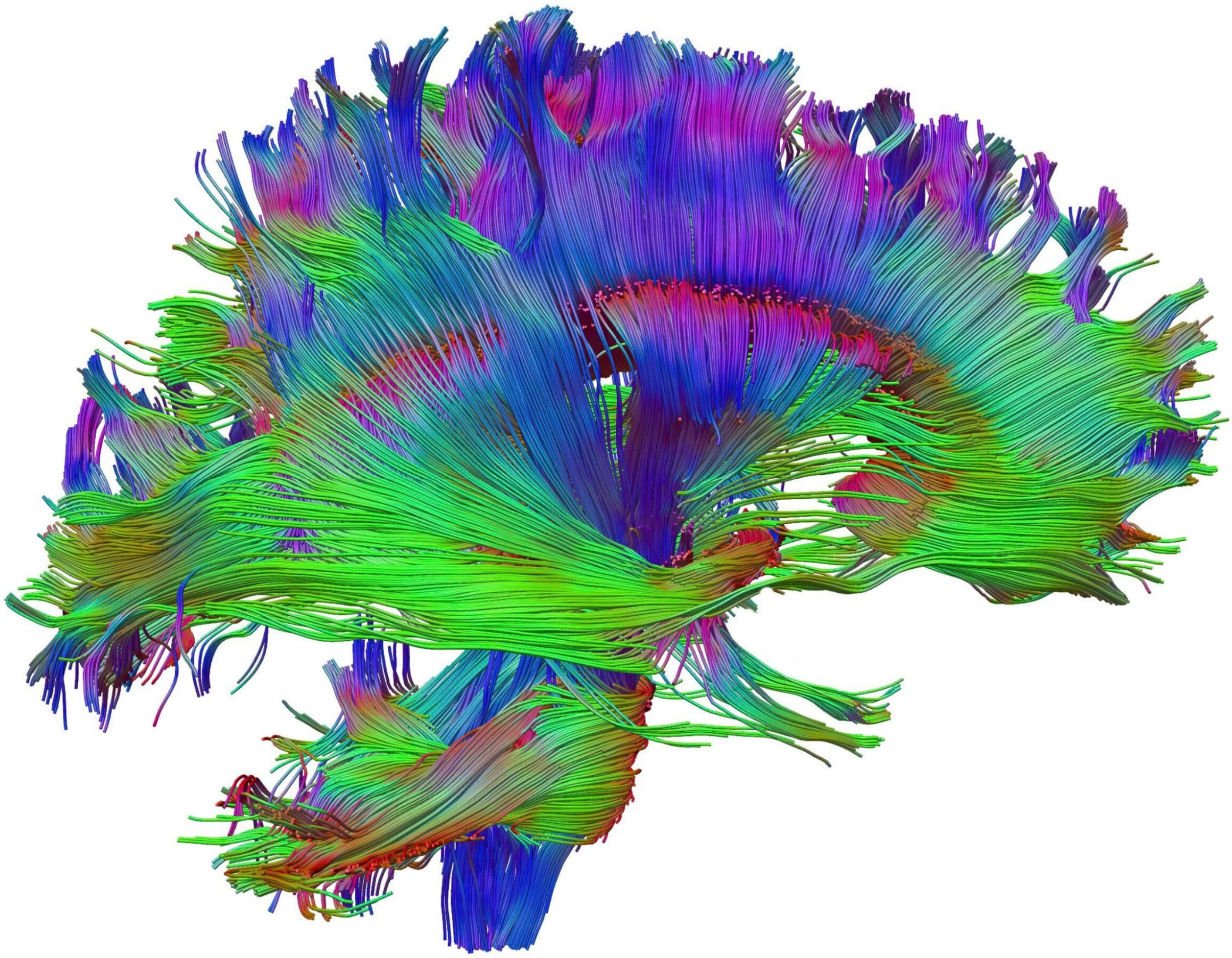


Vesalius got a little carried away in describing this view of the brainstem (Catani & Sandrone, 2015, pp 124-130). He envisioned the upper part of the brainstem as the male perineum, likening the pineal gland (D) to the penis, the superior colliculi (E, G) to the testes and the inferior colliculi (F, H) to the nates (buttocks). He was unclear as to how the cerebellum was attached to the brain stem, noting only the connections to the dorsal spinal cord through the inferior peduncles (I, K).

It is impossible to discern the functions of the brain stem by simply looking at its surface anatomy, and the names assigned to the surface features have little relevance to what goes on beneath. To understand the brainstem one first needs to determine the pathways between the different regions. The anatomy of pathways in the brain stem and cerebrum was determined in the 19th Century by dissection and later by histological studies. The following figure shows an illustration from the first edition of Gray's Anatomy (1858, p 453). This can be compared to a recent analysis of brain pathways obtained by Flavio dell'Acqua (Wellcome website) using Diffusion Tensor Imaging (DTI), a specialized form of

