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Neurotechnology: Scientific and Ethical Challenges

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Summary

- *As means of exploring or modulating the nervous system, neurotechnologies are increasingly used to treat or remedy disabilities. The private sector's growing interest in these technologies, particularly for creating brain-machine interfaces, raises the question of their non-medical applications.*
- *The research sector, in which France is and must remain highly ranked, still has many challenges to meet, most often in relation to improving the precision of the devices used. These advances are themselves linked to advances in knowledge of the brain.*
- *Increasingly complex ethical issues call for the regulation of these technologies, as shown by numerous initiatives at the international level. In the long term, vigilance must be exercised in response to the transhumanist project to create "augmented humans", as neurotechnologies must be used first and foremost for healing and repair.*

Patrick Hetzel, Member of the National Assembly, Vice-President

Neuroscience-related technologies

We have recently witnessed a resurgence of interest in neurotechnologies as **tools for measuring or modulating the nervous system**, especially brain activity, spurred on by initiatives launched by both public authorities and private companies,[1] but also by improvements brought about by digital technologies and the design of increasingly powerful interfaces. These techniques, whose forerunners include controversial methods,[2] and even abandoned practices in the case of lobotomies, **remain dependent on our currently incomplete knowledge of the functioning of the brain and its 100 billion neurons,** and more generally, of the functioning of the central and peripheral nervous systems.[3] Indeed, advances in neuroscience, which are dependent upon neurotechnologies, and which reciprocally help to improve these techniques, are hindered by the complexity of the brain, which remains the **most poorly understood human organ** by science.

Technologies used for investigating brain activity

Various imaging techniques can be used to investigate brain activity. Compared to other techniques, **electroencephalography** (EEG) is non-invasive and relatively inexpensive, and is therefore widely used. It measures electrical activity in the brain via electrodes placed on the skull, and has been used since the 1950s to diagnose and monitor a wide range of diseases (despite a spatial resolution of more than 1 cm^2). It is also used for studying sleep and, where necessary, its disorders. Electrocorticography (ECoG) and intracranial or stereotactic EEG (SEEG) are more efficient, but invasive (requiring surgery), variants of EEG. **Magnetoencephalography** (MEG) measures the weak magnetic fields generated by the electrical activity of a group of neurons (resolution of 2 to 3 mm^2), and has extensive clinical applications, e.g. for locating epileptic foci prior to surgery. EEGs and MEGs enable the recording of **evoked potentials** (EPs), which measure changes in the electrical potential of neurons after sensory stimulation and provide information about the functioning of the stimulated pathway (e.g. auditory, optic or motor nerves).

All of these techniques, which are based on electrical activity, usually produce less accurate results than other methods based on metabolic activity: **functional magnetic resonance imaging** (fMRI), for example, can show haemodynamic variations (local changes in blood flow) and changes in blood oxygenation linked to neuronal activity. Its average spatial resolution can be as detailed as 500 μm^2, although its temporal resolution is limited. Similarly, **positron emission tomography** (PET) and **single-photon-emission scintigraphy** (SPECT) use a camera to detect positrons or gamma rays, respectively, which are emitted by a radio-labelled tracer with known behavioural and biological properties, in order to monitor the concentration of radioactivity and the tissue kinetics of the radiotracer for the analysis of cell metabolism. Other techniques should also be mentioned, such as **transcranial ultrasound imaging** (which can facilitate stroke diagnosis and monitoring), and **functional near-infrared spectroscopy** or fNIRS (which measures brain oxygenation in order to infer its activity).

Neurotechnologies for healing

Neurotechnologies are widely used for **therapeutic purposes**, often in combination with the above-mentioned imaging techniques (especially EEG, MEG and fMRI). **Neuromodulation**, or neurostimulation, uses electric currents, light, ultrasound or magnetic fields to intervene on neuronal circuits. Non-invasive methods, such as **transcranial magnetic stimulation** (TMS) and **electrical stimulation** (transcranial direct-current stimulation – tDCS), whose effects vary according to the frequency of the current and the polarity (inhibiting on the cathode side, exciting on the anode side), are less accurate than invasive implanted stimulation because the administered or induced current is not precisely targeted. Although studied by medical research projects for the treatment of depression, pain, schizophrenia and neurological diseases, a consensus on their effectiveness has not yet been reached. Conversely, **deep brain stimulation** (DBS) produces undeniable results for the treatment of certain pathologies.[4]

Deep brain stimulation (DBS)

DBS is currently used empirically with success for the second-line treatment of Parkinson's disease, following research by Professor Alim-Louis Benabid (80% reduction in tremors, despite undesirable effects in a minority of patients such as apathy, speech problems and weight gain). It requires the extremely accurate implantation of two electrodes in the brain at the level of the subthalamic nuclei. These electrodes are connected to two electrical batteries implanted at the subclavicular or abdominal level, which deliver a direct current of 2 to 3 volts at 130 pulses per second, i.e. at a frequency of 100 to 200 Hz. Corrosion and tissue formation around the electrodes gradually reduce the signal over time. The batteries have a service life of around five years, depending on the intensity of the stimulation. Surgery is required whenever the equipment is changed, and batteries are currently being developed with a service life of 25 years. Other applications could include the treatment of Alzheimer's disease and mental disorders which are resistant to other treatments, such as severe forms of depression and obsessive-compulsive disorders.

