The Role of the Microbiota - Gut - Brain Axis in Mental Health

Visualizing the Invisible Influence

Claudia Amort

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The Role of the Microbiota-Gut-Brain Axis in Mental Health

by

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Table of Contents

Preface

The intersection of art and science has always held a special place in my heart. I am drawn to the mysteries of the human body, and I find it deeply fulfilling to try and understand the enigmas of our world. The challenge to unravel these is why I studied biomedicine and planned to pursue a career in research. Throughout my journey, I couldn't help but find countless ways to incorporate art with science. Whether it was through illustrating complex biomedical principles for presentations or infusing my scientific knowledge into my artistic work. I love to find ways to unite these two worlds.

Growing up, I used to spend so much time creating art and learning how to do that. I never thought that this would have a big practical application in my career. The process of creating and the sense of fulfillment it brought me in that moment is what I enjoyed. On YouTube I spent hours watching tutorials, simply because I loved seeing how other people brought their creations to life. And I created art for the sake of creating.

Despite initially not seeing the practical applications of my artistic pursuits, I am now realizing how I can combine them, as Steve Jobs once said "You can't connect the dots looking forward. You can only connect them by looking backward. So, you have to trust that the dots will somehow connect in your future." Now I am connecting these dots at a place where creativity and critical thinking intersect.

Introduction

The human body is home to trillions of microorganisms, collectively known as the microbiome. These tiny inhabitants within us play an important role in our overall health and well-being, influencing everything from our immune system to our mood. They do it by directly communicating with our gut and indirectly with our brain. This connection is called the Microbiota-Gut-Brain Axis.

The microbes in our gut help digest food that is otherwise indigestible by humans and produce some vitamins and other compounds which are essential for our health. Because their survival depends on the food we eat, these microbes found, over time, a way to influence our diet: what we want to eat, when we want to eat, and even how we perceive the taste of our food.

Fig. 1: The Microbiota-Gut-Brain Axis. Digital painting in Midjourney and Procreate.

In the gut itself, they protect us from harmful microbes. But they also look after the rest of our body by helping in the development of a healthy immune system. They are even involved in the defense of harmful toxins and pathogens from the brain by influencing the blood-brain barrier, which separates the central nervous system from the rest of the body and should only allow beneficial molecules to pass (1).

Studies have shown that mice that don't have a gut microbiota, have social deficits (2). The same effect can be found when animals are given antibiotics, which not only kill harmful bacteria but can attack all bacteria in the body, including the microbes in the gut (3). These social deficits can be reversed, when the microbiota is restored, which can be supported with supplements (4) or probiotics (5). The observed effects of reduced social behavior with poor microbiota can be seen in other cognitive functions as well like attention, memory, recognition, and learning (1).

These examples show how the microbiota affect the host, but the opposite is also true. As a host, we can also strongly influence our microbiota. With our diet, we can change the composition and diversity of the microbes. Even factors like stress can have an effect on them and they in return can influence how stress affects us and how we deal with it (1).

Seeing the important role that the gut microbiota in both the gut and the brain plays, it is probably not surprising, that researchers find more and more links between disruptions in the Microbiota-Gut-Brain Axis and many disorders, including digestive, mood, and neurological disorders. Therefore, research in this area is essential for understanding these systems and developing new treatments.

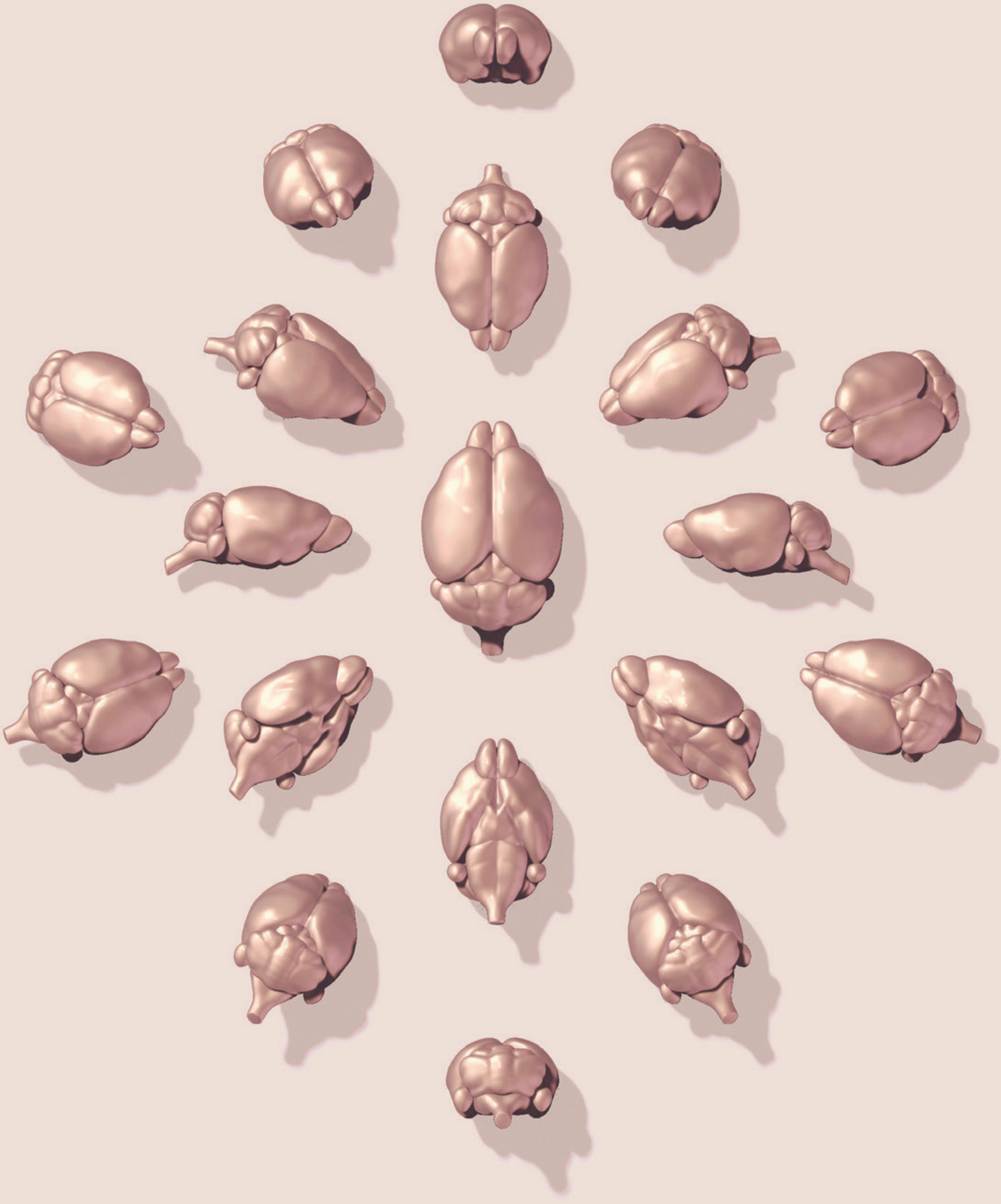


Fig. 2: Mouse brains. 3D sculpting in ZBrush.

project description

With my work, I want to support the communication and spread the knowledge of the processes and concepts of the Microbiota-Gut-Brain Axis. Specifically, my thesis project involves developing meaningful, functional, and effective illustrations for the Microbiome Institute at the University College Cork in Ireland.

To achieve this, I investigated various conventions and techniques used in creating illustrations. I explored ways to enhance existing illustrations to better convey information, particularly when visualizing abstract concepts such as social anxiety and attention deficits. I also identified the most suitable artistic technique to address specific problems, considering the visual style: realistic or graphical, format: static or animated, and visualizing it in 2D or 3D. I even investigated how an AI-based image generator could be useful for me as a scientific illustrator. Lastly, I analyzed how composition, layout, design, and level of detail can guide the viewer in understanding the illustrations effectively.

The Microbiota-Gut-Brain Axis has significant implications for human health and well-being and I hope to contribute with my work to advance the communication and understanding of this field among the research community.

Components
of the Microbiota-Gut-Brain Axis

Brain
Our brain is probably the most complex organ in our body. It enables us to act and react, it is the reason why we are able to think and feel. Most of the information of our body comes together and here we process and perceive the world around us. At its core, the brain consists of three parts: the cerebrum, the cerebellum, and the brain stem. The cerebrum is the largest part of the brain and is responsible for cognitive processes such as perception, thought, memory and voluntary movement. The cerebellum, located under the cerebrum, is responsible for balance and coordination. The brainstem connects the brain to the spinal cord and controls vital functions such as breathing, heart rate, and blood pressure.

Gut
The second component involved in the Microbiota-Gut-Brain Axis is the gut or gastrointestinal tract. It is a highly specialized organ system responsible for the mechanical and chemical breakdown of food, absorption of nutrients, and elimination of waste products. It consists of various segments such as the mouth, esophagus, stomach, small intestine, and large intestine. The intestines are also the home of the third component: the microbiota.

Microbiota
The microbiota are a diverse community of microorganisms that live within our gut. They are essential in the gut's maintenance and overall health of the body. They consist of bacteria, viruses and fungi. They help to break down undigested compounds, produce important vitamins such as vitamin K and B12, and support the immune system.

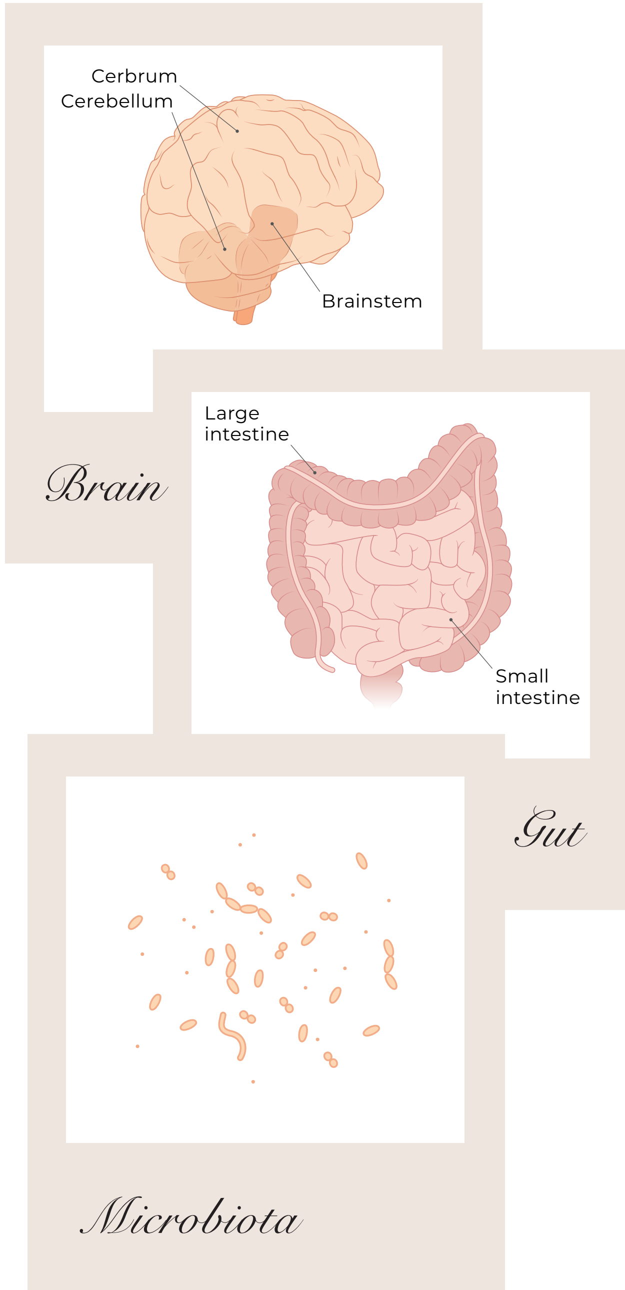


Fig. 3: Components of the Microbiota-Gut-Brain Axis. Adobe Illustrator.

How do these three components interact with each other?

