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Neurochallenges report

This document serves as an overview of NeurotechEU's deliverables related to the white papers on neurochallenges. The following deliverables on white papers have been added to this document:

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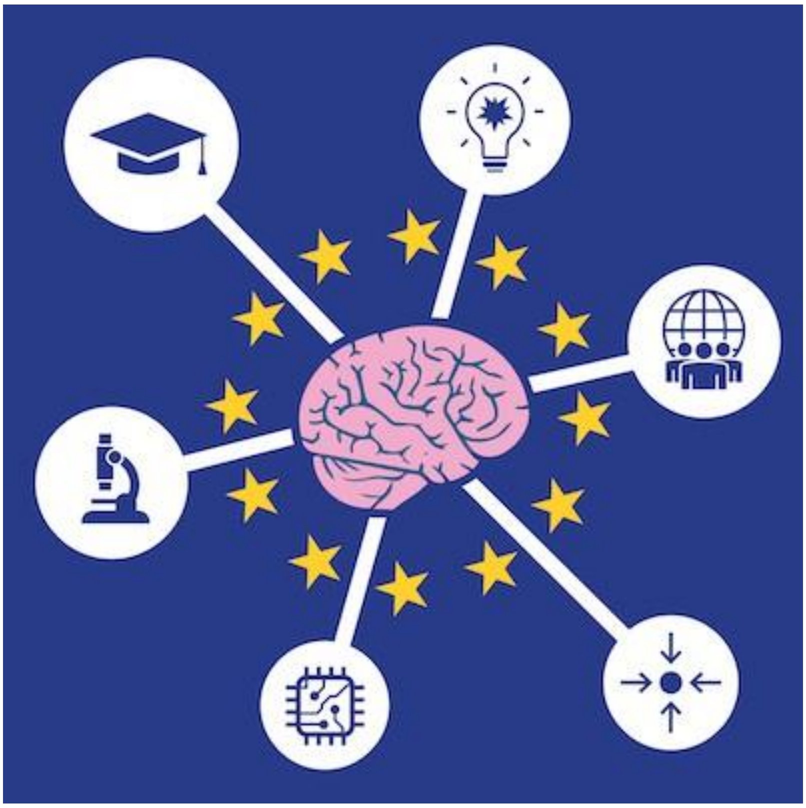

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Future Neurochallenges in Health and Healthcare

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Introduction

After more than two years since the beginning of the COVID-19 pandemic, the concepts of health and healthcare have never been as emphasized in our collective consciousness as they are now. While the world may have become fatigued by continuously worrying about the health of loved ones and fearing that the health systems they relied on were on the brink of collapse, this point in time offers an immense opportunity to piece together the emerging lessons and shape the healthcare of the future.

Before 2020, the public health landscape was characterized by a steady shift between the global burden inflicted by communicable diseases and the one imposed by non-communicable conditions [1]. The COVID-19 pandemic has completely altered this scenery by impeding the fight against infectious agents such as HIV [2] and tuberculosis [3], causing momentous disruptions in the delivery of essential health services all around the world [4] and creating major setbacks in health areas where progress was previously registered [5]. The full extent of the impact of these disturbances is yet to be determined, though it would be safe to assume that sudden changes might occur in the global epidemiology in the coming years. Moreover, among the list of long-term and yet to be fully understood impacts of the coronavirus pandemic also lies Long COVID [6], which might impose an additional unforeseen burden on society – considering that almost half of the world's population has been infected with SARS-CoV-2 at least once during the past years [7].

This whitepaper attempts to bridge the current status of healthcare and a vision for the future, identifying novel challenges in health that will likely materialize by 2040. The approach employed is designed to serve to tailor Neurotech^EU^ – the *European University of Brain and Technology* – educational and research programs and aid in developing innovative action plans to maximize the benefits of novel technologies and interventions for the European economy and society at large.

In addition, we will focus on neurochallenges – issues that can be addressed using a multidisciplinary approach at the intersection between neuroscience and neurotechnology. It is now unquestionable that intense cross-border and cross-disciplinary collaboration in research is the key for rapidly solving complex challenges, such as those posed by the myriad afflictions of the nervous system. The recently accelerated embracement of e-health is another essential component for tackling future neurochallenges, offering fertile ground for the development and implementation of innovative neurotechnologies. Considering the colossal burden posed by neurological disease on society – stroke, the second cause of death worldwide [1], being just one example – the interplay between neuroscience and neurotechnology has an immense potential of improving population health and relieving considerable pressure on health systems. For the remaining part of this whitepaper we focus on the following neurochallenges that health and healthcare will face in the next 20 years:

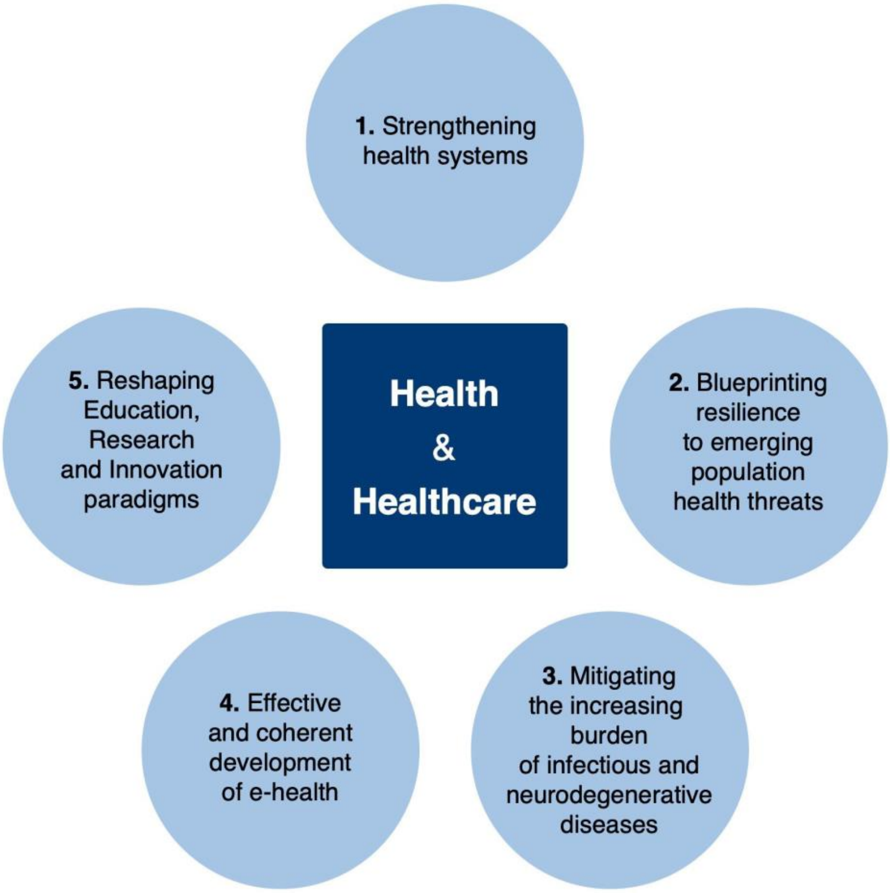

Figure 1 - Main Neurochallenges within Health & Healthcare.

Finally, we propose a roadmap to address at least some of these challenges so that it can be considered in future Neurotech[EU] strategies and programmes.

Strengthening health systems

Health system strengthening (HSS) is a term that has never been clearly defined. Originally, it came from the recognition that without strengthening of basic health systems, vertical programs targeted to address specific diseases and interventions would be unlikely to deliver as expected. The World Health Organization (WHO) defined HSS as "*any array of initiatives that improves one or more of the functions of the health systems and that leads to better health through improvements in access, coverage, quality or efficiency*". WHO has also defined 6 core components of HSS: (a) service delivery, (b) health workforce, (c) health information systems, (d) access to essential medicines, (e) financing, and (f) leadership/governance. WHO also defined several criteria to assess what is an intervention on HSS: they should encompass cross-cutting benefits, address identified policy and organizational constrains, produce long-term system impacts and be tailored in country-specific contexts with clearly defined roles for institutions. Other authors suggest the inclusion of other elements, such as the involvement of communities in the process of maintaining health, and financial protection. At present, several challenges related to HSS include:

- The lack of consensus on the assessment of the impact of health interventions (vertical interventions are the most common) on the broader health system.
- The lack of consensus on the assessment of the impact of health interventions on health status and access to health services.

In a recent review, Witter et al. (2019) [8] defined as intermediate outcomes of HSS interventions the following: service access, service coverage, and service quality and safety. Longer-term outcomes would be: improved health (morbidity and mortality); equity of outcomes/distributional effects; cost-effectiveness; responsiveness (such as patient-centeredness); and social and financial risk protection. These authors also reviewed studies on the evaluation of interventions of HSS and identified the following main categories of interventions:

- *Leadership and governance*: good governance, the involvement of different stakeholders and civil participation in the interventions as well as leadership capacity development and mentoring have proved to improve indicators of the health system such as service quality.
- *Workforce*: interventions in human resources for the health system are effective in improving support to HSS. Workforce interventions involving education, regulations, financial incentives and information systems are usually applied. Providing support from community health workers for particular areas of service delivery may improve health services. Well-designed performance management systems greatly influence individual performance of health workers.
- *Financing*: usually interventions combining financing and governance reforms are applied such as purchasing reforms, incentivisation, mix of public and private providers, and others.
- *Health information*: there is no clear evidence of its effect on health outcomes and indicators.
- *Pharmaceutical supply chain strengthening*: there is not enough research in this area to evaluate the effect of investing in the supply chain of medicines on the outcomes of health care.
- *Service delivery*: this is the most complex and broad area of intervention. It is widely accepted that strengthening primary care services has a positive impact on health outcomes. Basic or essential packages of health service and their design may be also relevant.

Under this scenario, the main present challenges for HSS are:

- Providing resources in time and adequate for providers able to have flexibility to provide services according to local needs.
- Capacity building (at individual, organizational and system levels) to face changing situations, such as emerging risks.
- Providing packages of services to a growing population (migrations and refugees), focusing first on vulnerable populations.
- Engaging communities into health programs (the voluntary adoption of healthy habits, citizens as being co-responsible for the health status of the population).
- Developing consensus methods to efficiently measure the impact of interventions for HSS, including resilience as an indicator of HSS plans performance.

Blueprinting resilience to emerging population health threats

Resilience of the healthcare systems has no standardized comprehensive definition, although it is widely accepted that it addresses the response to unforeseen threats and crises, rather than with daily challenges. According to the EU expert group "*Health system resilience describes the capacity of health to proactively foresee, absorb and adopt to shocks and structural changes in a way that allows it to sustain required operations, resume optimal performance as quickly as possible, transform its structure and functions to strengthen the system and possibly reduce its vulnerability to similar shocks and structural changes in the future*".

Haldane et al. (2021) [9] defined resilient health systems as systems that: (1) activate a comprehensive response (health, economic and social considerations); (2) adopt capacity within and beyond the health system to meet the needs of communities; (3) preserve functions and resources within and beyond the health system to maintain crisis-related and non-related routines and acute care, and (4) reduce health, well-being and financial vulnerability to catastrophic losses in communities.

Resilience can be divided into planned resilience (pre-disaster activities, plans to avoid and minimize crisis and adaptive resilience, risk management plans, among others) and adaptive resilience (develop new capacities by responding to emergent situations). Resilience as a process can be divided into phases: prepare, prevent, protect, respond, recover and re-imagine.

The One Health (OH) approach may also enhance resilience of health systems by including human, animal, plant and environmental health. Some burdens of disease are related to neglected zoonosis or tropical diseases, lifestyle or even from the social-ecological system in which they occur [10].

The COVID-19 pandemic has drastically reshaped our understanding of healthcare and our focus on health. During this time, the challenges previously faced by health systems have only been exacerbated, while numerous others have emerged. The pandemic has also demonstrated that when crossing paths with novel pathogens, common comorbidities such as diabetes or heart disease may have an unexpected and far-reaching impact – beyond their intrinsic pathophysiological processes. In the case of COVID-19, this has dramatically influenced the severity of disease, and ultimately its mortality [11,12]. Improving population health is thus in itself a measure of increasing our society's capacity to better overcome future pandemic threats, which is essential given that the probability of another extreme epidemic is not at all negligible [13]. The present COVID-19 pandemic has been a challenge for healthcare systems around the globe [14]. Factors that have proven to be responsible for successful pandemic response to COVID-19 have been state capacity, social trust and leadership. Countries with a competent health system in which citizens trust and listen to their leaders have performed the best. In order to set recommendations for resilient healthcare systems in emerging populations the main challenges are to:

- Develop an assessment framework for evaluating the resilience of healthcare systems, and include them when assessing HSS plans.
- Enhance public health preparedness and provide adaptability and sustainability to the health system.
- Continuously develop science-guided policies and procedures for the future prevention and control of outbreaks.
- Governance and social interventions to implement good governance guidelines, enhancing leadership and social trust.
- Develop community capacity for health protection and promotion.
- Including One Health approaches that consider the commonalities of human, animal, plant and environmental health.
- Finance all previous actions in the present scenario of reduced energy resources and humanitarian conflicts.

Mitigating the increasing burden of infectious and neurodegenerative diseases

Infectious diseases. The past two decades have been characterized an increasing burden of infectious diseases. The most recent (COVID-19) pandemic has currently had a death toll of more than 5 million people, with 30% of survivors reporting long-term neurological symptoms. Nevertheless, the COVID-19 pandemic showed us that vaccines and antivirals can be developed in record time through multidisciplinary efforts from basic research. Now similar efforts are needed for other infectious diseases such as HIV or Zika [15]. Moreover, many central nervous system infections are still largely undiagnosed [16,17] and therefore represent an important future neurochallenge. Developing sequencing methods that allow investigation of all non-human DNA in a single sample has the potential of addressing this challenge, improving the diagnosis of acute infections in a data-driven and hypothesis-free manner, and avoiding clinical biases [18]. We also expect that techniques such as multiplex PCR will be made more widely available in the future in order to identify multiple disease-related changes in a single patient [19].

Neurodegenerative diseases. Similarly, the more we learn about neurodegenerative diseases, the less confident we are that changes in single proteins are their causes, and that targeted pharmaceuticals might only be effective in a subset of individuals. For instance, most patients with Alzheimer's disease, fronto-temporal dementia or Parkinson's disease have multiple neuropathologies and comorbidities. They are normally excluded from clinical trials due to this multiplicity of symptoms that is expected to yield reduced clinical trial efficacy. Thus, personalized and targeted therapies are a future neurochallenge that we need to address in order to address multiple pathologies and the impact of concomitant diseases. Promising examples to overcome this challenge are engineering approaches based on newer-generation nanoparticles capable of delivering small molecules, peptides and antibodies to specific brain areas or neurons bearing pathology [20,21]. Moreover, building a better system to prevent or delay the effects of neurodegenerative disorders will be essential to overcome the challenges associated with neurodegeneration. To be successful, this will likely require societal action by creating policies that make healthy diets with reduced salt intake and more fruits and vegetables affordable and more widely available [22]. In addition, a life-course perspective of brain health, starting in early life, will be needed that facilitates physical activity, psychological health and better life-long education [23].

Caregiver burden. A substantial number of infectious and neurodegenerative disorders lead to a progressive impairment in physical and mental independence. When this occurs, patients start receiving help from family members or a caregiver, who, depending on the disease severity and behavioral impairment, are at higher risk of developing mental and somatic health problems themselves. This is an important neurochallenge because it will increase the prevalence of diseases and reduce the quality of care for patients with sick caregivers. Programs that provide support to caregivers should thus be implemented in the future and funded at a large scale in order to reduce caregiver physical and psychological burden. These programs should include social networks of other families going through similar experiences, financial support for persons with low income, and counseling from health psychologists in case they experience emotional distress [24].

Effective and coherent development of e-health

Technology is playing an increasing role in our health. Neuroimaging techniques such as magnetic resonance imaging (MRI) have become a standard procedure used at neurological and infectious disease centers around the word and in the coming years advances in portable MRI will create cost-effective opportunities to increase its widespread use even further. Wearable technology already exists to provide real-time, quantitative data on movement, sleep and other basic physiological functions [25,26]. A future neurochallenge will be to include form-factor improvements that embed these devices into our clothing and our homes. When coupled with future advances in batteries and sensor function, patients themselves will be able to access measures of their neurological function. These real-world data might be used to detect and monitor diseases or to get feedback for a neurosurgical implantable device. Moreover, once properly developed, virtual reality settings mimicking real life activities will likely be more sensitive in evaluating impairment than conventional measures of cognitive function obtained in a clinic setting, and potentially be used as cognitive stimulation therapies.

Reshaping Education, Research and Innovation paradigms

Development of human resources adapted to modern needs. One cannot approach the topic of human resources in health without first acknowledging the paramount role played by the health workforce during the COVID-19 pandemic. While the rest of the world was locking down to avoid crossing paths with the novel coronavirus, doctors, nurses and many other healthcare professionals stood their ground and risked their own lives to work in uncharted territory. It is estimated that more than 100,000 health and care workers have paid the ultimate price due to COVID-19 [5], and this calls for a thorough reassessment of the strategies for human resources in health. The healthcare workforce was facing numerous difficulties even before the pandemic. In recent years, enormous strain on the mental health of health professionals has repeatedly increased [27], the effects of which will likely extend over a longer period of time. The resulting neurochallenge implies designing and implementing concrete measures for the mental health and well-being of healthcare practitioners, thus ensuring a safer and more prosperous working environment – the benefits of which will ultimately extend to the safety outcomes of patients [28]. Furthermore, fully addressing the future health needs of the population requires increasing the number of healthcare workers, in conjunction with a broader set of actions aimed at optimizing human resources for health [29].

Funding for academic research of new treatments. In light of the powerful influences of cancer [30] or mental illness [31] on global epidemiology, it is vital for the academic community to quickly adapt to the emerging needs in research. However, this can only be done provided that the funding for academic research is aligned with both the current and the predicted burdens of disease. Using stroke as a reference case, the enormous toll that it currently takes on society, coupled with the predicted increase in its incidence and prevalence in the following decades [32], calls for appropriate funding for research directed towards alleviating its current burden – as a short and medium-term strategy – and, more importantly, towards prevention – as the only sustainable long-term approach. Funding for academic research should also encourage addressing the cost-effectiveness of interventions to ensure that their large-scale adoption is economically viable. Moreover, the judicious use of innovative approaches in research, such as the utilization of real-world evidence in drug development [33], can also be incentivized by designing appropriate financial pipelines for research.

Ethics and patient safety in health R&D. Building upon the idea of novel research approaches, we must also stress the importance of research being guided by robust ethical considerations and patient safety principles – which must never be sacrificed for the sake of innovation. The digital transformation of healthcare and the increasing use of real-world data in the development of medicines bring both challenges and opportunities for the future [34]. One of the great benefits that real-world data in health currently offers is the possibility to continuously assess the safety of new medicines and technologies beyond their development phase [35]. The vast amounts of data that are now increasingly available to researchers can also be swiftly analyzed using modern techniques such as machine learning. However, hasty use of such approaches poses the risk of nurturing social inequalities inside healthcare models, potentially leading to patient safety concerns. And the threat doesn't stop at ill-advised of data. Patients who rely on neurotechnology implants for the management of neurological disorders are particularly vulnerable to disruptions in the availability or support of these devices, highlighting the need for a patient-centered approach that could include designing sustainability schemes for such devices [36]. Considering the vastness of neurological disorders, the development of novel interventions in this field is likely to ramp up and diversify in the near future. It is therefore a neurochallenge for the research community to adopt a proactive stance for keeping ethics and patient safety at the core of the rapidly evolving research and development landscape in health.

Neurochallenges for 2040

- Ensure the mental health and well-being of healthcare practitioners through tailored programs and increase the number of healthcare workers to meet the present and future health needs of the population.
- Align research funding with the current and the predicted burden of neurological disease.
- Incentivize cost-effectiveness and the use of innovative methodologies by creating future-oriented financial pipelines for research.
- Adapt ethical considerations and patient safety approaches to the rapidly evolving research and development landscape in health.
- Fast development of vaccines to treat new emerging infectious diseases.
- Implement data-driven, multivariate methods in the clinic to assess multiple pathological processes.
- Apply precision medicine approaches that take into account individual characteristics and comorbidities.
- Develop a life-long system based on modifiable risk factors that can be changed to prevent neurodegenerative diseases.
- Provide funding for support programs for caregivers of disabled patients at a large scale.
- Install wearable devices in our clothes to monitor motor and cognitive functions to detect earlier signs of impairment.
- Application and use of virtual reality programs for cognitive rehabilitation therapies.
- Increase the resilience of healthcare systems by providing additional economical resources and better practice conditions.
- Promote transparency in government policies and select trustful leaders.
- Enhance population habit changes, farming and environmental changes to successfully face new threatening scenarios.

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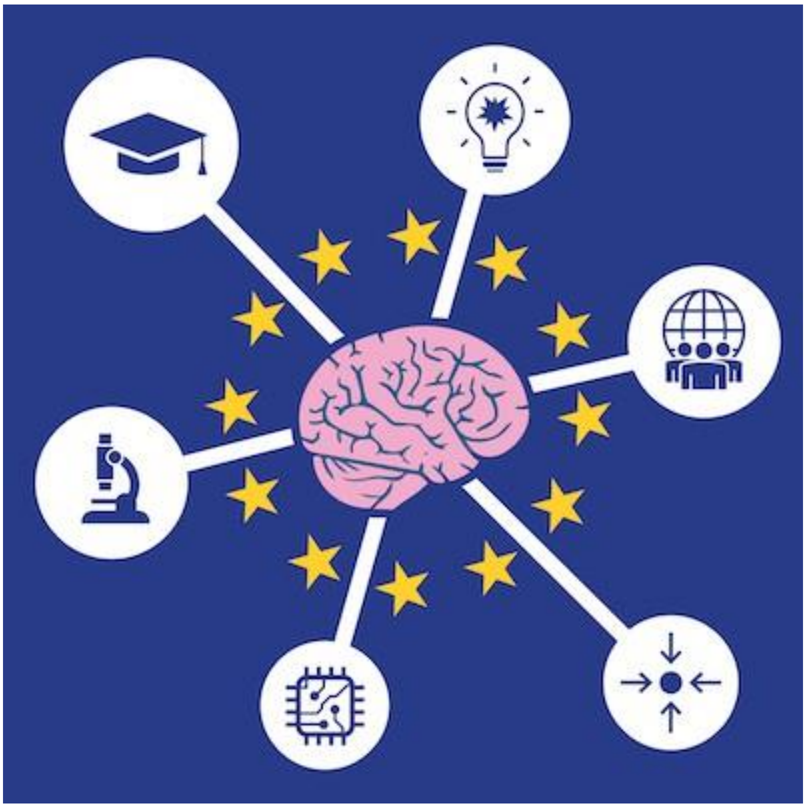

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Executive summary

This document is a study about the challenges in the learning and education aspects pertaining to the field of neuroscience. We focus on the neurochallenges in relation to 5 subfields within the realm of learning and education (data-based teaching and learning, artificial intelligence, virtual and augmented reality, lifelong learning, and open educational resources), which can be applied to 3 settings (life sciences, clinical settings, lay audience). In conclusion, 5 neurochallenges needed to be addressed by 2040 are presented:

1. Dealing with big data - a new generation of neuroscientists with data science expertise.
2. Personalizing learning paths using AI.
3. Improving study content comprehension using virtual reality and augmented reality.
4. Creating digitally-based life-long learning platforms.
5. Achieving synergy effects through open educational resources.

Future Neurochallenges in Learning and Education (2040)

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Introduction

During the past decades we have experienced a revolution in brain signal processing. New technologies such as electroencephalography (EEG), magnetic resonance imaging (MRI) and functional MRI (fMRI) have facilitated our understanding of human brain behaviour. Due to these technologies we are now able to study the neural processes that underlie learning, memory, cognition, emotions and social behaviour. Neuroscience has the potential to play a significant role in shaping the future of university education in a digitalized world. Concretely, neuroscience has contributed to a better understanding of the individual and neuroscience is in its various domains investigating personalized applications. Neuroscience is therefore in an advantageous position to shape a future personalized learning environment which respects individual differences in learning styles, cognitive abilities, and neural processing, thereby allowing for more effective teaching. Neuroscience can also contribute by applying the understanding of neural mechanisms underlying attention, motivation, and emotion, thereby educators can design digital learning environments that are more engaging and effective. Any critical approach of neurotechnology also cannot ignore the options of emerging neurotechnologies, of which neurostimulation or neurofeedback are the first baby steps, that might offer enhancement of cognitive abilities. Such an integration needs to be accompanied by a thorough evaluation of the ethical implications of their use in education. For example, brain-computer interfaces (BCIs) could potentially allow teachers to monitor students' brain activity in real-time, raising concerns about privacy and autonomy. Despite these ethical challenges that need to be solved in the long-run, combining BCI with artificial intelligence (AI) makes it possible to personalise the learning path for each student.

The efficient education of our schoolchildren and students at all educational levels is of utmost societal importance, as the future challenges for society will undoubtedly require critical and well-informed citizens. The expansion of technical innovations in general, but particularly within neurosciences, has generated a need for novel learning and educational approaches. In particular, the need for internationalisation and exchange of big data (i.e. within the human brain atlas or the human cell atlas) can be considered specific educational challenges within the neuroscience field.

In this document, we focus on the neurochallenges of 5 subfields within the realm of learning and education:

- **Data-based teaching and learning** - dealing and evaluating rapidly growing datasets.
- **Artificial intelligence** - teaching AI in different disciplines.
- **Virtual and augmented reality** – improving the learning process by using virtual and augmented reality.
- **Lifelong learning -** providing programs and training opportunities for adults.
- **Open educational resources** - digitalization of educational materials.

Figure 1 shows a simplified summary of these challenges, which are applicable to *life sciences, clinical settings* and the *lay audience.*

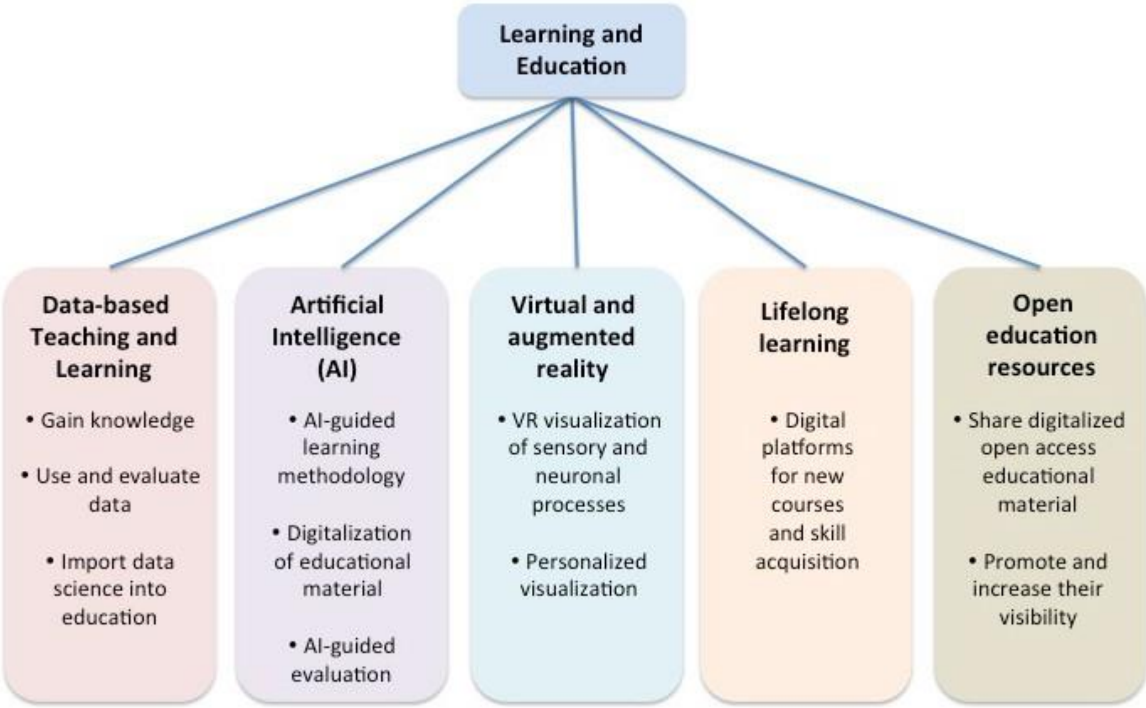

Figure 1 - Conceptual framework of future educational innovations.

Data-based teaching and learning

Across all disciplines, IT-supported research is currently undergoing a rapid development associated with an enormous increase in volumes of data. For students and future researchers, the ability to deal with large datasets in a planned and sustainable manner and to consciously use and evaluate data in the respective subject-specific contexts is therefore of great importance. As Brunton & Beyeler (2019) state:

"*The next generation of human neuroscientists will have access to genomic, anatomical, neural, and behavioral data of unimaginable richness and complexity. To take full advantage of this data, we need researchers who are fluent in the language of machine learning and adept in the practice of data science. A trans-disciplinary approach to academic training will be integral to producing, in Ed Lazowska's words, "π-shaped" individuals, who have deep expertise in both human neuroscience and in data science."* [1]

Life Sciences:

- The necessity to gain knowledge from vast data sets is increasing in life sciences and especially neuroscience. Drawing meaningful conclusions from these datasets will become more challenging and require knowledge in data science and AI in the future.
- In order to gain the ability to deal with data in any field of natural sciences, the implementation of data science in study courses is required to consciously *use and evaluate this data*.

To address this challenge we will need a concept of how to implement data science across all disciplines, but especially within neuroscience, to work with large datasets and to be able to evaluate these datasets. To this end, students will need to master programming languages that are required to work with data in a meaningful way. This has to be implemented such that it is not at the expense of basic biological knowledge, but in a way that supports the learning of this basic biological knowledge.

Teaching of data science has to be balanced against the duration of B.Sc./M.Sc./PhD programs. Thus, Neuroscience students will have to be multi-disciplinary team-science enabled researchers in the future.

Clinical settings:

- All points raised for Life Sciences are also applicable in Medicine or perhaps even more so due to the complexity of medical studies. A revision of the complete medical study courses is required for the implementation of data science across all medical disciplines. In Germany, for instance, the medical study courses are currently under revision according to the "national competence-based learning catalogue".
- A potential obstacle is the digitalization and sharing of patient data across Europe, which could be solved by implementing biomathematical approaches such as swarm learning.

Lay audience:

- A user-friendly interface, designed as an online tool, will help lay audiences to gain information about scientific projects such as the human brain atlas. Neurotechnology should build and empower a citizen science platform for neurotechnology, in which society gets the opportunity to co-create the future of neuroscience.
- On such a citizen science platform, there could be topics like nutrition, health, digitalization, education, the awe of neuroscience etc.
- Innovative apps that target the digital natives of Generation Z will be used for science teaching and healthcare. Examples are apps for children with cancer and asthma that help recognizing symptoms and monitoring of these diseases.[2,3]

Artificial Intelligence

The rapid developments in the use of big data are also driving an increased number of applications of AI systems. Higher education has a central role to play in this context: it must enable people to navigate in a *digitalised world of life and work* shaped by AI systems and to further develop these systems. Conversely, AI offers great potential for improving higher education by processing, analysing, visualising data, and by finding and structuring knowledge and information e.g. through the *personalisation of learning paths* and *tailored support*. AI has the potential to drastically change all areas of human life, students of neurotechnology will be at the forefront of shaping this future with design of AI systems and the human-AI integration as well as identifying, facilitating and supporting the learning needs of the general population in an AI influence future work environment.

Examples of AI systems based on machine learning (ML) are optimization algorithms that work with pattern recognition. These types of ML systems are therefore broadly applicable in research and, by extension, in educational settings. Students usually feel intimidated by lower-level programming languages. This creates a gap between students lacking programming experience and the use of new supportive technologies. Along with the need to close such gaps, students will undertake a basic formation in programming within their life science or clinical education. Additionally, the use and scale-up of support technologies will facilitate the creation of user interfaces that will be more widely accessible by students and society. Neurotechnology should take a strong position in shaping how AI is used, as we investigate and focus on the interface of the individual and technology for the betterment of humanity.

The developments in AI will lead to the automatization of processes and activities that are currently mainly or only performed by people. As an example of the rapidly evolving AI technological field, a brain computer interface was recently published[4]. The report describes a brain-to-text high performance interface that allows a spinal cord injury paralyzed man to type 90 characters per second with 94% accuracy, illustrating the rapid decoding of dexterous movements.

Life Sciences:

- Learning Neuroscience requires the interconnection of complex scientific concepts and generating associations between them. Building personalised study schedules using AI by focusing on each student's individual needs will improve personalised complex learning. An AI Neuroscience software will be required to integrate educational and learning theory and will have to be created based on a close communication between users and AI experts. This will be important not only for the technological design and development, but also to ensure constant updates in Neuroscience powered by AI.
- To provide personalised learning guidance and support to students in Neuroscience, an AI software can build and integrate individual learning status, students' preferences, personal characteristics, identify a student's weak points, provide assistance to students queries at any time, as well as alerting teachers to focus on re-teaching specific topics that were not properly learned, all thereby optimising the learning process. For example, cognitive tutor apps that offer feedback to students such as "*Lumilo*" already use AI to address students' problems.[5]
- AI Neuroscience softwares support learning at different levels based on the three AI paradigms: i) **AI-directed** (direct learning) - for example in mathematics we already have *Stat Lady*; ii) **AI-supported** (learners as collaborators), and iii) **AI-empowered** (learners' leading their own learning) - an example for learning in reading is the AI initiative "*Global Learning XPRIZE*" (https://www.xprize.org/prizes/global-learning).
- Creation of digital lessons (study guides, digital textbooks) and interconnection of visualisation, simulation and web-based learning. Educational outcomes obtained through AI methods need constant monitoring to ensure a high quality of learning. Digitalization can guarantee global access, including AI designs for students with special needs such as hearing or visual impairment, and/or adaptable to local culture and organisational level.
- Automatization of grading tests, evaluating homework, making progress reports, organising resources and materials for lectures as well as managing teaching materials. These administrative tasks can be managed using AI, thus optimising teachers' time to facilitate students' learning on high-order thinking and creativity tasks as well as critical reflection, discussion and debate with their peers. The 'Flipped classroom' concept will be greatly facilitated by digitally-assisted learning platforms that allow personalised study by students combined with face-to-face discussions to consolidate knowledge.
- The success of an AI learning software in Neuroscience depends on the teacher's technical knowledge, which has to be promoted by continued involvement and training in the effective orchestration of AI in their classroom. This has positive benefits in terms of learning behaviours and outcomes. It will therefore be a necessity to train the teachers to facilitate the full implementation of the digital teaching they will be expected to deliver.[6]

Clinical settings:

- Similar to a Neuroscience AI software used in Life Sciences, a personalised AI tool could provide feedback on ethics assays or actions in virtual reality surgery training, as well as, for learning new advances and complex topics in neuroscience in the clinic.
- Integration of patients' historical databases (personal information, previous illnesses, treatments, vaccinations, clinical evaluations, laboratory test results, genetic analysis, imaging) in an AI software will facilitate the examination of comprehensive patient information over time.
- AI interconnection of patient databases with their relatives (parents, grandparents) databases will allow faster and more efficient correlation between patient symptoms and relatives' genetic predisposition or current health status.
- Patient information management using AI will require additional efforts to safeguard private data.

Lay audience:

- To ensure a successful implementation of AI in education, engagement of lay audiences will be required. Daily life AI (navigation apps; facial recognition, spam filters, smart assistants) will need to be complemented with technological and AI-friendly platforms to communicate Neuroscience to lay audiences.
- AI technology will help individuals with hearing or vision impairment, and several AI innovations have already been created with this purpose.

Virtual and Augmented Reality

Students of all disciplines are faced with the great challenge of independently understanding the real facts of their subject and their complex interrelationships, as well as addressing their own misconceptions. An essential step for the individual development process of new contents and the reduction of existing misconceptions is the active examination of the newly acquired contents as well as the flexible application of the acquired knowledge. To make this possible, practice-oriented learning situations in real contexts are created in teaching-and-learning scenarios with the help of virtual reality (VR) and augmented reality (AR) to support the individual process of comprehending new study content. While VR creates a completely new immersive and interactive virtual environment, virtual objects in AR become added to existing reality. In all three domains at issue, both VR and AR will help making complex issues comprehensible by allowing an experiential and immersive learning approach within neurosciences.

In general, VR allows a reproduction and extension of the physical world in a digital setup. This includes basic learning infrastructures such as meeting rooms (e.g. Metaverse/Horizon Workspace), virtual laboratories and virtual versions of equipment. The benefit of VR is the simple scalability, ease of access such as *ad hoc* virtual classrooms without the necessity for physical presence and even allowing the erroneous use of expensive tools, as virtual tools do not break. One of the limitations of AR and VR is the missing haptic, meaning that virtual objects cannot be touched or do not produce any haptic feedback, thereby potentially breaking the emersion. However, by building an accessible virtual European Neurotech Campus, we could create a familiar environment, which could give us safety. Navigating the virtual campus of a partner university or engaging with the avatar of a colleague or teacher at another campus will familiarise students and researchers. VR does this in an even more powerful way than 2D video calls, and an AR-enriched campus can be a big learning bonus. Critically, we need to investigate and take good care of well-being and social aspects such virtual environments might make us face. Nevertheless, it should not be a story of alienation by technology, but we should explore and embrace the possibilities and apply individualised approaches to potential hazards.

Life Sciences:

- As versatile as life is, so versatile may be the future educational use of VR in the illustration and visualisation of life.
- Regarding education in foundational neurosciences, initial applications already exist that not only illustrate in 3D space different neuroanatomical structures, but also make these structures ‘enterable’ and actively explorable by means of VR. In this context, the "Virtual Brain Project" of Prof. Bas Rokers and Prof. Karen Schloss might be mentioned, who are currently working on developing 3D simulations of the visual system and other sensory systems, which can be entered and explored by means of VR technology.
- Similar simulations could also be produced for neuronal processes (e.g. cellular homeostasis, neurotransmission) and structures (e.g. limbic system, motor system, brain nerves, vegetative nervous system), both at extracellular and intracellular levels.
- Likewise, other structures and processes that are difficult to observe *in vivo* or *in vitro* such as cells, anatomical and physiological processes can be simulated in virtual reality, where function or structure can be added or removed as necessary for a deeper understanding.