Other **invasive but less profound neuromodulations** have also produced positive effects on treated patients, either by reducing chronic pain, eliminating the feeling of hunger in obese people, or preventing epileptic seizures (a helical electrode implanted around the vagus nerve stimulates it at regular intervals). Used in a medical context, **virtual reality** also yields promising results for mental disorders, especially in combination with other therapies.[5]

Neurofeedback and brain-machine interfaces (BMI)

The imaging techniques discussed above can be used as part of a "neurofeedback" process consisting of **feedback** loops between the nervous system and computers, which use information about a given function to control and modify that function, usually via EEGs. **Brain-computer interfaces**[6] (BCI), which are closely related to neurofeedback but often considered as a separate technique, have made a significant contribution to the neurotechnology field, with **neuroprostheses** being a spectacular example of this technology. BCIs are divided into unidirectional and bidirectional, invasive and non-invasive devices. After pioneering research on monkeys and then on humans in the 1970s and 1980s, and despite a mixed clinical assessments,[7] convincing results have been recorded more recently in the fields of **communication** (cursor movements, virtual keyboards, video games, etc.), **military** applications[8] and, above all, compensation for disabilities.

Compensating for certain disabilities

Neurotechnologies can provide solutions to aid recovery from **sensory** (hearing, visual) **and motor** (paralysis, loss of a limb, etc.) **disabilities**. Sensory neuroprostheses, which consist of information sensors and a processor to transform this information into electrical stimuli, are used to transmit sensory information to the brain via electrodes when an organ or the normal transmission chain fails. When the optic nerve is intact but the photoreceptor cells have degenerated (as occurs in pigmentary degeneration of the retina and age-related macular degeneration), **artificial retinas** can restore basic vision after the implantation of a chip in the retina which creates electrical currents to stimulate the cells leading to the optic nerve when the chip is exposed to light, or when an external camera sends visual information to the chip.[9] When deafness is accompanied by an intact auditory nerve, a **cochlear implant** can restore hearing as a second-line treatment, via a microphone that detects sounds and converts them into electrical signals, which are then applied to different parts of the helical structure of the inner ear in order to stimulate the auditory nerve.[10]

Several technologies can also compensate for **motor disabilities**, but they currently remain at the laboratory research stage (except for post-stroke rehabilitation). **Paraplegia** and **tetraplegia** – paralyses caused by an injury to the spinal cord that prevents nerve signals from flowing between the brain and the parts of the body situated beneath the injury – can be overcome by restoring the patients' control over their limbs by implanting a controller: functional electrical stimulation requires the application of low-level electrical stimuli to the nerves controlling the muscles, or directly to the muscles themselves, in order to assist or replace voluntary contractions. Highly complex electrical signals are transmitted to the muscles via electrodes placed on each muscle. However, the implantation process requires a very long surgical operation, the actions are slow, the muscles tire quickly, and the patient needs assistance from another person or a walker. BMIs are also used for patients with advanced amyotrophic lateral sclerosis. **Motor neuroprostheses** analyse voluntary motor information in the brain, interpret it, and transmit information about the mechanical actions to be performed to an **exoskeleton,**[11] or to a limb (real or artificial).[12] Finally, **bi-directional neuroprostheses** are composed of a motor prosthesis, sensors and proprioceptors. The latter provide feedback to the brain or to the controller about the action performed by the prosthesis, in order to help patients adapt their control over the movement, recover their sense of touch, and feel signals similar to pain.[13]

Growing private-sector interest and the question of non-medical applications

Tempted by the potential opportunities arising from the hybridisation of the brain with artificial intelligence (AI), more and more companies are investing in the field of neurotechnology,[14] following the example of **Neuralink**, founded by Elon Musk in 2017, whose targets include enabling paralysed people to walk again and treating neurological diseases, but also improving natural cognitive abilities. The latest version of its 23-mm diameter, 8-mm thick implant, recharged daily by induction and composed of 1,024 electrodes (extremely fine wires close to the size of a neuron), was tested in on pigs in 2020 (after initial experiments on rats and a monkey), and authorisation is currently awaited to begin clinical trials on humans.[15]

The corporate sector's growing interest in neurofeedback and BMIs is accompanied by **massive investments in research**, with a view to mainly non-medical applications despite a **restrictive legal framework.**[16] Examples include the marketing of consumer products with **often unproven effectiveness**, for controlling digital interfaces by thought (computerised transmission and receipt of information, entertainment and video games, etc.), as an aid to concentration, relaxation or sleep and well-being in general, or to improve cognitive and sporting performance. There is great potential for the development of EEG neurofeedback as an "individual" device, although the results are highly variable and tend to be **overestimated**, and not only as a result of promotional "hype".[17]

It can also be used to detect **losses of attention** when driving a car, in the classroom or at work. Several of the experts interviewed claimed that experiments on using BMIs to monitor the brain waves of students and workers are being conducted in China, in order to combat emotional states that are detrimental to concentration.

Meeting the challenges of research

This field benefits from major public and private research projects and is constantly progressing, with efforts focusing on **extending** the application of already known neurotechnologies to other pathologies (such as the use of deep brain stimulation to treat OCD, Tourette's syndrome, depression, etc.), and on increasing their **precision**.

In **brain exploration**, future progress will require the standardisation of measurements (each manufacturer has its own references), and the simultaneous use of fMRI and EEG or MEG. Advances in fMRI call for the deployment of high-resolution, latency-free, "high-field" imaging,[18] and small low-field devices to facilitate the dissemination of the technology. Progress in EEG will require **higher resolutions** (less than one cm^2), the simplification of sensor installation (often long and uncomfortable), and the ability to use dry electrodes. The objective for MEG is to enable the technology to function at room temperature[19] (versus near absolute zero at present).

