

Brain-Machine Interfaces: The Role of the Neurosurgeon

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1 **Abstract**

2

3 The neurotechnology field is set to expand rapidly in the coming years as technological
4 innovations in hardware and software are translated to the clinical setting. Given our unique
5 access to patients with neurological disorders, expertise with which to guide appropriate
6 treatments and technical skills to implant brain-machine interfaces (BMIs), neurosurgeons have a
7 key role to play in the progress of this field.

8

9 We outline the current state and key challenges in this rapidly advancing field including implant
10 technology, implant recipients, implantation methodology, implant function, ethical, regulatory
11 and economic considerations. Our key message is to encourage the neurosurgical community to
12 proactively engage in collaborating with other healthcare professionals, engineers, scientists,
13 ethicists and regulators in tackling these issues. By doing so, we will equip ourselves with the
14 skills and expertise to drive the field forward and avoid being mere technicians in an industry
15 driven by those around us.

16

1 **1. Introduction**

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3 Elon Musk’s August 2020 press conference outlining the progress of his new brain-machine
4 interface (BMI) company, Neuralink, captured the attention of neuroscientists and technology
5 enthusiasts around the world as he demonstrated the ability to record neurons from pig cortex in
6 real time. He had earlier promised to ‘merge’ humans with artificial intelligence (AI) when he
7 first announced the company.^{1,2} Neuralink’s novel BMI package comprises of 1024 contacts in
8 custom-built microelectrode ‘threads’, implanted into the brain by a robotic system and is able to
9 wirelessly transmit these signals in real time.¹ While this has received a lot of public interest,
10 many components of the proposed technology are not ground-breaking; systems with similar
11 capabilities have been published in the peer-reviewed literature as long as 17 years ago and other
12 simpler systems are being used clinically to treat a variety of neurological disorders.³

13

14 Neuromodulation technology, including deep brain stimulation, is already a mature market worth
15 over US\$ 5.8 billion in 2020 and set to expand rapidly in the coming years as technological
16 innovations are translated to the clinical setting, with one report forecasting a worldwide market
17 of \$13.3 billion by 2022.⁴⁻⁶ Neurosurgeons have a key role to play in its progression as we have
18 a unique relationship with patients affected by neurological disorders that may benefit from
19 BMIs, both as treating physicians and in guiding their decision making processes as to the best
20 choice of treatment. We also possess the skills and expertise to implant these new devices into
21 the nervous system. It is therefore easy to see how many neurosurgeons may be part of a
22 subspecialty of not just ‘*restorative and functional*’ but ‘*augmentative*’ neurosurgery.

23

24 In this article, we outline the current state and key challenges in this rapidly advancing field
25 including implant technology, implant recipients, implantation methodology, implant function
26 and implant regulation, ethical, regulatory and economic considerations. Our key message is to
27 encourage the neurosurgical fraternity to proactively engage in collaborating with other
28 healthcare professionals, engineers, scientists, ethicists and regulators in tackling these issues. By
29 doing so, we will equip ourselves with the skills and expertise to drive the field forward
30 responsibly and avoid being mere technicians in a field driven by those around us.

31

1 **2. Implant Technology**

2

3 Clinical indications should be considered in the context of neural interfaces that are currently in
4 use and those that are in development. Broadly, existing devices that interface with the brain can
5 be divided into ones that record or stimulate neural activity (Figure 1). Recording devices
6 include macroelectrodes such as stereoelectroencephalography (SEEG) electrodes or cortical
7 grids/strips and microelectrode arrays; there are adaptations of recording macroelectrodes with
8 microelectrode contacts, but these devices are currently used only in research settings.^{7,8} An
9 endovascularly implantable ‘stent electrode’ that is placed in the cortical vasculature has recently
10 received breakthrough device designation from the FDA and is undergoing clinical trials.
11 Stimulating devices are mostly in the form of deep brain stimulation (DBS) electrodes, although
12 other constructs, such as auditory brainstem implants also exist.^{9,10} Novel constructs such as
13 closed loop DBS and responsive neurostimulation (RNS) electrodes are capable of both
14 recording and stimulating, with the aim of optimizing stimulation in real-time based on the
15 activity recorded.^{11,12} The choice of device largely depends on the indication and the location of
16 recording/stimulation; some devices are better suited to record and stimulate cortical structures
17 whilst others are more suited to deeper brain structures.

