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Was the Nobel Prize Awarded Mistakenly? Should the Corpus Callosotomy be considered a Split-Brain Surgery?

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Abstract

One of the most controversial topics in neuroscience surrounds the Nobel Prize-winning split-brain experiments of Sperry and colleagues. Their experiments were carried out on patients who had undergone a callosotomy, which is a surgery that removes the corpus callosum-one of the commissures that connect the cerebral hemispheres. After years of research that have allowed us to address some of the major concerns regarding this work, scientists remain doubtful about the validity of Sperry's findings. This is due, in part, to the number of other commissures that also allow for communication between the hemispheres, including the anterior commissure, hippocampal (Fornix), septum pellucidum commissure, the interthalamic adhesion (intermediate mass), the habenular commissure, and the posterior commissure. Therefore, the original assumption made by Sperry, that severing the corpus callosum divides the brain, is an exaggeration of reality: while there is no doubt that the corpus callosum plays the largest contribution in the passage of information from one hemisphere to the other, it is not the only route. After reading and consulting the bibliography of this article, I hope that you will be able to formulate your own opinions about these questions.

Keywords: Commissures; Split-brain; Corpus callosum; Callosotomy; Epistemology; Neurophysiology

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Introduction

The Nobel Prize has always held a special place in my heart for its emphasis on the more positive aspects of humanity. When I was a child, I was often asked about the greatest thing that I hoped to accomplish when I grew up, and my answer was always the same: win a Nobel Prize. I don't believe I had a specific reason at the time, or maybe my reason was childish, but as I grew older, I began to ask myself why this dream was so compelling to me. The answer finally came to me upon attending my first class at UBA Medical School: because perfection is what we were created to aspire in every aspect of our lives and the Nobel Prize is awarded to those who have approached this perfection. The goal of this introduction is to express my appreciation for the prestigious foundation that awards the Nobel Prize and to clarify that I have nothing but respect for the foundation and for those who have achieved this honor.

In the fields of medicine and especially neurology, it is difficult to find anyone who is unfamiliar with the name Roger W. Sperry, whose work with split-brain patients led to his acceptance of the Nobel Prize in 1981. Some textbooks even refer to this work as "the ingenious experiment of Sperry." [1]. However, despite an abundance of contradictory information obtained prior to and following Sperry's work, students of medicine, neurology, and physiology still regard the results of Sperry's experiments as incontrovertibly true. Though many scientists have expressed their doubts regarding Sperry's research, I was unable to find any single article that discussed the experimental errors and contradictory evidence that might call his conclusions into question.

After days of searching, I realized that perhaps I should be the one to revisit Sperry's experiments and offer a more unbiased perspective. I was hesitant at first, as the task of writing a rebuttal against one of the most renowned scientific endeavours in neurology would require significant effort. Instead, I considered waiting for my medical career and devoting my time to Sperry's experiment. However, I also realized that, as time passes, more students will continue to accept Sperry's experimental results as truth, and perhaps tomorrow there will be more important cases meriting my focus and attention. Though we can never know what tomorrow holds, my former professor Brian Tracy once said: "No matter what it takes to accomplish something, when you feel the need to accomplish it, do it instantly. Later, you may miss the opportunity, and it could be a huge loss for your life and the lives of others." Therefore, I have halted much of my other work to focus on what I believe to be an issue of the utmost importance.

As scientists, it is our duty to be diligent observers of the true nature of reality. Often, however, individual philosophies can obscure or prevent a scientist's appreciation of the truth. In the first part of this article, I will cease to be a scientist, donning the skin of an epistemologist in order to raise questions regarding the validity of Sperry's work. In the second part, I will present the physiology of the nervous system as it relates to the different components of Sperry's experiments and begin to formulate conclusions regarding the matter. However, these conclusions will require further validation by you, the reader, and by other researchers, in order to gain validity and traction in the scientific community.

Epilepsy and Callosotomy

Epilepsy is a neurological disorder caused by increased electrical activity that can spread throughout the affected brain hemisphere. In the presence of the corpus callosum, such activity can also spread to the contralateral hemisphere, depending on its magnitude or intensity.

