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Oficina C

Report C

# Advances in neuroscience: applications and ethical implications

## Breakthroughs in neurotechnology





CONGRESO DE LOS DIPUTADOS

FECYT INNOVACIÓN

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## Production method

Reports C are brief documents on subjects chosen by the Bureau of the Congress of Deputies that contextualise and summarise the available scientific evidence on the analysed subject. They also inform about areas of agreement, disagreement, unknowns, and ongoing discussions. The preparation process for these reports is based on an exhaustive bibliographical review, complemented with interviews of experts in the field who subsequently conduct two review rounds of the text. Oficina C conducts this process in collaboration with the management team of the Spanish Parliament's Lower House Documentation, Library and Archive service.

To produce this report Oficina C referenced 285 documents and consulted 20 experts on the subject. Of this multi-disciplinary group, 42% of the experts were from the field of life sciences (neurobiology, clinical neuroscience, molecular biology, clinical psychology, medicine, virtual reality and neurotechnologies), 26% from physical sciences and engineering (biomedical engineering, neuroprosthetics, neurorehabilitation, robotics, systems neuroscience) and 32% from social sciences and humanities (legal science, philosophy , bioethics, business and public administration studies). 75% work in Spanish institutions or centres, whereas 40 % have affiliations with at least one institution outside Spain.

Oficina C is the editorial supervisor of this report.

# Summary C

*The report in 5 minutes*

## Relevance

The current frontier of knowledge in neuroscience is the connection between the physical brain and higher functions, such as consciousness, thought, learning, memory, motivation, emotions or language. Research has made advances in understanding brain activity to ascertain the mechanisms behind some of these functions, but to date there is no general theory of the brain that explains its structure and functions holistically. A great step achieved in 2023 was obtaining the first molecular atlas of the types of human brain cells, although understanding how they are organised in circuits and achieving a full map represents a real challenge for scientists who have, however, made progress on the models for animal like mice or flies.

In today's society, with a tendency to longer life expectancy, the proportion of people who live with neurological, mental or neurodegenerative diseases, mobility problems or chronic pain has significantly increased. Understanding and treating these conditions represents one of the biggest challenges science faces in the 21st century. Experts highlight the potential of new methods, neurotechnologies and devices, which could generate major developments in knowledge and address some of these diseases, because they facilitate direct interaction with the brain and nervous system.

### Neurotechnology

Neurotechnologies enable a direct connection between a device and the nervous system (central and peripheral) to record or modify nerve activity. They combine neuroscience with other advances in artificial intelligence, robotics or virtual reality to regulate or measure different areas of brain activity including consciousness and thought. In addition to the proven use of certain neurotechnologies in healthcare and their role in scientific development, expectation is growing in the commercial and economic sectors about the potential applications of neurotechnologies in entertainment, education, defence and security on the consumer market. Continuous progress and investment in neuroscience and neurotechnologies in the clinical setting, industry and commerce has opened up a debate that spans the legal, ethical and moral dilemmas related to the impact of these developments on our society

### Focal point

Recent years have seen great technical developments in the direct connection between the brain and a machine or computer through brain-computer interfaces. Such interfaces control a device, whether a computer program, a robot or a prosthesis, as the result of analysing neural activity. Despite of promising clinical demonstration models in the treatment of certain diseases, more scientific evidence is necessary before systematic clinical interventions that are robust, feasible and safe in the middle to long term can go ahead with these interfaces. Among other achievements, they can recover the mobility of hands paralysed after a stroke, or even the mobility of a tetraplegic patient's leg, with the aid of prostheses connected to the brain. Neuroprosthetics could also substitute, enhance or improve a cognitive or sensory mechanism that may have been damaged. A well-recognised example of this are cochlear implants, connected to the auditory vestibular nerve that restore the sense of hearing. Other research, at different stages of development, targets decoding signals associated with emotional states or consciousness, language, or auditory and visual thought in images and phrases. A common limitation is obtaining clear signals of neural activity. Current research is actively working on making electrodes more sensitive. This would increase the amount of data obtained, which would have to be properly analysed in a standard way. The role of artificial intelligence in this field is to help provide increasingly advanced understanding.

### On the horizon

In addition to a demonstrated usefulness in healthcare, expectations are growing in the commercial and economic spheres: 27% of companies focus on non-medical developments, and up to 54% of the scientific studies on non-invasive devices to record activity focus on cognitive monitoring, communication and controlling external devices. Since 2012, investment has multiplied by 21, reaching more than 30.000 million euros and is growing exponentially. The widespread interest in this field means that, within 5 to 10 years, it is expected to see technologies that record, evaluate, modify and improve our minds, cognitive capacity and state of awareness, among other breakthroughs.

The use of neurotechnologies poses major ethical issues.

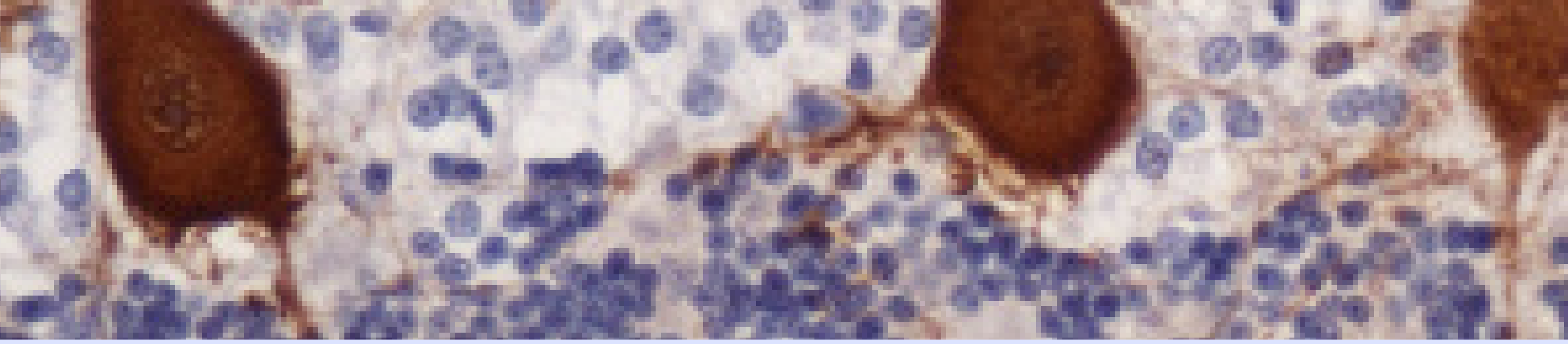

**Imagen FOTCIENCIA** Dance of Purkinjes © Daniela Alejandra López Espíndola

The main challenge is to guarantee mental privacy. Recent demonstrations of the possibility of decoding imagined images and words using non-invasive neurotechnology show the potential risks of extracting confidential neurodata from a subject and their possible use by private companies for commercial benefit. Other challenges are related with personal identity. Documented cases exist of patients whose impulsiveness has increased, or who have suffered from apathy after receiving deep brain stimulation to alleviate the effects of Parkinson's, and others have begun to doubt the origin of certain perceptions or behaviours (whether they are their own or caused by the implant). Another debate centres on the ethical consequences of increasing cognitive capacities. Neurotechnologies can offer strategic advantages for military personnel, such as improvements in cognitive skills, sensory processing or the control of weapons systems using brain-computer interfaces. In short, ethical dilemmas exist related to national security.