18

19 In terms of stimulating or modulating brain activity, current DBS strategies offer an ability to
20 modulate the pulse current, duration and frequency to a small number of electrodes (usually 4-
21 16) in a specific area of the brain. Targets are chosen based on the specific indication and patient
22 characteristics. Treatment is optimized by manually titrating the settings to the clinical response.
23 Novel strategies that are being employed to improve DBS include directional electrodes, closed
24 loop systems which are able to record and stimulate and connectomic strategies where individual
25 patient structural connectivity is used to optimize target location at the time of implantation.^{12,13}
26 DBS and RNS technology have a profound impact on people with movement disorders, epilepsy
27 and, increasingly, psychiatric disorders.^{9,11,12,14,15} In addition to deep brain stimulation, emerging
28 stimulation techniques for auditory and visual restoration hold promise; whilst auditory
29 brainstem implants have been in clinical use for many years, a number of research groups are
30 investigating broadly similar strategies for visual cortex stimulation based on information from a
31 camera mounted on the forehead or glasses.^{10,16,17}

1
2 Current stimulating technology is limited by small numbers of electrodes that are spatially
3 limited to small structures. Although not demonstrated in the recent preprint, novel BMI systems
4 such as those proposed by Neuralink are designed to be ‘precision’ systems with hundreds to
5 thousands of electrodes that allow programmed stimulation at each contact.¹ Although currently
6 hypothetical, this may, in time, allow the individual to ‘sense’ (somatic sensation, vision, smell,
7 taste) using external sensors or allow the device to alter brain connectivity, affecting cognitive,
8 psychological and emotional responses.

9
10 Devices that record neural activity can be divided into macroelectrodes that measure local field
11 potential (LFP) activity aggregated from many neurons and microelectrodes that are capable of
12 measuring extracellular action potentials from single neurons in addition to LFP. Both are
13 immensely powerful when combined with modern data processing and machine learning
14 technologies; cortical LFP signals can decode speech and existing microelectrode arrays have
15 been used to control a range of functions including prosthetic arm and cursor control in small
16 numbers of patients.^{18–22} Like with the stimulating electrodes, these are limited by the number of
17 electrodes and sampling from a small area of brain; current microelectrode arrays have in the
18 region of 100 electrode contacts and sample a 1cm² area of cortex. Newer devices may be able to
19 sample from thousands or tens of thousands of neurons but the advantages of recoding from
20 increasing numbers of neurons have yet to be realized.²³ Implanting hundreds of micro-scale
21 biocompatible wires into eloquent tissue also requires careful consideration of risks. Despite the
22 small scale, implanting microelectrodes into eloquent cortex has been shown to cause fine motor
23 deficits in animal models and the long-term impact of this requires evaluation.²⁴ Electrodes may
24 preclude or cause artefact on subsequent imaging, potentially interfering with diagnostic
25 accuracy and subsequent medical treatment. MRI compatible neuromodulation devices are
26 entering the market, but further work is required for specific BMI implants.

27
28 In addition to implants that interface with the brain, neural interface technology may also
29 interface with other elements of the nervous system such as spinal cord, peripheral nerves and
30 cranial nerves (including cochlear implants and vagal nerve stimulation).^{16,25} Although an in-
31 depth exploration of these specific technologies is beyond the scope of this review, it is

1 important to highlight that there is a lot of cross-fertilization of technological breakthroughs and
2 mechanistic insights across these different modalities.

3
4 There are a number of key areas of research with regards to improving this technology. The first
5 is the foreign body reaction, a classic physiological response of the body to implanted foreign
6 material.²⁶ In the context of BMIs, this affects both the short and long-term performance of the
7 device's recording and stimulation capabilities as the formation of fibrotic tissue around the
8 interface eventually causes an inefficient transduction of the electrical signal.^{27,28} Many factors
9 have been associated with the degree of foreign body reaction including surface properties of the
10 biomaterial (porosity, roughness, stiffness, and chemistry), shape, surface area and volume of
11 implant, degree of implantation trauma and mechanical mismatch between the implanted 'stiff'
12 material and the 'soft' biological tissue.²⁷⁻³⁰ Novel biocompatible implants have demonstrated
13 our ability to record microelectrode activity from large numbers of channels for up to 6 months
14 in animals.^{31,32} Clinically, we must approach this area with caution, warning patients that positive
15 effects may diminish over time and eventually render implants ineffective. In addition to the
16 basic science work that is being undertaken to understand the mechanisms of the foreign body
17 reaction and options for subverting it, we suggest establishing rigorous implant registries to
18 determine longer-term durability in humans. Other issues that warrant study include the impact
19 of electrode drift on the fidelity of the captured signals and the long-term impact of neural
20 implants on brain connectivity and function.

