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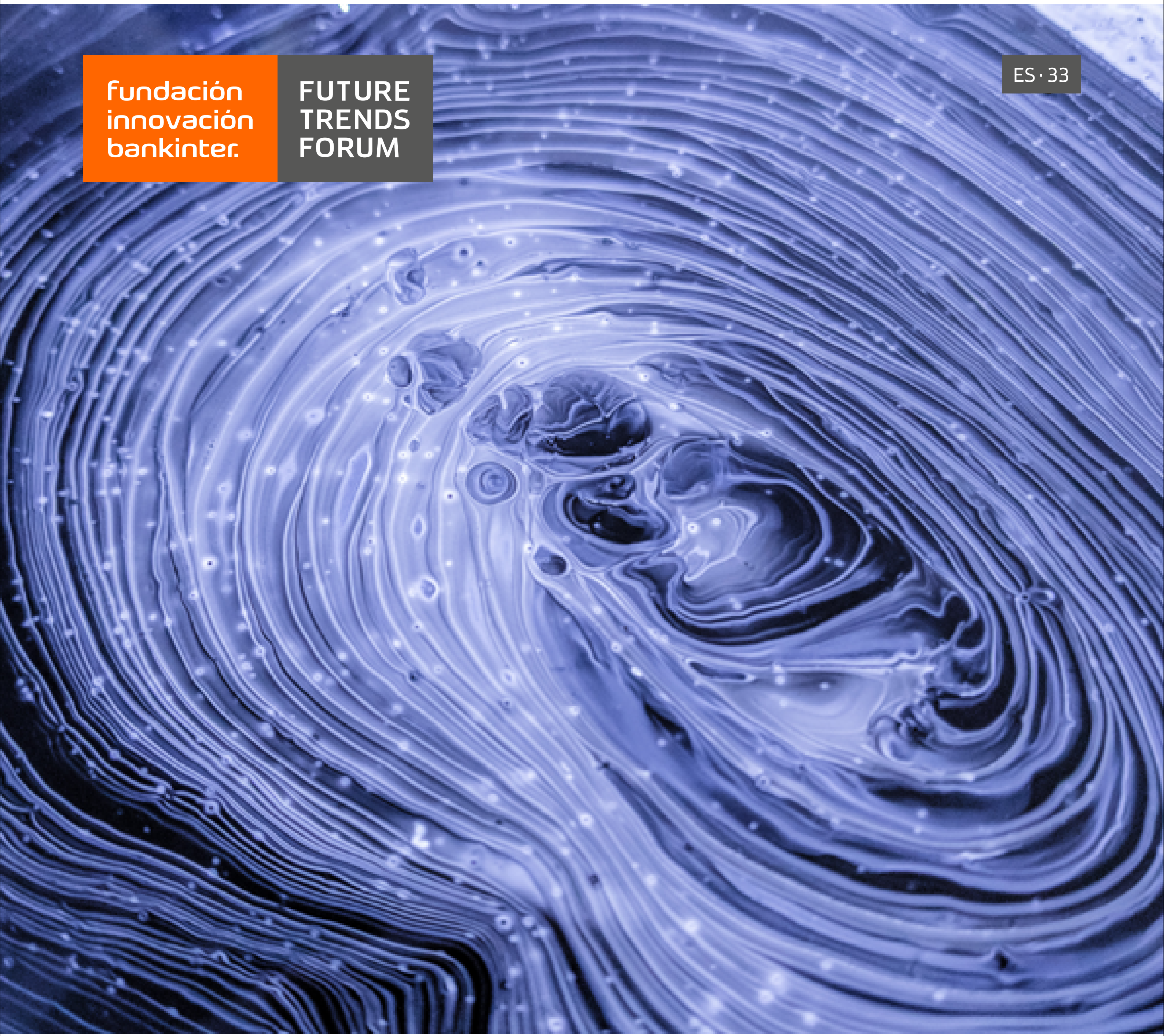
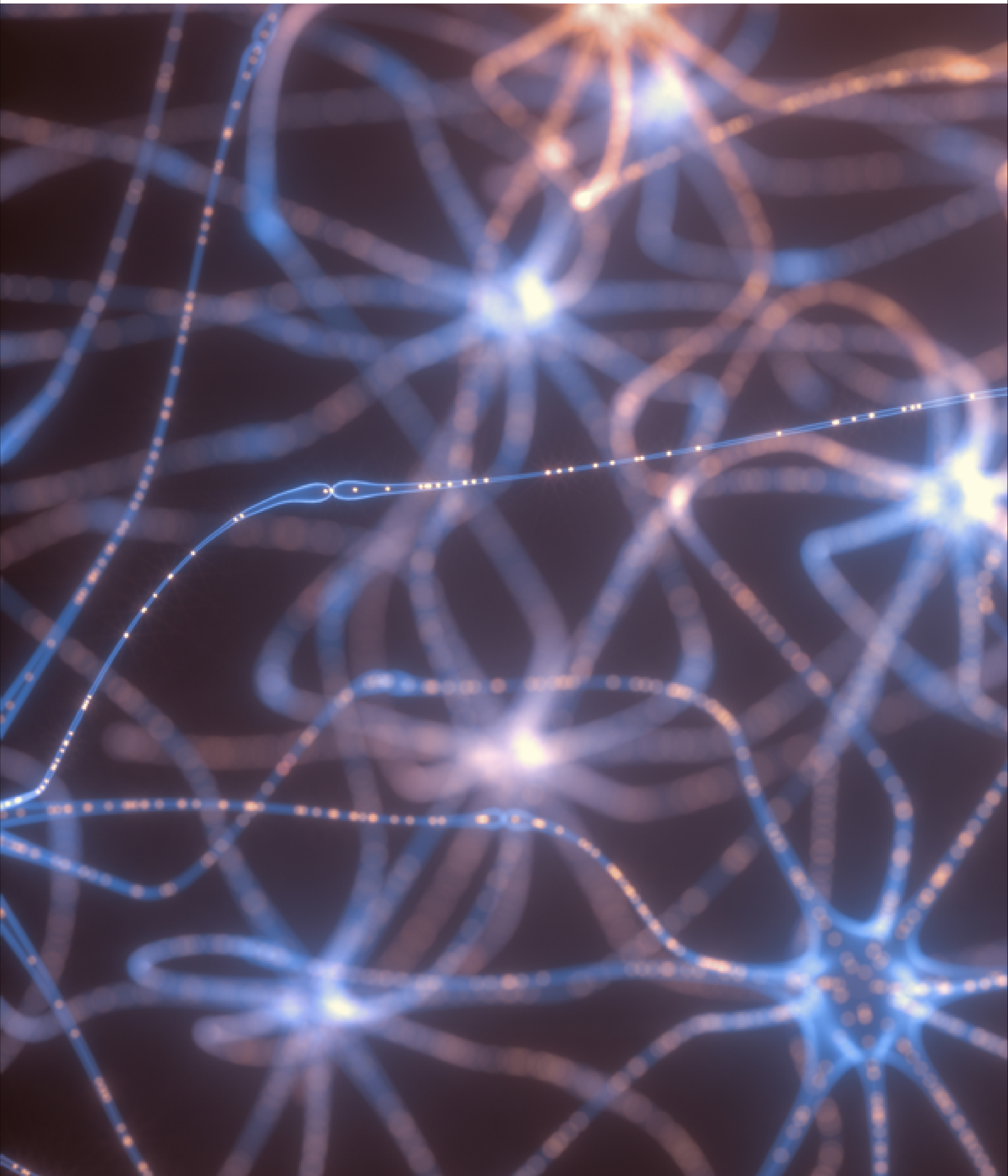


Neuroscience: The Next Brain



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The Next Brain

01

Neuroscience

Your **brain defines who you are**, how you process the world around you and how you respond to stimuli. Processes such as falling in love with someone, recognizing yourself, remembering a place by its smell, tolerating pain, and even mending a broken heart all take place inside the brain, thanks to the hormones it secretes and the thoughts it generates.

But the brain also causes you to feel threatened, not see specific colors, lose your sense of proprioception or your ability to communicate, forget about your daughter or lose interest in being alive. These are the consequences of dysfunctions caused by the diseases, injuries or developmental disorders that affect the chief organ in your body.

What is neuroscience?

Neuroscience studies all of these processes, but what is neuroscience? That is, without a doubt, a complicated question. The official Spanish definition describes it as the "science that studies the nervous system and each one of its diverse aspects and specialized functions." While this definition is correct, it leaves some elements out. Considering the complexity of the processes that take place inside the brain, a more accurate definition of neuroscience would specify its goal of understanding the functioning and structure of the nervous system using different approaches, methodologies and techniques.

This definition explains that the science of the brain requires cooperation among a myriad of disciplines to unravel the hidden details of the most complex organ in our body. Chemistry, physiology, psychology, pharmacology, genetics, different types of engineering, computing–all these disciplines are involved in neuroscience.

We are made of brain structures, neural synapses and mental processes, but also emotions and neurological and mental disorders. Every new finding makes it more evident that we must understand neuroscience from different perspectives. In fact, some people state that **there is no such thing as one type of neuroscience. Instead, there are several types of neurosciences, because multiple disciplines study the biological basis of behavior.**

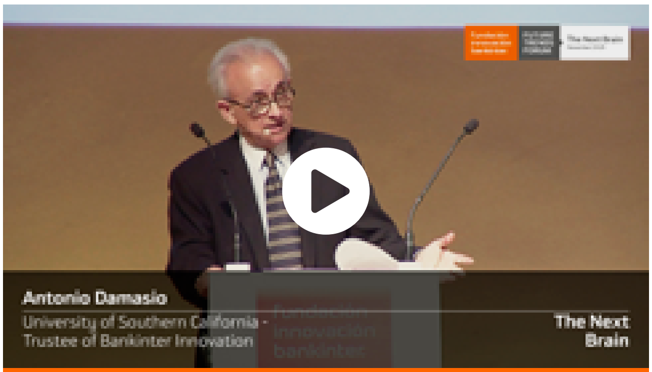
But that is not the full picture. If we truly want to understand neuroscience today, we need to take new technologies into account. Thanks to them, brain observation is as detailed as ever; we can enhance ourselves through brain-computer interfaces and even create machines with feelings due to artificial intelligence. The development of computing, big data, virtual reality, nanotechnology and DNA sequencing machines, among other technologies, are redefining this scientific discipline. Now, on top of understanding how the human brain works, we must take into account what we learn from machines and their ability to analyze information and predict, for example, connection patterns between neurons.

1.1

Beyond the Brain

Historically, neuroscience has focused on the brain. *"That is, of course, perfectly acceptable because we have been very successful in neuroscience. This has led us to think that we should only focus on the brain and leave everything else out of the conversation,"* says Antonio Damasio. This provides an innovative perspective that can help us better understand what neuroscience is beyond the brain.

Antonio Damasio
University Professor of Neuroscience at the University of Southern California



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There has been life on Earth for the last 4 billion years, and organisms with nervous systems have only existed for a very small fraction of that period, around 500 million years. Most of the time, our planet has been inhabited by unicellular living systems, such as bacteria. Though these organisms had an apparently simple structure, Damasio believes we should have paid more attention to them to understand the human brain. Why?

Matthew Hutson
Science and technology writer

"They present complex behaviors, the possibility to detect stimuli and respond to them (they have sensitivity, not awareness); they present complex metabolisms that regulate their vital processes, and also something that often times people do not associate with unicellular livings: socialization." They have the chance to form alliances, to cooperate, to fight. That leads us to the conclusion that "*there is intelligent life outside the brain; even bacteria can do things that not even the most intelligent robot can do,*" Matthew Hutson says about this issue.

But, in spite of proving to be very successful beings, they have gone unnoticed in the study of neuroscience and human behavior. "*I think it happened because neuroscientists have been very successful in studying, for example, perception, attention, reasoning, memory, movement, language...*" Damasio states. *"In fact, during the 20th century, the success of this approach came at the expense of connections with other aspects of neuroscience, such as affection, emotion and the possibility of feeling."* This made collaboration between disciplines more difficult.

"We need to realize that the nervous system, in all its complexity, does a very simple thing: it extends, expands and updates the homeostasis project." In the context of neuroscience, **homeostasis is understood as *"a collection of rules and regulations meant to preserve life in the future and resist illness and decline,"*** says Damasio himself. *"So, I really don't think there is a significant difference between what the nervous system does and how it does it, and what bacteria, those successful, amazing organisms, can achieve."* As said by Neil deGrasse Tyson, American astrophysicist and science educator: *"Everything we do, every thought we've ever had, is produced by the human brain. But exactly how it operates remains one of the biggest unsolved mysteries, and it seems the more we probe its secrets, the more surprises we find."*

1.2

The Basis for Neural Functioning

At the end of the 19th century, Santiago Ramón y Cajal established, for the first time, that neurons are individual elements of the nervous system: he suggested that they act as units that communicate with one another by meshing a network of connections. He became the first Spanish Nobel prizewinner, in the category of Medicine, in 1906. Today, it is an irrefutable reality that **neurons are the structural, functional units of the nervous system**. These cells receive stimuli from the environment, turn them into nervous stimuli and transmit them between neurons. Or they transfer them to a muscle neuron that will trigger a response.

