

DISTRACTED? BLAME YOUR CLAUSTRUM!

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YOUNG REVIEWERS:

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(SCIENCE-
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YOUTH)

AGES: 12–16



To succeed in reading these sentences, your brain must ignore a variety of distractions—sights, sounds, and smells. Resisting distractions is a vital ability for our daily lives, and it poses a unique challenge for people who are dealing with attention disorders. In a recent study, we asked whether an area in the brain called the claustrum supports the ability to ignore distractions. We developed methods that allowed us to silence the claustrum in mice. We challenged these mice with tasks requiring them to pay attention. We found that mice whose claustra were silenced were especially sensitive to distractions. These results provide an important clue about the function of the claustrum, and we hope that they will contribute to the development of new methods that will assist people dealing with attention disorders.

While reading these words, you are dedicating attention to the black letters on the white background. To do that, your brain must ignore a variety of other objects and stimuli from your surroundings. For

ATTENTION DISORDERS

Brain disorders that lead to difficulty following instructions, focusing while performing tasks, and efficiently finishing tasks. People with attention disorders tend to be easily distracted.

CLAUSTRUM

A thin, elongated region located deep within the Brain. It interacts with many other brain regions, involved in multiple brain functions.

example, you must filter out the white walls in your house or your keyboard keys. Your brain also needs to filter out noises from your environment and ignore your body position on the chair. Imagine for a moment what would happen if your brain could not differentiate between important information and distractions. If everything was important, would you be able to focus?

In other words, to help you pay attention, the brain needs to constantly perform two complementary actions [1]. It needs to highlight important and relevant information while, at the same time, it needs to ignore less important or irrelevant information. The ability to concentrate and ignore distractions is challenged in people with **attention disorders**. People with attention disorders can find it challenging to separate important events or information from those with lower priority that are safe to ignore.

How does all this relate to the brain? Although the brain is a single organ, we can define about 1,000 different parts or sub-regions of the brain. Each sub-region helps the brain to perform different functions, such as processing information from the senses, recording memories, directing thoughts, and sending instructions to the body's muscles. Now, let us assume that there is a part of the brain that specializes in filtering out irrelevant information. What sorts of features would you expect this area to have?

THE CLAUSTRUM—A MYSTERIOUS BRAIN AREA

To know what to ignore, a brain area that filters out irrelevant information should receive information from the senses, such as information about sights, sounds, and touch. Moreover, this area needs to communicate with other areas in the brain that direct our attention. One intriguing brain area that fulfills both requirements is called the **claustrum** [2, 3]. Although the claustrum is a relatively small brain area, it is the most connected brain region, relative to its size [4].

The claustrum is located deep inside the brain, and it has the shape of a long thin sheet (Figure 1). Its name corresponds to its location in the brain: in Latin, claustrum means “hidden” or “closed,” similar to “claustrophobia” (fear of closed or crowded spaces). The claustrum has captured the attention of researchers ever since its discovery. However, it has frustrated them too, because for a long time they were unable to understand its function. To understand the function of any brain area, researchers usually disrupt its normal activity, to see which abilities are then lost. This was almost impossible with the claustrum, due to its small size, unusual shape, and challenging location in the brain. This was the situation until Gal Atlan, Anna Terem, and others from the laboratory of Prof. Citri at the Hebrew University, found a way to selectively silence cells in the claustrum [5].

Figure 1

Connections between the claustrum and other areas of the mouse brain. A side view of the mouse brain shows that the claustrum (colorful area) communicates with a variety of other brain areas, including those responsible for sight (visual), hearing (auditory), touch (sensory-motor), and smell (olfactory). The claustrum also communicates with areas responsible for directing attention and controlling behavior, located in the prefrontal cortex (PFC) (Image credit: [2]).