Clinical settings:

- A profound knowledge of anatomy and physiology is essential not only for scientific work in the field of foundational neurosciences, but also for an in-depth understanding of all neurological and most mental diseases. In this respect the 3D simulations described above could also be used to improve the basic anatomy and physiology understanding of medical students.
- As an additional benefit, simulations can be personalized by using existing patient data from imaging or other sources to create personalized models.
- Clinicians can thereby train procedures to advance and encounter the same physiology as during the actual treatment.
- Furthermore, the 3D simulations could be extended to also illustrate the pathological mechanisms underlying neurological and mental disorders. For example, actively-explorable 3D simulations could illustrate how different stroke patterns can cause different motor impairments, or how neurodegenerative diseases change the brains' structure and function over time.
- Similarly, 3D simulations could be used to illustrate different treatment approaches and their individual modes of action.
- VR tools can be used to train diagnosis and treatment of patients with rare disorders, simulate difficult scenarios or train in areas or context that are hardly accessible to student groups. Examples of these are pilot on diagnosis of treatments of burn wounds in children, reanimation training, root canal treatment or high-security, operation room or emergency procedures. Virtual and extended reality can be used in 360 degree video tours with interactions, interactive simulations and offer an emersive and safe environment to train crucial skills and valuable experiences.

Lay audience:

- VR-based 3D illustrations of medical diseases could help making diseases intuitively understandable to lay people who have limited medical knowledge.
- In addition, VR can aid therapy or rehabilitation, by placing patients in a context that would otherwise be too costly or not feasible at all. For example, exposure therapy for phobias can use virtual replacements such as spiders, high buildings or narrow corridors to address different anxieties. In another example, burn victims playing a game in a soothing and cooling context (snowball fight in a winter surrounding) during bandage dressing change could relieve pain.
- However, lay people often require the involvement of trained personnel to utilize VR or AR tools due to the complexity in the setup and the specialization of the available applications towards specific diseases.

Lifelong learning

Knowledge and knowledge acquisition are crucial resources in the current society. This poses the challenge to design programs and structures for universities so that they become an institution of lifelong learning beyond the basic education of young people. Above all, digitally supported educational programs offer the potential for lifelong learning.

Life Sciences:

There are several aspects related to lifelong learning, i.e. before and after undergraduate and graduate education. On the one hand, schoolchildren and young adults need to acquire the necessary knowledge and skill sets that prepare them for studying at universities. In an ever-changing scientific landscape and with an increasing pool of knowledge and methods, it will be important to train educators and to directly provide content where necessary to facilitate efficient preparation for university. Conversely, it is necessary to extend the teaching opportunities at universities beyond graduation and obtaining a final/doctorate degree, both for employees and researchers at research institutions but also for industry. In this context, the following will be the main themes to address:

- Continuously updating knowledge about emerging concepts and techniques after curricular education: while working in Life Sciences often involves specialisation in specific (research) topics that inevitably leads to a narrower focus and expert knowledge, Life Sciences themselves continuously evolve and become broader regarding theoretical and technical knowledge. This gap needs to be bridged if people in the Life Sciences are to maintain a sufficiently good lifelong overview. Lifelong learning will therefore have to provide primers, overviews and introductory courses for new or changing fields and techniques. At the same time, they should provide entry points for further studies and specialised courses.
- Preparation for challenges in a working environment: education at the university traditionally concentrates on the acquisition of knowledge and on the skill sets to efficiently work with that and to build on that. However, further skills are required for productive work. Although the widespread introduction of so-called generic skill courses at the undergraduate and graduate levels addresses this to some extent, the opportunities beyond this phase of education are currently limited. For instance, how to organise and lead a team at the university or elsewhere is typically not covered or discussed. Similarly, the efficient and effective supervision of students and team members is a topic that is often neglected. Furthermore, in most cases it is left to individuals to acquire the skills for teaching (e.g. at a university) on their own. Structured introductions into teaching concepts, tools and platforms need to be provided.
- All of the above will need to be provided through appropriate digital platforms. This is because participants will take courses in parallel to their other (work) activities. Any offered content will therefore need to be flexibly accessible in terms of time and independence of geographical location.

Clinical settings:

Knowledge about a given disease regarding pathophysiology, diagnostics, treatment options and guidelines is rapidly growing. In order to enable postgraduate physicians to translate medical progress into clinical practice, clinicians are obliged to continue their medical education and lifelong learning. Further postgraduate medical education is challenged by strong time restrictions due to daily clinical practice on the one hand, and the vast amount of clinical and translational studies published every year on the other. Successful learning methods should thus allow regular and rapid updates, remote access at all time points and include learning modules with variable length. Learning modules are likely to include the following modalities:

- Streaming or downloading platforms containing summaries of controlled clinical studies, treatment guidelines and updates as short podcasts and teaching video clips.[7]
- Interactive computer-based education modules, enabling learners to work on clinical cases or to interpret diagnostic findings (e.g. EEG, ECG, ultrasounds, MRI etc.) with the help of an interactive computer-based teaching module, providing opportunities for immediate feedback.[8]
- Simulation tools by which learners can simulate clinical examinations, surgical interventions etc. to acquire skills and competencies, using e.g. virtual or augmented reality techniques.[9]

Open Educational Resources

Digitalisation opens up a wide range of opportunities for universities to make educational materials of any kind and in any medium available under an open license, i.e. free access as well as free use, editing, and redistribution by others without any or with only minor restrictions. This potential can be further exploited in the coming years to achieve synergy effects across institutions and disciplinary boundaries.

Life Sciences:

- Simply making material available to students will not automatically translate into improved learning outcomes. More research into the motives of students to use or not to use open educational resources is needed to determine how these resources can be incorporated in formal curricula.

- Students will require guidance on which resources to use and how they fit in with their individual study plan. Most importantly, using these resources must produce an added value for students (e.g. by virtue of credit points or useful qualifications).
- Likewise, educators need to be aware of the content and format of open educational resources recommended to their students. Teaching sessions need to be designed to help students apply their knowledge gained from open educational resources (OERs) to specific problems.
- Universities will need to agree on a shared pool of resources that will fit in the curricula at all sites - instead of one university providing material that will be most useful to their own students but less so for students at other sites. It will be difficult to tie these resources in with classroom teaching or real lab rotations.

Clinical settings:

- In the application of OERs to the clinical context, the focus should be on postgraduate training. Given that this is organised differently in each country, producing resources that will be meaningful and helpful to all potential users may prove a challenge. During undergraduate medical education, the most recent experience of making content available to all medical schools within Germany alone showed that most schools rather prefer producing their own content even if this means spending far more money than would be needed for a joint effort. A thorough analysis of the situation is required to elucidate the reasons for not sharing and/or using local resources even within the same study degree.
- In medical education, alignment of teaching content with assessment methods is crucial for student motivation. Thus, any open educational resources must be aligned to local curricula, and the content covered in these resources must be assessed in summative examinations. Otherwise students will view these resources as interesting at best - but when it comes to deciding which formats to spend time on, students will choose the one that is most likely to help them achieve a favourable score in upcoming exams. OERs must ‘tick a number of boxes’ to fulfil that requirement.
- If meaningful open educational resources can be produced and are actually used by students on a large scale, this opens up the opportunity of linking up teachers and learners from different universities, thus making the strengths of one site available to all teachers and students at all other sites. A prerequisite for this to happen is the implementation of an online digital resource portfolio tracking student activities and achievements across all sites and reporting it back to a student’s home university where they will receive credit points in return.

Lay audience:

- Resources explaining all kinds of things - including neuroscience - are abundant on the Internet. One important question is how members of the general public choose from the vast spectrum of information sources. Open educational resources designed for a lay audience need to be visible on popular channels, they need to be credible and recognisable (*branded*). Above all, they need to address issues that are relevant to the public and that can be presented in an accessible way. Research into user preferences, motivation and behaviours, as well as ideal modes of delivery and how to increase visibility of resources will be needed to inform the production of educational material for a lay audience. Given the large number of resources already available, gaps in the coverage need to be identified, or it will have to be argued why the same topic should be covered in a different way.

Neurochallenges for 2040

1. Dealing with big data - a new generation of neuroscientists with data science expertise.

Establishing a trans-disciplinary training in machine learning and programming languages, artificial intelligence and data science:

- Creating neuroscience bachelor and master programs with incorporation of data science courses.
- Implementing data science in regular courses - data science courses not as replacement but as a foundation for other courses.
- Implementing biomathematical approaches such as patient data sharing across Europe.
- International programs should train neuroscience students to be multi-disciplinary team-science enabled researchers

2. Personalizing learning paths using AI.

- Personalizing study schedules by emphasizing theory focusing on each student's needs using AI.
- Machine learning: Closing the gap between lack of programming background and the requirement of data scientific skills for students by creating user interfaces.
- Creating AI softwares, digital lessons, web-based learning and cognitive tutor apps as supportive learning tools for students.
- Synchronizing learning content - more unified, similar learning approaches and content across European universities.
- Facilitating patient information management.
- Positioning neurotechnology as THE discipline to guide society into the age of AI.

3. Improving study content comprehension using virtual reality and augmented reality.

- Connecting students all over Europe via digital workspaces and meeting rooms.
- Exchanging practical skills without traveling using virtual laboratories and VR surgery training.
- Realization of a virtual campus that augments the physical campuses and bridges nationalities and cultures.
- Personalizing simulations by using patient data to help diagnosis, treatment and practice for surgery.
- Implementation of VR in rehabilitation and cognitive therapy.

4. Creating digitally-based life-long learning platforms.

- Closing the gap between narrow expertise and constant evolvement of knowledge.
- Providing structured introduction into teaching concepts, soft skills and effective supervision on easily accessible digital platforms independently of geographical location.

5. Achieving synergy effects through open educational resources

The aim here is to make it possible for students to benefit from educational content of all European universities partnering up in NeurotechEU in order to receive the best possible education. NeurotechEU would therefore soften up boundaries of country-specific educational systems and help unifying the universities:

- Structuring credibility and module management for students across universities.
- Aligning open educational resources to local curricula.
- Presentation of open educational resources in an accessible way and highlighting the most suitable platform for specific purposes and lay audience.

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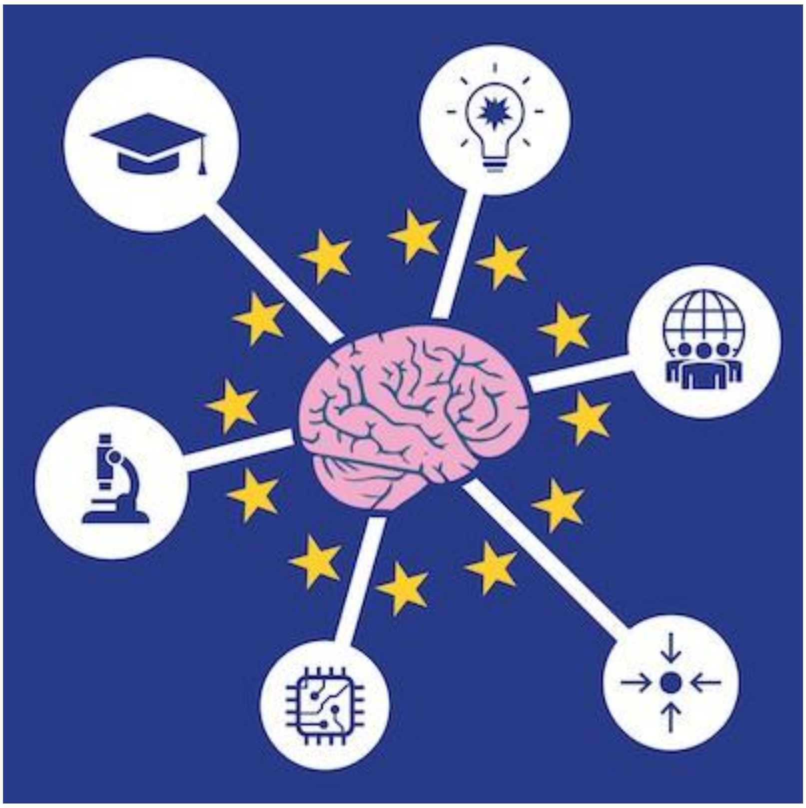

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Future Neurochallenges in Nutrition and Cognition

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INTRODUCTION

Suboptimal diets are responsible for more deaths than any other risks globally, including tobacco. In 2017, 11 million deaths and 255 million disability-adjusted life-years were attributed to unhealthy diets [1]. Overall, unhealthy dietary patterns and a sedentary lifestyle are major contributors to non-communicable diseases, ranging from cardiometabolic to psychiatric disorders. Therefore, dietary and lifestyle changes are keys to reducing societal and economic disease burdens, and understanding the behavioural bias in food selection and consumption becomes an urgent necessity. Moreover, sustainable and safe production of food are major challenges that also have to be considered, as they are of utmost importance for the population, as wellbeing is linked to optimal nutrition.

The impact of an equilibrated diet on cognitive function has been established [2], but the mechanisms supporting this interaction are not well known. Different bioactive compounds present in food such as vitamins, minerals, polyunsaturated fatty acids, or carotenoids, have been shown to beneficially affect brain function due to their antioxidant and anti-inflammatory effects, among others [3,4]. Likewise, inadequate levels of these compounds are associated with an increased risk of dementia, depression, and other neurological disorders [3,4]. The function of bioactive compounds takes place at the molecular level and leads to physiological effects directly related to cognition and mental health. Future studies should thus focus on exploring these mechanisms and on how different food components might affect the incidence of diseases that are very prevalent in different populations, such as depression or Alzheimer's disease. In this context, gut-brain interactions have emerged as key players in maintaining a healthy state, and any alteration in this bidirectional signalling leads to cognition and neurological disorders [5].

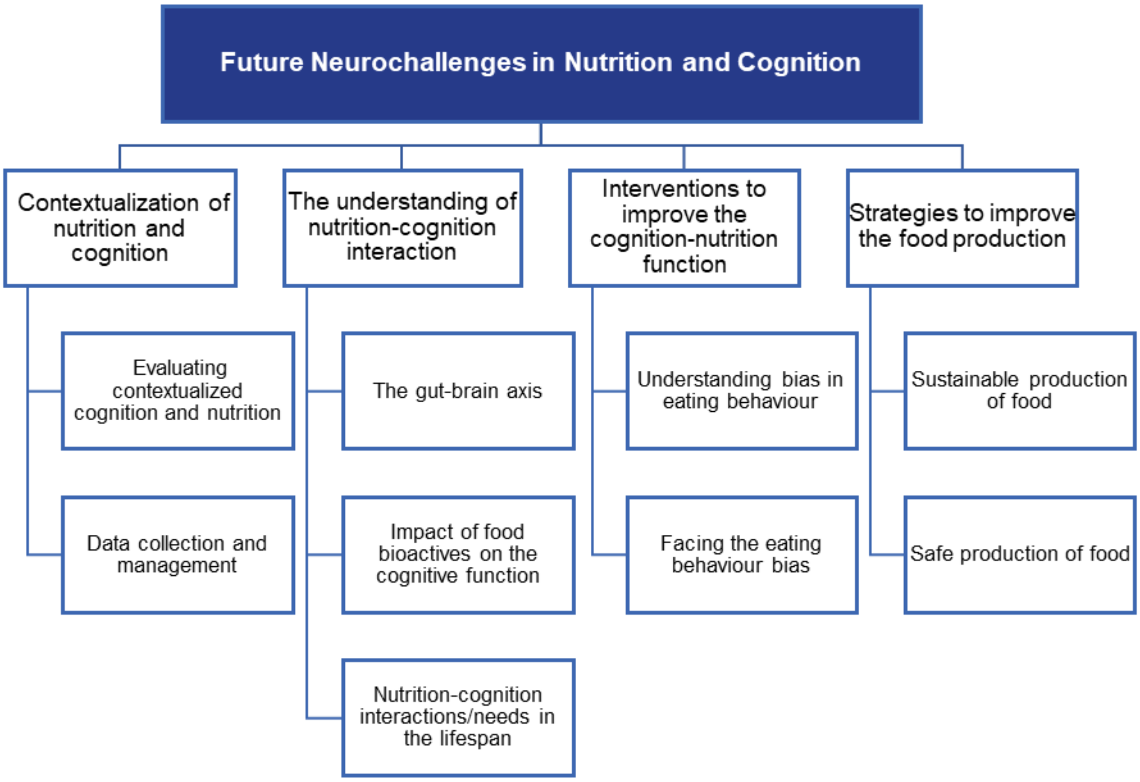

Figure 1 - Conceptual framework of future Neurochallenges in Nutrition and Cognition.

1. Contextualization of nutrition and cognition

1.1. Evaluating contextualized cognition and nutrition

Assessing cognition and nutrition under natural conditions and in context, away from the usual artificial laboratory situations, requires the development of innovative tests and an *ad hoc* theoretical framework. Development of sensors for continuous monitoring of physiological and biological markers related to cognition and diet in everyday life, would be essential. A major challenge will be the development of such sensors for continuous monitoring of behavioural and dietary biomarkers without interfering with the normal people's activity. Improvements to the existing wearable technology, like smartwatches, smart clothing and other health monitor systems, as well as the development of new devices that could be installed at home, are crucial. Conversely, the development of mobile applications that help to understand the nutritional information and that could instruct about different aspects related to diet and a healthy lifestyle is another challenge to be considered.

1.2. Data collection and management

Standardization is necessary to generate a trans-European database, including microbiome/metabolic/molecular and cognitive measures. This will allow us to advance in this and other areas, also incorporating cultural, socioeconomic, sex, gender and age variables, taking advantage of the multivariate complexity of the generated datasets and the latest advances in artificial intelligence (AI). In this regard, a decentralized data structure for nutritional and cognitive data should be developed to apply the principles of swarm learning to these data sets for AI-based analysis, as it is being developed by consortia such as COVIM (**CO**llaborati**V**e **IM**munity Platform of the NUM) for immunological data [6]. On this matter, patient data management by AI will require specific regulations to safeguard patient records private information.

The challenge will be to build an EU-wide population database to first investigate nutritional habits in relation to their cognitive habits and health outcomes, and then to follow the impact of different measures. These developments need to go hand-in-hand with those in section 1.1, to generate valuable datasets and results applicable in real-world conditions, outside of an artificial laboratory environment. Some efforts in data banking already exist. International organisms such as the European Food Safety Authority (EFSA) make some databases publicly available, namely, *Database on food consumption data*, that is essential for assessing how exposed people are to potential risks in the food chain; and *Chemical hazards database* (OpenFoodTox), important for the scientists to determine how chemicals may be hazardous for humans, animals and/or the environment [7]. In addition, the Food and Agriculture Organization of the United Nations (FAO) has FAO/INFOODS databases for different foods (pulses, fish, supplements), that are food composition databases of analytical data [8].

2. The understanding of nutrition-cognition interaction

2.1. The gut-brain axis

Unveiling the key cellular and molecular mediators within the brain-body axis that impact on neurons, networks, and eventually cognitive functions and capacities is a new challenge.

Gut-brain interactions have emerged as key players in maintaining a healthy status. The gut brain axis is defined as the bidirectional relationship between the gastrointestinal tract and the central nervous system. Undoubtedly, the impact of nutrition on cognition has a powerful intermediary in the gut microbiome. The gut microbiome is estimated to form a complex ecosystem containing more than a thousand different species of microorganisms [9]. Communication pathways between the gastrointestinal tract and the central nervous systems include endocrine, immune, and neural (via the autonomic nervous system and the vagus nerve) signalling pathways [10]. What is their relative contribution to human cognition? How can we beneficially manipulate these pathways? These are important issues that arise. A major challenge will be to understand the role of neurotransmitters in the gut on brain functioning, the bidirectional communication between the enteric and central nervous systems, and how to influence their interaction with nutrition.

2.2. Impact of food bioactive compounds on cognitive function

Diet is one of the main environmental factors that has an influence on the brain structure and function, particularly on brain plasticity throughout the lifespan [11].

Different bioactive compounds present in food exert actions that can be related to the improvement of cognition. The number of studies of these food components and their therapeutic effects in neurodegenerative diseases is growing. The potential application of functional foods as part of neurodegenerative disease management is one of the most studied areas. Some food components with neurological evidence include vitamins, minerals, polyunsaturated fatty acids, carotenoids, polyphenols, bioactive peptides, and probiotics, among others. The function of bioactive compounds takes place at the molecular level and leads to physiological effects directly related to cognition and mental health. However, the molecular mechanisms through which these dietary components exert their effects should be further investigated and clarified.

It has been demonstrated that patients suffering from cognitive disorders have a deficiency in essential vitamins and that inadequate levels of some vitamins are associated with an increased risk of dementia and depression [12–14]. Effects produced by essential vitamins such as vitamin E, D or B12 include a reduction in β-amyloid-induced cell death [15], and have implications in neurotransmitter synthesis [16,17]. Minerals are involved in multiple metabolic processes. Zinc, magnesium and iron insufficiencies are associated with neuropsychiatric manifestations like depression and anxiety behaviours, and with cognitive disorders such as autism or attention deficit hyperactivity disorder [18–23].
Polyunsaturated fatty acids influence brain plasticity. Omega-3 polyunsaturated fatty acids (n-3 PUFA) are classified as essential since their levels depend on dietary intake. Aging is associated with decreased cerebral n-3 PUFA levels due to their reduced absorption, their capacity to cross the blood-brain barrier, and to convert shorter chained fatty acids into longer fatty acids [24]. A deficiency in n-3 PUFA consumption in the diet can lead to neurodegenerative diseases, such as Alzheimer's disease, neuroinflammation and cognitive impairment [25]. n-3 PUFAs and their metabolites regulate microglia phenotype and function to exert their anti-inflammatory and resolving activities in the brain.

Carotenoids have also been proposed as potential bioactive compounds to be used for the management of mental diseases as they have high antioxidant and anti-inflammatory effects. Crocins administration through saffron extracts has been proposed as an effective strategy to reduce $A\beta_{42}$ levels in patients with Alzheimer's disease [26] and lycopene administration in depressed mice has demonstrated suppression of inflammatory responses in the brain and attenuation of depressive-like behaviours [27].

Polyphenols exert their neuroprotective actions through different mechanisms that include reduction of amyloid plaque density [28], increase in the expression of brain-derived neurotrophic factor (BDNF) [28], lipid peroxidation reduction [28], effects on mitochondria [29] and anti-inflammatory effects [30]. Bioactive peptides impact in mental health is illustrated by their capability to inhibit enzymes associated with neurological disorders, such as bipolar and schizophrenic disorders and Alzheimer's and Parkinson's diseases [3]. These enzymes include Prolyl Oligopeptidase (POP), Acetylcholinesterase E (AchE) and Angiotensin-converting Enzyme (ACE).

The intestinal microbiota can promote changes in brain function through short chain fatty acids, regulatory hormones and neurotransmitters and their precursors, due to bidirectional signalling between the gut and the brain [31]. Despite the great inter-individual variability of the intestinal microbiota, a clinical trial showed an altered microbiota composition in patients with depression compared to healthy controls [32]. In another intervention study, probiotic administration in patients with major depression disorder produced a significant reduction in depressive symptoms [33].

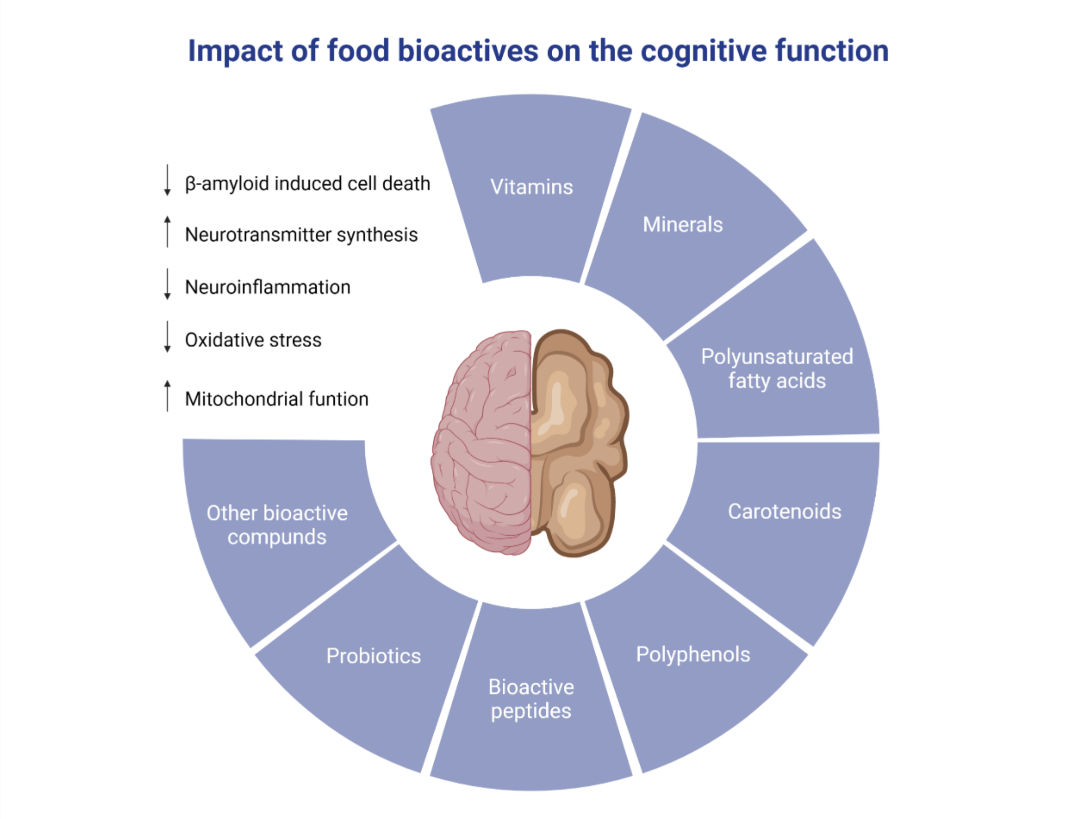

Figure 2. Impact of food bioactive compounds on cognitive function.

2.3 Nutrition-cognition interactions/needs in the lifespan

An ontogenetic dimension considering development stages, from neonatal through childhood, adolescence and the elderly, as periods with potentially distinct nutrition-cognition interactions would be required. Furthermore, research into the influence of dietary habits on future phases of life will be crucial. For instance, the importance of nutrition during the first 3 years for the later stages, as well as the importance of cardiometabolic health already in midlife for neurodegeneration in later life. Healthy nutrition is an essential element in every stage of human life and is crucial to protect against malnutrition and noncommunicable diseases (NCDs) [34]. A healthy diet has been defined as a diet that promotes health and prevents disease according to the Scientific Group of the United Nations Food Systems Summit 2021 [35]. It should provide adequate levels of beneficial nutrients (e.g., protein, vitamins, essential amino acids) and avoid the consumption of health-harming elements (such as saturated fats or sugars). In this context, the World Health Organization has created a series of guiding principles for healthy diet according to age [34].

Adolescents are considered the healthiest group among the entire population. However, because of the preferred fast food and ready meal consumption, they do not always acquire the essential nutrients required for their healthy development. This could affect their cognitive capacity and make them prone to overweight and metabolic disorders. According to the World Health Organization, the prevalence of overweight and obesity among children and adolescents aged 5-19 has risen dramatically from just 4% in 1975 to over 18% in 2016 [36].

Moreover, aging represents another problem to be addressed. Life expectancy has increased, mainly in developing countries. It is estimated that by the year 2030, one out of six individuals will be 60 or older [37]. Nowadays, the growth of the elderly population requires the prevention of the age-related cognitive decline, that is due to the impairment of the underlying cell processes in the brain [38,39]. It is well known that healthy habits during the lifespan, such as a balanced diet or the physical activity contribute to reducing the risk of age-related health decline.

Cognitive decline is closely associated with nutrition and lifestyle. Cardiometabolic health can be preserved by consuming bioactive components of food [40], which leads to a decreased risk of cerebrovascular problems including vascular dementia [41] . The knowledge of selective and healthy nutrient consumption is more important in people who are still cognitively healthy, and that could prevent the onset of neurodegenerative diseases. Currently, once neuron damage occurs no pharmacological treatments are effective to reverse or slow the progression of degeneration. Prevention and early protection of the complete brain-body system are currently the only strategy for keeping a healthy condition.

3. Interventions to improve the cognition-nutrition function

3.1 Understanding bias in eating behaviour

People's eating behaviour is conditioned by different factors. Geography and culture are important in determining eating habits and nutrition. As an example, the Mediterranean diet has become popular because of its health benefits. A meta-analysis showed that the Mediterranean diet can reduce the risk of Alzheimer's disease and cognitive decline [2]. As part of the cultural influence, religion is one of the most important determinants of the dietary habits, such as kosher foods that conform to the Jewish dietary regulations of kashrut (dietary law) or Halal foods that are permitted under Islamic law. Moreover, the way food is processed, and the ingredients used are determined by cultural factors intrinsic to different countries or regions and linked to traditional or cultural inheritance. While olive oil is a basic ingredient used in Mediterranean countries, butter and other vegetable oils are common in other countries.
There are other additional factors that could prevent people from having a healthy and balanced diet that should be taken into consideration, such as local availability and the affordability of food.
Nowadays, most of the population is aware of the negative impact of an unhealthy diet. Despite this, an unhealthy eating pattern is often preferred, with high consumption of indulgent foods rich in fats and calories. A busy lifestyle also makes the population prone to the selection of ready-to-eat meals that are not always equilibrated in their nutritional content. The use of flavour enhancers in these kinds of products leads to an even higher increase in their consumption, resulting in an unbalanced diet pattern. Together with this, recent data indicate that food allergies may be more prevalent among adult populations than previously acknowledged, and that they affect people of all races, ethnicities and socioeconomic strata [42]. The avoidance of food allergens directly affects dietary habits and can lead to unhealthy eating behaviours.

The challenge is to use an integrated approach to examine the influence of the different factors (social, cultural, psychological and biological) that contribute to the decision-making process in choosing between healthy and unhealthy eating behaviours.

3.2 Facing the eating behaviour bias

The *"WHO Global Strategy on Diet, Physical Activity and Health"* describes the actions needed to support healthy diets and regular physical activity. The Strategy calls on all stakeholders to act at global, regional, and local levels to improve people's diets and physical activity patterns [36]. Since December 2016, the current legislative framework of the European Parliament and of the Council in Regulation (EU) No 1169/2011 on the provision of food information to consumers makes it mandatory to include nutrition information on foods, which is generally presented in tables. However, there is evidence that this nutritional information is not well understood by the population and does not improve food purchasing and consumption decisions. In this context, additional forms of presentation of nutrition information provided by the European regulations, such as the front-of-pack labelling (FOPL), are crucial. Nutrition labelling models such as Nutri-Score should be developed, supported by extensive scientific evidence to facilitate the use and understanding of the mandatory nutrition information by consumers favouring healthier choices. The aforementioned wearable technologies, which enable continuous measurement, should facilitate the empowerment of the population by providing direct and up-to-date knowledge of the consequences of decisions taken. Gamification strategies should also be investigated to increase the spread of these technologies in the population.

Conversely, regulating advertising and content in general in the media (TV, social media, etc.) is important, particularly those aimed at children. Many advertisements promote the consumption of foods high in fats, sugar and salt that influence consumer's food preferences, leading to unbalanced diets. In this context, it is also crucial to raise consumer awareness of healthy food consumption through these media. The media and social networks also promote physical stereotypes that trigger the onset of eating disorders such as anorexia and bulimia, which have a neurological origin. Moreover, social media broadcast information promoting weight loss and techniques to achieve an ideal weight and shape. This also represents a danger regarding depressive behaviours and suicide, especially among young people. According to WHO, suicide is the 4th cause of death in 15–29-year-olds [37].

Another fundamental pillar to address the bias in the eating behaviour is education. In this sense, school campaigns that promote a healthy diet are essential. In addition, education about healthy habits together with the awareness of the risks associated with a poor diet, should also be expanded to upper educational stages, such as high-schools and universities. In those stages the neurological disorders related with eating behaviour are most prevalent. Another challenge will thus be the creation of educational programs that include content in healthy habits and their derived benefits.

4. Strategies to improve food production

4.1 Sustainable production of food

We need to reanalyse the entire food supply chain to raise quality and welfare standards across the food industry in an environmentally friendly manner, while addressing the major challenges of a growing population, climate change and dwindling natural resources.

Food production is heavily influenced by the environment, and climate change has a huge impact on agriculture. Local producers are constantly making adaptations to changing weather patterns (drought, extreme temperatures, rises in the sea level). In this respect, among the Sustainable Developmental Goals (SDGs), objective SDG13 is focused into the climate action that urges to take action to combat climate change and its impact on food production. Moreover, SDG12 ensures sustainable production patterns [43]. In addition to this problem, large supermarkets and multinationals harm the local producers with more competitive prices. In this regard, councils must support the local farmers by using extensively located banners and advertisements and by creating campaigns to encourage consumption in local businesses. Another aspect of this 'eat local' phenomenon is the renewed interest in grow-your-own food. Urban-based agriculture has gained a lot of importance in developing countries, and these kinds of initiatives should also receive formal institutional support as they can provide direct access to fresh food.

Another challenge within the sustainable production is to avoid the environmental impact generated by food production and waste, such as the environmental persistence of some chemicals and pesticides namely, DDT, polychlorinated biphenyls (PCBs) and polychlorinated dibenzo-p-dioxins (PCDDs)) and the nitrification of water produced by nitrogen fertilizers in agriculture (Increasing the organic production of food and making organic products affordable for consumers are therefore important challenges.

4.2 Safe production of food

As a result of known industrial activities and if no action is taken, food contaminants that have been shown to have neurological effects (mainly heavy metals and various persistent pollutants) are expected to increase. The population at risk of exposure may need an early diagnosis strategy and deeper knowledge of mechanisms of action. There is an urgent need to understand the effect of nanomaterials present in food and the environment (i.e. nanoplastics on gut health and gut-brain communication) in order to assess their safety.

Food packaging is crucial for the safe consumption of foods. The use of chemicals in food packaging should be subject to ongoing risk assessment. Some chemicals could represent a serious health threat as they can bioaccumulate and be potentially carcinogenic and endocrine disrupters. For example, bisphenol A (BPA) is a compound used in combination with other chemicals to produce polycarbonate plastics that will be in contact with food. It is also used to produce epoxydic resins for protective coatings in canned drinks and foods. BPA can migrate from the materials in contact with food to foods and beverages. There is evidence that BPA can be linked to neurodevelopmental disorders that are caused by changes in brain development, such as attention deficit/hyperactivity disorder, intellectual and learning disabilities, impairments in vision and hearing, and autism spectrum disorder (ASD) [44]. In 2021 the European Food Safety Authority (EFSA) published a scientific opinion that proposed to reduce the tolerable daily intake (TDI) of this compound, considering that the exposure of the population in all age groups to BPA is higher than the temporary TDI.

The safest way to consume food is to reduce the use of food packaging such as plastic packaging, cartons and film. This is the only way to minimise the possibility of harmful chemicals remaining in the environment and entering the food chain. The challenge here will be to change habits in the food supply chain. Alternatively, the challenge, of no lesser magnitude, will be to anticipate potential problems and design packaging that is safe for health and is environmentally friendly.

Neurochallenges for 2040

- Development of sensors and wearable technology for the monitoring of cognition and dietary biomarkers under natural (non-laboratory) conditions.
- Establish an EU-wide population database to investigate how nutritional habits correlate with cognitive habits and health outcomes taking advantage of the latest advances in Artificial Intelligence.
- Create personalized nutritional strategies by using analytical tools and wearable technology.
- Understand the gut-brain axis: How does gut function contribute to human cognition and how can the function be manipulated to promote neurological beneficial effects.
- Explore the molecular mechanisms exerted by bioactive compounds that influence cognition and mental health and how they affect the incidence of prevalent mental diseases such as depression and Alzheimer’s disease.
- Investigate how the interactions between nutrition and cognition change at different stages of life: from childhood to the elderly.
- Improve the comprehensibility of nutrition information for consumers by developing new, science-based models for nutrition labelling.
- Empower population by providing personalize and real-time information on the nutritional/health consequences of their eating behaviour (gamification).
- Tackle different social and cultural biases in eating behaviour by controlling media advertising content and by creating educational programmes that promote a healthy lifestyle and its benefits.
- Promote a more sustainable production of food by supporting local and organic food production.
- Improve environmentally friendly cultural practices in primary production.
- Promote a safer production of food.
- Increase food security by reducing the food waste and its environmental impact.

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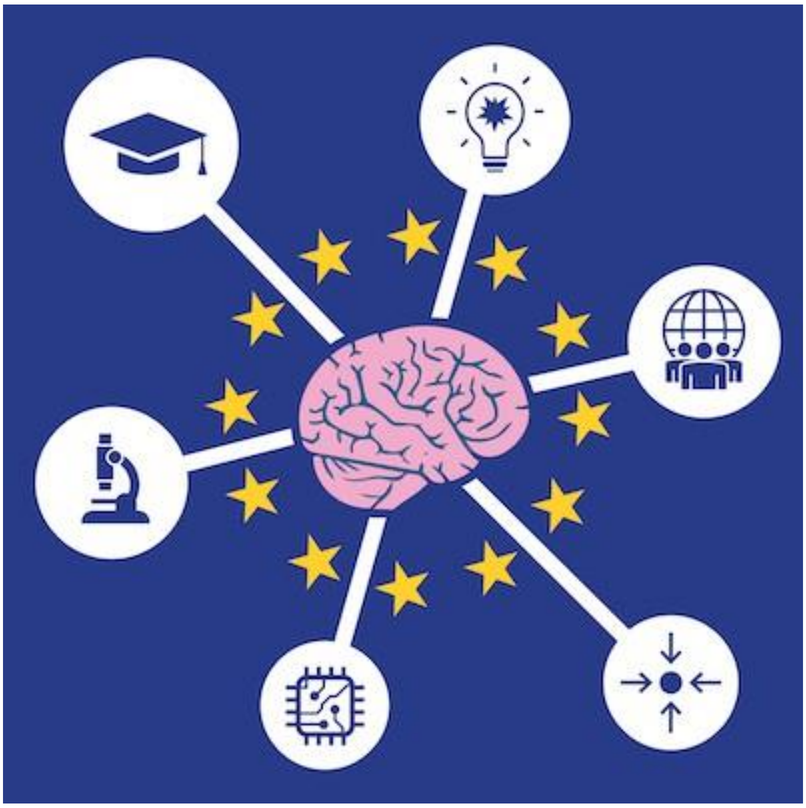

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Future Neurochallenges in Biological & Artificial Intelligence

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Introduction

Although there is not a generally accepted definition of artificial intelligence (AI)[1], AI has been proposed as the most promising strategy to enhance and expand human intelligence, in the same way that mechanization enhances and complements human physical strength. In addition to classical data processing techniques based on predefined algorithms, Deep Learning (DL) aims extracting patterns and learn within a given context, providing a new framework to train computers to perform complex tasks such as delivering accurate diagnosis, and handling vast data bases[2,3].

