Deep Brain Stimulation (DBS) Seminar, Group 2

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***Abstract*—Deep Brain Stimulation (DBS) is a mature neurosurgical therapy involving the delivery of targeted electrical pulses via implanted electrodes, and notably effective for Parkinson's disease, essential tremor, and dystonia. Technological advancements are driving DBS forward, switching from standard four-contact electrodes to directional leads for precise field steering and enhanced therapeutic windows. Since conventional DBS programming is empirically challenging, the field is rapidly adopting Adaptive DBS (aDBS); an innovative closed-loop approach that uses neural biomarkers and sensing technology to dynamically regulate stimulation, paving the way for a new era of research that promises greater clinical efficacy, fewer side effects, and significant reductions in battery drain. As DBS expands its application to complex neurological and psychiatric conditions, future success still relies on resolving technological challenges in biomarker identification and addressing ethical concerns related to cognitive system modulation and data security.**

I. Introduction

The advancement of technology and the miniaturization of electrical circuits, along with a better understanding of the human brain, have led to rapid advancements in research on human brain stimulation over the past couple of decades. The techniques used are various, but the most popular and well-studied technique is DBS.

DBS technology was initially developed by modifying the already existing pacemaker technologies [5], i.e., a pacemaker-like unit called **an Implantable Pulse Generator (IPG)**. The very first hypotheses about the mechanism of DBS were based on the similar effects of high frequency stimulation and lesions of some brain regions : *pallidotomy for the treatment of PD (Guridi and Lozano, 1997) or capsulotomy for the treatment of OCD (Jenike, 1998)* [4]. Initially, and for several years, progress in DBS technology was limited due to the lack of competition and the low diversity among device manufacturers. In the past decade, however, the field has witnessed a sizable leap forward, driven by the emergence of new companies and increased innovation; further improvements are to be expected over the next few years. [5]

Hereafter, we will closely inspect the fabric of the aforementioned advances in DBS from technological, medical, logistical, and ethical perspectives; along with the new horizons of research expected in the near future.

II. Understanding how DBS works

Deep brain stimulation (DBS) remains a therapy whose working mechanisms are only partially understood.
Early hypotheses suggested that high frequency stimulation acted in a manner similar to ablative lesions of the same brain regions, primarily by suppressing pathological neural activity [3]. According to the ***"Inhibition Hypothesis"*** DBS was thought to exert its effect by blocking the overactive basal ganglia neurons within the **subthalamic nucleus (STN)** or the **Globus Pallidus Internus (GPi)** [6]. Although this idea was compatible with the ***"Classic rate model"*** of basal ganglia physiology, future experiments demonstrated that DBS can *increase* neuronal activity [1], [3].

Later studies attempted to explain these contradictory results. While the exact mechanism of DBS remains unknown, the current consensus is that high-frequency stimulation produces a complex modulation of both afferent and efferent neurons by activating axons near the stimulation electrode while inhibiting somatic firing at the stimulation site [3].

One central observation in movement disorders (for example, PD, Essential Tremor or Dystonia) is that symptoms, in many cases, correlate with excessive, abnormal rhythmic brain activities, called **oscillopathies** [3]. In PD for example, exaggerated beta-band (12-30Hz) is linked to motor symptoms (especially bradykinesia and rigidity) and its reduction improves symptoms [1]

Many other mechanism hypotheses have been proposed to explain the positive impact of DBS on movement disorders:

- **Synaptic Filtering [2] :** High frequency DBS may act as a filter of neuronal activity, allowing physiologically relevant signals to propagate while blocking pathological low frequency activity. The high frequency stimulation generates action potentials in many axons, thus exhausting the amount of releasable neurotransmitter and inducing postsynaptic receptor depression, therefore acting as low-pass filters : The high-frequency components of stimulation are not transmitted and the sustained depression blocks the low-frequency oscillations that are linked to motor symptoms of disorders like PD.
- **Signal Disruption and Override [2], [6]:** High-frequency stimulation drives regular activity in surround-

ing axons, disrupting pathological signal patterns and preventing the propagation of abnormal activity. This can occur through two complementary mechanisms: (1) ***Information lesion***, mimicking a reversible lesion without structural damage by overriding pathological patterns, and (2) ***Jamming theory***, where the regular stimulation pattern overrides abnormal low-frequency activity, effectively blocking pathological signals.

- **Network Desynchronization [2], [6]:** DBS improves symptoms by disrupting the synchronous neural signals that are present in many movement disorders, leading to a desynchronization of the network. This restores a more physiologically variable neural pattern and thus reducing the transmission of disease-related activity.

Importantly, these mechanisms likely operate in parallel at different spatial and temporal scales [2]. The relative contribution of each mechanism may vary depending on the stimulation target, the specific disease being treated, and even individual patient characteristics. This multi-level, multi-mechanism framework helps explain why DBS remains effective across diverse targets and pathologies.