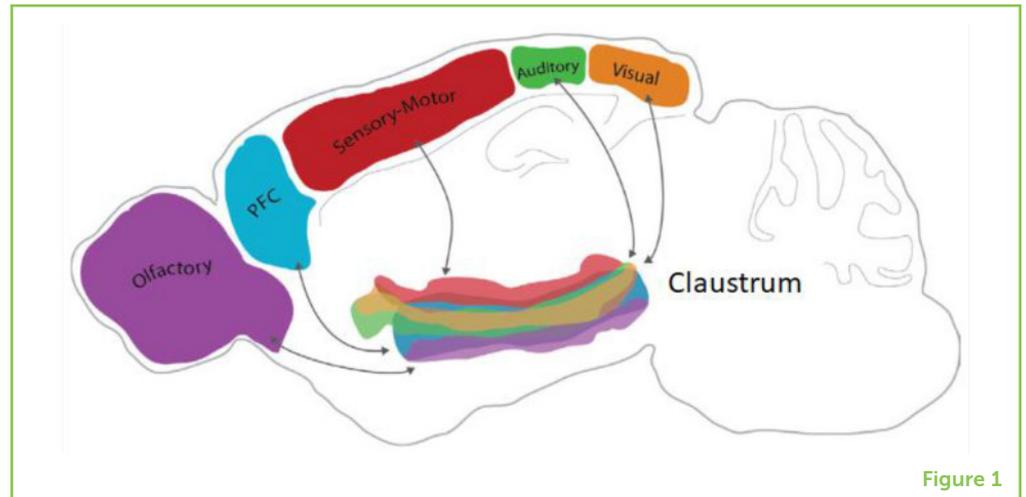


Figure 1

HOW DO WE SILENCE THE CLAUSTRUM?

To understand how these researchers managed to silence the claustrum, we first need to understand a fundamental characteristic of cells. The body is made from over 100 billion cells! All our cells share the same “code”—DNA—that is responsible for directing the main action performed by all cells—producing **proteins**. You can imagine proteins as small machines, each with a unique assignment. The different cell types in the body produce different proteins, allowing them to specialize in the tasks they perform. Hemoglobin, for example, is an oxygen-carrying protein, which is present in red blood cells.

Prof. Citri’s research group discovered that brain cells in the claustrum produce a protein called **Egr2**. This protein is not present in any other nearby brain cells, so it is therefore called a marker of claustrum cells. Researchers used a **virus** that was specifically created to infect and silence only cells that produce Egr2. They infected the brains of mice with this virus. The ability to selectively silence cells in the claustrum allowed researchers, for the first time, to examine the function of the claustrum.

THE WATER SOURCE EXPERIMENT

Once researchers were able to silence the activity of the claustrum, they could study whether the claustrum is related to attention. Does the claustrum help us to be focused and resist distractions? To answer this question, Gal and Anna, together with Noa Peretz-Rivlin, conducted an interesting experiment. Mice were placed in a cage with two water sources (Figure 2A). When a mouse approached these water sources, a light appeared for a short time above one of them. To receive a drop of water, the mouse had to pay attention to which light came on and had to respond quickly by licking the sensor under that light. In some cases, a noise was produced while the light was

PROTEINS

Tiny machines and building blocks within cells that are critical for almost all the actions performed by cells.

EGR2

Early Growth Response 2. It is a special type of protein that controls the production of many other proteins. Egr2 is produced in the Claustrum, but not in neighboring regions, making it a good marker for the Claustrum.

VIRUS

An infectious particle consisting of DNA or RNA, enclosed by a protein envelope. Genetically modified viruses can be created by scientists to target specific cells in an organism.

Figure 2

Silencing the claustrum makes mice sensitive to distractions. **(A)** When the mouse approaches the water sources, a light goes on above one source. The mouse must pay attention and quickly lick a sensor under the correct light, to get a drink of water. In some cases, a distracting noise is played. **(B)** Mice with normal claustra (control) performed the task successfully about 65% of the time, and the noise distractor did not significantly affect their success. However, in whose CLA was inhibited, the success rate dropped significantly, to about 40%, in the presence of the distracting noise.