The study of patients with epilepsy has allowed researchers to uncover a great deal of information regarding the higher functions of the nervous system. However, some of these discoveries occurred accidentally, as in the case of patient Henry Molaison 1926-2008. After exhaustive attempts to understand and treat H.M.'s seizures, which were extremely severe and life-threatening, his attending physician, Dr. Scoville, concluded that the only remaining solution was to remove part of the temporal lobe, including the hippocampus. He performed the surgery on September 1, 1953; it wasn't until later that scientists discovered that the hippocampus and other regions of the temporal lobe play critical roles in processing and storing information. Accordingly, H.M. lost the ability to store new memories and information. Although Dr. Scoville regretted his decision, the subsequent study of H.M.'s condition, until his death in 2008, unearthed a vast amount of information regarding the neural basis of memory and emotion.

Due to the extremely high levels of electrical activity that are associated with severe epilepsy, effective treatment options have yet to be identified. Current medications can suppress the negative effects of epilepsy and return the brain to a state of electrical homeostasis. However, any drug that exerts a negative effect on the generation of action potentials-as in the case of anti-epileptic agents-can have negative side effects on parts of the brain associated with different types of memory. In fact, anti-epileptics tend to affect both explicit and implicit memory since these two forms rely on the same short- and long-term potentiation processes. Moreover, anti-epileptic medication negatively impacts function in up to 90% of the forebrain, as well as the cerebellum, resulting in side effects on attention, emotional regulation, and memory.

During the 20th century, the corpus callosotomy became one of the most famous techniques for epilepsy management. The procedure was designed to prevent the spread of seizure activity from one hemisphere to the other by severing the corpus callosum and other commissures. Although Walter Dandy [2], a pioneer of this technique, first resorted to corpus callosotomy in the case of a tumor, the first such operations for the treatment of epilepsy were performed in the 1940s by William P. van Wagenen and Yorke R. Herren [3]. Specifically, the first operation occurred on February 6, 1939, which was reported in volume 44 of the Archives of Neurology and Psychiatry in 1940. Van Wagenen spent the rest of his life regretting his choice to conduct this procedure [4].

In 1960, the corpus callosotomy was again presented as a solution for severe epilepsy by Dr. Joseph E. Bogen. Patient William Jenkins, a World War II veteran, underwent the operation on February 6, 1962. After dramatic improvements were observed in the frequency and severity of WJ.'s seizures, five additional patients underwent the same operation. Under the care of Joseph E. Bogen and Vogel PJ, another group of patients underwent similar operations in which only 2/3 of the corpus callosum was severed (leaving the splenius of the corpus callosum intact) [4]. In the late 1950s, prior to these operations, neuropsychologists Roger W Sperry and Michael Gazzaniga had begun to study the behavior of animals with severed commissures [5-7]. Although William Jenkins expressed an interest in participating as a research subject after his corpus callosotomy, Bogen and Vogel instead motivated others to assist with further analyses and experiments.

Integration of the Experimental Data

Epistemology is critical for the advancement of science, enabling us to discover the truth by examining the relationships among language, logic, and reality. Regardless of our individual truths, the three above-mentioned elements are required for epistemological proof. Before moving on to Sperry's work, let us first consider the following: we know that neuroscience is the subdomain of biology that tells us about the anatomy and function of the nervous system, and that biology is an experimental science most often associated with hypothetical-deductive and inductive reasoning. To be accepted as valid, the results of any study in the experimental sciences (biology, physics, chemistry, etc.) must employ a specific method of reasoning. Specifically, the premise must support the conclusions. However, it must also be noted that validity and truth represent two different concepts. A valid argument says nothing about the truth of its propositions.

However, if an argument is valid and its premises are true, its conclusions will be true as well.

A → B

A

B

If I sever the corpus callosum → The brain is divided

I sever the corpus callosum

The brain is divided

Consider an example (illustrated above using notation familiar to many students of logic): if I sever the corpus callosum, it means that the brain is divided; the corpus callosum is severed, thus the brain is divided. This is a valid argument because its premises support its conclusion, but it tells us nothing about its truth. In fact, it is not true, and later we shall see why. This simple example serves as a basis for understanding the more complex analyses that will follow. Our analysis here will utilize the three aforementioned epistemological tools for understanding the truth of an experiment and its conclusions: the language used (what the researchers say), the logic (reasoning) used for the experiment, and the reality of the situation.