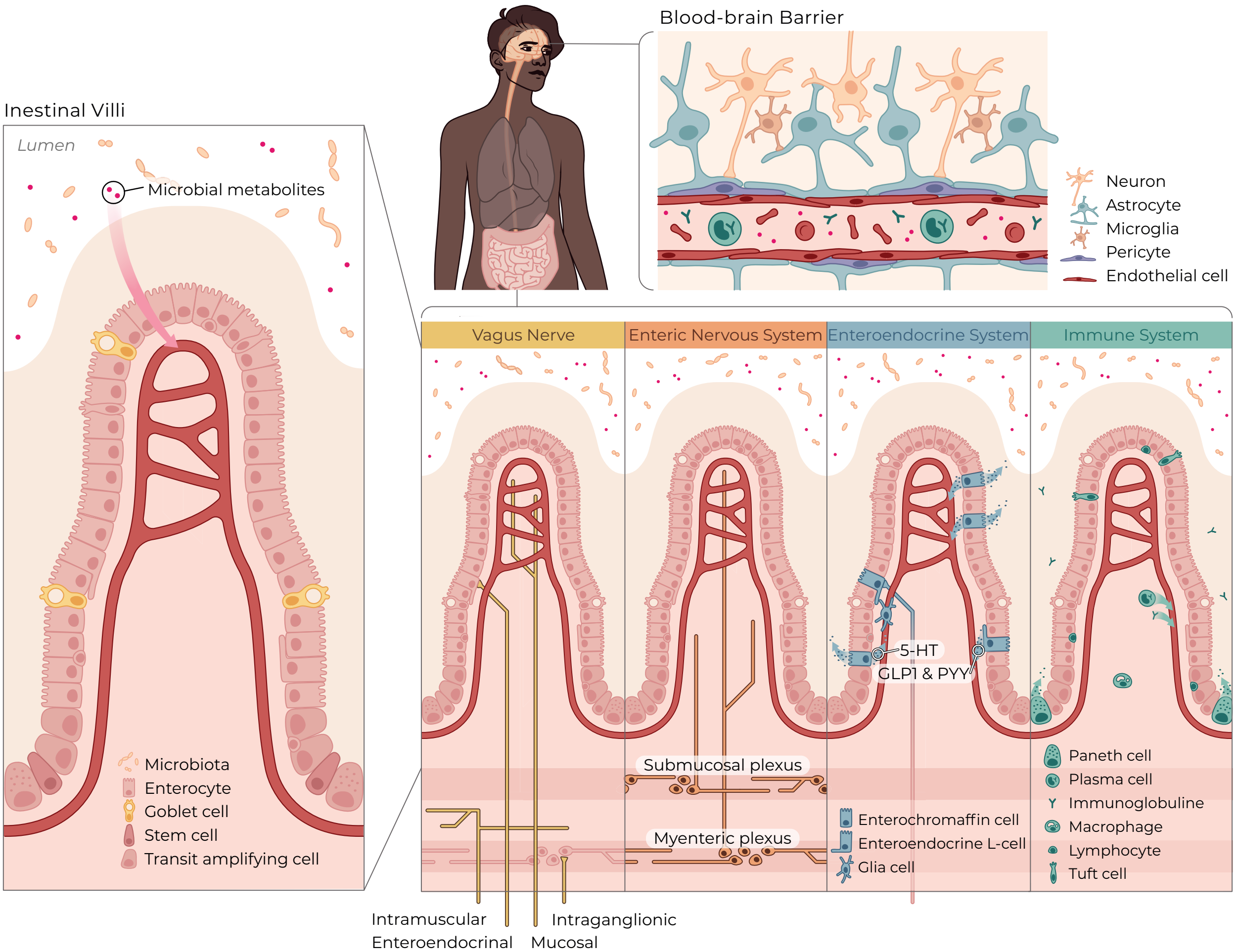


Fig. 4: Pathways of the Microbiota-Gut-Brain Axis. Adobe Illustrator.

Pathways

of the Microbiota-Gut-Brain Axis

There are several different pathways along which the microbiota, the gut, and the brain communicate. This always goes in both directions.

Blood-brain Barrier

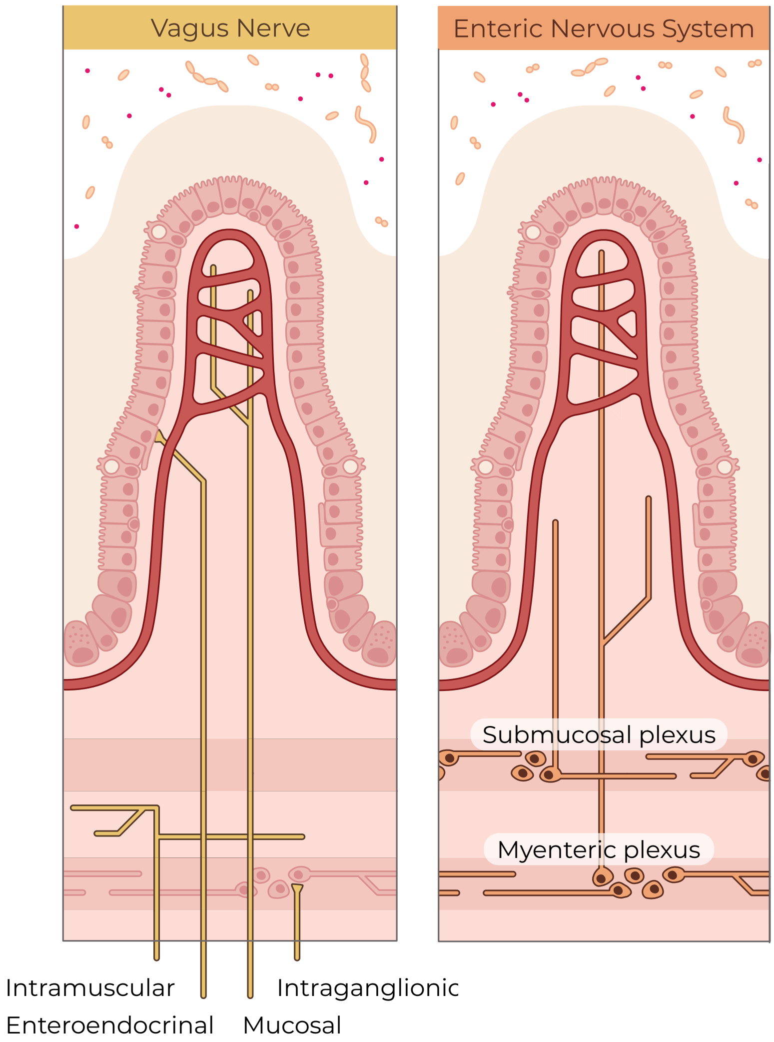
The blood-brain barrier is a specialized barrier that separates the brain and spinal cord from the circulating blood. It is made up of endothelial cells that line the blood vessels, which prevents most substances in the bloodstream from crossing into the central nervous system. Harmful toxins and pathogens stay out while some molecules and ions that are beneficial to the central nervous system are allowed to pass. Hormones, metabolites, and immune cells coming from the gut are able to cross this barrier and interact with the brain.

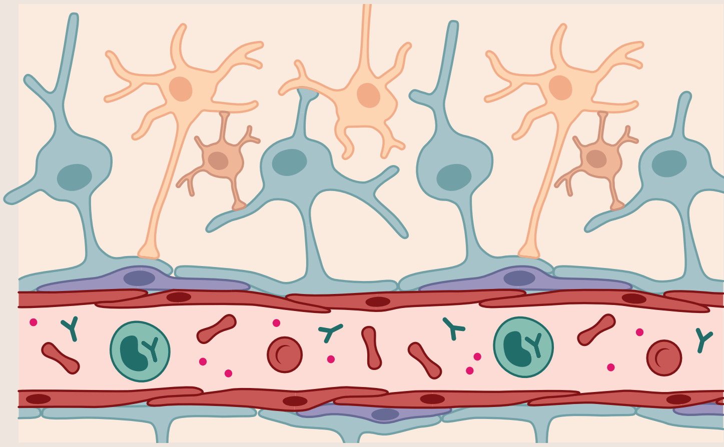
Vagus Nerve

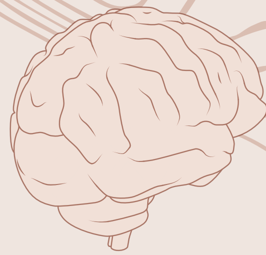
The vagus nerve is the primary neural pathway connecting the gut to the brain and vice versa. It is responsible for transmitting information mainly from the gut to the brain. It transfers different types of information such as stretch, tension, and molecular signals to the brain and it also modulates the immune system. More research is needed to understand the exact mechanisms of how the gut microbes use the vagus nerve to communicate with the brain, which allow for specific emotional and behavioral responses.

Enteric Nervous System

The enteric nervous system is a network of neurons located at the interface between the gut microbiota and the host. It controls gut functions such as motility and movement of its content. This communication enables factors derived from the gut lumen, including those coming from the microbiota, to influence both gut function and the central nervous system.







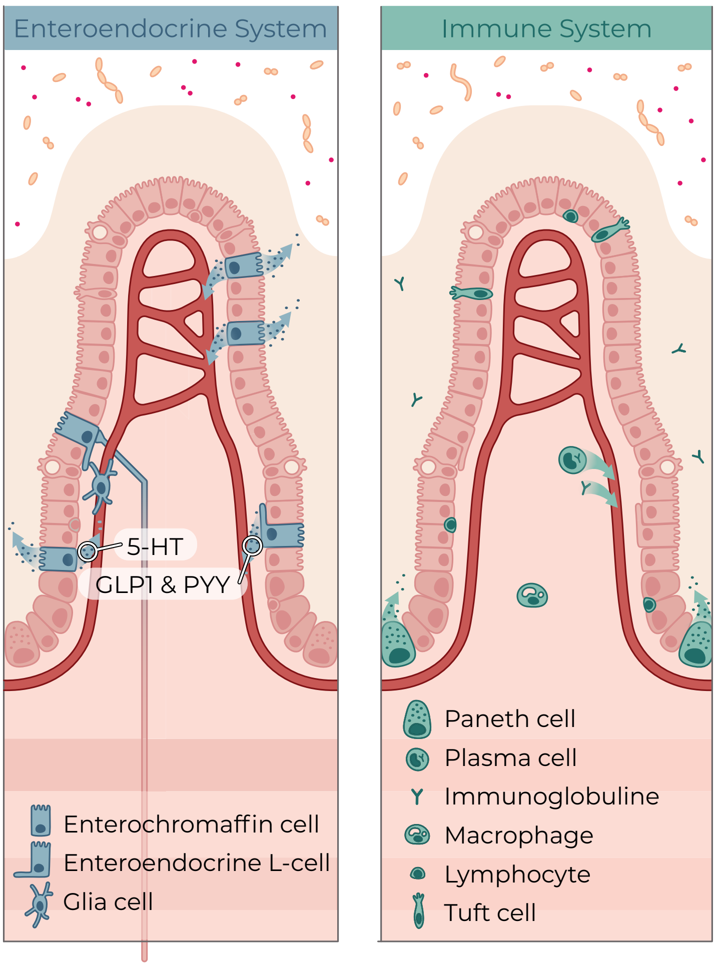


Fig. 5: Pathways of the Microbiota-Gut-Brain Axis. Adobe Illustrator.

Enteroendocrine System

This is a network of cells in the gut that release hormones. They coordinate changes in the gut's nutrient content with metabolic and behavioral responses. They regulate insulin secretion and influence food intake, ultimately affecting our body weight and metabolism. In obese individuals, for example, some of these hormones are decreased. Also, 95% of the body's serotonin is found in the gut. This intestinal serotonin although is unlikely to have a direct effect on the brain, because it cannot cross the blood-brain barrier.

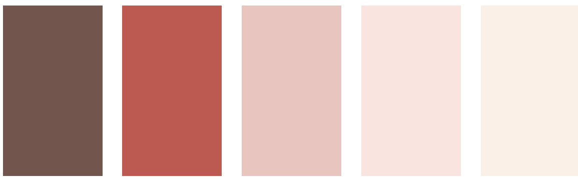
Immune System

The gut has the highest density of immune cells in the body and is constantly interacting with the trillions of microbes that reside in the gut. The interaction with these microbes is important for the development of a healthy immune system through the recognition of self and non-self-antigens. The gut microbiome also influences the relative populations, migration, and function of various subsets of immune cells.

I created this illustration as an introductory figure to explain the Microbiota-Gut-Brain Axis in my external advisor's publications. I obtained the biomedical background information for this illustration from a review on the Microbiota-Gut-Brain Axis (1). This helped me to understand the pathways and decide what to depict. I approached it from the perspective of a scientist who is trying to understand the pathways for the first time. At that moment I was this someone myself. So, when coming up with the first sketch, I consistently asked myself: what do I need to understand the concept? I believe that this situation benefited me greatly in creating an illustration that would be easily understood by viewers in a similar position.

When I had decided what I wanted to show in my illustration, the next step was to get references to have the information accurately visualized. For the anatomy in the orientation figure, I used the SOMSO model and anatomy books as references. For the microscopic view of the gut, I had histological sections that I could go back to.

I created two initial sketches. The first one has one insert with all four pathways on it: the autonomic nervous system, the enteric nervous system, the enteroendocrine, and the immune system. In the other sketch, I separated these pathways into four individual inserts.



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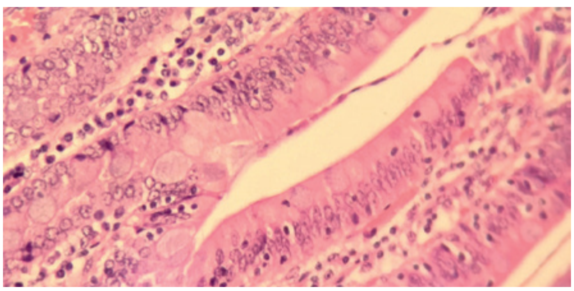


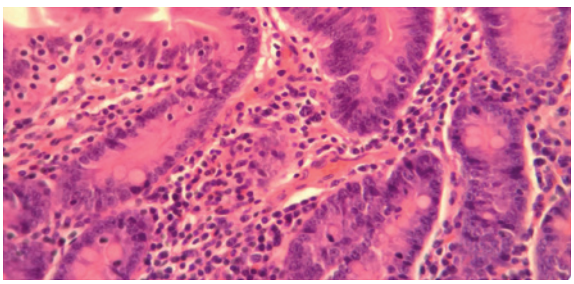
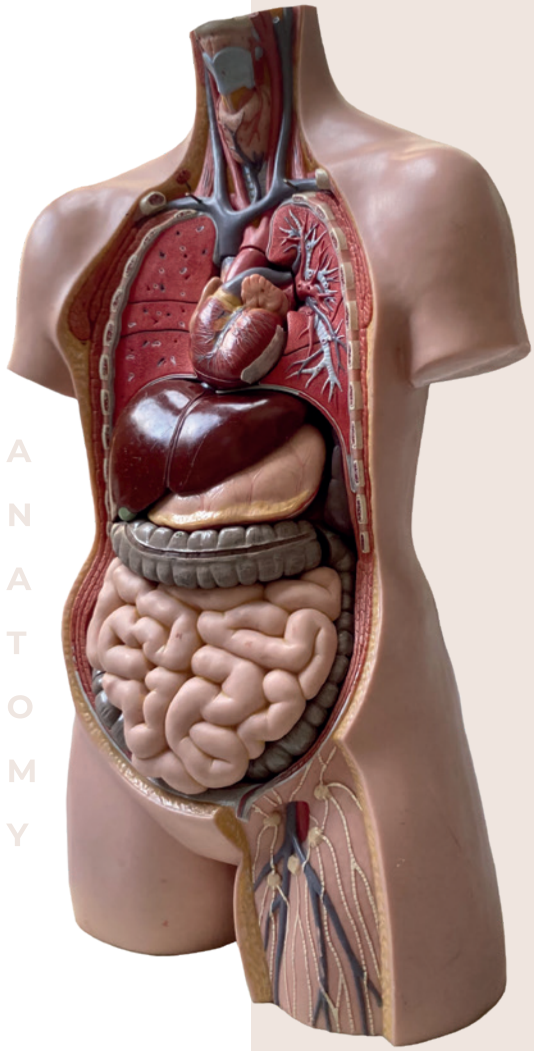
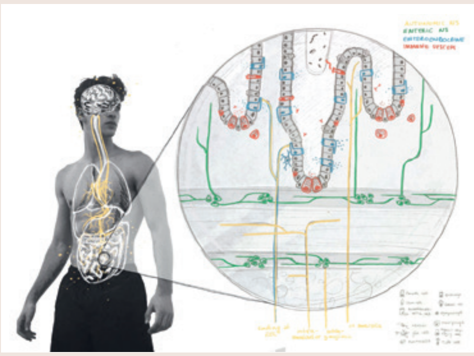


Fig. 6: Histological section of the duodenum (top) and jejunum (bottom). SOMSO model (right).