However, the flexibility and power of biological human intelligence makes it hard to replace in the complex scenarios that characterize the everyday work of healthcare professionals. This reality was acknowledged in the 2019 statement by the World Medical Association, which deemed the term “augmented intelligence” more appropriate to reflect the supporting role of AI in decision making, rather than a substitute, in clinical settings[4] (Statement on Augmented Intelligence in Medical Care Adopted by the 70th WMA General Assembly, 2019). Here, we review the current challenges and future perspectives of AI in healthcare. We focus on the following main neurochallenges:

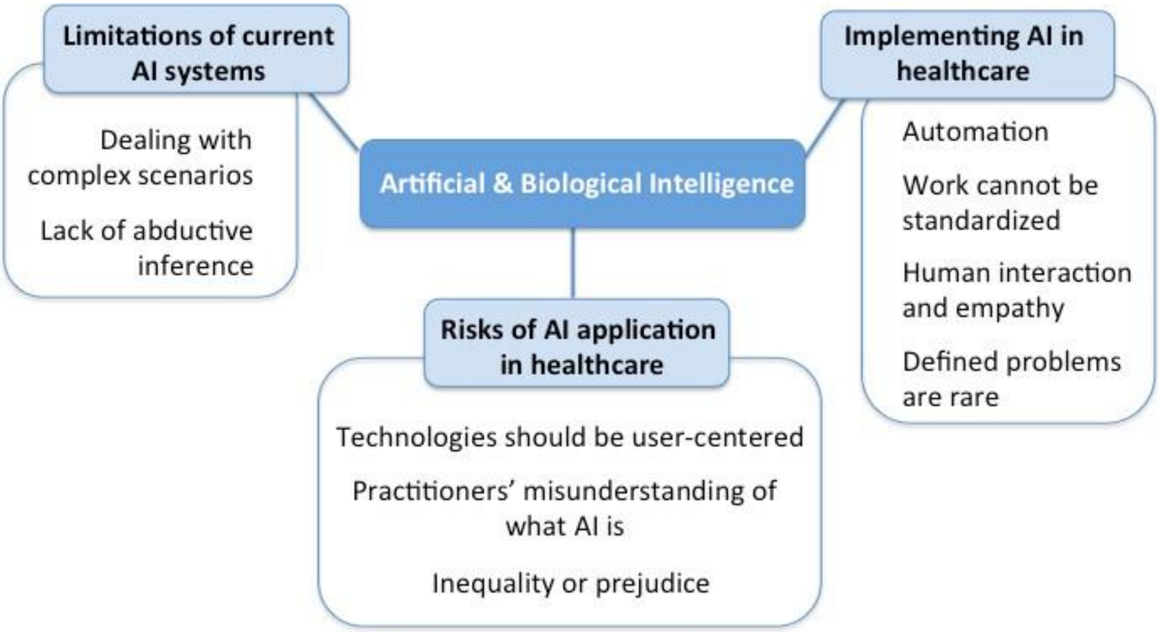

Figure 1 - Conceptual framework of future neurochallenges in Artificial and Biological Intelligence.

Implementing AI in healthcare

Despite centuries of advancement in mechanization, humans still perform difficult and physically taxing work, particularly in healthcare. The reasons precluding the replacement of human physical work mirror those that preclude replacing human intelligence: automation works best for repetitive actions in a predictable environment, which does not describe most healthcare situations[5]. Physical and intellectual work in healthcare is often too varied to be standardized, requires human intuition and empathy with persons in a vulnerable position, and is cheaper and quicker to be performed by a human, with some recent studies estimating that only 30% of the work performed by a nurse can be automated[5].

Furthermore, most of the work in healthcare is borne by nurses, nurse assistants or junior doctors whose salaries may not provide an adequate incentive for automation. At our current technological level, AI might help to decide but a human still needs to perform the action, a process that often occurs simultaneously during time-sensitive work such as emergency care in which adding an additional step involving AI may delay action with no measurable outcome improvement. Medical decisions conducted by senior consultants or specialists may be more cost-effective to replace, but they are also more specific, and may require an individual AI solution for each decision node, making the costs of replacement prohibitive. Machine learning solutions require a defined problem[6] which are rarely occurring in real medical environments in which decisions are usually the results of converging medical factors, social aspects, healthcare constraints, patient preferences, and a general impression of the patient's health which is difficult to put into words. In these situations, it is hard to specify a clear decision-making process, much less replicate it artificially.

Limitations of current AI systems

Inability to deal with complex scenarios. People's decisions are often biased in the direction of what best suits their interests. Even though people are influenced by the evidence they encounter, they are also biased both in choosing which evidence to acquire and in their interpretation of this evidence. In other words, human beings typically act like 'motivated Bayesians', and this inevitably leads to suboptimal decision-making. AI systems, on the other hand, could operate as 'classical Bayesians', seeking out the most informative evidence and processing it in an unbiased way. The current generation of AI systems, however, simply follow rules, "learn" and execute action sequences. This currently limits their utilization in cases of complex and uncertain decision-making, such as in healthcare settings.

Lack of abductive inference. Another challenge has to do with the open-ended nature of human intelligence, in particular the human capacity for abductive inference. Using abductive inference, we can quickly focus on what is relevant and select which hypothesis best explains the relevant evidence, out of a background of effectively infinite possibilities. This is a particularly important strategy when dealing with new and unexpected events, and when having to make decisions that cannot be fully captured by knowledge-based existing rules and regularities. Again, AI systems are typically based on either **deductive** (Good Old Fashioned Artificial Intelligence) or **inductive** (Deep AI) forms of reasoning.

In order to make more complex decisions, future AI systems require an architecture that allows for abductive inference. Here, a classical Bayesian predictive processing architecture coupling sensory information streams (acquired by a single agent, multiple agents, or distributed network of sensors) with action outcomes could provide the necessary closed-loop control solutions. As a Bayesian inference framework, this architecture would allow combining statistical distributions regarding the (possible) states of the world (i.e. internal models, or priors) to update the state of motor controller (posterior) in a context-specific manner. The control system would have to implement Bayesian inference for predictive as well as reactive control. While predictive control offers rapid action planning, its performance deteriorates under uncertainty and in complex (non-stationary) environments. Reactive control, based on continual update of the priors with sensory information, is slow, but ensures contextually relevant motor action selection even in the face of ever-changing sensory information.

Risks of applying AI solutions to healthcare

The incorporation of AI-based devices and wearables have the potential of dominating clinical practice so they must be accepted by most practitioners.
Most importantly, the application of AI in healthcare should always focus on human and cognitive factors. The design of healthcare tools and technologies should be user-centered, always keeping ergonomics and human factors in mind[7]. The application of DL techniques in ergonomics and manufacturing will bring opportunities for improvement of both devices and algorithms that will allow solving increasingly complex problems[8].

Nonetheless, their incorporation into the clinic is expected to have backsides: practitioners' misunderstanding of what AI is and what it can do, overreliance, de-skilling and acceptability have previously been identified[9]. Reliability and validity of training datasets and transparency have been identified as key components to applying AI to healthcare[9,10]. Liability and accountability for harm are also issues when physicians rely on AI to make decision[9]. Significant attention should also be paid to the potential risks of AI replicating or enhancing inequality or prejudice[2], although these tools could also be implemented to remove bias, standardize care or uphold quality.

Benefits of applying AI in healthcare

Despite the aforementioned challenges, AI applications have clear benefits for healthcare. In the same way that mechanization and automation replace and improve human work in areas that are dangerous, boring, repetitive, error-prone or require precision, AI may assist humans to increase the amount and quality of healthcare work. AI solutions may also remove factors that humans find tedious or irritating, improving workplace environments and reducing burnout. AI may have more success by identifying areas where human intelligence performs poorly, rather than attempting to replicate its strengths. Humans may miss details and can be prone to error and uneven performance, particularly in situations of stress and sleep deprivation: AI and digitalization measures supporting improved and more detailed analysis, standardization, equality, and quality of care are obvious first choices. In this context, AI solutions have already demonstrated value diagnosing different types of cancer[2, 3,11] or analyzing radiological images[12]. These are situations where all the relevant information is available in one image or can be complemented with a defined amount of information to be provided to the AI decision tool. A radiological image is a situation where there is a lot of information present, but it is defined to one place and finite: in these situations, AI may well surpass human intelligence. In contrast, situations in which information is undefined, messy, disperse and unarticulated may still present unsolvable scenarios for AI.

Neurochallenges for 2040

In summary, although full artificial intelligence solutions may not be feasible in the short-term, augmented intelligence is already being implemented in healthcare and can substantially improve quality of care. The race to discover and implement AI solutions in healthcare is dominated by North America and Britain: in one recent review Europe was severely underrepresented[9]. However, some neurochallenges remain:

1. Countries and governments need to decide their future aims in medical AI development and heavily invest if they are to have a leading position in this field. There is a cyclical tendency to hype new solutions to old problems. Minimal clinically relevant improvements need to be met for an AI solution to merit implementation[6]. The current hype of digitalization and AI posits that it is the solution to chronic and structural healthcare system problems, such as staffing and funding shortages, or increasing demographic pressure. Although technological solutions may increase efficiency, they are unlikely to solve these issues, particularly since increasing quality quickly becomes the standard of care and the baseline requirement for future care provision.

2. Currently, AI can only be implemented for defined problems and there are risks in relying on future technological advancement to solve healthcare systems' impending catastrophes.

3. Safety analysis are common in some branches of industry (rail, aviation) but rarely if ever implemented in healthcare[13,14]. In these industries, human error is expected and the systems default is to "fail soft" to avoid safety risks. New technologies should not preclude using existing tools such as these to improve safety and quality in healthcare. Implementation of AI solutions should not lead to de-skilling or overreliance, rather, they should increase safety and protect against error by providing a double check to clinician decisions[10,13].

Current and future implementations of AI in healthcare

Some solutions relying on digitalization and AI have already been implemented. For instance, prescription warnings (interactions, allergens, potential secondary effects) are currently integrated into medication prescription softwares, reducing errors and the need to memorize lists of medication interactions. Another potential application for AI/digitalization would be to provide "nudges" to encourage good practices: e.g. reminders to review prescription lists, inform patients of a specific secondary effect or prescribe a particular combination.

Smartphones and wearables are generating an explosion of medical data, providing precise knowledge regarding the evolution of a patient or a specific disease. These data allow a patient to interact with intelligent systems to manage the follow-up of his or her disease[15]. These systems have started to be timidly implemented in the clinic, and still rely on close supervision by physicians who integrate the emotional aspect required for providing a holistic approach to healthcare[16]. Assistance in data collection through increasingly less intrusive devices will allow for improved treatment of patients[17].

The ultimate goal of AI in healthcare is epitomized by the use of robots in patient care, particularly the elderly. Currently, people are reluctant to be cared for by robots, however a major focus of robotic research aims to improve both the appearance and the emotional management to generate humanized robots to support, and eventually replace, caregivers[18].

Undoubtedly, AI-powered solutions are bound to transform healthcare, with new opportunities for disease diagnosis and monitoring, clinical workflow augmentation, and hospital optimization. Although the roadmap for a successful implementation of AI-based techniques to improve upon traditional healthcare structures remains unclear, the intensification of different research lines will be crucial to overcome the challenges that currently prevent a comprehensive implementation of AI in clinical settings, some relevant ones are listed below:

Research line 1: Using AI for disease diagnosis and patient monitoring: Explore real-world applications of AI for diagnosis and patient monitoring, promoting developments in software and hardware.

Research line 2: Natural language processing and data analytics: Improve AI to extract value-adding outcomes from medical visits, literature and pathology reports.
Research line 3: Interpretability in machine learning: Improve the predictive power and interpretability of algorithms.

Research line 4: Patient risk stratification and augmenting of clinical workflows: Improve how AI can be applied to health care interventions and patient care.

Research line 5: AI-integrated approach to hospital management and optimization: Investigate a holistic approach to optimizing the different aspects required for patients´ treatment.

Although it may seem that the road ahead to reap the benefits of AI´s implementation in healthcare is long and uncertain, the benefits are worth it. In order to achieve this goal, not only healthcare professionals but the entire society should commit to new organizational architectures, processes, behaviors, and attitudes. Such change can be difficult to implement. It requires patience and flexibility, as well as the ability to adapt to new contexts and ways to receive clinical information and perform procedures. In order to achieve the full potential of AI, developing companies, medical organizations and governments must recognize that humans play an equally important role in the equation.

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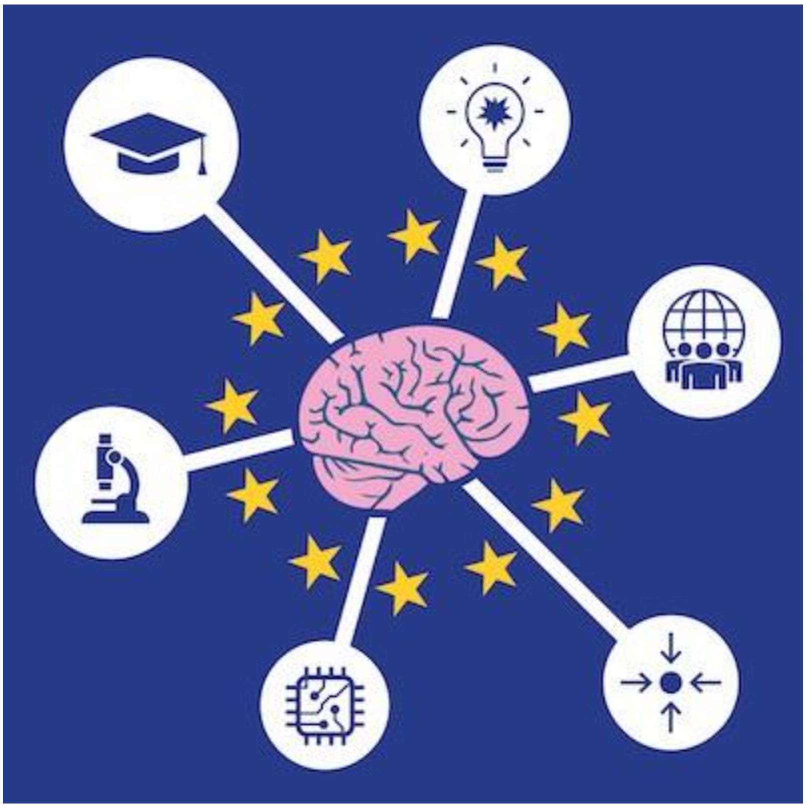

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Future Neurochallenges in Neurotechnology & Big Data

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Introduction

Neurotechnology and big data are two rapidly advancing fields that have the potential to transform our understanding of the brain and its functions. Advancements in neurotechnology have enabled researchers to investigate the function of the brain at unprecedented levels of granularity at the functional, molecular and anatomical levels. This has resulted in the collection of not only more data but also larger datasets – a trend that is expected to continue with the emergence of each new neurotechnology. Yet at the same time, neuroscience has been a hotbed of challenges in reproducibility, where small, underpowered studies, problems in experimental design and analysis, and lack of routine data sharing have led to difficulty in relying on published results [1].

To address these challenges, like many domains in biomedicine, neuroscience has adopted the FAIR Guiding Principles for scientific data management and stewardship in an attempt to make neuroscience results Findable, Accessible, Interoperable, and Reusable to both humans and machines [2]. The FAIR principles were formulated by a collective effort of several international groups based on practical experience in roadblocks encountered when trying to reuse data [2]. Some recommendations are domain independent, while others, particularly those that address interoperability and reusability, specifically delegate to individual scientific communities to define the relevant standards and best practices for their data types and protocols. To fully realize FAIR and to maximize investments in open data, neuroscience and neurotechnology must also embrace best practices, methods and tools for FAIR that support the reproducibility and replicability of scientific results [3].

The adoption of these best practices and tools is in turn critical to accelerating scientific discovery as it can expand collaboration, reduce errors and maximize reuse of data, code and tools [4]. However, brain science as a discipline faces considerable challenges in developing the necessary technical and human infrastructure for FAIR. It is a large, multidisciplinary field that is not served by a single or even a small number of data repositories. Instead, it is characterized by a large number of databases, both within and across international boundaries, specialized for different data types or subdisciplines [5].

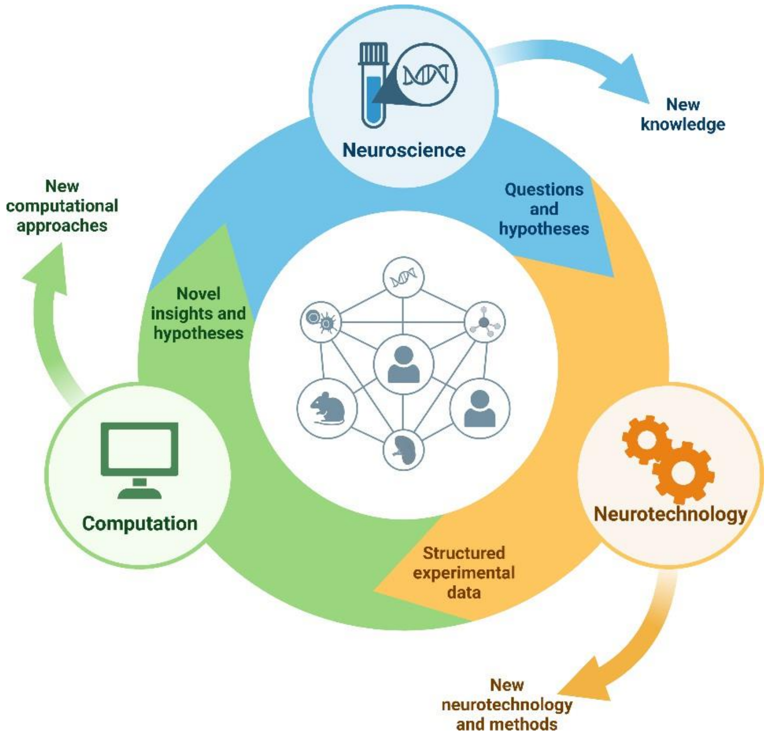

Figure 1. The important role played by neurotechnology in neuroscience .(Figure created with BioRender.com)

With its large number of subdisciplines, techniques, data types, and model systems, the roadmap to FAIR neuroscience (**Table 1**) provides a useful roadmap for identifying the neurochallenges that will impact neurotechnology and big data. History tells us that each new neurotechnology will be associated with an increase in the amount of data collected/generated and the need to integrate this data and make its supporting tools and infrastructure interoperable within the existing ecosystem of tools and infrastructure.

In the case of new data types, efforts will need to be undertaken to develop standards and to establish data quality and reliability metrics. The resulting increase in data volume will also require new data management and storage solutions, as well as new techniques for data analysis and interpretation. Moreover, neurotechnological advancements in the form of personal devices will require new solutions to protect privacy and require changes to current ethical and legal policies.

Table 1. Roadmap to FAIR neuroscience	
1	FAIR requires that the necessary infrastructure in the form of web-accessible repositories are available to neuroscientists for publishing data, code and workflows
2	Neuroscience needs the means to identify, define and support community-relevant standards both for data and metadata. With scientists increasingly acquiring and sharing multi-modal data across temporal and spatial scales, these standards must not work in isolation
3	A large, dispersed domain such as neuroscience benefits from centralized information hubs to make it easier for researchers to find FAIR data, tools and services for FAIR practices
4	Neuroscientists need training in how to share FAIR, including good data management practices in the lab, how to organize their data, how to use standards and find tools that are available to assist them

Neurochallenges in Neurotechnology and Big Data

1. Privacy, ethical and legal concerns

One of the major challenges that neurotechnology and big data researchers face is ensuring the privacy and security of the data they collect. Brain data is highly personal and sensitive, and its collection and use raise important ethical concerns, such as respecting a patient's autonomy *vs* provision of adequate consent, ensuring equity and respecting the individual's privacy. As the amount of data collected and analysed grows, it becomes increasingly difficult to protect individuals' privacy and ensure ethical use of their data. In addition to privacy and ethical concerns, another challenge that neurotechnology and big data researchers face is legal regulations that govern whether and how data can be shared. For example, General Data Protection Regulation (GDPR) in Europe and the Health Insurance Portability and Accountability Act and the Common Rule in the United States, regulate privacy and security in research and complicate efforts to share data across geographical boundaries. This is a must if we are to harness the full potential of neurotechnological advancements and big data.

As neurotechnology and big data continue to advance, it is important to recognize that the collection and analysis of brain data can reveal sensitive information about an individual, including their mental health, cognitive abilities and personal characteristics. This raises important ethical concerns related to data privacy and discrimination. For example, employers or insurers may use brain data to make hiring or coverage decisions, potentially discriminating against individuals based on their neurological traits. To address these concerns, researchers and policymakers must work together to establish ethical guidelines and legal protections to ensure that brain data is used appropriately, and that individuals have control over how their data is collected and used. Moreover, researchers must prioritize transparency and informed consent to build trust with research participants and promote responsible data sharing practices.

2. Integration and interoperability

Neurotechnology and big data research are highly interdisciplinary, with many different tools, platforms and data formats used to collect and analyse data. This can lead to a lack of interoperability between different systems, thus making it difficult to integrate data from multiple sources. Implementation of common standards by systems and data producers facilitates systems interoperability and data integration, but they must be developed to support each data and system type. This entails a rather lengthy process of development, validation and adoption. The standards landscape today is characterized by many competing, overlapping and incomplete standards – making it difficult for systems developers and data producers to select appropriate standards for their use cases. Moreover, the development of standards in neuroscience has often occurred *ad hoc* to serve the needs of the current project, with little regard to long-term sustainability and common adoption. The current state of the standards landscape is only expected to become more problematic as new neurotechnologies are brought online, since each new technology typically results in a new data type that requires standardization and new systems that need to be integrated into the larger landscape of systems.

Integrating data from multiple sources is essential to unlock the full potential of neurotechnology and big data. However, the integration of diverse data types is challenging due to the complexity of the data, the variety of collection methods and formats, and the lack of uniformity across different systems. Achieving interoperability between systems and data formats requires the development of common standards that enable seamless data exchange and integration across different platforms. For instance, the Brain Imaging Data Structure (BIDS) standard has been proposed as a common framework for organizing and sharing neuroimaging data. Other standards, such as the OpenEEG format, have been developed to promote interoperability among electroencephalography (EEG) systems. However, the adoption of common standards in neurotechnology and big data research has been slow, and the development of new standards can be time-consuming and resource-intensive. As such, it is crucial that stakeholders work collaboratively to establish common standards that are widely adopted and facilitate the integration of diverse data sources.

3. Data quality and reliability

Another challenge in neurotechnology and big data is ensuring the quality and reliability of the data collected. High-quality data are preconditions for analysing and using big data; however, judging data quality and reliability in big data is challenging due to the characteristics of big data: volume, velocity, variety and value [5]. Data quality and reliability are critical for the success of any neurotechnology and big data project. The use of different neuroimaging and electrophysiological modalities produces heterogeneous data, each with its own signal characteristics, acquisition protocols and preprocessing pipelines. Ensuring that data is of high quality and is reliable is particularly challenging in the context of big data due to the sheer volume and variety of data types that need to be integrated. Additionally, data quality can be affected by a range of factors, such as measurement errors, artefacts and poor data preprocessing. Quality control procedures should therefore be established to identify and remove poor-quality data. It is also essential to establish quality standards for neuroimaging and electrophysiological data, which would facilitate cross-study comparisons and meta-analyses. Finally, the development of automated methods for data quality assessment and data preprocessing pipelines would enhance the reliability of the data and reduce the risk of errors due to human intervention. Cai and Zhou reported in 2015 (**Table 2**) [6] three challenges for big data in terms of data quality and reliability that will hold true as new neurotechnologies are brought online.

Table 2. Challenges of Big Data	
1	The diversity of data sources brings abundant data types, complex data structures and increasing difficulty of data integration
2	Data volume is tremendous, and it is difficult to judge data quality within a reasonable amount of time
3	No unified and approved data quality standards have been formed

4. Data management and storage

The amount of data generated by neurotechnology and big data research is increasing exponentially, thus creating a challenge for traditional data management and storage solutions. Managing and storing large amounts of data can be expensive, and traditional data storage systems may not be able to handle the volume and complexity of brain data.

In addition to the challenge of storing large amounts of data, there is also the challenge of managing and maintaining the quality of the data. Proper data management is essential for preserving the integrity of the data, and it includes various aspects such as data documentation, metadata, data sharing policies, data curation and data preservation. Data curation is particularly important in neurotechnology and big data research, as it ensures that the data is properly annotated, curated and validated to improve its usability, reproducibility and long-term preservation. Furthermore, data sharing policies should be established to ensure that the data can be accessed and reused by others, thereby facilitating collaboration and knowledge exchange within the scientific community. A comprehensive data management plan that includes all these aspects is essential for neurotechnology and big data research, to ensure that the data can be managed, shared and reused effectively, which ultimately facilitates scientific progress.

5. Analysis and interpretation

Finally, one of the biggest challenges in neurotechnology and big data is analysing and interpreting the vast amounts of data generated. The complexity and variability of brain data make it difficult to draw meaningful conclusions and to develop accurate predictive models, and developing tools and algorithms to analyse and interpret data is a major area of research. The analysis and interpretation of brain data pose significant challenges in neurotechnology and big data research. In addition, there is a need for standardized protocols and methods for data analysis to ensure the reliability and reproducibility of results. Furthermore, the development of tools and algorithms for brain data analysis is an ongoing area of research that requires collaboration between neuroscientists, computer scientists and statisticians. One promising approach is the use of machine learning algorithms to analyse large and complex datasets, such as deep learning and convolutional neural networks. These methods are becoming increasingly important for the development of personalized medicine and the identification of biomarkers for neurological disorders. However, the interpretation of results from these methods requires domain expertise and a deep understanding of the underlying biology, making interdisciplinary collaborations essential for meaningful progress in this field.

Roadmaps to address the Neurochallenges:

1. Researchers and developers must work to establish strong ethical guidelines and data security protocols.

2. Federated data sharing platforms protect data by bringing analytical tools to the data, rather than permitting downloading the data for analysis, to allow analyses of multiple datasets without violating restrictions on the transfer of personal information mandated by privacy laws.

3. Develop standardized data formats and metadata: Developing standardized data formats and metadata can help facilitate data sharing, collaboration, and data integration across different research groups and institutions.

4. International agreement on types of data that can be shared and how they can be shared.

5. As we continue to generate vast amounts of data, it will become increasingly important to develop tools and platforms that can seamlessly integrate and analyse data from different sources.

6. Implement machine learning and artificial intelligence (AI) algorithms: With the rapid development of machine learning and AI, these technologies can be harnessed to accelerate data analysis, prediction and interpretation. These technologies can help to identify patterns and associations that may not be immediately apparent to human researchers, enabling more comprehensive and accurate data analysis. Caution is advised, as we are only at the beginning of the AI use.

7. To ensure that data is of high quality, researchers and developers must design rigorous data collection and processing protocols and develop tools to assess the reliability and validity of the data.

8. Researchers and developers must work to develop more efficient and cost-effective data storage and management systems.

9. Researchers and developers must continue to develop new techniques and tools for data analysis and interpretation, and work to ensure that these tools are accessible to the wider research community.

10. Foster interdisciplinary collaborations: Neurotechnology and big data research require expertise from various fields such as neuroscience, computer science, statistics and engineering. By using interdisciplinary collaborations, researchers can bring together diverse perspectives and expertise, leading to more comprehensive and innovative approaches to data analysis and interpretation. Interdisciplinary collaborations can also help to address the ethical, legal and social implications of neurotechnology and big data research.

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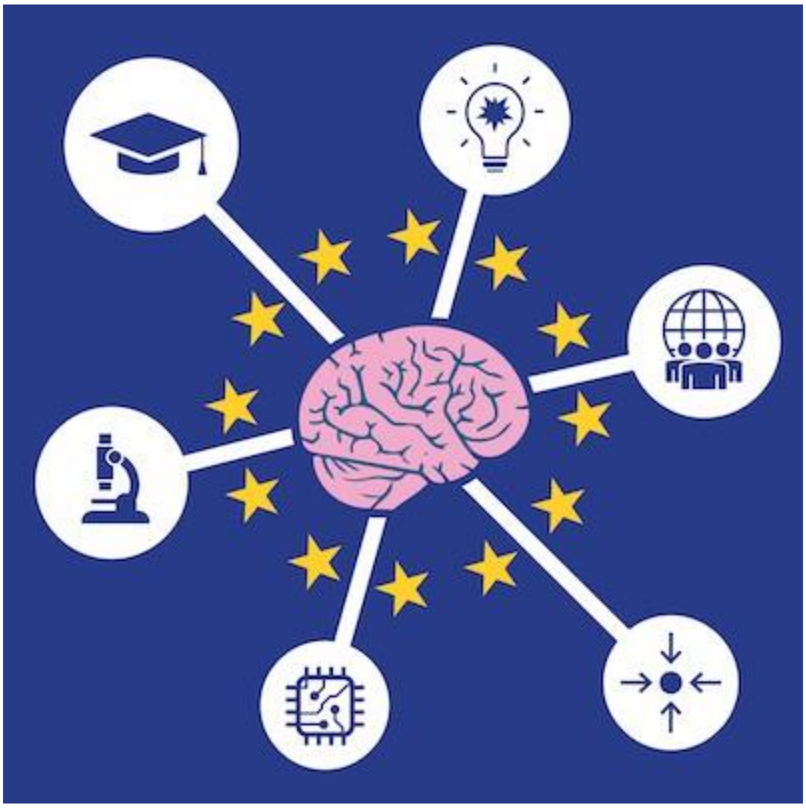

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Future Neurochallenges in Public and Ethics

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Introduction

Recent advances in neuroscience and clinical neurology have shown that there is an urgent need to reflect on the moral aspects and social consequences of these advances, while simulatenously taking into account their future gains, potentials, dangers and threats. In particular, the combination of science with medicine and technology requires a more focused moral control, which has prompted the development of a new field called ***neuroethics***, which is a branch of general bioethics. It is important to ensure that the research in neuroscience and clinical neurology follows the highest ethical standards and carefully considers the clinical application of new knowledge, practices, and technology to human individuals and animals. **In summary, we should apply the well-known four principles of bioethics: non-maleficence, beneficence, autonomy and justice.**

However, monitoring and regulating neuroscience, technology, and clinical practice requires more than simply applying the standard terms and theories of ethics. We should note that the basic principles and concepts of our moral landscape, such as freedom, autonomy, dignity and justice are highly sensitive to our conception about the functioning of the mind and brain. In this sense, neuroscience and neurology are specialised areas of science and medicine, as they have the potential to change the related identity and moral commitments, or even to undermine the basic pillars of our overall morality. These are fundamental challenges that are not evident in other fields of science, technology, and medical practice.

This whitepaper focuses on the future challenges arising within the folowing areas:

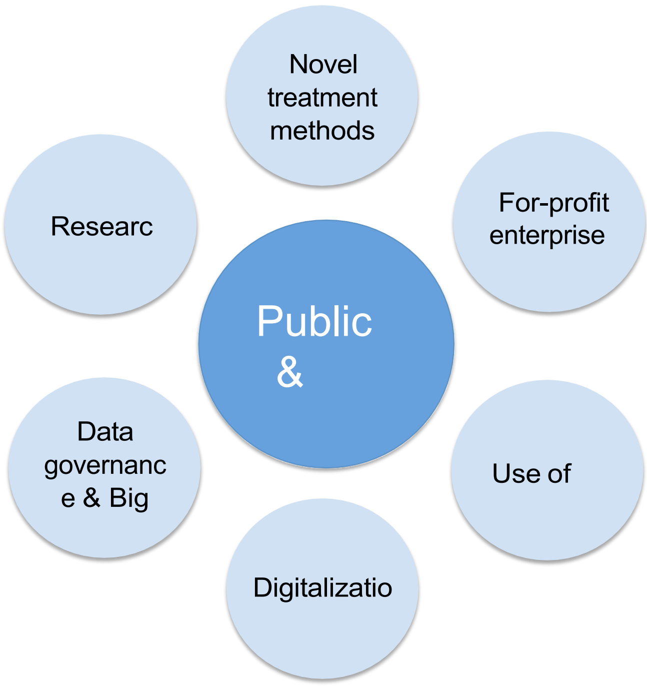

Figure 1 - Main Neurochallenges within Health & Healthcare.

Finally, we propose a roadmap to address at least some of these challenges so that it can be considered in future Neurotech[EU] strategies and programmes.

Novel treatment methods

There are several novel treatment methods now available within the field of health and healthcare for different brain disorders. A significant level of hope, excitement and belief is present within the scientific community, as well as among the clinical practitioners, patients and their families, that these therapies may lead to significant theraputical improvement.

The novel treatment options vary from the development of new drugs, including gene therapy, new neurostimulation methods and cognitive interventions. Novel predictive methods to detect disease at an early stage, including medical imaging, allowing for their earlier treatment are also being developed [1].

Similarly to the development and application of any new treatment, there are several related ethical challenges:

- The first set of ethical challenges are those associated with establishing a new treatment method as the standard one. How can this be performed? Do we test them against already existing treatments and/or placebo? How do we communicate this to the patients and their families? [2]
- The second set of ethical challenges raised are associated with the implementation of novel treatment methods in everyday clinical practice. Questions regarding proof of safety, efficacy and patient selection should be addressed. In other words, when is a novel therapy ready for clinical implementation? Are there any risks and unforeseen side-effects that we should consider, and have these been adequately communicated to healthcare workers, patients and their families? What does the novel treatment do: does it prevent the occurrence of the disease, provide the treatment for the disease itself, or delay the progression of the disease? What are the benefits and costs for the patient, family and the healthcare system? [3]
- The third set of ethical challenges is connected to predictive testing. In order to have better treatment outcomes for a disorder for which we have a novel treatment as well as a specific and sensitive screening test developed, the question is whether the already existing predictive testing should be transferred into population screening and at what cost/benefit ratio? Is there a need for general screening, or do we wait for the onset of the disease? What are the benefits and costs for the patients, their families and the healthcare system? [1]
- Finally, the fourth set of ethical challenges relates to the consequences that a novel treatment can have on patients, their families and society. What are the benefits and burdens of a novel treatment to the patient and the family? Does it provide higher quality to their everyday life and at what financial cost? Does it involve additional organizational burdens within the healthcare system? Does it reduce inequities within the healthcare system? Does it imply additional stigma to patients and their families? [4]

Increasing involvement of for-profit enterprises in the provision of healthcare

Every publicly funded healthcare system faces the same basic moral dilemma: since health resources are scarce compared to their demand, in what way should they be allocated? Such a moral dilemma represents the social problem that shapes the discipline of health economics. As the development of neurotechnology offers increasing 'high-tech' and high-cost goods and services, and as pressure on public funding increases, debates about the fairness of health care are ongoing [5]. This dilemma also applies to the funding of publicly funded research and patient care.

Publicly funded research often results in private Intellectual Property rights, which boosts the research interests of private institutes and other agencies. There are efforts in academia to make the results of publicly funded research open, but this is not yet the most common practice. An important additional initiative in research funding could be to prioritise research that is specifically aimed at developing affordable technologies.

However, the economic pressures on the healthcare system will increase and governments are likely to be forced to rely more extensively on privately financed/organized (for-profit) healthcare. At the same time the worsening health situation represents a market opportunity for private companies, which will be attracted to this area. Governments will probably have to carefully regulate the balance between profit generation and the quality/equality of health care in order to ensure that all those in need have access to high quality health care.

At the patient care level, the dilemma of allocation is obvious. Conflicting responsibilities to promote optimal patient care and financial responsibility can sometimes lead to a state of 'moral injury'. This describes the damage to a person's moral conscience and values that results from the experience of having committed a morally wrong action, which brings a sense of shame and guilt to the individual. Indeed, the moral injury risk may be particularly elevated in a for-profit health care settings with numerous factors other than patient care that influence treatment decisions [6]. The question is, what is the right balance between meeting the medical needs of patients and maintaining fiscal responsibility when making decisions for capital allocation? This question will become very acute as new procedures become very expensive.

Increasing use of AI

The use of robots. As robots are increasingly becoming part of our daily lives, entering our homes and helping us to care for patients, the need to develop control algorithms that adhere to moral norms is an urgent but as yet unmet need. How can we design robots that function as members of our society and make decisions in the service of our common interests? This is fundamental question about ethics and ethical decision-making.

The use of robots raises several questions that reside in the thin border between law and ethics. There is an obvious lack of transparency in using AI tools. The huge differences in the knowledge related to the algorithms that robots are based on are due to the diverse competence of society with respect to IT tools. This imposes an increased moral and legal burden on the IT developers to step up and protect the privacy and human dignity of human end-users. Encrypted channels, however, are not sufficient to guarantee equal access to the world of robots. A real governance should be given to the user that enables widespread control over the intervention robots and other AI systems provide. Wearable devices should be treated as a combination of extensive medical service providers and as a tangible property at the same time. The former aspect places the obligation on the medical service provider or the manufacturer of the device to provide for sufficiently detailed information for the purpose of using the device. It may be a diagnostic tool or part of the treatment; either way, to obtain informed consent in agreement with the existing legal standards, the medical service provider that recommends or prescribes the use of the device must consider the application of the wearable technology as part of the treatment or diagnosis. Conversely, the tangible property aspect provides the user full control and even the power to make adjustments (e.g. withdrawal or change) of the consent given to the medical service provider.