Sperry's split-brain experiment aspired to investigate sensory, motor, and higher-order functions, and was designed to deliver information only to a single hemisphere without giving the other hemisphere access to the same information. Based on the available archives, this methodology was most likely insufficient. The results of the experiment were so contradictory to current knowledge within the field of neuroscience that Joseph E. Bogen felt obliged to remove his name from the work, as there was no physiological explanation for the observed responses. Considering that Sperry received a Nobel Prize for his work, this may have seemed like a poor decision on Bogen's part. However, neither Bogen nor previous neuroscientists were wrong. Bogen opted for a physiological explanation rather than other interests, and this is the key to understanding the truth of the experiment. Not only was he the doctor who performed the operations, but he was also a witness to the development of the situation and to the relationships between the other researchers, such as that between Roger Sperry and Michael Gazzaniga. Consider the following quotes from the autobiography of Joseph E. Bogen [8].

"Even Sperry shrugged: what theoretical preconception would be falsified? His interest in 'useful information' can be illuminated by the time I returned from a meeting, finding him eager to hear what had transpired. I had been going on for about 5 minutes, when he asked, 'Was there anything that would change how we look at things?' By this time I had read almost all of his writing. 'Well, I think not.' He shrugged and was no longer interested in the report…"

"In the beginning Sperry was not that interested. He just thought he would let me and Gazzaniga do it. But it became apparent to Sperry after the second patient that anything you could do with a monkey you could do a lot faster with human beings. He got a lot more interested…"

"Derek Denny-Brown was very strongly opposed to the idea of complementary hemispheric specialization. And whenever someone would come up with some evidence from lesions that a right hemisphere was special in some way, he would come up with some kind of argument to show that it had been misinterpreted. But in spite of his strong feelings on the subject, he was apparently a man of open mind because in this International Congress he decided to put on a plenary symposium for everybody on cerebral dominance. It turns out that he invited Oliver Zangwill, Henri Hecaen, Wilder Penfield, Brenda Milner, and Roger Sperry. He asked Roger Sperry to bring Gazzaniga along but by this time he and Gazzaniga were not on speaking terms so he said, 'How about if I take you along?' I said, 'Sounds good to me.' I was kind of amused by this whole thing any-way…" [9].

"Mike Gazzaniga was a good friend of mine when we started out. But eventually I developed a bunch of negative feelings about him because I think he just kind of muddied everything up for everybody. He keeps changing what he says. I wrote him one time and said, 'I am going to criticize some of your views at the Neuroscience meeting, you may want to show up.' He wrote back that he had another meeting elsewhere. However, he said, his views were evolving. I would say they revolve from year to year. People have asked me, 'Do you agree with Gazzaniga?' When they ask me now my answer is, 'Which?'"

It is clear from the aforementioned quotations that the relationships among the three researchers involved in the original experiment were fraught with conflict. Ironically, the one who expressed no initial interest in the experiment would become the only one to win the Nobel Prize for the work.

A step towards the truth with CT and MRI

Doubts regarding Sperry's split-brain research continued to surface even after Sperry received the Nobel Prize. To resolve some of these concerns, both sides-those who had doubts and those who did not-reached an agreement and sought to confirm their respective positions using diagnostic imaging. The brains of the experimental participants were examined using computed tomography and magnetic resonance imaging. Michael Gazzaniga reported on three of the observed cases (J.W., P.S., and V.P.; December 1, 1985), while other researchers reported on different cases [10]. Magnetic resonance imaging revealed that the anterior commissure was intact in all three cases, and demonstrated an intact knee and splenius of the corpus callosum in one patient (V.P.) whose corpus callosum was thought to be completely severed. Another report indicated that certain parts of the cortex had atrophied in patient W. J. Furthermore, interthalamic adhesion, which could not be visualized using CT, was observed using magnetic resonance imaging in W. J. When Bogen was asked how and why complete commissurotomy was reported in these cases, he responded that he did not use a surgical microscope due to Vogel's renowned surgical skills, though he had begun to use one in 1970. This response calls into question why Bogen attempted to finish the operation in some bodies from the morgue and in his first patient, and why he would not use a tool as important as the surgical microscope to gain a greater appreciation of his colleague's work. We could also ask why patient V.P. exhibited intact portions of the knee and splenius of the corpus callosum even though his operation had occurred in 1979; almost a full decade after Bogen began to use a surgical microscope. Unfortunately, Bogen is no longer alive, and these questions must remain unanswered. Gazzaniga provided the same responses as Bogen, though he added that neuropsychological evaluations had also enabled them to conclude that complete disconnection of the hemispheres had been achieved: "Although surgery was not carried out under microscopic control, a neuropsychological assessment implied that hemispheric disconnection was complete." However, Gazzaniga left the following questions unanswered: when was a neuropsychological evaluation designed to confirm the disconnection of the two brain hemispheres? What convention established this assessment? What year? Are you not the first to have analyzed neuropsychological functioning in the split-brain condition?