As far as **brain stimulation** is concerned, the electrodes used, whose diameter is currently no smaller than 5 microns, will become progressively thinner in order to approach the neuron scale. In addition, the materials used will be **more flexible and biocompatible,**[20] in order to prevent them from being identified as foreign bodies and to limit signal loss. Finally, the circumferential electrodes that measure the potential in their entire vicinity will be replaced by **directional** electrodes, to reduce spurious signals. This increased accuracy will enable **more precise coverage** and the use of a greater number of electrodes, in order to reproduce local and overall variations in nerve impulses. The US-based Brain Initiative is developing mixed and scalable electrodes to record and stimulate neuronal activity electrically, magnetically and optically at different scales. These **mixed electrodes** hold great promise. **Optogenetics**[21] is another potentially exciting, but uncertain, field awaiting further exploration. Finally, the use of improved radiotracers will enable the development of **more precisely targeted therapies.**[22]

However, we must remain aware of the **limitations of** neurotechnologies (inconsistent performance, and side effects, as the implantation of electrodes in the brain may cause infections, haemorrhages and brain dysfunction). Electrical or magnetic stimulation may cause epileptic seizures, alter the brain's plasticity, and interfere with the patient's thoughts and emotions, or even his or her ability to exercise free will: consequences which raise major ethical issues.

Ethical issues

The use of neurotechnologies **affects the brain** – either as the intended purpose or as a side effect – and the patient's or user's personality may be altered, leading to depression or euphoria, for example. Insufficient long-term data is available to objectively assess whether the benefits of certain neurotechnologies far outweigh their side effects. In addition to these intrinsic risks, the use of neurotechnologies is also open to **potential abuses**. Low-cost devices for individuals are becoming more widely available and may be of poor quality, ineffective, or even dangerous (cases of cognitive damage or scalp burns).

More generally, neurotechnologies raise **ethical questions** about patients' rights to their data, which need to be protected as they could be used for discriminatory or malicious purposes. Therefore, concerted international efforts have been made recently to meet the ethical challenges posed by these technologies, as the 1997 Oviedo Convention on Human Rights and Biomedicine – the first legally binding international instrument for protecting rights against any misuse of biological and medical advances – is now insufficient. In December 2019, the **OECD** [(23)] formulated nine principles intended to regulate innovation in neurotechnology. This recommendation – the first international standard in this field – will be implemented at the national level. The French Ministry of Higher Education, Research and Innovation (MESRI) is collaborating with other actors on the adoption of a **charter for the responsible and ethical development of neurotechnologies in France.**[(24)]

Some initiatives go further than the usual rights of patients (including dignity, the integrity of the human body, the principle of informed consent, and the right to information), the protection of personal data, the reliability, safety and security of devices, and the prevention of abusive or even malicious uses: they concern the **protection of the personality** and the protection of the right to exercise free will.

For example, the report by the **UNESCO** International Bioethics Committee (IBC) on the "Ethical Issues of Neurotechnology",[(25)] published in 2022, calls for the creation of a new set of human rights, called **neurorights**, including the right to mental privacy and to exercise free will, which go beyond the traditional scope of the protection of human rights.[(26)] This report calls on each state to guarantee the neurological rights of its citizens by adopting laws that protect privacy, brain activity and freedom of thought in relation to neurotechnologies, and stresses the need to pay special attention to children and adolescents, due to the plasticity of their developing brains.[(27)] UNESCO has also announced that it is leading discussions on developing a roadmap that will serve as the basis for a global framework for the governance of neurotechnologies.

In October 2021, **Chile** anticipated these developments by passing a law protecting citizens' "brain rights", which covers the protection of neurorights,[(28)] including the rights to personal identity, free will and mental privacy.

The Office's recommendations

Following on from its previous work,[(29)] the Office proposes to **reinforce the coordination and unification of French** neuroscience and neurotechnology **research**, which is carried out by an excessively fragmented body of small, poorly funded teams (the number of permanent neuroscience researchers at the French National Centre for Scientific Research (CNRS) has declined by 20% in ten years).

The development of the research ecosystem should be encouraged by establishing a **consortium** (of the “Braingate” type in the United States), or even a **national neurotechnology research network** encompassing all the players: research institutes, hospitals, military researchers and industry.[(30)]

This is all the more important as France boasts many assets and is often **at the forefront of international neurotechnology research**, particularly for **clinical research** (deep-brain stimulation, cochlear implants, artificial retinas, neuroprostheses, optogenetics, etc.).

In partnership with the Institut du Cerveau and the Institut de la Vision, based in Paris, a centre of **excellence** in neurotechnology could emerge at Paris-Saclay, which is already a top-ranked institution for neuroscience (with NeuroSpin, NeuroPSI, etc.) and hosts excellent engineering schools.

The following recommendations are made with specific regard to the **ethics** of neurotechnology:

- continue the work on transposing the OECD recommendation on the regulation of innovation in neurotechnology into national law;

- define a **protective legislative framework**, similar to that adopted in Chile, with an emphasis on the safety of devices, respect for the right to maintain bodily integrity and the right to privacy, and the protection of personal data, including data from the recording of brain activity, while setting aside the excessively vague notion of free will;

- and ensure that this framework does not discourage research or reduce our competitiveness.

Even if the **transhumanist project** remains largely the stuff of science fiction at this stage, a certain vigilance is still required to counter the **temptation to create augmented humans**: first and foremost, neurotechnologies must **be used for healing and repair**.