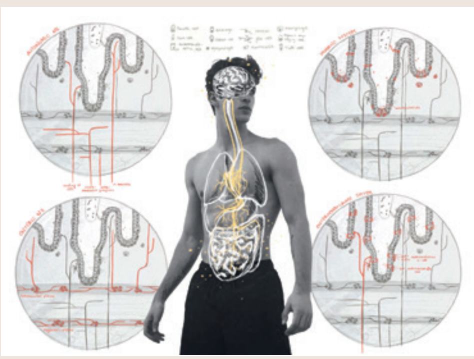
A N A T O M Y



The advantage of having one insert is its increased size. Larger illustrations allow for more fine details to be included, which is relevant when conveying precise information. When all four pathways are combined in one insert, it is also more crowded. To overcome that, I used color coding to distinguish the four pathways, which means, the illustration wouldn't work in a black and white version.



One insert

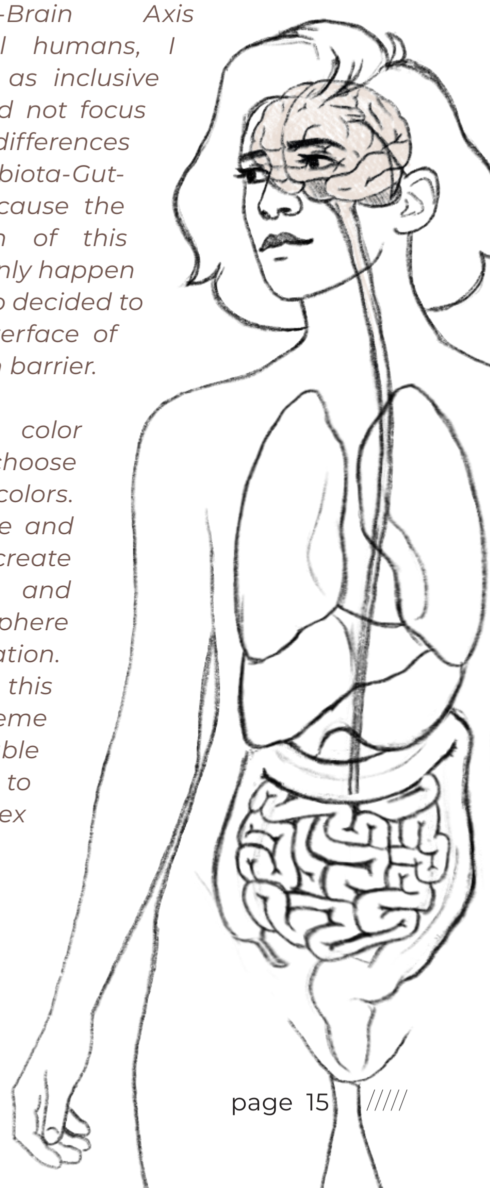


Four inserts

This is relevant because publications are sometimes printed in black and white and should therefore still contain all the information in such a version. To make it work, I could have used different patterns, dashed lines, and different line thicknesses, but I find that these can make the illustration even busier. When having four inserts, each insert contains less information and is therefore clearer. This version will also work in color and in black and white.

After reviewing my sketches, I decided to continue with four inserts. I changed the shape of the inserts from circles to squares, which are more space efficient and allowed for the main illustration to be larger. I also decided to show a gender-neutral figure instead of a man. Since the Microbiota-Gut-Brain Axis applies to all humans, I wanted to be as inclusive as possible and not focus on gender differences of the Microbiota-Gut-Brain Axis. Because the communication of this Axis does not only happen in the gut, I also decided to include the interface of the blood-brain barrier.

As for the color scheme, I choose soft pastel colors. They are gentle and delicate and create a calming and clean atmosphere in the illustration. I believe that this color scheme creates a suitable environment to take in complex scientific information.



The Microbiota-Gut-Brain Axis in Diseases

We all have a unique microbiome composition in our gut, which helps maintain the balance of our body and keeps us happy and healthy. For people with neurological and psychiatric disorders, this can be a bit different. When looking at the gut microbiome in disease, it is to find a signature and to correct a dysbiotic gut composition to help alleviate symptoms and in the best case scenario, result in individuals that are no longer clinical.

Depression

Studies have shown that people with depression have an altered gut microbiome compared to healthy individuals (6). This imbalance of microbes can be restored with probiotics. They can improve symptoms of depression (7) and could be potential therapeutic targets. Not only probiotics, but our diet overall influences the quality of our microbiome. Therefore, also a poor diet is a risk factor for depression (8). In one preclinical study with rats, the microbiota of people with depression was transplanted into rats. This was conducted to understand to what extent the microbiome influences the symptoms of depression. In fact, these rats started to show depressive and anxious behaviors after the transplantation (9).

Autism

Studies have shown that people with autism have lower levels of beneficial bacteria and higher levels of harmful bacteria (10). A small clinical intervention demonstrated that restoring the balance was effectively improving the gastrointestinal and behavioral symptoms of children with autism. The gut was repopulated with a balanced, diverse community of microorganisms by transplanting the microbiota of a healthy donor into the patients (11).

Obesity

In another study, the microbiota was transferred from an obese donor to a lean recipient, which then resulted in an increase in body fat and appetite in the recipient. This could mean that also the reverse is true, meaning that the transfer of the microbiota of a healthy individual could help decrease adiposity in patients (12). That a Western-style diet has a strong influence on obesity is

Fig. 7: Cognitive symptoms of schizophrenia. Digital painting in Procreate.

Inability to recognize social cues

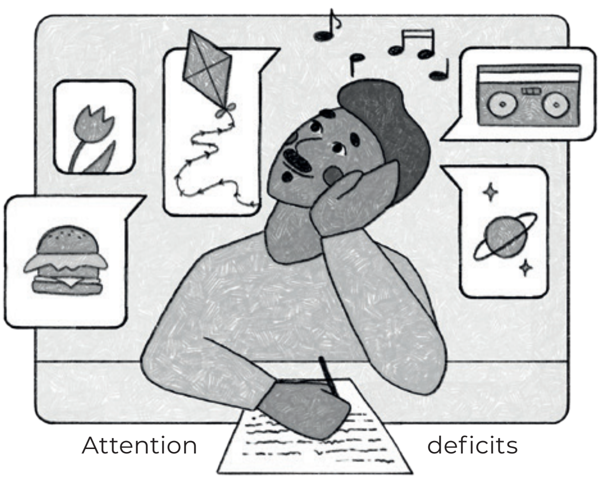
Withdrawal from social connection

undoubted and since the microbiota is highly influenced by diet, the microbiota could be a key factor in obesity (13). But there are more clinical trials necessary to prove this connection.

Eating Disorders

The survival of every microbial population in the gut is dependent on the nutrients they get from our food. Furthermore, they can influence our cravings and how food tastes to us. Since people with eating disorders have an altered gut microbiome, it is not surprising, that also their taste is different. People with obesity often have lower responsiveness to sweet and fatty. Therefore, they shift towards liking foods with more sugar and fat. Individuals with anorexia nervosa on the other hand have an impaired taste perception, meaning that they can lose part of their ability to taste. This improves when the patients start to gain weight again (14).

Inability to plan and organise tasks

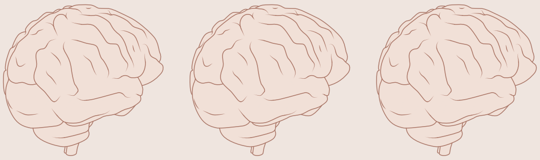


Attention deficits

Schizophrenia

Schizophrenia is one of the most common and difficult psychiatric conditions to treat. Patients describe hallucinations, apathy, and cognitive symptoms like problems remembering their past or having difficulties with social interactions. Currently, there is evidence that disruptions in the communication between gut microbes, vagus, and brain often accompany the core symptoms of schizophrenia (15). A strict ketogenesis diet for example, has been shown to improve the condition of some patients with schizophrenia (16).

Stimulation of the vagus nerve has improved memory in patients with Alzheimer's disease (17), which could be relevant for schizophrenia patients who also experience cognitive impairments. The vagus nerve pathway is a promising target for future treatments for schizophrenia.



Cognitive Symptoms of Schizophrenia

I made these scenes for my external advisor to help explain the symptoms people with schizophrenia are experiencing. I was attentive to include people from various ethnicities, so all patients feel addressed. In the first image, I wanted to show two women because women give more nonverbal cues in social interactions, or at least we associate women more with communicating non-verbally. In the fourth image, I specifically choose to depict two men hugging to go against the societal pressure that men can't show affection among men. In the fifth scene, I chose a woman wearing a hijab to also be inclusive of people practicing different religions. Artistically I chose very bold eyebrows to enhance and underline the emotions the characters are feeling.

After discussing with my external advisor, I decided to elaborate four scenes. These four are most representative of people with schizophrenia. In the scene where the woman pulls away from social connection, I also changed her hair to be messy. People with schizophrenia sometimes stop taking care of themselves and I wanted to include that too.

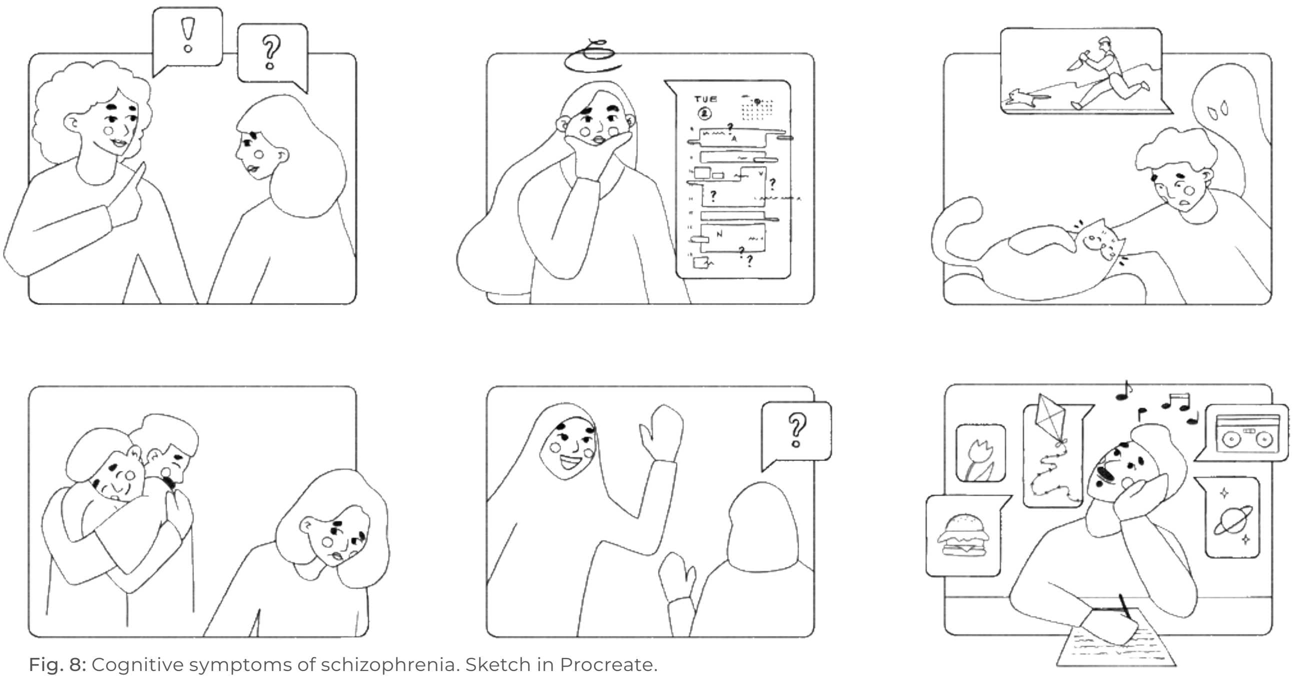


Fig. 8: Cognitive symptoms of schizophrenia. Sketch in Procreate.