In light of the abovementioned MRI evidence indicating the presence of commissures that had presumably been severed, researchers attempted to show that the statement of false information by Sperry and colleagues was not intentional. Gazzaniga himself went on to state that he doubted the capabilities of the equipment used, remarking that first-generation MRI may not have been entirely accurate. To this end, modern equipment has allowed researchers to observe the same findings visualized in the 1984 images with better detail. Thanks must be extended to the 2003 Nobel Prize winners Paul Christian Lauterbur and Peter Mansfield for their development of the MRI technique that has allowed us to shed light on this and numerous other issues in the field of neuroscience [11].

The language in the right hemisphere

The presence of a certain degree of expressive ability in the right hemisphere was the most controversial and discussed finding of the original split-brain experiment, among both scientists and laypersons. This finding was rejected by many neuroscientists, and even by one of the researchers involved in the original experiment (Bogen) due to the lack of a physiological explanation for the result. However, the public became fascinated by this new and contradictory idea, bestowing a type of social approval upon the results of the study. To researchers, the conclusion was akin to saying that humans can see with the nose as well as the eyes-absurd, yet there was no way to prove that it was untrue. Although most people would be thrilled to have an additional part of the body helping them appreciate the beauty of a morning sunrise, the only evidence we have to reject this notion is that people without eyes cannot see. Similarly, people with lesions in language areas of the left hemisphere cannot speak and/or understand language used by others. Luckily, there is a great deal of additional evidence regarding this argument, which I will develop throughout the article.

We should note that the original research asked us to bear in mind two important facts:

1. All patients had undergone a uniform [12,13] commissurotomy that included the corpus callosum in its entirety, the fornix, and the anterior commissure,
2. Information was successfully delivered only to one hemisphere [14]. Given this information, it would seem likely that, if patients were able to read words presented to the right hemisphere, the right hemisphere must have had some capacity for expression.

The issue of language was the only novel subject of the research, as the remaining subjects-such as lateralization of brain functions-had been debated since the 19th century by Wernicke, Broca, and Heschl, among others. However, while previous researchers had used the word "attention" in the discussion of their results, Sperry chose to use the word "consciousness". Strictly speaking, consciousness is not synonymous with attention, though it may be considered as such in a variety of situations by neuroscientists.

Consider the following example:

1. Miguel was concentrating on point A and was therefore not conscious (aware) of what was happening at point B;
2. Point A occupied the attention of Miguel, while point B did not.

Additional research was conducted in the 19th century regarding consciousness/attention by a number of researchers who had analyzed patients with problems of irrigation and drainage in the nervous system, which can cause damage to areas such as the posterior parietal cortex. The ideas expounded by this research prevailed until 1941, when Russell described for the first time a syndrome characterized by inattention or neglect. Following the advent of more advanced diagnostic imaging technology, we have learned a great deal about the phenomenon of neglect. Today, we know that deficits in attention can be related not only to injuries of the posterior parietal cortex, but also to those of the cingulate cortex, basal ganglia, and cerebellum. Electroencephalography and MRI have enabled us to observe increased activity in the cingulate cortex during tasks that require a high level of attention, such as in the Stroop task, in which participants are required to read a written color name while ignoring a non-matching ink color (i.e., the word red written in color blue).