Along similar lines, the capacity and suitability of the various national and international legal frameworks in existence on neurotechnologies are being questioned in terms of whether they properly protect citizens rights, and the term "neurorights" has been coined. Various international and national bodies, such as the Neurorights Foundation, the OECD, UNESCO or the Organisation of American States, have taken steps to identify the most suitable legal frameworks to manage the social, ethical and legal implications of neurotechnologies.

On the other hand, the scientific community notes that the ethical regulation of neurotechnologies need not necessarily be an obstacle to innovation. If control is addressed from the initial stages and throughout the research process, regulation could also be a key feature to help confront the future challenges that may arise from neurotechnologies. In Spain, the Charter of Digital Rights (2021), although not legally binding, includes neurorights among the rights of Spanish citizens in the digital era. For the EU, the 2023 "León Declaration" represents a first step in Europe's deliberation on promoting human-centric neurotechnologies, taking into account fundamental rights, and an acknowledgement of the international race to develop innovations. Legislation governing health technology assessment establishes the framework within which neurotechnologies can be developed and implemented and the guidelines, standards or criteria that authorities can use to certify or assess their functions and use. This also applies to devices without an intended medical purpose which, due to their similarity with medical and healthcare devices must be certified and assessed using the same criteria.

In addition to contributing its existing research structure, Spain joined the international community with the launch, in December 2022, of its National Neurotechnology Centre (Spain Neurotech). This multi-disciplinary organisation will pay particular attention to the ethical, legal and regulatory aspects associated to the field

# Advances in neuroscience: applications and ethical mplications

## Introduction

**The current frontier of knowledge in neuroscience is the connection between the physical brain and higher functions. One of the greatest challenges science faces in the 21st century is the treatment of human neurological diseases.**

In 1888, when the Spanish Nobel Prize laureate Santiago Ramón y Cajal first described nerve cells as possible functional units and noted the connections between them, he laid the foundations for the study of the brain and the whole nervous system[1]. This is the focus of neuroscience, a field of study that presents particular complexity in humans. Each person has an average 86,000 million neurons, three times more than other primates[2]. Their organisation and connections enable the transmission of information and signals that give rise to identity, consciousness, thought, memory, behaviour and emotions, among others[1]. The current frontier of knowledge in neuroscience is precisely this connection between the architecture of the physical brain and higher functions[3,4]. This development is still far from complete for the human brain, although significant steps have been taken in the right direction. The most advanced research has produced a precise map of the brain of a fruit fly larva, *Drosophila melanogaster*, synapse by synapse, of 3,016 neurons and 548,000 connections[5,6]. On the other hand, scientists have described an almost complete map of the types of cells and their position in the brain structure of mice, as well as the possibility of cell connections[7–9]. For humans, it was not until 2023 that an atlas of the types of cells in our brains was mapped, including characterisation at genomic, transcriptomic, epigenetic and functional levels[10]. However, achieving a complete map of all the cells, types and, in particular, their interactions represent a challenge: our brain is home to some 10 billion connections.

Traditionally, neuroscience has focussed on studying individual neurons in great detail, a task that new technologies are continuing to work on and achieve the cell atlases[7–10] mentioned above. Nevertheless, current thinking is that the real functional unit of the brain are neuronal groups, so the latest developments seek to understand how circuits form from groups of neuronal types in different proportions[11], as well as their real-time functioning in different regions of the brain[12,13]. Although, to date, there is still no general theory on the brain[3] that holistically explains its structure and functions, research has advanced in the investigation of and knowledge about brain activity. This has given us an understanding of the mechanisms of memory[14], language[15,16], behaviour and brain coordination[17], and the role of the cerebellum[18,19]. Likewise, we are gaining a deeper understanding of neural plasticity (changes in the organisation of connections between neurons over time), which has direct links with rehabilitation or learning after brain damage in terms of recovering impaired functions[20].

**Neurotechnologies have the potential to allow great developments in knowledge, confront problems related with the nervous system and generate new opportunities for innovation, commerce and the economy.**

The brain coordinates a wide range of cognitive and motor roles, which means that any defect in its functioning can lead to various diseases that are difficult to deal with, many of which still have no cure. In today's society, with a tendency to longer life expectancy[21,22], the proportion of people who live with neurological, mental or neurodegenerative conditions, mobility problems or chronic pain has significantly increased[23–26]. In 2017, 21 million people were suffering from neurological disorders in the European Union and 1.1 million people died because of their condition[27]. Despite what seems like a large number of cases, experts believe this only represents a small proportion[28] and highlights the increasing trend of diseases such as stroke or Alzheimer's[23,26]. In the European Union (EU), costs associated with neurological diseases in 2010 amounted to 800 billion euros, of which 60% went on direct costs (medical and other)[29].

· Higher functions: Mental processes that enable us to perform a task. In human beings, higher functions include consciousness, thought, learning, memory, motivation, emotions and language.
· Genomic, transcriptomic and functional level. Genomics refers to the study of the structure and function of genomes (an organism's DNA sequence). Transcriptomics is the study of the set of RNA molecules that are active at a given time. Functional level refers to full functioning of the different parts.

Understanding and treating human neurological diseases is one of science's greatest challenges in the 21st century. There are neurological diseases and mental disorders for which there is no effective pharmacological treatment[30], with the added difficulty that many drugs cannot penetrate the blood-brain barrier protecting the brain, slowing down innovation. Experts indicate the new methods, technologies and devices designed to study, interact with or modify the brain and nervous system as an area with the potential for major developments in knowledge to address diseases that affect the nervous system[31,32]. Collectively known as neurotechnologies, they afford a direct connection between a device and the nervous system (central and peripheral) to record or modify nerve activity[33]. These technologies combine neuroscience with other advances in artificial intelligence, robotics or virtual reality to regulate or measure different aspects of brain activity, including consciousness and thought[34,35]. Among the potential advantages in the clinical setting are highly personalised therapies, immediate, very localised effects, and a high degree of reversibility (e.g., the possibility of removing an implant)[30].

In addition to the proven use of certain neurotechnologies in the field of healthcare and their role in scientific advances, expectations are growing in the commercial and economic sectors about possible applications of neurotechnologies in entertainment[36], on the consumer market, education[37-39], defence[40,41] and security. Continuous progress and investment in neuroscience and neurotechnologies in the clinical setting, industry and commerce have opened up a debate that spans the legal, ethical and moral dilemmas related to the impact of these developments on our society[42-44].

## The advance of neurotechnology

**In the clinical setting, treatments with neurotechnologies focus on diseases that do not improve with any other therapies. These technologies can substitute, enhance or improve cognitive, sensory or motor mechanisms.**

Neurotechnology can be broadly classified into three categories: those that record and read brain activity (neuroimaging or electrophysiological techniques); those that are capable of modifying neural oscillations (neuromodulation)[45]; or those that combine the recording of signals with a neurofeedback response (**Box 1**). They can also be classified depending on how they connect with the nervous system. The technology may be invasive or semi-invasive when implantable, which entails a higher risk for the patient because of the need for surgery. If devices are placed on the outer part of the body and act from the skin, they are considered non-invasive[45,46].