Another ethical challenge concerning the use of robots is the uncertainty around the person who can be held liable for the consequences stemming from an unwanted operation or malfunction of such devices. The manufacturer is an obvious potential person obliged with liability. Product liability regimes place strict – no-fault – liability on the manufacturer of any device for the personal injury or other type of harm that the defective device may cause the user. It is highly questionable whether the mere existence of product liability could function as a beacon in identifying the person liable for the potentially bad decisions robots may make. The manufacturer typically does not tailor the products to the specific needs of one particular patient. The medical service provider is expected to decide whether the AI tool is beneficial for individual cases and to consider the risks associated with the use of the device based on the specific needs of the patient. In several cases a third party is also involved in this complicated relationship: the developer of the software that runs the device. It may be extremely difficult to identify what caused the harm or which part of the process malfunctioned. The concept of multiple individuals being responsible and the application of joint or several liabilities extended to all potential wrongdoers may sound a just solution from the perspective of the user. However, the purpose of the prevention may be completely overlooked if following this simplified approach. There is a trend that robots be recognized as legal persons and to make them individually liable for any damage they might cause; however, this proposition may ultimately jeopardize the reparation/compensation goals of liability in lack of assets owned by these newly constructed legal entities. Already existing and legally recognized persons should be identified as those obliged to recover damages as they (manufacturers, software developers, medical service providers) have the opportunity to make decisions regarding the functioning of robots, either in abstract or in real cases. Strict – no-fault – liability scenarios may be developed for such cases combined with product liability and the liability of medical service providers. Ultimately, any legal authority may only be addressed to these persons and not to the AI tool.

Robots are not always neutral. Their decisions may result in inaccurate or discriminatory outcomes and can be generally biased. Given the current stage of science and technology, it seems impossible to program algorithms that precisely reflect the decision-making process of human beings. As humans may be biased in given circumstances, robots may also seem discriminatory when making decisions simplified by algorithms. The elimination of the risk of bias motives and discrimination from the decision-making process of robots seems to be a technical challenge yet to be solved; liability rules may be the tools to correct such wrong-doings. As discussed above, an almost airtight liability system may ideally oblige players involved in the process to become more diligent (*theory of prevention*) in the stage of planning, or to be there to recover the damages inflicted on the user by the non-neutral decision-making robots.

The use of (non-robotic) AI systems. AI methods are already widely used in neuroscience and medicine. In general, those areas that involve data in the form of images are particularly well suited to the use of AI, as image recognition is one of the areas in which AI has made the greatest progress since the 2010s. The widespread use of MRI for imaging, both in clinical and purely scientific contexts, therefore prompted an alliance with AI, and specifically with the so-called *Deep Neural Networks* (DNN).

DNNs can help evaluate complex images of the brain. Renowned AI researcher Geoffrey Hinton, speaking in a panel at the *Machine Learning and Market for Intelligence Conference* in Toronto in 2016, suggested that radiologists are now like the coyote in a popular cartoon who has gone over the edge of a cliff without realizing he has no ground to stand on. Hinton went on to say that we should stop training radiologists when it is obvious that within 5-10 years AI systems will be able to do a much better job in diagnosing radiological images than can medical specialists. It is undoubtedly true that the field of activity of physicians has already changed due to the use of AI and will probably change even more in the coming years. Hinton's statement can perhaps be interpreted in this sense, as a call to take the changed requirements into account in the training of physicians, to a greater extent than has been the case to date.

To be more specific, the use of AI systems can raise questions of *epistemic transparency* and, related to this, questions of accountability. DNN have the property that their results cannot be traced back to the input data, or only to a very limited extent. In other words, it usually remains incomprehensible why a model has reached a certain result. This makes it difficult for physicians and even more so for patients to decide whether they should follow a diagnosis or a therapy suggestion, for example. The phenomenon described has been discussed for some time under the title '*black box'*. Researchers have now reacted to this and are working on methods to increase the epistemic transparency of such systems. '*Explainable AI*' should help to better understand the results of AI systems.

However, this only partially solves the second problem. This is the question of attributing responsibility in the event of errors and damage. Most agree that AI systems themselves are not moral agents to whom responsibility can be attributed. What is under dispute, however, is whether this creates a responsibility gap. There is an intense debate about this in both the fields of ethics and law. Either way, the distribution of responsibilities in the use of AI in medicine represents a major challenge for the future.

Increasing digitalization

Neurotechnology will help improve cognitive abilities in the years to come, by connecting the brain directly to digital networks. This will involve the systematic collection of neural data and the decoding of the individual's thoughts from their neural activities. However, the undoubted medical benefits of such advances should not overshadow the risks they pose. The potential benefits of neurotechnology enable greater access to and exploitation of neural processes, and its unregulated commercialisation and use represent an enormous threat to the ability of individuals to freely control their own behaviour. Indeed, these technologies have the potential to irreversibly destroy or disrupt the 'human soul' [7].

Data governance without limiting the impact of big data

Issues related to the dual-use of neurotechnology and wearables (legal-ethical challenges). The obvious challenge associated with the dual use of neurotechnology and wearables stems from the social cooling effect. Long-term negative effects of the data-driven innovation seem unavoidable. The interaction of humans with such wearables is driven by a massive exchange and share of data, mostly the personal data of the user. In IoT (*Internet of Things*) environments, the volume of data collected is continuously growing. The speed of the process and the variety of data sources IoT devices rely on results in increasing concerns for data protection and the freedom of information.

Analysis of the voice of the user and of the commands given to the device typically requires the data to be transmitted to remote servers: encryption is not only important locally, at the site of the device, but also at the place/data center to which the device transmits the information. The manufacturers of such wearables, therefore, face a constant duty to protect the user's privacy [8]. This duty does not end when the device is sold. Frequent firmware updates on the device, updates concerning the software running the device and the center of analysis are expected to always follow a strict protocol that respects data protection and freedom of information. Software and/or hardware features that enable the user to gain more control over what is transmitted may seem a good strategy towards a society that respects data protection and information freedom. It is impossible, however, to create a world in which the user has access to all elements of the system, as this could result in overcomplicated devices most users would not be able to operate. The lack of a uniform system of global data protection laws makes it extremely important for the manufacturers and other service providers to adopt and publish data privacy regulations they strictly follow, and that can be controlled by both governmental and non-governmental organizations. Self-governance (e.g. through associations or unions of manufacturers) is of outmost importance in this context, where guidelines and model laws could accelerate the process.

Impact of neurotechnology on personal privacy and autonomy. The brain is the most complex part of the human body, and it is intimately connected with our personality – our thoughts and feelings, our memories and desires. Interventions in the brain – whether for therapeutic or purely scientific purposes – are therefore associated with considerable reservations and potential risks. In the case of invasive interventions, the expected medical benefit must be rated sufficient enough to justify the risk of injury and potential long-term damage. This applies, of course, to all types of invasive therapies. However, interventions in the brain require special justification, since, among other things, they may result in changes in personality.

There are several non-invasive examination methods that are commonly used in medicine as well as in neuroscience. These include magnetic resonance imaging (MRI), positron emission tomography (PET), electroencephalography (EEG) and magnetoencephalography (MEG).

Within MRI, a technique called functional MRI (fMRI) allows deep insight into the mechanisms of the brain. Through fMRI images it is possible to visualize changes in blood flow in brain areas that are related to neuronal activity. The different magnetic properties of oxygenated and deoxygenated blood are visualized using fMRI (with BOLD contrast). Furthermore, experimental tasks can be performed by subjects during the imaging, so that the specific mechanisms of the brain can be investigated while using specific cognitive functions.

Additionally, there are also invasive as well as non-invasive methods to manipulate the brain, including deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS). Targeted impulses from outside or inside the brain are used with these techniques to treat neurological disorders.

Because of the close connection between brain and personality, observational as well as stimulating procedures targeting the brain may threaten the autonomy and privacy of persons. 'Looking into the brain' is in some ways more intimate than looking into other parts of the body. A key ethical challenge is therefore to implement the use of neurotechnologies in such a way that the autonomy and privacy of persons is always respected. This begins with ensuring that such technologies are only used when patients or subjects have given their informed consent. Again, of course, this applies to all medical and scientific procedures. However, in the field of neuroscience particular care must be taken to ensure that potential consequences are emphatically clear to those affected. In addition, collected data must be protected against misuse. In the research context, this amounts to, among other things, careful anonymization and clear regulations regarding data transfer.

The ethical challenges should not be exaggerated. A common concern is that researchers will – soon or sometime in the future – be able to read people's minds and manipulate their behaviors. However, for this to happen extensive data collection as well as the training of sophisticated AI models for each individual will be required. Nonetheless, there are narrow limits to mind reading, which will not change in the future. It will not be possible to read people's innermost thoughts and remotely control their behavior with a mysterious machine, even in the future. An important challenge is also therefore to educate people about the possibilities and limitations of neuroscience, and to dispel unfounded fears. Nevertheless, autonomy and privacy are core values. Neuroscientists must be aware of these and should always act accordingly.

Equitable access to neurotechnology. As was previously indicated, ethical concerns about neurotechnological advancement have been considered for quite some time. Even though the rights of equity, freedom and data protection are already protected by the majority of national and international legal systems [9], the current status of human rights might not be adequate to address these new concerns. It is therefore essential to debate the necessity of establishing a brand new class of human rights. Marcello Ienca and Roberto Andorno proposed four new human rights in 2017: "the right to cognitive liberty, the right to mental privacy, the right to mental integrity, and the right to psychological continuity" [10].

The widespread use of neurotechnology applications will provide many possibilities, for example the access and regulation of brain activity, potentially leading to a range of benefits [10]. The freedom of individuals to employ developing neuroethologies means that people will be able not only to use neurotechnology for therapeutic reasons but also to aid them in lifestyle habits or to modify their mental states using neurotools. This notion of equal or extensive access to neuroethologies raises significant issues.

The need to adopt the right to access neurotechnologies may affect societal structure. Due to their expected expensive price, only a minority of society would be able to utilize neurotechnologies, leading to widening of the social gap. This may result in issues related to the loss of diversity [11]. In addition, governments may face a new financial burden as a result of having to pay for the implementation of all developed innovative neurotechnologies using public funds under this new right.

Towards that direction, Yuste, Goering and their team proposed in 2017 four ethical priorities that should be emphasized: *privacy and consent, identity, augmentation* and *bias* [12]. Based on this, the *NeuroRight* initiative developed later in 2021 five specific neurorights: *the right to personal identity, the right to free will, the right to mental privacy, the right to equal access to mental augmentation* and *the right to protection against algorithmic bias* [9,13]. The neuroright to 'free will' ensures that any person should be completely in charge of their own decisions, and free from unknowable interference from external neurotechnologies. Other concerns related to the new neurotechnologies are addressed by the right of equal access to mental augmentation of access to mental enhancement. The *NeuroRight* initiative proposed the ensurance of equal access in society to neurotechnological tools without discrimination. In order to prevent technology from impairing the sense of 'self' of the individual, the boundaries of the personal identity rights need to be established. The initiative also proposed to initiate safety actions against algorithm bias. Algorithms can be very helpful, but they also have the potential to be programmed to discriminate particular groups. The neuroright to mental privacy means that all data gained from monitoring brain activities should be kept private [13].

Borbón *et al*. recently published an article suggesting that equitable access to neurotechnology should be used solely for therapeutic purposes [11]. The *Strategic Action Plan Human Rights and Technologies in Biomedicine* (2020-2025), adopted in 2019 by the Committee on Bioethics (DH-BIO), builds on the objectives of the Council of Europe Convention on Human Rights and Biomedicine (Oviedo Convention) to integrate human rights in the technological development of biomedicine. This Strategic Plan focuses on the use and regulation of such devices in healthcare and sets out recommendations for equal access to technology in health by 2025 [14].

With the rapid development of neurotechnology and in response to the potential dangers arising from the use of neurotechnologies, international treaties should protect the proposed neurorights [12]. It is urged that these neurorights be made operational immediately, with instructions for their proper implementation in accordance with international treaties [12]. Medical use must be approved and authorised by certain procedures. Individuals must be assured of the full protection of their neurorights. Neurotools should warn users of abuses to their privacy and mental integrity.

Although it is still a long and difficult route for neurotehnonlogy to be accessible to all individuals, companies and insurance providers should start working to guarantee widespread access to cutting-edge enhancement technologies. This proposal is designed to keep equity and access issues in the heart of the development progress [15]. Advisory Groups should facilitate an open dialogue between representatives of all groups in society to determine how these objectives can be translated into policies, including specific laws and regulations.

Research

The brain is unlike any other organ in the human body, with its structures being interconnected and responsible for several tasks. It is also a place for mental activities and what we call *mind*. Any intervention in the brain can potentially have multiple consequences.

As in other areas of research, the same ethical challenges are raised by research in neurosciences: animal protection, preventing harmful effects to research participants, protection of vulnerable research participants, quality and implementation of adequate informed consent procedures, and fairness and equity of access to the benefits of the research [16].

Animal research. However, even those issues raise additional ethical challenges. When it comes to animal research it is often difficult to translate research findings in animal models to humans, especially for disorders linked to complex human behavioral patterns. So the questions raised here are: How can we decide when to test basic science findings in humans? How do we know which animal models are relevant for studies in humans? [17]

Human research. Inadequate animal models for specific brain disorders often prompt us to focus more on research in humans (healthy volunteers and patients). Here the protection against harm to research participants is crucial. Moreover, some of the patients involved in brain research may have cognitive impairments that need to be studied. Here additional protection of vulnerable individuals needs to be in place. The following questions need to be asked: Is it necessary to involve these vulnerable individuals as research participants or can we include other research participants who are less vulnerable? How much harm to the research participants can our research methodology cause and can it be avoided? [18] A further dilemma is whether the use of patient subgroups with the mpdst advanced disease states (and thus less favourable prognoses) are the optimal individuals fofr tetsing of new therapies.

Ensuring adequate informed consent procedures is essential but in brain research using participants with cognitive impairment it is important to assess the capacity for consent not only at the beginning of the research but throughout the entire research period, meaning that the process should be repeated at several points in time to have adequate informed consent procedures in place [18].

Sharing benefits from research with the research participants and the community as well as providing everyone with access and participation in research is important without creating stigma and discrimination in the society. Therefore, when communicating research findings, scientists must be aware of possible societal implications [17,19].

Moreover, there are other ethical challenges raised by brain research. Some neuroscience research results may provide therapeutic benefits but may also be used for non-therapeutic purposes (human enhancement, economics, military purposes). The roles and obligations of scientists do not end with conducting their research and communicating it to their peers. They must fully comprehend the full consequences of their research and prevent its misuse [19]. In addition, if we consider that scientists transplant neural cells from fetuses into patients in order to treat diseases such as Parkinson's disease, we face another series of ethical issues. It is controversial whether one should implant foreign tissue into human brain or eventually destroy a fetus for therapeutic purposes, not to mention the problems concerning identity [20].

The most ethically important questions - concerning for example the topics of enhancement, cell transplants, informed consent of people with cognitive impairment, or new and risky interventions - can be very challenging to address. Scientists and other neurotech researchers, however, are not the only ones that are responsible for ensuring that no one abuses this revolutionary technology. Beyond the researchers' responsibilities we have to mention the legislator's responsability as well. Governments should set up the legal frameworks of research and application of neurotechnologies. With some governmental activity we could solve many problems, from winding up legal uncertainty to ensuring the ethical use of neurotechnologies, strengthening public trust in neurotech researchers' work and making reckless researchers accountable. This regulation should involve experts from the field of neurology, ethics and law, and a permanent commission should review it from time-to-time to keep pace with the changes in science and technology.

Conclusion

The moral aspects of brain research and medicine require a continuous public discourse among scientists, medical professionals, ethicists, philosophers, theologians and more generally, the citizens of our societies. It is important to consider the opinions, hopes and worries of every party involved and a diverse group of stakeholders. In addition to an expert discussion on the ethical questions in neuroscience and clinical neurology, we should create public forums to invite people to participate in these debates. Neuroscience is not just another field among the sciences, but it is deeply rooted in the fundamental questions of our humanity, the values and the identity of the human person.

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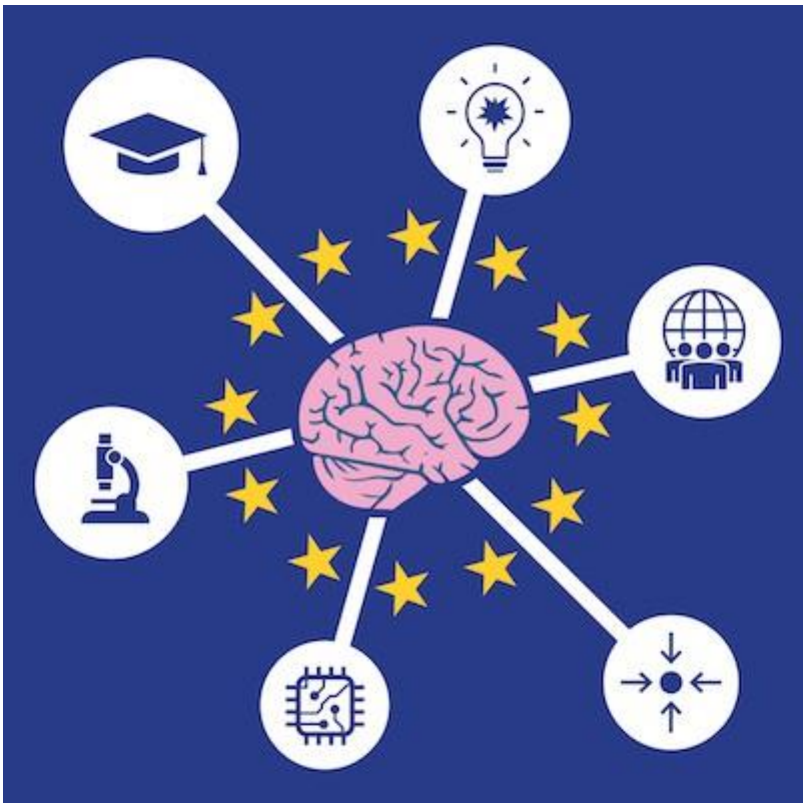

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Future Neurochallenges in Economy and Ecology

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Introduction

Driven by industrial and digital revolutions, humanity has seen a tremendous positive change since the eighteenth century. With eight-fold population growth and a proportional decrease in extreme poverty across all continents, we are now at the peak of human prosperity, notwithstanding an ongoing pandemic [1,2].

Despite the marked decrease in shares of populations impacted by critical livelihood troubles, the crude population impacted by poverty remains roughly the same as two centuries ago, albeit with encouraging trends in recent decades [3-6]. Societies are also as polarized as ever, with great differences in how wealth is distributed across population groups. While growing inequality could be blamed on globalization and technological innovation, the future is likely to be influenced by converging factors (i.e., sharp growth coupled with increasing inequality). Based on the work of Jason Hickel and other scholars, the consensus is that current economic growth trends are not sustainable within planetary boundaries. The continuous pursuit of economic growth, as measured by Gross Domestic Product (GDP), has been linked to the depletion of natural resources, climate change, and environmental degradation. These trends are threatening the long-term sustainability of our planet and the well-being of future generations. While economic growth has brought improvements in health and well-being to many people, it has also contributed to widening income and wealth inequality, social and political instability, and a range of environmental crises. To achieve a sustainable future, there is a growing need for rethinking our economic system and adopting more holistic approaches that prioritize human and ecological well-being over endless economic growth. [7]. Based on within-country inequality forecasts since 1980, the top 1% of revenue share may rise from nearly 20% to more than 24% in 2050, while the bottom 50% share could decrease from 10% to less than 9% [8]. Income inequality has striking implications for the well being of populations. As coined by Michael Marmot, the *social gradient in health* implies that people who are less advantaged in terms of socio-economic position have worse health (and shorter lives) than those who are more advantaged [9]. Nevertheless, the reality of inequality trends across countries shows that local political context plays a crucial role in shaping the phenomenon, suggesting an upside there may be ways to curve this unwanted side to economic growth [10].

Due to heavy use of fossil fuels, greenhouse gases and other pollutants have been increasingly dispersed in the atmosphere, leading to the growing concern about climate warming. Finally, in the 1990s, a consensus was formed due to the improved fidelity of computer models and observational work: greenhouse gases are causing remarkable changes to our physical environment, impacting nature, wildlife, and humans alike [11]. In 2015, United Nations Member States adopted the *2030 Agenda for Sustainable Development*, committing to joint efforts worldwide to tackle a wide area of societal issues, ranging from climate change to poverty, inequality and access to healthcare. The initiative is built around seventeen Sustainable Development Goals (SDGs). In a nutshell, these are a call to action for all countries, regardless of the phase of economic development. They recognize that ending poverty and other deprivations must be developed together with strategies that improve health and education, reduce inequality, and spur economic growth – all while tackling climate change and biodiversity loss. The United Nations offer substantive support and capacity-building for the SDGs and their related thematic issues, including water, energy, climate, oceans, urbanization, transport, science and technology [12]. Nevertheless, to transform SDGs into results, widespread and continuous buy-in is required by all involved stakeholders so that countries can stand a chance to implement their ambitious global goals.

This whitepaper glances into the future, imagining health-related economic and ecological challenges that society will likely face by 2040, aiming to highlight what should be done to improve the resilience of our health systems. Our approach is focused on ***neurochallenges*** or difficulties that can be met by *neuroscientific* and *neurotechnological* knowledge and solutions in the present and near future.

In a growingly digitized economy, further exploring neurochallenges related to brain skills such as self-control, emotional intelligence, creativity, compassion, altruism, systems thinking and cognitive flexibility is critical. Brain skills are cornerstones of *resilience and adaptability*. These two traits are now more critical than ever for individuals and populations, as healthcare systems face unprecedented financial, logistical, and innovation-related pressures [13]. Some countries have been more resilient to turbulence caused by the emergence of the novel coronavirus (SARS-CoV-2), while others have been profoundly impacted beyond the direct medical cost of COVID-19. Nowadays, understanding the determinants of system-level preparedness is of great interest among researchers and policymakers. Nevertheless, specific guidance on what resilience entails and how to measure or improve it is missing or insufficiently integrated into the academic policy [14,15].

The challenge of promoting brain skills is also intrinsically linked to health. In conjunction with the massive disease burden, compromised brain health leads to an increased risk of additional afflictions such as depression, anxiety, substance misuse, dementia, and neurodevelopmental and neurocognitive disorders, boasting devastating consequences for individuals and their families [16]. Around the mid-twentieth century, the World Health Organization defined health as *a state of complete physical, mental, and social wellbeing and not merely the absence of disease or infirmity* [17]. Since the brain is the agent of all our actions and the mediator of all our experiences, brain health is essential for overall health. Nevertheless, physicians, public health professionals, researchers, and politicians seldom work together to safeguard brain health at the population level. In 2021, Vladimir Hachinski and colleagues expanded the definition of brain health in adults as a state of complete physical, mental, and social wellbeing *through the continuous development and exercise of the brain*. This integrative vision reinforces the path presented by Martin Prince back in 2007 (i.e. "*no health without mental health")*, laying out a forward-looking framework for system-wide efforts to improve brain-related population-level health outcomes [18,19]. In recent years, the One Health concept has gained prominence in public health discourse as a holistic approach to address health issues. One Health recognizes the interconnectedness of human, animal, and environmental health and emphasizes the need for collaboration across sectors to address health challenges comprehensively. This approach acknowledges that human health is intimately linked to the health of animals and the environment. One Health offers an added value to the traditional health approach by recognizing that the health of humans, animals, and ecosystems is inextricably linked. By promoting the integration of public health, animal health, and environmental health, the One Health approach aims to improve health outcomes for all, including reducing the risk of zoonotic diseases and environmental hazards. It encourages cross-disciplinary collaboration, a critical step towards achieving more sustainable and equitable health outcomes.

Another essential concept that is linked to present and future neurochallenges in Economy and Ecology is *Planetary Health* - an interdisciplinary field that explores the intricate relationship between human health and the environment. The concept recognizes the impact of human activities on the planet's natural systems and the resulting consequences on human health and well-being. Environmental degradation, such as climate change, land degradation, biodiversity loss, and pollution, poses significant challenges to global public health. As with the health of human beings, Planetary Health involves a collaborative effort across disciplines and nations to address complex environmental challenges and promote sustainable development. Experts from fields such as ecology, public health, environmental science, and social science work together to develop solutions that are equitable, effective, and promote health. The field emphasizes the interconnectedness of human and environmental health and recognizes that human health is inextricably linked to the health of the planet. Addressing environmental problems and promoting healthy ecosystems is essential for the well-being of present and future generations.

The approach outlined in this whitepaper is envisioned to help to tailor Neurotech[EU] (The European University of Brain and Technology) educational and research programs and aid in developing an innovative action plan to maximize the benefits of the novel technologies and interventions for the European economy and society at large [20].

Today's challenges in Economy and Ecology

Health systems are challenged to keep up with demand while maintaining standards and incorporating innovation. There is a constant need to invest in health systems to meet Sustainable Development Goals [21]. This first section addresses the factors already impacting population health.

Rising costs of healthcare innovation

The paradigm of *health care cost containment* has come to an end. Instead, rising health care costs and medical innovation are considered the driver of health care costs, both now and in the future. The core issue of health innovation is that it fails to enhance net productivity - the relative output generated per unit resource consumed. The COVID-19 pandemic has confirmed this hypothesis [22-24].

Impact of changing age mix in the population (aging) on health budgets
This section will expand on the hypothesis that increasing the population's average age will increase the incidence of neurodegenerative diseases and pathologic cognitive decline, with negative consequences for individuals, their families and society at large. In addition, the increasing proportion of older people within the population of many countries (population age pyramid) exacerbates the challenge of aging population-related disorders and results in additional healthcare challenges [25].

The increasing burden of non-communicable diseases
Resource allocation mechanisms across many countries do not follow the burden of disease. Resource allocation is frequently based on precise, legacy-based approaches. Health Technology Assessment mechanisms are either unprepared to handle complex decisions at scale while accommodating disease-specific nuances or being avoided [26-28]. Besides having a substantial economic impact on society, climate change will also directly impact human health. Whereas brain health is perhaps not the foremost concern here compared to cardiovascular and respiratory problems, changing climatic conditions could increase pathogens that may impact the nervous system [29].

The threat of communicable diseases – lessons from COVID-19
Society will likely also face entirely novel health hazards and pathologies. A current example is the COVID-19 pandemic caused by a novel pathogen and exacerbated by an associated increase of indirect contributors to the disease burden [30].

The threat of communicable diseases is not only limited to novel pathogens but also stems from the interactions between humans and animals, which can increase the risk of zoonotic diseases spreading to humans. The COVID-19 pandemic, for instance, is believed to have originated from the animal-human interface. Therefore, it is crucial to consider the impact of human activities on the natural environment, including the destruction of habitats and the exploitation of wildlife, which can lead to the emergence and spread of zoonotic diseases.

Further scientific and technological advances are a central requirement to deal with novel health hazards efficiently and in an integrated manner throughout all relevant determinants [32]. Likewise, regulatory frameworks must be flexible enough to respond to novel conditions quickly. The ongoing COVID19 pandemic and the speedy development, approval and production of vaccines based on mRNA technology can serve as examples [32].

Lack of financial protection and access to healthcare
About 930 million people (12.7% of the world's population) incurred catastrophic health spending as they dedicated at least 10% of their household budgets to pay for healthcare out of their own pockets. About 90 million people (1.2% of the world population) are still being pushed into "extreme poverty" (living on $1.90 or less a day [1]) because they paid for health care out-of-pocket. Currently, at least half of the people in the world do not receive the health services they need. About 100 million people are pushed into extreme poverty each year because of out-of-pocket spending on health [33].

There are different ways of financing health systems to ensure that a population is financially protected. However, what is clear is that health systems need to predominantly rely on public revenue sources: mandatory, pre-paid, and pooled, rather than voluntary pre-payment mechanisms. Furthermore, entitlement and membership to a health coverage scheme are not guaranteed financial protection, as broader changes in the health system are required. Efforts are needed to align with SDG target 3.8, which focuses on achieving universal health coverage, including financial risk protection, access to quality essential healthcare services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all [34].

Overemphasis on curative *vs.* preventive care or personalized medicine
Due to a race to cure disease, science has rarely focused on identifying behavioral and environmental determinants of brain disorders and their impact and magnitude on specific afflictions. As a result, researchers and policymakers are currently operating with immature concepts based on scarce evidence regarding these determinants [35,36].

Limited access to data hinders the evaluation of health programs

Even in developed countries, access to high-quality data is problematic. The availability of robust data in weaker health systems is deficient. Population-level outcome assessment is limited without registries providing longitudinal effectiveness data [37].

Academia and governments must work together to produce synthesis, aggregation, appraisal and integration of clinical outcomes of patients (response to approved therapies) with associated financial costs in order to produce informed priorities for funding future research to address these identified unmet needs.

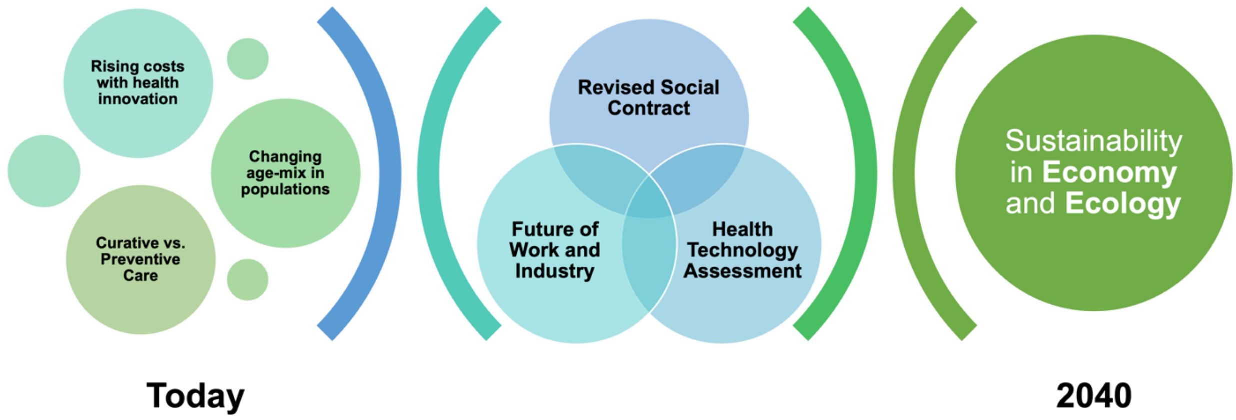

Figure 1 – Neurochallenges in Economy and Ecology from today to 2040.

Ecological determinants of health. Human health and diseases are determined by many complex factors. Health threats from the human-animal-ecosystems interface (HAEI) and zoonotic diseases (zoonoses) impose a continuously increasing risk to public health, with emerging pathogens being transmitted through contact with animals, food, water and contaminated environments. Food and environment is always a complex issue in human health, with many factors interacting and relating to each other. This is well illustrated by air pollutions, water pollutions, misuse of antibiotics and growth hormones, over-fishing, abuse of chemical usages, food fraud and overlook of food animals and poultry welfares, as well as other determinants of environmental contaminants, climate changes and food-producing systems.

Climate change, as a critical ecological determinant of health, demands greater attention in the context of Economy and Ecology. The direct and indirect impacts of climate change on human health are multifaceted and far-reaching. Extreme weather events, such as heatwaves, storms, floods, and droughts, have the potential to cause injury, illness, and death. Furthermore, climate change affects air quality by increasing ground-level ozone, particulate matter, and allergens, exacerbating respiratory and cardiovascular diseases. Warmer temperatures and altered precipitation patterns also contribute to the expansion of vector-borne diseases, like malaria and dengue, as well as waterborne illnesses, including cholera and other diarrheal diseases. The relationship between humans and nature is another essential aspect that warrants further exploration. Human encroachment on natural habitats, driven by urbanization and deforestation, increases the likelihood of zoonotic diseases spillover and diminishes natural buffers that keep pathogens at bay. A deeper understanding of how human activities affect ecosystems and biodiversity is crucial in mitigating these risks and promoting a more sustainable coexistence with nature. Moreover, the conservation of plant species and maintenance of genetic diversity within species offer promising avenues for advancing human health. Many plant species possess valuable bioactive compounds with potential therapeutic applications. Traditional medicine systems, such as Ayurveda and Traditional Chinese Medicine, have long recognized the healing power of plants. However, habitat loss, over-exploitation, and climate change threaten the survival of these species and their genetic diversity. By conserving plant species and preserving their genetic diversity, we can continue to explore their potential in treating diseases and develop novel therapies, ultimately benefitting human health. To better address the ecological determinants of health, a more comprehensive understanding of the impacts of climate change, the human-nature relationship, and the importance of plant species conservation is needed.

By incorporating these dimensions into the "One Health" vision and the Ecological Public Health Model, we can develop more effective strategies for sustaining our environments and promoting Planetary Health [38].

Neurochallenges for 2040

The market for health services and products is distinct from other markets in many ways. The demand for health services and products is largely decoupled from prices and customer preferences. Importantly, public healthcare reimbursement decisions regulate access and usage of new health technologies. Consequently, these decisions are the bottleneck for medical innovation in many countries with economic and social implications. Recent research identified several flaws in health economic concepts.

Additionally, the heterogeneous viewpoints of participating stakeholders are rarely systematically addressed in current decision-making. Multi-criteria Decision Analysis (MCDA) provides an opportunity to tackle these issues. In early innovation, MCDA can provide information about stakeholder preferences and evidence for further development. Such approaches increase the efficiency of the R&D process and facilitate access to most beneficial innovations [39].

The use of cost-effectiveness thresholds fluctuates at global level from one country to another [40]. Only a handful of high-income countries have constructed explicit cost-effectiveness thresholds based on country-specific rationale, while most countries do not utilize specific threshold values [41]. The dominant cost-effectiveness thresholds still being used in low- and middle-income countries are based on GDP per capita, despite growing criticism against them [42]. However, constant effort is being placed in constructing cost-effectiveness thresholds that better factor in the opportunity cost specific to each country [43].

As more and more countries are working to achieve universal health coverage, context-specific cost-effectiveness thresholds play an important role in ensuring the reimbursement of interventions that have the highest chances of improving population health [44,45]. Considering that cost-effectiveness thresholds have both advantages and disadvantages, the outputs of cost-effectiveness analyses should inform healthcare resource allocation in conjunction with other country-specific factors to ensure a transparent and consistent decision-making process [46]. Such broader evaluations of new health technologies are often performed under the umbrella-term "**Health Technology Assessment**" (HTA) by governmental or professional bodies specially appointed for this matter. For HTA, MCDA allows a more nuanced analysis in different settings and different countries by explicitly structuring decision criteria and providing a methodological framework for decision-makers to address the conflict between costs and medical benefit. However, further research is needed to define guidelines about the conditions of MCDA at specific phases of innovation [39].

In Europe, EUnetHTA was established to create an effective and sustainable network for HTA across Europe – we work together to help develop reliable, timely, transparent, and transferable information to contribute to HTA in European countries. EUnetHTA starts from the definition of *health technology* offered by the ***International Network of Agencies for Health Technology Assessment (INAHTA)***: *"Any intervention that may be used to promote health, prevent, diagnose, or treat disease, or for rehabilitation or long-term care. This includes pharmaceuticals, devices, procedures and organizational systems used in health care"* [47], defining HTA as *"a multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe effective, health policies that are patient focused and seek to achieve best value"*.

While HTA provides a technical solution for tackling current and future neurochallenges, the framework under which it is implemented must be carefully considered to reflect emerging population-level needs. A crucial aspect that warrants consideration in the assessment of health technology is its ecological sustainability. While Health Technology Assessment (HTA) focuses on medical, social, economic, and ethical issues, incorporating environmental impacts in the evaluation process is essential, given the pressing need for sustainable healthcare solutions. One key area to explore is the energy and resource consumption of digital health technologies. Data storage, analysis, and communication tools are indispensable components of modern healthcare systems. However, these digital tools require significant energy consumption, which contributes to greenhouse gas emissions and exacerbates climate change. Moreover, the production, use, and disposal of electronic devices generate electronic waste, posing risks to both human health and the environment. Therefore, regulators, policymakers and funders must assess the ecological footprint of digital health technologies and to promote the development and use of energy-efficient, low-resource alternatives.

The environmental impacts of pharmaceuticals are another significant concern. Active pharmaceutical ingredients can end up in water systems through human excretion or improper disposal, affecting aquatic ecosystems and potentially leading to antibiotic resistance among bacteria. Additionally, the production of pharmaceuticals often involves energy-intensive processes, resulting in substantial carbon emissions. To mitigate these adverse effects, it is essential to incorporate environmental considerations into the research, development, and manufacturing processes of pharmaceuticals, as well as to promote responsible use and disposal practices among consumers.

Incorporating ecological sustainability into HTA can be achieved through the integration of environmental criteria within the Multi-Criteria Decision Analysis (MCDA) framework. This approach allows decision-makers to systematically consider the ecological impacts of health technologies alongside other factors, such as costs and medical benefits. Furthermore, collaboration between stakeholders, including governments, healthcare providers, manufacturers, and patients, is vital to ensure the development and implementation of sustainable healthcare solutions.

Figure 2 - Domains of Health Technology Assessment. Adapted from Bridges and Jones (2007).

Revising the Social Contract

All countries in the world, regardless of their level of development, face limited public resources in general and in the field of health, where the expectations of society are growing. The position of the World Health Organization on addressing this reality is firm: **no government has the resources to provide universal coverage with quality medical services**.

Primary Health Care (PHC)

In 2018, The Lancet Global Health Commissions argued that in the drive towards universal health coverage (UHC) there was a moral imperative to consider a basic level of quality, showing that more people globally die from poor quality care than from lack of access to it. One of the four main recommendations of the Commission was that countries should redesign service delivery to maximise health outcomes, not geographical access, and one of the key elements of service redesign was a greater focus on primary health care (PHC). PHC is ideally suited to managing the rise of non-communicable diseases and, as the 2018 Astana Declaration reaffirmed, *"is the most inclusive, effective and efficient approach to enhance people's physical and mental health".* Throughout the Commission, the authors recognize that reorganising PHC financing is not merely a technical issue, but also a political issue. It will necessitate a clear vision, long-term commitment, and a whole-of-government approach. Such a holistic view could also apply to the research landscape [48].

Artificial intelligence (AI)

AI for healthcare presents potential solutions to some of the global challenges faced by health systems. However, it is well established that these novel technologies are often not well accepted by healthcare leaders, contributing to their slow and variable uptake. Although research on various stakeholders' perspectives on AI implementation has been undertaken, very few studies have investigated leaders' perspectives on the issue of AI implementation in healthcare. It is essential to understand the perspectives of healthcare leaders because they have a key role in implementing new technologies in healthcare. In a recent study healthcare leaders highlighted several implementation challenges in relation to AI within and beyond the healthcare system in general and their organizations in particular [49]. The challenges comprised conditions external to the healthcare system, internal capacity for strategic change management, and transformation of healthcare professions and healthcare practice. The results point to the need to develop implementation strategies across healthcare organizations and to address challenges to AI-specific capacity building. Laws and policies are needed to regulate the design and execution of effective AI implementation strategies. There is a need to invest time and resources in implementation processes, with collaboration across healthcare, county councils, and industry partnerships.