Forebrain Physiology

Due to the wealth of information available on the human forebrain [15], it is impossible to discuss the entirety of knowledge surrounding the physiological functioning of this region within a single article. However, we can use some of this knowledge to provide a physiological explanation for the results of Sperry's experiment. Let us return to our previous discussion of truth and validity, briefly:

$A \rightarrow B$

A

B

If I sever the corpus callosum, then the brain is divided; the corpus callosum is severed, the brain is divided. As previously discussed, this argument is a valid argument because its premises support its conclusion, but we must also consider whether the premises upon which the conclusions are based are true: is the corpus callosum the only structure to join the forebrain?

Though some consider the term “nervous system” to be a crude synonym for “brain”, our analysis will utilize the strict definitions of both words. The nervous system is divided into the peripheral and central nervous systems. The brain is part of the central nervous system. The forebrain includes the diencephalon and telencephalon, which are joined by various commissures that convey information between the hemispheres. These commissures are the corpus callosum, fornix (hippocampal commissure), anterior commissure, interthalamic commissure (intermediate mass or interthalamic adhesion), habenular commissure, and posterior commissure **(Figure 1).** Of note, a commissure is defined as a structure of the forebrain that allows the passage of signals from one hemisphere to another, though these structures are sometimes capable of providing secondary support to ventricles and other structures.

It should also be noted that neurological functions such as maintaining focus on a particular point, voluntary movement, or speaking a particular language occur via the integration of activity in many cortices that communicate via fibers that interconnect different regions within the same single hemisphere. If a given task requires the participation of the other hemisphere, information is exchanged via the commissures. A clear example of this complex interchange can be observed when making a movement to lift a heavy object in extra-personal space. Execution of any voluntary movement requires the activity of the primary motor cortex and basal ganglia, and the type of movement mentioned here requires additional activation of the premotor cortex. Furthermore, as this type of movement also requires an assessment of the distance to which the arms must be extended, cerebellar activation is required as well. Before the individual attempts to lift the object, the nervous system recognizes that one limb will not be sufficient for this task, and information is exchanged with the other hemisphere in order to recruit the assistance of the other limb. The entire process must occur within milliseconds in order to successfully complete the task and overcome any internal conflict. While the importance of commissural fibers and information exchange is apparent in such a simple example, let us consider a more complex scenario. Activation of Broca's and Wernicke’s areas is required for self-expression and language comprehension, respectively, in conjunction with activation of the motor cortices, basal ganglia, and cerebellum. Vocalization also requires the control of fine motor movements of the tongue and facial muscles. Moreover, a given individual must be aware of what he or she is saying, which requires the activation of yet another group of neurons in the posterior parietal and cingulate cortices.

In Sperry’s experiment, split-brain participants were able to read aloud words presented to the right hemisphere, which required the coordination of the bilateral tongue and facial muscles. If the opposite hemisphere was truly deprived of information (as the original researchers claimed), and each hemisphere acted independently, how would such a result have been possible? How can it be true that information was not transmitted from one hemisphere to the other in the absence of hemiplegia or paralysis of the contralateral side?

In stroke, hemiplegia is an important symptom that helps predict the hemisphere in which a stroke has occurred. Consider also the Duchenne smile, which involves the movement of nearly all the muscles of the face. Injury to one hemisphere in any of the frontal areas related to this smile task results in the patient’s inability to move muscles on the side contralateral to the lesion. Furthermore, injury to the supplementary motor cortex and/or cingulate motor cortex results in a phenomenon known as akinetic mutism, wherein the main characteristics include an inability to speak and an inability to initiate voluntary movement (even if the primary motor cortices remain intact).

At the time of their research, Sperry and colleagues claimed that the observed responses (i.e., the ability to read aloud words presented to the right hemisphere) were solely due to the activity of the right hemisphere. In what manner then was the right hemisphere capable of coordinating the facial muscles of both sides of the face? Given the aforementioned knowledge, it would seem that these researchers were suggesting that the right and left hemispheres acquired an ability to independently produce speech and bilateral muscle movement due to the commissurotomy.