21

22 **3. Implant Recipients**

23

24 Given our ability to record and stimulate neural activity, it is not surprising that indications for
25 BMIs include a wide range of neurological and psychiatric disorders that is constantly
26 expanding. Currently, there are approved indications for deep brain stimulation in Parkinson's
27 disease, essential tremor, dystonia and obsessive-compulsive disorder and emerging indications
28 in epilepsy, neurocognitive disorders, pain and other neuropsychiatric disorders.^{9,33} More
29 experimental indications for BMIs include controlling prostheses¹⁹⁻²¹, obesity, multiple
30 sclerosis, substance addiction and memory augmentation/editing.³⁴

31

1 Determining which patients are eligible to receive implants is an individualized risk-benefit
2 analysis, often undertaken by a multidisciplinary team consisting of neurologists, neurosurgeons,
3 neuroradiologists, psychiatrists and allied health professionals that weigh the risks of surgery and
4 implant maintenance against the probability of clinical improvement. Factors that are taken into
5 consideration include disease severity, associated comorbidities, imaging abnormalities and,
6 significantly, a lot of importance is given to patient preference. Especially when considering
7 novel or experimental indications, careful consideration must be given to the way in which these
8 are introduced into the clinical domain; we suggest that these are undertaken solely under the
9 auspices of a clinical trial using structured frameworks for the introduction of new technology
10 with adequate regulation and oversight.^{35,36}

11
12 In addition to medical indications, BMIs hold immense potential to augment function (e.g.
13 memory, cognition, sensation, language, motor control) in otherwise ‘normal’ individuals.³⁷
14 Although this is not be the focus of current research and may be seen as ‘unethical’ by some,
15 augmenting function is a natural corollary of developing technology for functional restoration in
16 those with neurological disorders. For example, non-invasive sensors and stimulators have
17 already been used to achieve direct brain-to-brain communication³⁸ and it is possible that
18 invasive strategies will only increase precision of such systems. If and when such a situation
19 arises, careful consideration must be given to the risk-benefit balance in the absence of disease
20 and what level of risk is acceptable, both at an individual and societal level. As medical
21 professionals and key members of the BMI community, neurosurgeons need to think carefully
22 about the medical, ethical and societal implications of this and, importantly, whether and how we
23 should be involved in such practices, especially in the context of healthcare systems with limited
24 resources.

25

26 **4. Implantation Methodology**

27

28 Perhaps the most straightforward challenge in this field involves achieving accurate, safe and
29 long-lasting implantation of electrodes. This has been a key driver behind neurosurgical
30 technology for decades, that started with frame-based stereotactic localisation based on air
31 ventriculography and resulted in the modern plethora of robot-assisted neuronavigation systems

1 that incorporate high levels of sub-millimeter accuracy and integrate with advanced vascular
2 imaging to ensure that blood vessels are avoided.³⁹ So far, these systems have all been
3 ‘supervisory control’ systems which require human input to control; there is scope for fully
4 automated systems that implant autonomously, which raises further issues such as responsibility
5 and liability that are actively being explored.⁴⁰ Microelectrode arrays and depth electrodes
6 require cortical penetration. Histological analyses from microelectrode arrays, implanted largely
7 in research contexts during short-term monitoring of epilepsy patients, confirm ‘minimal’ tissue
8 damage associated with pneumatic implantation devices designed to minimize trauma, but
9 implantation is not without risk.^{41,42} Surgical techniques must therefore be constantly evaluated
10 and rigorously audited to ensure the highest standards are maintained.