Digital Health Services (DHS)

The COVID-19 pandemic has given an unprecedented boost to already increased digital health services, which can place many vulnerable groups at risk of digital exclusion. It is necessary to identify and address the elements that may prevent vulnerable groups from benefiting from digital health services to improve the likelihood of achieving digital health equity. Several development needs in implementing digital health services were identified that could improve equal access to and future benefits gained from digital services. While digital health services are increasing, traditional face-to-face services will still need to be offered alongside the digital ones to ensure equal access to services [50].

Increased budgets are needed for health, but other resources are necessary to place performance, transparency, and predictability at the cornerstone of health systems. Moreover, the COVID-19 pandemic continues to exert pressure on human, financial, material resources and the legal provisions of countries worldwide. It is therefore critical to revisit some underlying assumptions of health insurance systems, stemming from the social contract, such as:

- New system-wide objectives to be fitted into health insurance mechanisms
- Fitting in universal health coverage (UHC) into health systems objectives

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- Assessment of financial capability in conjunction with service packages and coverage/access.

The role of precision medicine

Health systems and academia should focus more on identifying potential mechanisms of brain disorders, prevention, and early screening of genetic or metabolic conditions evolving into neurological diseases or neurodevelopmental disorders, using technologies such as genetic testing or biomarkers rather than mainly focusing on treating them.

New early biomarkers need to be identified for the diagnosis and prognosis of such disorders, and their widespread availability should be ensured [51]. For treatment, new drugs that lead to symptomatic relief and drugs that can alter the progression of neurodegenerative diseases need to be identified. Overall, a multi-disciplinary approach that combines genetics, immunology, and molecular biology, along with advanced technologies such as AI and machine learning, is likely to be the most promising strategy for discovering new drugs for neurodegenerative diseases [52].

The application of precision medicine to the treatment and prevention of neurodegenerative disorders appears to be highly promising in contrast to the traditional “one-drug-fits-all” approach. In fact, neurodegenerative pathologies can present variable clinical features even in patients with the same disease who are very unlikely to benefit from a single drug. In this context, developing a precision medicine approach could represent an excellent possibility to identify preclinical stages of disease, allowing an accurate differential diagnosis and providing timely and optimal treatments instead of the traditional treatments normally utilized at later stage of disease. The availability of social networks for the simultaneous sharing of huge amounts of data worldwide has allowed bridging of the gap due to geographical distance and difficulties in accessing this information. In this context, realizing a web-based network for neurodegenerative disorders can be decisive for implementing precision medicine strategies across different specialized centers [53].

Methodological advances in clinical trials and future AI-based analyses of all data could provide a more sustainable model of personalized, pragmatic and patient-participatory medicine aiming to improve population health and address equity, diversity and global access to therapies [54].

Strengthening Health Systems

Most health systems budgets are currently structured on service levels (e.g. primary care, hospital care, etc.). This approach is oblivious to patient pathways, as it ignores the interdependencies between services and access barriers (material, bureaucratic, legislative, and otherwise). In future decades there is a need not only for longitudinal thinking, aligned with patients' needs, but also for better coordination between service levels, as well as active partnerships with public, private, and civil society organizations to prevent and cover existing deficiencies.

Investing in **health policy and systems research (HPSR)** - an emerging field that seeks to *understand and improve how societies organize themselves in achieving collective health goals, and how different actors interact in the policy and implementation processes to contribute to policy outcomes*. By nature, HPSR is multi and interdisciplinary, a mix of health economics, public health, epidemiology, and other fields working together to provide a high-level overview of how health systems function, adapt to challenges, and most importantly how effective policies can influence population level outcomes.

High-burden diseases disproportionately affect low- and middle-income countries (LMIC), largely due to health system organization and healthcare service delivery issues. LMICs in Eastern Europe and Asia are characterized by growing economies but relatively poor health infrastructures. Additionally, these countries face important challenges regarding availability of health system information, including complete absence of injury surveillance and acute lack of epidemiological data, rendering evidence-based policymaking a real and daunting challenge.

Finally, monitoring policy implementation is seldom provided sufficient attention in health systems [54]. According to the United States Center for Control and Disease Prevention (CDC), effective health program evaluation is a systematic way to improve and account for public health actions by involving procedures that are useful, feasible, ethical, and accurate:

- Improving surveillance in health and climate-related areas
- Widespread implementation of health program evaluation
- Capacity building in Health Technology Assessment to empower inverting the pyramid of medical services.

Figure 3 - Centers for Disease Control and Prevention. Framework for program evaluation in public health. MMWR 1999;48 (No. RR-11)

One Health Concept Implementation

One Health is a collaborative, multisectorial, and transdisciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment. One Health issues include zoonotic diseases, antimicrobial resistance, food safety and food security, vector-borne diseases, environmental contamination, and other health threats shared by people, animals, and the environment [55].

The Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the United Nations Environment Program (UNEP) and the World Health Organization (WHO) welcome the newly formed operational definition of One Health from their advisory panel, the One Health High Level Expert Panel (OHHLEP), whose members represent a broad range of disciplines in science and policy-related sectors relevant to One Health from around the world. The four organizations are working together to mainstream One Health so that they are better prepared to prevent, predict, detect, and respond to global health threats and promote sustainable development [56].

The future of work and industry

Through technological developments, health care may drift away from hospitals. Furthermore, the value-based approach will require new roles, skills, and relationships among healthcare professionals. Likely trends include (57):

- **A move out of the office**, driven by convenience for consumers and a move toward less costly service sites, requires an entirely new set of skills to deliver care across different settings. Health providers will need to operate in non-traditional locations and use technology to access and integrate care, engaging patients in unique ways as consumer expectations evolve.

- The **shift to value-based care** and new models of care requires a more holistic view of patients and new roles. As a result, care teams must be increasingly multidisciplinary.
- **Scientific advances** create significant unknowns, for which there is no workforce supply model yet.
- The need to **innovate quickly**.

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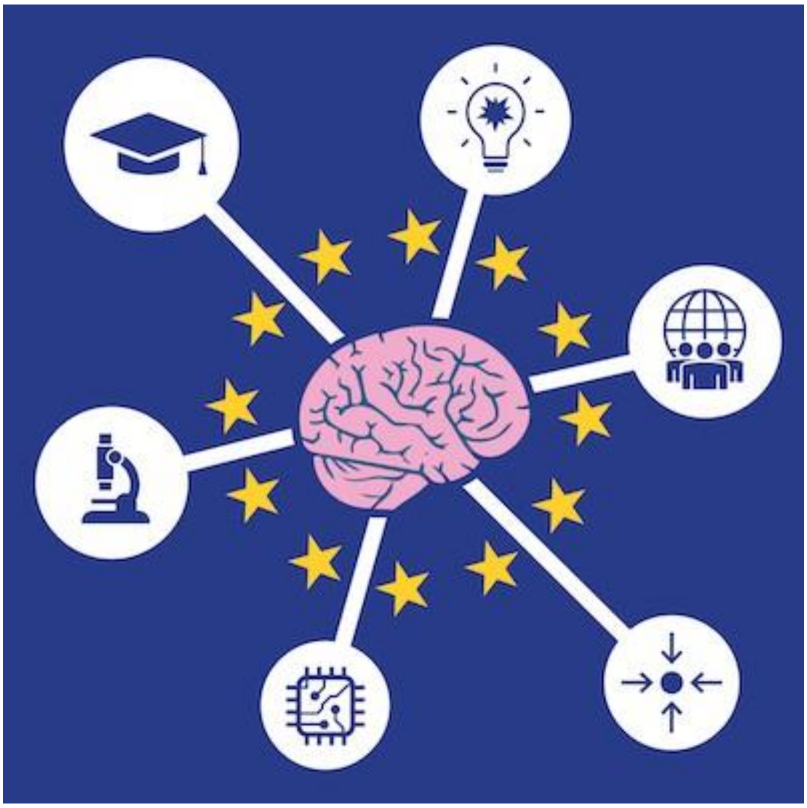

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Neurochallenges in Smart Cities: State-of-the-Art, Perspectives, and Research Directions

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Abstract

Smart city development is a complex multi- and transdisciplinary challenge requiring adaptive resource use and context-aware decision-making practices to improve human functionality and capabilities while respecting societal and environmental rights and ethics. Experts in a wide range of fields agree that real-time sensing designs and control algorithms inspired by the brain could help build and plan urban systems that are healthy, safe, inclusive, and resilient. This vision of the nexus of neuroscience and technology, urban space, and society requires co-producing knowledge towards a hybrid intelligence, whereby education and research, technological innovation, and societal innovation are interrelated in key focus areas. There is an urgent need for action, especially (a) to enhance the health and well-being of individuals residing in cities while ensuring that no one is excluded from urban development (e.g., through the intelligent design of public space and incorporation of neuroaesthetics), and (b) for resilience and sustainability (e.g., through improved disaster management, planning of city logistics, waste management and energy efficiency). Against this background, this perspective paper will first review the state of knowledge in the literature based on a bibliometric analysis to describe how neuroscientific and neurotechnological expertise and solutions are currently used in smart cities. The paper will then delve deeper into some emerging themes. Understanding emerging themes around neuroscience and technology as applied to smart cities will help us identify novel challenges in this arena and where we want to go, given societal needs and some legal and ethical concerns.

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1. Introduction

Smart city development is a complex multi- and transdisciplinary problem that requires adaptive resource use and context-aware decision-making locally to improve human functioning and capabilities while respecting societal and environmental rights and ethics (March, 2019; Townsend, 2013). While there is not a unified and universally accepted definition of smart cities, it is expected that a broad and inclusive framing of the concept will link and localize a comprehensive set of UN Sustainable Development Goals (SDGs): Goal 3 (good health and well-being), Goal 4 (quality education and lifelong learning), Goal 7 (affordable and clean energy), Goal 9 (industry, innovation, and infrastructure), Goal 10 (reduced inequalities), Goal 11 (sustainable cities and communities), Goal 13 (climate action), Goal 16 (peace, justice, and strong institutions). Considering this list, there appears to be a need for urgent action, especially (a) to enhance the health and well-being of individuals residing in cities while ensuring that no one is excluded from urban life and (b) to ensure that urban development and planning play a positive synergetic role for resilience and sustainability.

In this context, planning for smart cities, viewed as complex systems to improve the quality of life, requires a transdisciplinary approach that includes multiple domains and stakeholders. Experts in different fields agree that real-time sensing designs and neuro-inspired control algorithms could help local initiatives, thereby supporting the development and planning of urban systems that are healthy, inclusive, safe, and resilient. This vision of the nexus of neuroscience and technology, urban space, and society requires co-producing knowledge towards a hybrid intelligence, whereby education and research, technological innovation, and societal innovation are interrelated, as discussed below.

1.1. The nexus of Neuroscience and technology, urban space, and society

A smart city vision, depicted in Figure 1, at the nexus of neuroscience and technology, urban space, and society, requires an interdisciplinary and integrative approach that would address the critical issues and concerns of urban development and planning by allowing the communication of multiple codes and perspectives consistently and coherently (Kourtit and Nijkamp, 2012; Castells, 2000). As Ancora et al. (2022) highlight, recent years have seen significant advancements in our understanding of brain functioning, with the field of neuroscience expanding its applications across various domains, such as marketing, economics, decision science, and educational sciences. This expansion has been aided by technological advancements such as wearable devices and software applications. A novel field known as 'neurourbanism' has also recently emerged, integrating theoretical perspectives and analytical methods inspired by the brain. The aim is to deepen understanding of human needs, behaviors, and decision-making processes in urban environments and, ultimately, to enhance service design and implementation throughout cities in a context-aware manner.

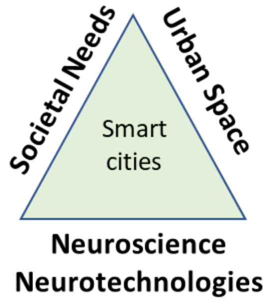

Figure 1: Smart cities as hybrid intelligence in the nexus of neuroscience/technologies, urban space, society

In this context, the particular neurochallenges in smart cities would involve using or being stimulated by principles of cognition and neuroscience to comprehend and anticipate human behavior and requirements within urban environments. Subsequently, appropriate solutions would be devised and implemented utilizing neurotechnologies to enhance the quality of life of present and future generations. It goes without saying, "going smart" also raises significant ethical and privacy concerns, which need to be carefully managed in any smart city initiative. Therefore, the ultimate goal is not just to improve effectiveness but also to ensure that these technologies serve the purposes of healthier and sustainable urban planning and design (Pykett et al., 2020). Undoubtedly, this can be achieved only through strong collaboration among governments, industry, academia, and civil society organizations (Breuer et al., 2019).

1.2. Objectives and scope of the paper

With this background, this perspective study first examines the structure of current knowledge in the literature regarding neurosciences and technologies, urban space, and the society nexus, using bibliometric analysis. It then discusses how knowledge and solutions from neuroscience and neurotechnology have been applied in smart cities. Specifically, we map the neuroscience and neurotechnology literature for smart cities based on 2018–2022 data extracted from the Scopus database using a list of terms and themes identified within the scientific community. We conducted this analysis initially on a broad basis without disciplinary constraints, subsequently narrowing our focus to four specific sub-disciplines: computer sciences, engineering, social sciences and environmental sciences.

Understanding emerging topics in neuroscience and neurotechnology as they apply to smart cities will help us to determine our current state of knowledge, assess what has already been accomplished in this area, and identify what issues to be addressed considering the societal and environmental challenges of the 21st century, along with associated legal and ethical concerns. We aim to provide insights into potential future trajectories. In particular, we argue that neuroscience and neurotechnology can contribute to progress in smart cities in two focal areas that require urgent action in the urban public domain: (I) improving people's health and well-being in cities and ensuring that no one is left behind in urban development, for example, through the intelligent design of public spaces, mobility, and transportation; and (II) ensuring resilience and sustainability, for instance, by improving resource planning, disaster and waste management to maintain ecosystem health. We visualize our scope in Figure 2, where the blue parts indicate where a more in-depth discussion for future neurotechnology research is recommended, directly aligning with the SDGs outlined earlier. The pink areas then show cross-cutting issues that need to be kept in mind and thought about simultaneously. This is because public decision-making processes in the two focal areas need to be supported by institutions that enhance data-based governance with the collaboration of multiple constituencies, and that promote transparency and accountability. In addition, the initiation of new educational and research programs such as NeurotechEU, as well as discussions around the adoption of regulatory frameworks and ethical codes, are urgently needed.

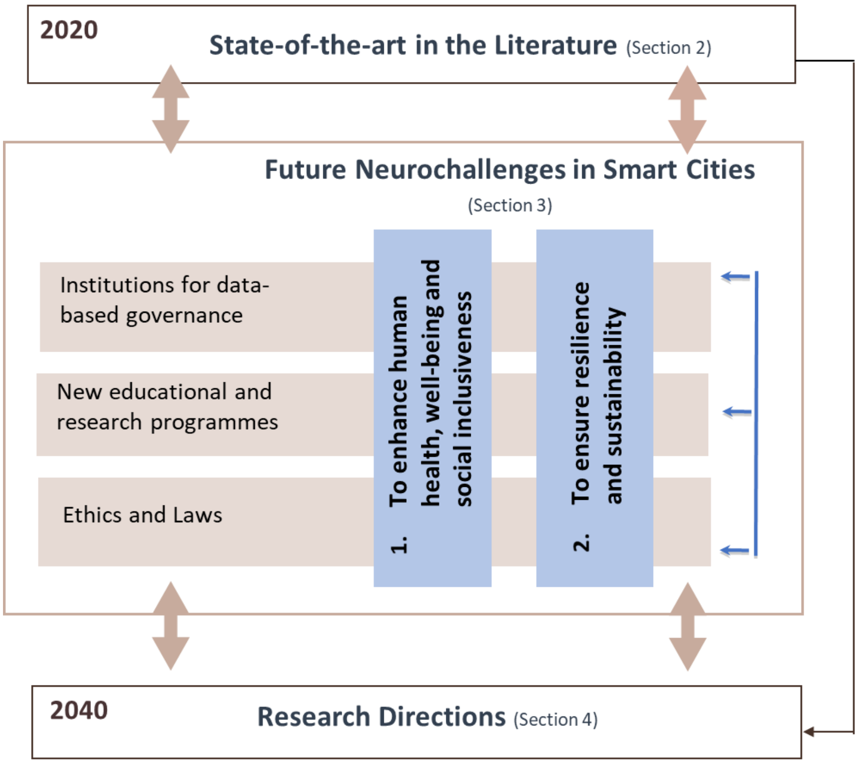

Figure 2: Focal areas for neuroscience and neurotechnologies in smart cities

The structure of this perspective paper is as follows. In Section 2, we present the state-of-the-art in the literature by offering a bibliometric analysis of neurochallenges within the context of smart cities. After explaining the methodology followed and describing the data sources used for the bibliometric analysis, we present our findings and illustrate how the contributions in the core literature share common aspects and how they can work together to create new synergies and complementarities. Based on these findings, Section 3 delves into more detail to illustrate key research grounds from different fields of study, focusing on challenges, neurotechnology solutions, and their potential use in smart cities. In particular, we consider the implications of neurotechnology in the two focal areas: (1) for human health, well-being, and social inclusiveness, and (2) for resilience and sustainability. For the former, we focus on neuro-design and neuro-architecture, followed by a discussion on mobility and access to transportation. In the latter, we specifically investigate waste management for ecosystem health. Lastly, Section 4 suggests possible directions for future research in the field.

Overall, this perspective study is an academic endeavor, a systematic exploration that fosters inquiry by raising awareness and encouraging engagement and action among researchers.

Importantly, this type of analysis also enables us to identify potential synergies and partnerships, not only within different academic disciplines but also between academia, industry, and civil society. Stakeholders in this process may play various roles at different levels or from diverse perspectives to strengthen the efforts towards creating a more sustainable and livable urban space.

2. A bibliometric analysis of neurochallenges within the context of smart cities

In this section, we introduce the details of our research, presenting the methodology and initial outcomes. We first explain the way we conducted the bibliometric analysis and the sources from which we extracted data. This is followed by the presentation of the co-word analysis conducted on all selected articles. We then shift to a more discipline-focused perspective, conducting a co-word analysis with a particular disciplinary emphasis. Finally, we present the critical insights derived from our bibliometric analysis.

2.1. Methodology and data sources

The main goal of our bibliometric study is to reveal the intellectual structure and important themes in the field of research. To achieve this, we initially generated a draft list of terms and refined and augmented them into a finalized list through consultation with experts, as can be seen in Table 1. This represents the first step in our bibliometric methodology. In the second step, we ensured the relevance of our bibliometric analysis to smart city research by narrowing our search to those papers where the “smart cities/city” keyword appeared, along with terms and themes representing Neuroscience and Neurotechnology in relation to Smart Cities (listed in Table 1) or terms and themes characterizing a Smart City concept (listed in Table 2). When one searches these lists with the concept of a “smart city,” the evolution of the idea becomes apparent. It shifts from being primarily about technology to focusing on people, eventually embracing inclusive and participatory governance.

Table 1: Terms and Themes representing Neuroscience and Neurotechnology in relation to Smart Cities

- Neuroaesthetics
- Neurolaw
- Neurophilosophy
- Neuroethics
- Mental health
- Neuroarchitecture
- Neurourbanization
- Neuroart
- Neuro design

Table 2: Terms and Themes characterizing Smart City concept

- Mobility
- Access to public transportation
- Micro-mobility problems
- Socially inclusiveness
- Care solutions
- Physical and social landscapes
- Comfort and well-being
- Harmony
- Smart design of public space
- Frugal technologies
- Resilience
- Real-time resilience
- Adaptation
- Human-centered design
- Disaster management
- Resource-aware planning
- Nudges
- Bottom-up governance
- Data-based governance
- Evidence-based decision-making
- Societal innovation
- Open-data platforms
- Technology as commons
- Technological literacy
- Dissemination
- Citizen science
- Waste management
- Classification for recycling
- Recycling of plastics
- Water management
- Sustainability
- Interaction of autonomous vehicles

In the third step, we searched the Scopus database, preferring it over the Web of Science due to its larger number of indexed journals. Using the query function, we looked for articles containing these terms in the article title, abstract, or author-defined keywords, covering all years and research institutions. For this step, following typical literature review practices, we restricted our search to peer-reviewed journal articles and conference publications, thereby excluding gray literature and books. Furthermore, we only included articles in English. Our search criteria and terms yielded 27,346 peer-reviewed manuscripts. In the final stage, to streamline the data in our bibliometric analysis, we also created a thesaurus and combined or recoded some words in accordance with bibliometric analysis guidelines (Donthu et al., 2021), addressing variations in term usage across different publications, such as the singular or plural forms or the use of acronyms. For instance, we made no distinction between “smart city” and “cities” or between “mobile crowdsensing” and “mcs”. This enabled us to generate a reliable list of author keywords our dataset.

We also analyzed the disciplinary foundations of the bibliometric data at our disposal. Figure 3 illustrates the diversity of fields covered by the literature, each highlighting different aspects of smart cities and reflecting the varied goals and priorities that stakeholders may have.

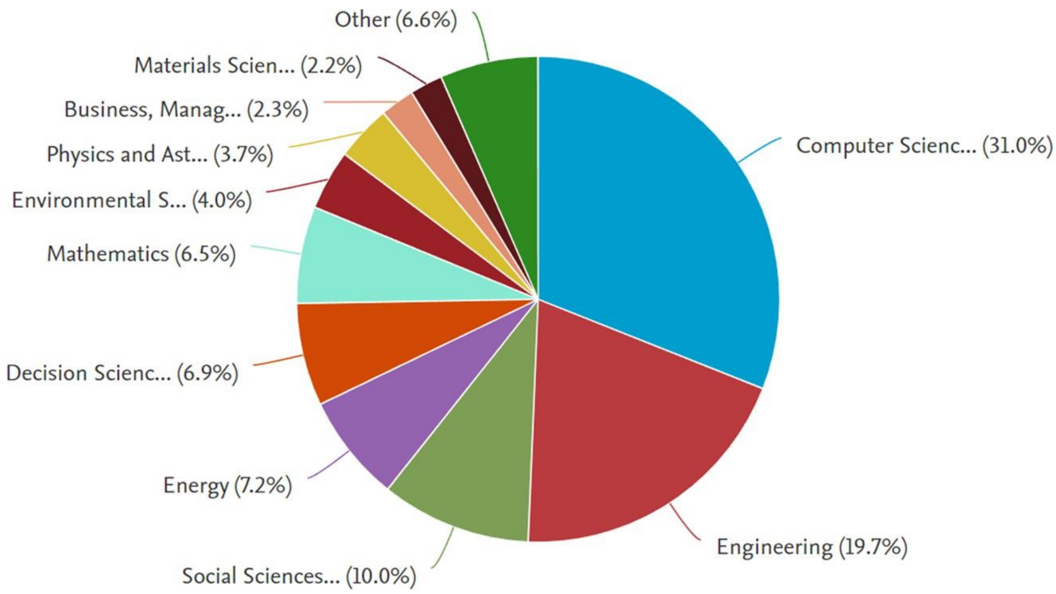

Figure 3: Bibliometric analysis: Share of various disciplines (2018-2022) for Smart-city/cities + Terms/Themes (from Table 1 and Table 2)

Approximately a third of the studies (31%) fall under the computer sciences discipline, while nearly a fifth (19.7%) are categorized under engineering. The remaining half of the studies are spread across various disciplines, with social sciences accounting for a significant share (10%). This distribution signals opportunities for dialogue and collaboration between the dominant disciplines and those with smaller representations. Neurosciences, for instance, as a field that does not appear to be dominating the scene now, might become prominent in the future, given its potential for new collaborations with other disciplines.

2.2. Co-word analysis for all articles selected

We conducted a co-word analysis, also known as ("author keyword co-occurrence"), on the selected articles (27,346 in total) in the VOSviewer software. This method identifies keywords that frequently appear together in the content of the articles, indicating thematic relationships. Figure 4 presents one such bibliometric analysis result, a general one conducted without disciplinary filtering. While it is always possible to generate images for different periods, the image below represents the last five years, from 2018 to 2022. We used the VOSviewer clustering algorithm (with the counting method fractional counting, and the normalization method based on association strength), which allowed us to generate a number of clusters based on topics. In our analysis, it seemed adequately meaningful to interpret the thematic groups within five clusters.

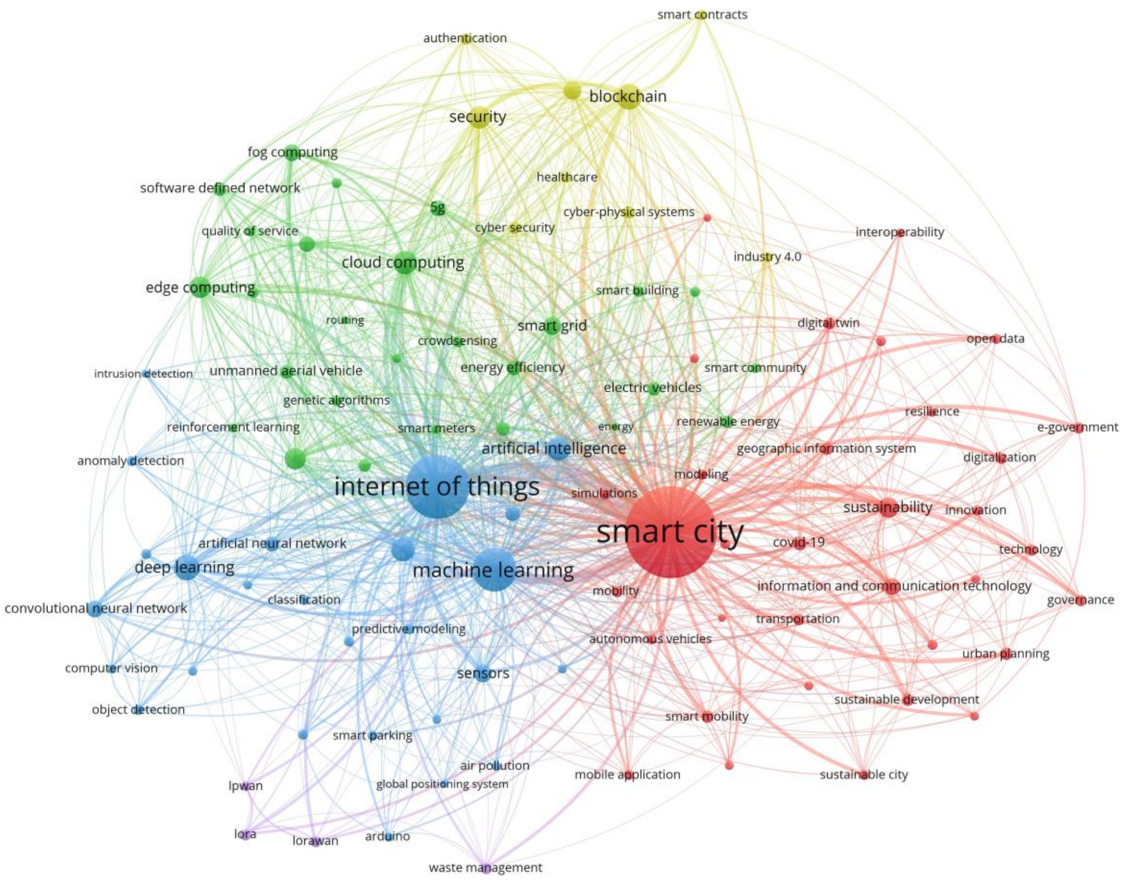

Figure 4: Co-word network visualization for Smart-city/cities + Terms/Themes (in Table 1 and Table 2) (2018-2022)

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Each node in this network represents an author-defined keyword, such as “smart city,” “internet of things,” “machine learning”, or “urban planning.” The size of the node represents the frequency of the keyword appearing, i.e. how many times “smart city” appears. As node gets bigger, the associated keyword occurs more frequently. A link between two nodes implies that the two keywords appear together in the articles. The link strength or thickness, with has a positive numerical value, indicates how often two keywords appear together or how often they “co-occur.” Each color represents a distinct thematic cluster. The nodes and links within a cluster help explain the range of topics (nodes) covered by that theme (cluster) and how those topics (nodes) are interconnected (links) (Donthu et al., 2021). To fully interpret the results of the bibliometric analysis, our team convened to discuss the interpretation of each thematic cluster and the significance of the keywords within publications in that cluster. The following are some preliminary observations drawn from these results.

The red cluster in Figure 4 focuses primarily on sustainability issues, exploring strategies for more sustainable urban development, planning, and governance, which a key driving force in existing smart city literature (Caragliu et al., 2011). This includes leveraging innovative technologies such as e-government, geographic information system, and information and communication technologies (ICT) to manage and operate a sustainable city and improve the quality of life. The green cluster centers around using specific digital technologies for addressing specific problems, such as energy consumption and efficiency, smart grids, smart meters, electric vehicles, and edge computing. The blue cluster highlights the "smart city" concept, emphasizing techniques from areas like “machine learning,” and “artificial intelligence.” The yellow cluster addresses privacy and security concerns, touching on topics such as “authentication” and “smart contracts”. Lastly, the purple cluster may be considered a niche theme, delving into network and gateway protocols like LoraWAN and LPWAN.

2.3. Co-word analysis with a disciplinary focus

In recognition of the integral link between smart cities and the vision of context-aware decision-making, we also aimed at establishing stronger connections to specific SDGs, in particular focusing on SDG3 (good health and well-being), SG7 (affordable and clean energy), SDG9 (industry, innovation, and infrastructure), SDG10 (reduced inequalities), SDG11 (sustainable cities and communities), SDG13 (action on climate change) and SDG16 (peace, justice, strong institutions). To this end, we narrowed our search to papers within four primary disciplines: computer sciences (relevant to SDGs 3, 9, and 11), engineering (relevant to SDGs 7, 9, and 11), social sciences (relevant to SDGs 3, 10, and 16), and environmental sciences (relevant to SDGs 11 and 13).

When we limit the analysis to certain subject areas or subsets of disciplines, more specific thematic groups, or clusters, emerge. This is because each discipline—Computer Sciences, Engineering, Social Sciences, and Environmental Sciences—might have its unique perspective on smart cities. The themes identified from the bibliometric analysis and how they are interpreted in these four disciplines give us which keywords are most frequently used in each field and how many are shared across disciplines. This understanding can facilitate discussions on potential disciplinary partnerships. Each figure also provides insight into the meanings of the clusters. While some clusters in these figures seem more goal-oriented or challenge-driven, others are techniques, methods, or technologies.

Bibliometric analysis under computer sciences:

The analysis under computer sciences was based on 19,910 documents (including peer-reviewed articles and conference papers) and 38,189 author keywords. In Figure 5, we visualize the top 100 keywords with the highest occurrence (the minimum number of author keyword occurrences being 66) under five clusters. This gives us a general overview of the main topics authors are exploring in computer sciences within the context of smart cities. The blue cluster reveals that a significant portion of research in computer sciences, as expected, relates to the 'internet of things' and techniques such as machine learning, deep learning, image processing and classification. The red cluster focuses on digital technologies and their infrastructure, encompassing aspects such as cloud computing, wireless sensor networks, edge computing, fog computing, 5G, and the internet of vehicles. The green cluster corresponds to research on the practical concerns and challenges of smart cities. Specifically, it represents areas where digital technologies and AI techniques from the blue and red clusters can be applied, such as public transport, smart mobility, information and communication (ICT) technology, e-government, smart governance, smart community, and augmented reality, among others. The purple cluster centers around a niche topic, and explores issues around gateway protocols. Lastly, the fifth cluster, indicated in yellow, emphasizes privacy and cybersecurity concerns. (see Appendix 1 for a detailed breakdown of the keywords in each of the five clusters, along with their frequency of occurrence).

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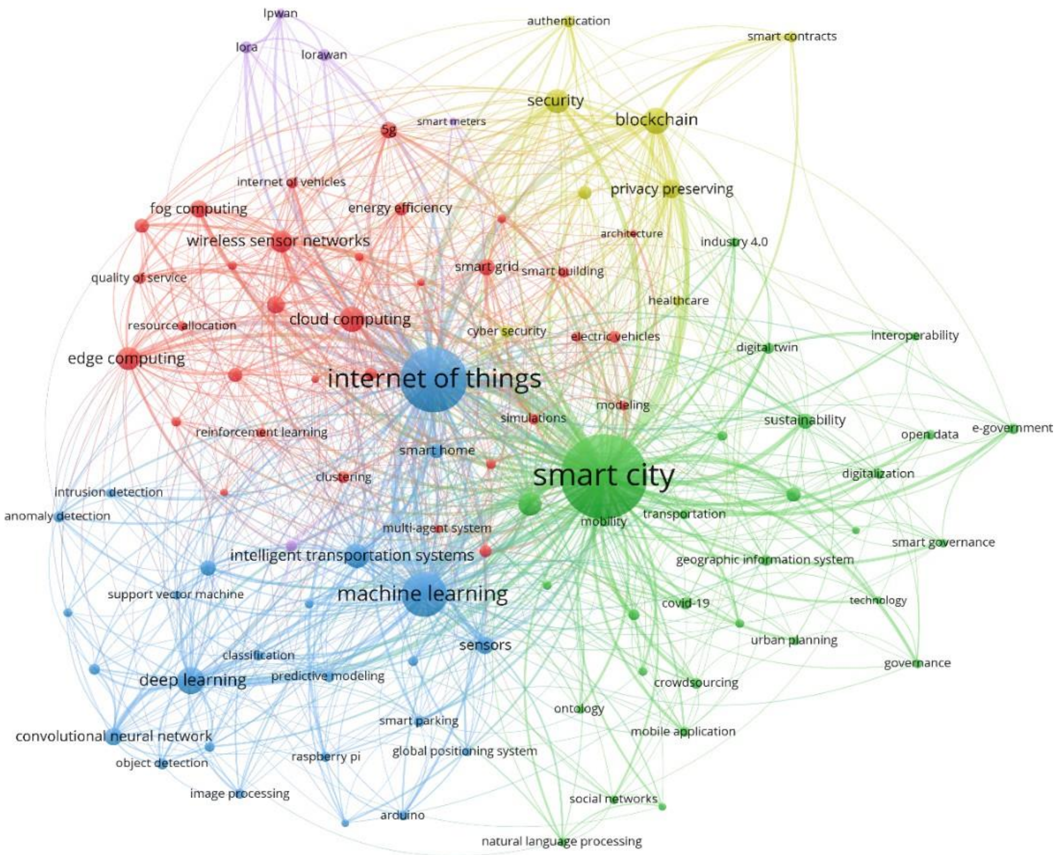

Figure 5: Co-word network visualization in Smart-city/cities + Terms/Themes (in Table 1 and Table 2) with Computer Sciences focus (2018-2022)

Bibliometric analysis under engineering:

The analysis under engineering was conducted on 11,893 documents (peer-reviewed articles and conference papers), and over 24,695 author keywords. We then visualized the top 100 keywords (Figure 6), with the highest occurrence (the maximum number of keyword occurrences being 3957 and the minimum being 41) falling into five clusters. The yellow cluster with "smart city" as its central node signifies some primary challenges for engineering encompassing sustainability, urban planning, mobility, resilience, and governance issues. The red cluster centered around the “internet of things” incorporates technologies such as object detection, and techniques like deep learning, machine learning, and deep neural networks. These are deployed for specific purposes, such as in smart homes, smart parking, and classification, all represented within the same cluster. The green cluster, though diverse, contains a bunch of innovative information and communication technologies (ICT) infrastructures and uses, such as 5G, fog computing, edge computing, blockchain and the internet of vehicles. The blue cluster focuses on energy-related topics, such as energy efficiency, renewable energy, smart grid, smart meters, electric vehicles. The purple cluster features a large central node that connects the "artificial intelligence," to cyber security, and information models and systems (see Appendix 1 for a detailed breakdown of the keywords in each of the five clusters, along with their frequency of occurrence).

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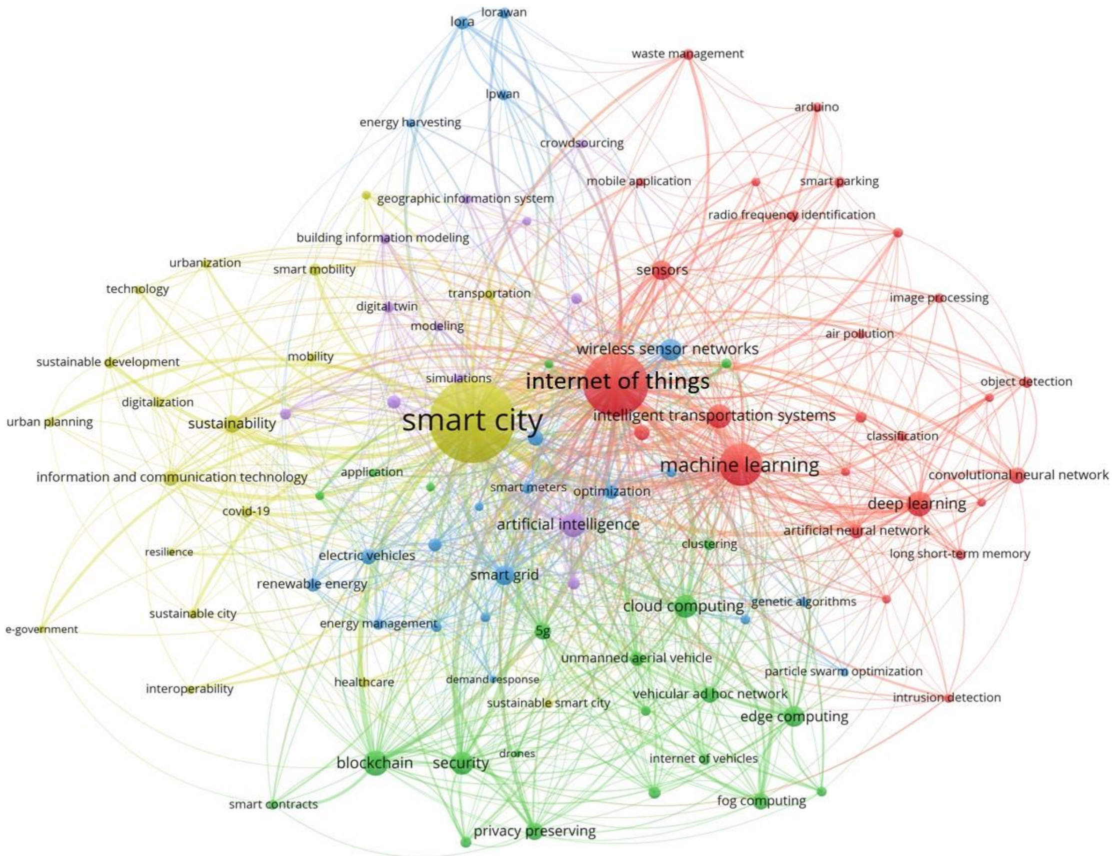

Figure 6: Co-word network visualization in Smart-city/cities + Terms/Themes (in Table 1 and Table 2) with Engineering focus (2018-2022)

Bibliometric analysis under social sciences:

In social sciences, we conducted the analysis on 6138 documents (peer-reviewed articles and conference papers) encompassing 15,693 author keywords. In Figure 7, we visualize the top 100 keywords with the highest occurrence (the maximum number of keyword occurrences being 2364 and the minimum 21) in five clusters.