Neurons are the structural, functional units of the nervous system

Tens of years later, research in neuroscience has led us to find out amazing information about neural functioning. We have a complete understanding of their morphology and that they have a core, dendrites and an axon; we know how they communicate with one another. We also know how nerve signals are transmitted from one neuron to another; we know that some neurons are specialized in the visual system and others in the auditory system. Some help us remember things and some help us recognize faces. We have also learned that there are no specific anatomical regions for all these systems. Instead, neural networks are reinforced by every new connection.

Even though we now know much more about neural functioning than a century ago, some mechanisms still remain a mystery to the scientists that, on a daily basis, work to unravel them. One of the most interesting questions that currently comes up in this area is, what determines the way in which different brain regions connect to one another? Alex Fornito spends much of his time trying to answer that question. Fornito studies neural connections and models the brain as an interconnected network. A major concept in his field of work is the connectome, a map of connections produced between neurons that draws out how different brain regions relate to one another. *"The connectome is the basis of the approach that understands the brain as an integrated unit; instead of presenting different regions with very specific functions, the brain is shaped based on its connections,"* explains Fernando Maestú, professor of Psychology at the Universidad Complutense in Madrid.

Álex Fornito
Turner Institute for Brain and Mental Health at Australia

The connectome is the map of connections in the brain

Duration: 10:00 min

In order to understand the existing connection patterns and what determines them, Fornito and his team scanned and analyzed brain connections in different people. They used a model that allowed them to define which brain regions communicated with one another. *"We divided the brain in different regions. Each of them became a point or a node, and we drew lines to connect them."* That is how they obtained a graphic representation of the networks. *"This is a very flexible model that allows us to conduct different types of analysis,"* Fornito explains. *"For instance, we can generate maps that show which specific brain circuit is affected in a person with depression, ADHD or schizophrenia, so we can start looking for similarities and differences among several disorders."* But Fornito and his team went beyond that: they conducted a 'topological analysis' in order to quantify different aspects about the organization of brain connections in greater detail.

When they analyzed brain connections in depth, they realized that brains can be divided into modules. **Brain modules are not anatomical regions, they are sets**

of connections. "*Strongly linked connections make up a module. We think they respond to related functions,"* explains Alex Fornito. For instance, there is a module for the auditory system and another one for the visual system. The points connecting the modules within those systems are called 'nodes', and nodes that receive a larger influx of connections are called 'hubs'.

These strategic points in the brain are key to communication between different brain regions. But they are also the brain points that consume the most, and they are the most vulnerable to disease. That is at least the conclusion that Fornito and his team drew. *"If we map the cortex regions where we know some hubs are located, and we also map regions that show glucose consumption at rest, we observe that the regions overlap. Brain hubs are expensive, metabolically speaking, because they take up a lot of energy, but they contribute high functional value by integrating several parts of the brain."* They use a lot of energy but they are very useful, because they connect brain regions to one another.

On top of that, this high demand for glucose makes hubs particularly vulnerable to disease. *"If we map the brain of someone with Alzheimer's disease, we will observe that the areas with the highest concentration levels of amyloid, a key protein in the development of the disease, correspond to the brain hubs. We observe that in several disorders such as schizophrenia, depression or epilepsy,"* Fornito points out.

Therefore, **hubs are key points in the brain that draw together a large amount of connections, which allows different regions in the brain to communicate. In turn, hubs take up a lot of energy and are vulnerable to disease.** "*They are very valuable because of the function they perform, but it comes at a very high cost,"* Fornito explains.

Hubs are key points in the brain that draw together a large amount of connections

There is a basic question that we have not posed yet: where do hubs come from? How is their organization in the brain determined? It seems that genetics has something to do with it. Fornito's team has been working on this aspect for the last few years, focusing specifically on human twins in order to quantify genetic influence. As a result, the team found out that there is a greater genetic influence in the connections between hubs. This means that it is not distributed homogeneously throughout the brain; instead, it especially impacts hubs. Genes perform a very important role in connectivity.

1.2.1
Connection Patterns

By studying neural connections, we can learn more about how different parts of the brain communicate with each other. We can observe, for instance, which specific brain circuits that are affected in people with depression, ADHD or schizophrenia.

The approach suggested by Sean Hill allows us to observe, additionally, how changes in neural excitability and sleep alterations are also related to different neurological, psychiatric and drug-abuse disorders. Hill and his team address this issue through comprehensive modelling in Blue Brain. This 15-year-old project aims to **decode and study brain structures in detail.** To do so, the team is developing a simulation of the entire organ at a molecular level. They are creating a digital map that recreates, as precisely as possible, neural paths of the human brain and the way they activate. Their job is to integrate thousands of data to digitally reconstruct brain circuits and structures.

Sean Hill
Krembil Centre
for Neuroinformatics

Then, they introduce the electrophysiological and synaptic attributes to build a model of the circuits. This model shows aspects such as the slow oscillation of neural networks, an intrinsic property of brain cortex. These oscillations appear especially during sleep stages, and they are neural activity waves that travel from one point of the cortex to another every one to four seconds. The digital model designed by the Blue Brain project leverages only on data to integrate this low frequency oscillation.

As an example of how useful these advances are, Hill explains how transitioning from wakefulness into sleep causes significant changes in neural activity. More specifically, he explains that wakefulness and sleep stages are not fully binary. What does this mean? It means that when we are sleeping, our brains are not necessarily asleep; when we are awake, our brains are not necessarily awake. Let's go back to slow oscillation to understand how this is possible.

Duration: 09:50 min

As we were saying, these waves travel all around the brain cortex during some sleep stages. Even though it is counterintuitive, these waves that lead us to sleep appear when specific neurons are activated. "*When the excitability of a microcircuit increases, there is a change that makes it more likely for us to enter into a sleep stage. It tends to produce more slow frequency oscillations, which are typical of sleep periods, than when excitability levels are balanced*," Hill explains. During wakefulness, excitability is at a normal level and *"the answer to stimuli is proportional and integrates inputs properly."* During sleep, that circuit goes into hyperexcitability, and slow oscillation appears.

But wakefulness does not always come with normal excitability, and sleep does not always come with hyperexcitability. Slow waves can also appear during wakefulness. "*During wakefulness, cortical neurons are triggered at irregular intervals*," Hill explains. This means that there are slow wave micro-intervals, typical of sleep, even when we are awake.

Something similar happens during sleep. Slow wave oscillation consists of an inactivity stage (typical of wakefulness) followed by a rise stage (typical of sleep). "*We observe a very abrupt transition between these two stages*," Hill explains. This is why "*there are parts of the brain that are asleep when we are awake, particularly when we have a lack of sleep.*"

Neuron excitability also affects how other brain regions connect. *"If we stimulate a specific point during wakefulness, we observe diverse activation of the brain across the brain network,"* Hill explains. *"During sleep, the same circuit produces an only-local response that does not expand through the brain."* There is a dramatic difference in brain connectivity when we are awake and when we are asleep. One of the most widely supported processes that explain this is the synaptic homeostasis hypothesis, which suggests that sleeping at night is the price we pay for the brain plasticity that we use during the day. *"If we don't use a specific brain region during the day, that local area will see a reduction in sleep at night."*

Neuron excitability also affects how other brain regions connect

With this approach, Hill's team tries to answer the questions of what different brain states entail, and how they relate to other types of excitability and to the entire brain. As an example, he uses another data-based approach, Janelia's MouseLight project, which identifies and monitors every individual neuron in the brain. *"This gives us a very different perspective than the one we have had so far in terms of the impact that an individual neuron might have on the entire brain in just milliseconds,"* Hill assures. *"This is transforming the way in which we perceive and understand the role of each individual neuron in the brain."*

One of the most important steps that has been taken to integrate all this information is to build a predictive connectome of the entire brain at a synaptic level. "*By integrating all these data, we can predict all the brain synapsis in a mouse's brain,*" Hill claims. **This means that not only can we study how the brain is connected at that very moment, but we can also predict how future connections will be made.** "*This is just the starting point; the process is constantly changing.*"

1.2.2

The Jennifer Aniston Neuron

For 15 years, Rodrigo Quian has observed the behavior of both individual neurons and groups of neurons in patients with epilepsy that received intracranial electrodes implanted to fight their disorder. **He showed photographs to the patients and realized that there is a group of neurons that only respond to pictures of Jennifer Aniston.** Nothing else. It does not matter what the picture looks like: the neuron will respond to it. "*That is what people call 'the Jennifer Aniston neuron', you might have heard about it,*" Quian explains. "*And, similarly, I found another neuron that responds to Halle Berry, to any picture of Halle Berry; another one responds to Luke Skywalker, another one to the Sydney Opera House, another one to Maradona, etc. It also happens when we write, for instance, Oprah Winfrey's name: I write down 'Oprah' and the neuron responds. I say 'Oprah' and it also responds.*"

Rodrigo Quian
Centre for Systems Neuroscience of University of Leicester

Quian claims that there are neurons in the brain that only respond to concepts, regardless of the context: they respond to the idea of Jennifer Aniston; not to specific pictures of her, but to the idea of her. **These neurons have been named 'concept cells'.** The person's memory, the things that matter to them and what they decide to remember is what determines which concepts are associated with a group of neurons and which ones are not. Additionally, these neurons are found in the hippocampus, a brain region that engages memory. Considering this, Quian wonders, why are there neurons that respond to concepts in a memory region?

In order to answer this question, several experiments were conducted based on the assumption that we tend to remember concepts and forget details. "*We have observed that these neurons can code associations (the basis for memories) in just one try. Therefore, if I have a Jennifer Aniston neuron and I pair it up with, let's say, the Eiffel Tower, the neuron will code the memory of Jennifer Aniston and the Eiffel Tower and will form a new association. This association coding will remain over time,*" Quian explains.

Duration: 06:38 min

Additionally, we currently know that these concept cells are only found in humans. "*So far, we have not found these neurons in any other animal. We have looked for them in rats and monkeys, and we have not found anything remotely alike,*" Quian explains. "*This leads me to think that these neurons might be related to the basis for human intelligence, for superior cognitive abilities.*"

Concept cells can only be found in humans:

They have found out that, in other animals' hippocampi, these cells depend on context. A rat's neuron responds to a microphone on the podium, but if we put the microphone on the ground, another set of neurons will be activated. "*My theory is that these abstract representations might be the key to high-level human thinking, to the capacity to make analogies, inferences and different associations. Context-independent, abstract representations might be related to human thinking and intelligence.*"

1.2.3

Technology that Enables Brain Observation

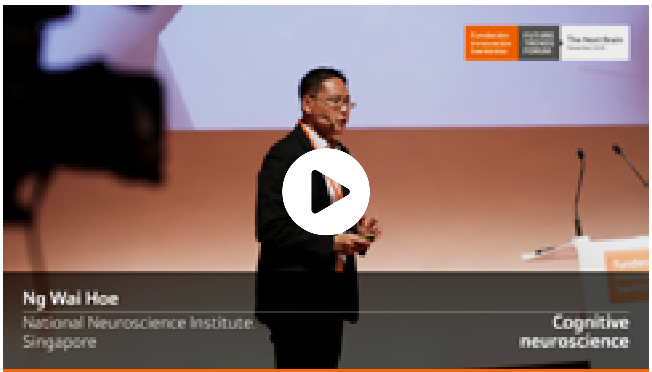
All neuroscience findings bring us closer and closer to a better understanding of how the brain works on a cellular level. This is possible thanks to technological developments that enable us to observe this organ at different scales and with various techniques. Naturally, **the more sophisticated the imaging methods are, the more rigorous, detailed and valuable the information will be.** Currently, there are many neuroimaging modalities, such as magnetic resonance, magnetoencephalography or electroencephalography. There are also more detailed techniques such as the optical coherence tomography or the transcranial direct-current stimulation. Overall, we can place them in two categories: neuroimaging techniques that study structural and anatomical features, and imaging modalities that study functional aspects.

We will obtain rigorous, detailed and valuable information

What do we use these techniques for? Currently, we mainly use them for clinical diagnosis and research. Ng Wai Hoe explains that neuroimaging techniques can be useful in many other areas as well, such as ageing and neurorehabilitation or childhood learning. They can even be applied to fields like artificial intelligence, computational neuroscience, materials science, hardware engineering, biomedical engineering and biotechnology. *"It is interesting to use research in neuroimaging in order to understand human behavior in business, society and social science,"* Ng Wai Hoe adds.

Ng Wai Hoe
National Neuroscience Institute at Singapur

More specifically, the NNI (National Neuroscience Institute de Singapur has several working groups focused on observing and studying different disorders through different neuroimaging techniques. For example, one of their teams uses probabilistic and deterministic tractography to study Parkinson's disease. "*We are also applying this technology and this research to longitudinal population studies in an attempt to assess how the brain changes when it ages or develops a neurodegenerative disorder such as dementia*," Ng Wai Hoe explains. In the case of Parkinson's disease, they also use neuroimaging techniques to monitor neuron transplants' response to treatment. His team also focuses on another disorder: normal pressure hydrocephalus, which affects the elderly populations by causing them trouble walking, dementia and urinary incontinence. This research might help them find the perfect patient for a specific cerebrospinal fluid diversion therapy or to adapt patients' treatments.