The Office's websites:

http://www.assemblee-nationale.fr/commissions/opecst-index.asp
http://www.senat.fr/opecst

Références

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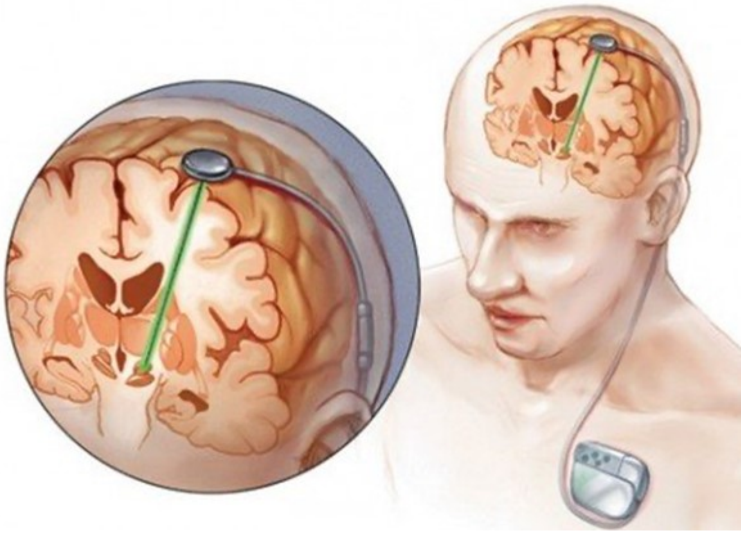
[1] *Examples of such initiatives by the public authorities include major research projects on the functioning of the brain, in conjunction with the private sector. In 2013, the* "Brain Research through Advancing Innovative Neurotechnologies" *(or* "Brain initiative"), *was launched in the United States, with $4.5 billion in funding allocated over twelve years. In the same year, the European Union launched its* "Human Brain Project" *with €1 billion in funding over ten years. China has also launched its own* "China Brain Project" *on a similar scale, and many other states, including Japan, Israel, and Australia, have also established major national initiatives). For their part, private companies – especially US firms – are making unprecedented investments in neurotechnology research, and particularly in brain-machine interfaces (BMI). Neuralink, founded by Elon Musk and benefiting from investments totalling several hundred million dollars, is the highest-profile example, but other cases can also be mentioned: Meta/Facebook (purchase of CTRL-labs in 2019 for $1 billion dollars and Oculus in 2014 for $2 billion dollars); Kernel, Synchron, Allen Institute, the Braingate consortium with Cyberkinetics, Blackrock Neurotech, the Wyss Center and General Motors, and smaller examples such as Muse, Halo, Emotiv, etc. French examples include BrainTech, NextMind, Clarity and Dreem.*

[2] *Electroconvulsive therapy (ECT), known as "electroshock therapy", is probably the most famous of these methods. In psychiatry, its effectiveness for treating depression and manic, paranoid, catatonic or psychotic states (especially schizophrenia) is proven, despite its sometimes traumatic and even dehumanising aspects. Exactly how this technique functions is still poorly understood but it probably relates to the reduction of brain connections in the dorsolateral prefrontal cortex. Lobotomy, a practice which began to decline in 1960s before being completely abandoned in the 1980s, most often entailed a transorbital resection of the white matter in the frontal lobe (the "ice-pick" method, which replaced even cruder and more invasive leukotomy practices). Before the advent of neuroleptics, this form of surgery was used in psychiatry for treating psychotic conditions such as schizophrenia and severe depression. The overwhelming majority of patients were women, indicating a link between medical practices and power relationships in society, especially gender bias. In general, there is still considerable uncertainty about how both lobotomy and electroshock actually function from a scientific standpoint. See the history of lobotomy by Louis-Marie Terrier, Marc Levêque and Aymeric Amelot, published in the* Lettre des Neurosciences, *No. 55, 2018, and by the same authors: "Most lobotomies were done on women",* Nature, *volume 548, No. 523, 2017* https://www.nature.com/articles/548523e

[3] *The central nervous system or neuraxis comprises two main organs: the brain, on the one hand, which ensures cognitive functions and integrates information (e.g. sensory information) required for the command and control of motor skills, and the spinal cord, on the other, which transmits nerve impulses to and from the brain (bi-directional logic) and co-ordinates motor actions, particularly reflexes. Nerves are responsible for transmitting nerve impulses between the spinal cord and the organs. The brain consists of two hemispheres (right and left) and the cerebellum, which controls the body's balance. The hemispheres can be divided into lobes: the frontal lobe (reasoning, language, voluntary motor coordination), the parietal lobe (awareness of the body and surrounding space), the occipital lobe (integration of messages), and the temporal lobe (hearing, memory and emotions). The main information circuits are the loop between the thalamus and the sensory cortex for processing incoming sensory information, the loop involving the striatum, motor cortex, cerebellum and thalamus which generates complex motor commands, and the memory circuit comprising the hippocampus and the cingulate and temporal cortices. The brain contains a network of nerve cells called neurons, in which information flows in the form of high-speed electrical impulses. Each neuron consists of a body containing the nucleus, dendrites which collect signals from other neurons, and an axon that sends signals to them. The axon is protected by a myelin sheath, which also improves the quality of signal transmission. These neuronal signals are electrical currents called "nerve impulses" or "action potentials". Each axon in a neuron is connected to the dendrites of other neurons via synapses (up to 100,000 per neuron, with an average of 10,000). When a nerve impulse reaches the synaptic terminal, chemical neurotransmitters are secreted into the extracellular environment in order to inhibit or excite the connected neurons by binding onto their transmembrane receptors. The brain also contains at least the same number of glial cells (astrocytes and oligodendroglia) as neurons, i.e. 100 billion. Glial cells are essential to and responsible for performing homeostasis (maintenance of the conditions required for a stable internal operating environment), producing myelin (the insulating sheath surrounding neurons), providing support for brain tissue, supplying nutrients and oxygen to neurons, and in the specific case of microglial cells, eliminating dead cells and pathogens. These cells are therefore responsible for destroying foreign bodies or covering them with rigid tissue. The spinal cord is composed of the same cells and transmits sensory information upwards towards the brain, and motor information downwards towards the different parts of the body. Different nerves emerge around the spinal cord, forming the peripheral nervous system; they are composed of sensory and motor neurons, which innervate all the organs (skin, muscles, viscera etc.) and connect them to the central nervous system.*