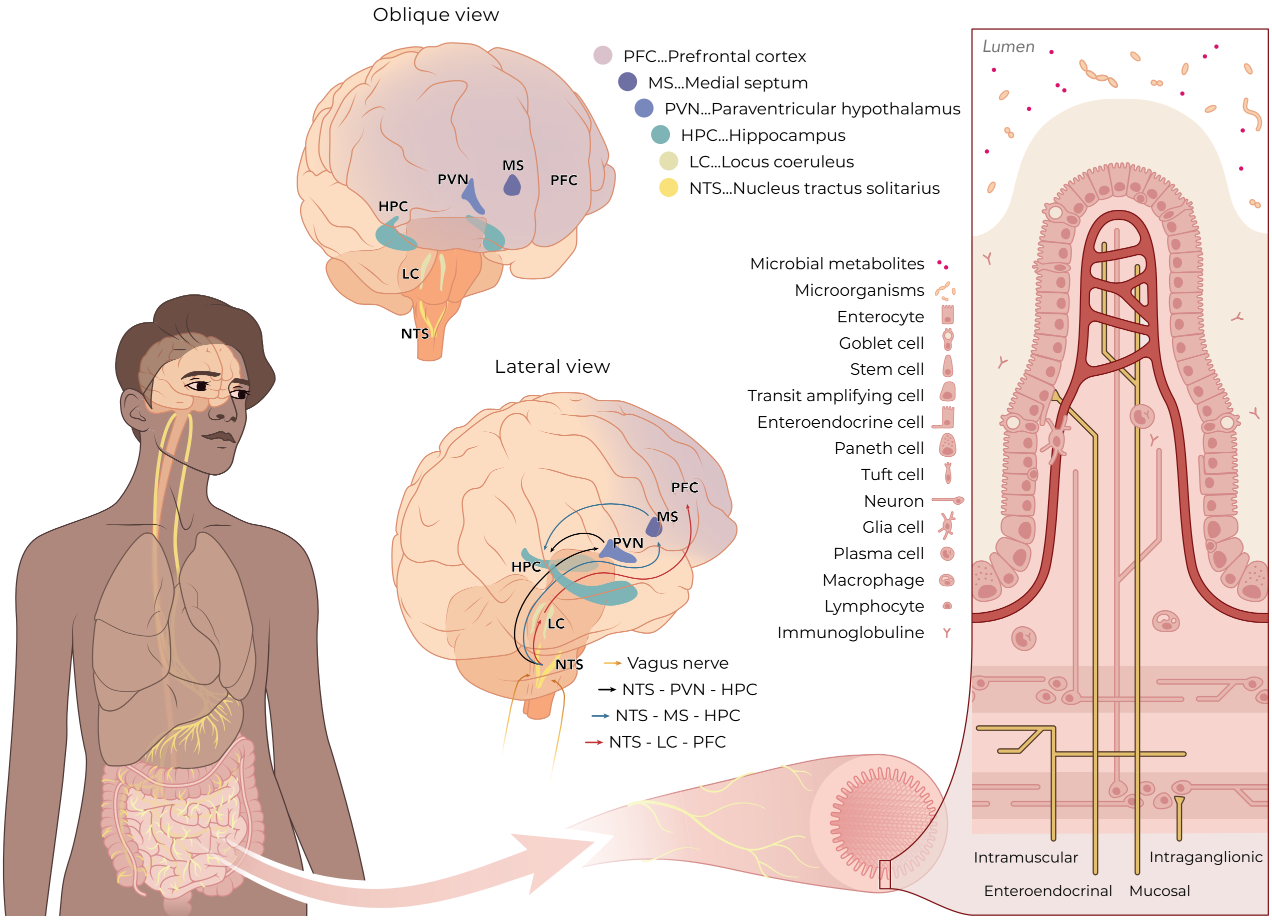


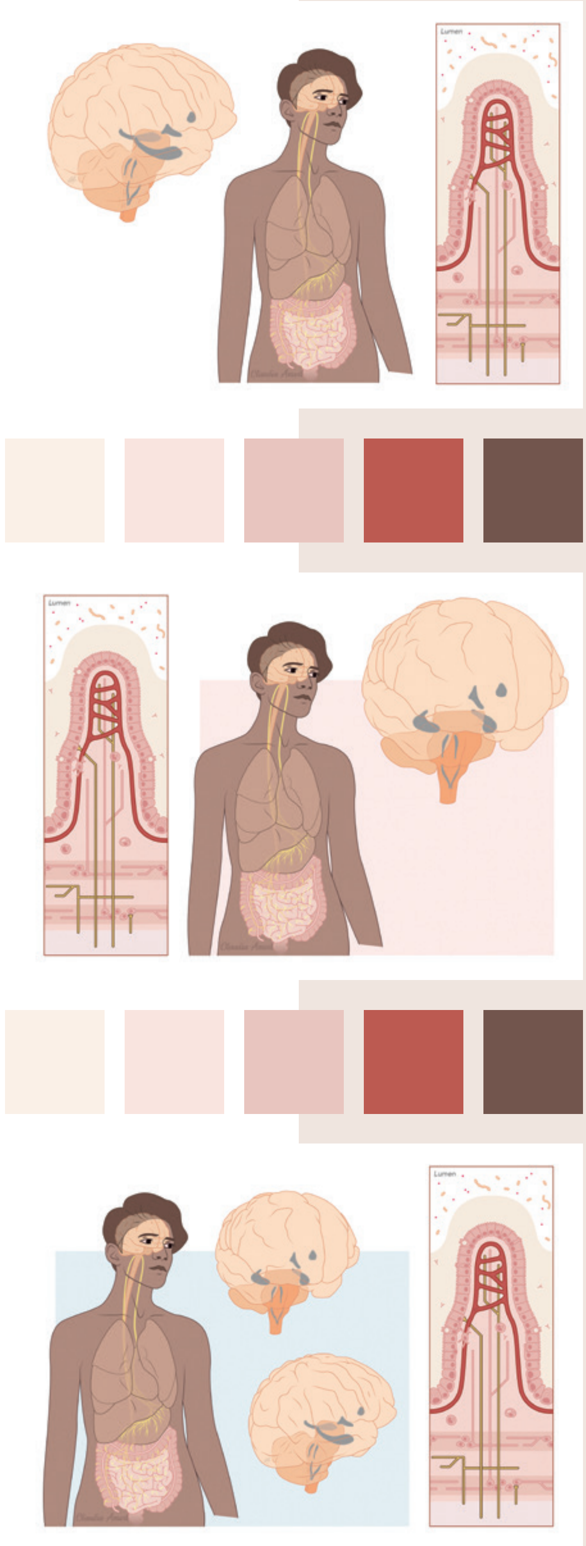
Fig. 9: The vagus nerve in the Microbiota-Gut-Brain Axis. Adobe Illustrator.

The pathway of the vagus nerve is the main pathway along which the brain and the gut communicate. Once the signals from the vagus nerve enter the brain at the brainstem, very little is understood about how this information is processed. But there are thought to be three different areas of the brain, which receive and process signals coming from the vagus nerve.

Finding New Treatments for Schizophrenia

Within the next couple of years, my external advisor will investigate the role of the vagus nerve in schizophrenia. She will also examine whether it could be a potential target for new treatments for cognitive symptoms like the ones I described in my previous chapter. I made this illustration as an introductory figure to explain where the vagus nerve gets its inputs from the gut and to which areas they get transmitted in the brain.

In the color palette and style, I chose to stay consistent with the infographic I made on the pathways of the Microbiota-Gut-Brain Axis. This way, I could reuse the insert of the vagus nerve in the gut and use my previous orientation figure as a base for this one. This was not the only reason, I also wanted all illustrations that I make for the research group in Cork to be consistent. I intend to create a recognizable corporate identity for that research group. When audiences read the paper and see the graphics, they immediately make a connection to that research group. This can be important for them to help people remember their institution and to support their impact in the scientific community. Branding like this can create loyalty, trust, and credibility for the research group within their readers, but also with institutions that give grants for new research. Branding is crucial for any business and can therefore also be beneficial for a research institution to help ensure their long-term success.



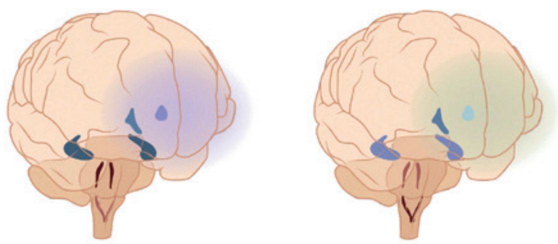
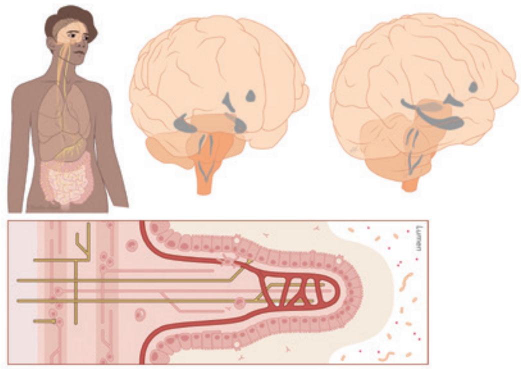
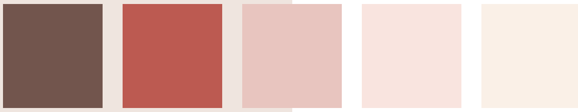
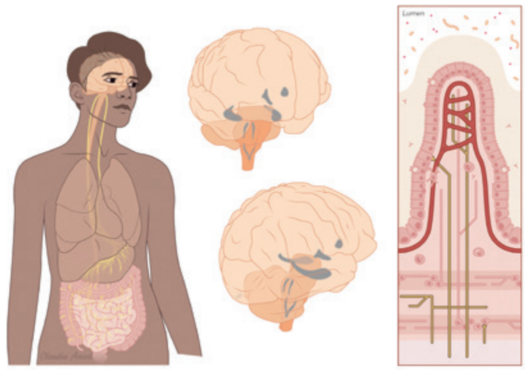
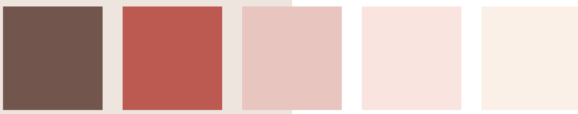


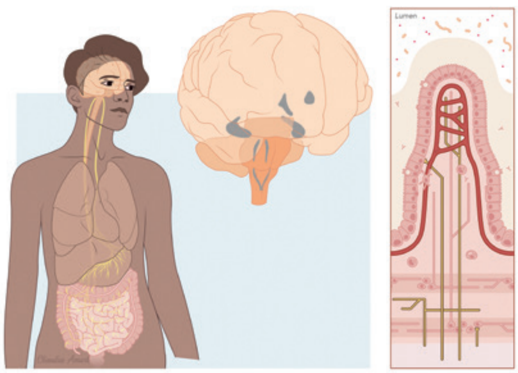
Fig. 10: Different versions for the layout and color. Adobe Illustrator.







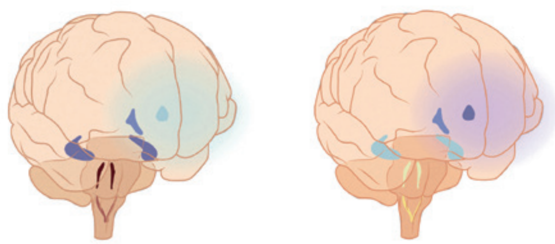




When creating the layout, I went through many different versions to finally get to this one. The challenge for me was to create something aesthetically pleasing and to give the elements in focus the attention they should have. I had versions with only one orientation of the brain but decided to show two because this gives the viewer a better 3D understanding of the location of the structures in the brain.

When distributing the elements, it would have been practical to place the section of the gut horizontally. This would have allowed for both brains and the gut section to be the largest and given them the most attention. However, I chose to position it vertically to maintain consistency with the traditional depiction of a cut in the gut, with the villi facing upwards and the lumen on top. This orientation is easily recognizable and understandable without requiring additional thought from the viewer.

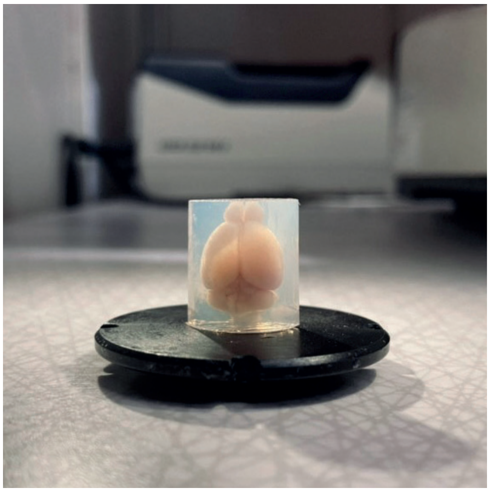
I also experimented with some background colors to have a cool element contrasting the mostly orange and pink color scheme. I found the background made the graphic busier, so I decided to go without it and therefore chose more cool colors for the structures within the brain. Since the vagus nerve sends signals to the Nucleus Tractus Solitarius (NTS), I ended up coloring the NTS yellow in order to visually strongly connect the two structures by using a color commonly associated with the nervous system.



Research in Mice

As discussed in the previous chapter, the pathways in the brain that respond to signals induced by the gut and their microbiota entering via the vagus nerve remain poorly understood. To shed light on this, my external advisor's research group will stimulate specific brain regions to investigate their effects. Because the required methods to investigate this are invasive, they cannot be performed in humans and are therefore performed in mice.

While animal models have been used in research for a long time, there is an ongoing debate about the ethical implications, as well as the extent to which animal models accurately represent human physiology and disease. A lot of research is going into the development of alternative methods, such as in vitro studies and computer simulations, that may be able to replace some animal models in the future. For now, animal studies remain necessary, especially in the brain to understand biological processes and study potential treatments.



Mouse brain

The fundamental structures in the brain of mice and humans are quite similar, except for the prefrontal cortex (PFC) and the topography. In mice there is no PFC, instead, they have an infralimbic and prelimbic cortex. These areas contain neurons that are involved in decision-making and cognitive tasks, comparable to the PFC of humans. Therefore, these areas are accepted within the cognitive biology field to be similar enough for mice to be used as reliable research models for studies involving the PFC.