There are three large clusters (red, green and blue) with many keywords and two relatively smaller groups that stand out (see Figure 7). The green group considers the core of smart cities in sustainable urban development, urban planning, governance, participation, and quality of life. These ideas are presumably made workable by connecting them to the other large cluster, the red areas, where techniques such as internet of things, machine learning, and AI are used. The blue cluster, in the social sciences, covers issues surrounding intelligent transportation systems linked to smart mobility and public transport. The yellow cluster then examines the uses of technologies such as data visualization, virtual reality, and augmented reality. The purple cluster is small, featuring social media and smart tourism as niche topics.

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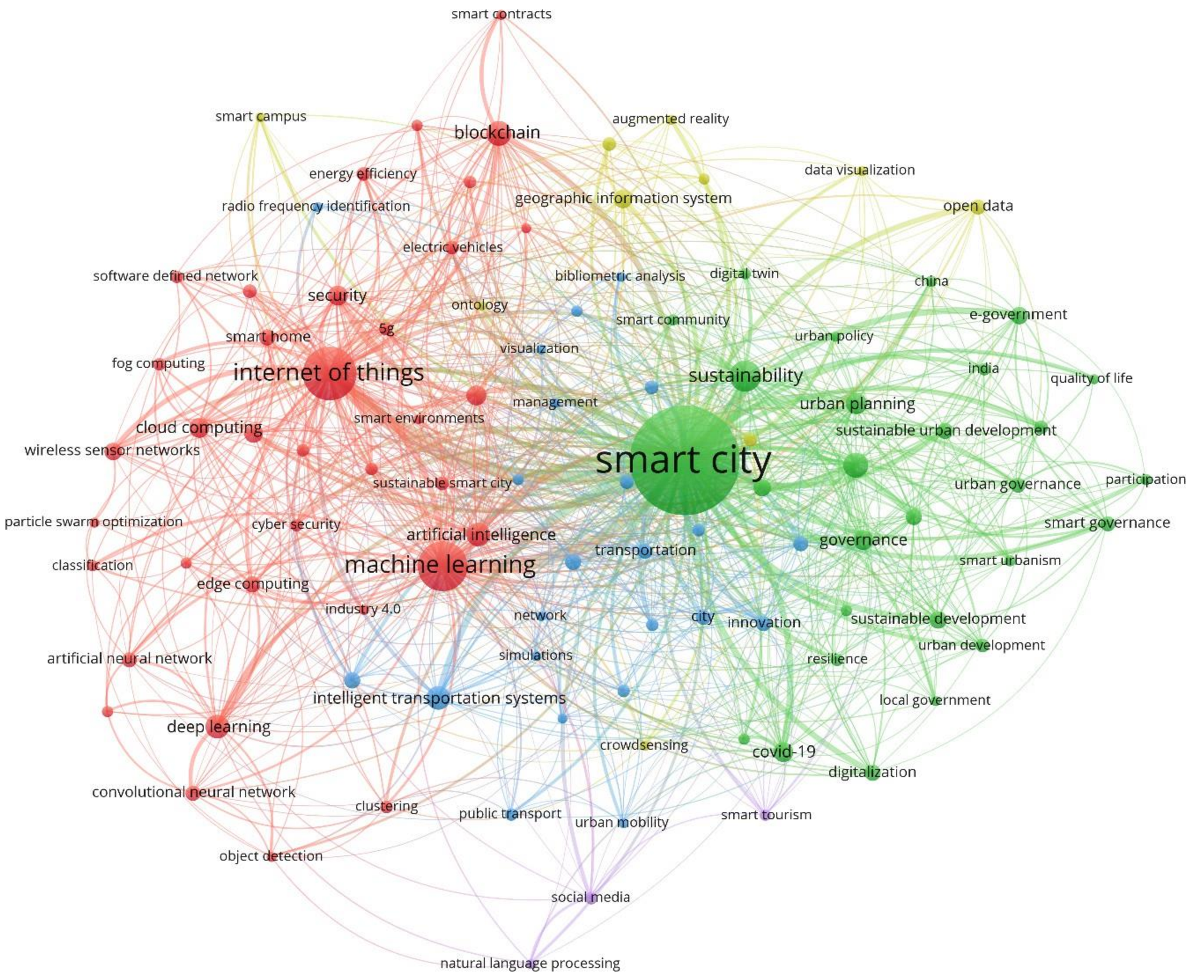

Figure 7: Co-word network visualization in smart-city/cities + Terms/Themes (in Table 1 and Table 2) with Social Sciences focus (2018-2022)

Bibliometric analysis under environmental sciences:

The analysis of 2,433 documents (peer-reviewed articles and conference papers) within environmental sciences gives us 6288 author keywords. Figure 8 reflects the top 100 keywords with the highest occurrence (the minimum number of keyword occurrences being 8). The red cluster of the network represents challenges such as eco-cities and sustainable urban development from an environmental science perspective and includes issues such as air quality, climate change, energy transition, urban transformation, and the circular economy. The green cluster again with sustainability and quality of life concerns, has a focus on planning and decision-sciences, where optimization, indicators, infrastructure policies play a role. The blue cluster is centered mainly around internet of things and machine learning, representing computer sciences solutions along with sensors, data visualization and image processing. The purple and yellow clusters seem small niche areas around energy and security.

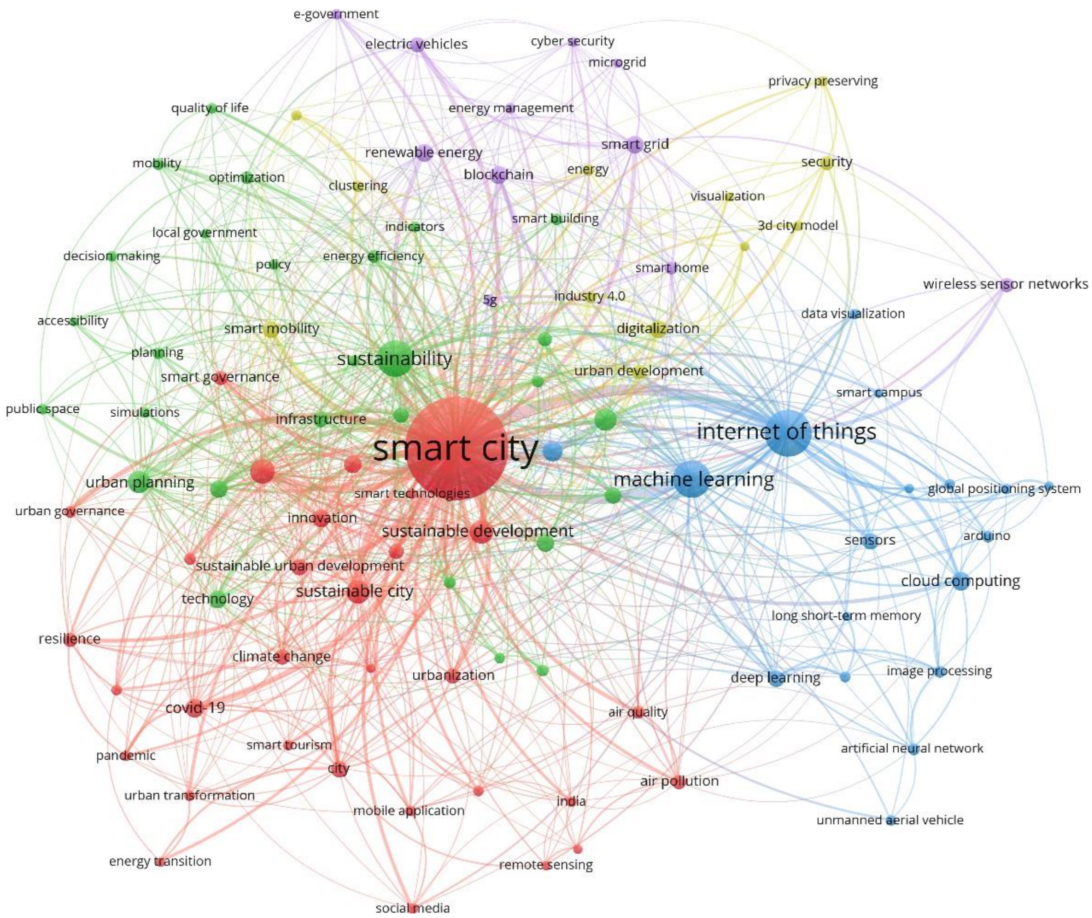

Figure 8: Co-word network visualization smart-city/cities + Terms/Themes (in Table 1 and Table 2) with Environmental Sciences focus (2018-2022)

2.4. Key insights from the bibliometric analysis

Our analysis provides compelling evidence that smart city development encompasses various dimensions, thereby necessitating the utilization of multiple perspectives against the societal and environmental challenges of the 21st century in urban settings. Throughout our bibliometric analysis, many author keywords repeatedly surface, indicating recurring themes and shared terminologies among disciplines in the intersection of neuroscience and technology, urban space, and society.

Smart city discussions typically revolve around the following core themes: urban planning, sustainability, e-government, smart governance, climate change, resilience, healthcare, smart mobility and intelligent transport systems, energy efficiency, air and water quality, and smart home. At the same time, these discussions also highlight some key technologies that play a crucial role in developing smart cities. These include, for instance, the internet of things, machine learning, data mining, wireless sensor networks, blockchain, edge computing, smart grids, and mobile applications.

Identifying these commonalities across disciplines holds significant value for academics and policymakers, providing them with insights to establish synergies and complementarities. Understanding these shared issues and technologies could enable researchers and policymakers to comprehend the intricate interconnections between different aspects of smart cities and foster an awareness of potential disciplinary bridges. This comprehension is essential for formulating cohesive and integrated strategies and advancing smart city initiatives in alignment with SDGs.

Obviously, there is also some divergence in core focuses across disciplines reflecting the diverse goals and priorities that researchers and stakeholders with different lenses might have. The computer sciences perspective, for instance, seems centered on the role of technological solutions and ICT infrastructures. The engineering perspective is more driven by problem-solving approaches. The social sciences perspective emphasizes theoretical and conceptual frameworks that shape urban development and address organizational concerns such as e-governance and citizen participation. The environmental perspective integrates high-tech solutions with green interventions to achieve environmental goals.

Here, we see a potential danger of fragmentation, resulting from any incoherent and inadequate implementation or neglect of coordination in addressing common urban challenges. Overall, the complexity of smart city development always contains the risk of seeking some short-term gains through black-box technological solutions. Based on these insights, in Section 3, we offer some concrete perspectives from different fields of study on the implications of neurotechnology in smart cities with specific reference to challenges, technologies, and solutions, as well as any open issues.

3. Perspectives on implications of neurotechnology in smart cities

The discussion in this section is structured in two parts. The first part will focus on neurochallenges in smart cities to enhance human health, well-being, and social inclusiveness, and the second part will focus on improving resource planning and waste management for resilience and sustainability.

3.1. Neurotechnologies in smart cities for human health and well-being

3.1.1. On Physiological Sensing-based Emotion Regulation with Wearables across Smart Cities

Challenges: Modern urban life is very demanding regarding economic and physical resources. Moreover, more crowded, more complex city life increases the time pressure on the urban citizen. It has been shown that the major source of the increased stress in everyday life is the mismatch between these demands and the individual's available resources. The European Environment Agency describes this as “urban stress” (EEA, 2020). Although some stress can be beneficial for increased alertness, athletic ability, or better focusing during an exam, it is well known that long-term urban stress can be harmful to the human body. Emotion regulation techniques such as meditation, yoga and walking outdoors may help to reduce stress.

However, urban lifestyles such as long working hours and commutes prevent the most well-known emotion regulation techniques.

Today, designers also need a better understanding of the psychological and emotional impacts and threats of changing physical and social landscapes. Neuroaesthetics, which studies the neural basis of aesthetic experiences, can play a crucial role in informing the design of public spaces that create positive emotional responses in individuals. For instance, incorporating natural elements such as green spaces and natural lighting can enhance mood, promoting a sense of calm and well-being. In contrast, exposure to unnatural light sources can adversely impact mental health, intensifying feelings of anxiety and depression. The understanding and regulation of these emotional shifts can be enriched by applying neurotechnology. Consequently, there are two significant challenges here: Firstly, sensing stress, fatigue, anger, and other potentially harmful emotional or physical states, and secondly, facilitating emotion regulation in urban environments.

Technologies and Solutions: Since smart watches, smart wristbands and other smart wearables such as rings have become pervasive and their sensing modalities have increased, sensing emotional states has become feasible using wearables (Y.S. et al., 2019). There are observable physiological changes in the human body such as a reaction to stress. Heart Rate Variation (HRV) and Electro-Dermal Activity (EDA) are well-known stress indicators. Most wearables have Photoplethysmography (PPG) sensors that could be used for measuring HRV, which changes quickly in a stressful situation. In addition, some wearables have Galvanic Skin Response sensors for detecting EDA. Although an EDA reaction is slower compared to an HRV response, it has been shown that multimodality improves the emotion/fatigue sensing capability (Y.S. and Ersoy, 2023).

The ubiquity of wearables is not the only reason for the improvements in emotion sensing. The sensors create multiple streams of time series data. Recent advances in machine learning (ML) techniques, such as deep learning and faster ML hardware, have enabled more accurate models for emotion sensing. If the available data is not large, an acceptable sensing accuracy can be achieved using classical ML techniques such as support vector machines and decision trees. With larger physiological data from wearable sensors, better overall emotion-sensing performance can be obtained using deep learning techniques. However, there are increased privacy concerns about health-related data. Federated learning, like new techniques, also facilitates privacy-aware emotion sensing with better accuracies (Y.S. and Ersoy, 2021).

Open issues: Most of the successful ML techniques are supervised. In other words, they require labeled data. Most data labeling techniques expect individuals to frequently fill out standard surveys. However, collecting reliable surveys every several hours is a significant challenge in modern urban life. Semi-supervised or unsupervised ML techniques are required to reduce the burden of ground truth collection. The other major issue is acting to regulate emotions after detecting the emotional states while living in urban environments, such as working in the office or commuting. One EU-funded H2020 research project targeting these issues was Affectech: Personal Technologies for Affective Health (https://cordis.europa.eu/project/id/722022). In that project, interactive tools and wearable actuators with vibrotactile and temperature-changing elements were recommended for emotion regulation in urban environments. In that context there is much room for improvement in urban spaces.

3.1.2. On Crowd-sensing with Mobile, Wearable and IoT Devices across Smart Cities

***Challenges**:* One of the important building blocks of smart cities is the sensors that can be statically deployed around cities. They enable monitoring of key parameters about the city, such as noise, air pollution, traffic levels, or availability of parking places. Sensors are mostly used as data loggers, and raw data from the nodes can be transmitted, mostly through wireless interfaces, to a server or cloud where further inference of the data takes place. Data can only be monitored, visualized and shared with the stakeholders, or actions can be taken according to the incoming data as a response by the governors of the cities. Deploying the sensors around a city and in large quantities presents the challenge of installing a complex and costly infrastructure. In addition, questions such as how to power the devices and maintain/replace them in case of failures, are arising. Cities already face the challenge of replacing old infrastructures, such as water distribution and sewer infrastructures, and installing a new fracture is challenging. There is thus a requirement to use easy-to-deploy/maintain/deploy sensing systems.

Technologies and Solutions: Crowd-sourced or participatory sensing enables the collecting of ambient or personal data, particularly from the devices carried/worn/owned by people. Smartphones, wearables and IoT devices are the ideal platforms for sensing applications with the integrated rich set of sensors, their ubiquity, ease of use, support for mobility, and wireless interfaces (Incel and Ozgovde, 2018). Consider the sensors available in today's smartphones: microphone, camera, GPS, light, accelerometers, gyroscope, compass, GPS, pressure, temperature, magnetic field, humidity and heart rate, among others. The sensor set can be extended by those not integrated into the device but can be connected via wireless interfaces, such as gas and occupancy sensors. They can also communicate and complement existing, statically distributed sensing infrastructures. These devices gather ambient information and collect data about the context, such as activities, location, emotional states and health status, of the users carrying them. Users can also act as sensors by reporting their observations (Berntzen et al., 2016) through app interfaces. Programming such devices is easy, and the applications can be delivered to large populations worldwide through app stores. Hence, they enable global mobile sensor networks.

Typical applications of crowd-sourced systems in smart cities include environmental monitoring, traffic and transportation monitoring, and monitoring road conditions such as detecting road obstacles. Normally these devices are personal, and the sensing applications are for personal purposes, such as step counters, fitness tracking and well-being monitoring. However, context recognition of crowds and communities rather than individuals enables a new set of application domains in urban planning and transportation. By monitoring what is happening in urban environments, for example, it will be possible to discern those regions' typical/routine actions: which regions in the city are used and for which activities? By analyzing common activities, transportation modes in certain areas, suitable areas, and times for cycling, for example, can be marked on maps. Alternatively, extraordinary situations can be monitored, and possible emergency or disaster situations can be detected: what if many users start running in an area where people normally sit or walk? In addition, people's transportation modes such as cycling, car/bus and train/metro, can be tracked, thus laying the groundwork for applications such as extracting transportation-type maps of cities.

Open Issues: The use of crowdsensing via the devices carried/worn/owned by people for urban sensing is not new (Lane et al., 2010). There are still open issues to be considered for the practical implementation of smart city applications: *i) Respecting the privacy of users*. The devices considered are mostly used for personal purposes, and using the data for large-scale applications should not violate privacy. Regarding privacy, people's persuasion to share data is another challenge. *ii) The target devices are operating with a battery, and they are for personal use.* Battery and power management are important. They are also resource constrained in terms of computational capability. Running complex data processing and machine learning tasks may not be possible using such devices, and solutions such as edge computing or simplification of tasks can be utilized. *iii) The data processing is often offloaded to a server/cloud.* However, users may not be willing to upload their data. If possible, data can be processed in the device, but in that case, for example, a machine learning model trained for a specific device may not benefit from data from other devices. In this regard, distributed machine learning tasks such as federated learning are gaining attention from the research community.

To achieve the desired results, designers must collect and manage local and remote sensing data and adopt a user-centered approach that prioritizes the well-being of individuals. Nudges or subtle environmental cues that encourage positive behavior can also be incorporated into the design of public spaces to promote healthy habits, such as walking or socializing. In addition, smart layouts and sound systems can further enhance the safety and accessibility of public spaces.

3.1.3. On Mobility and Transportation

Challenges: As the social economy develops there is a rapid increase in both the global population and private automobiles. The increasing demand for mobility burdens the existing transportation infrastructure, resulting in increased road accidents, congestion, and inefficient use of energy resources, consequently causing environmental, economic and societal impairments. Rather than building more roads, a feasible solution therefore involves more efficient use of currently available means of transportation. The development of Cooperative Intelligent Transportation Systems (C-ITS) technologies can contribute to this goal by enabling more efficient planning of transportation and logistics in addition to regulating traffic flow, throughput and its safety.

Technologies and Solutions: In traffic, automated vehicles need to interact with other vehicles, bicycles, pedestrians and other road users, as well as with IoT services (including via Road-Side-Units), over Dedicated Short Range Communication (DSRC) or 5G-V2X networking (Zhang et al. 2023). Information exchange between Connected Automated Vehicles (CAVs) through Vehicle-to-Vehicle (V2V) and Vehicle-to-Infrastructure (V2I) wireless communication enables automated vehicles to cooperate and interact within their (socio)-cyber-physical environments. Connected automated vehicles (CAVs), forming the so-called *Internet of Vehicles*, are predicted to transform transportation and urban life (Loke, 2019). Other automated vehicles, such as self-driving wheelchairs and self-driving motorcycles, are also being developed. In addition, cooperative Intelligent Transport Systems (e.g. cooperative driving) is an active area of research.

- *On Cooperative Logistic Delivery with UAV and AGV:* The demand for faster, less energy-consuming and autonomous delivery methods is increasing in the logistics industry within the scope of last-mile delivery. Cooperative delivery mission planning for the UAV and the AGV was considered an alternative solution for the last-mile delivery missions instead of conventional methods. Synchronization of Unmanned Aerial Vehicles (UAV) with Automated Ground Vehicles (AGV) provides the advantage of delivering hard-to-reach places. In addition, heterogeneous mobile platforms offer variability of strategies considering e.g. operational time, delivery time and fuel consumption. UAVs offer several advantages compared to conventional delivery methods. Since the UAVs cruise through the air, the delivery is independent of roads, traffic lights, speed limits and pedestrian crossings. Especially in urban areas, too many external factors influence ground deliveries.

- *On Cooperative Adaptive Cruise Control:* In today's traffic, limited human perception of traffic conditions and human reaction characteristics constrain the lower limits of achievable safe intervehicle distances. In addition, erroneous human driving characteristics may cause traffic flow instabilities, which result in so-called shockwaves. For example, in dense traffic conditions, a single driver overreacting to a momentary disturbance (e.g. a slight deceleration of the vehicle immediately in front) can trigger a chain of reactions in the vehicles following. The amplification of such a disturbance can bring the traffic to a full stop kilometers away from the disturbance source, and cause traffic jams for no apparent reason. In this respect, attenuating disturbances across the vehicle string, covered by string stability, is an essential requirement for vehicle platooning. Wireless information exchange between vehicles provides the means for overcoming sensory limitations of human- or ACC-operated vehicles and, therefore, can significantly improve the traffic flow, particularly on highways. Cooperative Adaptive Cruise Control regulates inter-vehicle distances to achieve improved traffic flow stability and throughput. CACC extends the currently available Adaptive Cruise Control (ACC). Improved performance is achieved by utilizing wireless information exchange between vehicles through Dedicated Short Range Communication (DSRC) in addition to local sensor measurements (Öncü et al., 2012; Öncü et al. 2014). The general objective of a Cooperative Adaptive Cruise Control (CACC) system is to pack the driving vehicles together as tightly as possible to increase traffic flow, while preventing the amplification of disturbances throughout the string, known as string instability. Potential fuel benefits are high, especially for trucks, due to their larger frontal surface area within a platoon where vehicles are closely packed (Nieuwenhuijze et al., 2012). As a result, aerodynamic losses are reduced, especially during highway operations. For example, in (Alam et al., 2010), the inter-vehicle distance between two heavy-duty trucks varied between 3-10m, resulting in a fuel reduction of 10-12% for the following truck and a fuel reduction of 5-10% for the leading truck.

Open Issues: Decision-making under conflicting objectives and liability, such as autonomy versus heteronomy, must be considered when examining automated vehicles. It is not enough to view these vehicles as autonomous entities that only sense and react to their immediate environments and goals; they should also be seen as a form of social AI that can develop cooperative awareness and behavior. To facilitate this cooperative awareness, shared perception is necessary. This can be achieved through a shared ontology called CAM, which enables vehicles to exchange information, not only about their immediate dynamic states, but also their intentions, dynamic capabilities and limitations, and perceived environments. Cooperative map generation tools such as ADASIS (Ress et al., 2008) and SENSORIS (Eichberger, 2017) can also aid in this process by allowing for shared data that reduces the sensing and computation requirements of individual vehicles, thereby promoting the adoption of new technologies.

3.2. Neurotechnologies in smart cities for resilience and sustainability

3.2.1. On Waste Management

Challenges: Developing built environments that meet people's needs while avoiding social and environmental impacts is a challenge (Hamilton et al., 2002). There is therefore a need for concerted action in maintaining a virtual cycle between human well-being and ecosystem health. In this context, the issue of urban waste, an unprecedented amount of waste produced in cities, is becoming increasingly pressing as cities grow in size and population. However, current waste management practices face several challenges, including inadequate infrastructure, limited funding and public awareness about the importance of waste reduction and recycling. To address this we need new solutions that prioritize waste reduction, recycling and proper disposal practices, while also considering the unique needs and characteristics of each urban environment.

Technologies and Solutions: Neurotechnology applications in smart cities for using the Internet of Things (IoT) in waste management and classifications. RFIDs, sensors, and cameras are used with a special emphasis on dynamic route optimization of waste collection vehicles while allowing citizens to access real-time data of waste collection processes. These sensors also aid in automated waste segregation to increase recycling efficiency. In particular:

- *On the Internet of Things*: Smart waste management utilizes various Internet of Things (IoT) applications to improve waste collection, separation, data monitoring and illegal disposal mapping. Sensors that measure different parameters such as weight, temperature, or volume of waste, microcontrollers and cloud technologies that gather, analyse and store data are used to promote waste collection (Shyam et al., 2017; Srikanth et al., 2019). Garbage bin locations, as well as routes of collection vehicles, are optimized by RFIDs (Radio Frequency Identification), cameras, drones, WSNs (Wireless sensor networks) and GPS (Global Positioning System) to increase citizens' convenience and financial benefits to the waste management system (Sosunova and Porras, 2022; Topaloglu et al., 2018). Sensors and actuators also aid in automated waste segregation to increase recycling and recovery efficiency (Esmaeilian et al., 2018; Batais et al., 2020). Utilizing ICT contributes to real-time data monitoring and communication between members, hence supporting decision-making in waste management systems (Hannan et al. 2015; Akram et al. 2021). Additionally, detecting and tracking illegal waste disposal that poses a major threat to the ecosystem is crucial for improving waste management. These illegal waste-handling sites are monitored and mapped by remote sensing techniques, sensors and spatial data integration to geographic information systems (GIS) (Karimi et al., 2022; Sliusar et al., 2022). The integration of such technologies to waste management systems can positively influence the environment and social life, thus encouraging citizens' adaptation to the smart city concept.

- *On Sensors:* Low-cost sensors and wireless sensor networks monitor environmental parameters such as water quality, air quality, agriculture systems, hazardous materials, odour and noise nuisance. Water quality measures including pH, dissolved oxygen (DO), conductivity and dissolved metal ions, are observed in real time by solid-state sensors (Chawla et al., 2020). Low-cost air quality sensors are employed to record outdoor and indoor air quality and personal exposure levels to mitigate the effects of air pollution (Kang et al., 2022). The sensors used in agriculture, with a particular emphasis on precision agriculture, provide real-time monitoring of crops, soil quality, weather conditions and characteristics below and above the ground to increase the productivity and quality of the product (Kumar et al., 2018; Ragaveena et al., 2021). Using sensors to detect hazardous substances in different ecosystems can protect human life and the environment from the detrimental impacts of these materials (Zhao et al., 2022). Gas sensors and electronic noses are used to identify odour nuisance (Jonca et al., 2022), while both level and source of noise can be detected through sensors and wireless sensor networks, enabling citizens to avoid the negative consequences of these issues (Picaut, 2020). The availability of such sensors supports citizen science with robust and low-cost sensor and networking technology. In addition, such networks offer improved data coverage (especially in remote or data-scarce regions).

- *On Satellite Data:* Remote sensing technologies are also used in ecosystem assessments. For example, public data supplied by the Earth Observations (EO) data monitor ocean temperature, quantify disturbance activities, monitor vegetation health, detect land change and analyse the impacts of climate change. The publicly available EO data has applications in agriculture, regional planning, marine studies and forestry. In addition, the availability of such spatially and temporally continuous data increases the precision of ecosystem assessments.

Open issues: Key issues related to environmental monitoring are spatial coverage, time resolution and cost of implementation. Some critical indicators such as land and water surface temperature, ground vegetation and change in water color can be observed from satellite images with wide spatial coverage; however, the frequency of measurements is sensitive to atmospheric conditions, with gaps on cloudy days. In addition, the spatial resolution of satellite imagery is currently 30m-1km resolution, useful for regional studies, but ground verification might be required for local studies.

4. Future research directions and concluding remarks

This paper started by reviewing the current state of knowledge in the literature on using neuroscience and neurotechnological solutions in smart cities based on bibliometric analysis. It then explored some emerging themes in greater detail, mainly in relation to issues where there is urgent need for action, namely on human health and well-being and on resilience and sustainability, which are also very much in line with SDGs. Understanding these emerging themes around neuroscience and neurotechnology related to smart cities is critical in identifying novel challenges in this field and discussing where we need to go, considering human health and well-being and sustainability purposes.

4.1. On identifying novel challenges and opportunities

To what extent does the current state of affairs in the smart city agenda directly influence and contribute to addressing societal needs and environmental concerns and achieving SDGs? Can we better align adaptive resource use and context-aware decision-making-focused research and practices with societal and environmental goals and principles? It is true that ICT technologies and their infrastructures are crucial means for developing smart cities. However, there is little reason to assume that human well-being and sustainability objectives will naturally be served by the free play of uncontrolled forces and actors' will. A holistic understanding of smartness requires the active involvement of stakeholders and the inclusion of dimensions beyond technology that can purposefully solve urban challenges. Overall, how the relationships between technology, community, and urban space will develop over time seems to be a key future research agenda.

From a societal and governance point of view, the role of institutional arrangements will be central when selecting, adopting, designing, implementing, and using these technologies. The analysis presented here made it clear that we still have some way to go, as there is a need to better establish direct links to the SDGs and embrace a multi-faceted approach fostering interdisciplinary collaboration going hand-in-hand with systemic governance. Overall, to address any urban challenge effectively in line with SDGs and the vision of a smart agenda, society needs discuss in detail how we can generate reliable data, process information, promote transparency, and ensure accountability. Equally, new institutions must be established to enhance public decision-making processes involving different social groups living in the city.

Hence, the deployment and successful implementation of smart city initiatives also depend on the availability of an enabling environment where there is citizen participation and active engagement with the community. In this context, new educational and research programs such as Neurotech-EU and lifelong learning for capacity building and citizen engagement in smart city projects, are important for healthy development of smart initiatives. Appropriate governance mechanisms should also be in place to evaluate choices, and outcomes and deliberate on key questions of phronetic planning (Flyvbjerg, 2001), such as "where are we going", "is this development desirable" and "what, if anything, should we do about it?"

4.2. Addressing legal and ethical concerns

Two other concerns that are important in smart city development are legal frameworks and ethics, since the way and the extent to which they are adopted would make a difference in smart city outcomes. Moreover, in the presence of scientific and technical uncertainties, disagreements regarding the visions of smart cities and associated policies will become particularly apparent. When uncertainties and social controversies hinder

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consensus on factual matters, it becomes crucial to establish and protect the legitimacy of diverse viewpoints and value commitments while addressing issues effectively. Therefore, it is very important to prioritize the development of laws and ethics that are aligned with emerging technologies and their implications. This will ensure that technological advancements are deployed in a way that is both socially responsible and sustainable.

Overall, there is consensus on the fact that by creating platforms that allow for the sharing of resources and knowledge, technology can be harnessed as a force for positive change in urban settings. However, it is also well known that excessive or irresponsible use of technology, a digital divide, or ineffective citizen participation may always compromise SDGs. Therefore, a comprehensive understanding of smartness necessitates moving beyond sole reliance on technological solutions and purposefully establishing coherent policies to improve human functionality and capabilities while respecting societal and environmental rights and ethics. Attention to detail will be essential, as disparities in the framing and implementing smart city initiatives will significantly influence policy outcomes in practice.

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Appendix – Cluster lists for Maps

Cluster Lists for General Map without disciplinary focus (Figure 4)									
Cluster 1 Keywords	**Occurrences**	**Cluster 2 Keywords**	**Occurrences**	**Cluster 3 Keywords**	**Occurrences**	**Cluster 4 Keywords**	**Occurrences**	**Cluster 5 Keywords**	**Occurrences**
smart city	9591	cloud computing	662	internet of things	4748	blockchain	754	LoRa	171
sustainability	470	edge computing	545	machine learning	2251	security	620	waste management	151
information and communication technology	337	wireless sensor networks	524	deep learning	798	privacy preserving	391	LoRaWAN	150
COVID-19	222	smart grid	398	intelligent transportation systems	656	cyber-physical systems	190	LPWAN	121
geographic information system	199	fog computing	335	artificial intelligence	649	cyber security	181		
smart mobility	194	vehicular ad hoc network	317	sensors	379	authentication	157		
sustainable development	183	5G	294	convolutional neural network	330	smart contracts	141		
urban planning	182	energy efficiency	254	artificial neural network	274	Industry 4.0	134		
digital twin	172	electric vehicles	239	smart home	249	healthcare	125		
digitalization	168	unmanned aerial vehicle	227	anomaly detection	139				
simulations	158	software defined network	218	long short-term memory	139				
governance	157	optimization	206	object detection	137				
e-government	154	clustering	187	smart parking	135				
transportation	145	renewable energy	178	predictive modeling	131				
mobility	144	smart building	170	classification	124				
technology	144	crowdsensing	151	radio frequency identification	117				
crowdsourcing	136	internet of vehicles	143	Raspberry Pi	117				
autonomous vehicles	133	smart community	126	computer vision	113				
urbanization	133	quality of service	123	Arduino	110				
open data	131	energy management	121	air quality	104				
mobile application	127	resource allocation	118	image processing	103				
sustainable city	126	genetic algorithms	115	air pollution	100				
innovation	124	reinforcement learning	114	support vector machine	98				
building information modeling	116	smart meters	108	smart environments	96				
modeling	116	energy consumption	101	global positioning system	86				
smart governance	110	routing	90	intrusion detection	86				
public transport	106	energy	87						
social media	97								
infrastructure	96								
resilience	92								
interoperability	91								
ontology	91								
sustainable smart city	90								
architecture	86								

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Cluster Lists for Computer Sciences Map (Figure 5)									
Cluster 1 Keywords	**Occurrences**	**Cluster 2 Keywords**	**Occurrences**	**Cluster 3 Keywords**	**Occurrences**	**Cluster 4 Keywords**	**Occurrences**	**Cluster 5 Keywords**	**Occurrences**
cloud computing	581	smart city	6584	internet of things	3959	blockchain	645	LoRa	143
edge computing	501	artificial intelligence	518	machine learning	1851	security	542	LoRaWAN	133
wireless sensor networks	438	sustainability	225	deep learning	693	privacy preserving	339	waste management	120
fog computing	303	information and communication technology	190	intelligent transportation systems	533	cyber-physical systems	157	LPWAN	108
vehicular ad hoc network	283	COVID-19	132	sensors	298	cyber security	155	smart meters	66
smart grid	265	geographic information system	123	convolutional neural network	292	authentication	141		
5G	257	digital twin	122	artificial neural network	235	smart contracts	123		
software defined network	199	crowdsourcing	114	smart home	200	healthcare	95		
unmanned aerial vehicle	186	smart mobility	111	anomaly detection	126				
energy efficiency	179	e-government	109	long short-term memory	117				
optimization	149	digitalization	101	object detection	117				
clustering	147	mobile application	101	smart parking	112				
electric vehicles	143	open data	100	predictive modeling	109				
crowdsensing	136	mobility	99	classification	104				
internet of vehicles	126	smart community	96	computer vision	102				
simulations	126	Industry 4.0	93	Raspberry Pi	102				
smart building	120	transportation	92	radio frequency identification	101				
quality of service	110	ontology	82	Arduino	94				
reinforcement learning	102	smart environments	80	image processing	89				
resource allocation	99	urban planning	78	support vector machine	80				
genetic algorithms	96	social networks	77	deep neural network	76				
renewable energy	95	governance	76	intrusion detection	75				
autonomous vehicles	89	interoperability	74	air quality	70				
modeling	88	public transport	74	global positioning system	70				
routing	80	natural language processing	73	traffic congestion	69				
energy consumption	76	augmented reality	72						
energy management	73	smart governance	71						
multi-agent system	70	technology	69						
wireless communication	69	sustainable development	67						
particle swarm optimization	68	social media	66						
architecture	67								
federated learning	67								

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Cluster Lists for Engineering Map (Figure 6)									
Cluster 1 Keywords	**Occurrences**	**Cluster 2 Keywords**	**Occurrences**	**Cluster 3 Keywords**	**Occurrences**	**Cluster 4 Keywords**	**Occurrences**	**Cluster 5 Keywords**	**Occurrences**
internet of things	2337	blockchain	348	wireless sensor networks	286	smart city	3957	artificial intelligence	319
machine learning	1010	security	312	smart grid	219	sustainability	185	cyber-physical systems	97
deep learning	355	cloud computing	308	electric vehicles	144	information and communication technology	140	cyber security	85
intelligent transportation systems	316	edge computing	247	energy efficiency	141	smart mobility	84	digital twin	74
sensors	222	privacy preserving	176	optimization	114	sustainable development	74	simulations	71
convolutional neural network	150	vehicular ad hoc network	166	renewable energy	100	transportation	70	autonomous vehicles	69
smart home	129	fog computing	159	LoRa	98	COVİD-19	66	Industry 4.0	69
artificial neural network	127	5G	150	smart building	97	digitalization	62	building information modeling	66
predictive modeling	75	unmanned aerial vehicle	126	energy management	78	healthcare	58	geographic information system	63
waste management	73	software defined network	90	LoRaWAN	77	sustainable city	56	modeling	52
long short-term memory	72	clustering	77	LPWAN	76	urban planning	55	augmented reality	45
object detection	72	authentication	73	smart meters	73	public transport	51	crowdsourcing	43
radio frequency identification	72	internet of vehicles	68	smart community	63	technology	51		
smart parking	71	crowdsensing	65	microgrid	58	interoperability	47		
Raspberry Pi	65	quality of service	65	energy consumption	56	urbanization	46		
Arduino	58	resource allocation	60	genetic algorithms	54	mobility	45		
classification	55	smart contracts	58	reinforcement learning	54	sustainable smart city	45		
image processing	54	wireless communication	47	energy	46	e-government	41		
computer vision	52	architecture	44	particle swarm optimization	44	resilience	41		
anomaly detection	51	application	43	energy harvesting	43				
mobile application	51	reliability	43	demand response	41				
intrusion detection	49	drones	41						
support vector machine	48								
global positioning system	46								
air pollution	43								
deep neural network	43								