Physiology of the thalamus and the forebrain commissures

The thalamus is a center of information integration that processes external and brainstem-level signals before they reach the level of the cerebral cortex, with the exception of olfactory information (which is relayed directly to the cortices via the olfactory bulb). The lateral and medial geniculate nuclei of the thalamus are responsible for the integration of visual and auditory information, respectively, while the posterolateral ventral nucleus is responsible for the integration of pain, temperature, and touch signals for the whole body, with the exception of the face (these signals are integrated by the posteromedial ventral nucleus). However, one group of thalamic nuclei has reciprocal connections with the association cortices: the pulvinar, lateral, posterior dorsolateral, and dorsomedial nuclei. Relatively little is known about the function of these nuclei, though the pulvinar nucleus is better studied than the others. The pulvinar nucleus has reciprocal connections with each association cortex, receiving, sending, and processing various types of information (for more information about the pulvinar nucleus, refer to the work of Javier Cudeiro, Carlos Acuna, and Kenneth L. Grieve). Therefore, an important question is whether there exist commissures that allow for the integration of the activity of these thalamic nuclei. If so, in a callosotomy or commissurotomy, these commissures

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must be severed as well to ensure that information transfer between the hemispheres does not occur.

The septum pellucidum is another commissure of the forebrain; yet, the precise function of the septum pellucidum in the transmission of information from one hemisphere to the other remains unclear. The hippocampal commissure or fornix allows for the passage of information from the hippocampus of one hemisphere to the other and connects the hippocampus with various structures of the limbic system, including the hypothalamus.

However, the two most important commissures for communication between different parts of the telencephalon are the anterior commissure and the corpus callosum **(Figure 1).** The anterior commissure is responsible for the passage of information between the frontal lobes (and especially between the basal ganglia). The larger and more important commissure for communication between the different structures of the cerebrum is the corpus callosum. The corpus callosum is composed of different parts, starting from the peak, through the knee, followed by the truncus or body, and ending in the splenium. This commissure plays the most well-known role in integrating the information of both hemispheres. Patients who have lost 2/3 of the corpus callosum, but retain the third that corresponds to the splenium, demonstrate awareness of what happened in the other hemisphere, while the absence of this third results in the opposite phenomenon.

As the primary motor cortex is the last superior processing center for the execution of a voluntary movement, the posterior parietal cortex seems to be the last center involved in the processing of motor and sensory information necessary for comprehension and expression. Information in this cortex is exchanged reciprocally via the splenium of the corpus callosum, which may explain patients' (Neglect syndrome) inability to understand and express what happened in the right hemisphere. Lesions of the primary motor cortex affect fine motor movements of the tongue and fingers as related to spoken and signed language, but do not affect all voluntary movements due to the ability of other cortices (e.g. the supplementary motor and premotor areas) to convey information via the pyramidal and extrapyramidal tracts. The parietal cortex seems to be the principal center for attention, not only because the cingulate cortex spans the length of the corpus callosum in its entirety, but also because this area plays an important role in the execution of complex movements and tasks that require a high level of focus. The interthalamic adhesion that connects the bilateral nuclei of the thalamus is very important for the exchange of information between hemispheres.

Finally, we must consider two other essential commissures in the forebrain: the habenular commissure and the posterior commissure. These two structures have a close anatomical and physiological relationship with the pineal gland, separated by only a few millimeters. As such, it is almost impossible to completely sever these commissures despite modern technological and surgical advancements **(Figure 1).** The habenular commissure connects the bilateral habenular nuclei and primarily serves in limbic functions related to memory, attention, emotion, personality, and behavior. Though little is known regarding the posterior commissure, research has revealed that visual information from the optic nerve passes through this commissure to reach different nuclei (e.g. the pretectal nuclei), which in turn connect with the Edinger-Westphal nucleus, which then sends information through the third cranial nerve (oculomotor) for contraction of the eye muscles.

The Brain, Plasticity and Decisions

The word plasticity is used to define changes that occur within the nervous system over time in response to external and internal stimuli. In the present context, however, plasticity does not refer to the ability of the brain to activate new genes for transcription, differentiation, and maturation. Instead, the plasticity to which I refer here is defined by the following four characteristics:

1. Plasticity is related to an increase in synapses between neurons.
2. Plasticity is related to a decrease in synapses between neurons.
3. Plasticity is related to an increase in action potentials.
4. Plasticity is related to a depression of action potentials.

A clear example involving these four points occurs during the chronic stage of spinal shock, in which an increase in synapses between afferent (sensory) neurons and interneurons that activate motor neurons, as well as a decrease in synapses between afferent fibers and inhibitory interneurons, may occur. Nicotinic acetylcholine receptors also increase their affinity for acetylcholine, which positively influences the generation of action potentials. No new genes and/or increases or decreases in transcription are known to be required in these cases.