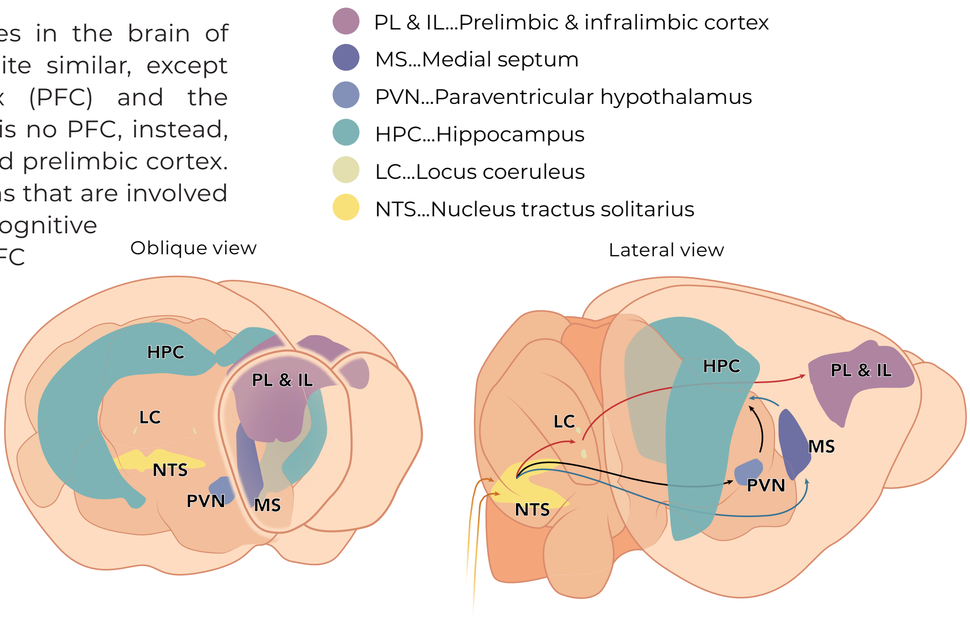
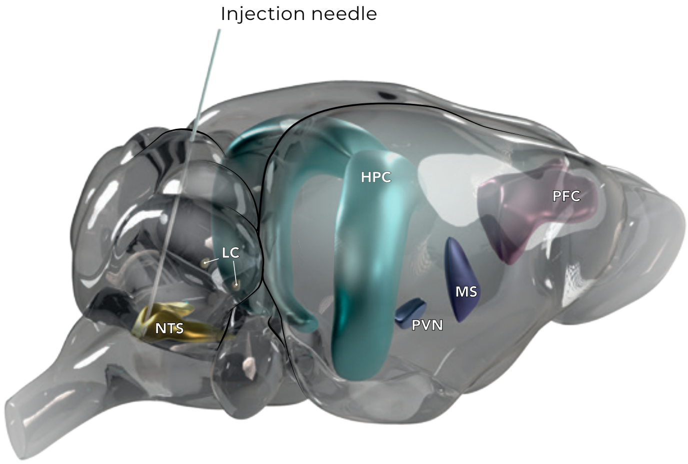


Fig. 11: Areas and pathways in the Microbiota-Gut-Brain Axis in the mouse brain. Adobe Illustrator.

The groups of neurons in the brain that the research group in Cork wants to stimulate are located in the NTS. This is the first entry point in the brain of the afferent signals along the vagus nerve from the gut. The neurons there send signals along three pathways to the hippocampus (HPC) and PFC. Therefore, when the neurons in the NTS are stimulated, it will likely affect the neurons in the HPC and PFC. The question is which effect does it have?

The following will be done to answer that question. First, to stimulate the areas of interest in the brain, these neurons need to receive a specific protein. This protein makes the cells reactive to light, meaning that when shining light on the neurons, they can be switched on or off. This protein is delivered using a virus as a transporter to carry the gene encoding the protein which gets incorporated into the genome of the cell where the cell natively expresses the viral gene product.



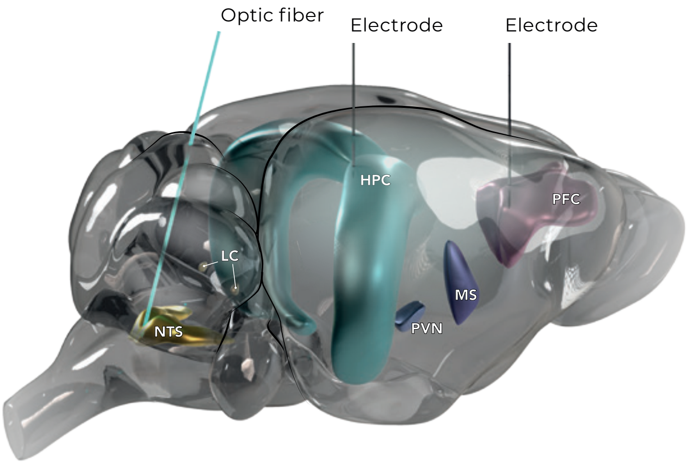


Fig. 12: Viral vector delivery into the NTS (top). Stimulation with optic fibers in the NTS and recording in the HPC and PFC with electrodes (bottom). 3D sculpting in ZBrush.

After the neurons have become reactive to light, they can be stimulated with light carried along glass optic fibers. These fibers emit light at their tip and are placed within the brain. As I described before, the stimulation of the neurons in the NTS will influence the neurons in the HPC and PFC. This electrophysiological effect will be recorded using electrodes placed in the HPC and PFC.

Fig. 13: Rat brains in formalin.

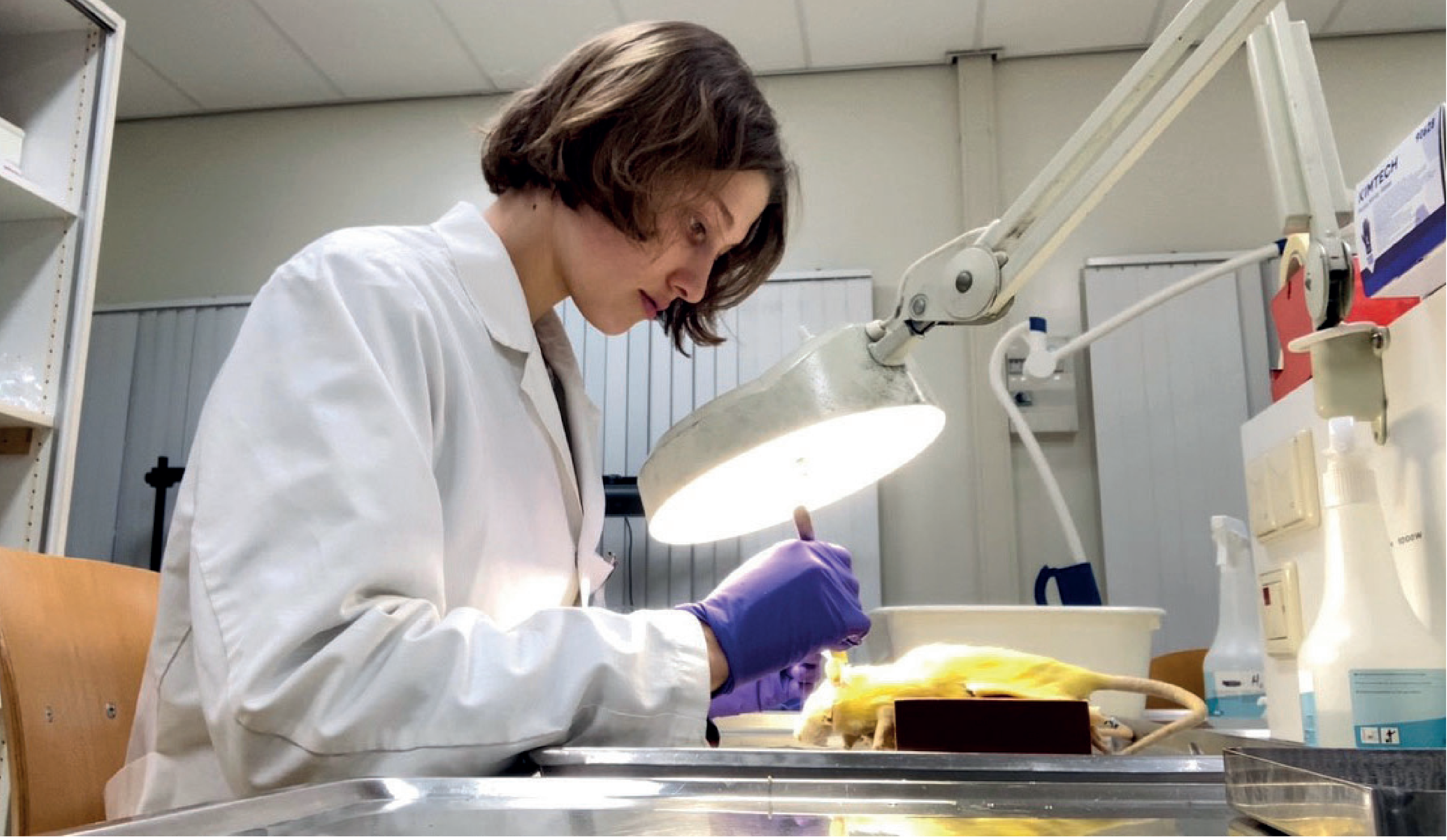


Fig. 14: Dissection of the rat brain.

To explain the methods of this study, I decided to make a 3D Model of the mouse brain. For this, I mainly used an online 3D atlas as a reference for the shape and position of the brain and each area of interest within the brain. Additionally, I used a mouse brain atlas of coronal and sagittal sections to verify my model and I dissected a rat to have a first-hand reference for the shape of the brain.

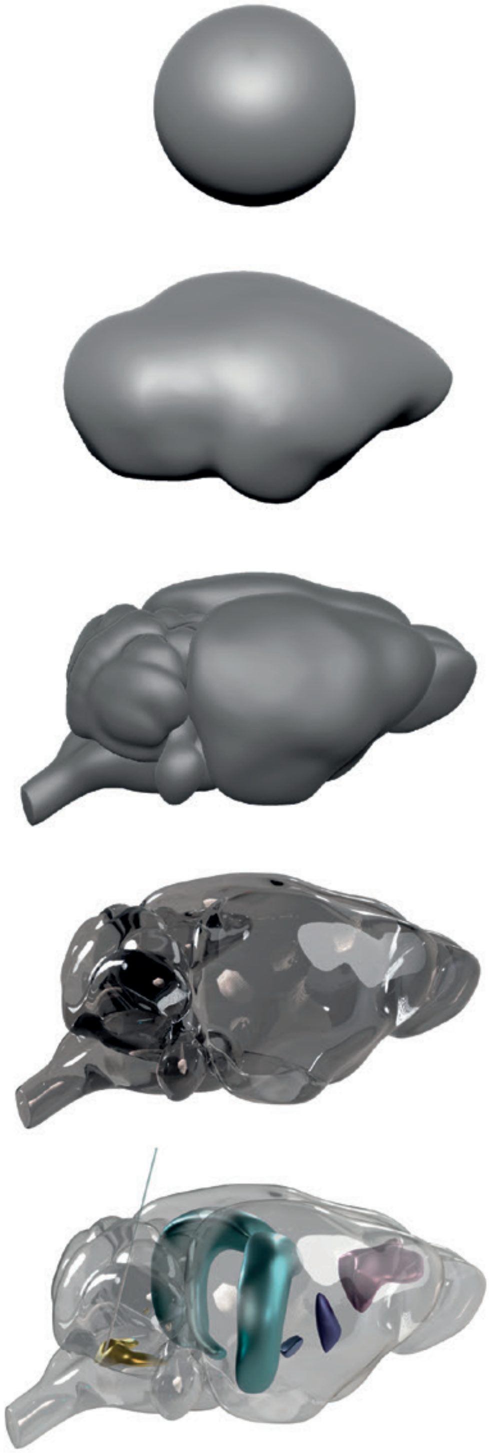


Fig. 15: Process of sculpting the mouse brain in ZBrush.

When comparing the time required to create a 3D brain model versus a graphical illustration, the difference is significant: 2 days versus 2 hours. However, in general, the actual time investment may vary depending on the technique and level of detail. For example, a highly detailed pencil drawing could be just as time-consuming as a 3D model. However, the 3D model offers the added benefit of interactivity and highly accurate lighting and shading. Although shading may not always be necessary, as shown in the illustration I made of the vagus nerve, flat fills can be better to show different structures of the brain. If time was the only variable I wanted to optimize for, I could have used the illustrations of the mouse brain I already made and just place the glass pipette, optical fiber, and electrodes on top. However, in the process of this thesis, I also wanted to explore different techniques and determine when which technique would be most beneficial for which purpose. Compared to a traditional illustration, the 3D model provides an improved understanding of the placement and shape of individual brain areas and the components involved in the study. Ultimately, in this case, the time investment required to create a 3D brain model is well worth the benefits it provides. I also believe the 3D model is very eye-catching and I will likely reuse it in the future, for other visualizations of the mouse brain.

Three Chamber Test

The stimulation of the NTS causes physiological changes in the brain, which then may lead to behavioral changes in the animal. To see the altered behavior, different tests can be performed. One of them is the three chamber test.