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In spite of everything that current neuroimaging techniques can achieve, the development of new tools is ongoing. *"New techniques will help us obtain more knowledge and implement it, they will help us educate and train our brain capacity, and predict diseases better,"* Ng Wai Hoe assures. *"One of the challenges we face is that of passing this knowledge on in order to commercialize it and regulate it properly."* It is a significant challenge: research in neuroimaging poses many questions on the subject of ethics. Ng Wai Hoe points out some of them: how can we address the results we obtain accidentally? In the case of criminals whose imaging results show they have different attributes, do these attributes make them guilty or are criminals still responsible for their own actions? *"There are also legal problems, such as privacy issues. Data resulting from neuroimaging techniques can be used to put our privacy in danger, which also entails consequences for public society."*

1.3
Mental Health

According to the World Health Organization, more than 300 million people in the world struggle with depression. *"It is already one of the main causes of disability not just in the United States, but all over the world,"* Mustafa Husain explains. Another 260 million people have anxiety, according to the WHO. These two disorders are the most widespread across the planet, but they are not the only disorders that cause damage. The number of schizophrenia and bipolar disorder diagnoses, including autism spectrum disorder, keeps increasing.

These disorders are truly challenging for both neuroscience and society as a whole. *"They not only affect the patient,* *but their entire environment, including their productivity,"* Husain explains. *"Some people talk about depression as if it was a contagious disease, because it affects the patient's entire family and environment."* Their long-term effects take a toll on society. Data support this theory: the WHO estimates that anxiety and depression affect workers so much that they cost us a billion in productivity losses every year.

Mustafa Husain
University of Texas
Southwestern Medical Center

On top of mental, emotional and developmental disorders, there are other neurodegenerative disorders, such as Alzheimer's or Parkinson's. Neuroscience studies them to learn about how they affect the brain. It is difficult to find a cure for these disorders, and even to improve their treatments. They almost always appear in the elderly and completely infringe upon the patient's quality of life.

According to some researchers, the earliest symptoms of Alzheimer's disease appear around 20 years before its onset. How can we design a clinical study that helps these patients? This is one of the questions that Juan Carlos López, neuroscientist with broad experience in drug discovery, tries to answer. According to him, it is one of the challenges that neuroscience needs to face.

Juan Carlos López
Haystack Science

The same thing happens with people that have neurological developmental disorders. If you give medication to a child that has struggled with brain connectivity problems for ten years, how long do they need to take it for in order to reverse the situation? These questions are still unanswered, partly because *"all new ideas for therapies come from trials with animal models, but no trial is good enough to represent a neurological disorder that can be replicated in humans."*

Neuroscience still needs to face challenges, but so far, the development of this discipline has allowed us to learn many other things about mental and neurodegenerative disorders. *"Alzheimer's disease, depression and a myriad of mental disorders put primary feelings, their management and their organization at risk,"* Antonio Damasio states. **By improving our knowledge about the functioning of the brain, we can better understand how mental disorders affecting this organ work.**

As we have seen, the more sophisticated the observation techniques are, the more rigorous, detailed and valuable the information will be. Singapore's National Neuroscience Institute is already applying them to longitudinal population studies in an attempt to assess how the brain changes when it ages or develops a neurodegenerative disorder such as dementia. They also use them to assess how patients with Parkinson's disease respond to neuron transplants.

According to Alex Fornito, studying neural connections allows us to learn which specific brain circuit is affected in the case of patients with depression, ADHD or schizophrenia. We can then look for similarities and differences among several disorders. *"We also know which connections are related to each mental disorder,"* Mustafa Hussein says. How are these connectivity patterns impacting the development of therapies? Fornito explains, *"If you can identify a dysfunctional network, you can use that to select a specific target, either in a non-invasive way or surgically."* However, he warns that the area is developing rapidly and *"we still have to find out the best way to approach this, especially in the case of non-invasive brain stimulation in deep brain regions."*

One of the most innovative contributions comes from Sean Hill. *"I'd like to emphasize that wakefulness and sleep stages are not completely binary"*, he explains. "*Local sleep intrusion in wakefulness has very strong implications to understand cognition and mental health disorders."* Hill also points out that *"in order to improve mental health, we do not need to understand how the brain works in its entirety."*

How can neuroscience help treat these disorders? Manuel López Figueroa, managing director of capital risk firm Bay City Capital in San Francisco, believes that by learning more about these disorders, we can perfect their treatments. His company is well-known for its investments in technologies that have a great impact on psychiatry or neurology patients. Figueroa, together with other researchers, is a member of the Pritzker Neuropsychiatric Disorders Research Consortium, which strives for a better understanding of psychiatric disorders and the discovery of new biomarkers and targets.

Manuel López Figueroa
Bay City Capital

Duration: 08:26 min

"Last year, several drugs were approved, such as esketamine (a fast-acting antidepressant) and postpartum depression compounds", López Figueroa explains. He and his team have observed that there is a new approach that focuses on specific symptoms or concrete medical needs. Research tends to personalize treatments as much as possible. *"We try to focus on subsets, on the specifics. Psychotic depression, for instance: is that psychotic disorder different from the one present in Alzheimer's or Parkinson's patients, the disorders drugs are discovered and approved for?"* López Figueroa wonders.

The Pritzker Consortium gathers experts that apply non-invasive medical devices. "*We use functional magnetic resonances to determine the brain core that we need to intervene; we also use TMS with specific algorithms that allow the patient to receive treatment for a couple of hours, instead of several hours a day during a whole week. We have tried to direct ultrasounds to target specific brain vesicles that allow us to release said drugs. This could potentially reduce adverse effects for the patient.*"

1.3.1
Future Prospects

Our experts foresee **a promising future for mental health**: they assure that progress will continue, particularly regarding depression, its effects and its evolution. *"Treatment-resistant depression will probably be the next thing we will address; there are already some approaches in clinical trials that might help,"* López Figueroa claims. *"We will see progress even in the field of diagnostics."* His colleagues agree: they predict that we will be able to predict some mental disorders even before patients ask for professional help.

A promising future for mental health

Experts believe it will not take long. They predict that ten years from now we will have much more detailed knowledge about the different types of cells. We will also have much more thorough brain connections maps that will increase our knowledge about which circuits are affected by different mental and neurodegenerative disorders.

More specifically, Alex Fornito believes we will have **a more holistic understanding of the brain**. *"We won't think of the brain as an isolated element. We will be able to understand how it interacts with the immune system, for instance, and we will use that knowledge to develop more treatments for different disorders."* Experts agree that developing small molecules will make all the difference when treating neurodegenerative and neuropsychiatric disorders; it will be an essential aspect of mental health. Technology will also be a turning point, *"particularly wearable devices, which will be helpful in the treatment of psychiatric disorders such as anxiety and depression, or neurological disorders like migraines or epilepsy"*, Ng Wai Hoe states.

1.3.2
Cost of Medication

Mental, neurological and neurodegenerative disorders are some of the main areas that neuroscience studies. All the efforts towards research, clinical trials and regulation aim to improve patients' health and even cure diseases whose cures still seems out of reach, such as Alzheimer's disease. Despite the challenges it faces, neuroscience allows us to know the human brain better, as well as the disorders that affect it the most. This, in turn, allows us to perfect treatments. Juan Carlos López is a neuroscientist with broad experience in drug discovery, and he recommends that we consider several aspects regarding medication and its cost.

We need to take into account the following considerations:

1.Treatment Personalization. *"Biology tells us that mental illnesses are really a compilation of disorders,"* López states. There is not one single type of diabetes, it varies depending on the person. The same thing happens in the case of schizophrenia: if we observe 100 schizophrenic patients, we will see they all have different symptoms. That is why we need personalized treatments. The problem is that medication tends to be more affordable when developed with a large group of people in mind. The price of these treatments increases when we personalize them. "*When does the development of a specific therapy for a limited group of patients stop being affordable?*" Juan Carlos López wonders. Rare diseases are interesting cases that attract attention, but they increase the cost of treatments. *"If the group of patients that will use that medication is very limited, then you can be certain that the cost of that medication will be very high."*

2.Therapeutic Modality. One of the decisions that needs to be made during a drug discovery process is what the treatment will be based on, which also affects its price. *"If we are talking about developing small molecules, then it might be cheap. But if we want to develop antibodies, RNA therapies, gene editing, gene therapies or cell-based therapies, then we are facing many limitations that clearly determine their cost,"* López points out.

3.Regulation. This is about how to put products on the market. One of the key questions when releasing a new drug is, what do you claim your product does? Are you saying it cures Alzheimer's? Or does it make people feel a little bit better, but it does not really cure it? *"The regulatory process to put a product on the market is different in these two situations. In the second one, you might have access to the market earlier. It might be cheaper, too, because development costs are cheaper, and they are the ones determining the price."*

4.Dycotomy between new and existing technologies. Another important problem regarding price is how good the new technology is compared to the already existing standard of care. *"In some cases, it might already be very good,"* **López says.** *"If we release something just a little bit better, but much more expensive, it is not going to work."* This especially concerns cognitive enhancement. Caffeine is a clear example. We could say that caffeine improves cognition, but if we invented something just a little bit better than caffeine, why would we buy it? It would have to be a truly revolutionary product for us to consider it a better alternative to what we now have.

5.**Access.** Cost will determine who has access to these technologies. If they are very expensive, then maybe only a few people will be able to afford it. If they are very cheap, they will be available for everyone. *"This has an impact on society,"* López explains. When something is very cheap and everyone has access to it, then we must face another issue: coercion. Would your employer make you use this new product for you to increase your productivity? If everyone is more productive when they use it, will you feel forced to use it as well? *"It is worth reflecting upon this type of coercion, because it is quite serious."*

02

Making Neuroscience Approachable

As we have seen, the study of neuroscience gives us truly valuable information about disorders and their treatment. Researchers, scientists, doctors, technologists and, overall, experts in the field, can use that information in their scientific studies and their labs to obtain an even deeper knowledge of the brain.

They are also drawing attention to the importance of making neuroscience approachable to citizens and their daily lives. They are the ones who fight to take neuroscience out of the lab and into society. The goal is not just to contribute new, valuable information on brain functioning in a more realistic setting, but also to find more useful applications for this science.

Taking this science out of the lab and into society

2.1

Devices

"I guess there are three things that everyone studying the functioning of the brain wants to do: understand the brain, manage mental health; and prevent, monitor, treat and cure progressive pathologies," **Ricardo Gil Da Costa** states. *"To do that, we need to move out of the lab. Obviously, there are lots of essential information and techniques inside a lab, but we need to create systems that people can use in their everyday life," Da* Costa adds. He has worked for years at the US National Institutes of Health and the Salk Institute for Biological Studies.

Da Costa has worked day after day on imaging techniques, precisely on electroencephalography (EEG). According to him, one of the main problems he and his team still face—one that is particularly frustrating—is that many of these techniques do not have solutions that can be applied outside the lab. Why? A home health device must comply with some requirements. *"It cannot be a commercial system: it needs to be reliable, affordable and easy to use for a large-scale audience; it needs to be reliable, but compatible with research techniques,"* Da Costa lists.

Ricardo Gil Da Costa
Neuroverse, Inc.

Duration: 8:52 min

Once outside the lab, when researchers want to have large-scale recordings, they must create different uses for the device, well beyond the compilation of data. For instance, a device that just sends data to a lab is a much less attractive option than a device people can use to know how many calories they burnt and how many steps they took. That feedback is what motivates users, who therefore use the device in a genuine way. *"We need to start developing ways to integrate them into our daily lives. We need to create actual use cases across pathologies and normal, healthy behavior. People need to use devices because they are beneficial in some kind of way, not because they provide researchers with data."* To do that, Da Costa believes they need to be reliable, but also customized. *"We need to create systems that we can adjust and adapt to each person so they find them useful,"* he states.

The ultimate goal in the use of these devices is to include performance, prevention and detection for early diagnosis of disorders and pathologies' progression and treatment. In other words, devices must be focused on two aspects of brain functioning: mental health (this is, medical pathologies) and mental fitness and prevention. To meet these two goals, Da Costa and his team have created a system called **Brain Station**, which is, in essence, an EEG wireless system. The device is placed on the user's forehead to scan brain activity.

This device has been found useful in patients with migraines. The team collaborated with the University of Lisbon in a paper where they explained that the patients took the system home with them and self-recorded for two weeks. In a nutshell, they were able to show that they can predict an upcoming migraine 24 hours in advance. Mental health patients (for instance, the ones with a generalized anxiety disorder) can also benefit from this device. Da Costa and his team have partnered with **Justin Feinstein,** a neuropsychologist at the Laureate Brain Research Institute. He's using an innovative technique based on the use of flotation tanks (sensory deprivation tanks) to do interventions on anxiety patients. *"We are able to record throughout the whole process and then explore different neurofeedback ways to compare it with that they have on the chamber."*

The team is also collaborating with the University of California San Diego, specifically with schizophrenic patients. The idea is to use the device to observe which brain markers are different in schizophrenic patients versus other individuals.