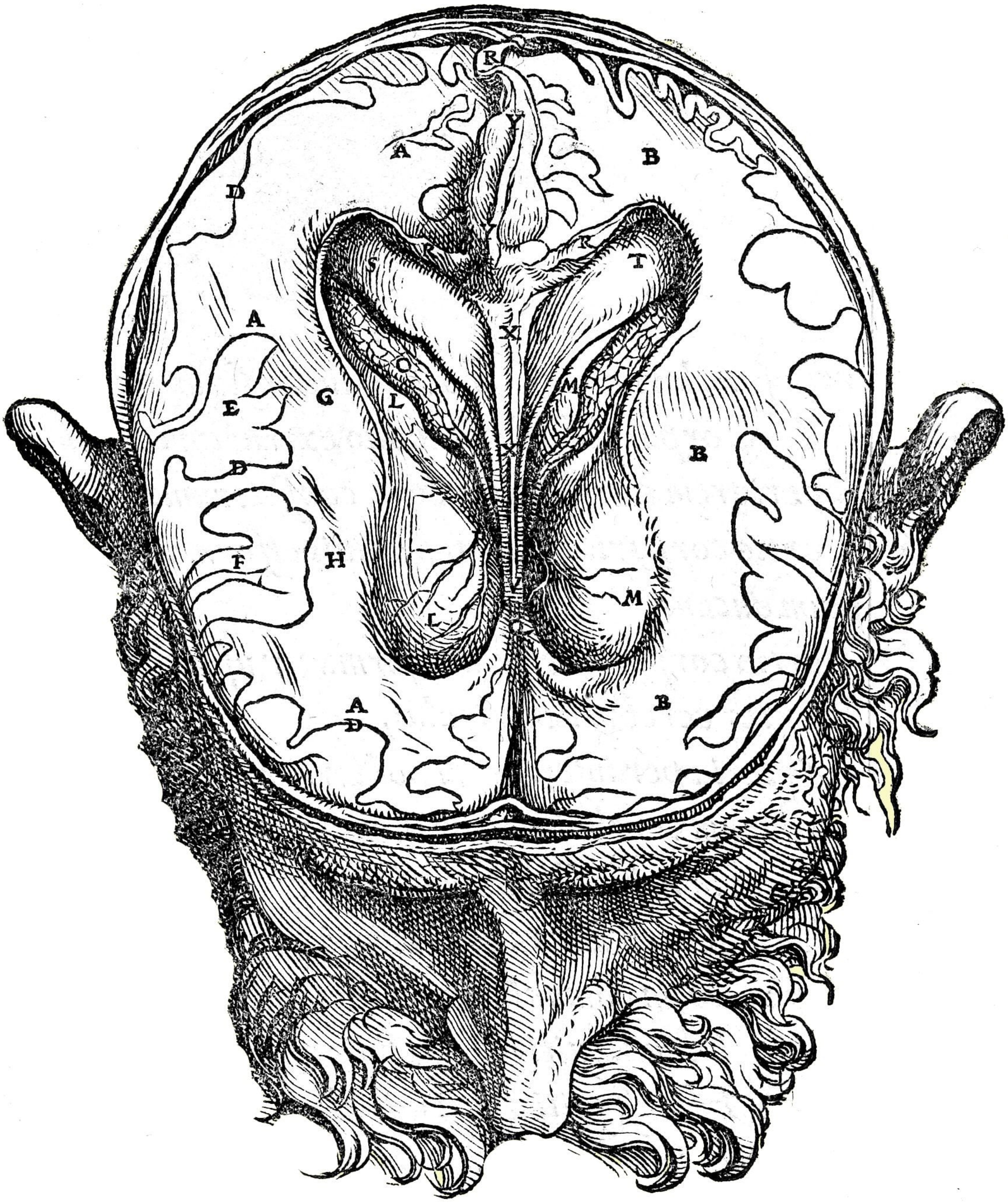
Magnetic Resonance Imaging (MRI). Pathways connecting different regions of the brain are colour-coded: fibers travelling up and down are blue, front to back are green, and left to right are red. The DTI image has been left-right reversed to facilitate comparison. The red fibers in the upper part of the figure represent the commissural fibers of the corpus callosum. The green fibers in the lower part of the figure show the ponto-cerebellar fibers connecting the nuclei on the pons to the cerebellum through the middle cerebellar peduncle. These fibers are not seen in the illustration of Gray and Carter.