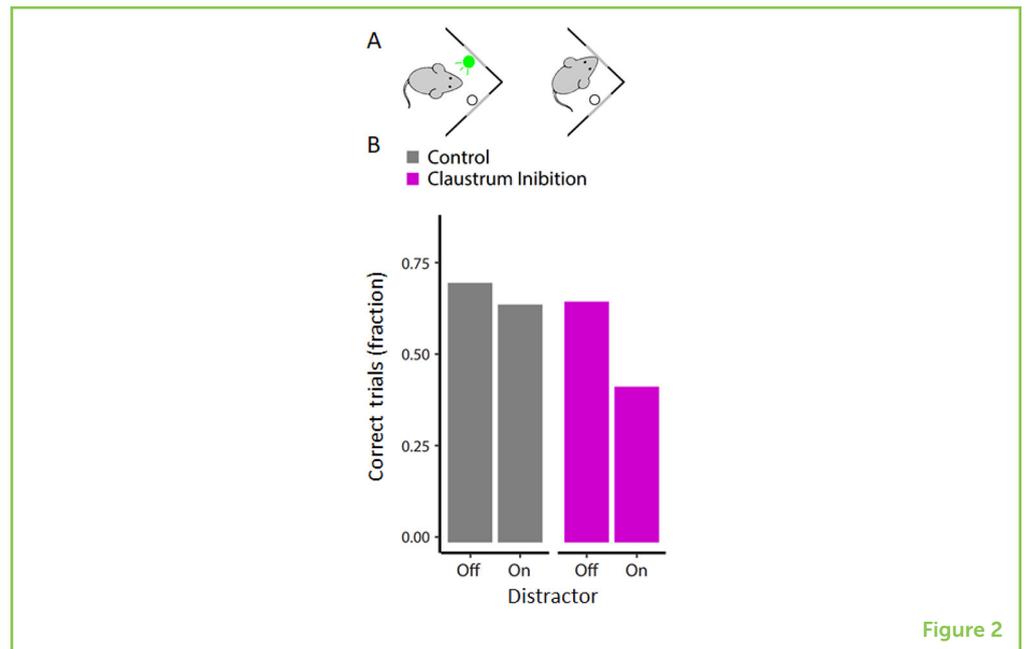


Figure 2

turned on, serving as a distraction. The performance of the mice was measured as the percentage of times they licked the correct sensor and were rewarded with a drink of water.

The researchers compared mice whose claustra were silenced with control mice, which had intact claustra. They noticed an interesting pattern: in the absence of distractions, the two groups of mice exhibited similar performances—both licked the correct sensor and got water about 65% of the time. In comparison, when there was a distraction, mice with silenced claustra succeeded in only 40% of the trials. The control group with normal claustra was not affected by the distraction (Figure 2B).

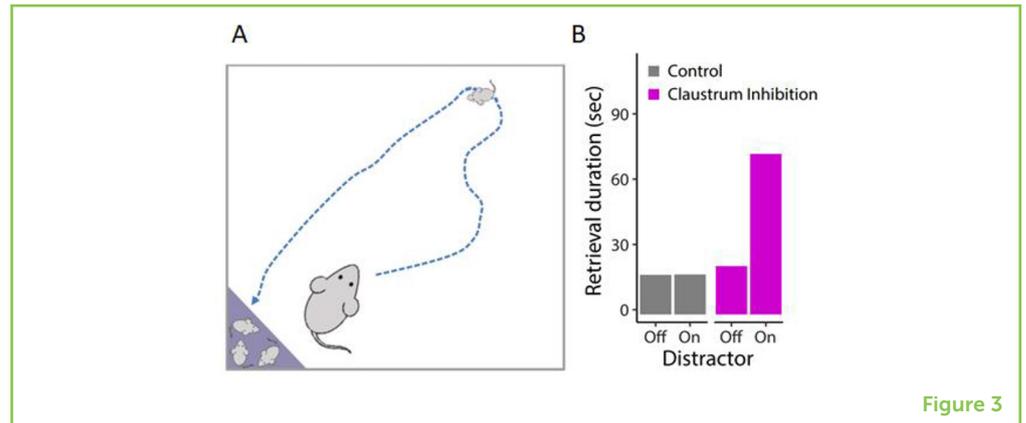
THE PUP RETRIEVAL EXPERIMENT

Results from the water source experiment taught us that proper functioning of the claustrum is crucial for mice to ignore distractions. It is important to emphasize that this was a very artificial experiment—mice in nature do not need to lick a water source marked by a light to receive a drink of water. To test the role of the claustrum in a more natural activity, Gal and Anna conducted another experiment. Mothers in nature (not only mice) tend to keep track of their pups using all their senses, to collect them back to the nest if they stray. Imagine you are responsible for your young siblings in a mall or a movie theater. Could you allow yourself to be distracted and not pay attention to them?