The placement of the device is one of the main challenges this research is facing. To address the different use cases of the devices, tracking different mental processes is essential, and that requires different placements for the technology. At least that is what Javier Mínguez, BitBrain's co-founder, believes. Da Costa recognizes this as one of the main challenges to monitor the full brain while leaving the smallest mark, or at least making the process as invisible as possible. *"Even so, the frontal device provides us with lots of information about the brain,"* he states.

2.2

Legal Implications

It's easy to understand the need to bring devices closer to people's daily lives. Some other aspects are not that obvious, but they still have an impact on the development of research and innovation regarding wearables. We're referring to privacy issues. A watch that monitors your pulse while you're running might be useful to adapt the physical activity to your needs and learn how your body responds. But that medical data about your physical condition could be very valuable for several advertising (or even medical) companies that might make money out of it.

This situation is quite new. It poses questions that **Amanda Pustilnik** tries to answer. *"So far, we have had privacy. We have been able to determine what we want to share and what we don't, because our brains are wrapped in this wonderful protective device: the cranium,"* Pustilnik explains. She works for the Center for Law, Brain and Behavior at the Mass General Hospital and the University of Maryland. However, *"one of the problems in the legislation of brain devices are brain-computer interfaces."*

Duration: 08:35 min

Amanda Pustilnik
University of Maryland Francis King Carey School of Law.

As brain monitoring devices and emotion recognition technologies become increasingly popular, we address issues such as how to allow third parties access to the information we generate, and if we can deny them that access. More specifically, Pustilnik uses the example of a person that we'll call 'Guy'. Let's imagine that Guy has bipolar disorder. He uses brain-computer interface devices for gaming, sleep tracking and meditation. These devices pick up information on him, his state and his traits all the time. *"If these devices are used in a positive way, I guess they can compile information that shows how Guy is headed towards a maniac episode. That information could be used to alert either him or the people in his network to whom he has previously authorized, who could step in and help him, or at least intervene early to mitigate the effects of the episode,"* Pustilnik claims. Maybe the device can also communicate directly with Guy's healthcare providers.

However, this information can also be used in a negative way. For instance, if the information is sold to data brokers, for instance, that then make it available as a product or as a service to other companies. In that case, Guy might start seeing ads for online gambling, expensive luxury goods or high-risk financial products. These are the kinds of things he will be so much more prone during a manic episode, and that could in fact precipitate or exacerbate it. *"The fact that data is available to data brokers, for example in our social media, is a foreseeable misuse,"* Pustilnik states.

Let's go one step further: data compiled by these systems could be used by employers or law enforcement to make hiring, screening and promotion decisions. Pustilnik believes this opens the door to misuse and bad use. *"By 'misuse', I mean taking data and using it in non-rigorous ways, but attractive as a shortcut for decision makers. And by 'wrong usage', I mean the use of information that could be scientifically legitimate, but socially or regulatorily objectionable and harmful to the other goals of society that we value. So, the conventional legal responses might be privacy law, consent and anti-discrimination law,"* she states.

This is a complicated problem to solve, and so are its solutions. Privacy is problematic, first of all, because no one is truly sure about what it means or what it protects. *"It can also be overly constraining. If our answer is This data has to be in a closed loop system and it has to be purged every night', that limits the opportunity for Guy himself to engage in these potentially productive uses of the data with his provider or for his healthcare. It also limits the future development of other technologies,"* Pustilnik believes.

So far, those in charge of regulating this situation have decided that one solution could be to compile data only when people consent to it. The famous privacy terms and conditions. However, Pustilnik thinks that *"consent is inadequate as a model, legally, because we usually don't know what we're consenting to."* It's not just that no one reads the endless privacy terms and conditions before accepting them: it's also that we don't know what will happen with that data. *"I consent to have my brain data monitored by this game I want to play now. But I'm not thinking that five years from now, there could be a warrant for that data from a law enforcement agency,"* Pustilnik explains.

Given the situation, what should we do? "*We're left in a moment right now where we don't have any really good legal models for dealing with this,*" Pustilnik acknowledges. She suggests considering the situation from three different perspectives.

- Individually. We should be aware of the positive and negative uses of brain data and make good choices, as consumers, to the best extent that we can.
- As technologists, designers and investors in technology. We need to agree to principles that drive independence and are person-centered.
- Legal and regulatory. We need to try and determine the antidiscrimination paradigms that we want for this type of data, so that we don't wind up recapitulating with brain data the forms of discrimination and determinism that we've tried to prevent in other realms.

Given the fast development of these devices, regulatory bodies have started working already on the implementation of regulation to organize the current situation. **Roland Pochet,** secretary general of the Belgian Brain Council, knows quite well the European Union's situation regarding regulation and policy enactment. Pochet assures that, according to the experts he's been in touch with, trust is key to policy enactment. *"The EU'S Directorate-General for Health believes it is a major issue. If there is no trust between companies, if there's no trust between the academia and the industry, things won't work at all. Solving this lack of trust is essential,"* Pochet explains.

Roland Pochet
Belgian Brain Council

However, our expert highlights the importance of the culture we legislate in. *"In Europe, we are fragmented in cultures with rules, standards, controls and strategies. A safer European Union will depend far more on a major cultural change than on a new regulatory regime,"* Pochet states.

Despite this statement, Europe has been developing a General Data Protection Regulation for the last few years, which was enforced on May 25, 2018. This new regulation promises to dramatically change the way in which companies process our information, and it is the strictest data protection regulation there is. It aims to protect citizens' privacy and give them more decision-making power.

This legislation aims to protect citizens' privacy and give them more decision-making power

This legislation regulates how companies utilize the user data they collect. For example, the regulation allows us to request that our personal data be erased when the company no longer needs it or if it had been collected illegally (without users' consent). However, consent is not enough. *"Consent as a key to data processing is losing relevance because it has been proven that we don't understand what we're consenting to, or we don't even read it,"* says **Raúl Rubio, director of the data protection program at IE Law School** [link in Spanish]. Most times, privacy terms and conditions are too hard to understand, or they're explained in a convoluted way.

Rubio adds an interesting fact: *"The legislators' concern is that our data is not used in an abusive way, but that could lead to us–not just companies– being the ones benefitting from our privacy or, rather, lack thereof."* The massive amount of data collected by companies and governments nowadays entails significant challenges regarding citizens' privacy and security. *"People should have control over their data and know what is being done with it, and now's the time to make that possible,"* says **Alex Pentland, director of the MIT Connection Science and Human Dynamics Lab** [link in Spanish]. *"We have to express our rights as users, so we can prevent the misuse of our data."*

This regulation is facing the challenge of addressing different regions. The General Data Protection Regulation (GDPR) is a step in the right direction, but since it is an exclusively European regulation, it is not enough to address a challenge that spans borders.

2.3

Applications in Society

2.3.1

Neuroscience in the Classroom

The study of the brain generates a large amount of data that can be applied in different areas of society. One of those areas is education: *"The main goal of neuroeducation is to close the gap between neuroscience and education,"* says **David Bueno**, director of the Chair of Neuroeducation at the University of Barcelona. According to him, the goal is *"to bring all data we have on the human brain, understand the way the brain acquires new knowledge, and use that to optimize and enhance children's capabilities."*

David Bueno
Chair of Neuroeducation at the University of Barcelona UB-EDU1ST

Duration: 09:02 min

So, understanding how the brain analyzes and draws conclusions about the world might be extremely useful in the optimization of learning processes in the classroom. One of the main functions of the human brain is to learn from the environment to adapt to changes. How do children do this? *"We have observed that children in the preverbal stage before they start talking, use some philosophical reasoning systems to anticipate what is going to happen,"* Bueno explains. *"For example, they use a philosophical paradigm called 'disjunctive syllogism'. They also use the scientific method to analyze the environment."* Understanding this, how children use their brains (even in developmental stages when they haven't started talking yet), could help teachers optimize their job and the children's education.

Education professionals should also take into account the functions of each part of the brain. The brain develops and matures over time, from the embryological stages throughout our whole life. If we understand which areas and regions of the brain are maturing at each stage, we can take advantage of that to provide the students with the best possible education. *"That includes the cortex, for instance, where most of our reasoning processes are based on, but also the limbic system, which includes the hippocampus for memory and the amygdales for emotion,"* Bueno claims.

The limbic system is essential. It has been proven several times that emotions are crucial to learn. They make learning much more efficient. In an interview with El País, José Ramón Gamo says, *"Our brains need to get excited in order to learn."* Gamo is a child psychologist and the director of the master's degree in Neuroeducation at the Rey Juan Carlos University [link in Spanish]. Gamo and his team used proprietary as well as external scientific research to conclude that, in order to acquire new knowledge, the brain tends to process data from the right hemisphere, which is related to intuition, creativity and images. Gamo adds, *"In those cases, linguistic processing is not the main actor, which means that talking does not work. Facial expressions, body language and context play a very important role."*

But the information we obtain from studying the brain poses some ethical questions as well. *"Of course, all the students are genetically different: some students are more prone to creativity, empathy, working memory... every mental process that you can imagine has a reflection in our genes,"* Bueno explains. Taking into account that there are differences, the same education system is not useful for all students.

"The question is, what should be the main aim of education? What are the ethical limits when enhancing cognitive capabilities? What are the limits when tracking brain function during learning? Some schools have started tracking their students' brain activity during the learning process. Which capabilities should be enhanced from a medical, educational and humanistic point of view? Where is the line between normal and atypical?", these questions remain unanswered.

"The main goal we strive for in my Chair is to help people grow with dignity," Bueno sums up. What does 'with dignity' mean? He's referring to social issues, to giving everyone the best possible opportunities to learn and get to know themselves. *"These are some of the principles behind the idea of dignity: understanding the origin of biological differences and the way the brain acquires new knowledge. Giving everyone the best opportunities to develop cognitively as much as possible. Enhancing these cognitive*

capabilities in an ethical way, always understanding that ethics depends on each society."

The brain is flexible and constantly creates connections, so the capacity level can be improved by using said flexibility to create new connections that are adapted to the children's genetic capacity and developmental stage. These strategies have an impact on brain connections; they influence the mental life the person will have in the future. Therefore, it is important to define the goal of education, just like Bueno suggests.

▪ We will need to design education strategies based on the new brain connections

What are the major challenges of this approach? One of the main problems is to translate all neuroscientific information into educational, pedagogical systems. *"First, most people involved in pedagogy have no idea about the brain,"* Bueno explains. *"I think it's very important to design new pedagogical strategies. Pedagogues should learn about neuroscience, just like teachers. This topic should be present in schools."* Bueno believes that education professionals should know how the brain of their students work, because that's what they work with. *"They should have basic knowledge, like executive functions, emotions, memory, maturity processes... so they can adapt the education system to each specific situation."*

2.3.2

Neuroscience in the Workplace

In the last few decades, constant research in neuroscience has revealed major ideas about brain functions that have different applications at work, such as memory, thinking and emotions. If we can apply the knowledge that we have about these functions to our day-to-day work, it could help us manage stressful situations and prevent worker burnout. The latter is already included in the World Health Organization's (WHO) International Classification of Diseases (ICD-11). The emotional burnout syndrome, as described in this new classification, is associated with chronic workplace stress. It is characterized by increased mental distance from one's job, physical and emotional burnout and reduced professional efficacy. Experts estimate that burnout affects 10% of workers, and between 2% and 5% of them suffer from the most serious forms of burnout.

There are many reasons why workers might develop this syndrome. Emotions are one of them. Several neuroscience research projects have proven that mood is contagious when people share experiences and spaces for an extended period of time. According to the Official Association of Psychologists, stress is contagious; people who suffer from stress tend to work in the same groups. A research project led by several German universities found that 26% of people suffer an increase in their cortisol levels just by observing a tense person.

Daniel Goleman is a psychologist, anthropologist, journalist and a prominent figure in the field of emotional intelligence. He analyzes how this contagion happens among a company's top management and its employees as well as the potential impact on the company's performance. In his latest research, Goleman found that, of all components that affect final performance, the leader's mood and behavior have a strong influence.

Who is responsible for this relationship between a leader's emotions and their employees behavior? The **limbic system**, a brain structure that is the emotions management center in humans. It is an open system whose management depends on external sources. What happens in the world around us conditions our limbic system's activity. Our mood is determined by our connections with others. Research in neurobiology claims that people transmit signals that can alter other people's hormonal levels, cardiovascular functions, sleep cycles and immunological functions. This emotional contagion happens unconsciously, unless we develop the necessary tools to manage work relationships and teamwork, therefore mitigating our responses. Neuroscience can help.

▪ Neuroscience can help us manage work relationships and teamwork

This research is relevant because many corporate areas still believe that emotions have no place in business, even though they are as important to human functioning as any of the so-called rational processes. A recent study provided illuminating information on the costs of emotional suppression, which is still a normal tactic in most workplaces. When we contain our emotions, the resources involved come from the very same brain region that deals with problem solving and analytical thinking. This can affect our productivity. The implications of these findings in the workplace are fascinating. When we are busy suppressing our emotions (sometimes we call this 'being professional'), we're not only denying our own psychological experience, but also damaging our cognitive functions.