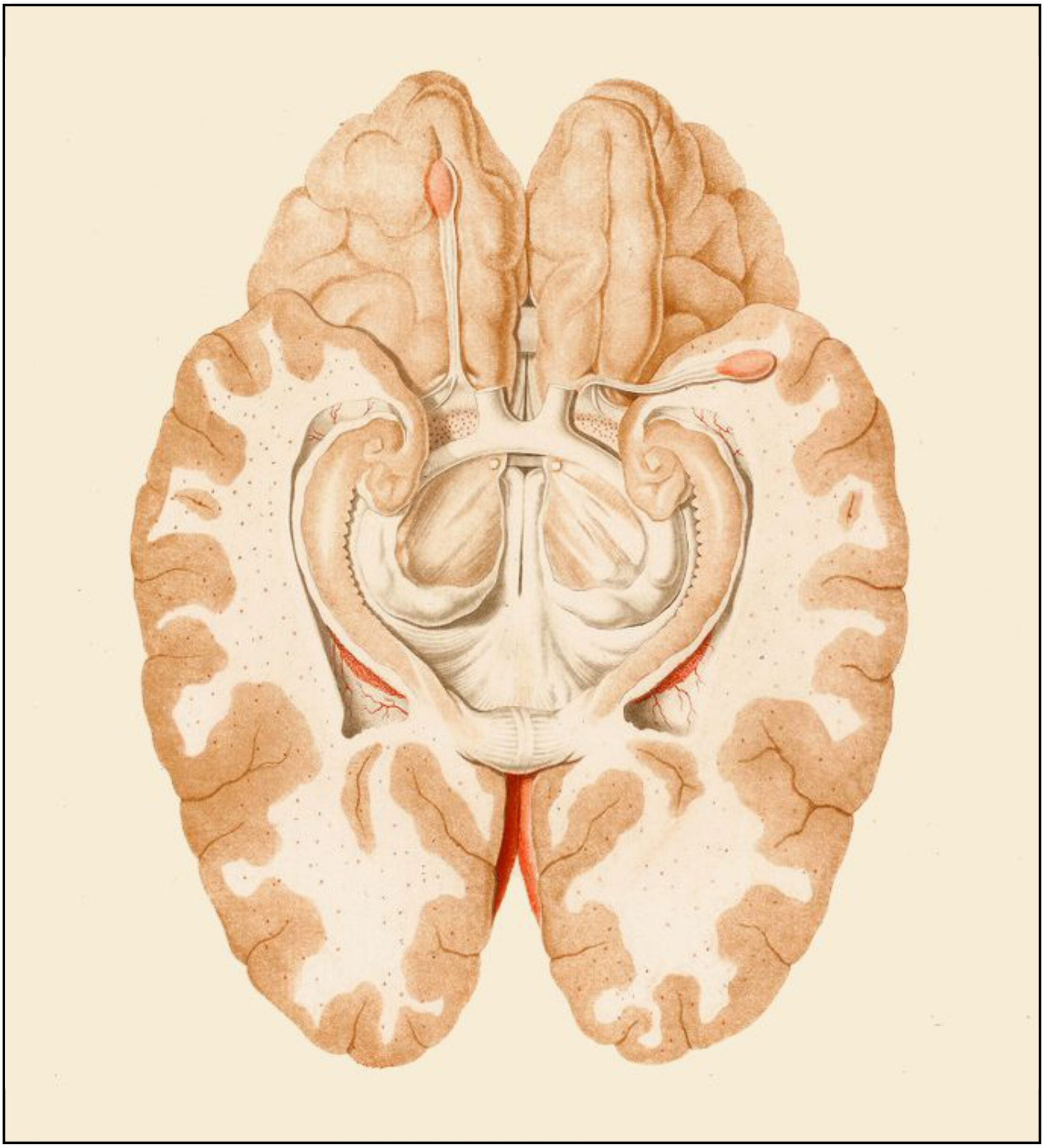


The Brain in Axial Section

Vesalius included in his book several sections though the brain, one of which is shown below. He was mainly concerned with the cerebral ventricles, which were then thought to contain the vital spirits. In the illustration, the anterior portion of the corpus callosum (R) and much of the septum pellucidum (Y) have been bent backward to reveal the lateral ventricles. The lower part of the septum (X) remains. Within the ventricles can be seen the choroid plexus (O). Vesalius distinguished between the gray and white matter but did not otherwise concern himself with the internal structure of the cerebral hemispheres.

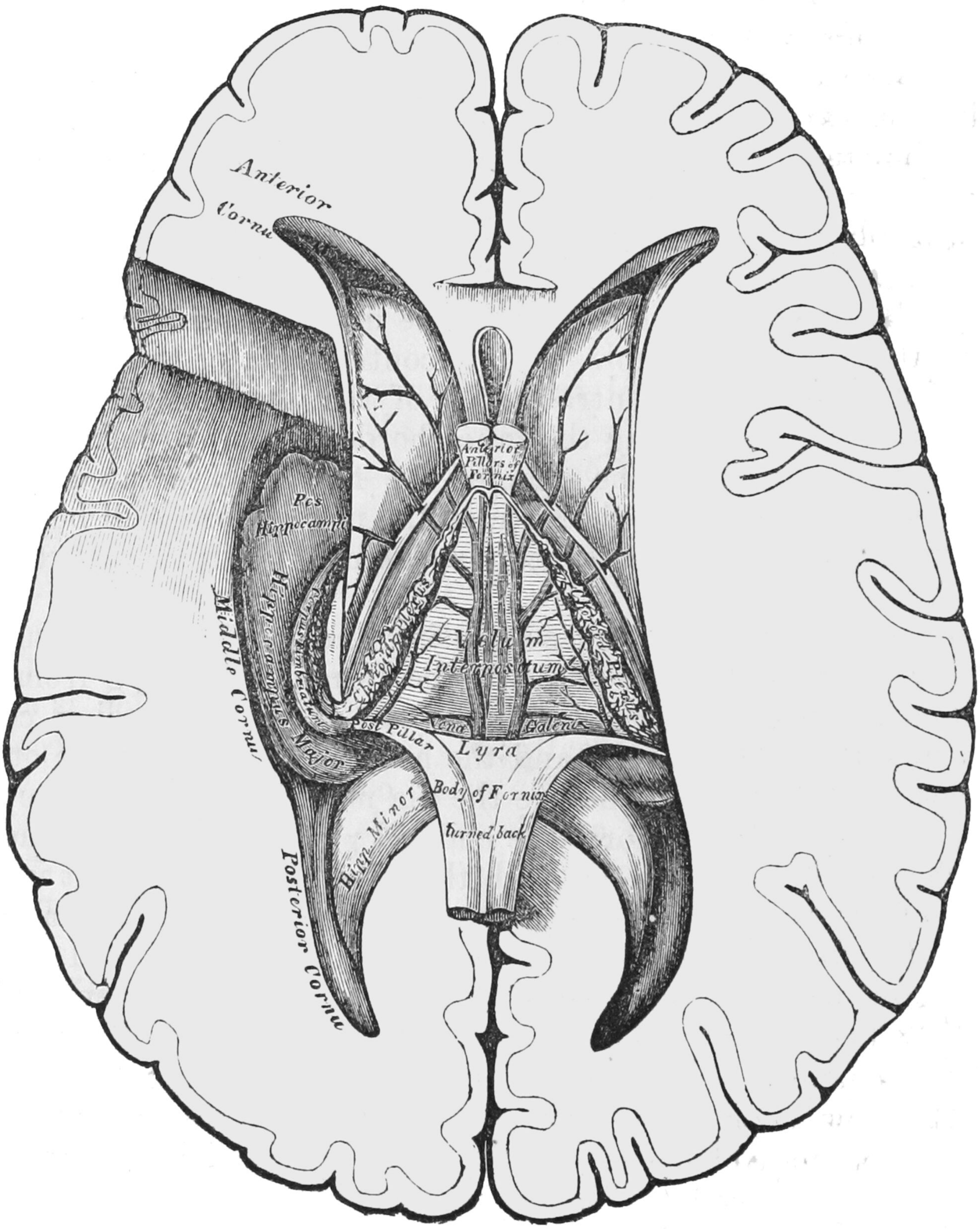


The following illustration is from Vicq d’Ayr’s 1786 treatise shows a section through the brain at a lower level than in Vesalius’ section. The illustration also differs from Vesalius by viewing the section from below rather than from above and by placing the front of the brain at the top. The section shows the hippocampus in the medial wall of the temporal horn of the lateral ventricle. The viewer is charmed by the fact that the left olfactory tract and bulb have been insouciantly turned to lay laterally over the cut surface of the anterior temporal lobe.

