



WHY DO BRAIN CELLS NEED “ANTENNAS”?

Mariana Martins^{1,2,3†}, Luísa Amado^{1,3,4†}, Mariana Laranjo^{1,3,4}, Sílvia Santos^{5,6}, Cláudia Cavadas^{1,2,3}, João Peça^{1,3,7} and Catarina Morais Seabra^{1,3,4*}

¹CNC-UC, Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal

²Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal

³CIBB, Center for Innovation in Biomedicine and Biotechnology, University of Coimbra, Coimbra, Portugal

⁴Institute for Interdisciplinary Research, University of Coimbra, Coimbra, Portugal

⁵CEIS20, Center for Interdisciplinary Studies, University of Coimbra, Coimbra, Portugal

⁶Faculty of Arts and Humanities, University of Coimbra, Coimbra, Portugal

⁷Department of Life Sciences, Faculty of Science and Technology, University of Coimbra, Coimbra, Portugal

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Our brains are like incredibly complex puzzles, with billions of pieces that have been growing and developing since before we were born. But did you know that tiny, hair-like structures on our cells called primary cilia play a big part in this process? Primary cilia act as antennas, helping our brain cells communicate, travel, and even build connections, by guiding the assembly of this big puzzle. However, when primary cilia cannot form properly or cannot function smoothly, this can impact the development of many organs, including the brain. Scientists have found that shorter or fewer primary cilia are linked with conditions that may affect brain development, including a group of disorders named ciliopathies. By



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EMBRYOS

The earliest stage of development after fertilization in many species, where a group of cells has the potential to grow into a complete organism.

STEM CELLS

Stem cells are cells that can become many different types of cells in the body. They play a key role in development, growth, and repairing damaged tissues or organs.

Figure 1

(A) The embryo is made of stem cells. (B) Stem cells in the embryo divide, and some become NPCs. (C) NPCs can divide to generate neurons and glial cells. (D) Newly formed neurons must migrate using glial cells as guides. (E, F) Neurons connect with other neurons through synapses, which allow communication using chemical signals. (G) Neurons connect like a large puzzle, where each piece is essential. (H) The completed puzzle forms the complete brain, with each region performing a specific function.

understanding the importance of primary cilia, we can find out more about brain development and the role cilia play in the assembly of this big puzzle.

HOW IS THE BRAIN FORMED?

The human brain is truly remarkable, consisting of around 86 billion tiny cells that work together to control every function and action of our bodies. But how does such a complicated organ come to be? It all started before we were born, when we were just tiny **embryos** (Figure 1A). At this stage, **stem cells** are constantly dividing and creating all the various types of cells that make up our body parts. By receiving signals from surrounding cells, the stem cells in an embryo start to piece themselves together and become more specialized, taking on specific roles like transmitting information as **neurons**, supporting brain function as **glial cells**, or even forming muscles, skin, or blood. In the brain, the stem cells with some degree of specialization are called **neural progenitor cells (NPCs)** (Figure 1B).