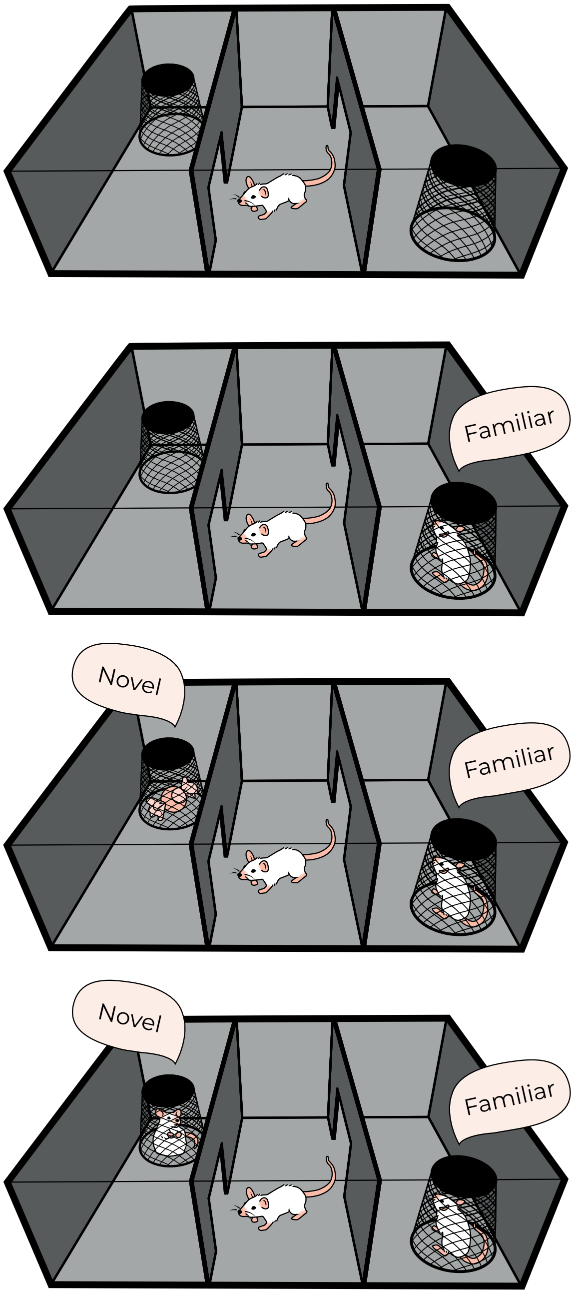


Fig. 16: Three chamber test. Adobe Illustrator.

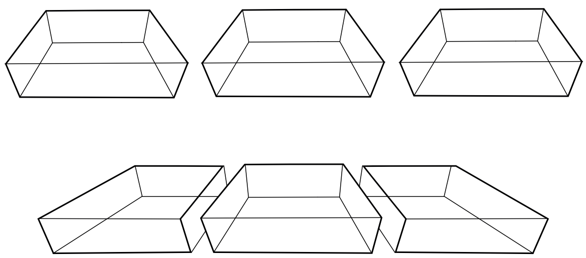
This test can be used to assess sociability and interest in novelty in mice. The setup is as follows: a mouse is placed in a box that has three chambers with openings between the chambers and upside-down pencil cups in the left and right chambers. In the first of four rounds, both pencil cups are empty, and the mouse is placed in the middle chamber and left to explore the arena. In the second round, a familiar mouse is placed under one pencil cup. The mouse that is studied is again placed in the middle chamber. In the next round, an object the mouse is not familiar with, is placed under the other pencil cup, the rest of the setup is as before. In the fourth and last round, a never-before-met mouse is placed under the pencil cup where the novel object was before.

Normally, mice like to investigate new objects and spend more time with other mice, they don't know yet. Therefore, the time spent sniffing each pencil cup, the entries, and the time spent in each chamber are measured. The quantification of possible deficits in social behavior in mice will give insights into the pathways involved in the symptoms people with schizophrenia experience in social situations.

To create the scene, I first made a model of the arena in Sketchup with cones representing the upside-down pencil cups. I wanted to use this as a reference and test which viewpoint would work best to visualize the scenes.

When the view is not frontal the perspective distortion might lead to questions of whether all chambers have the same size. To avoid these, I went with the frontal centered view. The symmetric view makes it also very easy to spot the differences among the three chambers. I used this view as a reference for all four scenarios.

When the individual scenes are placed next to each other horizontally the perspective is interfering. Even though it is coherent within one scene, it is not when looking at all of them together.



During my thesis, I also once went to Cork to meet the research team I have been working with. There, I was able to see the animal facilities and the behavioral tests. On the left it's me all dressed up to go to see the animals.

To solve this, I then decided to depict the scenes underneath each other. This makes the graphic look calmer, even though they still don't follow one perspective. But distortions along the y-axis seem to be more acceptable to our brain than distortions along the x-axis.

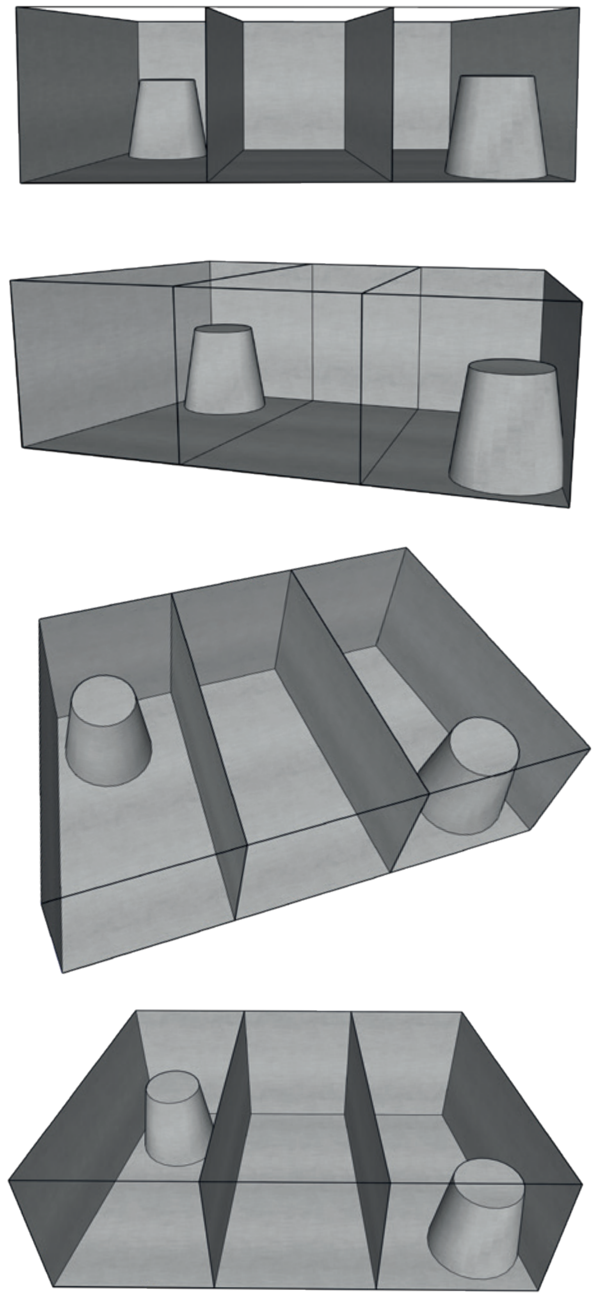
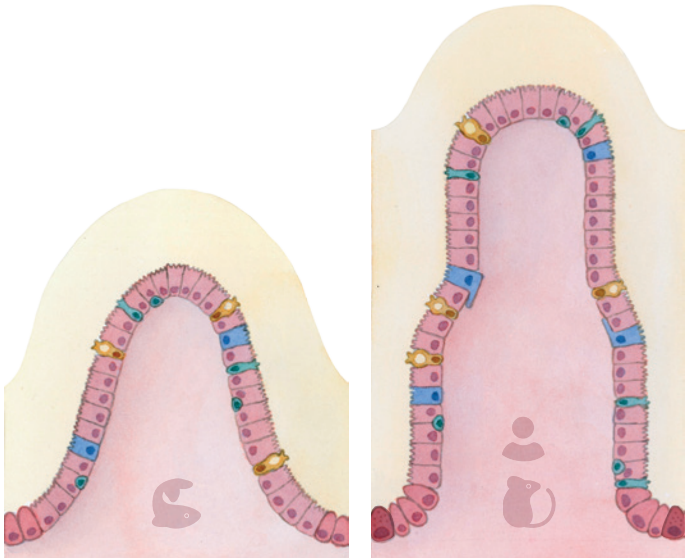


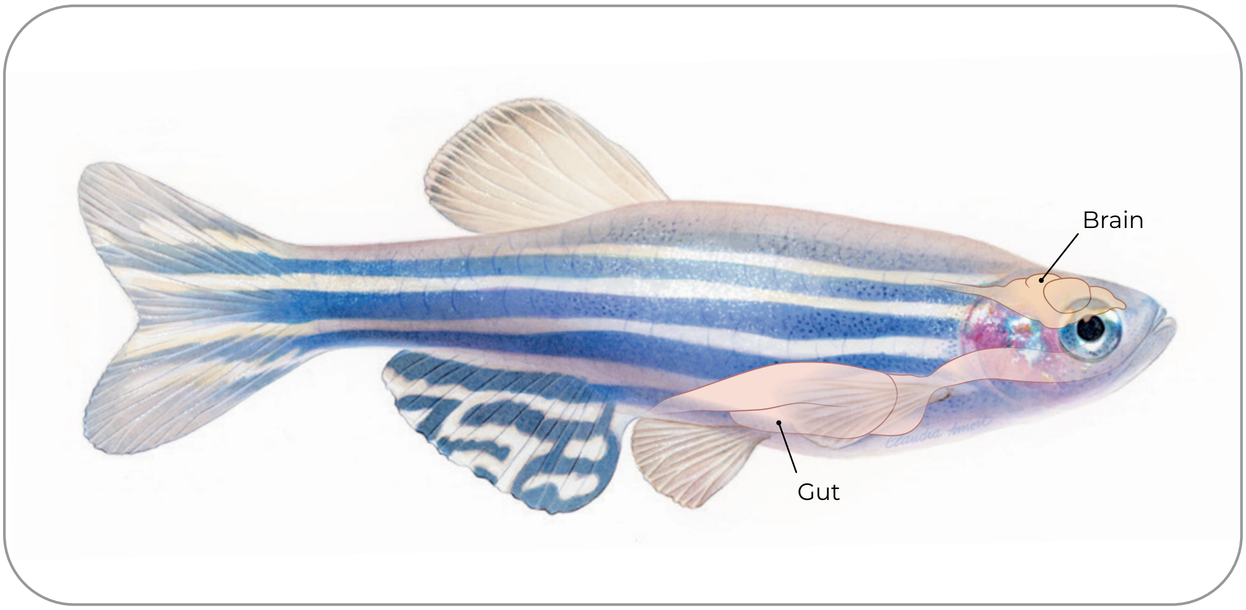
Fig. 17: References for the chambers. 3D modelling in SketchUp.

Research in Zebrafish

Apart from rodents, zebrafish are sometimes used as an animal model to research the Microbiota-Gut-Brain Axis. They have some similarities and differences compared to mice and humans, which I wanted to highlight in this infographic.

Cells of the Gut			
Enterocyte	✓	✓	✓
Stem cell	✓	✓	✓
Paneth cell	✓	✓	
Goblet cell	✓	✓	✓
Enteroendocrine cell	✓	✓	✓
Lymphocyte	✓	✓	✓
Tuft cell	✓	✓	✓





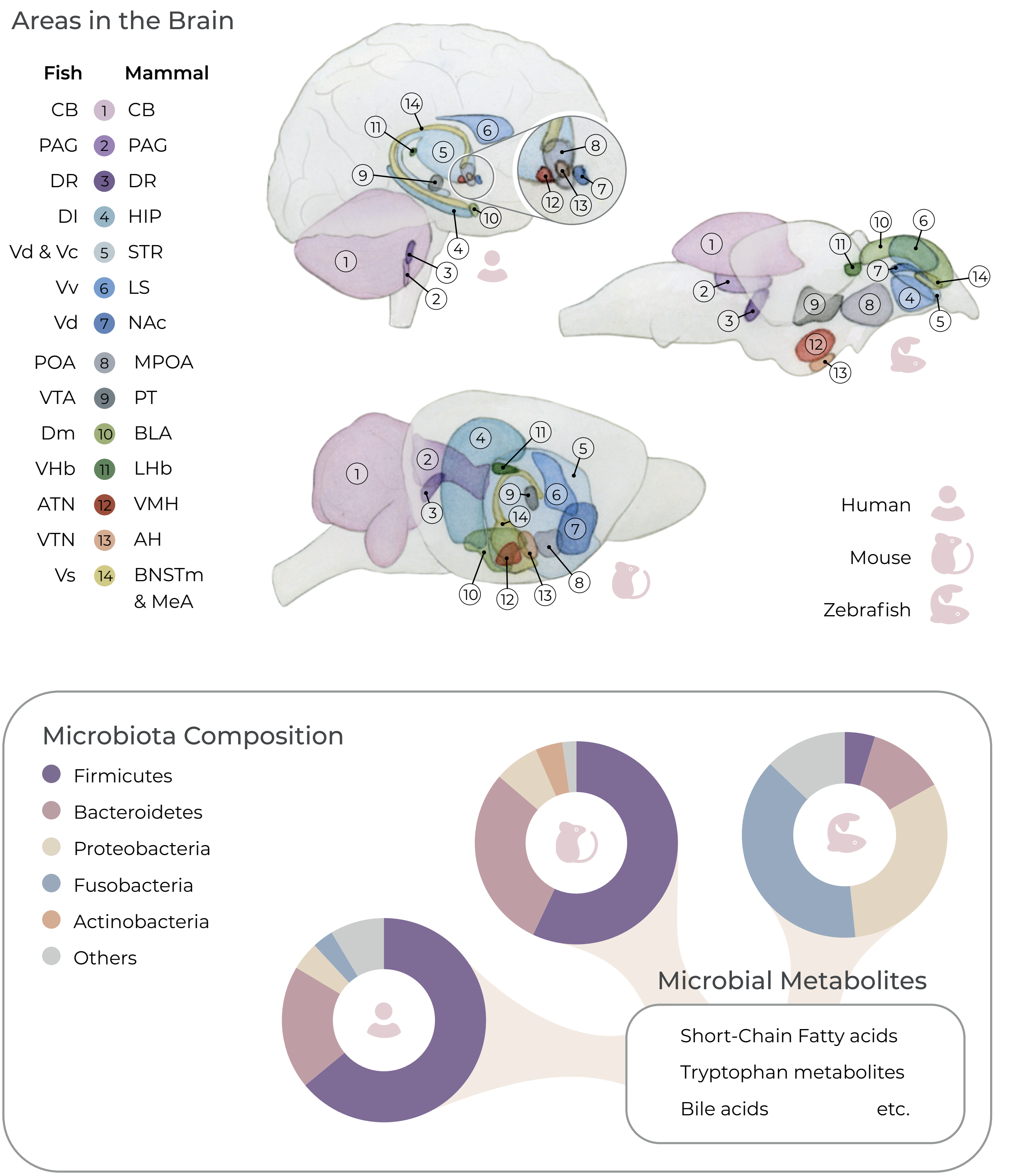


Fig. 18: Comparing the Microbiota-Gut-Brain Axis in humans, mice and zebrafish. Watercolor and Adobe Illustrator.