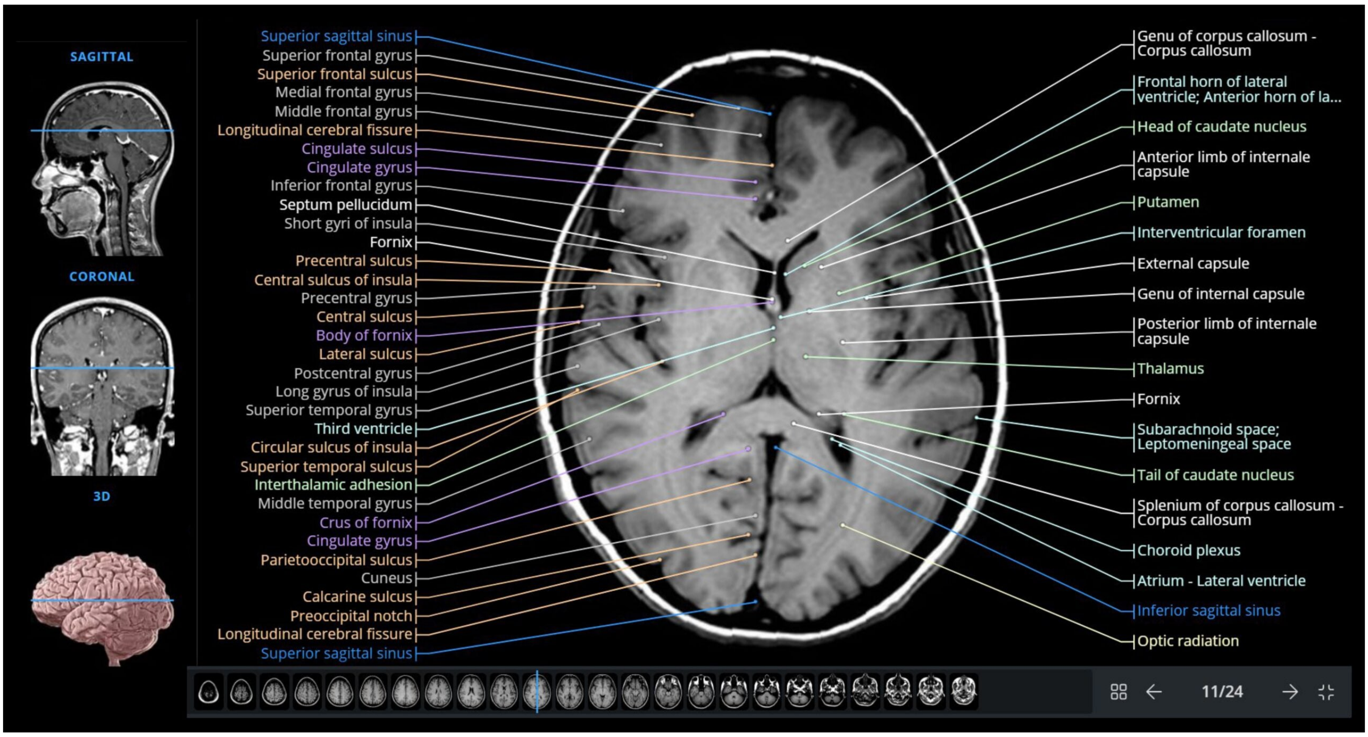


Vicq d’Azyr was fascinated by the structures lying deep within the brain that we now call the limbic system (Parent, 2007). He showed that the major output from the hippocampus was through a bundle of fibers called the fornix that arched around underneath the corpus callosum and then descended to the mammillary body in the hypothalamus. The mammillary bodies than connected to the anterior nucleus of the thalamus through the mammillo-thalamic tract, often known as the tract of Vicq d'Azyr.

The relations between the Vesalius section and that of Vicq d'Azyr can be understood by studying an ingenious illustration from the first edition of Gray's Anatomy (Gary & Carter, 1858, p 464) The right side of the illustration is similar to the view of Vesalius. On the left side, the section has been dissected more deeply to reveal the hippocampus as in the section by Vicq d'Azyr. The triangular membrane beneath the corpus callosum (*lyra*) has been cut through the descending parts of the fornix and bent backwards. This both reveals the superior aspect of the thalamus and also allows one to imagine the true course of the fornix as it curves upward, forward and then back down. This approach derives from a similar (though less effective) illustration from Vicq d'Azyr (Plate XIV). The drawing by Henry Vandyke Carter is a marvelously lucid (Richardson, 2008). One of Carter's characteristics was to write the name directly on the illustrated structure.