Recent years have seen remarkable technical developments in the direct connection between the brain and a machine or computer through brain-computer interfaces (BCI)[69]. These interfaces control a device, whether a computer programme, robot or prosthesis, by analysing neural activity. Recently, research has begun into the use of interfaces in cerebral organoids (**Box 2**). Despite promising clinical demonstration models in the treatment of certain diseases[70] a lot more scientific evidence is necessary before systematic clinical interventions that are robust, feasible and safe in the middle to long term can go ahead with these brain-computer interfaces[71]. Treatments with neurotechnologies in the clinical setting have focussed on diseases that do not improve with any other therapies[72,73]. They can also substitute, enhance or improve a cognitive, sensory or motor mechanism[35,74].

· Artificial intelligence: The group of analytic and information science technologies that can achieve complex objectives based on information.
· Virtual reality: An environment of simulated 3D scenes and objects with real dimensions. It may consist of an immersive experience or may be augmented reality (a combination of real-world images with virtual elements).
· Brain-computer interface: A type of neural interface (a connection between an external device and a part of the nervous system) that captures the electrical activity of neurons and transmits them to an external device for interpretation. They contain a sensor of brain activity, a processor, and a control element that directs a device. They are classified as unidirectional or bidirectional, invasive or non-invasive.

**Neuroimaging measures the brain's structure and function. Neuromodulation changes neural activity, and neurofeedback seeks to link brain activity with a response.**

### Box 1. Types of neurotechnology

**Neuroimaging.** The structure and activity of the brain can be measured by means of changes in electrical, optical, magnetic or acoustic patterns, or blood flow. These can be represented as an abstract space-time 'image'. Functional magnetic resonance, the non-invasive technology that gives good recording of brain activity, requires a large apparatus and immobilisation of the patient for an extended period of time. This fact limits its usability despite its good spatial resolution (although it has low temporal resolution) in detecting of brain activity patterns. It is habitually used in hospitals, for instance, to diagnose cancer or determine the effects of a stroke[47,48] and in different basic research projects on the brain. Researchers can obtain high-quality signals using invasive methods to measure the electric signals directly in contact with neurons. However such procedures are restricted to the clinical setting. Non-invasive techniques, such as the surface electroencephalogram (EEG) and magnetoencephalography (MEG), are being worked on, and are gradually reaching the quality standards of implantable technologies, thus increasing both their usability and user comfort[49].

**Neurostimulation.** It includes techniques to modulate neural activity to achieve a direct therapeutic effect (using electric, magnetic, chemical or acoustic signals or even pulses of light). A valid example for clinical practice is the electric stimulation aimed at the deepest part of the brain. This invasive treatment is used for Parkinson's disease[50-52]. Implantable devices are in direct contact with the brain and can regulate and interpret signals with greater precision than non-invasive techniques (e.g., transcranial magnetic stimulation, which is delivered from outside the brain[53]; which, despite significant reservations, is already used to treat resistant depression[54,55]). It is also possible to stimulate the peripheral nervous system[56], which involves fewer issues of safety or ethics and therefore presents numerous clinical applications. The Spanish Network for Health Technology Assessment of the National Health System, RedETS, has assessed tools to treat chronic pain[57], chronic cluster headaches (migraines)[58] and urinary incontinence[59].

**Neurofeedback.** Neurofeedback is based on neural plasticity to achieve changes that endure over time[60]. It is a psychophysiological process in which the information of the measured neural activity is linked to a response[60]. The reading is usually presented to a patient, who can then learn to control their own brain activity through real-time observation on a screen or through other senses[60,61]. It has been successfully used to reduce postoperative pain among lung cancer patients[62] or to mitigate the effects of tinnitus[63]. Non-medical devices for assisted meditation have also been marketed[64-66]. Another form of use involves directing a response, which can be aimed at a stimulation device that regulates its effect depending on the activity being performed. In 2020, the first device of this kind received approval for treating Parkinson's, and it is now on the market[67,68].

**Combining cerebral organoids with brain-computer interfaces could pave the way for enormous advances in the study of neurodegenerative or developmental diseases and biocomputing.**

### Box 2. Organoid intelligence

In 2022, cultivated neurons connected to a neural interface in a laboratory "learned" to play the computer game 'Pong'[75]. Aside from this example, a scientific consortium has reported that combining cerebral organoids (neural 3D cell culture) with brain-computer interfaces could enable enormous advances in the study of neurodegenerative or developmental diseases and biocomputing[76]. This field of research, which is still in its infancy, has been called "organoid intelligence". It is based on the idea of creating new forms of computing that could be faster, energetically efficient and more powerful than silicon-based computing. Although there is still much work to be done to make organoid intelligence a reality[76], experts highlight that we should anticipate the need to develop it in an ethical, socially responsible way. The signatories of the 2023 Baltimore declaration call on the international scientific community to explore the potential of this field while confronting and acknowledging the associated ethical implications[77].

## Technical limitations and artificial intelligence

The main technical limitations of neurotechnologies are monitoring resolution, regulation of neural oscillations, and managing the large amount of data that could be recorded.

Technical developments to improve the interpretation and modification of brain activity are essential to understanding the brain and developing neurotechnologies aimed at improving people's health or other potential applications. Advances in this field are complex and restricted by both the degree of spatial resolution the brain can achieve and the management of the large amount of data that may be recorded. In terms of resolution, it is currently possible to obtain the neural activity of specific brain regions, but is not possible to achieve a high level of detail about their connections with other regions, particularly when using non-invasive devices[78,79]. To overcome these hurdles, in the short term, new types of electrodes are being developed to record neural activity with increasing precision using new materials like graphene[80-82] or with long-term stability[78]. Advances include new multimode probes that allow simultaneous recording and management of brain activity[83,84] or use nanoparticles[85]. Progress is also being made in implanting electrodes with increasingly safe, minimally invasive neurosurgery[86,87]. With the increasing sensitivity of electrodes, the amount of data that must be analysed, standardised and included in large databases increases[88], which means that another limiting factor is the capacity to suitably analyse all of this information (**Box 3**)[89]. Artificial intelligence and machine learning can be helpful to analyse large amounts of data. When the information that comes from neural recordings is obtained, it includes signals from numerous simultaneous processes and activities mixed together, as well as different levels of detail. Before useful information can be obtained there needs to be a process of understanding or decoding, in which each signal is isolated and associated with a neural function or activity[90]. Combining clinical data with artificial intelligence and existing knowledge of a disease enables the design of more effective neurofeedback and neurostimulation techniques[91-93], and feedback intervention strategies to detect and regulate activity patterns in real time[94]. In brief, increased resolution accompanied by developments in data analysis opens the door to more precise treatments.

As the market for brain-computer interfaces grows, large volumes of brain data, which could contain personal information, may be collected.