[4] *This device, costing around €30,000, is shown in the following diagram:*

Deep brain stimulation (DBS) device



Source: Mayo Clinic

[5] *Some new therapies combine virtual reality with neuroimaging and/or MRI in order to stimulate certain brain areas and treat psychiatric disorders or even impaired motor function, e.g. following a stroke, with the aim of restoring brain plasticity (e.g. the Hemisfer project conducted by INRIA and Rennes University Hospital).*

[6] *The term brain-machine interfaces (BMI) is used, along with brain-computer interfaces (BCI) and direct neural interfaces (DNI). The BMI concept is the most widely used: DNIs and BCIs usually connect the nervous system to a computer, whereas neuroprostheses connect the nervous system directly to a prosthesis. See one of the first books published in French on this subject: Maureen Clerc, Laurent Bougrain and Fabien Lotte (eds.),* Les interfaces cerveau-ordinateur, *éditions ISTE, 2018, as well as the report by Bernard Bioulac, André-Raymond Ardaillou and Bruno Jarry* Interfaces cerveau-machine : essais d'applications médicales, technologie et questions éthiques*, published in December 2020 by the Academy of Medicine and the Academy of Technologies* https://www.academie-medecine.fr/rapport-20-06-interfaces-cerveau-machine-essais-dapplications-medicales-technologie-et-questions-ethiques/

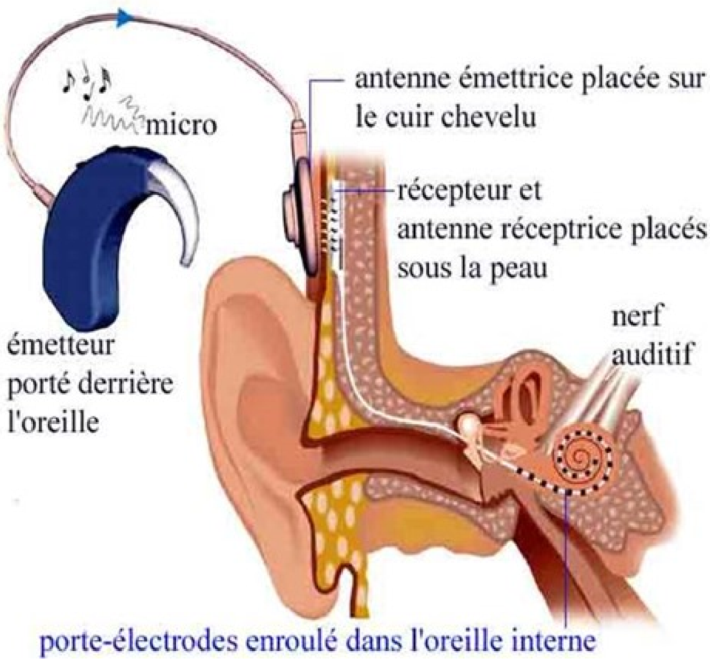
[7] *The available studies show that BMIs with* neurofeedback *have limited effects on health problems, except in the case of stroke rehabilitation, for which they appear to be effective. See the only available meta-analysis, which focuses on chronic pain: Kajal Patel et al. "Effects of neurofeedback in the management of chronic pain: A systematic review and meta-analysis of clinical trials", European Journal of Pain, volume 24, n 8, 2020* https://onlinelibrary.wiley.com/doi/full/10.1002/ejp.1612

[8] *Military applications include exoskeletons and prostheses, analyses of brain activity (to fire a weapon more quickly or control soldiers' vigilance, for example), brain training, etc. In its opinion on the "augmented soldier" of 18 September 2020, the French Defence Ethics Committee stated that it was in favour of developing these augmentation technologies, but called for a risk-benefit analysis to evaluate their impacts on soldiers' physical and mental health. It also recommended establishing the principle of the soldier's consent, with the provision of prior information about the risks involved, and stressed the need to support the Armed Forces' Health Department throughout the life cycle of an augmentation and in its efforts to ensure reversibility. Finally, to encourage further research on the augmented soldier and avoid any risk of loss of military capability for our armed forces, the opinion recommends the prohibition of any enhancement liable to reduce control over the use of force, undermine the exercise of free will, or infringe the principle of human dignity. See* https://www.defense.gouv.fr/salle-de-presse/communiques/communique_le-comite-d-ethique-de-la-defense-publie-son-avis-sur-le-soldat-augmente

[9] *The aim is to be able to recognise faces, read or even move around independently, for which a resolution of 600 to 1,000 pixels is sufficient. However, the best state-of-the-art implant with 1,500 electrodes currently struggles to achieve these levels: increasing the number of electrodes does not necessarily improve the resolution because this is degraded by the inflammatory reactions of tissues around the implant, which complicate the targeting of the electrical currents. Each device costs approximately €90,000.*

[10] *The lifespan of a cochlear implant is approximately 20 years. It should be noted that the sounds perceived, processed and transmitted in digital form are very different from those obtained naturally by a normal ear, and require a period of adaptation and re-education of one year with a speech therapist. If the auditory nerve is affected, a hearing implant can be connected to the cochlear nucleus, but the sound quality is no longer sufficient for understanding speech, and only helps with lip reading. Each device costs around €23,000.*

Cochlear implants



Source: Isabelle Mosnier and Yann Nguyen, APHP and Sorbonne University

[11].