DBS could also have some positive impacts that go beyond alleviating disorder's effects. Some evidence shows that DBS may have **neuroprotective effects** on dopaminergic cells by protecting them from the degenerative effects of the different diseases, suggesting that DBS could play a role in slowing down pathology progression [6].

Despite the numerous uncertainties that remain concerning the underlying working mechanisms of DBS, this technique is widely used to treat many pathologies, and its parameters need to be tuned depending on the disease to maximize its benefits.

III. Treated diseases and stimulation Sites

DBS has been tested on multiple diseases with varying results. The earliest clinical trials focused primarily on motor disorders, including Parkinson's disease (PD), dystonia, and essential tremor. These conditions demonstrated the most consistent benefits, leading them to become the only FDA-approved indications for DBS [1]. Other conditions are still under study (Table I), producing limited results. It has been shown that different stimulation regions have different effects on patient symptoms (in the case of PD). Thus, the choice of the target stimulation region is crucial and may differ for different conditions. To give an exemple, PD treatment has been tested at different brain locations (STN, GPi, VL thalamus and others). Further information about precise stimulation sites can be found in [2].

Moreover, the time it takes for DBS to take effect and the types of symptoms that are treated widely depend on the disease. (See figure 1)

IV. Electrodes : Characteristics

Once the electrode have been implanted, the system must stimulate the chosen target stimulation region correcly, that is the **volume of tissue activated (VTA)** must also be accurately

TABLE I
DEEP BRAIN STIMULATION (DBS) DISORDERS (INSPIRED FROM [3] AND [5]

Disorder	Circuit	Stage of study	Efficiency
Parkinson disease	Motor	Standard of care	high
Essential tremor	Motor	Standard of care	high
Dystonia	Motor	Standard of care	high
Major depression	Limbic	Phase III	variable
Obsessive-compulsive disorder	Motor / limbic	Phase II/III	promising
Alzheimer disease	Cognitive and memory circuits	Phase II/III	inconclusive
Pain (different kinds)	Sensory systems	Phase I/II	limited
Anorexia nervosa	Reward / mood	Phase I/II	promising
Epilepsy	Various	Phase I/II	moderate
Tourette syndrome	Motor / limbic	Phase I	limited

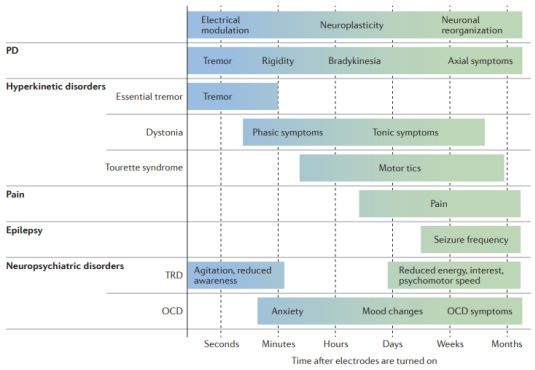

Fig. 1. Timing of the effects of deep brain stimulatio [6]

reached. To this end, the implanted electrode characteristics must allow for flexibility in targeting the VTA more precisely to the therapeutic region while avoiding side-effect prone region. A simple cylindrical electrode produces a cylindrical VTA with little post-implantation parameterization possible. Therefore, new electrode designs with multiple programmable contacts (Fig. 2) have been developed to achieve directionality through **field steering**. This allows for better control of the VTA, thereby improving symptom suppression and reducing side effects [1], [3]. The most commonly used DBS electrode is the four-contact design.

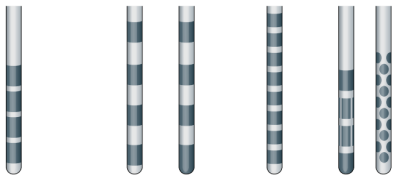

Fig. 2. DBS electrode configurations (from : [5]) most left : standard 4 contacts electrode

The electrodes must also meet several material and mechanical constraints, including inertness (to ensure biocompatibility), durability and stability, as well as appropriate

electrical properties. Platinum-iridium (Pt-Ir) alloys are often used in DBS electrodes because of such properties. Antibiotic coating can also be used on the implantable electrodes to reduce the risks of infection. [5]

V. Stimulation Methods

DBS can be delivered through a variety of stimulation patterns. Traditionally, DBS used monophasic cathodic pulse trains with passive recharge that is programmable in amplitude, frequency and pulse width. But, with recent hardware developments, new stimulation patterns are possible and need to be evaluated through blind studies. A key consideration is whether stimulation is delivered in a current-controlled or voltage-controlled mode. Recent studies seem to show that current-controlled stimulation produces better results (due to the inflammatory response around the electrode changing the impedance of the tissues) [5]. Another consideration is the choice of the stimulation waveforms. In this context, studies indicate that biphasic active recharge pulses produces great result for PD and tremor patients, at the cost of higher power consumption. [1]