Gal and Anna wanted to see if mother mice depend on their claustra to retrieve their pups in the presence of a distraction. They placed the

Figure 3

Inhibition of the claustrum distracts mothers during pup retrieval. **(A)** Researchers placed the pup a certain distance from the mother and measured the time it took her to bring the pup back to the nest. **(B)** Control mice with normal claustra took about 15 s to retrieve their pups, both in the presence and absence of distracting noise. When there was no distracting noise, mice with silenced claustra took about the same amount of time to retrieve their pups as did the control mice. However, in the presence of distraction, their average time increased significantly, to over 1 min.



young pups, one after another, a short distance away from the mother (Figure 3A). They compared the time it took mothers with normal claustra to bring their pups back to the nest, compared to mothers whose claustra were silenced. Like the previous experiment, in some cases they included noise as a distraction. As you can see in Figure 3B, the distraction did not influence the mothers' performance in the control group with normal claustra. In contrast, the noise distraction had a dramatic influence on mothers whose claustra were silenced. The average time it took them to retrieve the pups increased from 20 s to more than 1 min.

THE CLAUSTRUM: YOUR SHIELD FROM DISTRACTIONS

To maintain attention, the brain needs to filter out a huge amount of irrelevant information. Our research group hypothesized that the claustrum could be a good candidate for performing this task. To test our hypothesis, researchers used a special virus to silence the claustrum, and compared mice with silenced claustra to mice with normally functioning claustra. When there was no distraction, the two groups behaved similarly. But in the presence of the distraction, there was a decrease in the functioning of mice whose claustra was silenced.

Could this information help us understand the function of the claustrum in humans? Generally, yes. Information from mice can tell us a lot about the function of various brain areas in humans. Humans and mice have high levels of similarity in brain structure, in the division of the brain into separate areas, and even in the relationships and connections between areas.

This research raises several interesting questions. In a world full of distractions, could we make the claustrum work harder than usual, to improve the ability to pay attention? How does the claustrum know what information is important and what it should filter out? What does the claustrum do to help us filter out irrelevant information?

What are the other roles of the claustrum? And finally, can we use our knowledge of the claustrum to help people who are dealing with attention disorders? The research we are currently conducting aims to answer these important questions.

ORIGINAL SOURCE ARTICLE

Atlan, G., Terem, A., Peretz-Rivlin, N., Sehwat, K., Gonzales, B. J., Pozner, G., et al. 2018. The claustrum supports resilience to distraction. *Curr. Biol.* 28:2752–62. doi: 10.1016/j.cub.2018.06.068

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SUBMITTED: 06 May 2021; **ACCEPTED:** 09 June 2021;

PUBLISHED ONLINE: 30 June 2021.

EDITED BY: Idan Segev, Hebrew University of Jerusalem, Israel

CITATION: Fatal Y and Citri A (2021) Distracted? Blame Your Claustrum! *Front. Young Minds* 9:706131. doi: 10.3389/frym.2021.706131

CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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YOUNG REVIEWERS

NOAR SHOHER MADA TAU (SCIENCE-ORIENTED-YOUTH), AGES: 12–16

We are five kids aged 12–16; we are all science-oriented and love the scientific field. We are studying in middle school and dream of pursuing a future in science. We participate in the Science-oriented Youth at Tel Aviv University. We reviewed the article together, on Zoom, each contributing from their own experience, and in the process, we learned and broadened our horizons. We thank Lior Abramson for guiding us through the article review process.

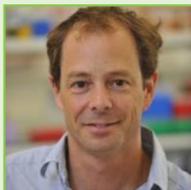
AUTHORS

YONATAN FATAL



I am an 18-year-old from Jerusalem. I have always loved asking questions and finding their answers. What is the distance to the moon? How many cells are there in the body? How can the brain perform so many actions in parallel? In the last few years, I have had the privilege of studying biology for B.Sc. in the Open University, and to work in the research lab of Prof. Citri. Excitingly, my job is exactly what I love doing—asking questions and performing focused experiments to find their answers. I am fascinated by the way single cells in the brain can influence entire brain regions, and in turn direct the behavior of animals and humans.

AMI CITRI



I am a professor of brain sciences at the Hebrew University. I get excited about imagining how my brain functions while I perform different actions, like writing this sentence. How does my brain organize my thoughts and express them by tapping my fingers on the keyboard? Brain science offers us an unusual opportunity to ask questions about ourselves, while we develop insights about the basic brain mechanisms that define who we are, and the circumstances influencing our behavior. *ami.citri@mail.huji.ac.il