The Clinatec exoskeleton

Source: Clinatec, CEA, LETI, Grenoble University Hospital

[12] The motor information originates either from muscles which are still linked to the brain, via an electromyogram, or from the nervous system through electrodes. For complex applications such as hand prostheses or exoskeletons, internal brain electrodes implanted in the motor cortex are preferred.

[13] Patients suffering from hemiplegia often struggle to walk normally. They cannot lift the balls of their feet before they touch the ground, as this requires a nerve impulse that cannot be transmitted. This impulse can be recreated by an electrode, and it is activated via a link established between sensors and the controller. For amputees, mechanoreceptors integrated into their prostheses enable them to regain feeling in their limbs, in order to protect the patient's body and the prosthesis by reactions to pain, or to improve control over their prostheses by feeling the pressure applied to an object.

[14] Back in 2017, the Office raised the alarm about the predominance of private research and the key ethical issues related to artificial intelligence technologies in its Report No. 464 (2016-2017) by Mr Claude de Ganay, MP, and Ms Dominique Gillot,

Senator, "Pour une intelligence artificielle maîtrisée, utile et démystifiée" (Towards controlled, relevant and demystified forms of artificial intelligence). See the links available on the Senate website http://www.senat.fr/notice-rapport/2016/r16-464-1-notice.html and also on the National Assembly website https://www.assemblee-nationale.fr/dyn/14/dossiers/intelligence_artificielle_maitrisee_utile

[15] *Eventually, Neuralink is aiming to produce 4 mm by 4 mm chips equipped with 10,000 electrodes, capable of exchanging information with the outside world via Bluetooth for a smartphone application, based on the observation that our ability to communicate with our smartphones remains limited. The surgical procedure for implanting the electrodes is expected to be automated, minimally invasive and scarless. Questions have been raised about these projects, especially as this company is driven by a transhumanist project to enhance natural cognitive abilities, which goes beyond the dimensions of repair or medical care. For the time being, the demonstrations have concerned established techniques used by research laboratories for at least 20 and sometimes even up to 50 years, occasionally on humans, and without always requiring invasive sensors: See the cases of a monkey controlling a cursor and subsequently a robotic arm by neuron activity alone, in 1969 and 2003 respectively, (both using an invasive BMI), followed – in humans – by using a non-invasive BMI to play pong, in 2007.*

[16] *In France, for example, the Law of 2 August 2021 on bioethics added Article L. 1151-4 to the Public Health Code, which provides for the prohibition by decree of "acts, procedures, techniques, methods and equipment having the effect of modifying brain activity and posing a serious risk or suspected serious risk to human health". Article 16-14 of the French Civil Code, as revised by the Law of 2 August 2021 on bioethics, stipulates that "brain imaging techniques may only be used for medical or scientific research purposes, or in the context of judicial expertise, excluding, in this context, functional brain imaging", which is consistent with the Office's position on limiting the use of brain imaging in court (Laura Pignatel's PhD thesis on this issue and, more generally, on the emergence of "neurolaw", defended in 2019, is worthy of note). See Report No. 476 (2011-2012) of the Office, by Mr Alain Claeys and Mr Jean-Sébastien Vialatte, Members of the French Parliament, entitled "L'impact et les enjeux des nouvelles technologies d'exploration et de thérapie du cerveau" (The impacts and challenges of new technologies for brain exploration and therapy), published on the Senate website https://www.senat.fr/notice-rapport/2011/r11-476-1-notice.html and on the National Assembly website, https://www.assemblee-nationale.fr/13/rap-off/i4469.asp in addition to the Office's Science and Technology Briefing No. 20, on "Neurosciences et responsabilité de l'enfant" (Neurosciences and children's liability by Mr Michel Amiel, Senator (November 2019), also available on the Senate website https://www.senat.fr/fileadmin/Fichiers/Images/opecst/quatre_pages/OPECST_2019_0090_note_neursociences.pdf and on the National Assembly website https://www2.assemblee-nationale.fr/content/download/181379/1817000/version/3/file/OPECST_2019_0090_note_neurosociences.pdf*

[17] *As shown in the meta-analysis by François Gonon, Estelle Dumas-Mallet and Sébastien Ponnou, on "Media coverage of scientific observations concerning mental disorders", the choice of subjects covered by the media significantly accentuates the distortions already found in the scientific literature, i.e. publication biases favouring initial observations and those reporting a positive effect. As a result, the media rarely inform the public about the uncertainties surrounding initial studies, and neglect to mention studies reporting an absence of effects. In particular, biomedical observations reported by the media are often contradicted by subsequent research, about which the public is not informed. See https://cahiersdujournalisme.org/V2N3/CaJ-2.3-R045.html*

[18] *The high-field fMRI system at the French Alternative Energies and Atomic Energy Commission (CEA) Neurospin centre in Saclay – the world's most powerful model with a magnetic field of 11.7 teslas – produced its first images on 7 October 2021.*

[19] *This is the objective of Mag4Health, a start-up launched by CEA-Leti engineers in September 2021. See https://www.leti-cea.fr/cea-tech/leti/Pages/actualites/News/Magnetoencephalographie--vers-la-haute-resolution-a-temperature-ambiante.aspx*

[20] *Polymer-metal-polymer composites and silicones could ensure the biocompatibility, flexibility and durability of the electrodes, despite their extreme fragility.*