The stimulation pattern and intensity as well as the VTA can usually be programmed. The programming procedure can be done regularly in order to accommodate the patients' needs and improve efficiency while minimizing side effects. This is, however, a long empirical process that requires an experienced clinician. [3] Adjustment of parameters works relatively well if the disease affects the patients' motor system, as the symptoms can be directly assessed. However, with other diseases involving long term effects (such as depression), programming becomes really difficult as there is no direct feedback, leading to a higher risk of not providing the right amount of stimulation to the patient (overdosing stimulation). [2]

VI. Closed-Loop DBS :

DBS is effective for movement disorders, but conventional systems apply constant stimulation that does not respond to changes in symptoms, medication levels, or side effects. Using biomarkers, i.e. measurable physiological signals that reflect the patient's disease state, to track disease state and automatically adjust stimulation parameters to the patient may improve outcomes and extend battery life. This patient-specific approach is known as **closed-loop DBS** [1].

Closed-loop DBS relies on biomarkers to determine *when* and *how intensely* to stimulate. These biomarkers may come from pathological neural patterns or peripheral measurements and do not need to reflect the disease mechanism directly, as they simply must correlate with symptom severity and treatment response [3].

Currently, most closed-loop DBS applications target movement disorders such as Parkinson's disease and essential tremor. Two main neural signals are used for control:

- **Beta-band activity (20 Hz)** recorded locally from the stimulation electrode which allows simultaneous sensing and stimulation with minimal hardware.

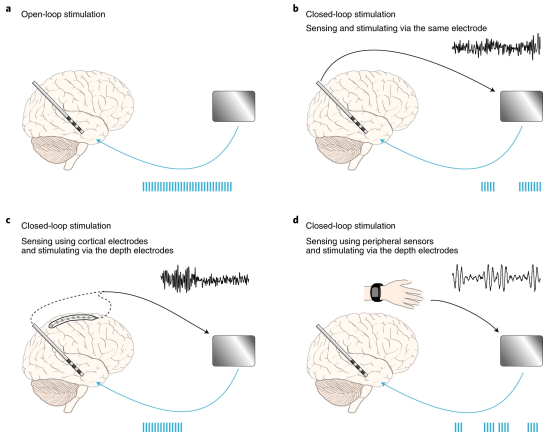

Fig. 3. A comparison of different stimulation strategies – From [3]

- **Gamma (75 Hz) or movement-modulated beta activity** recorded from the motor cortex and offers cleaner signals with reduced artifact contamination.

These neural features enable adaptive therapeutic modulation based on real-time brain activity. [3]

Advances such as chronic neural signal recording, cortical ECoG electrodes, and wearable sensors help identify reliable markers, however, recording neural signals from the same electrode used for stimulation introduces artifacts because stimulation voltages are much stronger than neural signals [1]. Wearable sensors (e.g., tremor monitors) may also provide useful external biomarkers, though they respond only after symptoms appear and raise technical challenges such as communication and power consumption. Despite limitations, they hold promise for continuous, objective symptom tracking. [2]

VII. Problems and Risks

A. Ethics, Invasiveness and surgical procedures

Even though DBS is considered a minimally invasive procedure, its implementation in the body requires surgical interventions that introduce risks of hemorrhage, skin erosion or infection. In fact, 5 to 10% of chronic DBS patients experience infections due to the implantable devices [5]. In addition to that, side effects occur in around 50% of cases [3]. This led to a difficult patient selection and raised some ethical challenges, as the disease had to be quite serious for a patient to take the decision to undergo surgery and suffer the subsequent complications.

Furthermore, the success of DBS in treating conditions like PD has motivated the scientific community to further experiment with this technology on a wider range of diseases. Consequently, these experiments included patients whose conditions can be managed by medication intake; which constitutes an ethical issue given the relatively higher risk of this emerging treatment protocol. [2].

It is also important to keep in mind the ethical implications of tempering with the human cognitive system and potentially

influencing decision making. This raises questions about the concepts of **"Neurosecurity"** and **"Brainjacking"** and how to protect patients from attacks towards their neurostimulation systems [5].

B. Power Consumption

It is important to reduce power use of DBS stimulation devices to have a prolonged battery life resulting in fewer device replacement surgeries, thus, reducing the risk of infections. This is especially important for young patients, since they commit to a lifelong implant.