During my time in Cork, I had the opportunity to dissect a zebrafish, which provided me with firsthand knowledge of its anatomy. Although the fish had scoliosis, I used it as a reference for the colors in my final illustration, which was done in watercolor. This technique gave the fish a soft, smooth feel that was well-suited to its appearance. I painted the fish first, then digitally incorporated the anatomy, allowing me to experiment with different ways to integrate the anatomy. This way I will also be able to reuse the watercolor of the zebrafish for future projects where I might want to highlight other elements of the anatomy. I also chose to leave out reflections in the watercolor to save time and instead added sparkles and shine digitally.

Dissection

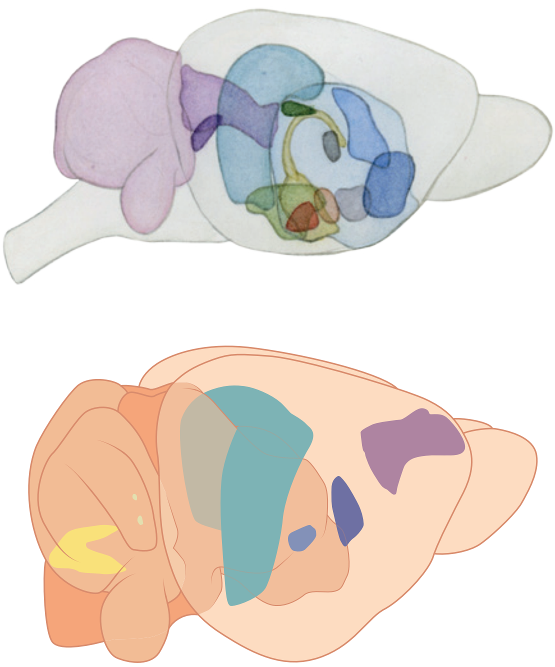


Fig. 19: Mouse brain. Watercolor (top) and Adobe Illustrator (bottom).

For this infographic, I could have reused some elements from previous illustrations, such as the gut and brain of humans and rodents. I could have done that to save time, but I wanted to maintain consistency in style in this infographic and also explore another technique for presenting the same information. I found that watercolor has a high aesthetic appeal and creates an organic feel. Because I shaded the elements in the watercolor, they have more depth and give further information about the volumes and texture. However, if shading is not necessary, it can sometimes distract from the information that needs to be conveyed. Additionally, the final colors of the illustration in watercolor can be a bit more unpredictable, because they are built up layer by layer. Although when following specific rules, such as creating an underpainting and adding yellow tones in the light and blue tones in the dark areas, can help harmonize the final product. Graphical artworks compared to watercolor for me offer more precise control over the colors.

Fig. 20: Zebrafish. Pencil sketch (top), underpainting in watercolor (middle) and final artwork in watercolor and Procreate (bottom).

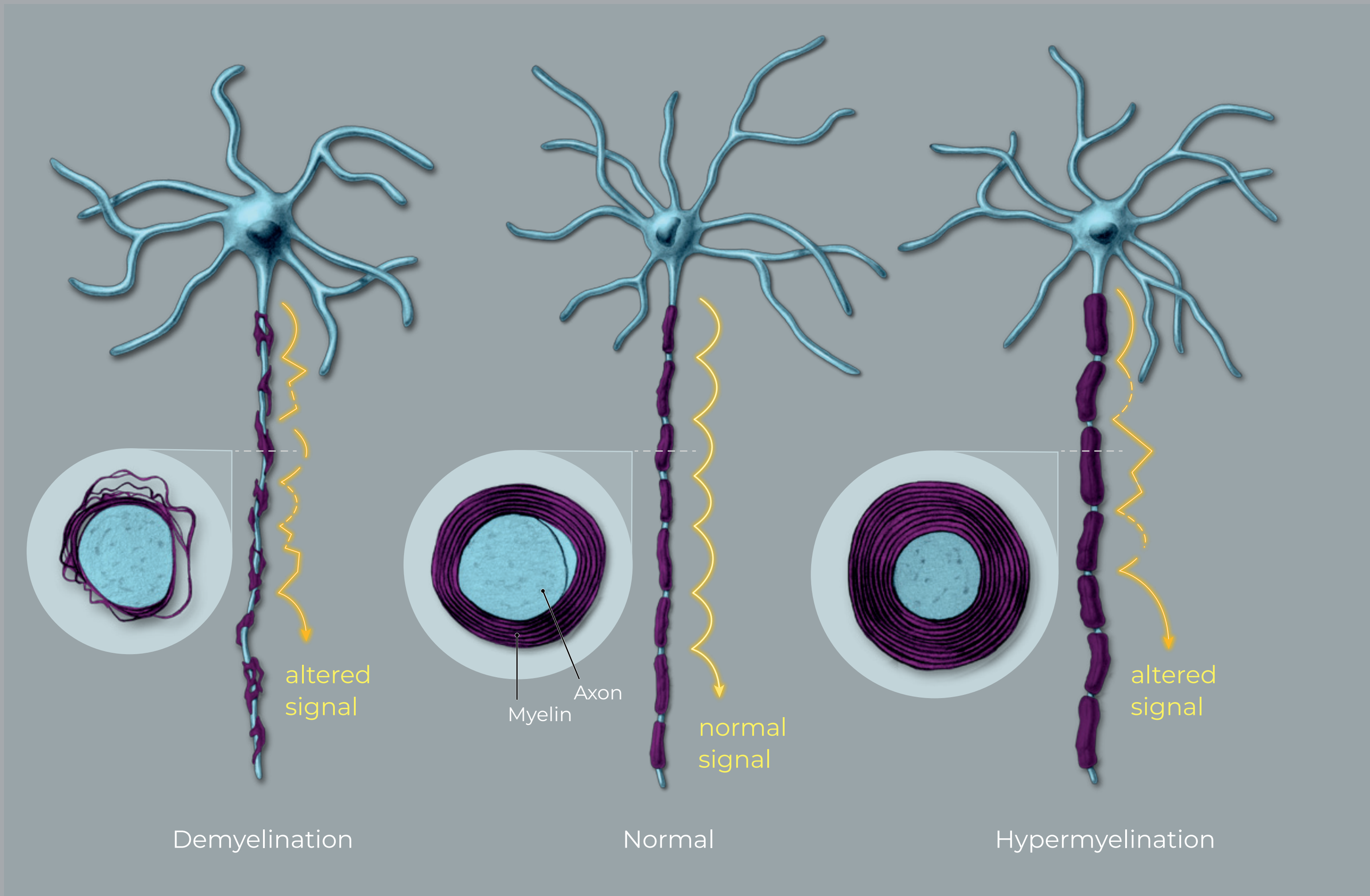


Fig. 21: Myelination of neurons. Pencil and Adobe Illustrator.

Myelination of Neurons

In the course of my thesis, I wanted to explore another technique: frame-by-frame animation. Static images are very effective when conveying information, especially for a single idea or a moment in time. They are quicker to create and can show the information in a wider context, in instances where playing a video is not possible, like in prints. Animations on the other hand, allow me to show a process more comprehensively. Additionally, the audience can take in the information in a more memorable and entertaining way.

The choice between animation and static images depends on the purpose and content. For this project, I chose to make an animation and a static version of the illustration. I believe that the animation is more appealing to audiences when shown in a presentation. However, as I mentioned before, sometimes it is not possible to show an animation. For that case, I made a static version of it as well.

I made different color versions of the illustration. In the beginning, I left the neurons grey with dark blue myelin and turquoise signal. I found this color scheme very aesthetically pleasing but felt like the neurons were not standing out enough on the light background and the myelin was overlooked on the dark background. Then I made a version where I colorized the neurons in more conventional colors making them yellow. I wanted to try what it would look like with different color combinations as well: green neurons with red myelin and a yellow signal. This one made the neurons look slimy or swampy, which is not the atmosphere I was going for. Next, I made the neurons blue with purple myelin and yellow signal. I found this very appealing, but still felt like the myelin wasn't getting enough attention. Since the graphic is about the different myelin sheath thickness around the axon, I decided to go back to a light background and removed some of the graphical elements, because they were not necessary and made the graphic noisier.

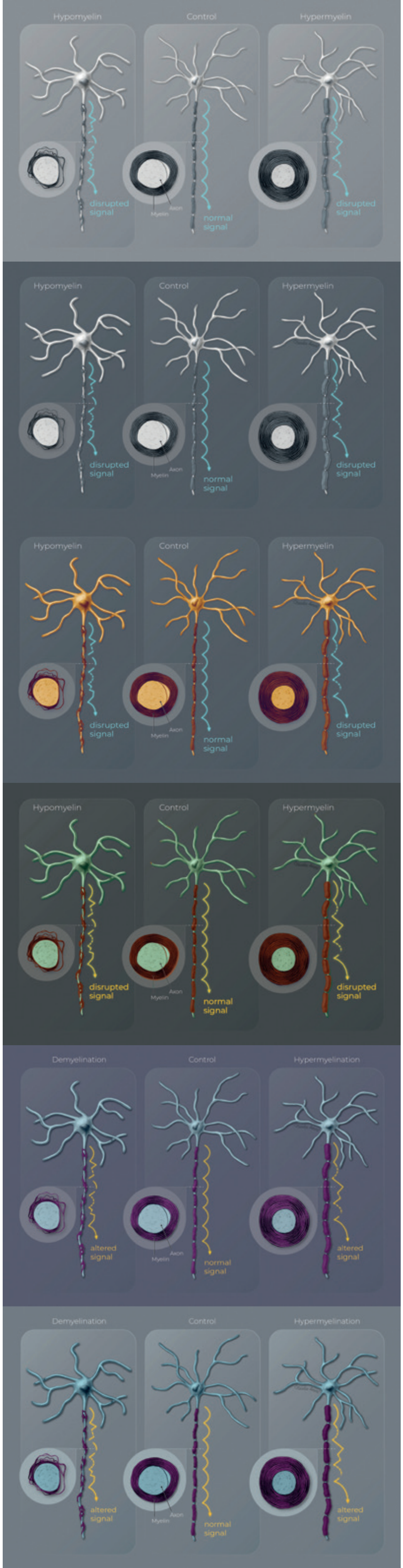


Fig. 22: Different versions for the layout and color. Pencil and Adobe Illustrator.

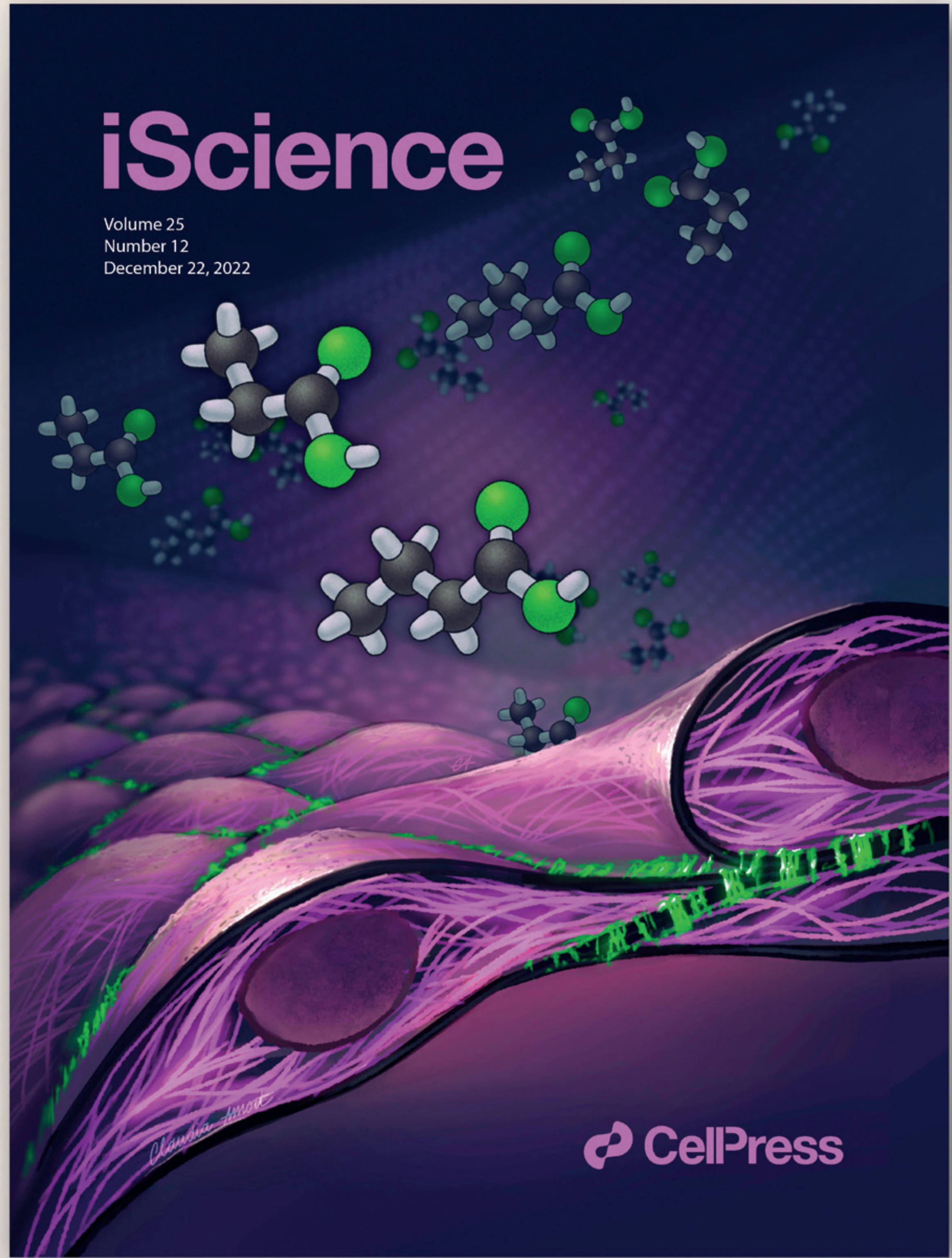


Fig. 23: Cover for iScience. Digital painting in Procreate.