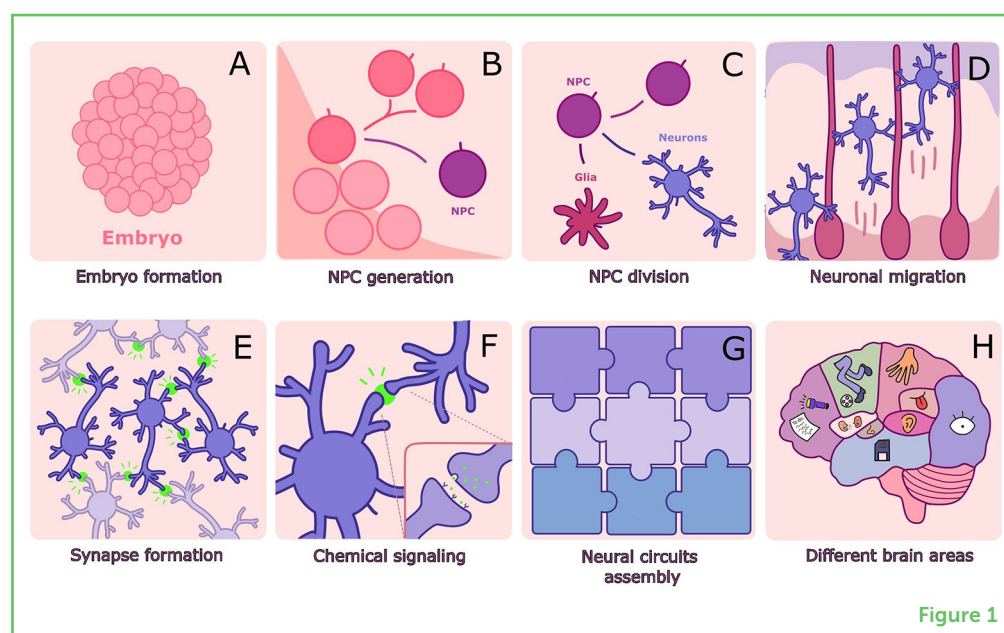


Figure 1

Neural progenitor cells have an extraordinary power: they can transform into two kinds of more complex cells—they can become either neurons or glial cells (Figure 1C). Neurons are specialized brain cells that can receive and send information, not only to other neurons but also to other types of cells. Neuron activity and communication allow us not only to think and create memories but also to see, move, talk, and even listen to sounds. Glial cells have other important roles, such as supporting neurons and cleaning up their waste products, protecting the brain from infections, helping fix things when there is a problem, and ensuring everything runs smoothly in the brain. In a sense, glial cells are like the glue keeping the neurons well

NEURONS

Neurons are nerve cells that carry messages in the brain and throughout the body. They help us think, move, feel, and remember by using mostly chemical signals to communicate.

GLIAL CELLS

Glial cells are important support cells in the brain. They protect neurons, provide them with nutrients, clean up waste, and help them communicate, ensuring the brain stays healthy and works well.

NEURAL PROGENITOR CELLS (NPCS)

Cells in the developing brain that can either divide or generate brain cells called neurons and glial cells.

SYNAPSES

A small gap between neurons where signals are transmitted, enabling brain cells to communicate and coordinate functions such as thinking, moving, and sensing.

NEURAL CIRCUITS

Neural circuits are networks of connected brain cells that send and process information, like tiny electrical highways. They control everything from breathing to thinking, helping the brain respond to the world.

DIFFERENTIATION

The process where stem cells become specialized, turning into different types of cells with specific jobs, like neurons or glial cells.

attached—that is precisely what the word “glia” means (glue, in Greek).

When a new neuron is formed in a developing brain, it needs to travel to its specific place (Figure 1D). As neurons piece themselves together to form the structure of the brain, connections between neurons form, which are called **synapses** (Figure 1E). Synapses make it possible for neurons to communicate with each other, mostly through chemical signals (Figure 1F). Like puzzle pieces, neurons need to fit together effectively and build just the right number of connections. As more and more neurons connect with each other, a big, intertwined web is created, forming what are known as **neural circuits** (Figure 1G). When this happens, the different parts of the brain become organized into regions that may each play a more specific role in thinking, learning, speaking, seeing, or controlling body movements (Figure 1H).

However, brain development does not stop there. As we grow and learn new things and develop new interests like sports or music, our neurons can form even more synapses. This ability to change connections between neurons is called plasticity, and in this way the brain is always changing and adapting—thanks to the hard work of brain cells and their special “antennas”, the primary cilia.

WHAT ARE PRIMARY CILIA AND HOW DO THEY PARTICIPATE IN BRAIN FORMATION?

Primary cilia are tiny, antenna-like structures, with each cell having just one. They help the cell sense signals and communicate, like mini satellite gathering information. For neurons and glia, this antenna helps send and receive signals between brain cells. This function is especially important when the brain is developing because primary cilia help cells capture important chemical messages that tell them when to perform certain tasks, such as dividing and making more copies of themselves, becoming more complex “adult” cells (which is called **differentiation**), or migrating to a specific place in the brain (Figure 2) [1–3].

For example, the primary cilia of NPCs tell them when to divide into either more NPCs or into neurons or glia, which do not divide anymore. This way, the brain has a mechanism to ensure that it has precisely the right number of cells it needs to work in a healthy way. After neurons differentiate, they need to know where to go in the brain—that is where their antennas come into play once more. Primary cilia capture signals from neighboring cells that tell these neurons where they should go and even where to form new synapses. Based on the signals that primary cilia collect, more synapses are made, and these connections help to create mature neural circuits.