Many parameters can influence power consumption. Optimizing stimulation patterns and electrode design in addition to using biomarker feedback in closed loop DBS or computational tools could improve battery lifetime while the communication with wearable devices can drain the battery more quickly. [1]

VIII. Beyond DBS

So far, we have examined the limitations of DBS as a technology, particularly its invasive nature, potential risks and fluctuating clinical effectiveness. This encouraged the scientific body to explore new venues and search for alternative technologies capable of modulating neural activity without surgery. Thus, a renewed interest was born that contributed to the development and clinical adoption of **non-invasive brain stimulation (NIBS)** techniques, which proved to be efficient, cheaper and especially safe for patients [7].

Multiple NIBS techniques exist, each characterized by distinct applications and implementation protocols *(see figure 4)*.

Compared with DBS, NIBS techniques offer non-invasive, lower-risk ways to modulate the same large-scale networks, without surgery, implanted hardware or hardware-related complications. Furthermore, stimulation can be delivered repeatedly, even at home.

Method		Stimulation approach	Mechanism of action	Targeting precision	Context of use
Targeting superficial cortical areas					
Transcranial magnetic stimulation (TMS)		Electromagnetic pulses that activate brain cells	Directly triggers brain cell firing using suprathreshold electric fields	Moderate (≈ 3-5 cm^3)	Specialized centres only; use of the device requires a trained professional
Transcranial electrical stimulation	Transcranial direct current stimulation (tDCS)	Weak constant electric current	Modulates brain cell excitability without directly firing	Low to very low; diffuse spread; improved by optimized electrode placement	Research setting; some experimental home-based protocols
	Transcranial alternating current stimulation (tACS)	Weak alternating sinusoidal electric current	Tunes brain oscillations without direct firing		
	Transcranial random noise stimulation (tRNS)	Weak random (noise-like) electric current	Increases brain responsiveness using random noise signals		
Also targeting deep brain areas					
Transcranial temporal interference stimulation		Two weak high-frequency electric currents that interfere to create a low-frequency effect	Modulates deep brain activity by targeting regions where electric fields overlap, without triggering immediate firing	Low (≈12 cm^3)	Research setting; potential for home-based protocols
Transcranial-focused ultrasound (tFUS)		Low-intensity focused ultrasound (mechanical pressure waves)	Alters brain cell behaviour through mechanical effects on cell membranes and ion channels	Very high (<0.5 cm^3)	Experimental use; requires trained professional

Fig. 4. Key characteristics of non-invasive brain stimulation methods [7]

- **TMS** provides relatively focal cortical modulation and has shown "probably effective" benefits on global cognition and associative memory in Alzheimer disease, and on selected executive functions and dual-task gait in Parkinson disease (PD), although effects are heterogeneous and often based on small samples [7].
- **tES** is above-all non-invasive, more accessible, cheap and portable, making long-term and home-based protocols feasible. By contrast, DBS remains superior for robust motor symptom control in PD [7].
- **tTIS** is capable of selectively modulating deep brain structures by exploiting interference between two high-frequency electrical currents applied via scalp electrodes. Unlike traditional NIBS, it can reach targets such as the subthalamic nucleus or globus pallidus without surgical implantation. Recent studies in PD demonstrated DBS-like effects while remaining well tolerated [8]. Although its mechanisms differ from DBS and further research is needed to optimize parameters and confirm long-term efficacy, *"tTIS represents a novel and potentially transformative approach of non-invasive DBS"*. [8].

Overall, these techniques complement DBS by providing safer, network-level neuromodulation with broader accessibility, but current evidence for disease-modifying or large, durable clinical effects remains preliminary and inconsistent across disorders.

IX. Future of DBS

DBS is progressing from a simple reversible lesion approach to a precise and adaptive neural prosthesis capable of restoring function based on real-time neural dynamics. Improvements in **electrode resolution** and **temporally patterned stimulation** are enabling therapies that better match individual symptoms and clinical states. Achieving this vision requires reliable biomarkers and refined control algorithms that remain computationally feasible. Broader technological trends such as device miniaturization, secure wireless telemetry, cloud-based processing and rechargeable systems will support continuous monitoring and more complex adaptive stimulation while preserving safety and efficiency [3].

X. Conclusion

Deep Brain Stimulation has recently progressed from an experimental surgical intervention to an established and effective treatment for movement disorders and neuro-degenerative diseases. Recent advances including directional electrodes, refined stimulation paradigms and adaptive closed-loop control have improved therapeutic precision and reduced side effects. However, DBS requires invasive surgeries and remains technically demanding, as well as ethically complex, particularly as its use expands toward neuro-psychiatric applications where biomarkers are less clearly defined.

Parallel developments in non-invasive neuro-modulation, such as TMS, tES, and tTIS, offer promising alternative strategies capable of modulating large-scale neural circuits without surgery. While these approaches currently lack the robust clinical efficacy demonstrated by DBS, rapid progress suggests a future where invasive and non-invasive stimulation technologies coexist and converge toward individualized brain therapies.

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