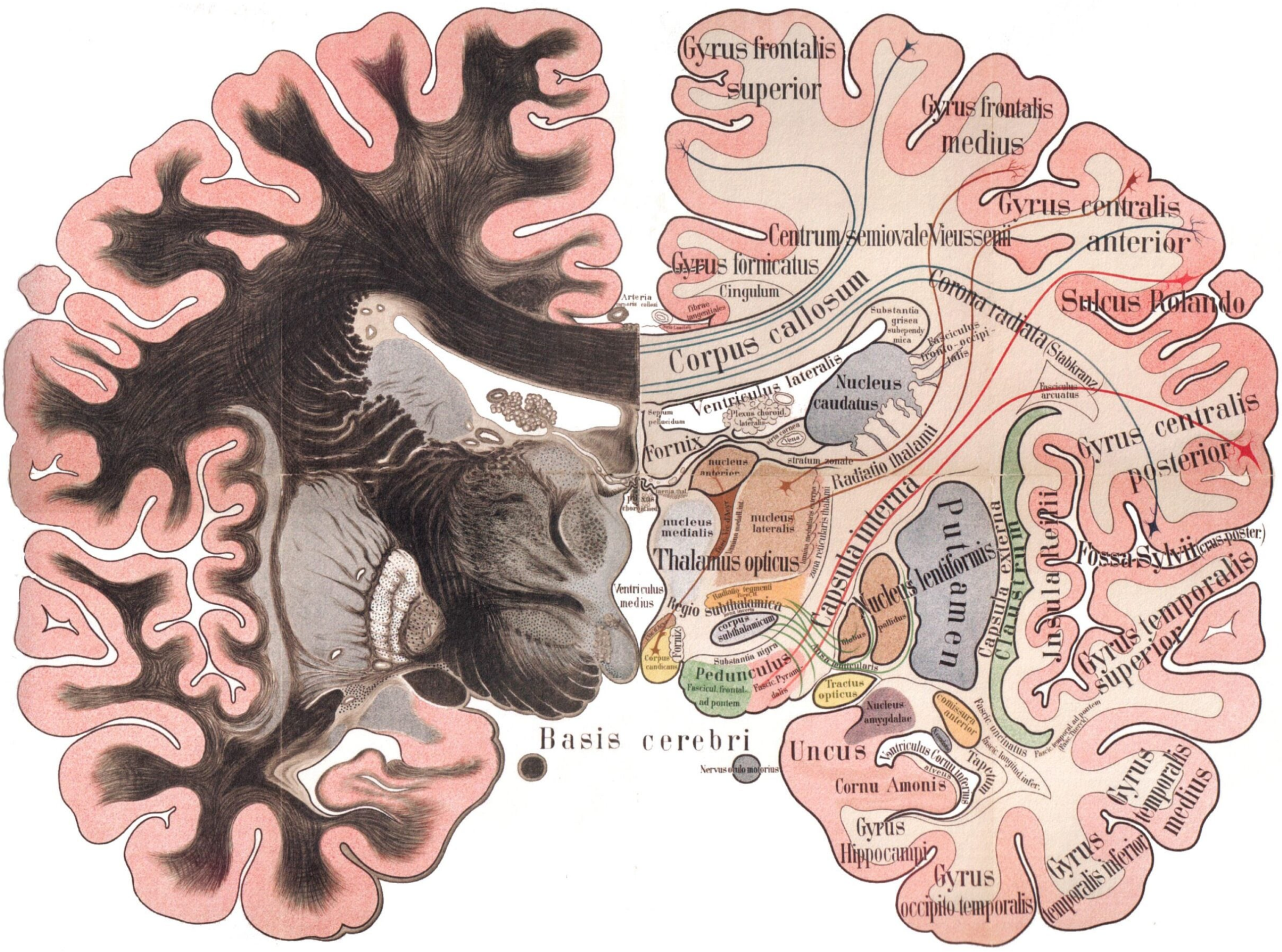
The illustration below shows a modern Magnetic Resonance Image of an axial section of the normal human brain (IMAIOS.com). The section is located between the levels of the Vesalius section and that of Vicq d’Azyr:



The Brain in Coronal Section

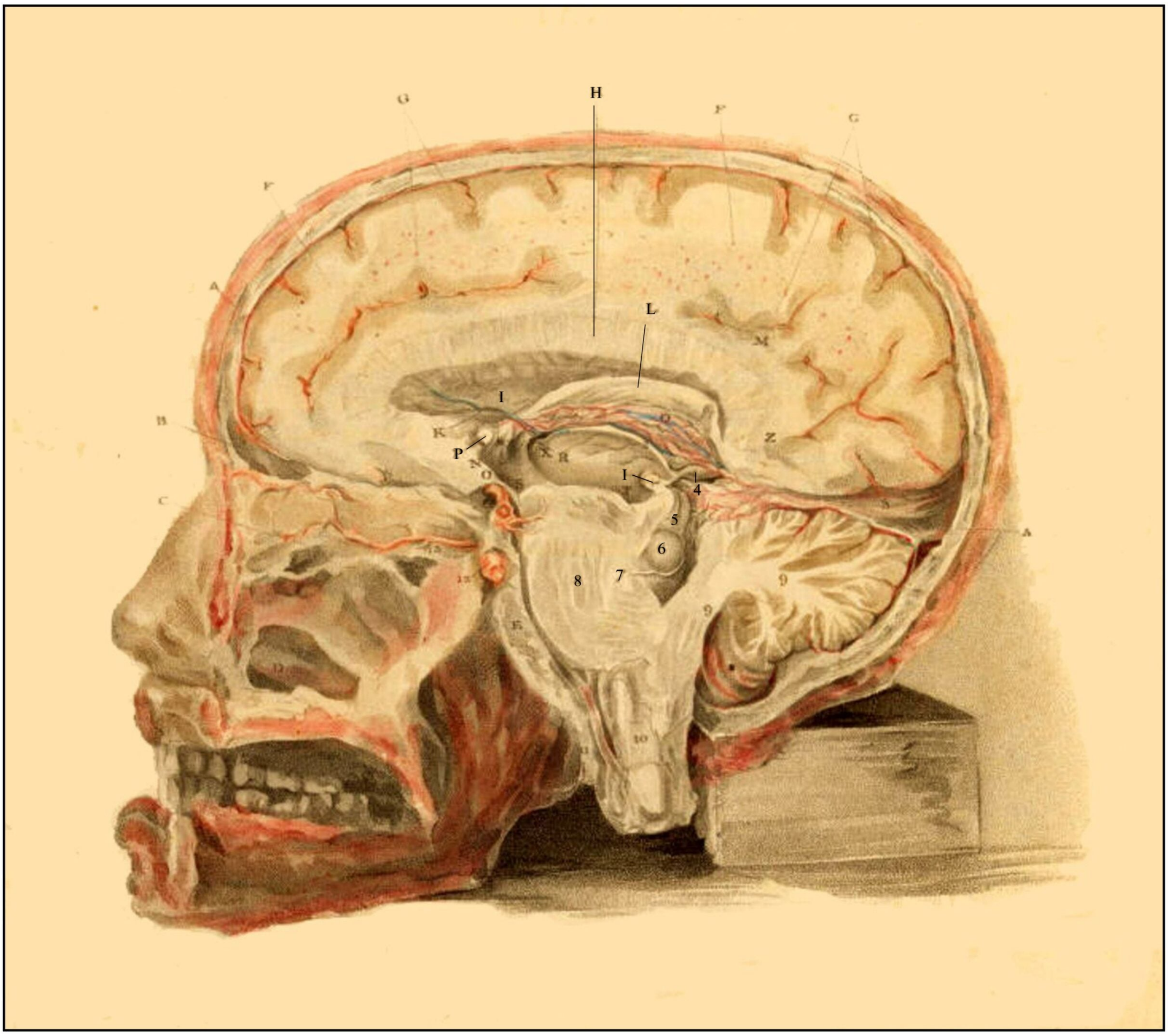
Vicq d'Azyr included several coronal sections of the brain in his 1786 treatise, one of which (Plate XXVI) is shown at the top of the next page. The structure of the nuclei and pathways are only faintly indicated, and the reproduction has been digitally darkened to enhance them. At the top can be seen the corpus callosum connecting the two hemispheres. In the center of the section are the basal ganglia (with their characteristically striped appearance: the corpus striatum) and the thalami. Below the basal ganglia can be seen the hippocampus in cross section.

The structural details of the brain are better seen if the section is stained with chemicals that distinguish the grey and white matter. These only came into use in the late 19th Century. At that time physiologists began to study the connections between regions of the brain using electrical stimulation, and tracts were traced by studying the degenerative effects of focal lesions. At the bottom of the next page is a poster published in 1897 by Adolf von Strümpell, one of the founders of German neurology (Engmann et al., 2012). The left side of the poster reproduces a stained section, and the right side shows a diagram delineating the nuclei and their connections. The descending fibers of the pyramidal tract are indicated in red: these fibers have their cell bodies in the pre-central cortex and travel through the internal capsule into the cerebral peduncle. Fibers connecting between the hemispheres through the corpus callosum are shown in grey. The green fibers represent the connections between the nuclei of the corpus striatum and the midbrain.