Cluster Lists for Social Sciences Map (Figure 7)									
Cluster 1 Keywords	**Occurrences**	**Cluster 2 Keywords**	**Occurrences**	**Cluster 3 Keywords**	**Occurrences**	**Cluster 4 Keywords**	**Occurrences**	**Cluster 5 Keywords**	**Occurrences**
internet of things	575	smart city	2364	intelligent transportation systems	112	geographic information system	72	social media	36
machine learning	498	sustainability	191	smart mobility	58	open data	44	smart tourism	28
blockchain	125	information and communication technology	130	sensors	54	building information modeling	41	natural language processing	21
artificial intelligence	116	urban planning	95	urbanization	51	crowdsourcing	38		
deep learning	110	COVID-19	87	innovation	50	virtual reality	27		
cloud computing	82	governance	84	city	48	augmented reality	23		
privacy preserving	81	sustainable city	68	transportation	47	crowdsensing	23		
security	80	sustainable development	66	mobility	42	smart campus	23		
smart grid	69	e-government	62	infrastructure	38	data visualization	22		
wireless sensor networks	68	digitalization	55	autonomous vehicles	36	ontology	21		
edge computing	57	technology	53	planning	33				
smart home	53	sustainable urban development	52	public transport	32				
convolutional neural network	48	smart governance	46	case studies	31				
artificial neural network	47	urban governance	44	modeling	29				
5G	42	citizen participation	42	decision making	25				
sustainable smart city	40	urban development	42	management	24				
unmanned aerial vehicle	40	resilience	35	mobile application	24				
electric vehicles	39	India	31	visualization	24				
energy efficiency	38	China	29	urban mobility	23				
clustering	36	digital twin	28	radio frequency identification	22				
cyber security	36	climate change	27	bibliometric analysis	21				
renewable energy	35	pandemic	27	network	21				
optimization	34	smart community	27	simulations	21				
cyber-physical systems	32	smart urbanism	27						
fog computing	32	participation	26						
software defined network	31	local government	24						
smart building	30	quality of life	24						
predictive modeling	27	urban policy	23						
classification	26								
long short-term memory	25								
Industry 4.0	24								
object detection	23								
particle swarm optimization	23								
smart contracts	22								
architecture	21								
smart environments	21								

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Cluster Lists for Environmental Sciences Map (Figure 8)									
Cluster 1 Keywords	**Occurrences**	**Cluster 2 Keywords**	**Occurrences**	**Cluster 3 Keywords**	**Occurrences**	**Cluster 4 Keywords**	**Occurrences**	**Cluster 5 Keywords**	**Occurrences**
smart city	862	sustainability	113	internet of things	183	digitalization	25	renewable energy	28
information and communication technology	53	urban planning	42	machine learning	118	smart mobility	22	smart grid	28
sustainable development	47	artificial intelligence	40	intelligent transportation systems	35	urban development	18	blockchain	26
sustainable city	45	governance	28	cloud computing	29	security	16	electric vehicles	21
COVID-19	32	geographic information system	27	sensors	23	clustering	12	wireless sensor networks	16
innovation	27	technology	25	deep learning	22	energy	12	smart home	14
sustainable smart city	27	waste management	22	artificial neural network	13	Industry 4.0	12	5G	12
sustainable urban development	24	infrastructure	21	arduino	12	sustainable transport	10	e-government	10
city	22	transportation	19	image processing	12	3D city model	9	energy management	9
urbanization	21	building information modeling	17	convolutional neural network	11	privacy preserving	9	cyber security	8
climate change	20	energy efficiency	15	global positioning system	11	environment	8	microgrid	8
circular economy	19	optimization	15	data visualization	10	visualization	8		
resilience	18	bibliometric analysis	13	LoRa	9				
smart governance	17	planning	13	unmanned aerial vehicle	9				
air pollution	16	built environment	12	global system for mobile communication	8				
air quality	15	mobility	12	long short-term memory	8				
sharing economy	13	smart building	12	smart campus	8				
urban governance	13	sustainable development goals	12	smart meters	8				
India	11	case studies	11						
mobile application	11	quality of life	11						
urban transformation	11	public space	10						
pandemic	10	smart urbanism	10						
smart technologies	10	decision making	9						
smart tourism	10	indicators	9						
eco-city	9	policy	9						
social innovation	9	simulations	9						
social media	9	accessibility	8						
energy transition	8	local government	8						
remote sensing	8								
urban heat island	8								
urban policy	8								

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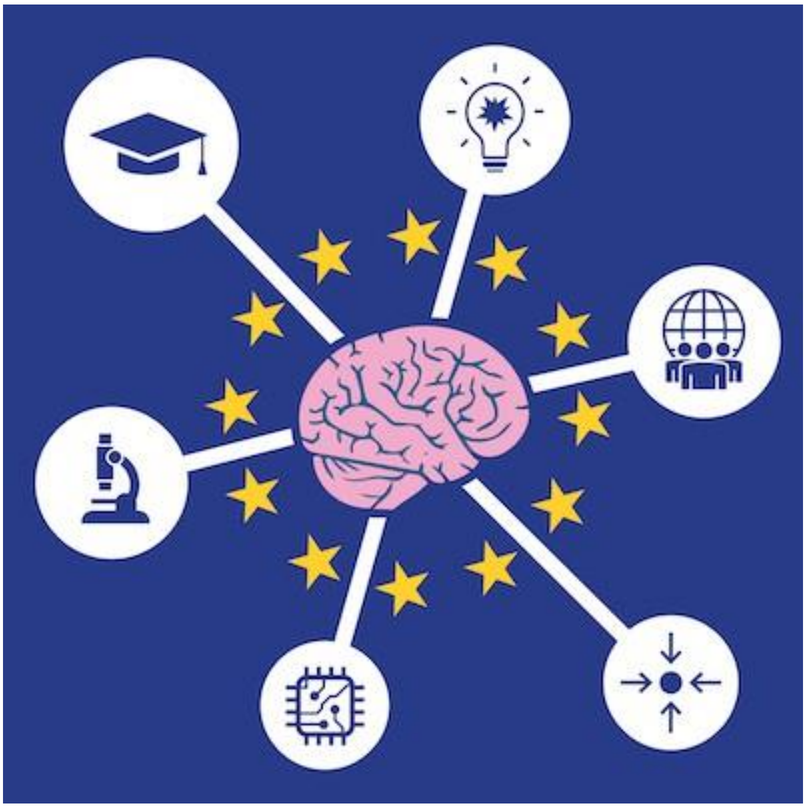
Neurotech^{EU}

The European University of Brain and Technology



[D6.2]
[White Paper on Neurochallenges in Societal Innovation]

Deliverable information	
Work package number	WP6
Deliverable number in work package	D6.2
Lead beneficiary	BOUN
Due date (latest)	30/04/2023

Document History		
Version	*Description*	*Date*
1.0	Draft by BOUN, based on online meetings between members of the WP6 subgroup "Understanding Societal Challenges (USC)" (see Appendix 1 for members of subgroup)	01/02/2023
1.1	Final version	12/04/2023

Executive summary

Futuristic universities like Neurotech[EU] and the technological innovations they advance will not only shape society, but also serve and require support from society. Yet, neuroscientists, neuro-engineers and other innovators do not typically reach out to the public to better understand and address their challenges. Therefore, the overarching goal of this deliverable is to understand our Neurotech[EU] nations' perspectives about neuro-technological advances, and to integrate these perspectives into the scientific process. We hypothesize that our efforts in the advancement of neuro-technologies do not completely meet the challenges of our Neurotech[EU] nations or are understood by them, resulting in mistrust and non-acceptance. To test our hypothesis, we will generate statistical data related to i) the population characteristics of our Neurotech[EU] nations and ii) their needs for, interest in, access to, knowledge of, and trust in neuro-technologies, and their views on policymaking regarding the development of new neuro-technologies. To address i), we have developed a form that asks about the characteristics of our nations ('Understanding Societal Challenges – Demographics (USCD)' – refer to Appendix 2). To address ii), we have developed a trans-national questionnaire ('Understanding Societal Challenges Questionnaire (USCQ)' – refer to Appendix 3) that asks about the 6 interest domains (needs, interest, access, knowledge, trust, and views on policymaking). The resulting data will allow for comparisons between different nations and between different demographics within a nation. The study will launch following the pilot testing of our forms within the Neurotech[EU] community and the approvals of our study from the relevant ethics committees. Changes in societal perspectives about neuro-technological advances, e.g. as a result of information campaigns and continuing education initiatives, will be studied longitudinally. The data collected in this study will help elucidate the challenges of our Neurotech[EU] nations related to neuro-technological advances. The data will inform the Neurotech[EU] research community about societal needs, interests, and trust issues related to neuro-technologies, among other, and will allow the researchers to provide better service and help innovate society through public outreach.

Introduction

Futuristic universities like NeurotechEU and the technological innovations they advance will not only shape society, but also serve and require support from society. Yet, neuroscientists, neuro-engineers and other innovators do not typically reach out to the public to better understand and address their challenges. Therefore, the overarching goal of this deliverable is to understand our NeurotechEU nations' perspectives about neuro-technological advances, and to integrate these perspectives into the scientific process. We hypothesize that our efforts in the advancement of neuro-technologies do not completely meet the challenges of our NeurotechEU nations or are understood by them, resulting in mistrust and non-acceptance. To test our hypothesis, we will generate statistical data related to i) the population characteristics of our NeurotechEU nations and ii) their needs for, interest in, access to, knowledge of, and trust in neuro-technologies, and their views on policymaking regarding the development of new neuro-technologies. To address i), we have developed a form that asks about the characteristics of our nations ('Understanding Societal Challenges – Demographics (USCD)' – refer to Appendix 2). To address ii), we have developed a trans-national questionnaire ('Understanding Societal Challenges Questionnaire (USCQ)' – refer to Appendix 3) that asks about the 6 interest domains (needs, interest, access, knowledge, trust, and views on policymaking). The resulting data will allow for comparisons between different nations and between different demographics within a nation. The study will launch following the pilot testing of our forms within the NeurotechEU community and the approvals of our study from the relevant ethics committees. Changes in societal perspectives about neuro-technological advances, e.g. as a result of information campaigns and continuing education initiatives, will be studied longitudinally.

Material and methods

Participants

Participants will consist of NeurotechEU researchers (n = 5 per nation) for initial proof- and acceptance reading of our materials. For reliability testing of our forms, we will recruit n = 100 participants per nation who will provide their responses online. We will collect 1000+ data from a representative sample of each nation for a final data set. We will determine the recruitment strategy for our final sample in a work group meeting in February, 2023. While many participants can be reached online in a short time, such a sample may not be representative. It was suggested to find the participants in their day-to-day environments. A random sampling procedure would be ideal. The participants will not be promised any rewards a priori but will be offered a personality analysis as a free gift after the responses are received. The participants will provide written informed consent (refer to Appendix 4) before providing their data. All procedures will be approved by our local ethics committees and conducted in accordance with the Declaration of Helsinki.

USCD

The USCD is shown in Appendix 2. Responses to this form will help us gather information on the population characteristics of our NeurotechEU nations. Our expectation is that demographics, such as age, sex, education, upbringing, and belief systems influence attitudes about futuristic enterprises and technological advances. We will therefore not only compare our nations' demographics with each other, but will also compare different demographics within a nation to better understand where, as scientists, we could do better connecting with and serving the public. 'Doing better' could involve innovating for specific needs, educating, and improving rapport through public outreach. We have constructed the USCD for trans-national studies among NeurotechEU nations, having considered our diverse educational systems, cultural norms, and sensitivities.

USCQ

The USCQ is shown in Appendix 3. Responses to this questionnaire will help us better understand societal challenges related to neuro-technological advances. Specifically, we will inquire about our nations' needs for, interest in, access to, knowledge of, and trust in neuro-technologies, and their views on policymaking regarding the development of new neuro-technologies. We expect to find gaps between our efforts as scientists in the advancement of neuro-technologies and the ways that our societies relate to them. We have constructed the USCQ as a trans-national questionnaire that should be applicable to any of our NeurotechEU nations following the translation into the respective official language.

Past and future

So far, the main work group consisted of NeurotechEU members from BOUN (project lead), OXF (past), RU, UMH, KI, UBO, and UD (refer to Appendix 1). Next, we will seek support from principal investigators (PIs) of the remaining NeurotechEU countries as well.

The current work group has developed the USCD and USCQ in seven online meetings (minutes are available, if desired), which took place between November 2021 – January 2023. We will continue to meet approximately once per month to resolve any remaining issues and follow the study as it unfolds.

We have agreed to test the English versions of our forms with NeurotechEU researchers for proof- and acceptance reading. We expect to make only small changes hereafter. Next, the PIs will lead the effort to translate the English forms into the official languages of the respective NeurotechEU countries. Each partner will then seek approval for the study from the relevant ethics committee. Using the translated material, each NeurotechEU country will collect data from 100 participants online for reliability analysis. This will give credence to the reproducibility and thus quality of the questions asked. We expect to make only small changes as a result of this analysis. Finally, we will collect 1000+ data from a representative sample of every NeurotechEU nation. We will discuss recruitment strategies in our upcoming meeting in February, 2023.

Dissemination

We are currently drafting a first manuscript to be submitted to Frontiers in Neuroscience, specifically, a collection on The NeurotechEU (https://www.frontiersin.org/research-topics/47939/neurotechnology-state-of-the-art-perspectives-and-research-along-the-lines-of-dimensions-and-neuroch). In this manuscript, we will publish the methodology of our study upfront. In a follow-up submission, we will publish the results of the study. Once the manuscript is submitted to Frontiers in Neuroscience, any content related to the project will be made visible through NeurotechEU channels and by partners at the local level.

• Appendix 1: The NeurotechEU-WP6 project subgroup "Understanding Societal Challenges (USC)"

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PIs from the other Neurotech^EU nations will be recruited.

● Appendix 2: USCD

Understanding Societal Challenges – Demographics (USCD)

From health and healthcare to learning and education, neuroscience shows great promise to become also an applied science that could benefit society and kindle a new economy in Europe. The European University of Brain and Technology (Neurotech^EU) aims to be the backbone of this new vision. Neurotech^EU was funded by the European Commission to create an ecosystem that fosters neuroscience education, research and innovation, and creates societal impact resulting from the development of new neuro-technologies.

Neurotech^EU is a network of 10 universities from across the European Union and Associated Member States: Radboud Universiteit (The Netherlands), Universidad Miguel Hernández de Elche (Spain), Karolinska Institutet (Sweden), Rheinische Friedrich-Wilhelms-Universität Bonn (Germany), **Boğaziçi Üniversitesi (Turkey)**, University of Oxford (The United Kingdom), Universitatea de Medicină și Farmacie „Iuliu Hațieganu” din Cluj-Napoca (Romania), Debreceni Egyetem (Hungary), Université de Lille (France), and Háskólinn í Reykjavík (Iceland), and over 250 associated partners consisting of companies, technology transfer offices, and regional innovation networks, among other.

As researchers of Neurotech^EU, our goal is to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process. <u>Your answers to this form</u> will help us generate statistical data related to the population characteristics of *Turkey* (insert your country). **The data will be compared with those from other Neurotech^EU countries. Please answer the questions as viewed by you from your country of residence today.**

Scroll for page 2

1. **I am _________ years old.**
2. **I am** □ male □ female □ other
3. **Education (check all that apply)**
    a. **number of years in school (other than university): __________**
    b. **university degrees (check all that apply):** □ Bachelor □ Master □ Ph.D.
4. **Mother's education**
    a. **number of years in school (other than university): __________**
    b. **university degrees (check all that apply):** □ Bachelor □ Master □ Ph.D.
5. **According to *TÜIK*, the mean annual equivalized (for size and composition) household income for *Turkey* in 2020 (calculated in 2021) was 37,400 TL net (3,116.67 TL per month). My income fell**

    □ below □ near □ above this national average
6. **Occupation: __________________**
7. **Marital status**

    □ Single □ Live with partner, not married □ Married □ Married, but separated □ Divorced □ Widowed
8. **Children**

    □ 0 □ 1 □ 2 □ 3 or more
9. **I was born in: ___________________**
10. **I consider myself to be a ___________________ national**
11. **I grew up (check all that apply)**

    □ rural □ urban, small city (< 300,000) □ urban, big city (> 300,000)
12. **My current environment is**

    □ rural □ urban, small city (< 300,000) □ urban, big city (> 300,000)
13. **Current resident country: ___________________**
14. **I have lived in □ countries for more than 3 months**

    □ 1 □ 2 □ 3 □ 4 □ 5 or more
15. **Native language: _________________**

16. I speak □ language(s) fluently

□ 1 □ 2 □ 3 □ 4 □ 5 or more

17. Do you identify as religious?

□ Yes □ No

18. Do you identify as political?

□ Yes □ No

19. My position in politics is

□ far-left □ left □ center-left □ center □ center-right □ right □ far-right
□ not interested □ don't want to say

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● Appendix 3: USCQ

Understanding Societal Challenges Questionnaire (USCQ)

From health and healthcare to learning and education, neuroscience shows great promise to become also an applied science that could benefit society and kindle a new economy in Europe. The European University of Brain and Technology (NeurotechEU) aims to be the backbone of this new vision. NeurotechEU was funded by the European Commission to create an ecosystem that fosters neuroscience education, research and innovation, and creates societal impact resulting from the development of new neuro-technologies.

NeurotechEU is a network of 10 universities from across the European Union and Associated Member States: Radboud Universiteit (The Netherlands), Universidad Miguel Hernández de Elche (Spain), Karolinska Institutet (Sweden), Rheinische Friedrich-Wilhelms-Universität Bonn (Germany), **Boğaziçi Üniversitesi (Turkey)**, University of Oxford (The United Kingdom), Universitatea de Medicină și Farmacie „Iuliu Hațieganu" din Cluj-Napoca (Romania), Debreceni Egyetem (Hungary), Université de Lille (France), and Háskólinn í Reykjavík (Iceland), and over 250 associated partners consisting of companies, technology transfer offices, and regional innovation networks, among other.

As researchers of NeurotechEU, our goal is to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process. Your answers to this form will help us generate statistical data related to our nations' needs for, interest in, access to, knowledge of, and trust in neuro-technologies, as well as our views on policymaking regarding their development. The *Turkish* data will be compared with those from other NeurotechEU countries. Please answer the questions as viewed by you from your country of residence today.

Neuro-technologies encompass a broad range of technologies that allow for a better understanding of how the brain works and help prevent, diagnose, and treat diseases of the brain. Examples include brain scanners and other medical devices, genetic technologies, and artificial intelligence.

I. Needs for neuro-technological advances

1) In your opinion, how important are neuro-technologies for society?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

2) Do you think society needs new neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

For which purpose(s) or condition(s)? ________________________

3) To what extent do neuro-technologies play a role in your life?

□ 1 not at all □ 2 slightly □ 3 moderately □ 4 very much □ 5 extremely

4) Do you have needs for new neuro-technologies?

□ 1 not at all □ 2 slightly □ 3 moderately □ 4 very much □ 5 extremely

For which purpose(s) or condition(s)? ________________________

5) Do you have any neurological condition?

□ yes □ no

If yes, to what extent does it compromise your daily functioning?

□ 1 not at all □ 2 slightly □ 3 moderately □ 4 very much □ 5 extremely

II. Interest in neuro-technological advances

6) How often do you read about neuro-technologies?

□ never □ once a year □ once a month □ once a week □ daily

7) How often do you read about the brain and behavior (any topic)?

□ never □ once a year □ once a month □ once a week □ daily

8) How often do you visit science museums or science exhibitions?

□ never □ once a year □ once a month □ once a week □ daily

9) How often do you watch web media (e.g. documentaries) about the brain and behavior?

□ never □ once a year □ once a month □ once a week □ daily

III. Access to neuro-technological advances

10) Where do you most commonly find out about science?

□ social media □ Wikipedia □ scientific websites □ scientific journals □ TV
□ newspapers □ radio □ ads or posters □ other □ I don't follow science

11) In how many languages do you follow scientific news?

□ native language □ in two languages □ in three languages □ in 4+ languages
□ I don't follow scientific news

12) Do you use Google translator or other online translators to access articles in foreign languages?

□ yes □ no

IV. Knowledge of neuro-technologies

13) Which of the following technologies are you familiar with? Check all that apply.

□ PC □ tablets □ mobile phones □ wearable technologies □ fitness tracker □ apple watch
□ oximeter □ health apps □ hearing aid □ bionics □ robotics □ machine learning
□ artificial intelligence □ ultrasound □ computed tomography □ X-ray □ EEG
□ magnetic resonance imaging □ positron emission tomography □ psychotropic drugs
□ pharmacotherapy □ implantable drug delivery systems □ deep brain stimulation
□ optogenetics □ CRISPR-Cas9 □ genetics □ behavior tracking software
□ nutrition apps, smart tools, websites, videos □ sleep apps □ exercise apps
□ exercise equipment □ motion-assistive devices □ virtual reality

14) Which of these technologies are currently important for your life or have been in the past? Check all that apply.

□ PC □ tablets □ mobile phones □ wearable technologies □ fitness tracker □ apple watch
□ oximeter □ health apps □ hearing aid □ bionics □ robotics □ machine learning
□ artificial intelligence □ ultrasound □ computed tomography □ X-ray □ EEG
□ magnetic resonance imaging □ positron emission tomography □ psychotropic drugs
□ pharmacotherapy □ implantable drug delivery systems □ deep brain stimulation
□ optogenetics □ CRISPR-Cas9 □ genetics □ behavior tracking software
□ nutrition apps, smart tools, websites, videos □ sleep apps □ exercise apps
□ exercise equipment □ motion-assistive devices □ virtual reality
□ other (please state): _______________

15) What do you <u>feel</u> about 'neuro-technologies'? And to what extent? <u>Please circle</u>.
1 = low 3 = intermediate 5 = high

Fear:	1	2	3	4	5
Uncertainty:	1	2	3	4	5
Control by external powers:	1	2	3	4	5
It's important for medicine:	1	2	3	4	5
It will facilitate our lives:	1	2	3	4	5
Joy:	1	2	3	4	5
Curiosity:	1	2	3	4	5
Relief:	1	2	3	4	5
Helplessness:	1	2	3	4	5
Anger:	1	2	3	4	5
Sadness:	1	2	3	4	5

□ I don't know
□ Other (please state): _____________

V. Trust in neuro-technological advances

16) Do you generally trust the news about neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

17) Do you generally trust neuro-technologies that comply with European regulations?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

18) Do you generally trust U.S. Food and Drug Administration (FDA)-approved neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

19) To what extent do you think that data obtained by neuro-technologies can reveal thoughts or feelings that you would rather keep to yourself?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

20) Do you believe that using neuro-technologies can be a threat to your privacy?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

21) To what extent do you think neuro-technologies might help you understand yourself better?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

22) Do you believe that data obtained by neuro-technologies can be used or abused for commercial purposes?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

VI. Perspectives on policymaking

23) Should policymakers follow the recommendations of scientists?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

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24) Should policymakers push for the development of new neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

25) Should policymakers monitor industry as it develops new neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

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Appendix 4: Informed Consent

Understanding Societal Challenges (USC) – Informed consent

From health and healthcare to learning and education, neuroscience shows great promise to become also an applied science that could benefit society and kindle a new economy in Europe. The European University of Brain and Technology (Neurotech^EU) aims to be the backbone of this new vision. Neurotech^EU was funded by the European Commission to create an ecosystem that fosters neuroscience education, research and innovation, and creates societal impact resulting from the development of new neuro-technologies.

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As researchers of Neurotech^EU, our goal is to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process. To achieve this goal, we will generate statistical data related to i) the population characteristics of our Neurotech^EU countries and ii) our needs for, interest in, access to, knowledge of, and trust in neuro-technologies, as well as our views on policymaking regarding their development.

Neuro-technologies encompass a broad range of technologies that allow for a better understanding of how the brain works and aim to prevent, diagnose, and treat diseases of the brain. Examples include brain scanners and other medical devices, genetic technologies, and artificial intelligence.

Scroll for page 2

Participant Number:

INFORMED CONSENT

I state that I am eighteen years of age or older and wish to participate in a program of research conducted by (*contact*) at the national level and by members of Neurotech^EU across nations.

The purpose of the research is **to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process.** First, I will answer demographic questions about myself. Then, I will fill out the 'Understanding Societal Challenges Questionnaire'. Data collection will take approximately 15 minutes.

I furthermore consent to allow the data that have been obtained of me to be used in the research. I understand that the data will be used for research purposes only, and no one else except the researchers will ever know my identity.

I understand that participant numbers will be used to identify the data, and that all written material that I contribute will be kept separate from my identity. As a result, it will not be possible to connect my name to my participant number.

I understand that the study is not designed to help me personally, but that the researchers **will generate statistical data related to i) the population characteristics of our Neurotech^EU countries and ii) our needs for, interest in, knowledge of, access to, and trust in neuro-technologies, as well as our views on policymaking regarding their development.**

I understand that I am free to ask questions or to withdraw from participation at any time without penalty.

Signature:

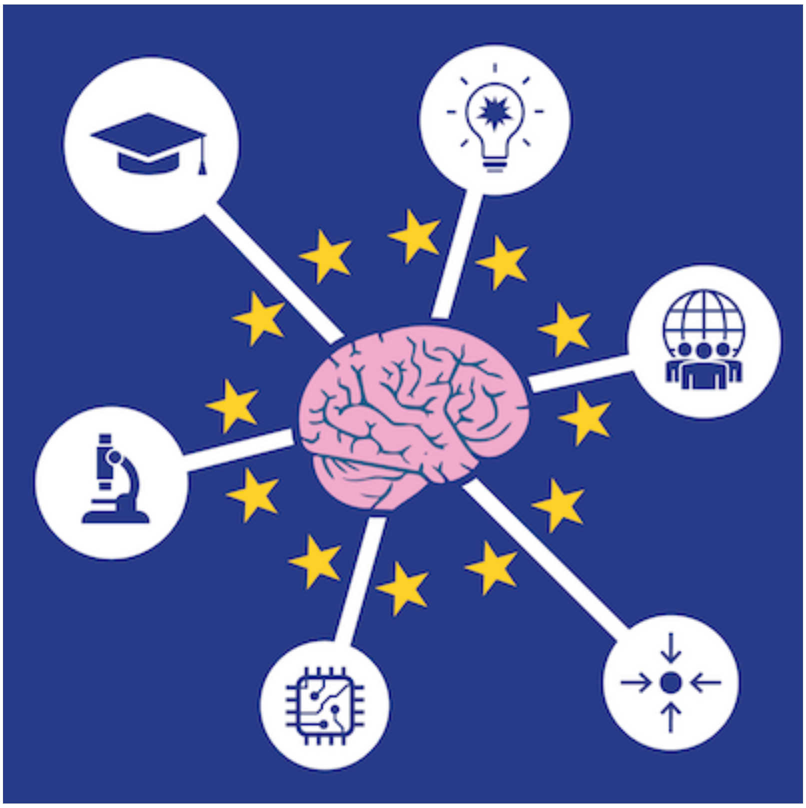
Date:

Email:

PI contact information

Neurotech^EU

The European University of Brain and Technology



[DL6.3]
[White paper on Neurochallenges in Societal Innovation]

Deliverable information	
Work package number	WP6
Deliverable number in work package	D6.3
Lead beneficiary	BOUN
Due date (latest)	31/10/2023

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Executive summary

Futuristic universities like The Neurotech^EU and the technological innovations they provide will shape and serve society, but will also require support from society. Positive attitudes about neuro-technologies will increase their reach within society and may also impact policy-making, including funding decisions. However, the acceptability rates especially of invasive neuro-technologies are quite low, and the majority of people are more worried than enthusiastic about them. The question therefore arises as to what neuro-technological advances should entail. In a rare effort to reach out to the public, we propose to conduct a trans-national survey with the goal to better understand the challenges of our Neurotech^EU nations. We aim to compare and contrast our nations specifically with respect to their perspectives on neuro-technological advances, i.e. their needs for, interests in, access to, knowledge of and trust in neuro-technologies, and whether these should be regulated. To this end, we have developed the first version of a new tool – the *Understanding Societal Challenges Questionnaire (USCQ)* – which assesses all six of these dimensions (needs, interest, access, knowledge, trust, and policy-making) and is designed for administration across EU/AC countries. In addition to trans-national comparisons, we will also examine the links of our nations' perspectives on neuro-technological advances to demographic and personality variables, for example, education and socio-economic status, size of the residential area, the Big Five personality traits, religiosity, political standings, and more. We expect that this research will provide a deeper understanding of the challenges that our nations are facing as well as the similarities and differences between them, and will also help uncover the variables that predict positive and negative attitudes toward neuro-technological advances. By integrating this knowledge into the scientific process, The Neurotech^EU may be able to develop neuro-technologies that people really care about, are ethical and regulated, and actually understood by the user.

1. Introduction

Neuro-technologies are tools and methods as diverse as cochlear implants, neuroimaging, deep brain stimulation, drug delivery systems and pharmaceuticals, machine learning and artificial intelligence, digital medicine and wearable sensors, mobile apps, and virtual reality games (Sveistrup, 2004; Friston, 2009; Macherey et al., 2014; Elenko et al., 2015; Habets et al., 2018, 2020; Heijmans et al., 2019; Adepu and Ramakrishna, 2021; Berisha et al., 2021; Chen et al., 2022; Park et al., 2022; Abd-alrazaq et al., 2023). Neuro-technologies are employed to diagnose and treat medical conditions like Parkinson's disease, stroke, chronic pain, obesity and depression, but can also help to prevent disease or enhance life quality by improving sleep and attention, relieving stress, supporting weight loss, and reducing the risk of falls in the elderly (Anguera et al., 2013; Cheatham et al., 2017; Habets et al., 2018; Chen et al., 2019; Tegeler et al., 2020; Chen et al., 2022; Abd-alrazaq et al., 2023; Fisher and Lempka, 2023; Wang et al., 2023). Neuro-technologies are also predicted to have economic growth potential (Garden et al., 2019; Neurotech Reports, 2022), attesting to their significance for society.

The European University of Brain and Technology (Neurotech[EU]) was funded by the European Commission to foster neuroscience education, research and innovation, and to generate societal impact through the development of new and improved neuro-technologies (https://theneurotech.eu/). Futuristic universities like Neurotech[EU] and the technological innovations they provide will shape and serve society, but will also require support from society. That's because public opinion matters; trust in and thus acceptance of new technologies will determine consumer reach. Public opinion also influences policy-making, where salient topics with coherent opinions about them are more likely to become integrated into programmatic priorities (Burstein, 2003; Christian, 2008; Spendzharova and Versluis, 2013; Bromley-Trujillo and Karch, 2021). However, there seems to be a gap between science and the public (McFadden, 2016; Coates McCall et al., 2019). While neuroscientists, neuro-engineers and other innovators interact with government agencies to secure funding for research, and exchange ideas with each other, they typically do not reach out to the public to decide on the technologies they wish to develop (Figure 1). Even engineers and clinicians, who develop and apply the technologies respectively, do not communicate enough (Weber, 2019). In the meantime, public opinion is shaped through the media. Policy-makers themselves shape public opinion, but many other influences exist, including misinformation (fake news) spread online (Funk, 2020; Cacciatore, 2021). Therefore, it is important that scientists, too, connect with the public, understand their challenges, and integrate this knowledge into the scientific process.

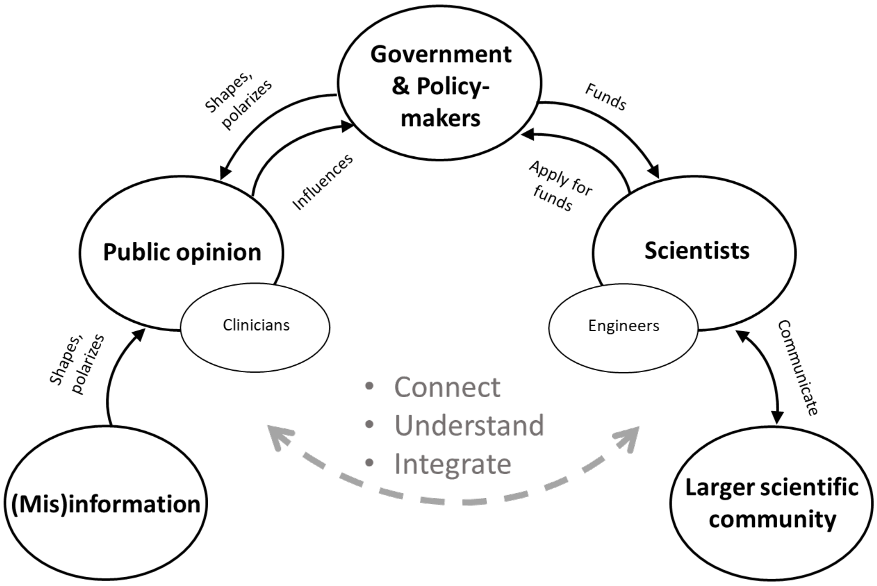

Figure 1 The scientist's web. Neuro-engineers and other innovators typically interact with government agencies to secure funding for research. They submit research proposals in response to specific calls that are based on programmatic priorities. Scientists also interact with each other to exchange ideas, for example, at scientific venues. Communication with the public is rare, however. Even engineers who develop the technologies and clinicians who apply them do not communicate enough (Weber, 2019). In the meantime, public opinion is shaped through public media, including misinformation spread online.

Evidence suggests that the level at which the general public and patients, in particular, accept and welcome new neuro-technologies is variable. Sattler and Pietralla (2022) found, for example, that the moral acceptability rate and willingness to use brain stimulation devices were 25.5% and 28.7%, respectively, indicating that the majority of the participants – a representative sample of the adult German population – is not fully embracing this technology. The results were similar for brain-computer interfaces, the second type of technology examined. The use of these technologies for treatment was more acceptable than their use for self-enhancement, and noninvasive applications were preferred over invasive ones. Sociodemographic characteristics, specifically, being female, older, and religious also contributed to a lower acceptance rate and/or willingness to use one or both technologies (Sattler and Pietralla, 2022). A US-based survey found that the public was much more worried than enthusiastic about gene editing, brain chips, and synthetic blood used for self-enhancement (Funk et al., 2016). While the interest in using assistive technologies was high in patients with spinal cord injuries, the acceptability rate of invasive technologies was still less than 50% (Huggins et al., 2015). Non-invasive technologies are clearly preferred, but even these have their barriers in actually getting used; patients with Parkinson disease reported a low usability, discomfort or pain, and a lack of familiarity with such technologies (Laar et al., 2023).

As Neurotech[EU], we will be confronted with many different attitudes about what neuro-technological advances should entail. Somewhat representative of the complexity that makes up the European Union (EU) and its Associated Member States (AC), our Neurotech[EU]countries – The Netherlands (NL), Spain (ES), Sweden (SE), Germany (DE), Türkiye (TR), Romania (RO), Hungary (HU), France (FR), and Iceland (IS) who are represented by Radboud University, Miguel Hernández University of Elche, Karolinska

Institutet, University of Bonn, Boğaziçi University, Iuliu Hatieganu University of Medicine and Pharmacy, University of Debrecen, University of Lille , and Reykjavik University, respectively – differ in social, cultural and individual characteristics that may translate into differences in opinion, both at the expert level and our broader societies. To serve everyone in the best ways possible, we therefore propose to conduct a trans-national study with the goal to better understand the challenges of our nations, specifically, their needs for, interests in, access to, knowledge of and trust in neuro-technologies, and whether these should be regulated. To our knowledge, no other trans-national studies have examined these variables before. We expect that, in the short-term, our study will provide a deeper understanding of the challenges that our nations are facing, the similarities and differences between our countries, and that through the process of science we will integrate our countries more. In the long run, we hope that our insights will benefit The Neurotech^EU in its efforts to develop neuro-technologies that people really care about, are accessible, useful, trusted, ethical, regulated, safe, research-based, new and proven, and are actually understood by the user. Connecting with the public, understanding their challenges, and integrating this knowledge into the scientific process may also result in a greater sense of inclusion and more excitement about the opportunities that come with research and innovation.

To achieve our goal, we have developed the first version of a new tool – the *Understanding Societal Challenges Questionnaire (USCQ)* which assesses people's perspectives on neuro-technologies by focusing on six question domains (needs, interest, access, knowledge, trust, and policy-making) – that can be administered across EU/AC nations. We aim to compare and contrast our nations specifically with regard to these categories, but will also examine their associations with demographic and personality variables, for example, education and socio-economic status, size of the residential area, the Big Five personality traits, religiosity, political standings, and more. The first task will be to establish the reliability of our tools across the Neurotech^EU nations. While we assume face validity of our measures at this point, we will probe into prediction and construct validity through simple correlation and multi-factorial analyses, including factor and structural equation analyses. We hypothesize that the domain means of the USCQ will vary across nations but that the factor structure will be invariant. We expect that age, gender, and religiosity will predict the general acceptability of neuro-technologies (Sattler and Pietralla, 2022; Funk et al., 2016), but that our nations will differ in other societal, cultural, and individual variables.

2. Material and methods

2.1 Study design

The design of our study is summarized in Figure 2. While we have established face validity of our forms in English language, these will be translated into the official languages of each participating Neurotech^EU country. Bilingual specialists will use back-and-forth translation to ensure that the translations are accurate and the meanings of the items comparable across languages. Next, ethics approvals will be sought by each participating Neurotech^EU country (refer to Section 4. Ethics). The translated forms will then be administered online for initial reliability testing of conceptually similar items. The English forms will be provided as a choice to the participants and tested alongside the translated versions in each country. The scales will be trimmed, if necessary, to achieve acceptable reliabilities (Cronbach's alpha > 0.70).

Finally, we will collect field data from a representative sample of each NeurotechEU country. Among other, the reliability analyses will be repeated, the factor structures of the USCQ determined, country means compared, and the influence of population characteristics on attitudes regarding neuro-technological advances assessed (refer to section 2.6 Statistical Analyses). The results will be disseminated to the NeurotechEU community and beyond.

