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Recommendation for the use and development of non-invasive brain stimulation— insights from a trans-European participatory stakeholder study

Dear Editor,

Non-invasive brain stimulation (NIBS), especially repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) is advancing into different facets of our society-from research and the treatment of medical conditions [6,7] to cognitive enhancement in healthy individuals, including the military and 'neurodoping' in sports [1]. The rise of some of the NIBS applications poses ethical considerations and apprehensions concerning its societal consequences [2].

In a multicenter study, within ERANET NEURON's 2020 call for Ethical, Legal, and Social Aspects of Neuroscience, we implemented participatory processes to analyze the perspectives, wishes, and fears of different stakeholder groups involved in NIBS, with the goal of shaping its utilization and future development. We used tailored design-based and co-creative workshops [10] including seven stakeholder groups related to NIBS: 1) patients who received NIBS interventions, 2) clinical practitioners involved in the treatment of patients, 3) students with basic knowledge and experience with NIBS, 4) representatives of NIBS companies building tDCS and TMS devices for research and therapeutic use, 5) tDCS home users using devices self-built or bought online without medical prescription or supervision, 6) policy experts, and 7) philosophers. The qualitative and inductively evaluated results from the workshops were compiled and assessed by 15 experts from the fields of medicine, neuroscience, psychology, law, ethics, philosophy, and innovation management to develop a set of recommendations for policymakers, health authorities, healthcare providers, industry, researchers, and research funding agencies regarding NIBS technologies on a two days expert workshop in April 2023. Here, we highlight the key issues in the field of NIBS and their relevant solutions, which were derived from the expert workshop findings and our previously published recommendations submitted as a white paper to the European Union (EU) Parliament [8].

Compared to the USA and some non-EU countries, only a few insurance companies reimburse treatments with rTMS and tDCS. In most of the European countries, the treatment should be paid privately. This limits the availability and accessibility of NIBS to underprivileged patients [3]. Stakeholders encouraged policymakers to ensure equal access to safe and effective NIBS by making it available for both inpatient and outpatient settings, including home-use, and spurring public health insurances to cover the intervention fees.

A common wish shared across all the stakeholder groups was the broader administration of tDCS for home use by healthcare authorities and its further development by researchers in academia and industries to make the technology easier to use and more accessible for patients living far from NIBS centers, as well as to reduce the workload of clinical practitioners in hospitals while providing for secure medical data transfer and acquisition. Research funding agencies were prompted to promote this direction and to fund research to ensure better efficacy, maximal safety, user-friendliness, and secure data transmission related to the home-technology. Unfortunately, some companies are currently selling tDCS devices for home use without proven efficacy and safety, while advertising misleading promises [4].

The recent non-evidence-based and controversial reclassification of non-medical NIBS devices in the Class III category (same level of risk as invasive brain stimulation devices) [3] and the tightening of the medical device regulations (MDR) in the EU currently hinder the testing of novel NIBS protocols and increase the administrative burden associated with grant writing and ethical approval. While demanding the reclassification of NIBS to Class IIa (moderate risk), stakeholders and experts in our study also stressed the need for public health authorities to provide trustworthy information about NIBS, backed up by quality research and to ensure that the quality standards of the technology are met through the monitoring of its manufacturing, marketing, and development. Evidence-based quality information from these specific bodies should be used by policymakers to make regulatory decisions regarding NIBS. Moreover, there is a need for an EU-wide certification system and standardized training for healthcare practitioners and researchers, similar to the current certification program in Germany [9].

Experts requested the establishment of a governing body for neuroscience and neurotechnology such as NIBS at the EU Level, which would provide specific guidelines for NIBS manufacturers and monitor a pan-European registry for research findings and side/adverse effects of the technology. Currently, the registration of side/adverse effects is well-regulated under the MDR. While the central registration of research/clinical studies is mandatory in numerous countries, the imposition of a regulatory governing body at the EU level might exacerbate bureaucratic impediments at the present stage.

A major concern shared by stakeholders was the management and protection of NIBS brain data. Policy experts emphasized that the use of NIBS-related personal data should respect neuro- and mental privacy rights by abiding by the guidelines of the Council on Responsible Innovation and Neurotechnology. Policymakers should also establish a clear definition of brain data, including the limits of its use and access while respecting the current data protection and human rights regulations (EU's General Data Protection Regulation and European Convention on Human Rights), and accounting for the current and upcoming legal developments in the neurorights debate [5].

While stakeholder engagements can be time-demanding and difficult to coordinate, participants in the final two-day expert meeting highlighted the importance of involving all relevant stakeholders in decision-making and public deliberations to address the medical, social, ethical, political, and legal aspects, including patients and carers, healthcare

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bodies, insurers, researchers, industries, international/regulatory organizations, ethicists and lawyers. It was also suggested to include all of the relevant stakeholders in therapy planning to deliver optimal and if needed, personalized NIBS treatment for patients. The engagement should consider patients with lived experience, the expertise of nurses in accompaniment and treatment settings, perspectives of medical doctors on therapeutic or technological issues, as well as psychotherapists and physiotherapists for add-on support before, during, and following the NIBS therapy.

Compared to other non-pharmacological interventions such as physiotherapy and electroconvulsive therapy, NIBS is relatively young, with its full potential remaining elusive. Despite the evidence-based application of NIBS in many disorders (e.g. major depression), stakeholders encouraged scientists in academia and industry to focus research on determining more reliable therapeutic biomarkers and developing risk/benefit assessment guidelines relating to the use of artificial intelligence in NIBS and the development of personalized precision-based NIBS interventions. They underscored the importance of unraveling currently unknown neuropsychological mechanisms of NIBS (e.g. dose-dependency, combination of NIBS with other methods to increase efficacy and to decrease treatment variability). Furthermore, they highlighted the need for research funding agencies to better promote exchange between academia and the industry through dialogues, conjoint grants, and collaborations as well as open access to data and results, while maintaining data protection regulations.

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CRediT authorship contribution statement

Perianen Ramasawmy: Writing – original draft, Conceptualization. **Andrea Antal:** Writing – review & editing, Validation, Supervision, Conceptualization. **Moritz Julian Maier:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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