[21] *Originating from the observation of a light-sensitive protein discovered in an alga (channelrhodopsin) in 2002, optogenetics involves the genetic manipulation of nerve cells in order to enable their electrical activity to be controlled by light. Targeted neuronal cells are modified via viral vectors and then optically stimulated in order to excite or inhibit a defined number of neurons. Clinical applications in humans will depend on the quantification of the side effects caused by the genetic engineering and the implantation of optical devices that channel light into the brain through the skull. Indeed, the spatial and temporal accuracy of this technique is highly dependent upon these optical illumination devices, which are currently under development. One short-term application prospect concerns the recovery of vision by optogenetic stimulation of the retina: the first successful clinical application of optogenetics took place at the Institut de la vision in Paris, as described in an article published in the journal* Nature *on 24 May 2021, see José-Alain Sahel et al., "Partial recovery of visual function in a blind patient after optogenetic therapy" https://www.nature.com/articles/s41591-021-01351-4*

[22] *Examples include the visualisation of neuroinflammation in Parkinson's patients with radiotracers that facilitate the evaluation of specific anti-inflammatory drugs.*

[23] *The following principles of Recommendation 457 were laid down by its Council of Ministers: promote responsible innovation; prioritise safety assessment; promote inclusivity; foster scientific collaboration; enable societal deliberation; enable the capacities of oversight and advisory bodies; safeguard personal brain data and other information; promote cultures of*

stewardship and trust across the public and private sectors; anticipate and monitor possible unintended use and/or abuse. See *https://legalinstruments.oecd.org/fr/instruments/OECD-LEGAL-0457 Back in 2017, Marcello Ienca and Roberto Andorno had called for such an approach in their article entitled "Towards new human rights in the age of neuroscience and neurotechnology" cf. https://lsspjournal.biomedcentral.com/articles/10.1186/s40504-017-0050-1*

[24] *The Ministry coordinates a national task force on the implementation of OECD Recommendation 457. The charter being developed could address the recognition of patients' and users' rights, the protection of brain data, the reliability, safety and security of devices, the ethics and rules of professional conduct for communication, the prevention of abuses, and the deterrence of malicious applications. This task force* has been *discussed in several articles published in an issue of the Annales des Mines journal* Réalités industrielles*, No. 3, August 2021, entitled "Neurotechnologies et innovation responsable" (Neurotechnologies and Responsible Innovation): See https://www.cairn.info/revue-realites-industrielles-2021-3.htm*

[25] *See https://en.unesco.org/news/unescos-international-bioethics-committee-recommendations A draft but more complete version of the report is available via the following link https://unesdoc.unesco.org/ark:/48223/pf0000378724*

[26] *In the United States, the NeuroRights Foundation, chaired by the professor of neurobiology at Columbia University Rafael Yuste, is also campaigning along similar lines.*

[27] *The Office's Science and Technology Briefing on "Neurosciences et responsabilité de l'enfant" (Neurosciences and children's liability) clearly underlined the slow pace of brain maturation, with cognitive capacities approaching those of adults acquired at around 16 years of age, and psychosocial maturity only attained at around 22-23 years.*

[28] *See this legal analysis by the lawyer Thierry Vallat https://www.thierryvallatavocat.com/2021/10/la-premiere-loi-sur-la-protection-des-donnees-neuronales-a-ete-adoptee-le-30-septembre-2021-au-chili.html*

[29] *See the Office's report No. 476 (2011-2012) by French Members of Parliament Messrs Alain Claeys and Jean-Sébastien Vialatte, entitled "L'impact et les enjeux des nouvelles technologies d'exploration et de thérapie du cerveau" (The impact and challenges of new technologies for brain exploration and therapy), published on the Senate website https://www.senat.fr/notice-rapport/2011/r11-476-1-notice.html and also on the National Assembly website https://www.assemblee-nationale.fr/13/rap-off/i4469.asp in addition to the Office's Science and Technology Briefing No. 20 "Neurosciences et responsabilité de l'enfant" (Neurosciences and children's liability by Mr Michel Amiel, Senator (November 2019), available on the Senate website https://www.senat.fr/fileadmin/Fichiers/Images/opecst/quatre_pages/OPECST_2019_0090_note_neursociences.pdf and also on the National Assembly website https://www2.assemblee-nationale.fr/content/download/181379/1817000/version/3/file/OPECST_2019_0090_note_neurosociences.pdf*

[30] *Particular mention should be given to the transport and automotive industries, which are already developing neurotechnology-based solutions for their future products.*

People consulted

Scientific Board of the Parliamentary Office for Scientific and Technological Assessment (OPECST)

- Mr Raja Chatila, Professor Emeritus at Université Pierre et Marie Curie, former Director of the Institut des Systèmes Intelligents et de Robotique (ISIR – Sorbonne University)
- Mr Béchir Jarraya, neurosurgeon at Hôpital Foch in Suresnes and University Professor (PU-PH) at Université Versailles-Paris-Saclay, researcher at NeuroSpin-CEA Saclay, and member of the French Academy of Medicine
- Mr José-Alain Sahel, member of the French Academy of Sciences, former Director of the Institut de la vision (INSERM, CNRS, Université Pierre-et-Marie-Curie, Hôpital des Quinze-Vingts, member of Paris City Council, Île-de-France Regional Council and six companies), clinician-researcher in the field of vision
- Mr Hervé Chneiweiss (former member of the Office's Scientific Board), Director of Research at the CNRS, Director of the Paris-Seine Neuroscience Laboratory (Inserm/CNRS/UPMC), neurologist at Hôpital Pitié Salpetrière, Chairman of the INSERM Ethics Committee and of the UNESCO Bioethics Committee, former member of the French National Consultative Committee on Ethics (CCNE)