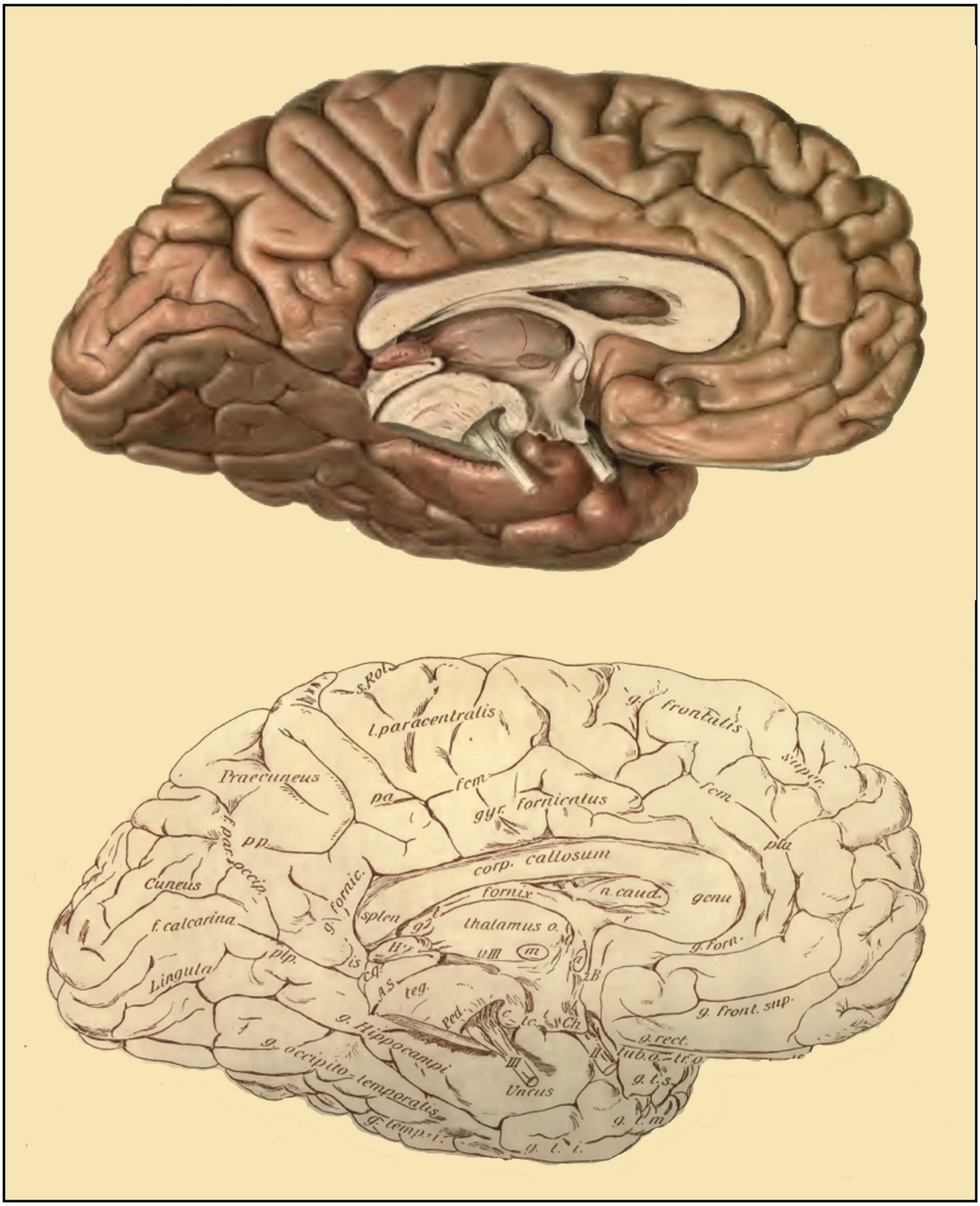
The Brain in Sagittal Section

Charles Bell included in his 1802 series of engravings an illustration of the brain as viewed in a sagittal section taken just to the left of midline (Plate VII). Some of the lettering has been enhanced to facilitate the identification of the structures:

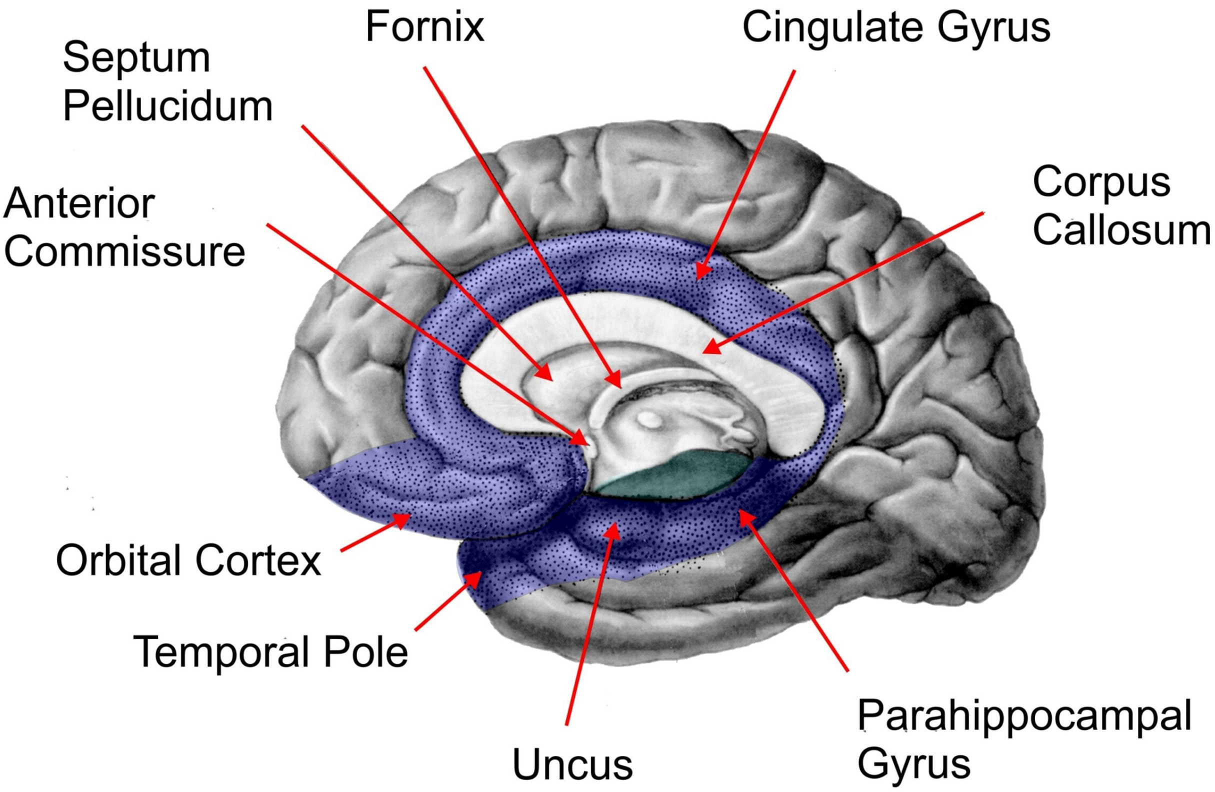


The section shows the corpus callosum (H), above the lateral ventricle (L) through which can be seen the septum pellucidum at the midline, the fornix (L), the anterior commissure (P), the third ventricle (R). Bell also identified the posterior commissure (1), the pineal gland (4), the superior and inferior colliculi (5, 6), (the testes and buttocks of Vesalius), the trochlear nerve (7) and the pontine nuclei (8).

The mesial surface of the forebrain is shown in an illustration on the following page from Christfried Jakob's 1899 *Atlas of the Nervous System* (Plate 4). Jakob, who had served as an assistant to Adolph von Strümpell, produced the first edition of his magnificent atlas in 1895 when he was only 29 years old. The second edition (1899) was soon translated into English.