Knowledge on neuroscience might also improve problem solving and teamwork. Many research projects call attention to the fact that cognitive diversity has proven to be crucial to teams' efficiency. It is about the way employees think, how to approach a problem and the way in which we process data and grasp things rationally. **The most recent study has been conducted over the last 12 years**, and it concludes that teams composed of people who think in divergent ways solve problems faster. Mental frames are established during childhood, and they are independent from education, culture and social status, although they are related. A lack of diversity reduces our ability to see things from a different perspective, interact in a different way or create new alternatives. This may take a toll on innovation. To overcome these challenges, companies need to make sure that their employee-selection processes prioritize the cognitive differences among recruits.

Attention is another mental process that plays a determining role in the workplace. Full attention has proven to be very useful in improving concentration and efficiency in the workplace. **A team of researchers from the University of California** describes full attention as paying attention to feelings, present emotions and body sensations. As a result, the amygdala is less active and emotions are less intense. Other studies show that full attention has significant benefits in reducing stress and anxiety.

These new findings about the brain and its effect on our well-being and work performance are very promising. But, according to experts, companies still need to get involved and include this information in their organizations and work dynamics.

2.3.3
Neuroscience in Business Areas

Another work-related field is the application of neuroscience to different departments inside a company, such as neuromarketing or behavioral economics, as well as new disciplines such as neuroarchitecture. Findings in these disciplines determine a company's business development and help it meet clients' needs.

Neuromarketing

Neuroscience applied to the study and analysis of consumer behavior. This application has gone beyond the academic field to burst into the corporate world and address the general public. To slightly broaden its definition, we could say neuromarketing uses neuroscience findings to analyze, understand and predict people's behavior regarding the market.

▪ Neuromarketing is neuroscience applied to the study and analysis of consumer behavior

It seeks to understand how the brain activates in response to stimuli generated by marketing techniques, in order to **identify brain activity patterns that show more information than that is which is revealed by consumer behavior.** According to neuromarketing studies, consumers' purchase decisions are not entirely based on incentives such as price or product. They are, to a greater extent, based on emotions that finally lead them to buy.

According to the review Neuroscience and neuromarketing. Literature review on the relationship between neuroscience, marketing and economics, [link in Spanish], disciplines such as economic, statistics, mathematics, psychology and anthropology collaborate with neuroscience to learn about consumer behavior. Roberto Álvarez del Blanco, an expert in neuromarketing, explained back in 2011 that if we want marketing to be effective, it needs to respond to consumers' needs, aspirations, frustrations, impulses and deep emotions; consumers usually make decisions in an irrational, unwitting and impulsive way.

He also points out that neuromarketing, based on the study of brain functioning, contributes to a better knowledge of the stimuli that condition market decisions. According to Braidot (2005), neuromarketing fundamentally seeks to analyze the neural complements in purchasing processes, brand familiarity or product preference to clearly understand how and why consumers make their choices and, most importantly, to know consumers in a reliable, anticipated way.

More specifically, neuroscience allows us to know how the nervous system translates most of the stimuli it is exposed to. It allows us to predict consumers' behavior when faced with those stimuli to identify the best format and the most efficient means that will help the potential consumer remember the message easily.

There are increasingly more companies that apply neuromarketing as a key to understand consumer behavior in order to be more efficient in their relationship with consumers.

Neuroeconomics

Neuroeconomics, yet another field, is also related to the previous point. Lately, neuroscience has been applied to the study of the neuroanatomical and neurophysiological bases of economic behavior. It seeks to use our knowledge on brain functioning to better understand the financial and economic decisions that consumers make. Therefore, professional economists study the behavior of consumers' brains using imaging technologies such as magnetic resonances in order to learn how they reacted when presented with different stimuli or actions. Neuroeconomics studies brain activity during economic decision-making processes.

> Neuroeconomics uses knowledge on brain functioning to better understand the financial and economic decisions that consumers make

Some of the questions that drive neuroeconomics are related to issues such as why we choose a specific option out of two equal ones or why our economic behavior differs despite the existence of rational models that can predict it. One of the decisive milestones in this variant of neuroscience came from Daniel Kahneman, psychologist and author of several best-sellers and winner of the Nobel Prize of Economics in 2002. Kahneman states that our economic decisions are less rational than we think they are and that we don't always choose the most logical option.

There are different mechanisms that affect these decisions, such as the reward system that is activated when we find something enjoyable or the aversion system that is activated when we want to avoid negative consequences. On the other hand, the effects of hormones such as cortisone, testosterone or oxytocin set the balance among risky, greedy and prosocial decisions. Knowing how these systems work, what activates them and how they affect our behavior, is essential to understand citizens' economic behavior.

According to current research, emotions drive both engines virtually every time. Tens of studies show that when there's damage in the brain regions that connect the limbic system (responsible for stimulating basic emotions) to the prefrontal cortex (responsible for planning), people find it harder to make optimal or coherent decisions. This means that they make decisions that go against the concept of economic rationality, which is about choosing among different alternatives by taking into account objective data such as cost and value.

Knowledge of the different neural functionalities and the role they play in several brain systems in decision-making might be a determining factor in explaining risky economic transactions and even the creation of bubbles. To understand these processes, we need to consider that expectations and emotions such as fear and greed affect economic predictions. If we want to make a prediction, we need to have all this neuroscientific information.

Neuroarchitecture

This subfield of architecture uses neurophysiological data, such as electrocardiograms and electroencephalograms, to measure in real time the brain's response to different architecture-related stimuli. This means that buildings are based on the present or future inhabitants' emotions and the architect's desired effect.

> Neuroarchitecture designs taking into account how the brain reacts to the building

"It is complicated to explain the scientific component to a client. It is not very common to tell them about encephalograms or skin sensors that measure sweating. We want to create objectivity with the emotions that a specific material provokes. We want to go beyond their personal taste," says Antonio Ruiz, a neuroarchitecture specialist at ARK Arquitectos.

No one has written the rules of neuroarchitecture yet. However, thanks to previous research, neuroarchitects have detected some common behavior patterns that people display when presented with specific stimuli. For example, the knowledge that optimal thermal balance is essential for well-being or that abrupt changes generate hostility are essential to designing homes that match their residents' needs.

Likewise, natural lighting and plants affect melatonin and sleep quality. Natural fragrances such as citrus reduce stress. Something similar happens with blue and teal colors. Even the use of curves helps people relax much more than angular spaces.

Putting neuroarchitecture into practice generates a massive amount of data. Both big data and machine learning have become two essential tools. They help identify emotions in lines and numbers and interpret the results. Recorded signals might be hard to interpret for the architects. These new technologies make traditional metrics understandable.

Neuroscience then becomes an additional pillar that supports architecture. The trend of incorporating neuroscience and applying it to different disciplines keeps growing. In Spain, more and more companies leverage neuroscience to develop their businesses. In the United States, even universities have included neuroarchitecture in their course catalog.

2.3.4

Living with a Mental Disorder

We have already seen that some aspects of neuroscience might change society thanks to what we know now about the human brain and its functioning. Every day, there are new advances, so it is interesting to think about how new knowledge might change the life of people with different needs in the medium term. The experts gathered at the Future Trends Forum tried to predict how a day in the life of a patient with schizophrenia, Alzheimer's or Down syndrome could change.

> How new knowledge might change the life of people with different needs in the medium term

Charles Bolden
NASA & The Bolden Consulting Group LLC

Early intervention in schizophrenic patients. Currently, the quality of life of schizophrenic patients largely depends on the type of disorder they have. Some disorders are incapacitating while others allow patients to lead normal lives. In the most serious cases, day-to-day life can be very difficult, particularly regarding integration in society. Symptoms might make working or maintaining close relationships difficult. Also, the medication that is currently available may have detrimental side effects, as pointed out by **Charles Bolden,** former NASA administrator.

That is the starting point. But taking into account the progress we are observing in the field of neuroscience and the evolution of technology, experts predict that the day-to-day of a schizophrenic patient will dramatically change. Thanks to the improvement of biological interventions, schizophrenic patients will *"have it easier to get out and socialize with others. They will be better integrated in society."* Also, their caregivers will have more technological tools available to help them, and, as experts predict, cognitive enhancement medication could help patients concentrate better.

> We will be able to know how the disorder affects each person in particular

One of the points that could make a difference is personalized treatment—not in finding a cure for the disorder, but rather in knowing how the disorder affects individual patients. The progress we make in terms of knowledge and techniques will help us diagnose the disorder earlier, and the tools to manage it will be more useful. An early diagnosis will facilitate early intervention.

More integration for people with Down syndrome. Today, some people with Down syndrome still have problems finding a job or integrating in social groups, even though there are hundreds of stories that prove they are perfectly capable of leading a normal life. According to experts, neurotechnologies could help those whose capabilities are particularly affected by the syndrome.

These advances will be key to help them increase their cognition, maintain attention and solve problems, which will directly impact their quality of life. It will help them be more independent and integrate better in their social environment, and they will therefore contribute more to society. By applying neuroscientific advances, experts anticipate that people with Down syndrome will no longer need to worry about being discriminated against at work and that other people will acknowledge the perspectives and unique skills that people with Down syndrome can contribute to projects and their jobs.

New treatments for Alzheimer's disease. Currently, Alzheimer's disease is the most common form of dementia. It accounts for about 60%-70% of cases. Furthermore, according to the World Health Organization (WHO), dementia is one of the main causes of disability and dependency among the senior population across the world. And, since it can be prevented, researchers keep working to find out how to treat it.

Experts predict that during the next few years we will be able to conduct a better assessment and early diagnosis of the disease, which will allow us to implement preventive measures. Also, the use of wearables and technologies such as machine learning will improve the management of the disease and its symptoms. Experts also strongly believe in immunotherapy, neuroimaging advances and the discovery of new biomarkers.

But society will not only see progress in treating diseases or improving patients' quality of life. We will also see progress in the cognition and work performance of healthy individuals, such as ER doctors. The emergency room is a very stressful environment and often times entails a huge workload. Experts predict that we will be able to use robots, which, thanks to artificial intelligence, would be able to conduct an initial assessment of the patients and classify them by the urgency of their treatment.

Also, we are currently making progress in developing software that can detect abnormalities in scanned images. The most recent example is an algorithm developed by scientists at the University of California. It has achieved better results than two out of four radiologists in finding small brain hemorrhages in scans. According to the scientific magazine PNAS, this could help doctors treat patients with traumatic brain injuries, cerebrovascular accidents and aneurysms.

To monitor doctors' performance and heath, we have wearables that measure doctors' well-being and tell them if they need to sleep, if their attention is decreasing or if their sugar levels are less than optimal.


MINDMAP
What will the impact of
SOCIETY

03

Cutting-Edge Technologies

Today's digitalization process has completely changed the way we connect with the world. The way we communicate, work, move in our environment and meet new people–all of this has changed thanks to the arrival of new technologies and the exponential development of technologies that already existed but have grown due to the evolution of the Internet.

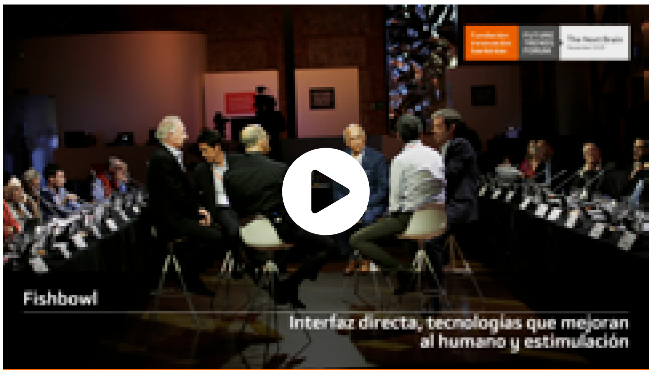
The field of healthcare has been particularly impacted by new technologies like artificial intelligence, big data, virtual reality and new imaging techniques. Neuroscience is one of the areas that has been most impacted by technology. For example, thanks to new techniques in the field of neuroscience, brain observation is as detailed as ever; brain-computer interfaces enhance our performance, and we can even create machines with feelings thanks to artificial intelligence. The development of computing and big data, together with the arrival of virtual reality, nanotechnology and DNA sequencing machines (among other technologies), are redefining this science. Now, on top of understanding the way human brains work, we also need to take into account what we learn from machines and their capacity to analyze and predict information, such as neural connection patterns.

It looks like this is just the beginning. *"We will have a very powerful evaluation and intervention systems thanks to emerging technologies,"* says **Walter Greenleaf**, our expert in virtual and augmented reality from Stanford's Virtual Human Interaction Lab. "*They will play a significant role in our lives in the future. First, they will change communication platforms, then entertainment platforms, then the way we work, how we interact with technology… This will result in both clinical and research applications.*" Experts at the Future Trends Forum talk about the improved tools used in the study and analysis of neuroscientific data: machine learning, new computational approaches, the network analysis mentioned by **Alex Fornito** or the modeling and prediction of all brain synapses that **Sean Hill** explains. Other experts talk about analyzing signals with an EEG, through forehead patches or body sensors; they mention neural dust and other types of brain-computer interfaces.