11
12 A more complicated challenge in implantation is accurately identifying the appropriate region of
13 the brain to target. Traditionally, implantations have focused on anatomical structures that can be
14 visualized on MRI. For instance, DBS for the treatment of Parkinson’s is targeted toward the
15 subthalamic nucleus or globus pallidus internus. However, the true functional target is the motor
16 subset of these structures, and additional information from microelectrode recordings or
17 advanced imaging techniques is necessary for accurate placement.^{43–45} However, as more
18 complex disorders are treated, especially those related to mood or cognition, identifying the
19 appropriate target becomes more complex and may require a combination of advanced structural
20 and functional imaging techniques and electrophysiology to help guide pre-operative assessment.

21
22 Novel constructs, especially those seeking to record macro-scale signals may be implanted
23 through endovascular routes, with the ability to record and stimulate when implanted into
24 cortical vessels. This would preclude the need for a craniotomy although it would be limited by
25 the location of cortical vessels. One such device is currently undergoing first-in-human trials and
26 has received Breakthrough Device Designation from the US Federal Drug Administration.^{46,47}

27
28 It is possible that some future neurosurgeons will be ‘*implant neurosurgeons*’ and we also need
29 to adapt our curricula to equip future surgeons with the required technical and non-technical
30 skills. Specialist societies must issue guidance on training requirements, and national and

1 international implant registries will aid ongoing audit and oversight of efficacy and complication
2 rates.

3

4 **5. Implant Function**

5

6 As mentioned earlier, recording electrodes can be divided into traditional macroelectrodes and
7 novel microelectrodes depending on the size of the recording contacts. Microelectrodes record at
8 frequencies around 30kHz and capture multiscale electrophysiological data, including local field
9 potential (LFP, 1-100Hz), high frequency oscillations (HFOs, 80-500Hz) and extracellular action
10 potentials (>300 Hz) from neurons; these frequency bands are somewhat arbitrary and have been
11 determined by identified features of interest in each. In epilepsy monitoring, microelectrodes
12 have been shown to capture neural signals that are not captured by current clinical
13 macroelectrodes.^{8,48} Extracellular action potentials are recorded from a minority of
14 microelectrode contacts and require ‘spike sorting’, a computationally intensive process that
15 ascribes particular action potential waveforms to putative neurons.⁴⁹ Whilst significant progress
16 has been made in spike sorting algorithms, the fidelity of ‘on-line’ (real time) spike sorting over
17 longer timescales that a few hours has not been established. Even if spikes cannot be sorted,
18 much can be gleaned from unsorted multi-unit activity.³ Factors such as electrode drift and signal
19 decay from the foreign body reaction will need to be evaluated. Action potentials from single
20 neurons can then be analysed in a number of ways including the rate of firing, timing of firing in
21 relation to the underlying LFP phase and population firing of multiple neurons.

22

23 Historical understanding of these electrophysiological signals has been limited to pattern
24 recognition on visual inspection but progress in computational power has enabled the application
25 of signal processing tools to better understand them, to the extent that we are developing atlases
26 of ‘normal’ intracranial EEG dynamics.⁵⁰ Machine learning algorithms that are being applied to
27 these signals will need to incorporate data from all these scales in order to optimize the output of
28 BMIs, a field that is in its relative infancy but one that has shown immense promise.¹⁸ These
29 algorithms may benefit from incorporation of novel approaches such as network science that
30 provides a natural language to model the complex, changing system of the brain.⁵¹ Although
31 there is a growing wave of clinician-scientists who have the computational knowledge to be able

1 to design and deploy these algorithms themselves, dealing with such data and the code behind its
2 processing is probably best served by close collaboration with computational neuroscientists,
3 engineers and mathematicians.

