S T I M C O D E

Participative developed recommendations for non-invasive brain stimulation in the European Union

Background

The EU is facing a severe mental health crisis worsened by the COVID-19 pandemic, with insufficient treatment options exacerbating the situation. Access to mental health services is inadequate in many EU countries, contributing to high levels of neuropsychiatric problems. It is therefore crucial to prioritize mental health by investing in comprehensive accessible and cost-effective healthcare. Prioritizing the wellbeing of EU citizens is essential for building resilience and a healthier future, thus respecting the principles of dignity, equality, and the right to health.

Therapy for mental health - The technical solution

What is non-invasive brain stimulation (NIBS)? NIBS allows stimulating the brain from the outside, that is, on the surface of the skull as distinguished from the inside of the brain (invasive as in deep brain stimulation). This non-surgical approach involves using electromagnetic or electrical currents to target specific regions of the brain in an indirect way known as transcranial stimulation. As such, NIBS includes a variety of different techniques including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS).

Recent developments show that NIBS emerges as an increasingly promising and innovative therapy for mental diseases. TMS and tDCS have demonstrated potential in improving symptoms of various conditions, including depression, anxiety, and schizophrenia. By modulating brain activity, these techniques offer new avenues for symptom relief and improved wellbeing. As research continues to advance, NIBS holds great promise in changing and improving, if not, revolutionizing the treatment landscape.

Touchpoints to the EU and its policy makers

The topic touches on numerous issues important for the EU as NIBS has a direct impact on the effectiveness, safety, and affordability of healthcare, and consequently on fundamental rights and freedom of EU citizens. NIBS helps to:

I. **Improve mental health and wellbeing** in the general population.
II. **Enhance personalized and outpatient treatment** by increasing digitization, while at the same time giving rise to relevant data security issues.
III. **Strengthen supply chain security in healthcare** by moving away from pharmaceuticals towards technological solutions.
IV. **Improve control of escalating healthcare costs** in several countries in the EU through wider use of the technology, especially in an ambulatory or domestic setting.

Given the great relevance of NIBS technologies for the people of the EU, it is essential for decision-makers, including regulatory body, to address them at the earliest possible stage.

The participatory processes of recommendation adoption

The following recommendations were formulated on the basis of a participatory process involving seven groups of stakeholders (patients, students, home-users, caregivers, industry representatives, philosophers and public policy experts). Representatives of the stakeholder groups were invited to workshops to freely share and discuss their expectations, fears and opinions regarding NIBS technologies. Based on their input, a shared vision of NIBS 2030+ for the EU as a preferable future was formulated. The final set of recommendations was developed by 15 experts from the fields of neuroscience, medicine, law, ethics, innovation management, philosophy, and psychology, based on the stakeholders' contribution.

The vision for NIBS 2030+ in the EU describes a preferable future based on the input of various stakeholder workshops.

Key elements include:

1. **Home Treatment:** NIBS is accessible at home after mandatory medical prescription with supervised application and strongly supported by digital monitoring.
2. **Supportive Environment:** Optimized clinical environment for better healing during NIBS treatment.
3. **Integration and Training:** Standard therapy options with mandatory professional training for practitioners.
4. **Insurance Coverage:** EU-wide coverage aligned with treatment guidelines.
5. **Personalized Treatment:** Tailored approaches for increased effectiveness.
6. **Regulations:** Safeguards against misuse, ensuring privacy and data security.
7. **Research and Innovation:** Funding promotes collaboration between academia, grant agencies and industry.
8. **Information and Education:** Resources inform patients about NIBS possibilities, limits, and risks. Focus on accessibility, safety, effectiveness, and transparency in NIBS treatment.

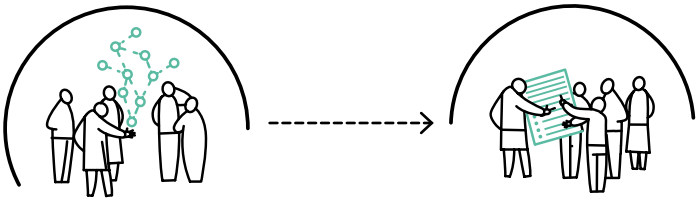
Why participation?

Participatory processes enhance decision-making by
- ensuring inclusivity and diversity of needs, interests, and opinions,
- improving quality and effectiveness,
- empowering individuals,
- promoting transparency and accountability, and
- fostering sustainable outcomes.

In addition to these benefits, the participatory process is in line with the concept of responsible research and innovation and the EU's better regulation guidelines.