- Neuroscience is impacted by new technologies like AI, big data or virtual reality

Even though they are independent, these disciplines are related and studied together. Wearables are useful because they are connected and compile information that they analyze and draw conclusions from thanks to artificial intelligence, which is also embedded in brain-computer interfaces. All these technologies have great potential to detect and treat disorders or enhance the capabilities of healthy individuals.

Walter Greenleaf
Stanford Virtual Human Interaction Lab



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3.1

Artificial Intelligence

Computers are not only used to understand brain data and information about the brain. The brain is actually used as an inspiration to develop artificial intelligence. Among other things, AI is widely used to help experts personalize treatments. **Ricardo Gil Da Costa** is a cognitive neurophysiologist who has worked for years at the US National Institutes of Health and the Salk Institute for Biological Studies. He affirms that *"the more data we compile, the more we can personalize patients' treatments."* By applying AI to the data we compile, we can find patterns and connections that we cannot appreciate on the surface.

Da Costa uses a practical case as an example. He and his team have been able to determine that neurovascular inflammation preceding a migraine increased between 6 and 72 hours before the initial onset of symptoms. This means that we can act earlier and reduce the duration and severity of the crisis. *"This makes us think that it would be really helpful to develop a non-invasive device that patients can use at home every day to analyze their organism's information; they could personalize it and find out when a crisis is coming in their specific situation,"* Da Costa explains.

This is already a reality thanks to the Internet of Things. By adding artificial intelligence to the equation, the device can learn about each individual patient. Da Costa states, *"we would go one step beyond if we could use the device to compile information on sleep (which affects virtually all neurological and psychiatric disorders), and we could connect these data to existing data to correlate them... then we would go one step beyond."*

> AI's data analysis will allow us to learn about each individual patient

Ng Wai Hoe is the medical director at Singapore's National Neuroscience Institute. He also works in a research group that applies artificial intelligence and machine learning to results obtained from magnetic resonances. Research teams all over the world have developed algorithms that can analyze thousands of resonances and detect alterations in them, to the point doctors in the right direction.

This is precisely one of the applications that **Ng Wai Hoe** promotes. How can AI release us from routine, mundane work and let us do the most complex, sophisticated tasks? There are many projects that focus on researching how artificial intelligence can be used to interpret images in traumatic brain injury and brain tumor cases. *"Regarding traumatic brain injury, our goal is to allow AI's paradigm to do a quick triage of the image. Then, it marks it up and tells the radiologist they need to look at the image immediately,"* **Ng Wai Hoe** explains. *"We have actually already started applying it in our emergency room to observe how integrating this software with imaging techniques leads to faster patient triage and more immediate intervention."*

This application seems useful, but it also sparks debate. The fear that machines will replace humans has been festering for many years, and those that are more skeptical do not believe that machines will function adequately. *"A very common misconception about artificial intelligence and its applications to magnetic resonance interpretation and neuroimaging techniques is that, oftentimes, we conceive this as a human versus machines issue,"* **Ng Wai Hoe** points out. *"It would be more accurate to think about it in terms of humans and machines versus machines themselves."* In other words, cooperating with machines and leveraging the advantages they offer.

3.2

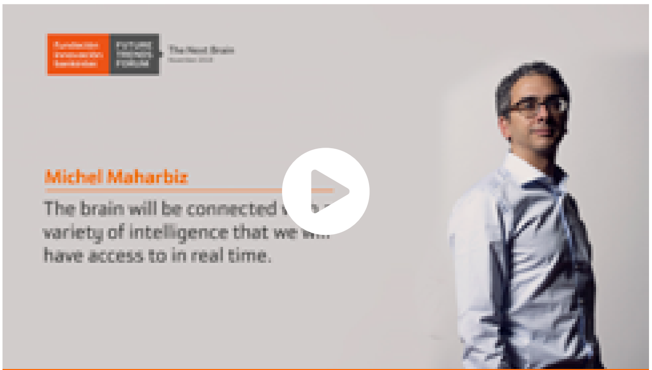
Brain-Computer Interfaces

Some of the most promising, cutting-edge technologies in the field of neuroscience are brain-machine interfaces. They are devices that capture brain waves to later process and interpret them in a machine or computer. This technology allows the human brain to communicate with a machine, which paves the way for interacting with technology through our thinking. Many projects are already studying the development of brain-computer machines. The most well-known project is that of tech entrepreneur Elon Musk, through his company Neuralink. This project focuses on the development of an interface to connect sensors to the human brain by sewing them on with microscopic threads. These threads will enable communication between different areas and with the outside.

> Some of the most promising, cutting-edge technologies in the field of neuroscience are brain-machine interfaces

Operating a machine with our brain is one of the most interesting applications that Neuralink promises. However, the extended use of brain-computer interfaces could significantly improve the study of brain connections and the compilation of information on neural functioning. Even so, this technology faces a huge challenge going forward. *"Today, there is not one single implantable neural interface that lasts for an acceptable period of a person's lifetime,"* **Michel Maharbiz** points out. He is a professor at UC Berkeley and the cofounder of a company called Iota Biosciences. The other cofounder is **Jose Carmena**, an electrical engineering and neuroscience professor at the same university. *"It is a fundamental fact that determines clinical studies, and it is still unsolved."*

Michel Maharbiz
iota Biosciences & University of California, Berkeley



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Maharbiz points out that all companies, including Neuralink, are trying to solve this. Maharbiz and Carmena's contribution was founding their company, Iota Biosciences, which produced what has been called 'neural dust.' It consists of tiny, wireless brain implants that can monitor muscles, organs and nerves deep inside the body in real time. They could treat disorders such as epilepsy and also, in the future, control prosthetics. These neural dust sensors communicate through ultrasound with a patch that activates them and receives information for any specific therapy. Their promoters believe they could be implemented in just a simple outpatient procedure, in the same way someone gets a piercing or a tattoo, according to Agencia Sinc [link in Spanish.]

"We have been dreaming for a very long time about having very small, completely wireless implants, completely unconnected. They would be great for diagnostic purposes, for recording brain states or for the neuromodulation of peripheral nerves because they would be able to focus on small nerves and specific brain processes," Maharbiz explains. *"The right way to do that is through the physics of ultrasound. It allows you to drive and build a bidirectional communication interface with items that currently measure just a few millimeters."*

Jose Carmena
iota Biosciences & University of California, Berkeley

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The researcher compares this to the idea of placing a Fitbit bracelet (which monitors the user's sport activity) around the liver. *"This means going one step beyond brain states and peripheral modulation,"* Maharbiz explains. What would happen if you were prone to developing fatty liver disease because you have the genotype, and you know you're at risk? *"At Iota, we put a spot in the portal vein that monitors oxygen levels coming from the liver as well as the liver's state every morning. Then, it beeps, and you take your medication. A wearable device cannot do that."* The question is, when will we get to the point when something like this is minimally invasive and transparent enough? According to José Carmena, on top of the technology used to develop these interfaces there is a second block of artificial intelligence and machine learning. It compiles information about the functioning of internal organs and acts accordingly.

"We can learn the most significant principles about how the brain learns new skills. We can use those to empower a healthy individual and give them more control, more freedom in the world, in a more or less invasive way," Carmena explains. *"We can also use them to help people with disabilities, which is what brain-computer machines are used for today."*

"Brain-computer machines and their applications are rapidly expanding in the field of mental health and are called 'mental prosthetics' in that area," Carmena says. This field is growing very fast in order to leverage all the knowledge provided by these technologies and to take advantage of what experts can do with these closed systems to treat psychiatric, neural disorders in a completely different way than they could pharmacologically.

> Brain-computer machines and their applications are rapidly expanding in the field of mental health

"It is, essentially, mapping out the patient's physiological systems and identifying the nodes in the network that cause specific disorders, such as post-traumatic stress disorder, anxiety or depression. Then, we apply an intervention such as stimulation, for instance, to alleviate the patient. Maybe the goal in the long term will be to cure, to unlearn said disorders," Carmena explains.

However, is it possible to cure these disorders? **Mustafa Husain** is a professor of psychiatry, neurology and medicine. He points out that, as we have seen, neuroimaging techniques tell depression, schizophrenia and anxiety apart. *"Once we understand those neural systems and their mechanisms, as well as the cause of those problems, then the possibilities are endless,"* Husain states.

3.3 Virtual Reality

Virtual reality is well-known for its applications in the entertainment industry. Little by little, we immerse in new worlds to consume cultural content (such as concerts or exclusive movie content), but above all, we play videogames. The main criticism in these cases has to do with image quality and loading time: the content needs a large processing capacity to meet the expectations. However, these handicaps are minor in the healthcare field.

So far, there are several projects dedicated to the development of programs to apply this technology in hospitals and healthcare facilities. Hospital Universitario La Paz launched the VTR project [link in Spanish] to improve psychological assistance for minors undergoing transplants as well as their family members throughout the entire treatment. *"It is essential to prevent children from living in stressful situations. Sedation or IV drips are a clear example. Virtual reality helps us teach them and makes everything easier,"* says Erika Guijarro, director of the initiative, in an interview with El País Retina [link in Spanish]. The initiative focuses on three goals: prevention, distraction and awareness. Hospital La Princesa, in Madrid, has also started a clinical trial that applies immersive virtual reality to multiple sclerosis patients undergoing rehabilitation. Around 50 people use special glasses with programmed exercises to optimize their time at home.

One of the world's leading experts on this technology is our own **Walter Greenleaf**, a scholar from Stanford University's Virtual Human Interaction Lab. *"I was honored to be involved in the very beginnings of virtual reality over 33 years ago. In fact, I participated in the discussion on what to call it,"* Greenleaf claims. *"I am against the term 'virtual reality', I think it's too simple. I supported giving it a very scientific name. I have been working on the field of technologies for virtual and augmented reality and their applications for many years."*

Greenleaf is also a behavioral neuroscientist who does basic research on new interventions for depression, autism, Asperger's, and addiction. He also works as a medical product developer, trying to transfer some of the neuroscientific results onto new products. With this wide experience, Greenleaf focuses on virtual reality's application to the medical field. *"We can take some of the lessons learned from gamification and apply them to medical interventions to promote adherence and engagement."*

Virtual reality is a powerful tool for research and intervention

"When treating an addiction, we can offer the patient a virtual setting to practice their rejection skills or their situational confidence. With autistic patients, we can rehearse social interactions and exaggerate non-verbal communication, body language, facial expressions…," Greenleaf explains. There are multiple ways in which this technology can be applied to help patients recover.

"Virtual reality is a powerful tool for research and intervention", he adds. It can contribute lots of social information on how we behave. *"We also capture people's small movements (micromovements) in order to understand some of the most basic interpersonal dynamics. Not just to understand how people interact in those specific situations, but how large groups of people work."*

Initially, virtual reality was perceived as something exclusive to gaming environments. However, now it has moved into the corporate area, where big tech players have invested billions of dollars in development. *"They're not going to recoup that investment through the gaming and entertainment industry,"* Greenleaf states. *"The medical field is making some of the greatest investments in this area."*

3.4

Wearables

There's more beyond sport devices that compile data such as our pulse, respiratory rate or body fat. In the healthcare field, wearables have become much more sophisticated and professional. **Didier Stricker** leads a group that focuses on augmented vision at the German Research Center for Artificial Intelligence. The team is specialized in the development of algorithms and machine learning methods for the processing of images through artificial vision and body sensor networks. Currently, some members of the team focus on autonomous driving, while others deal with perception or artificial vision and augmented reality.

Didier Stricker
University of Kaiserslautern & German Research Center for Artificial Intelligence

All this information can be transferred to wearable devices that help us, for example, understand how patients move. *"We try to go from traditional augmented reality to 'cognitive augmented reality', as we call it,"* Stricker explains. *"How do we get that information and how can we deduce someone's intentions? We have developed several techniques,"* he adds. *"We place around 20 body sensors and try to capture people's behavior. We also use a camera to see how they do things. The system is similar to a robotic system."*

It helps obtain information on the users, on how they do things, like repairing an item or even playing golf. *"We capture their experience or skills and digitalize them, so we have plenty of data,"* Stricker says.