**Box 3. Neurodata**

Neurodata are data types containing information about the user's brain activity. To date, the technical knowledge necessary to decode thoughts or a person's unconscious mind from such data does not exist [42]. However, some personal details can be inferred, such as emotional state or cognitive health[95-98]. On the other hand, recent studies indicate that it is possible to decode visual thought and language with non-invasive technology[99,100].

While the market for brain-computer interfaces is growing, brain data may be collected in large volumes, not only for medical or healthcare purposes, but also to design business strategies[95,101]. Companies that develop or use non-medical brain-computer interfaces might use personal data for their benefit, for instance, by designing advertising targeted at specific individuals[36]. Likewise, connecting brain-computer interfaces to the internet opens the door to potential cyberattacks[102] that attempt to steal data or obtain control of devices[44,103]. To guarantee the patient's privacy in neurotechnology research, particularly in neuroimaging and brain activity data research, the General Data Protection Regulation[104] allows sharing pseudonymised data (personal identifiers are not linked to the data) within the European Union[105]. To share such data outside the EU, a contract must be signed guaranteeing the protection of the data[105].

On the other hand, the scientific community has voiced concern about a replication crisis in studies on recording brain activity[106,107]. As a solution, work is underway on harmonising the neuroimaging data obtained in a standard way, following Brain Imaging Data Structure (BIDS)[88], in accordance with FAIR principles (Findability, Accessibility, Interoperability, and Reuse of digital assets)[108,109]. These initiatives facilitate collaboration along the lines of Spain's National Open Science Strategy (ENCA)[110], allowing the use of data for purposes other than those for which they were initially intended[105].

· Machine learning A sub-discipline of AI in which a programme "learns" based on experience (from databases or physical sensors). This learning can be maintained over time while new experience is acquired and enables the extraction of new patterns and information not previously known.

## Neuroprosthetics and neurorehabilitation

**Neurotechnology research and the use of brain-computer interfaces has concentrated on healthcare, and on the neurorehabilitation of patients with sensory and motor disabilities..**

Estimates suggest that one in every four people in the world will suffer a stroke at some time in their lives[111], and the principal sequelae include significant deficits in mobility and speech. There are also patients with mobility problems due to spinal cord injuries or neurodegenerative diseases like amyotrophic lateral sclerosis -ALS- or Parkinson's[26]. Their prevalence has meant that much of the research into neurotechnologies and using brain-computer interfaces has concentrated on healthcare and the neurorehabilitation of patients with sensory and motor disabilities[112-114].

Although work is underway to interpret or decode the brain activity related to mobility, most applications are in the research phase, with a low translation rate to the clinical setting[113,115]. Even so, several specific devices exist to recover mobility, mainly of upper limbs. The effectiveness of brain-computer interfaces combined with physiotherapy has been tested on patients with serious stroke sequelae to recover mobility in paralysed hands[116].

Clinical demonstration models also show us that when a patient's intention and willingness are associated with a real movement facilitated by robots or neuroprosthetics **(Box 4),** neural plasticity is stimulated. Likewise, partial neurological recovery is possible for different types of paralysis, as seen in paraplegic and post-stroke patients[117]. These prostheses can include touch or pain sensors in the limb to improve postural control by means of neurofeedback[118]. Conversely, when the nerve circuits for motor control are intact, they can be directly activated. For instance, two patients with upper limb paralysis recovered mobility in their arms and hands using a signal from the brain and artificial stimulation of their muscles[119]. In the case of tetraplegic patients, there are promising, increasingly advanced proofs of concept of enabled leg mobility recovery. The brain activity associated with movement is interpreted by a device, which transmits the decoded information directly to the limbs by means of stimulation[120-123]. The main difficulty resides in achieving autonomous walking with sufficient balance[124]. Interfaces are also being designed with the ability to move an exoskeleton, artificial limb or wheelchair with a controller supported by brain activity[124-128].

**In Spain, about 19,500 people have cochlear implants that restore hearing using a microphone which detects sound and directly stimulates the auditory vestibular nerve.**

**Box 4. Neuroprosthetics to restore the senses**

There are devices at different stages of development connecting with the nervous system to restore the senses of sight or hearing. In the case of hearing, cochlear implants are clinically successful and can restore hearing with a microphone that detects sound and directly stimulates the auditory vestibular nerve[129,130]. Such implants are indicated in certain cases of severe deafness when treatment with conventional hearing aids does not work[131]. The first implant was performed in France in 1957, and these implants are currently among the portfolio of services offered by the Spanish National Health System[132]. In this country, approximately 19,500 people already have cochlear implants[131].

Retinal implants are being actively developed to recover sight. They can detect light and transmit information to the optic nerve, retina or even the visual cortex1[33]. However, the most advanced devices are still unable to process details of images (they cannot recognise faces or read but can distinguish colours or large shapes), and technical obstacles must be overcome before they are safe for use in the clinical setting[134].

· Neurorehabilitation: A multi-disciplinary treatment for patients with central nervous system lesions whose ability is impaired. It can minimise, compensate or even restore functional impairments derived from a disease or an accident.
· Neuroprosthetics: Devices that can substitute, enhance or increase a sensory or motor mechanism which may have suffered damage (vision, hearing or movement). Their basis is the direct electric stimulation of the nervous system to perform a function and they sometimes use brain-computer interfaces.

## Decoding language, visual thought and emotional states

**Scientists can interpret emotional states or states of consciousness, language, auditory and visual thought, as well as the mental processing of images or text from measurements of brain activity.**

Brain activity signals contain information about different aspects of our thoughts, emotions and behaviour. Much research has focussed on motor signals, which is why advances have been made in controlling robotic arms using neural oscillations[119]. However, other research has targeted decoding the signals associated with emotional states or consciousness, language, or auditory and visual thought into images and phrases.

**Speech and language.** Understanding the information of neural oscillations enables communication for people with paralysis who cannot speak. Ongoing research is looking into interfaces that allow these patients to surf the internet[135] and access its services by just thinking a word or phrase in front of a computer screen[136]. These developments translate the patient's intentionally generated brain activity into phrases that a computer can read[100,137–139]. Although they have shown a certain degree of inaccuracy in practical conditions[140], increasingly higher rates of success are achieved by using language models[141,142]. The results of Meta researchers show the possibility of decoding spoken, heard or read language in real-time with non-invasive techniques[100,143]. One clinical trial has shown the possibility of using neuroprosthetics to recover communication for people who cannot speak due to a certain degree of paralysis, with a speed of 62 words per minute, which is close to normal speech[144].

**Visual thought.** Although still in its infancy, some studies have managed to reconstruct photos or faces of people from signals of the observer's brain activity[99,145], proving that it is possible to link neural oscillations with visual perception[146–148]. This research is the basis for the systematic decoding of visual thought. Currently, the main limitation is the need for the observer to simultaneously view the image in order to identify it[99], and it is not possible to reconstruct images from memories[149], although this is possible for simple forms and imagined colours[149]. Another consideration is that recognition varies between individuals or even for the same person at different times.