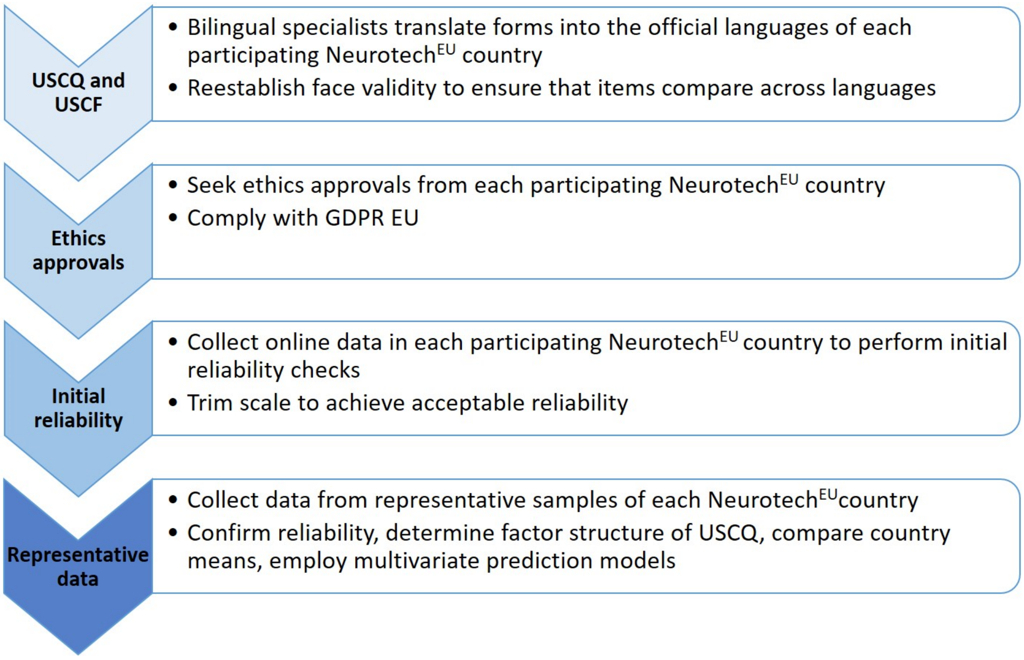

Figure 2 Study design. The progression of steps to be implemented next in Phase 1 of project 'Understanding Societal Challenges: A NeurotechEU perspective'. Phase 2 is planned as a follow-up study to assess longitudinal changes based on (e.g. educational) interventions that address the challenges of our societies. GDPR EU = General Data Protection Regulation EU (2016/679).

2.2 Participants

Our participants will be 18 years of age or older. Females and males will be represented in about equal numbers. All education levels will be included for analysis (refer to Appendix 2 – Understanding Societal Characteristics Form (USCF) for demographic information and more). For initial reliability testing of our forms, we will recruit 100 participants per nation who will provide their responses online. We will collect 1000+ data from a representative sample of each nation for a final data set. These participants will be found in their day-to-day environments. If possible, a random sampling procedure will be used for recruitment. Professional companies experienced in social research, such as Frekans in Türkiye (https://frekans.com.tr/tr/sosyal-arastirma/), will be hired to support the data collection phase. The participants will not be promised any rewards a priori but will be offered a personality analysis as a free gift after the responses are received. The participants will provide written informed consent before data collection (Appendix 4). All procedures will be approved by our local ethics committees and conducted in accordance with the Declaration of Helsinki and the directives of the General Data Protection Regulation EU (2016/679).

2.3 Understanding Societal Characteristics Form (USCF)

To generate statistical data related to the population characteristics of our NeurotechEU nations, we developed the 19-item-long USCF (Appendix 2), which asks about demographic variables and more, such as education and socio-economic status, size of the residential area, religiosity, and political standings. The USCF was designed for administration across EU/AC countries and is therefore taking the diverse educational systems, cultural norms, and sensitivities of our countries into account. We will use the information provided by this form to better understand the similarities and differences between our nations and to determine the characteristics that best predict positive and negative attitudes about neuro-technological advances.

2.4 Big Five personality traits

Personality is an important predictor of attitudes about health-related issues, such as mandatory vaccinations during the Coronavirus disease 2019 (COVID-19) pandemic and related restrictions imposed by the government (Lippold et al., 2020). Personality also predisposes to risky behavior (Reuter et al., 2002), which might influence perceptions on the use of risky technologies. Moreover, personality mediates the influence of political ideology on societal attitudes (Grünhage and Reuter, 2020). Given its importance, we plan to include personality as a potential predictor of our nations' perspectives on neuro-technological advances. The "Big-Five" is the most accepted model of personality; it assumes that personality has five dimensions, i.e. openness to experience, conscientiousness, extraversion, agreeableness and neuroticism (Costa and McCrae, 1992). These dimensions can be assessed efficiently with the 10-item short version of the Big Five Inventory (BFI; Rammstedt and John, 2007), which we will employ in the present study. The factor structure of the BFI has been demonstrated to be invariant across countries and cultures, and its psychometric properties were found to be excellent (Kajonius and Giolla, 2017). Personality is considered a stable trait. Accordingly, twin studies provided substantial heritability estimates of .40-.60 for the Big-Five dimensions (Bouchard and McGue, 2003).

2.5 Understanding Societal Challenges Questionnaire (USCQ)

The first version of the USCQ (Appendix 3) specifically asks about the respondent's perspectives on neuro-technological advances. The form has 27 items which cover 6 question domains – needs, interest, access, knowledge, trust, and policy-making. These domains contain 5, 4, 5, 3, 7, and 3 items, respectively. A Likert scale with five response categories is used as a format for most of the items, where 1 = not at all, 2 = slightly, 3 = moderately, 4 = very much, and 5 = extremely, or where 1 = never, 2 = once a year, and 3 = once a month, 4 = once a week, and 5 = daily. Items 5 and 12 have a dichotomous response format (yes/no). Item 5, for example, inquires whether the participant has any neurological condition. Three items (10, 15, 16) use a multiple-select format. E.g. item 10 asks 'Where do you most commonly find out about science?' and possible responses include social media, scientific journals, and the physician's office. Finally, item 17 (What do you feel about 'neuro-technologies'? And to what extent?) uses a multiple-choice format in which the participants rate several different feelings on a 5-point Likert scale.

2.6 Statistical Analyses

The reliability of the USCQ will be measured with Cronbach's alpha. The Likert-scale items in each domain – needs, interest, access, knowledge, trust, and policy-making – will be analyzed separately. Items with a low reliability (item-total correlation < 0.25 and if item deleted, alpha increases) will be removed from the questionnaire and, if necessary, replaced by new items. Cronbach's alphas of > 0.70 will be considered acceptable.

Once we obtained the field data from our representative samples, the factor structure of the USCQ will be determined. We will employ confirmatory factor analysis (CFA), in a structural equation model framework, to test the hypothesis that the structure of the USCQ is formed by six latent variables that correlate predominantly with the respective items in the six question domains of the USCQ. The fit between our theoretical model and the empirical data will be tested using fit indexes, including the chi-square test, root mean square error approximation (RMSEA), and the comparative fit index (CFI). The CFA will be applied to the data from each Neurotech[EU] country. If found invariant, the data from all countries will be pooled for a final analysis.

All data measured on a ratio scale will be checked for normality and equal variance of the distributions, using the Kolmogorov-Smirnov test and Levene-statistic, respectively. If results allow for parametric testing to be used, group comparisons will be performed using ANOVA models. If the assumptions of normality and equal variance are violated, we will apply non-parametric statistics to the data. The Kruskal-Wallis test will be used to compare three or more groups. The Mann-Whitney U test will be used for post-hoc comparisons. Z-score statistics will be employed for standardization of the data across countries.

To test for linear associations between the variables, we will apply the Pearson or Spearman rank-order correlation. Multivariate prediction models, i.e. path analysis and multiple regression will be used for mediation and moderation analyses. Continuous input variables will be centered to reduce multi-collinearity. These analyses will be conducted to identify the characteristics, e.g. demographic and personality variables, that reliably predict positive and negative attitudes about neuro-technologies.

All tests will be two-tailed and $P \leq 0.05$ will be considered a measure of effect.

3. Discussion

In summary, this study was designed with the goal to better understand the challenges of our Neurotech[EU] nations, specifically, their needs for, interests in, access to, knowledge of and trust in neuro-technologies, and whether these should be regulated. The data collected in each participating country will be used to determine the similarities and differences between our nations, and the characteristics that best predict positive and negative attitudes about neuro-technological advances. In the long run, the insights gained will benefit The Neurotech[EU] in its efforts to develop neuro-technologies that people really care about, are accessible and understood by the user, are ethical, regulated and safe, based on research, and are new and clinically proven.

Studies have shown that healthy people as well as patients prefer non-invasive over invasive neuro-technologies (Huggins et al., 2015; Sattler and Pietralla, 2022). Surprisingly however, it is common that neuroscientists and neuro-engineers develop cutting-edge technologies that are highly invasive, but are considered the next frontier, and then face a myriad of challenges in translation (Weber, 2019; Shen et al., 2020). Also, despite their great potential, neuro-technologies used in preventive medicine have received much less attention than technologies that treat symptomatology (Elenko et al., 2015). Neuro-technologies that focus, for example, on sleep, diet, exercise and cognitive biases, which are often impacted early in the development of psychiatric and neurological diseases, might help prevent the transition from these early changes into full blown conditions that are hard-to-treat by the time clinical diagnoses are made (Schulz, 2020). Therefore, the NeurotechEU has a great opportunity to set its mark as a leader in the advancement of neuro-technologies that take attitudes of people into account, and focus on prevention and health in addition to (or more than) disease and treatment.

The proposed study is novel in several ways. Firstly, we are not aware of other trans-national studies that have asked the general population about their perspectives on neuro-technological advances across the six domains covered in the USCQ (needs, interest, access, knowledge, trust, and policy-making). Furthermore, we will focus our inquiry on a more general set of neuro-technologies rather than a few specific ones, as is common in other surveys (Funk et al., 2016; Sattler and Pietralla, 2022), because neuro-technologies are diverse, and we wish to be encompassing and avoid biases towards a specific topic. Previous studies have identified a few characteristics that predict positive and negative attitudes about health-related issues, including age, gender, religiosity, political standings, and personality (Funk et al., 2016; Grünhage and Reuter, 2020; Lippold et al., 2020; Sattler and Pietralla, 2022). Here, we will inquire about these variables and more, using the USCF which we devised for application across EU/AC countries, taking the diverse educational systems, cultural norms, and sensitivities of our countries into account. Compared to other cross-country studies, which collected their survey data online or both online and offline (Kajonius and Giolla, 2017; Lippold et al., 2020; 3M State of Science Index, 2022), we aim to collect field data from representative samples of each Neurotech^{EU} nation. While this is difficult to achieve, we will seek support from research companies specialized in collecting such data. Finally, to avoid sampling biases by including only participants who are fluent in English, we will translate our forms into the official languages of each participating Neurotech^{EU} country.

In conclusion, our attempt at bridging the gap between science and the public may result in neuro-technological advances that our broader societies will value more. We further expect to highlight the importance of non-invasive over invasive neuro-technologies, and technologies used in preventive medicine over those used to treat symptomatology. In the long run, the insights gained in the present study may benefit The Neurotech^{EU} in devising interventional (e.g. educational) strategies that aim to innovate our societies.

4. Ethics

This study has been designed to ensure compliance with the ethical principles set out by each participating nation as well as the international standards described in the Declaration of

Helsinki (2013). It furthermore takes into account the directives provided by the General Data Protection Regulation EU (2016/679). Data collection in each participating Neurotech^EU country will commence only after all regulatory requirements and legal obligations have been assessed and ethics approvals were sought.

Before enrollment, all participants will be fully informed about the study. Only participants older than age 18 will be recruited. All participants will provide written informed consent to the processing of personal data in anonymous and aggregate form, by authorized personnel involved in the research, for up to 20 years from the conclusion of the study.

All data will be digitized, made anonymous, and archived on a centralized and secure IT platform in Germany or another EU member state involved in the study. The data will be coded with numbers and will not be associated with the name of the participant or any personally identifiable information.

5. Dissemination

We had the opportunity to present the ideas for this project at the NeurotechEU Technological/Societal Innovation Summit 2023 that was held in Bodrum, Türkiye, between 2-5 October, 2023, and were able to recruit ULille and UR as new partners into the project.

Furthermore, we have submitted a first manuscript to Frontiers in Neuroscience – Neural Technology (Research Topic on NTEU found at https://www.frontiersin.org/research-topics/47939/neurotechnology-state-of-the-art-perspectives-and-research-along-the-lines-of-dimensions-and-neuroch) on 30 October 2023. In this manuscript, we describe the study protocol presented here in deliverable D6.3.

We plan to publish the progress of this study in follow-up submissions to peer-reviewed journals and at scientific meetings. We expect that the data will also benefit The Neurotech^EU and its stakeholders in its mission to foster neuroscience education, research and innovation, and to generate societal impact through the development of neuro-technologies that are aligned with its values.

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• Appendix 1: Core contributors to project "Understanding Societal Challenges (USC) – A NTEU perspective" and authors of a manuscript submitted to Frontiers in Neuroscience – Neural Technology (Research Topic on NeurotechEU) on 30 October 2023

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Note that,

Begüm Özkaynak (BOUN; begum.ozkaynak@boun.edu.tr) wishes to get involved at data collection stage.

Representatives from ULille and UR have verbally agreed at the NeurotechEU Technological/Societal Innovation Summit 2023, Bodrum, Türkiye, to also participate in the project.

• Appendix 2: Updated "USCF"

Understanding Societal Characteristics Form (USCF)

From health and healthcare to learning and education, neuroscience shows great promise to become also an applied science that could benefit society and kindle a new economy in Europe. The European University of Brain and Technology (Neurotech[EU]) aims to be the backbone of this new vision. Neurotech[EU] was funded by the European Commission to create an ecosystem that fosters neuroscience education, research and innovation, and creates societal impact resulting from the development of new neuro-technologies.

Neurotech[EU] is a network of 9 universities from across the European Union and Associated Member States: Radboud Universiteit (The Netherlands), Universidad Miguel Hernández de Elche (Spain), Karolinska Institutet (Sweden), Rheinische Friedrich-Wilhelms-Universität Bonn (Germany), **Boğaziçi Üniversitesi (Turkey)**, Universitatea de Medicină și Farmacie „Iuliu Hațieganu" din Cluj-Napoca (Romania), Debreceni Egyetem (Hungary), Université de Lille (France), and Háskólinn í Reykjavík (Iceland), and over 50 associated partners consisting of companies, technology transfer offices, and regional innovation networks, among other.

As researchers of Neurotech[EU], our goal is to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process. Your answers to this form will help us generate statistical data related to the population characteristics of *Turkey* (insert your country). **The data will be compared with those from other Neurotech[EU] countries. Please answer the questions as viewed by you from your country of residence today.**

Scroll for page 2

1. **I am __________ years old.**

2. **I am** □ male □ female □ other

3. **Education (check all that apply)**

   a. **number of years in school (other than university): __________**

   b. **university degrees (check all that apply):** □ Bachelor □ Master □ Ph.D.

4. **Mother's education**

   a. **number of years in school (other than university): __________**

   b. **university degrees (check all that apply):** □ Bachelor □ Master □ Ph.D.

5. **According to *TÜIK*, the mean annual equivalized (for size and composition) household income for *Turkey* in 2020 (calculated in 2021) was 37,400 TL net (3,116.67 TL per month). My income fell**

   □ below □ near □ above this national average

6. **Occupation: ____________________**

7. **Marital status**

   □ Single □ Live with partner, not married □ Married □ Married, but separated
   □ Divorced □ Widowed

8. **Children**

   □ 0 □ 1 □ 2 □ 3 or more

9. **I was born in: ____________________**

10. **I consider myself to be a ____________________ national**

11. **I grew up (check all that apply)**

    □ rural □ urban, small city (< 300,000) □ urban, big city (> 300,000)

12. **My current environment is**

    □ rural □ urban, small city (< 300,000) □ urban, big city (> 300,000)

13. **Current resident country: ____________________**

14. **I have lived in □ countries for more than 3 months**

    □ 1 □ 2 □ 3 □ 4 □ 5 or more

15. **Native language: ____________________**

16. **I speak □ language(s) fluently**

    □ 1 □ 2 □ 3 □ 4 □ 5 or more

17. Do you identify as religious?

□ Yes □ No

18. Do you identify as political?

□ Yes □ No

19. My position in politics is

□ far-left □ left □ center-left □ center □ center-right □ right □ far-right
□ not interested □ don't want to say

• Appendix 3: Updated "USCQ"

Understanding Societal Challenges Questionnaire (USCQ)

From health and healthcare to learning and education, neuroscience shows great promise to become also an applied science that could benefit society and kindle a new economy in Europe. The European University of Brain and Technology (Neurotech[EU]) aims to be the backbone of this new vision. Neurotech[EU] was funded by the European Commission to create an ecosystem that fosters neuroscience education, research and innovation, and creates societal impact resulting from the development of new neuro-technologies.

Neurotech[EU] is a network of 9 universities from across the European Union and Associated Member States: Radboud Universiteit (The Netherlands), Universidad Miguel Hernández de Elche (Spain), Karolinska Institutet (Sweden), Rheinische Friedrich-Wilhelms-Universität Bonn (Germany), **Boğaziçi Üniversitesi (Turkey)**, Universitatea de Medicină și Farmacie „Iuliu Hațieganu" din Cluj-Napoca (Romania), Debreceni Egyetem (Hungary), Université de Lille (France), and Háskólinn í Reykjavík (Iceland), and over 50 associated partners consisting of companies, technology transfer offices, and regional innovation networks, among other.

As researchers of Neurotech[EU], our goal is to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process. Your answers to this form will help us generate statistical data related to our nations' needs for, interest in, access to, knowledge of, and trust in neuro-technologies, as well as our views on policymaking regarding their development. The *Turkish* data will be compared with those from other Neurotech[EU] countries. Please answer the questions as viewed by you from your country of residence today.

Neuro-technologies encompass a broad range of technologies that allow for a better understanding of how the brain works and help prevent, diagnose, and treat diseases of the brain. Examples include brain scanners and other medical devices, genetic technologies, and artificial intelligence.

Scroll for page 2

I. Needs for neuro-technological advances

1) In your opinion, how important are neuro-technologies for society?

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
not at all	slightly	moderately	very much	extremely

2) Do you think society needs new neuro-technologies?

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
not at all	slightly	moderately	very much	extremely

- For which purpose(s) or condition(s)? ___________________________

3) To what extent do neuro-technologies play a role in your life?

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
not at all	slightly	moderately	very much	extremely

4) Do you have needs for new neuro-technologies?

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
not at all	slightly	moderately	very much	extremely

- For which purpose(s) or condition(s)? ___________________________

5) Do you have any neurological condition?

☐ yes ☐ no

If yes, to what extent does it compromise your daily functioning?

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
not at all	slightly	moderately	very much	extremely

II. Interest in neuro-technological advances

6) How often do you read about neuro-technologies?

☐ never ☐ once a year ☐ once a month ☐ once a week ☐ daily

7) How often do you read about the brain and behavior (any topic)?

☐ never ☐ once a year ☐ once a month ☐ once a week ☐ daily

8) How often do you visit science museums or science exhibitions?

☐ never ☐ once a year ☐ once a month ☐ once a week ☐ daily

9) How often do you watch web media (e.g. documentaries) about the brain and behavior?

☐ never ☐ once a year ☐ once a month ☐ once a week ☐ daily

III. Access to neuro-technological advances

10) Where do you most commonly find out about neuro-technologies?

□ social media □ Wikipedia □ scientific websites □ scientific journals □ TV
□ newspapers □ radio □ ads or posters □ physician's office □ other □ I don't care

11) In how many languages do you follow scientific news?

□ native language □ in two languages □ in three languages □ in 4+ languages
□ I don't follow scientific news

12) Do you use Google translator or other online translators to access articles about science in foreign languages?

□ yes □ no

13) To what extent does cost prevent you from accessing neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5	□ 6
not at all	slightly	moderately	very much	extremely	don't know

14) To what extent do regulations prevent you from accessing neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5	□ 6
not at all	slightly	moderately	very much	extremely	don't know

IV. Knowledge of neuro-technologies

15) Which of the following technologies are you familiar with? Check all that apply.

□ PC □ tablets □ mobile phones □ wearable technologies □ fitness tracker
□ apple watch □ oximeter □ health apps □ hearing aid □ bionics □ robotics
□ machine learning □ artificial intelligence □ ultrasound □ computed tomography
□ X-ray □ EEG □ magnetic resonance imaging □ positron emission tomography
□ psychotropic drugs □ pharmacotherapy □ implantable drug delivery systems
□ deep brain stimulation □ optogenetics □ CRISPR-Cas9 □ genetics
□ behavior tracking software □ nutrition apps (and/or smart tools, websites, videos)
□ sleep apps □ exercise apps □ exercise equipment □ motion-assistive devices
□ virtual reality

16) Which of these technologies are currently important for your life or have been in the past? Check all that apply.

□ PC □ tablets □ mobile phones □ wearable technologies □ fitness tracker
□ apple watch □ oximeter □ health apps □ hearing aid □ bionics □ robotics
□ machine learning □ artificial intelligence □ ultrasound □ computed tomography
□ X-ray □ EEG □ magnetic resonance imaging □ positron emission tomography
□ psychotropic drugs □ pharmacotherapy □ implantable drug delivery systems
□ deep brain stimulation □ optogenetics □ CRISPR-Cas9 □ genetics
□ behavior tracking software □ nutrition apps (and/or smart tools, websites, videos)
□ sleep apps □ exercise apps □ exercise equipment □ motion-assistive devices
□ virtual reality
□ other (please state): _______________

17) What do you <u>feel</u> about 'neuro-technologies'? And to what extent? <u>Please circle</u>.
1 = low 3 = intermediate 5 = high

Fear:	1	2	3	4	5
Uncertainty:	1	2	3	4	5
Control by external powers:	1	2	3	4	5
It's important for medicine:	1	2	3	4	5
It will facilitate our lives:	1	2	3	4	5
Joy:	1	2	3	4	5
Curiosity:	1	2	3	4	5
Relief:	1	2	3	4	5
Helplessness:	1	2	3	4	5
Anger:	1	2	3	4	5
Sadness:	1	2	3	4	5

□ I don't know
□ Other (please state): ______________

V. Trust in neuro-technological advances

18) Do you generally trust the news about neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

19) Do you generally trust neuro-technologies that comply with European regulations?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

20) Do you generally trust U.S. Food and Drug Administration (FDA)-approved neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

Co-funded by the Erasmus+ Programme of the European Union

21) To what extent do you think that data obtained by neuro-technologies can reveal thoughts or feelings that you would rather keep to yourself?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

22) Do you believe that using neuro-technologies can be a threat to your privacy?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

23) To what extent do you think neuro-technologies might help you understand yourself better?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

24) Do you believe that data obtained by neuro-technologies can be used or abused for commercial purposes?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

VI. Perspectives on policymaking

25) Should policymakers follow the recommendations of scientists?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

26) Should policymakers push for the development of new neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

27) Should policymakers monitor industry as it develops new neuro-technologies?

□ 1	□ 2	□ 3	□ 4	□ 5
not at all	slightly	moderately	very much	extremely

• Appendix 4: Informed Consent

The following is a draft that will be adjusted to accommodate national and international (EU) regulations:

Understanding Societal Challenges (USC) – Informed consent

From health and healthcare to learning and education, neuroscience shows great promise to become also an applied science that could benefit society and kindle a new economy in Europe. The European University of Brain and Technology (Neurotech^EU) aims to be the backbone of this new vision. Neurotech^EU was funded by the European Commission to create an ecosystem that fosters neuroscience education, research and innovation, and creates societal impact resulting from the development of new neuro-technologies.

Neurotech^EU is a network of 10 universities from across the European Union and Associated Member States: Radboud Universiteit (The Netherlands), Universidad Miguel Hernández de Elche (Spain), Karolinska Institutet (Sweden), Rheinische Friedrich-Wilhelms-Universität Bonn (Germany), **Boğaziçi Üniversitesi (Turkey)**, University of Oxford (The United Kingdom), Universitatea de Medicină și Farmacie „Iuliu Hațieganu" din Cluj-Napoca (Romania), Debreceni Egyetem (Hungary), Université de Lille (France), and Háskólinn í Reykjavík (Iceland), and over 250 associated partners consisting of companies, technology transfer offices, and regional innovation networks, among other.

As researchers of Neurotech^EU, our goal is to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process. To achieve this goal, we will generate statistical data related to i) the population characteristics of our Neurotech^EU countries and ii) our needs for, interest in, access to, knowledge of, and trust in neuro-technologies, as well as our views on policymaking regarding their development.

Neuro-technologies encompass a broad range of technologies that allow for a better understanding of how the brain works and aim to prevent, diagnose, and treat diseases of the brain. Examples include brain scanners and other medical devices, genetic technologies, and artificial intelligence.

Scroll for page 2

Participant Number:

INFORMED CONSENT

I state that I am eighteen years of age or older and wish to participate in a program of research conducted by (*contact*) at the national level and by members of Neurotech[EU] across nations.

The purpose of the research is **to understand our nations' perspectives on neuro-technological advances and to integrate these perspectives into the scientific process.** First, I will answer demographic questions about myself. Then, I will fill out the 'Understanding Societal Challenges Questionnaire'. Data collection will take approximately 15 minutes.

I furthermore consent to allow the data that have been obtained of me to be used in the research. I understand that the data will be used for research purposes only, and no one else except the researchers will ever know my identity.

I understand that participant numbers will be used to identify the data, and that all written material that I contribute will be kept separate from my identity. As a result, it will not be possible to connect my name to my participant number.

I understand that the study is not designed to help me personally, but that the researchers **will generate statistical data related to i) the population characteristics of our Neurotech[EU] countries and ii) our needs for, interest in, knowledge of, access to, and trust in neuro-technologies, as well as our views on policymaking regarding their development.**

I understand that I am free to ask questions or to withdraw from participation at any time without penalty.

Signature:

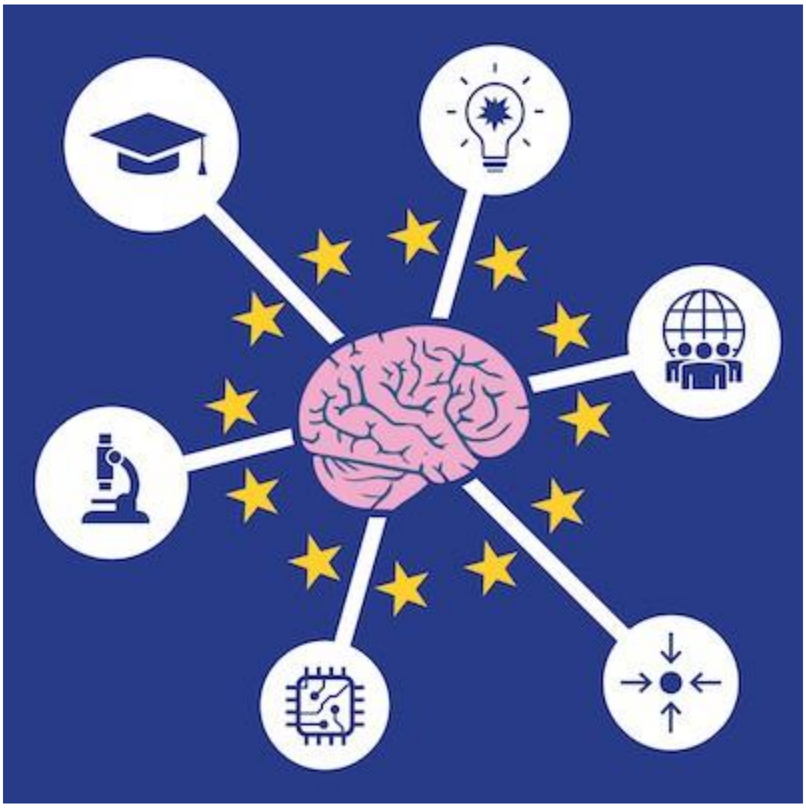
Date:

Email:

PI contact information

NeurotechEU

The European University of Brain and Technology



Deliverable 6.5: White papers on the new educational programmes needed to address societal neurochallenges

Deliverable information	
Work package number	WP6
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Deliverable [6.5] – [White papers on the new educational programmes needed to address societal neurochallenges**]**

Authors
This document was developed by faculty and administrative staff from the founding universities of Neurotech^EU - the European University of Brain and Technology, an initiative that aims to build a trans-European network of excellence in brain research and technologies to increase the competitiveness of European education, research, economy, and society. Neurotech^EU Alliance partners are listed below in the order of their assignment to project work packages:

- Radboud Universiteit (The Netherlands)
- Universidad Miguel Hernández de Elche (Spain)
- Karolinska Institutet (Sweden)
- Rheinische Friedrich-Wilhelms-Universität Bonn (Germany)
- Boğaziçi Üniversitesi (Turkey)
- Universitatea de Medicină și Farmacie din Cluj-Napoca (Romania)
- Debreceni Egyetem (Hungary)
- Université de Lille (France)
- Haskolinn i Reykjavik EHF (Iceland)

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1 Introduction

This deliverable described the educational program we consider essential for preparing the future neurotechnologists to make meaningful contributions to addressing societal neurochallenges. As our partners are identifying their scientific and technological strengths and weaknesses in the eight dimensions of neurotechnology defined within our alliance, we won't delve into the specifics of individual courses. Instead, we will focus on the components that emerge from various perspectives. In the following sections, we first summarize our definitions of societal challenges and the resulting specific challenges for education and learning. Following that, we present a summary of the main take-home messages from the UNESCO- symposium on neurotechnology held in July 2023. Lastly, we present our perspective on the integration of these points into components that need to be included in future educational programs.

2 Alliance view on societal challenges

During phase 1 of our European University Alliance we discussed societal challenges in neurotechnology between partners. These discussions resulted in eight white papers as deliverables 3.1 to 3.8. We defined the focus of our challenges as follows:

1. Health and healthcare: (a) Strengthening health systems; (b) Blueprinting resilience to emerging population health threats; (c) Mitigating the increasing burden of infectious and neurodegenerative diseases; (d) Effective and coherent development of e-health and (e) Reshaping education, research and innovation paradigms.
2. Learning and education: (a) Dealing with big data; (b) Personalizing learning paths using AI; (c) Improving study content comprehension using virtual reality and augmented reality; (d) Creating digitally based life-long learning platforms; (e) Achieving synergy effects through open education resources.
3. Nutrition and cognition: (a) Contextualization of nutrition and cognition; (b) Understanding of nutrition-cognition interaction; interventions for improved cognition-nutrition function; strategies for improving food production.
4. Artificial and biological intelligence: (a) Implementing AI in healthcare; (b) Risks of AI application in healthcare; (c) Limitations of current AI systems.
5. Neurotechnology and big data: FAIR Guiding Principles (Findable, Accessible, Interoperable and Reusable) consisting of (a) Necessary infrastructure are available to all neuroscientists; (b) Identify, define and support community-relevant standards for data and metadata; (c) Beneficial centralized information hubs; (d) Training of neuroscientists in the use of FAIR Guiding Principles.

Co-funded by the Erasmus+ Programme of the European Union

6. Public and ethics: (a) Novel treatment methods; (b) For-profit enterprises; (c) Use of AI; (d) Digitalization; (e) Data governance & Big data; (f) Research.
7. Economy and ecology towards 2040 and beyond 2040: (a) Revised social contract; (b) Health technology assessment; (c) Future of work and industry; (d) Sustainability in economy and ecology.
8. Smart cities as hybrid intelligence: (a) Neuroscience/neurotechnologies; (b) Urban space (c) Societal needs.

Each white paper described the current situation within the predefined domains plus the expected situation in the near, intermediate, and far future. These views then lead to a set of challenges for that domain. Challenges can be grouped towards research-, treatment-, education-, product development- and ethical-related topics; for a detailed list of all the challenges see the whitepapers. The following challenges, mainly coming from our white paper on learning and education were specified for educational programs:

a. Creating neuroscience bachelor and master programs with incorporation of data science courses.
b. Implementing data science in regular courses - data science courses not as replacement but as a foundation for other courses.
c. Implementing biomathematical approaches such as patient data sharing across Europe.
d. International programs should train neuroscience students to be multi-disciplinary team-science enabled researchers
e. Personalizing study schedules by emphasizing theory focusing on each student's needs using AI.
f. Machine learning: Closing the gap between lack of programming background and the requirement of data scientific skills for students by creating user interfaces.
g. Creating AI software, digital lessons, web-based learning and cognitive tutor apps as supportive learning tools for students.
h. Synchronizing learning content - more unified, similar learning approaches and content across European universities.
i. Positioning neurotechnology as THE discipline to guide society into the age of AI.
j. Connecting students all over Europe via digital workspaces and meeting rooms.
k. Exchanging practical skills without traveling using virtual laboratories and VR surgery training.
l. Realization of a virtual campus that augments the physical campuses and bridges nationalities and cultures.
m. Closing the gap between narrow expertise and constant evolvement of knowledge.
n. Providing structured introduction into teaching concepts, soft skills and effective supervision on easily accessible digital platforms independently of geographical location.
o. Structuring credibility and module management for students across universities.
p. Aligning open educational resources to local curricula.
q. Presentation of open educational resources in an accessible way and highlighting the most suitable platform for specific purposes and lay audience.

3 Take home messages from the UNESCO symposium on Ethics of Neurotechnology

On July 13, 2023 UNESCO organized an International Conference on the Ethics of Neurotechnology on the theme "Towards an Ethical Framework in the Protection and Promotion of Human Rights and Fundamental Freedoms". This conference can still be viewed online through the following link: https://webcast.unesco.org/events/2023-07-neurotech/ and a summary can be found here: https://www.unesco.org/en/articles/ethics-neurotechnology-unesco-leaders-and-top-experts-call-solid-governance. During the UNESCO conference , leaders and top experts call for solid governance. Our take home messages towards education programs from this symposium include:

a. Neurotechnology requires an ethical framework;
b. Human rights and technology must evolve together;
c. We must create a moral compass;
d. We need anticipatory governments;
e. We must prevent technophobia;
f. Standards about data, such as data collection, data protection and data sharing (and selling) are important;
g. We need to move from the proof of concept stage to more scalability and wide usage and adoption of neurotechnology;
h. Society needs to be involved in discussions on how to incorporate ethics of neurotechnology, and any kind of technology, in the education systems;
i. It is important to include genders, minorities and all ages in the development of data and technology;
j. Discussions need to start around natural vs enhanced.

4 Towards an integrated view on components for future educational programs

Neurotechnology is an emerging field with rapid advances in scientific and technological insights and possibilities. This draws a lot of attention from governments, policy makers and the general public. On the one hand we experience excitement about new possibilities, be it wearables that enhance our daily life or treatments for pressing neurological disorders. On the other hand, it raises concerns about our privacy and freedom of thought as big datasets are involved, and the boundaries between our physical world and digital experiences fade. This wide range of views on neurotechnology leads to demands and expectations on the neurotechnologists of the future that we need to address in our educational programs on bachelor, master, Ph.D. and life-long learners' level. Whereas traditional educational programs from universities focus on excellence in scientific and technological knowledge, it becomes clear that neurotechnologists of the future also need excellent knowledge and skills in fields like ethics, law, data management and entrepreneurship that will facilitate them in discussions about the societal placement of their neurotechnological advances.

As mentioned in the introduction, our partners are currently outlining their scientific and technological strengths and weaknesses within the eight dimensions of neurotechnology. It becomes clear that with this rapidly developing field, none of the partners can be an expert in all eight dimensions. As a result, we need to search for synergies between partners to reach our potential level of excellence in our education. Appendix 1 gives a description of our initial outline of each partner's strengths and proposed educational contributions. Synergistic education can be developed in dimensions with strength across multiple partners, e.g. ‘basic and clinical neuroscience’. Such synergy strengthens collaboration between the research of these partners while at the same time assuring an international approach to the education (see deliverable 7.3) while reducing workload for teaching staff. Likewise, for dimensions with few partners contributing, synergy can be sought between partners, or collaboration with external partners can be developed, to avoid weaknesses in content and create excellent educational programs for our learners.

The Neurotech[EU] alliance sees the future of pan-European teaching in a further blending of online and on-campus activities. For this, we need to further develop our digital platform Campus+ to remove borders between institutions and become fully student-centric. We have recently developed the first version of the module Neurospaces, where students, administrators and lecturers can discuss all topics Neurotech[EU] related. Future development of this module can transform it into a digital workspace for collaboration. Campus+ also fits the growing need for enhanced teaching opportunities, including virtual reality and artificial intelligence. These novel technologies will not be suitable for all courses and we need proper guidelines to assist teachers in their implementation. For the use of artificial intelligence, it is prudent to have proper expectation management, as learning of the AI system can take a long time and needs large amounts of data, which will not always be readily available. Finally, teaching lab skills is traditionally performed during internships in a master-apprentice model. Use of virtual teaching labs in combination with physical teaching will diminish travel costs and reduce the carbon footprint of the alliance. These virtual components can be purchased (e.g. clearpixelvr.com) or developed in-house, as we currently do for MRI scanning.

Incorporation of the societal aspects in our educational programs is mainly covered in dimension 8: Neurometaphysics, where we need to cover aspects of law, ethics, and philosophy as outlined in the previous sections. In our view, neurotechnologists of the future need to be well-equipped to contribute to discussions about these topics, are critical thinkers who can integrate neurotechnology-specific content with societal aspects, and prepare the next generation of neurotechnologists, thereby creating a sustainable educational environment. We, therefore, advise to critically evaluate the summary of the UNESCO symposium (https://www.unesco.org/en/articles/ethics-neurotechnology-unesco-leaders-and-top-experts-call-solid-governance) to determine necessary components. Modules to be included concern learning materials on (1) determination and safeguarding of ethical and legal standards towards fundamental human rights in neurotechnology; (2) implementation of ethics in the design and development phase of neurotechnology; (3) involvement in public awareness and contributions to multi-stakeholder discussions; (4) data standards with respect to collection, protection and ownership, including frameworks of strengths and weaknesses of AI in research and education; (5) entrepreneurship to bridge the gap between the proof of concept stage to a more widely useable and scalable product; (6) inclusiveness of gender, race and age to harness the full potential of neurotechnology towards (mental) health and disease.

In summary, together with the technical and scientific content from the other seven dimensions it will be impossible for our learners to excel at all societal aspects. We foresee a choice structure where each student must follow at least three of these modules. Our learners should be given freedom of choice, but for the consortium to exist as one balanced university, collaboration between companies and government bodies is essential to define and maintain the modules.

5 Acknowledgements

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