All the information compiled by the sensors helps them interpret what people do. *"Once we know what they're doing and what others have done before them, once we know the workflow, then we try to deduce the intentions,"* Stricker says. The body sensor network captures people's biomechanics. *"There is lots of machine learning behind that; we try to learn by leveraging data."*

Today, thanks to all the information that wearables compile, we can observe fatigue and exhaustion. *"And we would love to be able to detect depression from our data."* In order to be more precise in their diagnoses, now they are working on making wearable devices that record more precise, smaller neurological signals and include physiological data. *"The idea is to use them to create improved assistance systems and new therapeutic systems."*

> Neurowearables could capture intention, reaction and emotional state

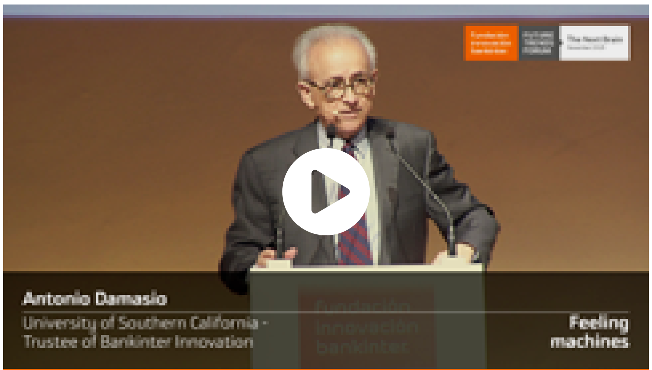
This system can form a set of emotion sensors that could capture intention, reaction and emotional state. *"We managed to make them so small that you can wear them on your clothes. We took technology out of the lab."* In order to do that, they have used different techniques. *"One of them is self-calibration. You have the sensors on; they start working, and everything calibrates automatically. We have managed to make them stable for hours, not just minutes."*

Mustafa Husain wonders if this system might help researchers develop specific sensors for particular disorders, such as panic disorder. *"It is a very specific disorder: rapid breathing, accelerated pulse, increased heart rate... and the earlier we identify it, the better we can treat it."* Indeed, Stricker's group has started working in that area. *"The body sensor network we've developed allows us to obtain a person's kinematics with a great level of detail. Now, we are focusing more on physiological sensors,"* Stricker explains. *"We need to combine this information with more behavior-oriented systems."*

3.5

Machines with Feelings

The most innovative proposals in artificial intelligence all have something in common: they try to go beyond the use of machine learning to analyze enormous amounts of information. They also venture into researching the most human aspects of artificial intelligence. A clear example is designing machines that are able to feel emotions or that are aware of their own existence. **Antonio Damasio** has recently published a paper where he explains this project. The idea is to develop machines that can feel, have feelings and, therefore, consciousness.



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Damasio explains that, in the beginning, he was agnostic regarding this issue. He said, *"I love machines, but they'll never be like me, they'll never have neither feelings nor consciousness."* But then, he and his team started thinking about deeper questions. Why don't we make vulnerable machines? Machines with feelings could be useful in two different aspects: first, as experimental testing platforms, a way to study human feelings and consciousness outside the human body. Secondly, they were hoping to create something quite intriguing, an even more intelligent machine. *"What living machines do is worry about their own life and protect it unconditionally."*

"For a long time, I've said that if we wanted to destroy a machine (especially a robot like the ones we have today, built with invulnerable, hard materials), we would need to split it with an ax blow." Damasio says. *"Those machines are not going to have feelings and, therefore, will be deprived of the possibility of feeling, which entails the possibility of having consciousness as well."*

Creating more intelligent machines that, by having the possibility of feeling, can have consciousness

That is why Damasio believes in the development of soft robots, made of hyperflexible materials, that can twist, bend and stretch. In rigid robotics, the material's flexibility is reduced to increase precision and power. However, soft robotics favors a safer interaction with the environment. Because of their composition, soft robots are very useful for any activity related to interacting with human beings.

In addition, Damasio's proposal includes intellectual capacity as well; instead of setting up a very complex device, cognitively speaking, our expert suggests weakening its design and introducing vulnerability and risk. The idea is that this robot with great intellectual capacity could evolve and develop the capacity to defend itself and be more intelligent due to its need for adaptability. *"People would find it easier to accept, so to speak, and there would be many interesting ways to apply it."*

In summary, Damasio and his team propose machines that could develop feelings and consciousness but, above all, the awareness of danger to themselves. *"Luckily, there are some new developments that might turn this into reality in the future. For example, soft robotics, the fact that there are new materials that can be deformed, instead of being rigid like steel."*

In order to perceive danger and develop the need to stay alive, machines need something more than just a vulnerable body: they need to be able to feel. *"One of the aspects that truly sets humans apart from other creatures that came before us is that we have a specialized mind,"* Damasio states. *"Only those creatures that have a nervous system, like us, have the ability to access feelings like comfort, discomfort or pain. They can also access feelings related to more complex emotional processes, such as joy, fear, anger or compassion."*

Feelings guide our lives. They affect everything we do. *"This possibility we have of feeling comfort, pain, longing or desire, among many others, is what truly dictates our life. These feelings mean we have consciousness."* Damasio says.

After all, consciousness is the ability to have a mental experience, determined by two critical components. Self-reference: when you are aware of something and you know it refers to you; more specifically, to your body. Mental experiences need to be associated with feelings. It's not that there might be a feeling or not; feelings are inherent to the experience process. A feeling is a sort of classification of the state of life at a specific moment in time. Damasio suggests creating vulnerable machines that are able to have feelings and, therefore, be aware of themselves and the risks they are subject to.

One of the main axis of this proposal is the concept of consciousness. **Manos Tsakiris** studies the connection between the body and the self from the perspective of psychology and cognitive neuroscience. Knowing how these two concepts relate to each other could be essential to develop machines with emotions.

Modern psychology has always focused on how we perceive the body from the outside, as when we recognize ourselves in the mirror, for example. That is an ability that we share with some other non-human primates, and a foundational point in the development of the self. In neuroscience, we're also using body illusions to try and model the feeling that our bodies belong to us. Tsakiris explains that *"This kind of advances have been quite influential in giving us a good understanding of how the brain creates a sense of body ownership and control over our own bodies."*

Manos Tsakiris
Royal Holloway, University of London

This has significant implications about how we relate to others, and technological implications about how we can experience ourselves in virtual reality environments. There are some studies that try to find out the neural network involved in that, in the feeling of control over our own actions from an outside perspective. However, we have been ignoring other side of this issue, what we call the 'interoceptive body': the body as experienced from within. It concerns sensations (like intuition, heartbeat or respiration), and it is crucial to ensure the stability of the organism, for homeostasis.

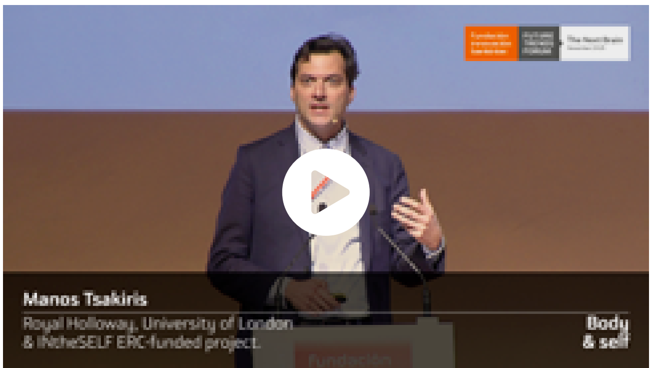
The question is how this self-consciousness impacts the brain. In the last 10 years, there has been an exponential increase in the number of articles covering interoception. According to Tsakiris, *"Now we know that deficits in how the brain is processing information from the body affect a series of mental and physical health conditions, as well as decision-making, emotional cognition, emotional regulation, time perception, and self-consciousness in general."*

The brain's capacity to process this information is related to another issue: that of the technologies that we use to complement the affective or interoceptive experience of our bodies. For instance, wearable devices that measure all sorts of variables about our physiological functioning, from the number of steps we take to our glucose levels or our heartbeat.

"The question is, what do we actually achieve by giving people this kind of explicit information? Not a first-hand experience of how they feel, but a read-out of what their bodies are doing. Are we turning them into anxious accountants that go through their spreadsheets, trying to figure out whether they're taking the right number of steps or whether their heart rate is appropriate?" Tsakiris wonders. He suggests an alternative approach with wearable technologies that are a bit more embodied, embedded and empathic.

Tsakiris points out another two unsolved issues. The first one is loneliness, *"which is becoming a quite significant epidemic,"* he assures. *"One of the challenges that we'll have to face in the future is the impact of loneliness on mental and physical health and how to use the technologies that we are discussing here to mitigate some of those risks."* Social robots are considered a potential solution for the question of loneliness, especially for an ageing population. *"We can think about this kind of hard robots that will interact with ageing population. Or we can think about soft robotics, along the lines of what* ***Antonio Damasio*** *has proposed, about robots that have similar properties to the ones we have in terms of vulnerability and risk."*

The second issue is related to affectant feelings. According to Taskiris, *"Usually, what's wrong with most people who seek treatment because of mental health issues (also in the case of many psychiatric conditions), has to do with feelings and how people actually experience themselves in relation to others."* We are not rational decision-makers. We're influenced by our emotions, and the more we think about how our emotions take part into our everyday life and decision-making processes, the more we will know and understand about why it's so important to make people 'emotionally literate'. Tsakiris assures that *"This is not trivial, and probably we will need to consider more radical technologies that will allow people to actually experience their own bodies, rather than just measure their experience."*



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04

The Future of Neuroscience

One of the factors that could contribute to progress in neuroscience is the investment by private companies or the development of businesses related to this science.

4.1

What Companies Will Bring to the Table

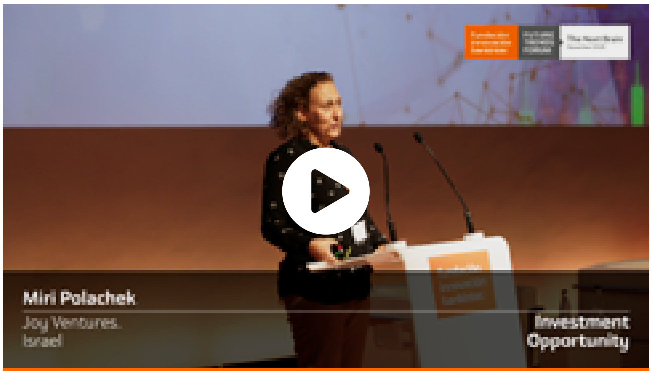
A good example of the first case is **Manuel López Figueroa**, managing director at risk capital firm Bay Capital in San Francisco, which invests in companies that have a great impact on psychiatry or neurology patients. For example, Civitas, which according to López Figueroa has developed a form of inhaled levodopa (L-DOPA), the most efficient medication to treat Parkinson's disease.

One of the goals that Figueroa and his team have is **to start companies based on what they believe will have the greatest impact in the next 10 years.** Some of the most innovative companies are working on neurotechnology and the development of medical devices. For example, Nevro, which came up with the concept of spinal cord modulation with special probes to treat spinal cord injuries and reduce pain. And it seems that their proposal is quite convincing: it has become a publicly traded company worth one billion dollars.

There are some other companies, such as Brain Cells, based on the concept of modulation of neurogenesis for the treatment of psychiatric disorders, and also Reset Therapeutics, based on the concept of the modulation of circadian rhythms as a way to treat central nervous system disorders. In fact, according to López Figueroa, many companies focus on innovation in the central nervous system, *"that is where ideas are and where the money is."* To give you an idea of the magnitude of these proposals, last year the Nobel Prize in Medicine was awarded to pioneers in this field. The investor and entrepreneur also highlights the use of other technologies related to pharmacological treatments. He mentions that there are companies, like Pearl Therapeutics, Aquila o Click, which try to combine different types of treatments.

According to López Figueroa, what all these companies have in common is that *"they present very exciting new approaches, such as the application of genetics and other molecular tools in personalized medicine, predisposition and to gain a better understanding of the state of the patient. In the next ten years, we will see the results."*

Joy Ventures is another investment fund that has its sights set on the future. Its goal is to develop science-backed, consumer products for emotional well-being. First and foremost, that involves trying to figure out what a typical human experience could look like in the future, to develop devices that are aligned with it. **Miri Polacheck,** Joy Ventures' CEO, points out that *"At the end of the day, you can have great science and great technology, but if* *you're not able to create a truly meaningful human-centered experience for people, they're not going to emotionally connect with that technology or with that product."*



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Miri Polacheck
Joy Ventures. Israel

Today, we spend lots of time trying to imagine what daily life will look like in the future, how we will interact with each other and with technology. Polacheck explains, *"I recently attended a session where they had us imagining that we wake up in the morning and turn to our bathroom mirror".* Obviously, it would be a smart mirror. And we would look in that mirror and it would tell us 'Hey, you didn't sleep that well last night, you look tired, you look sad'. It would give us some feedback and suggest different types of activities or interventions, maybe a specific supplement personalized for that moment. That technology would seamlessly interact with us throughout the day: at work, before we go to bed, as we sleep... it wouldn't only be in the mirror, but in many other objects as well.

According to Polacheck, *"In the future, the vision is that all those digital and physical products will be integrated in our daily lives to help us lead happier lives and maintain our well-being. That's what we try to envision when we think of future products that we would like to invest in."* For this interaction to be fruitful, one of the requirements that the device must meet is to provide some sort of feedback and to be user-friendly, reliable, and entail a significant change for users. The idea is not that consumers use the product once, but that they buy it and keep using it because they find it helpful or it offers them something,

To have devices that help users feel better in the future (no matter what they are), we need to keep researching emotional behavior. In the last few years, we have seen that emotion detection and analysis, the whole field of affective computing, is really growing very rapidly. *"The ability to analyze our emotions through various types of inputs, whether they're sensors, our voice, speech, facial expressions and gestures, etc.; and the ability to understand the user's state and respond with some kind of recommended content to somehow influence whatever it is that the person is doing,"* Polacheck explains.