Overall, primary cilia play an important role in putting together and organizing the puzzle pieces that form the brain, and it is very

Figure 2

When primary cilia on NPCs detect certain signals in their environment, they tell the cell to either **(A)** divide, **(B)** differentiate into neuronal cells, or **(C)** migrate to a different location in the brain. All these processes are crucial for healthy brain formation. **(D)** A microscope image showing healthy cells, with primary cilia colored green and the nucleus colored blue. Each cilium measures about 5 micrometers in length—about 1/4 the diameter of a strand of hair (microscopic image collected by the Peça Lab at CNC-UC).

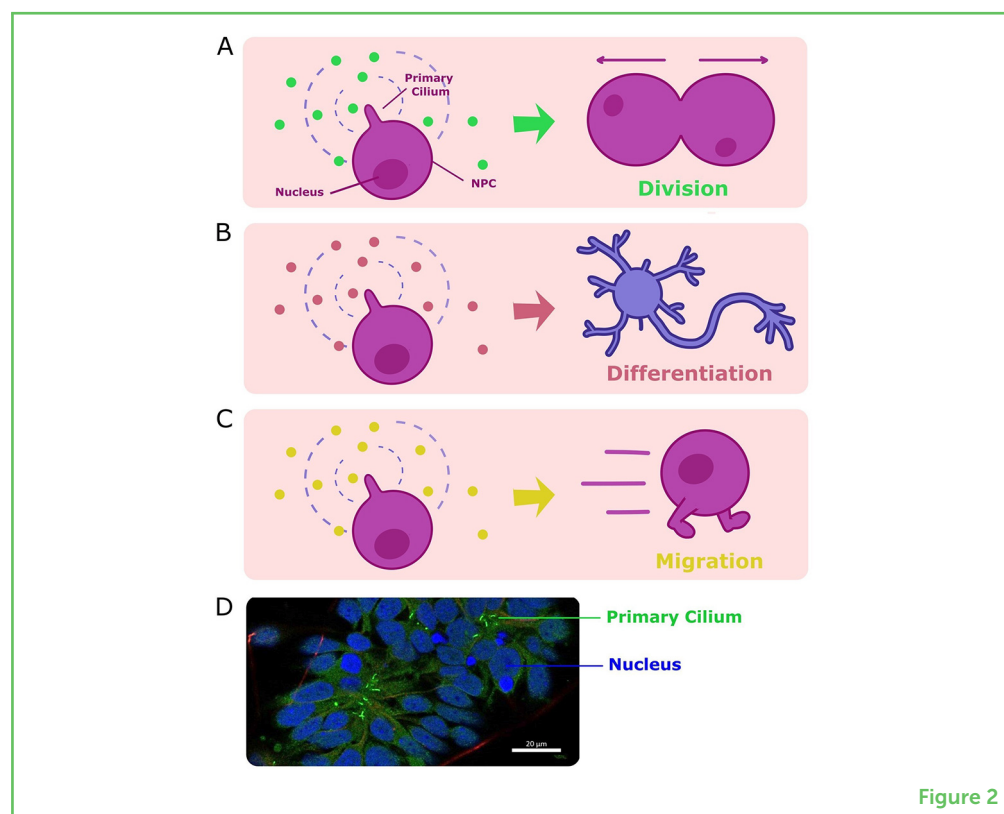


Figure 2

important that they do this job just right. When a piece is out of place, out of order, or even when there are too many pieces, health problems can result.

WHAT HAPPENS WHEN PRIMARY CILIA DO NOT WORK PROPERLY?

When primary cilia are either formed incorrectly or cannot be formed at all, they will not function properly, and diseases can result, including a group of diseases called **ciliopathies**. Ciliopathies can affect a few organs or multiple organs, including the brain, liver, and kidneys; in severe cases it can even be lethal for the developing embryo. When the brain is affected by ciliopathies, its puzzle pieces—the neurons and glia—have trouble connecting and communicating with each other. If this happens, the person will have difficulties with some activities, like learning new things. Altered primary cilia are also linked to **neurodevelopmental disorders** such as autism spectrum disorder and intellectual disability, in which brain development is impaired. Neurodevelopmental disorders can affect not only how people learn but also the ability to communicate or even move, making life more challenging.