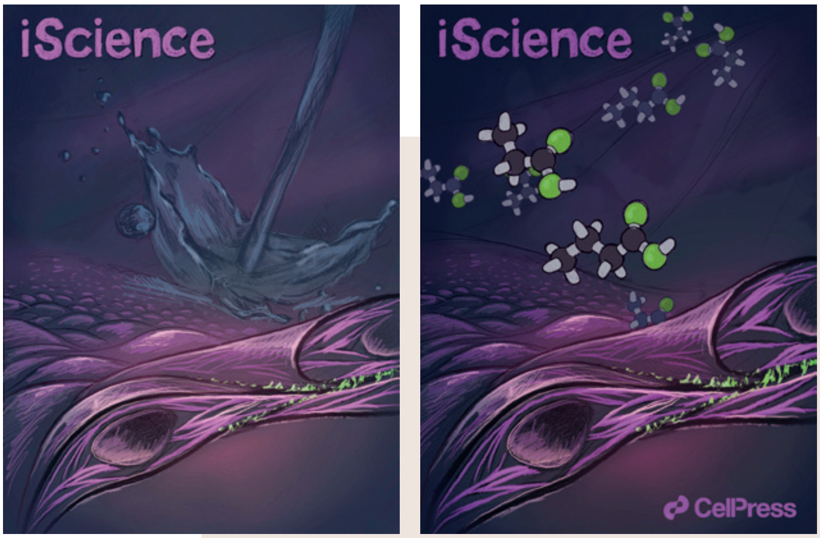
Cover for iScience

One of the papers my research group wrote was published in iScience, a scientific journal. For that, I had the opportunity to create a cover illustration. The publication was investigating how metabolites from the gut microbiota influence the blood-brain barrier. Specifically, they investigated how butyrate and propionate affect the actin cytoskeleton and tight junction protein structure of the blood-brain barrier. On the cover, I highlighted the epithelial layer with its cytoskeleton and tight junctions. In the background, I wanted to show the metabolites that were added to the cells.

At the time, Midjourney, an AI that can generate art based on a prompt given to it was just released. The AI uses machine learning algorithms to create unique and original artwork. This includes but is not limited to digital art for prints, logos, brochures, posters, websites, or other marketing media. It can generate game assets, designs for clothes and accessories, and even furniture and home decor. The possibilities are endless because it can create such a range of artwork in so many different styles and purposes. I wanted to see if this tool could also be useful to me as a scientific illustrator. I tried to explain my vision to the AI and let it generate images.

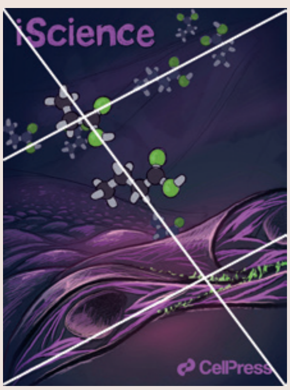
Fig. 24: Images generated by Midjourney. Prompt: pipette squeezing water on a carpet of cells, HD, 8k, hyper realistic, dramatic lighting, molecular biology.

The images don't really capture the idea, I was going for and I feel like the AI didn't understand my prompt. Maybe that is something that can be improved if I had more experience in how to communicate with Midjourney. Overall, I believe this is a tool that can be very useful to create digital art and graphic design, and more because it can produce a wide range of art quickly and easily. However, when it comes to scientific illustrations, the accuracy and precision of the information depicted are crucial. Scientific illustrations are used to communicate complex information, and the slightest inaccuracies can lead to confusion and misinterpretations. Therefore, the use of an AI-based art generator may not be suitable as it lacks the level of accuracy and attention to detail required. I also believe that the AI was trained with more general art which is closer to the real life of most people. If it would be trained with more scientific illustrations, it could get very interesting in the future. But I believe that a scientific illustrator or expert in the field will always need to validate it on the accuracy and relevance. Still, I believe that AI-based art generators can be useful for scientific illustrators to create some first conceptual illustrations or to get inspiration for composition and color combinations.



After I played around with Midjourney and recognized that I would not be able to use the generated images for this illustration, I went back to sketching. I decided to remove the solution in the background and to include Butyrate and Propionate as their chemical structures instead in the illustration.

Fig. 25: First concepts. Digital sketches in Procreate.



I choose to place the elements of interest along the golden triangles, which are based on the golden ratio. This creates harmony and a sense of direction in the image that guides the viewer's eye through the composition. It also creates depth and a hierarchy with the elements placed on the intersections appearing more prominent and to be closer.

Fig. 26: Composition in golden trangles.

The color choices I made were based on the fluorescent proteins the researchers used to visualize the actin cytoskeleton in pink and the tight junctions in green. This not only thematically, but also visually closely connects the cover page with the paper. I kept the background in a dark blue because this color together with the pink is the split complementary to the green. This gives additional tension to the artwork.

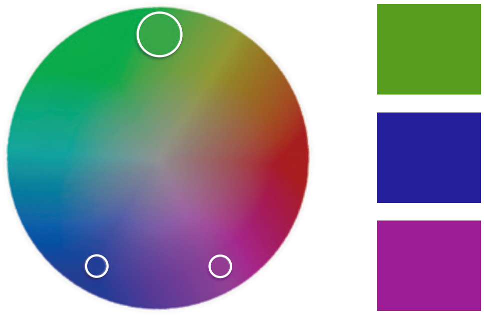


Fig. 27: Split complementary.

Cover for My Thesis

Towards the end of my thesis, I experimented with Midjourney again to create a cover for my thesis. I wanted to see how the art generator improved over the previous six months and if I could use this tool to create a base illustration to elaborate and tailor to my vision.

I experimented with submitting different promts until I was satisfied with the artwork the AI system created. I used that image as a base and painted the brain, gut and microbiota on top. This worked brilliantly, I could speed up my workflow and at the same time keep the anatomic accuracy I needed.

Using an AI that generates art, such as Midjourney, raises some ethical concerns, which are improtant to consider. For one, the question of ownership becomes complex. Is the creator of the AI system the owner, the person who trained the AI, the user who generated the artwork or the AI system itself? As of now users who purchase a membership with Midjourney are the owners of the artwork they create with Midjourney having non-exclusive copyrights to them as well.

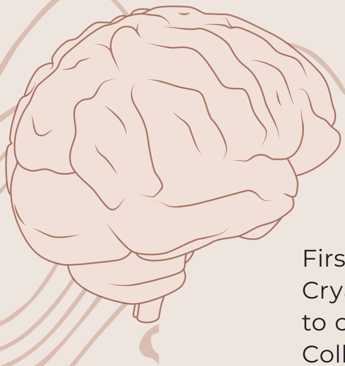
Another ethical concern involves plagiarism. AI systems are often trained on existing artworks, which means that the art it generates may closely resemble the existing work it has been trained on. The system learns patterns and features from a dataset and generates new artwork based on it. Here the line between inspiration and plagiarism can be very fine. Is the AI system copying the style and content of existing works, or is it creating something new that has been influenced by the training data?

As AI systems have the potential and sometimes already are able to replicate the quality of human art, it may be threatening to economic prospects for artists. The impact of AI on careers overall is a very real and challenging concern. For me personally, I believe that I can use Midjourney and other AI based systems as tools to improve and increase the efficiency of my work. I hope to incorporate AI systems into my workflow rather than being replaced by them.

Conclusion

As I reach the final pages of my thesis, I am filled with so much excitement and anticipation for my future. As a child, the first thing I would say to someone asking for my future job, was being an artist. And now, here I am, making that dream come true. I can't wait to learn more about science and art. I can't wait for the first big collaborations and for the first month of solely living from my freelance work. Armed with the foundations I have learned over the years, I am ready to face a chapter that may also bring its own challenges and uncertainties. I will go into the future with curiosity, passion and dedication.

Acknowledgements



First, I want to thank my supervisors Professor John F. Cryan and Ken O'Riordan for giving me the opportunity to create illustrations for their research at the University College of Cork in Ireland. It was such a delight working with your research team.

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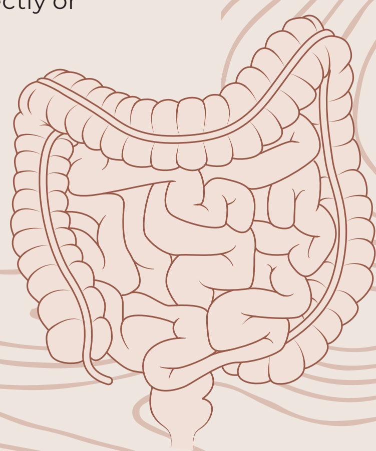
Lastly, I want to thank all the people not mentioned yet, who have supported me to complete my work directly or indirectly.



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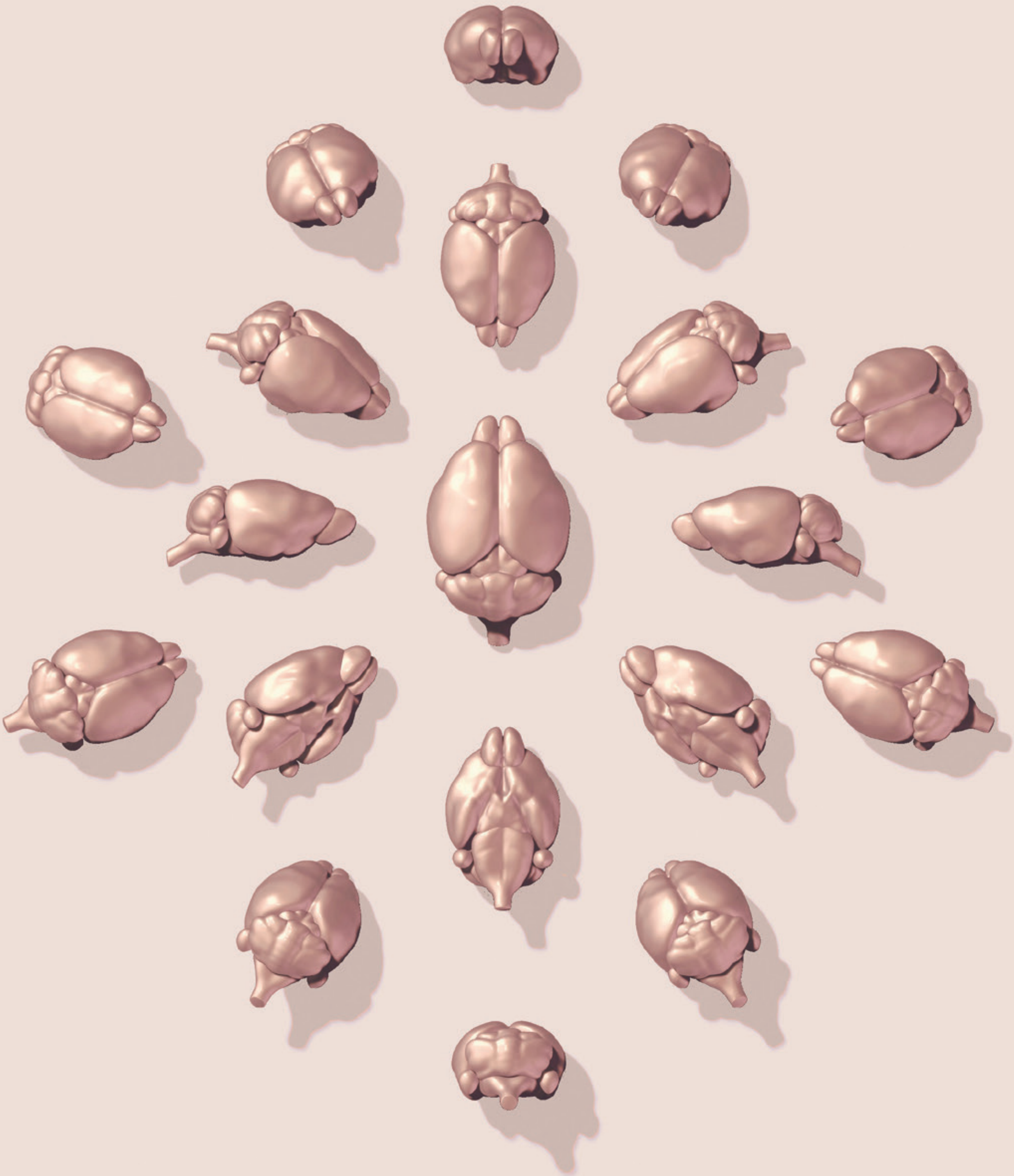

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