**States of consciousness and emotions.** It is possible to discover whether a patient with severe brain damage or paralysis who does not show any physiological response is conscious or not[150]. This is important to provide patients who are aware but immobile with a means of communication through brain interfaces. Decoding states of consciousness is also useful for people with sleep problems. Clinical trials conducted in this field have tested devices that emit acoustic signals in accordance with brain activity, which are specially adapted to improve the sleep quality or autonomous functions (like heart rate, digestion or urination)[151]. Simple devices have also been tested to guide meditation or promote attention[152]. On the other hand, research efforts exist to decode emotional states based on brain signals[153]. This understanding could be particularly useful in the treatment of diseases such as depression[154,155] or in recovering emotions affected by neuropsychiatric disorders[156].

## Relationship with virtual environments

**It is possible to move around virtual reality environments by means of non-invasive brain-computer interfaces.**

Virtual reality environments can potentially be combined with brain-computer interfaces. In the video game industry, simple games have been produced that are accessible for children with paralysis who would otherwise not be able to play[157] and for people whose mobility is reduced due to lesions or neurological disorders[158]. In another experiment, a tetraplegic patient could activate their movement in a virtual environment solely from the readings of neural oscillations recorded with non-invasive technologies[159–161]. Although this kind of demonstration has been conducted for years, many developments have not reached society as a whole because the systems were too expensive to leave the laboratory[158] or because they were not ready for public rollout[162]. Nevertheless, these systems are becoming more affordable and spreading to areas like neurorehabilitation or psychological therapy and are at an incipient stage in pain treatment. Extensive research and technological development underway, but it is difficult to predict the practical potential of these applications[158]. The metaverse, as a virtual environment, may be one of the main places where brain-computer interfaces could interact, even with each other, given the interest and investments of big business[46].

## Non-clinical applications

**As well as the demonstrated usefulness of neuro-technologies in healthcare, the world of business has great expectations for its application in sectors like entertainment, marketing, education, defence or national security.**

The business sector has made significant investments in neurotechnologies[163]. Among the major companies in this sector, 65% are located in the USA, and of these, 53% focus on developing devices that are able to read and modify neural activity, almost all within the therapeutic context. Only 3.5% are located in Spain[34], where most start-ups are in the area of neuroimaging[164]. In addition to a demonstrated usefulness in healthcare, expectations are growing in the commercial and economic spheres: 27% of companies focus on non-medical developments[165] and up to 54% of scientific studies on non-invasive devices for recording activity focus on the cognitive monitoring, communication and control of devices[166]. Along these lines, worthy of note is Apple's patent for wireless earbuds that can be used to record brain wave activity[167]. Since 2012, investment has multiplied, with an exponential growth that exceeds 30 thousand million euros[168]. Such widespread interest means that in the medium term (5-10 years), among other expected breakthroughs, we will see the technologies to record, assess, modify and improve our mind, cognitive capacity or state of consciousness[169]. These technologies have potential in other sectors: the consumer market (e.g., in the video game industry)[36], education[37–39] or in the area of defence[40,41].

In publicity, neuromarketing is a discipline where brain-computer interfaces could be used to measure the physiological and brain activity of people. At the same time, they read or see content related to a brand or product[170,171]. The goal is to obtain information about preferences, emotions, interests and purchasing decisions in order to design sales strategies that are more effective and personalised, as already happens on social networks[172]. Legal challenges are on the horizon when it comes to drawing the line between the civil liability of the individuals who make use of these types of technology and the validity of the data collected using neurotechnology as legal evidence[173]. In conclusion, the possible penetration of neurotechnologies in fields not related to healthcare opens the doors to new dilemmas and moral considerations.

# Ethical and social implications

**Debate exists on ethical and legal matters attempting to better understand the impact of these developments on our society.**

The use of neurotechnologies poses major ethical doubts[44,174,175]. In addition, any device that includes AI in its design is subject to the ethical challenges of AI as a whole[176]. The following section details some specific challenges facing neurotechnologies, many of which are under consideration by UNESCO's bioethics committee[43].

## Main challenges

**The main challenges are mental privacy and the management of confidential information, the identity and free will of people, as well as aspects related with increased cognitive capacities. sociedad.**

The main ethical challenge of neurotechnologies is mental privacy. The recent demonstration of the possibility of decoding imagined images and words using non-invasive neurotechnology[99,100,143] shows the potential risk of extracting confidential brain data or neurodata (**Box 3**) from a subject and their possible use by private companies for commercial gain. Debate on this subject is analogous to the discussions about technologies based on artificial intelligence[176]. Another consideration is that devices connected to the internet may be the victims of cyberattacks[36,44,102,177] and are, therefore, vulnerable to security breaches or malicious use that violates privacy and may coercively modify a user's behaviour[178].

· Metaverse: The term used to describe a shared, virtual, immersive space that extends beyond physical reality.

Some neurotechnologies can elicit changes in a person's thoughts, feelings and behaviour, blurring personal identity[43]. Documented cases exist of patients whose impulsiveness has increased, or who have suffered apathy after receiving deep brain stimulation to alleviate the effects of Parkinson's[175]. With the same technique, some patients have come to doubt their identity and decision-making capacity, questioning the origin of certain perceptions or behaviours (whether they are their own or caused by the implant)[179]. People do not know if the decisions they take are made because they want to, or whether they have been influenced by the device, thus generating a feeling of artificiality[180]. This means that neurotechnologies can affect an individual's free will[43].

As with any other therapeutic intervention, the patient's informed consent is required before performing neuromodulation treatment of the nervous system. This ethical-legal process ensures that patients are aware of the possible associated risks, which include alteration of personal identity, the use of neural data, or a potential modification of cognitive capacities[43]. Experts warn of the need to ensure that patients and their families are at the centre of the process, with greater participation in medical decision-making[181]. Another debate centres on the ethical consequences of increasing cognitive capacities (**Box 5**). Developing neurotechnologies for this purpose could bring benefits in areas like education and help improve people's mental health. However, unequal access to this kind of technology might contribute to an increase in economic, social or cultural inequalities[43].

**Businesses are developing devices to improve concentration, memory or learning speed, many of which are non-invasive; however, results and evidence vary.**

**Box 5. Learning, memory and cognitive enhancement.**

Neurotechnologies can be used to make learning easier. Some companies sell non-invasive interfaces that work with neurofeedback to improve concentration[182], facilitate meditation[64,65], or reduce attention deficit [183,184] although their results vary. There are also an increasing number of headband-type interfaces on the market to record brain activity for use in cognitive monitoring[166].

Despite the early stage of this research, neurotechnologies are being developed that could boost cognitive skills beyond the brain's normal functions[79]. A recent study has managed to increase short and long-term memory in both patients and healthy people, opening the door to cognitive enhancement with non-invasive techniques[185]. Devices are available for purchase online that provide transcranial stimulation to increase learning speed, although there is little evidence about their validity, robustness or safety and they are not certified for legal sale in Europe[33,186].