Institutions

French Ministry of Higher Education, Research and Innovation (MESRI)

- Mr Pascal Maigné, Project Manager, French Delegate to the OECD Working Group on the "Ethics of Neurotechnology"

French Academy of Sciences (Académie des sciences)
- Mr Yves Agid, neurologist and University Professor Emeritus (PU-PH) at Université Pierre et Marie Curie, founding member and former scientific director of the Paris Brain Institute, former director at INSERM and former member of the French National Consultative Committee on Ethics (CCNE)
- Mr Alim-Louis Benabid, neurosurgeon and University Professor (PU-PH), founder and former President – until 2021– of Clinatec (CEA, INSERM, Grenoble University Hospital and université de Grenoble)
- Mr Stanislas Dehaene, Professor at the Collège de France, Director of NeuroSpin, a joint INSERM-CEA unit, President of the Scientific Board of the French National Education System

French National Academy of Medicine (Académie nationale de médecine)
- Mr André-Raymond Ardaillou, nephrologist (PU-PH) and former Permanent Secretary of the Academy
- Mr Bernard Bioulac, former Member of the French Parliament, neurobiologist (PU-PH), former Deputy Scientific Director of the CNRS, former Head of Neuroscience at the CNRS, former director of the ITMO (Multi-Body Thematic Institute) for Neuroscience, and of the Institut des Neurosciences in Bordeaux

French Academy of Technology (Académie des technologies)
- Mr Bruno Jarry, former President of the Académie des technologies, Director of IFPEN, former advisor to the President of Institut Curie, former Vice-President of the Lafarge Group, former R&D Director of the Amylum Group, former Scientific Director of the Tate & Lyle Group, former Director of the École supérieure de biotechnologie de Strasbourg

French National Agency for Medicines and Health Products (ANSM)
- Mr Frederic Dittenit, Deputy Director of Legal and Regulatory Affairs
- Mr Pascal Di Donato, Product Manager for Neurology

French Embassy in the United States
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- Mr Jean-Baptiste Bordes, Science and Technology Attaché, San Francisco
- Mr Karim Belarbi, Science and Technology Attaché, Los Angeles
- Mr Julian Muller, Policy Officer to the Scientific Advisor, Washington

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- Mr Luc Estebanez, CNRS Research Fellow, Paris-Saclay Institut des neurosciences
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National Institute for Research in Digital Science and Technology (Inria)
- Mr Jean-Frédéric Gerbeau, Deputy Director General for Science
- Ms Sandrine Mazetier, Director of Public Affairs
- Mr Frédéric Alexandre, Inria Senior Researcher and visiting researcher at Microsoft
- Ms Christine Azevedo-Coste, Inria Senior Researcher, Head of the "Camin" project team
- Mr David Guiraud, Inria Senior Researcher, seconded to the Neurinnov as the firm's Scientific Director
- Mr Anatole Lecuyer, Inria Senior Researcher, Head of the "Hybrid" project team
- Mr Fabien Lotte, Inria Senior Researcher, "Potioc" project team
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- Mr Etienne Hirsch, Director of Research at INSERM, former President of the French Neuroscience Society
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- Mr Bertrand Thirion, Inria Senior Researcher, Scientific Delegate of the Inria centre in Saclay, Head of the "Parietal" project team at NeuroSpin (CEA-Inria)
- Mr Philippe Vernier, CNRS Director of Research, Director of the Institut des sciences du vivant Frédéric Joliot (CEA-Saclay), founder of the Paris-Saclay Institut des Neurosciences (NeuroPSI - CNRS/University Paris-Saclay)
- Mr Guillaume Charvet, Director of the Medical Device Development Laboratory at Clinatec (CEA, INSERM, Grenoble University Hospital and Université de Grenoble)

Institut de la Vision
- Mr Serge Picaud, Director of Research at INSERM, Director of the Vision Institute (INSERM, CNRS, Pierre-et-Marie-Curie University, Quinze-Vingts Hospital, Paris City Council, member of the Île-de-France Regional Council and six companies)

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- Mr Antoni Valéro-Cabré, Director of Research at the CNRS, Institut du Cerveau
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Universities and teaching hospitals
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- Mr Renaud Jardri, child psychiatrist and University Professor (PU-PH), Lille University Hospital, Head of the "Plasticity & Subjectivity" team at the "Lille Neuroscience & Cognition" Centre
- Marc Ferro, Stanford University researcher and entrepreneur
- Ms Isabelle Mosnier, Deputy Head of the ENT Department at Hôpital universitaire de la Pitié Salpêtrière, Head of the Hearing Implant Functional Unit, referral centre for cochlear implants, Director of the Adult Audiology Research Centre
- Mr Yann Nguyen, ENT surgeon and University Professor (PU-PH), ENT Department at Hôpital universitaire de la Pitié Salpêtrière
- Ms Nina Miolane, Assistant Professor at the University of California at Santa Barbara (UCSB), researcher at Stanford University
- Ms Sonia Pujol, Assistant Professor and researcher at Harvard Medical School (Brigham & Women's Hospital/HMS)

<u>Firms</u>

France Biotech, an association of French biotechnology and health innovation companies
- Mr Franck Mouthon, President
- Mr Olivier Chabanon, General Delegate
- Constance Montazel, Institutional Relations and Public Affairs Officer

<u>Lawyers</u>

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- Mr Raphaël Liotier, lawyer at the Alain Bensoussan practice
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