Conversely, the transcription of new genes is required for any cell to fulfill a new function; for example, for a cell of the stomach to fulfill the functions of a cell in the duodenum it must express the genes related to that function. Moreover, for neurons in the right hemisphere to accomplish the functions of neurons in the left hemisphere, or for a part of the cortex to fulfill the functions of another, the transcription of new genes related to those functions must occur. However, at present, neuroplasticity is unrelated to the transcription of new genes in groups of neurons (cortex or hemisphere).

Methodological validity

Finally, it is important to consider the methodological validity of Sperry's experiment. In the absence of the corpus callosum, the process of integration between the two hemispheres may be slowed or absent, depending on the duration of the stimulus. Additionally, when delivering information to only one hemisphere in a patient, such as by placing an object in the patient's left hand, care should be taken to ensure that the right hand is not touching anything (e.g. the patient's clothing or body). If a patient has both eyes open instead of one, each visual cortex is connected to its posterior parietal cortex for attention (consciousness); due to the absence of the corpus callosum and the duration of the stimulus, a patient can say he sees nothing when the information goes to the right posterior parietal cortex. These precautions (hands and eyes) will prevent the two hemispheres from receiving different information at the same time, which could lessen the effects of an absent corpus callosum. So, we must then ask the following: were the researchers aware of this when designing and conducting the original split-brain experiment and did they take the necessary precautions? A review of videos, on the Nobel Prize organization's website and others, that illustrate the development of the experiment indicates that they did not [16,17]. The algorithm in relation with the difference between Commissurotomy and Callosotomy, which case gives place to Split-brain for the study of single hemisphere functioning **(Figure 2);** it helps us to understand that the term split-brain is not fitted for Sperry investigation [18]. One possible investigation with the participants of Sperry could be the roles of other commissures in the absence of the Corpus Callosum.

Sperry is not the most recognized psychologist in his field. In fact, he was ranked as the 44th most influential psychologist in the 20th century [19]. The relevance of his experiment, however, resulted in his acceptance of a Nobel Prize in 1981 [20].

Considering the aforementioned discussion, accepting the entirety of Sperry's experiment as true seems to negate a vast amount of epistemological and physiological knowledge. Epistemology tells us that, in order to consider a definition or fact as true, it should be irrefutable. For example, in order to state that every mammal is warm-blooded, no examples of cold-blooded mammals should exist. Similarly, to say that the corpus callosum is severed and thus the brain is divided, there should not exist even one commissure that unites the two hemispheres. Yet, we have discussed several commissures that connect the two hemispheres **(Figure 1)** and, moreover, provided evidence that some of these commissures were not or could not have been severed at the time of Sperry's experiment. The improper experimental conditions, the inability of the present technology to conduct a complete comissurotomy, and results of neuroimaging (studies indicating intact commissures in experimental patients) are all evidence that Sperry's experiment was not as ingenious [20,21] as others scientists have considered it to be.

I would like to conclude with a discussion of a question I once asked my father: "Daddy, my teacher says that the brain is the most sophisticated and perfect machine that ever existed in the universe. If this is true, why do we use it to do such silly things like fight or lie?" My father told me that he had no perfect answer and that, if the answer was important to me, I should take care in learning more about this machine. After I learned a great deal more about the extent of the brain's capabilities -its incredible speed of information processing and the billions of connections contained within it. I knew that the answer was worth pursuing. The vast number of connections makes it difficult to fully understand all of the brain's functions, and we should be careful not to accept theories about the brain simply to satisfy our desire for knowledge. Instead, we strengthen our desire and willingness to learn and ask questions in the pursuit of a higher level of perfection.