In the future, devices must help users improve their emotional state

This is already widely used by major companies, even though in their cases the final goal is more oriented towards marketing and product sales: **detecting the emotional state of a potential buyer might help influence the user's behavior by modifying the information that is shown to them.** But, regarding healthcare, *"this is a huge part of what will ultimately enrich and facilitate human-machine interaction, and it will make it very meaningful. This is one of the areas that we look at and that I think are important to follow."*

Polacheck mentions several companies that are working in this area. One of them is **Affectiva**, which was started by Rosalind Picard, a pioneer in affective computing, at the Massachusetts Institute of Technology (MIT). There's also an Israeli company called The Elegant Monkeys that Joy Ventures is following. *"This is a very interesting space that we see as a great opportunity. Adoption of these technologies is increasing, and so is their ability to enable brain augmentation,"* Polacheck points out.

More and more people are open to using these non-invasive technologies to manage or to somehow influence their emotional stage. Obviously, these are being used for both clinical and non-clinical applications, as we have already said. Experts state that the key is to make them more reliable, affordable and user-friendly over time. But there's still some challenges ahead of them. *"People will start to see that they influence their state over time. We need to make sure that there's no habituation to these technologies and that someone who wants to use it for attention or any other kind of improvement can continue to get that effect overtime,"* Polacheck claims.

We already carry a part of that future with us. Our smartphones are truly becoming extensions of ourselves. It's just another way in which technology is connected to us. And it's not just our phones, but also the wrist watches that we wear and any other wearables that are now connected to us. In the future, these devices will be able to analyze us and capture our data 24/7. And again, this data can provide us with meaningful experiences, such as digital therapeutics that can be offered through these phones in a personalized way, or various applications that are digitizing psychology and different types of well-being methodologies, like CBT and mindfulness.

"These types of methodologies will be more accessible for people through their phones," Polacheck explains. That is another key point related to solutions for specific populations. *"We see that there are more and more specific solutions offered to different population groups,"* Polacheck explains. She's referring to solutions for the ageing population, for instance, or solutions just for women, or just for young people in college or in high school.

These solutions address very specific needs of those population groups and, according to experts; over time we're going to see specific answers to unique issues that certain populations experience. Regarding women, for example, there is a whole host of women's health experiences throughout a woman's lifetime that strongly affect their emotional well-being. Polacheck adds, *"That's something that historically has not been addressed. So, the ability to take these different technologies and provide specific solutions to women is also very exciting to see."* The same goes for ageing: we have mentioned social robots and cognitive training, which are being offered specifically to the ageing population, as well as some tools that are being offered to young people, like those with ADHD.

4.2

A Promising Future

As we have seen, companies are already focused on the developments we will see in the next years, which are all related to new treatments for diseases, improved health, increase in well-being, information analysis and device personalization. So, they're useful for several groups. Research processes are slow and still need to overcome several challenges regarding the regulation of new technologies and their use in humans. However, **the Future Trends Forum experts predict that some developments in the next few years will change many peoples' lives.**

4.2.1

Evolution in Neuroimaging Techniques

In the last few years, the development of brain observation technologies has been exponential. Experts predict that these systems will continue to be developed. We keep acquiring new knowledge, but, by 2030, technological development will allow us to have more information about different types of brain cells and their connections. We will acquire this knowledge thanks to evolved neuroimaging techniques, which will presumably improve thanks to the development of optical signals.

Given the fact that the brain is still a mystery, development of these techniques is very promising: it will allow us to know more about the types of neurons and how they connect with each other. It will also allow us to go deeper into connection patterns and their relationship with different disorders. Lastly, it will allow us to unravel the functioning of different mental processes such as memory or sleep, which is involved in many pathologies.

> We will acquire new knowledge on the brain thanks to the development of neuroimaging techniques

4.2.2

A Different Treatment for Everyone

In the last few years, the word 'personalization' has been increasingly popular in the technological field, like the personalization of advertising to obtain more sales or the personalization of entertainment content to match the users' taste. but the one field where personalization can save lives, that's healthcare. That is why experts agree that by personalizing treatments, we can adapt them to each patient's specific needs. Depression affects everyone in a different way, at a biological level as well.

We will soon see the development of technological tools that will predict disorders and will therefore allow us to manage them better. We will treat every single human in a different way, and we will personalize and design tailor-made treatments for everyone, in the field of mental health, for instance. As we said, depression is different depending on the patient. That will motivate us to find a way to identify concrete, individual aspects about it, as well as specific ways to address it. But we must overcome certain challenges: how can we handle ethical issues involved in predicting a disorder? How will this new knowledge affect people and society?

▪ We will develop technologies that will allow us to personalize treatments for everyone

4.2.3

More Knowledge, Improvement for Everyone

According to experts, technology will help us unravel the mystery of the human brain.

▪ Technology will help us unravel the human brain

Even though knowledge has a less direct impact on society,

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4.2.4

Enhanced Humans

This knowledge, on top of personalizing treatments and finding new more efficient ones, can also be used to select and improve the lives of healthy individuals. Smart sensors and the development of neurotechnology-based wearables will contribute to the enhancement of human capabilities. These will be developed to the point that some experts believe that humans will be able to communicate telepathically by 2050. But before we get there, experts predict that augmented communication and smart devices will help reduce loneliness and increase the autonomy of disabled people. They also believe that consumers will widely adopt cognitive- and emotional-well-being technologies to face their daily challenges and improve their quality of life.

▪ Neurotechnology will enhance human capabilities

4.2.5

Closer to Regulation

These ideas about enhancing human capabilities always have great ethical implications. For example, how do we use technology that analyzes the brain to decide who is worthier of attending college? To what extent should technology be used to improve intellectual performance? Where's the limit? Will we become super humans? Experts predict that the industry will be regulated in a balanced manner regarding the use of endophenotypes in education, employment, and other social aspects.

4.2.6

Healthcare through Devices

Knowledge will have the greatest impact on the field of technology development for disorder treatment and improvement in citizens' quality of life. Throughout history, technological research and development has significantly reduced the number of patients who die from disorders. These illnesses used to be fatal but can now be treated.

▪ We will make the greatest advancements in the field of wearable devices for healthcare

This knowledge will result in the creation of mobile technology that is accessible everywhere, like wearables. This will have an impact on education, telemedicine, disorder diagnosis and even finance. More specifically, these technologies might affect healthcare, since symptoms will be monitored and treated remotely. This understanding will also lead to improvements in education, which will be personalized for students depending on their capabilities. Mental health will be treated more adequately, since we will be able to prevent mental issues even before patients need to request medical treatment. We will also see an increase in our well-being by developing devices that will help us track our health conditions daily.

4.2.7
Curing Incurable Disorders

All the information we have access to now is already part of our reality, *"and it's perfectly obvious that it's going to be more so in the years to come,"* says Antonio Damasio. It can be applied to several areas, such as mental health, degenerative disorders or Alzheimer's disease, specifically. *"It's a fact that we will find far better treatments for many of the human pathologies in the field of neurology and psychiatry than the one we have today. We all want that and hope it will eventually happen,"* he adds. *"I'd like to see efficient treatments for some of the worse scourges in the field of psychiatry, particularly the area of dementia. Let me point out that the field of Alzheimer's disease is where there is, in fact, great hope."* In fact, experts assert that we will discover the primary causes of Alzheimer's and that treatment will be available for the public in 2026. They also say that, just a few years later, we will find a cure for Alzheimer's. Some of them even elaborate and say that people with disabilities or a specific syndrome will be integrated in both the labor market and society. In addition, experts say that a team of scientists with Down syndrome will discover a new system for the early detection or treatment of Alzheimer's. This could stem from another of our experts' predictions: by roughly 2027, **we will discover pre- and post-natal treatment for intellectual or learning disabilities.**

4.2.8
Mental Health: New Perspective and Treatments

Mental health is one of the main drivers of current research in neuroscience. There are still unanswered questions, such as why the same disorder might have different symptoms, what treatment is better depending on the personal characteristics of each patient or why brain connections vary depending on the disorder. However, experts agree that we will make great progress in this field in the medium and long term.

More specifically, they believe we will develop not-so-invasive treatments to address central nervous system disorders such as depression or bipolar disorder. Technology will facilitate the creation of devices that will allow us to treat these disorders in a less invasive way than those that are currently available. One of the keys to developing new techniques and treatments is to keep researching and expanding our current knowledge. Experts predict that by 2026 we will have a better understanding of the neural base involved in mental disorders. This will facilitate the development of neurotherapies that will help patients unlearn that behavior. By knowing more about neural functioning, we will be able to apply our knowledge to the development of innovative treatments.

Technology will allow us to treat mental disorders in a less invasive way

Even so, and despite the advancements, it is essential to be aware that a decade is a very short period of time to make unequivocal predictions and that, most likely, psychiatric or neurological disorders will not have a cure by 2030. There is still a long way to go before we reach that goal, but experts are already taking the steps to get closer to it, such as equally prioritizing mental health and physical health.

Currently, mental health disorders are taboo and many patients might feel stigmatized because of them, particularly at work or in social situations involving something other than their families or trusted networks. Experts predict that this situation will change little by little, and those suffering from mental disorders will function in society in a more natural way. Ultimately, everyone will accept them in the same natural way that they accept patients with any physical disease.

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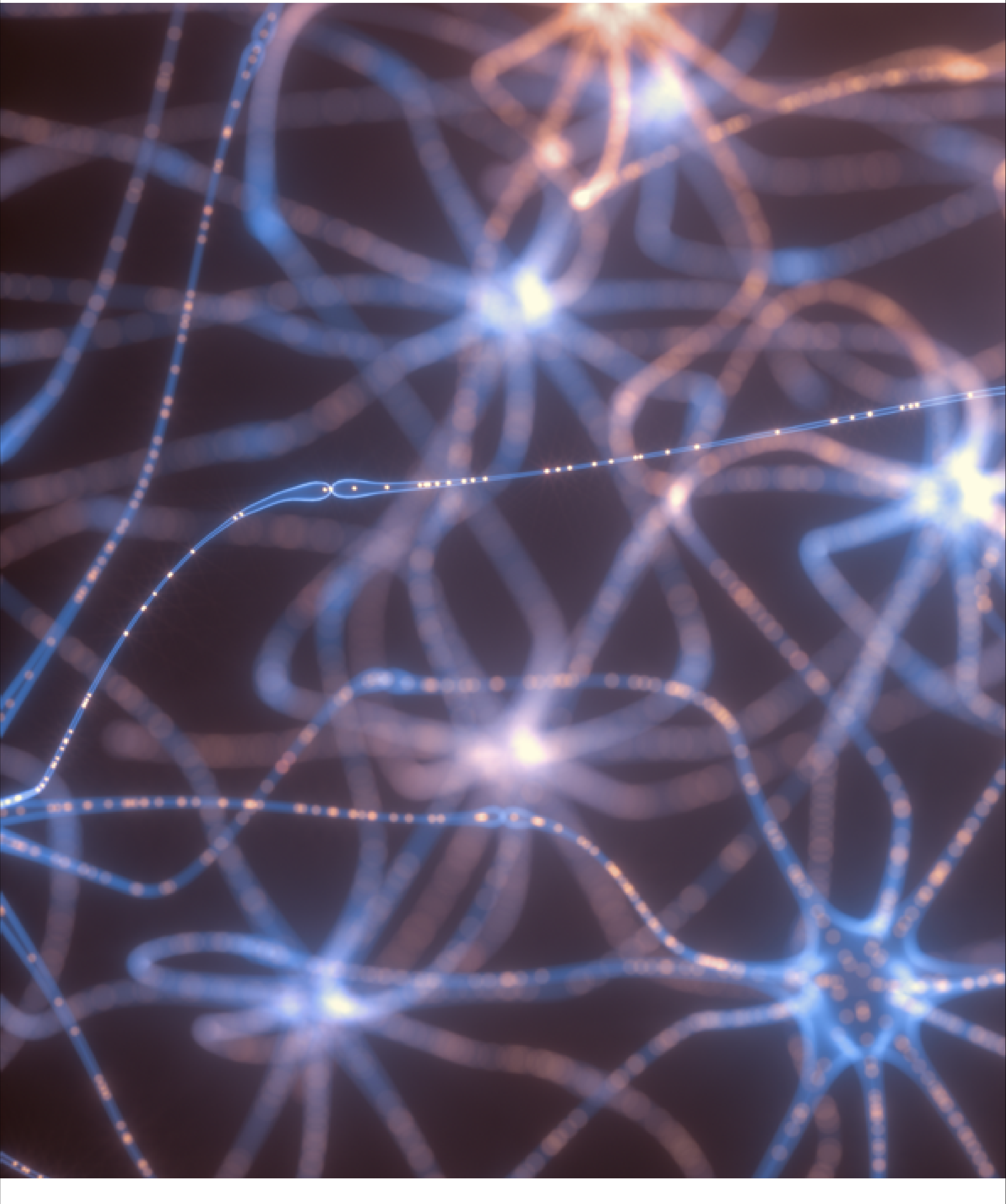

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