In experiments on animals, researchers have implanted rats with prostheses with an infrared lens[187], or nanoparticles[183], which enabled their brains to learn to perceive new stimuli and thus achieve night vision. This research could have implications for the recovery of damaged sight in humans. Nevertheless, there may be a downside to these improved capacities if we consider the hypothesis that the brain could be a "zero-sum" system[189,190]. Our brain has a finite biological capacity, and if it is forced to learn or improve one skill, it may stop expending energy on other functions[190]. This could result in bad functioning of another brain activity or in unexpected changes in behaviour[175]. The immense difficulty of detecting this type of undesired consequence should be noted: modification of a certain brain activity may offer an initial benefit, but years later it could result in disease or disability. So, scientists warn of the risks of neurotechnologies outside the clinical setting (non-invasive brain stimulation techniques, among others[191]).

Optogenetics is another technique that is taking its first steps, with basic research on animal models to observe and manipulate neural activity in live organisms. The technique is based on the genetic manipulation of neurons to make them sensitive to pulses of light[192,193] and may help us understand processes that involve multiple areas of the brain, such as memory. In the long term, optogenetics could be used to eliminate the memories associated with phobias or intrusive thoughts related with post-traumatic syndrome and to improve memory or create false memories that could help prevent destructive behaviour[79]. The idea of using this technique to manipulate the memory of humans is still subject to research and debate: any potential application in this field would require careful consideration of the possible risks and benefits, in addition to strict ethical and legal regulations[194–197].

## National security

**Some countries are funding projects to research brain-computer interfaces for achieving better performance of the military personnel.**

Neurotechnologies can offer strategic advantages for military personnel, such as improvements in cognitive skills, sensory processing[198] or the control of arms systems using brain-computer interfaces[199]. Indeed, this has opened up ethical dilemmas associated with national security[200]. Several countries are looking into enhanced cognitive skills in the area of defence. In the USA, the Defense Advanced Research Projects Agency (DARPA) funds numerous projects that research non-invasive brain-computer interfaces to achieve better performance of military personnel and strategic analysts[201]. In France, the Military Ethics Committee has approved research into neurotechnologies that enhance the cognitive capacities of French soldiers[202]. On an ethical level, experts question whether military personnel will be able to choose to receive or refuse these enhancements[203]. Likewise, decoding the images obtained from brain activity or improvements in lie detection could allow access to information that is confidential or that a person does not wish to divulge[33,206]. Conversely, neurotechnologies could be used to lie better[205] although none of these systems has yet been perfected[173]. It has been suggested that the results of such tests may not have been shared with the scientific community.

The control and regulation of exports in dual-use neurotechnologies (applications with both a civilian and military use) is the responsibility of national authorities, in compliance with the EU regulations specifically approved for this purpose[206-208]. Within the EU, the list of controlled products and technologies is the result of systematic harmonisation and identification. In Spain, the authority responsible is the JIMDDU (the Spanish acronym for Inter-ministerial Regulation Committee for Foreign Trade in Defence and Dual-use Materials), which reports on changes in the regulations on foreign trade for defence materials and dual-use technologies.

## Social perception

**Few studies exist on social perceptions, but their use in healthcare or for cognitive enhancement seems to be generally accepted, while there is greater distrust of developments for non-medical or military purposes.**

The participation of society in the process of designing and developing new technologies can facilitate public trust[209]. Nevertheless, to date there are still very few studies on social perceptions about applications derived from neurotechnologies. Some reports indicate that the public accepts its use in medicine, whereas non-medical uses cause more distrust[210,211]. On the other hand, one study on the use of deep brain stimulation techniques found that people in high-stress, low-productivity situations were more willing to accept the risks of devices that could generate increased cognition[212]. In fact, Spain is at the top of the ranking of European countries with up to 60% of the population who would be willing to accept some type of cognitive enhancement[213].

The general public, however, rejects its use for military, national security or defence purposes. The dual use of neurotechnologies represents a concern both for the general public and for different actors in the field of R&D&i. This sector considers that given the difficulties of managing an arms race based on this technology, controls on its design need to be established[211]. Other concerns expressed are a lack of equal access, the control and transparency of personal data, and the development of technologies that might be able to read or control behaviour without a person's consent[210]. Finally, some have suggested that lousy management of unduly high expectations coupled with bad communication could elicit a negative response. This might result in a limited adoption of this type of solution by people who could have benefited from these technologies[214].

## Legislative approaches

**The debate on governance is being led by experts in neuroscience, philosophy, ethics and legislation concerned about the suitability of current legal frameworks to ensure the adequate protection of neurotechnology-related citizens' rights.**

Current scientific and technical developments in the fields of neuroscience and neurotechnology have recently rekindled debate on their legal and ethical implications, led by the neuroscience community with the participation of experts in ethics, legislation and philosophy. The scope and suitability of the different existing national and international legal frameworks applicable to neurotechnologies are being questioned with regard to their protection of citizens' rights, resulting in the term "neurorights" being coined[103,215] (**Box 6**).

Various international and national authorities have taken initiatives to identify the most suitable legal frameworks to manage the social, ethical and legal implications of neurotechnologies. One of the first proposals for an international standard to anticipate the challenges posed by neurotechnologies was prepared in 2017 by the Morningside scientific group, in representation of the brain projects of the USA, Europe, China, Canada, South Korea, Japan, Australia and Israel[103].

In 2019, its proposals were followed by the recommendations of the OECD (Organisation for Economic Co-operation and Development) Council[222]. In 2022, UNESCO's International Bioethics Committee highlighted the need to implement neurorights within a global neurotechnology governance framework, with guarantees of rights within member states[43]. This resulted in a preliminary study on technical and legal aspects related to the advisability of a regulatory instrument governing the ethics of neurotechnology[223]. Likewise, the Organization of American States' Inter-American Juridical Committee has presented two reports[224,225] contributing to the materials on neuroscience, neurotechnologies and neurorights for that region, and on legal protection in case of damages. The *Red Iberoamericana de Protección de Datos* (Ibero-American Data Protection Network - RIPD) has endorsed these two reports and created a specific working group on the subject[226] Finally general debate on this topic continues within the United Nations.

**Neurorights are a proposed extension of existing human rights to guarantee exhaustive coverage in the face of the potential of neurotechnologies.**

**Box 6. Neurorights**

Neurorights are a proposed extension of the human rights already enshrined in international treaties[103,215,216]. There is an active debate among experts about how to address these rights in legislation. Some suggest that existing rights offer sufficient coverage and question the need for the addition of neurorights to the international treaties already in force[217,218]. However, most experts argue that current human rights do not offer exhaustive coverage, bearing in mind the potential of neurotechnologies, and the Neurorights Foundation exits to work in this area[219]. Specifically, experts highlight ambiguities regarding the right to free will[103,204,220]. In 2023, the Valencia Declaration was presented in Spain to promote the inclusion of these rights in the International Declaration on Human Rights[221].

The proposed neurorights are: 1) the right to mental privacy, which protects the neural data of people from intrusion or unauthorised use by third parties; 2) the right to personal identity and mental integrity that comes from any interventions that could manipulate personality; 3) the right to free will, which guarantees a person's decision-making without external influences; 4) the right of fair access to cognitive enhancement to guarantee human dignity, autonomy and equality; and regarding artificial intelligence, 5) the right to prevent the bias that can result from a deficient use of data or badly designed algorithms in neurotechnologies, which could reinforce discrimination against vulnerable groups.