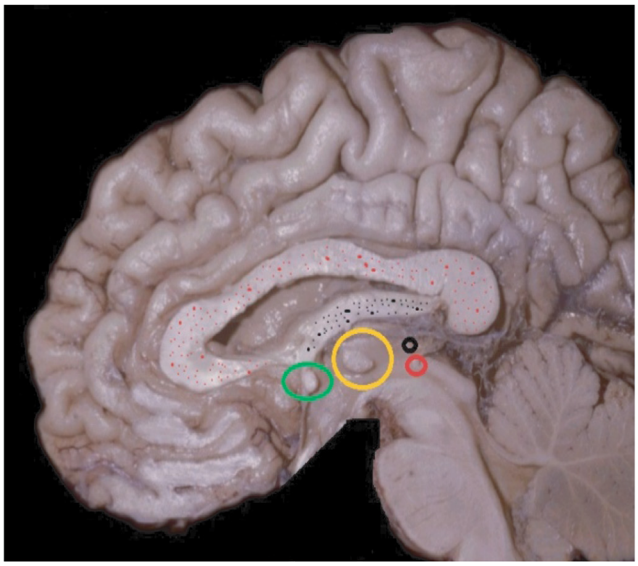

Figure 1 Commissures of the forebrain in a sagittal section. In the figure, the six commissures connecting the diencephalon and telencephalon can be seen. The red dots correspond to the corpus callosum, the black dots indicate the fornix, the green circle indicates the anterior commissure, the yellow circle indicates the interthalamic commissure, the black circle indicates the habenular commissure, and the red circle indicates the posterior commissure.

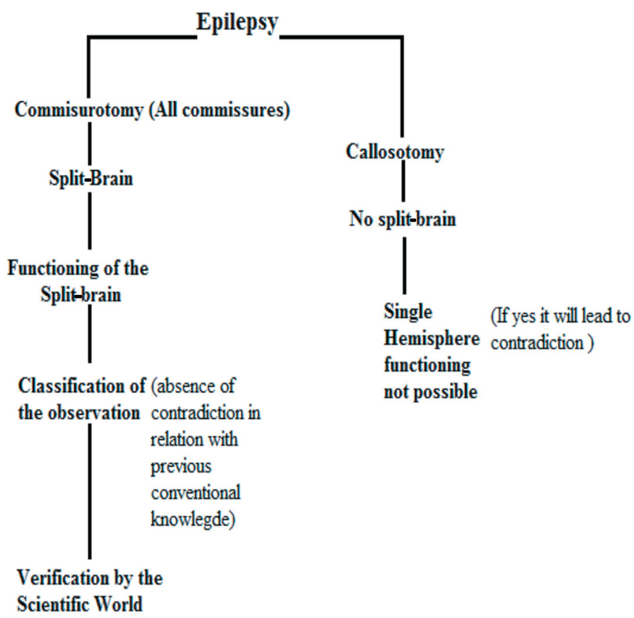

Figure 2 The algorithm in relation with the difference between Commissurotomy and Callosotomy, which case gives place to split-brain for the study of single hemisphere functioning.

If society could function and integrate information like the human brain, we would arrive at solutions much more quickly than we do now. I remember reading an article about human immunodeficiency virus and thinking to myself, "maybe we already have the solution." Maybe we only have to integrate all of this data in order to solve the problem. During this time, I began to believe quite deeply that perhaps the solution we were looking for was not contained within the defense system of a mammal but within that of an insect. We know that mosquitoes cannot transmit the virus from one person to another because of the concentration of the virus and the complete elimination of the virus in the digestive system. I thought that perhaps this process was due not to a decrease in pH (which occurs in the gut of all mammals) but to a more specific defense reaction. Two years later in 2015, I came to learn that the University of Washington had come closer to a solution, discovering a protein called melittin in bee venom [22].

Conclusion

Consider also the case of an English patient, a former military officer (identified only as W.O.), who lost his memory after going to the dentist for a root canal treatment. W.O. exhibited anterograde amnesia at the age of 38 in March of 2005. Though no diagnosis was ever offered, I believe that the key to an accurate diagnosis lies in the presentation of the case. For example, the integration of data from the past regarding memory loss for more than 12 hours, following the consumption of alcohol, may lead to an appropriate diagnosis. Data integration may also help solve the riddle of Alzheimer's disease if recent Nobel Prize-winning work were to be considered in conjunction with the abundance of available data. If we were able to integrate all of the data that has been obtained over the years, we could solve a great deal of problems much sooner than previously thought possible. Instead, the desire to be a pioneer or achieve recognition too often makes us focus on only the results of our solitary investigations, without considering the work of others. Yet, I am confident that modern research groups, both small and large, still have the desire and ambition to solve the greatest mysteries of science through the integration and communication of data.

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Declaration of Interest

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