To learn more about neurodevelopmental disorders and primary cilia, scientists did experiments using mouse brain cells and even human cells from individuals with disorders including **fragile X syndrome**,

CILIOPATHIES

A group of rare disorders where the primary cilia do not work properly, causing various problems.

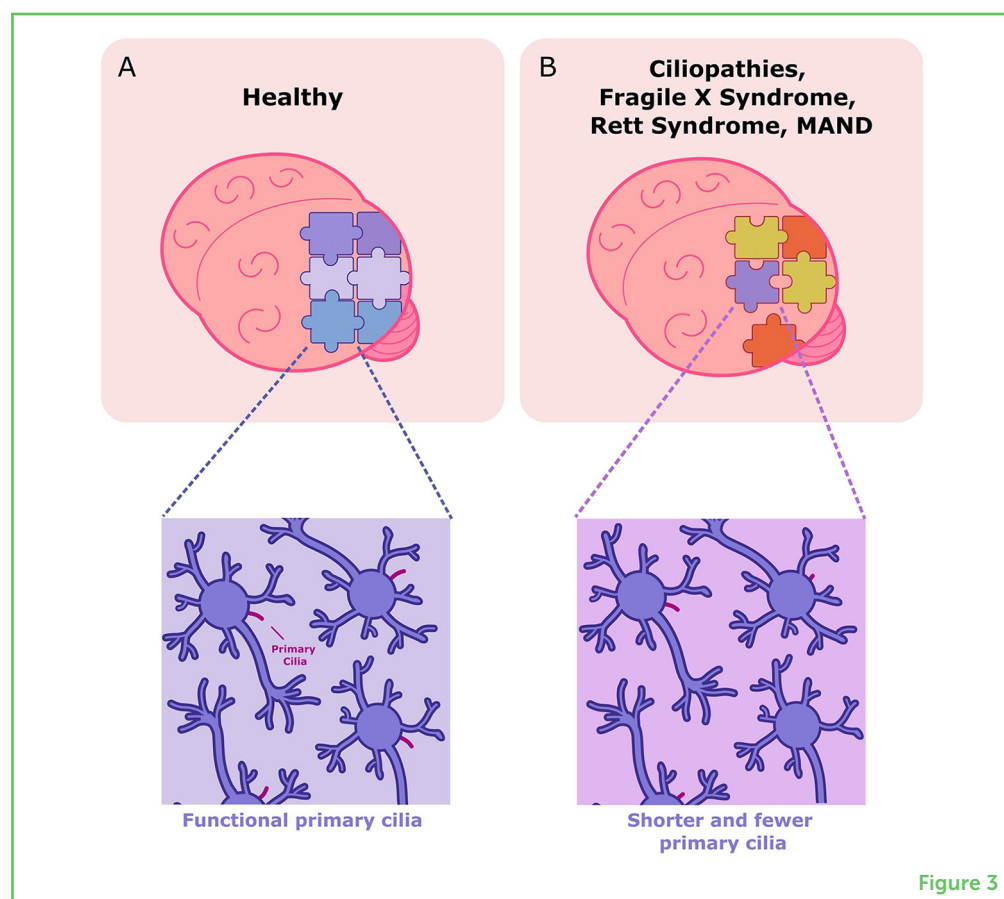
NEURO-DEVELOPMENTAL DISORDERS

Conditions that affect brain growth and function, often starting in childhood. They can impact learning, behavior, or movement, like autism spectrum disorder and intellectual disability.

Rett syndrome and MBD5-associated neurodevelopmental disorder (MAND) [4–6]. These scientists made an intriguing discovery—the primary cilia in these cells appeared to be shorter and fewer in number compared to cells from healthy mice or people without these disorders (Figure 3). Since primary cilia play a crucial role in brain development, these findings suggest that primary cilia could be involved in these neurodevelopmental disorders, as the brain cells might become “lost” without functional antennas.

Figure 3

(A) In a healthy brain, each brain cell has a functional **primary cilium** and the brain cells come together properly, completing the “puzzle”. (B) In diseases like ciliopathies, fragile X syndrome, Rett syndrome, or MAND, neurons have fewer primary cilia or these structures can be shorter or even absent. In these cases, the brain’s puzzle pieces might not assemble correctly.