At the European level, the Council of Europe's Commission for Human Rights adopted the Strategic Action Plan on Human Rights and Technologies in Biomedicine (2020-2025) in 2019. The purpose of this document is to protect human dignity, human rights and the fundamental freedoms of individuals in the fields of biology and medicine, and it explicitly addresses the debate on neurotechnologies[227]. Nevertheless, to date, these debates and ethical implications have not been addressed with legislation in the European Union. This is because existing legislation on healthcare has been relied on to cover needs in the field of neurotechnologies[228]. The European Parliament approved a resolution in 2017, with recommendations to the European Commission on Civil Law Rules on Robotics, with mentions of neuroscience[229]. However, the lack of specific legislation within the European Union does not mean these technologies are not subject to EU legal frameworks such as the Law on Protection of Personal Data and Guarantee of Digital Rights[104] or the AI Act[230]. Specifically, in its terms the AI Act forbids the cognitive behavioural manipulation (techniques that transcend awareness) of vulnerable people and groups[230]. After analysing the different legal frameworks of EU countries related to neurotechnology, an expert report offered certain recommendations for EU institutions[231]: 1) acknowledge and define neurorights within the framework of the European Union's fundamental rights[232]; 2) define the legal status of the brain and of neural data in the General Data Protection Regulation (GDPR); 3) address loopholes related to justice, equality and discrimination related with neurotechnology devices; 4) assess the regulatory frameworks regarding neurotechnology devices for both consumption and dual-use; and, 5) define the type of use of AI-based neurotechnologies in accordance with current legislation[230]. Along these lines, the recently issued "León Declaration" on European neurotechnology opened the debate on promoting human-centric, fundamental rights-oriented neurotechnologies, and acknowledged the international race to develop innovations within neurotechnology ecosystems[233].

In Spain, although not legally binding, the Charter of Digital Rights (2021), includes neurorights in the rights of Spanish citizens in the digital age[234]. Moreover, although the Spanish law on Biomedical Research 14/2007 does not explicitly refer to neurotechnologies[235], its cornerstones are the protection of fundamental rights and public freedoms, the protection of identity and personal autonomy, and the right to not be discriminated against, among others[236]. In addition, the Spanish Bioethics Committee[237] and the Spanish Research Ethics Committee[238] have powers over conflictive aspects of biomedical research including neurosciences and neurotechnologies.

**Neurorights have generated debate in international organisations, within the European Union, and in various countries. Chile was the first country to guarantee neurorights in its constitution. Spain includes these rights in its Charter of Digital Rights.**

The French Ministry of Higher Education, Research and Innovation (MESRI) is currently working on a Charter for the Responsible and Ethical Development of Neurotechnologies[239]. Likewise, in 2021, France included the possibility of using specific neural data as legal evidence in its Civil Code[239]. Another example is Italy, which extended the safeguards enshrined in its Declaration of the Rights of Citizens (2015) related to the internet to the field of neurotechnology[240].

Some Latin American countries, like Argentina[241] and Mexico[242] have recently amended their Codes of Criminal Procedure to introduce the use of brain activity data originating from neuroimaging techniques or other types of neurotechnology as legal evidence. Data related to mental activity will only be used after informed consent of the individual involved. Mexico also included neurorights in its digital rights charter[243]. The case of Chile is noteworthy because it was the first country to include the protection of neurorights in its constitutional framework[198,244]. In addition, in 2021, the Chilean Senate approved a bill on the protection of neurorights, mental integrity and the development of research in neurotechnologies[245] that is going through the final stages of the Chilean Congress. The Chilean Supreme Court has issued its first sentence compelling a company to eliminate personal neurodata it had stored[246]. In 2022, Brazil drafted a bill that included amendments to the General Data Protection Law of 2014, introducing a regulation to protect the neural data of Brazilian citizens collected by invasive and non-invasive devices[247]. Further work continues on different legal levels. Finally, in 2023, the Latin American Centre for Development Administration (CLAD), which has 24 member countries, included neurorights in its Ibero-American Charter on Artificial Intelligence in Public Administrations (*Carta Iberoamericana de Inteligencia Artificial en la Administración Pública*)[248].

## Regulatory and assessment frameworks

**Currently regulated devices include ones that combat the effects of stroke, Alzheimer's and Parkinson's.**

Current legislation on health technology assessment and regulation establishes the framework for developing and adopting neurotechnologies. This may be supplemented by any guidelines, standards or criteria that the authorities may use to certify or evaluate their functions of use. The following section provides details of the approaches current in 2023, distinguishing between neurotechnologies for the clinical setting and devices without an intended medical purpose.

### Clinical setting

**Robust clinical evidence needs to be compiled about the usefulness, safety and effectiveness of neuro-technologies before their sale or inclusion in the portfolio of services offered by the Spanish National Health System.**

The competent authority for the regulation of medical and healthcare devices in Spain, including active implantable medical devices, is the Spanish Agency of Medicines and Medical Products (AEMPS in Spanish), which applies European Regulation 2017/745[228] dated 5 April and Royal Decree 192/2023, dated 21 March[249]. This decree includes the obligatory requirements of the European Regulation as well as the additional aspects that had been left open for each member state to address.

The new regulations require any medical and healthcare device (including those whose function is based on neurotechnologies) to be used on/by people for medical purposes to pass a strict clinical assessment process demonstrating its clinical benefits, safety and effectiveness[228]. In this context, scientists highlight the difficulty of standardising certain diseases[250], which heightens the need for personalised treatments tailored to each patient. Another challenge, in the case of certain neurotechnologies, is the difficulty of designing research that proves a clinical benefit in the treatment of certain diseases, such as fibromyalgia[251,252]. Although there is potential, and initial evidence exists for its treatment[253-255], the participants in one trial who formed part of the placebo group (which did not receive therapy) reported the same improvements as the group who did receive transcranial stimulation. This could indicate that the mere fact of attending a session to receive an innovative therapy has a positive effect on people, which makes it difficult to prove the possible clinical benefits of neurostimulation for the treatment of fibromyalgia[251]. In most cases, the potential side effects of the use of these technologies is unknown in the middle to long term, and further, solid scientific evidence needs to be compiled both to confirm a clinical benefit and to rule out the emergence of negative side effects[256].

A clear regulation also needs to be defined for the removal or maintenance of implants in patients who have participated in clinical research. Whether the research process should also include removal of the device is another aspect of this debate[257]. Conversely, the debate also covers whether patients who have improved their symptoms should have their implant removed, either because the clinical research has ended or when there is a change in the manufacturer's priorities[258], circumstances that both the scientific community and patients warn about[259].