Removing the brainstemfrom the hemisphere allows one to see the mesial surface of the temporal lobes, in particular, the hippocampal gyrus and the uncus (hook, a term coined by Vicq d'Azyr) at its anterior end. Paul Broca (1878) proposed that the regions of the cerebral hemisphere surrounding the upper end of the brainstem formed an evolutionarily ancient limbic (*limbus*, edge) lobe of the brain (Pessoa & Hof, 2015). This region of the brain appeared to mediate visceral sensations and emotions. The following modern illustration is derived from Martin (2012):

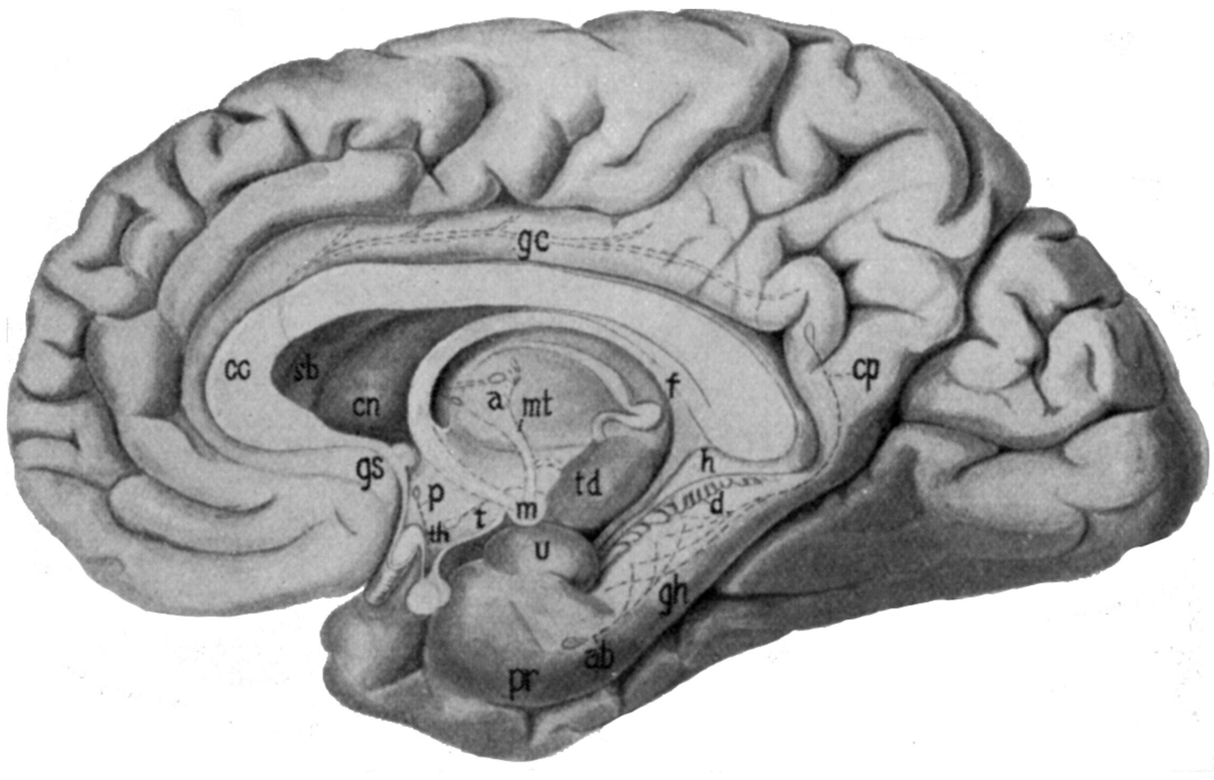


In 1937, the American neuroanatomist James Papez proposed that circuits connecting the regions of the limbic lobe to the hypothalamus mediated the experience of emotions:

> The central emotive process of cortical origin may then be conceived as being built up in the hippocampal formation and as being transferred to the mamillary body and thence through the anterior thalamic nuclei to the cortex of the gyrus cinguli. The cortex of the cingular gyrus may be looked on as the receptive region for the experiencing of

emotion as the result of impulses coming from the hypothalamic region, in the same way as the area striata is considered the receptive cortex for photic excitations coming from the retina. Radiation of the emotive process from the gyrus cinguli to other regions in the cerebral cortex would add emotional coloring to psychic processes occurring elsewhere. This circuit would explain how emotion may arise in two ways: as a result of psychic activity and as a consequence of hypothalamic activity.

The following illustration is from his paper. The most important structures in the Papez circuit are the hippocampus (gh), the uncus (u), the fornix (f), the mammillary body (m), the mammillothalamic tract (mt), anterior nucleus of the thalamus (a), the cingulate gyrus (gc), the hypothalamus (p).



Papez’s studies were expanded by Paul MacLean (1949) who proposed that these structures composed a “visceral brain.” The ideas of Papez and MacLean were originally proposed by

Christfried Jakob in the early years of the 20th Century (Triarhou, 2008; Catani & Sandrone, 2015, pp 104-115). However, he had moved to Buenos Aires, and his papers, published in Spanish, were not as widely read as they should have been.

The connections between the limbic structures and the rest of the brain are far more complex than originally proposed (Kamali et al, 2023; Nieuwenhuys et al., 2008). The amygdala nucleus located in the temporal lobe anterior to the uncus, and the nucleus accumbens in the basal forebrain were not considered in the original formulation of the limbic system. We still do not fully understand the workings of the limbic system, which we now know to be intrinsically related to memory as well as emotion.

Envoi

All that we experience – our thoughts, feelings, memories, and dreams – are somehow mediated by the brain. Over the years we have developed more and more accurate images of this organ of the mind. We now know the place but do not yet fully understand what happens there.

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Note on the illustrations:

The illustrations were derived from digital representations of the original publications (listed above). I have digitally enhanced the illustrations as best I could in an attempt to reach what I imagine was their original state.

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