4 5 **6. Implant Regulation & Monitoring**

6 7 6.1 Implant Monitoring

8
9 Two specific challenges in this area include dealing with large volumes of data, data security and
10 ownership. Microelectrode recordings generate significant volumes of data (250 channels at
11 30kHz is roughly 115GB per hour). This amount of data is difficult to store and process on many
12 of the computer systems currently in place in many hospital systems. However, development of
13 high performance computing (HPC) systems and cloud-based computing may provide a solution
14 that can scale with ever increasing demands on data storage and computation.^{52,53}

15
16 Data security is of utmost concern as altered functioning or disabling of neuro-implants can have
17 devastating consequences. System vulnerabilities may be exploited, leading to malicious
18 alterations to inbuilt algorithms, termed ‘brainjacking’.⁵⁴ Furthermore, even without malicious
19 intent we must safe guard against inadvertent access that can be caused by the user, interactions
20 with other systems (wireless networks and hardware that create electromagnetic signals), or even
21 errors during desired software upgrades. Most devices avoid data security issues by acting as a
22 closed system, where information is not stored externally and can only be adjusted in person.
23 Although there are wireless implantable devices on the market, they are typically secured using
24 external relay devices, where a physical object is required to be placed near the device to gain
25 access to the signal.⁵⁵ However, such a system necessarily limits the ability to monitor signals in
26 real time and make simultaneous adjustments. To unlock this potential, systems must be design
27 to ensure access is limited to only trusted vendors.

28
29 Data protection is also a key consideration, both in terms of outright theft and ensuring that data
30 is used only for its intended purposes. Frameworks must clearly delineate who owns the data,
31 who is responsible for its safe storage, where it is stored and the rights of the individual, medical

1 professionals, companies and governments to access, use and monetize such data. Existing
2 regulations, such as General Data Protection Regulation, may largely cover these requirements.

3 4 6.2 Implant Regulation

5
6 New active implantable medical devices and their accompanying software require careful
7 evaluation both prior to and during human trials. Whilst an efficient approval process is crucial
8 for clinical translation and patient benefit, this must not occur at the cost of robust evaluation of
9 the clinical efficacy and risks. Established approval processes for medical devices (CE marking
10 and FDA approval) will need to be adapted and expanded to increase the quality of ongoing
11 robust evaluation of new technologies, specifically to consider carefully individual and
12 population level thresholds for risk-benefit considerations, where indications for invasive
13 stimulation are for wellness or augmentation of physiologic function. Frameworks such as
14 IDEAL-D, that seek to end the dichotomy of ‘approved’ versus ‘not approved’ must be adopted
15 and we, as the responsible clinicians, must champion these approaches.³⁵

16
17 Software development is likely to play a pivotal role in the neurotechnology sphere. Whilst
18 network and artificial intelligence-based algorithms are rapidly being developed to improve
19 recording and closed loop technology, robust evaluation of these novel algorithms is crucial, as
20 are other aspects such as the data used to assess them. Existing frameworks such as the FDA’s
21 Software as a Medical Device are being adapted for artificial intelligence and machine learning
22 algorithms⁵⁶ and may require further modification specific for neurotechnology and BMIs.
23 Although patient data must be sufficiently protected, open science and open datasets have
24 hastened progress in recent years. Regulations must balance both sides and novel constructs such
25 as ‘data obfuscation’ should be used to allow pretraining of machine learning algorithms whilst
26 preserving confidentiality⁵⁷. In circumstances where the decision-making is difficult, ‘citizens’
27 juries’ may be used to decide whether data may be shared with other parties for research and
28 commercial purposes.

29 30 **7. Ethical Considerations**

1 The ‘merging’ of humans with machine interfaces (potentially with a superimposed machine
2 learning application layer) raises serious ethical issues.^{59,60} Firstly, issues of consent that apply
3 at present to individuals without capacity and children, would continue to be relevant, with the
4 added burden of the psychological impact of BMIs.⁶⁰

5
6 Devices that record from the brain may (intentionally or inadvertently) have access to ‘private’
7 or intimate thoughts not meant for the public world, an issue both in terms of recording and
8 storage of such information. There may be questions of the right and extent to which privacy
9 should be preserved in these situations - if thoughts can be interpreted through BMIs as
10 demonstrating risk of public danger, society must accept trade-offs between autonomy, privacy
11 and public security. However, the use of such devices to tailor marketing campaigns or other
12 commercial activities should be safeguarded against in the interest of the patient. Situations may
13 arise involving employers and insurance companies mandating such implants as has already been
14 seen in peripherally implanted microchips.⁶¹

15
16 Stimulating devices raise issues of autonomy – whilst they have the ability to increase the
17 functional independence of those with progressive neurological disorders, is the individual still
18 ‘self-governing’ and to what extent are they still accountable for their actions?^{60,62} By extension,
19 ethicists have debated whether BMIs become part of the ‘body schema’ and integrate into the
20 person, both from legal and philosophical standpoints.⁶² Augmenting function in otherwise
21 ‘healthy’ individuals also raises issues of risk and societal implications, with entrenched and
22 widening social inequalities between those who can and cannot afford such implants.