The figure (page 4) demonstrates the adopted participatory process for developing six sets of recommendations – each targeted at a different group of stakeholders. In the following, we spell out each of the recommendations (blue quadrats) by describing its respective main features. Note that sometimes similar or resembling items and recommendations are mentioned more than once under the umbrella of the recommendations to different stakeholders; this is to point out their relevance for the respective stakeholder.

Process of the participatory workshops and recommendations



Input from **9 workshops** with **91 participants**

Expert workshop for final recommendations adoption

RECOMMENDATIONS TO

01 **Policy Makers**

- Establish one governing EU-level body on neuroscience and neurotechnology, including NIBS
- Ensure equal acces to safe and effective NIBS
- Engage stakeholders in decision making
- Ensure data protection

02 **Health Authorities**

- Provide trustworthy information about NIBS
- Collaborate with EU-level body
- Monitor quality standards

03 **Healthcare Providers of NIBS**

- Engage stakeholder in therapy planning
- Improve treatment setting
- Get certified

04 **Industry**

- Develop home-use NIBS
- Develop NIBS clinics

05 **Researchers in Industry and Academia**

- Focus research and higher effectiveness
- Develop biomarkers
- Develop NIBS for home-use options

06 **Research Funding Agencies**

- Fund research for effectiveness, biomarkers, and home-use
- Promote industry academia exchange
- Promote open access
- Fund projects for enhanced ergonomics of NIBS

Policy Makers

01

(on European and national level)

Establish one governing EU-level body on neuroscience and neurotechnology, including NIBS

Have one governing body for Europe, which stimulates and supports NIBS research, establishes quality criteria for NIBS trainings, develops a regulatory infrastructure and NIBS specific guidelines for manufacturer as well as runs a pan European registry for adverse and side-effects and incidental findings. This should avoid:

- small-scale country-specific regulations
  - "NIBS therapy tourism" between different countries should be avoided by all means which is possible by setting European-wide binding legal regulations if not also international regulations
- sale for non-medical use, such as neuroenhancement, of NIBS within the European Union unless allowed for specific non-medical purposes by regulatory authorities, which should be determined specifically at the EU level

Ensure equal acces to safe and effective NIBS

NIBS shall be made available:

- to all patients on prescription only
- in all EU countries regardless of the patients' financial and educational status
- by public health insurance rather than being limited to private health insurance
- for both inpatient and outpatient settings, including home-use

Engage stakeholders in decision making

Engagement of all relevant stakeholders in public discussions on medical, ethical, social, legal, and political aspects of NIBS as well as in decision making processes regarding NIBS development, approval, application and distribution. The relevant stakeholders include:

- patients, their families, and patients' organizations,
- healthcare organizations and healthcare professionals such as physicians, nurses, psychotherapists, physiotherapists, and social workers,
- health insurers, both private and public,
- scientists and researchers, including basic and clinical,
- industry, including research & development and marketing,
- ethicists and lawyers,
- international organizations (such as the UN and World Health Organization) and regulatory institutions at the level of the European Union, and at the national level of member states

01

Ensure data protection

Establish data management and data protection (neurorights). This should allow for:
- the use of personal data with NIBS that respect neuroprivacy and mental privacy rights, following the recommendation of the Council on Responsible Innovation and Neurotechnology
- the promotion and development of a clear definition of brain data according to the principle of responsible innovation, particularly with regard to the possibilities and limits of access and use of this data, towards a framework in line with and complementary to current regulations (European Union's General Data Protection Regulation, OECD's Privacy Guidelines and the European Convention on Human Rights) taking into account current and potentially future legal developments in the neurorights debate
- develop data management policy covering informed consent specific issues (broad consent, secondary use for research purposes, handling of incidental findings in harmonization with the right-not-to-know, etc.)

RECOMMENDATIONS TO

Health Authorities

02

Provide trustworthy information about NIBS

Public health authorities should act as information providers and monitoring bodies for NIBS technology. In particular, they should:
- provide information to the general public about the latest developments in NIBS technologies
- provide access to information about advantages and disadvantages of NIBS to general public; ideally, this should include different fields of NIBS applications such as treatment, enhancement and research, thereby promoting and safeguarding respect for patients' autonomy
- provide lists with potential contact persons, points of contacts within industry, end users, and researchers to facilitate findability of reputable actors

Collaborate with EU-level body

Relevant information should be reported by national health authorities to the above mentioned EU body on neuroscience and neurotechnology or an alternative EU-level database. This information should include:
- incidents and anomalies with NIBS
- home-users' experiences with NIBS

02

Monitor quality standards

Public authorities should ensure the quality standards of NIBS by monitoring its developments, manufacturing and marketing and establishing training standards. They need to:

- monitor and support development of new promising NIBS technologies (even in statu nascendi)
- develop and establish training standards for researchers and healthcare practitioners working with NIBS
- provide a certification system for NIBS manufacturers and guidelines regarding their informational obligations towards NIBS users, both healthcare professionals and patients
- provide a EU wide certification system for NIBS practitioners

RECOMMENDATIONS TO

Healthcare Providers of NIBS

03

Engage stakeholder in therapy planning

Engagement of all relevant stakeholders and healthcare professionals in treatment decisions and processes. Such involvement should consider:

- lived and first-person experience of patients in setting up treatment plans
- the patients' targets for the treatment outcomes in co-designing and co-setting up treatment plans together with their respective caregiver, nurse, and physician
- the opinions of medical doctors on technological and therapeutic issues
- nurses' expertise in accompaniment and treatment setting
- psychotherapists for the psychological support before, during and after the NIBS therapy
- physiotherapists for the arrangement of proper setting and physiotherapy before, during and afterwards

Improve treatment setting

Improve treatment setting and equipment (for example, comfortable rooms and ergonomic instrumentation)

Get certified

Get a regular certification for NIBS practitioners as the field of NIBS is growing fast and continuously

RECOMMENDATIONS TO

Industry 04

Develop home-use NIBS

Development of home-use NIBS for medical purposes. This includes:
- development of simple and easily accessible NIBS for home-use, so that the technology is even accessible for people living alone
- provision of secure data acquisition for the transfer of medical data in a home-use setting

Develop NIBS clinics

Development of NIBS clinics and ambulances. These shall allow for:
- providing the latest and novel state-of-the-art NIBS technologies (which are not already in use for medical home-use)
- providing more than one NIBS method
- close collaboration with the research & development in either industry and/or academia
  - This makes them suitable to conduct larger-scale clinical trials on novel NIBS protocols and technologies, whereby first results should be published in reputable scientific journals (Q1-Q3)

RECOMMENDATIONS TO

Researchers in Academia and Industry 05

Focus research and higher effectiveness

Researchers are encouraged to explore NIBS underlying mechanisms, risks, and potential benefits. Research in these areas should focus on safety and effectiveness of NIBS treatment.
This should allow for:
- unravelling and identifying the basic neuronal and psychophysical mechanisms of NIBS
- more precise diagnostic and individualized therapy
- determining biomarkers for therapeutic monitoring (see below)
- developing various alternative treatment settings for more individualized precision-based treatment
- developing treatment guidelines in collaboration with healthcare providers and regulatory authorities
- developing guidelines on risk/benefit assessment and informed consent guidelines pertaining to research on AI use in the field of NIBS

05

Develop biomarkers

Development of biomarkers. This should allow for:
- determining biomarkers on neuronal, physiological, and psychological levels
- distinguishing between biomarkers of responders vs. non-responders
- developing biomarkers for differential-diagnosis (symptoms based) of different mental disorders, such as depression and anxiety
- developing biomarkers for the treatment monitoring
- linking the biomarker development with healthcare providers/insurers as to translate them into clinical practice

Develop NIBS for home-use options

Development of home-use NIBS. This should allow for:
- research into custom-made home-use NIBS device
- the development of user friendly and easy applicable home-use NIBS
- making available proper information and on-line support for home-use NIBS
- making available also on-line therapeutic monitoring for home-use NIBS
- research into the use of artificial intelligence in an ethically and legally compatible way (including the development of specific informed consent documents)

RECOMMENDATIONS TO

Research Funding Agencies

06

In general, we encourage research funders to take reasonable risks and also fund early-stage or experimental research projects. Furthermore, we suggest increasing the efficiency of grant-writing by lowering administrative burdens, so that researchers can put more capacities into research.
In addition, the following recommendations could be derived based on the needs of the individual stakeholders:

Fund research for effectiveness, biomarkers, and home-use

In order to promote home-use of NIBS in a medical context, targeted research should be funded for establishing:
- efficacy and safety of NIBS devices in home-use
- user-friendliness of NIBS devices in home-use, for an easier application
- technologies for the application and monitoring of NIBS devices at home
- technologies for secure data transmission from home-use NIBS

In order to increase the efficacy of NIBS treatments, research projects should also be funded with the following aims:
- increase the efficacy of treatments
- decrease adverse effects
- develop individualized treatment options in a precision-based way
- customize to different subgroups of patients by finding the best predictive and diagnostic biomarkers or a combination of biomarkers
- develop protocols that promise longer lasting effects (also with longitudinal studies)
- develop protocols for maintenance treatment (as for electroconvulsive therapy)