When the clinical evidence on the usefulness and safety of therapies based on neurotechnologies has been collected in the trials, developments may be certified for sale with the CE marking. Once they are on the market, in the case of assessment for inclusion in the portfolio of services offered by the Spanish National Health System, the competent authority is the Spanish Network of Health Technology Assessment Agencies (RedETS in Spanish)[260]. The network compiles the scientific and clinical evidence available on the effectiveness and safety of devices, as well as any considerations for their implementation. It reports on its decision-making process about whether a medical and healthcare device can be added to the portfolio. The portfolio currently contains some neurotechnologies, such as deep brain stimulation for the treatment of Parkinson's or epilepsy[72,132]. The Network also prepares clinical practice guidelines with recommendations on interventions and treatments, although it is

- CE marking: Certification indicating that a product or device meets the environmental health and safety standards established by the European Union. In the case of medical and healthcare devices, the device must have passed through the approval process of a notified body.
- Portfolio of services: The set of healthcare assistance, services and technologies that the public healthcare system provides equally for all citizens throughout the national territory following criteria of quality and effectiveness.
- Deep brain stimulation: Surgical technique that consists of the placement of electrodes in certain areas of the brain to administer electrical pulses.

not possible to recommend interventions that are not currently included in the portfolio[132], as is the case of transcranial magnetic stimulation for treatment-resistant depression (which is commercially available and is offered at a number of Spanish hospitals)[55,261]. A final consideration about neurotechnologies is intended purpose: although a device may be approved for clinical use in the treatment of a specific disease, it must undergo a new process for any other circumstance of use.

### Regulation of devices without intended medical purpose

**Non-invasive stimulation neurotechnologies without an intended medical purpose are certified and assessed under the umbrella of healthcare regulations.**

Sections of the scientific community recommend that regulating authorities categorise neurodata as sensitive health data and apply the regulations corresponding to neural devices[262]. The same line of thought was adopted by the European Commission when they approved Commission Implementing Regulation (EU) 2022/2346 on 2 December 2022, by virtue of compliance with Regulation (EU) 2017/745 dated 6 April, on medical devices. This implementing regulation lays down the common technical specifications for certain groups of products without an intended medical purpose (included in Annex XVI) which, due to their similarity with medical and healthcare devices in terms of functioning and risk, must be certified and assessed in a similar way to such devices. Non-invasive neurotechnologies with the purpose of transcranial stimulation to modify neural activity outside the clinical setting are categorised among these devices[263]. Annex VII of the regulation explicitly states that the published specifications do not apply to invasive cranial stimulation devices without an intended medical purpose, i.e., under strict control of the health regulations -which are excluded from the scope of this legislation[264]. On the other hand, it should be noted that non-invasive devices which do not stimulate are not included in the list that figures in Annex XVI; such devices are currently subject to European legislation in force governing the sale of devices in general[265]. The Spanish Bioethics Committee advocates express prohibition of the use of any neurotechnology for non-therapeutic purposes[237]. Nevertheless, the Charter of Digital Rights advocates regulation of this technology[234].

Currently, work is underway to implement common technical specifications for devices without an intended medical purpose, which establishes the need to conduct an exhaustive risk analysis, with a list of warnings, side effects and contraindications that must be communicated to the user[264]. These devices will be included in the EUDAMED database[266,267]. Manufacturers of neurotechnology devices without an intended medical purpose that were already on the market before this legislation came into force must compile the relevant scientific evidence by means of clinical research to achieve certification[263].

## Research and state-of-the-art innovation

**An ethical approach to neurotechnologies from initial stages and throughout the innovation and development process can enable their safe, responsible use, and make it easier to solve potential challenges should they arise.**

Since 2013, large investments have been made in brain related research projects in the United States[268,269], Europe[270], China[271,272], Japan[273] Australia[274], Canada[275] and South Korea[276], united in a coordinated global initiative[277]. Among the projects with most funding are the US BRAIN initiative[268,269], specifically centred on the development and application of neurotechnologies to decode the dynamics of neural activity and circuits and how they shape our cognitive and behavioural capacity[278]. One of the main initiatives in Europe is the Human Brain Project (HBP) which employs supercomputing technologies to construct computer models and simulations of the human brain. The use of big data provides researchers with new mathematical tools to confront various neurological, neurodegenerative diseases and other conditions[270,279]. Lines of action in the field of neurotechnology have likewise focussed on the creation of scientific infrastructures, digital platforms and best practice protocols to facilitate access to data, modelling tools and computing resources for scientists, healthcare and business professionals and, in short, achieve a better understanding of the brain[32,280,281].

In this context, the scientific community recommends more funding and coordination of research, in addition to promoting an interdisciplinary approach that addresses real clinical challenges and needs[32,282]. To transfer the advances made to clinical practice and society as quickly, equally and efficiently as possible requires the integration of different areas of knowledge. These include neuroscience, biomedical engineering, computer science, physics, chemistry, molecular biology, medicine as well as social sciences like psychology, philosophy, ethics and other fields relevant to the study of the social and cultural issues related with health and disease. Likewise, as new results emerge, the scientific community highlights the importance of large projects coming together to achieve consistent, reproducible developments in our knowledge of the brain[283].

On the other hand, scientists note that the ethical regulation of neurotechnologies need not hinder innovation. If control is addressed from the initial stages and throughout the whole process, it could also be a key feature to help confront the challenges that neurotechnologies might present in the future[45,284]. The first international standard to foster responsible innovation in neurotechnologies was prepared in 2019 by the Council of the Organisation for Economic Co-operation and Development (OECD)[222]. Business is acknowledged as a critical stakeholder in the ecosystem, particularly through its participation in international consortia for collaboration between research, innovation and industry, such as NSF Brain focusing on technological transfer[25].

In addition to contributing its existing research structure, Spain joined the international community with the launch, in December 2022, of the first National Neurotechnology Centre (SpainNeurotech). This multi-disciplinary organisation will pay particular attention to the ethical, legal and regulatory aspects associated with this field[285].

## Key concepts

- The current frontier of knowledge in neuroscience is the connection between the physical brain and higher functions, like identity, consciousness, cognitive and motor skills, and a person's behaviour or emotions. Understanding these things is vital to address one of the greatest challenges facing science in the 21st century: treating neurological diseases.
- Neurotechnologies are tools designed to interact with the brain and the rest of the nervous system. According to experts, these technologies have a great potential to generate advances in knowledge and tackle nervous system disorders.
- Validated neurotechnologies already exist for the treatment of neurological diseases, as do some promising clinical demonstration models that fight the effects of stroke, Alzheimer's, depression or Parkinson's. Nevertheless, certain technical limitations exist, and more scientific evidence is necessary before feasible, safe clinical interventions become commonplace.
- Research is underway into understanding the brain activity associated with emotional states and consciousness. Other ongoing research is related to communication and language, or with thought and visual or auditory processing.
- The demonstrated usefulness of neurotechnologies in the health sector has created expectations in the commercial sphere, with potential applications in entertainment, education, defence and national security and on the consumer market.
- The continuous progress of research and business investment in neuroscience and neurotechnologies is interlinked with ethical debate about the impact of such developments on our society.
- In terms of governance, the debate has been driven by the research communities in neuroscience, philosophy, law and ethics regarding the adaptation of existing legal framework to ensure proper protection of citizens' rights in neurotechnologies. This is the context that gave rise to the term "neurorights."
- The scientific community notes that the ethical regulation of neurotechnologies need not necessarily be an obstacle to innovation. If these aspects are tackled from the initial stages and throughout the development process, safe and responsible uses can be authorised, making the resolution of future technical challenges less complicated.

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