23
24 Bioethicists have identified that current human rights principles may be insufficient for dealing
25 with the advances in neurotechnology and have identified 4 new guiding principles (Table 1).⁶³
26 What is particularly interesting about this framework is the aspect of *cognitive liberty* that gives
27 people a right to alter their mental state. If neurosurgeons are to be involved in altering the
28 mental state of otherwise ‘normal’ individuals, we must think carefully about the levels of
29 acceptable risk, informed consent frameworks that protect both individuals and ourselves and, in
30 the context of research evaluations, our post-trial responsibilities to the participants and the
31 public.

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8. Economic Considerations

Economic considerations can be broken down into 3 pertinent questions. The first question is who will develop BMIs. The possible archetypes of organization are universities, hospitals, non-university state-owned research facilities, small and large companies. At different times, different organizational archetypes may be best placed to deliver on different steps such as ideation, productization, adherence to regulatory standards, quality control and assurance, business development and marketing. An important consideration is the incentives for each type of organization, including scientific progress, betterment of health and profits. Irrespective, progress must be evaluated objectively, and all organizations must be held to the same exacting standards. As neurosurgeons, we hold a unique position to generate insights into product development and utility; indeed clinicians can play important roles in developing relevant organizations.⁶⁴ One concern we must therefore keep in mind is potential conflicts of interest that might arise due to financial interests in commercial organizations.

The second question is who will fund the development. Funding may be institutional (governmental, non-governmental or private) or deployed capital from venture capital firms. The scales of money available through these different routes is likely to be vastly different. For example, Neuralink has amassed over US\$150 million of funding in its short history but such funding may come with the expectation of return on invested capital.⁶⁵

The third question is who will pay for BMIs. For BMIs that are developed to enable return to function for patients who have lost abilities which they previously had, or might reasonably be expected to have, the starting point will be existing payor mechanisms, such as governments or insurance companies depending on health economy. For augmentation of normal function, our assumption is that the payment burden will be on the individual. This has the potential to exacerbate and entrench existing inequalities within society and place neurosurgeons in a position of ethical dilemma when considering participation in such activities.

9. Conclusion

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The road ahead for the BMI community is long, both in terms of technological innovation and ethical & moral considerations. There is no certainty that Elon Musk and Neuralink will provide the breakthrough in this field but there is a clear direction of travel with an increasing range of medical and non-medical uses. We have not even considered the vast range of non-invasive stimulation strategies that will sit alongside invasive implants, some of which have been commercialized for improving cognitive performance.⁶⁶

Clinicians, and specifically neurosurgeons, hold a unique position in this field as our skill set makes us ‘gatekeepers’ to the clinical application of such technology. We must therefore take leadership roles in shaping the field. We need to continue working closely with the engineering and computational neuroscience communities to improve implant materials, minimize the foreign body reaction, ensure surgical implant techniques minimize risk and optimize efficacy, and optimize algorithms for understanding and stimulating the brain. Given the rapid pace of technological advancement, we also need to be involved in pre-emptively shaping the legislative and policy agenda to ensure such technology is introduced with adequate regulation and used for ethical indications. Some of the key challenges for the BMI community, highlighting areas where active clinician involvement is crucial to progress are outlined in Figure 2. National and international neurological and neurosurgical bodies should lead the charge in setting up task forces for these purposes. We, the neurosurgical community, must engage now to avoid becoming mere ‘technicians’ in this rapidly advancing field.