Promote industry academia exchange

In particular, research projects that ensure the transfer of scientific findings into technical implementation and treatment should also be promoted as to strengthen the:
- technologies that need to be developed given the recent therapeutic effects and their deficiencies
- dialogue between researchers and industry as well as users and regulatory authorities, which includes the elaboration of best regulatory practices in adapting technological progress with ethical considerations and legal requirements
- conjoint grants for industry and university/academia (for example, funding schemes by the European Union for start-up companies)
- combined research-industry collaborations and consortiums in providing novel more effective stimulation technologies

Promote open access

A prerequisite for any funding should be that the results are made available in open access. This should provide the:
- convergence of open access of data and results with and adjusted to data protection strategies
- development of novel data access and protection strategies including those for home-users of NIBS
- publication of the results in open access journals with the continuously increasing article processing charges being taken over either by the grant agencies and/or the universities. This action would defray these costs from the researchers' budget as to maximize that for research-related efforts
- giving incentives to private organizations that share results whenever they publish preprints or press releases involving the evaluation of neurotechnologies

Fund projects for enhanced ergonomics of NIBS

To enable easier use and better ergonomics for practitioners and patients, specific research projects should be funded. This should provide:
- development of more comfortable, easier and cheaper technologies for home-use NIBS
- development of more digital, technologically mature and sophisticated NIBS home-use technologies following the hospital NIBS standards
- standard proper information and guidance for the home-use of NIBS

GLOSSARY

Non-invasive brain stimulation (NIBS)

Non-invasive brain stimulation refers to a group of techniques that aim to modulate brain activity without the need for surgery or the insertion of any invasive devices. These techniques involve applying electrical, magnetic, or other forms of energy to the scalp or other external parts of the body to influence the neural circuits and activity within the brain. The goal of NIBS is to induce changes in brain function that can have therapeutic or research implications, such as enhancing cognitive abilities, treating neurological or psychiatric disorders, or investigating brain-behavior relationships.

Transcranial magnetic stimulation (TMS)

Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique that uses magnetic fields to induce electrical currents in specific regions of the brain. TMS involves placing a magnetic coil on the scalp, which generates brief and focused magnetic pulses that can penetrate the skull and reach the targeted brain areas. These magnetic pulses create small electric currents that stimulate the neurons in the targeted region, thereby modulating brain activity.

Transcranial direct current stimulation (tDCS)

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that applies a weak direct electrical current to specific areas of the scalp to modulate brain activity. It involves placing two or more electrodes on the scalp: an anode (positive electrode) and a cathode (negative electrode). The anode delivers a low-intensity electrical current, while the cathode acts as a reference point for the current flow.

Biomarkers

Biomarkers are measurable indicators or characteristics that can be used to assess biological processes, physiological states, or pathological conditions within an organism. They can be molecules, genes, proteins, imaging features, or other measurable entities found in body fluids, tissues, or cells. Biomarkers serve as objective measures that provide valuable information about normal biological functions, disease progression, response to treatment, or overall health status. They can be used for early detection, diagnosis, prognosis, monitoring treatment efficacy, and prediction of outcomes of various diseases or conditions.

Enhancement

Any modification aimed at improving individual human performance and brought about by science-based or technology-based interventions in the human body.

Individualized treatment

Individualized treatment refers to an approach in healthcare where medical care, interventions, or therapies are tailored to meet the specific needs, characteristics, and preferences of each individual patient. Rather than employing a one-size-fits-all approach, individualized treatment takes into account the unique biological, genetic, physiological, and psychological factors of a person to design a personalized plan. Individualized treatment is particularly relevant in fields such as precision medicine, oncology, pharmacology, and mental health, where variability among patients is observed and treatment responses can vary widely.

Open access

Open access refers to the principle of unrestricted and free access to scholarly research outputs, such as journal articles, research papers, and data, via the internet. It allows anyone, regardless of their institutional affiliation or financial resources, to read, download, copy, distribute, and reuse these research materials without legal or financial barriers.

IMPRINT

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This research project was funded within the ERA-NET NEURON framework by

- Federal Ministry of Education and Research (BMBF) (grant numbers [01GP2124A] & [01GP2124B])
- Canadian Institutes of Health Research - Institute of Neurosciences, Mental Health and Addiction (CIHR- IRSC) (grant number [CIHR 34786])
- Institute of Health Carlos III (ISCIII) (grant number [AC20-00074])

How to cite this document:
Maier, M. J., Antal, A., Oliviero, A., Breuer, J., Ramasawmy, P., Baeken, C., Hölzle, K., Paulus, W., Rozynska, J., Ryan, D., Salardi, S., Tankisi, H., Vidalis, T., Zilio, F., & Northoff, G. (2023). STIMCODE Participative developed recommendations for non-invasive brain stimulation in the European Union. Fraunhofer-Publica. http://dx.doi.org/10.24406/publica-1569

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