PRIMARY CILIUM

A tiny antenna-like structure on each cell that helps receive signals and communicate. The plural is primary cilia.

Scientists are working hard to understand more about these special cellular antennas that help healthy brains develop. We know now that they are crucial for neuron division, differentiation, and migration. However, we do not know exactly which chemical signals are involved in this communication. By studying more patients and coming up with creative ways to study this problem, scientists can generate new ideas for research, which could eventually lead to treatments for people with these conditions. Uncovering the secrets of the tiny primary cilia will bring us a step closer to solving the incredible and complex brain puzzle.

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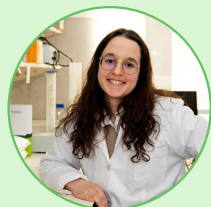
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The reviewers, 8 in total, were students in the honors track who have a passion for all things science, even staying after school to discuss this paper!

SWOPE MIDDLE SCHOOL GIFTED AND TALENTED SCIENCE CLASS, 7TH AND 8TH GRADE, AGES: 12–13

8th graders from Reno Nevada. Studying the brain and cells. Excited to learn!

AUTHORS

MARIANA MARTINS

I am a PhD student in Lisbon, Portugal, where I study tiny lab-grown mini-brains to uncover what goes wrong in rare disorders that affect how the brain develops. I work closely with patient associations to better understand these conditions and how to possibly treat them. Ever since I was a kid, I have been fascinated by how the brain works, and now I get to turn that curiosity into discoveries that could one day make a difference. When I am not in the lab, I love getting lost in a great novel, scrolling on TikTok, and spending time with my family and friends.

LUÍSA AMADO

I am a PhD student at the University of Coimbra, Portugal. In my project, I am trying to understand what happens to the communication between brain cells when alterations associated with autism occur. In the lab, I take care of cultures of human neurons, which are very similar to the neurons that exist in our brains! When I am not busy with experiments or culturing cells, I really enjoy drawing, hiking, and reading.

MARIANA LARANJO

I am a scientist passionate about neuroscience and how our brain works. I am also committed to science communication, and education. During my PhD, I studied how the brain is affected by neurodevelopmental disorders, particularly the contribution of inhibitory neurons to this phenomenon. In my spare time, I love to go to the gym, travel, and walk in nature.

SÍLVIO SANTOS

I am a professor at the University of Coimbra. My teaching and research areas are mostly focused on radio and journalism. I also have a specific interest in what is happening with fake news online. I am really passionate for sound and words, I was a radio producer for several years before becoming a professor and I still love to record my voice. Currently, I am also the university's theater director. Outside of academia I love riding my bike in the forest and gardening.

**CLÁUDIA CAVADAS**

I coordinate the Neuroendocrinology and Aging group at the Center for Neuroscience and Cell Biology, University of Coimbra, where we study how cells and body age. I am also a professor at the Faculty of Pharmacy, teaching Pharmacology and related subjects. As Vice-Rector for Research at the University of Coimbra, I launched innovative ideas across many areas of science. I am passionate about sharing science beyond the lab - especially with young minds! I also love drawing, reading, learning new things, and laughing -these keep my creativity and scientific curiosity alive.

**JOÃO PEÇA**

I love discovering how the brain works! I am a professor at the University of Coimbra in Portugal, where I lead a team of researchers studying how different parts of the brain help us think, move, and feel. I started studying biochemistry in Portugal and then worked at MIT, USA, to explore and better understand autism. Now, my team and I use incredible tools like optogenetics (using lights to control brain cells!) and mini-brains grown in the lab to uncover more about how the brain functions. When not working, I love spending time with my wife and children!

**CATARINA MORAIS SEABRA**

I have always been naturally curious, initially fascinated by how something as tiny as our DNA can hold the secrets to creating a fully developed being. For my PhD in the USA, I learned more about how alterations in DNA can lead to specific diseases, including autism. Later, in Portugal, I developed mini-brain models from patients to investigate this condition. Now, I am committed to promoting education and understanding of neuroscience, as well as guiding scientists in their careers. Outside work, I love following protocols to make cakes, dancing, and hairstyling.

*cseabra@cnc.uc.pt

[†]These authors have contributed equally to this work and share first authorship