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3 **Figures Legends**

4

5 *Figure 1: Schematic illustration of the current scope of brain-machine interfaces that splits the*
6 *field into recording and stimulating devices*

7

8 *Figure 2: Framework outlining some of the key challenges for the BMI community, highlighting*
9 *areas where active clinician involvement is crucial to progress.*

Table1[Click here to download Table\(s\): Table 1.docx](#)

Cognitive Liberty	The right to alter one's mental state with the help of neurotechnology as well as to refuse to do so
Mental Privacy	The right to one's own brain data. It should not be recorded, shared or used without explicit consent
Mental Integrity	Organizations and governments should not alter the computation of the brain without consent
Psychological Continuity	Personal identity should not be compromised

Table 1: New human rights principles in the era of neurotechnology and neuroprostheses.⁵¹

Figure1

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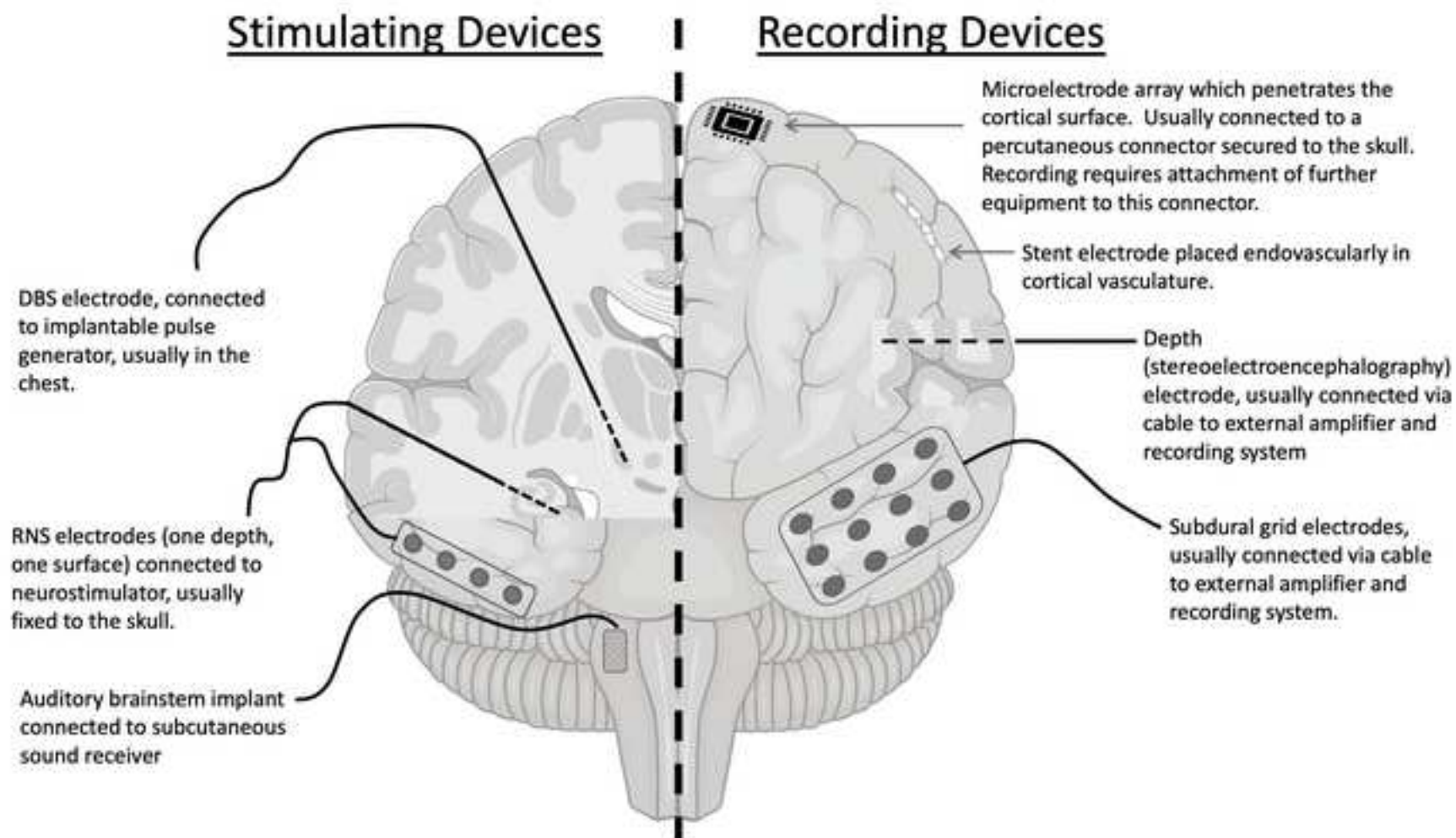


Figure2

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