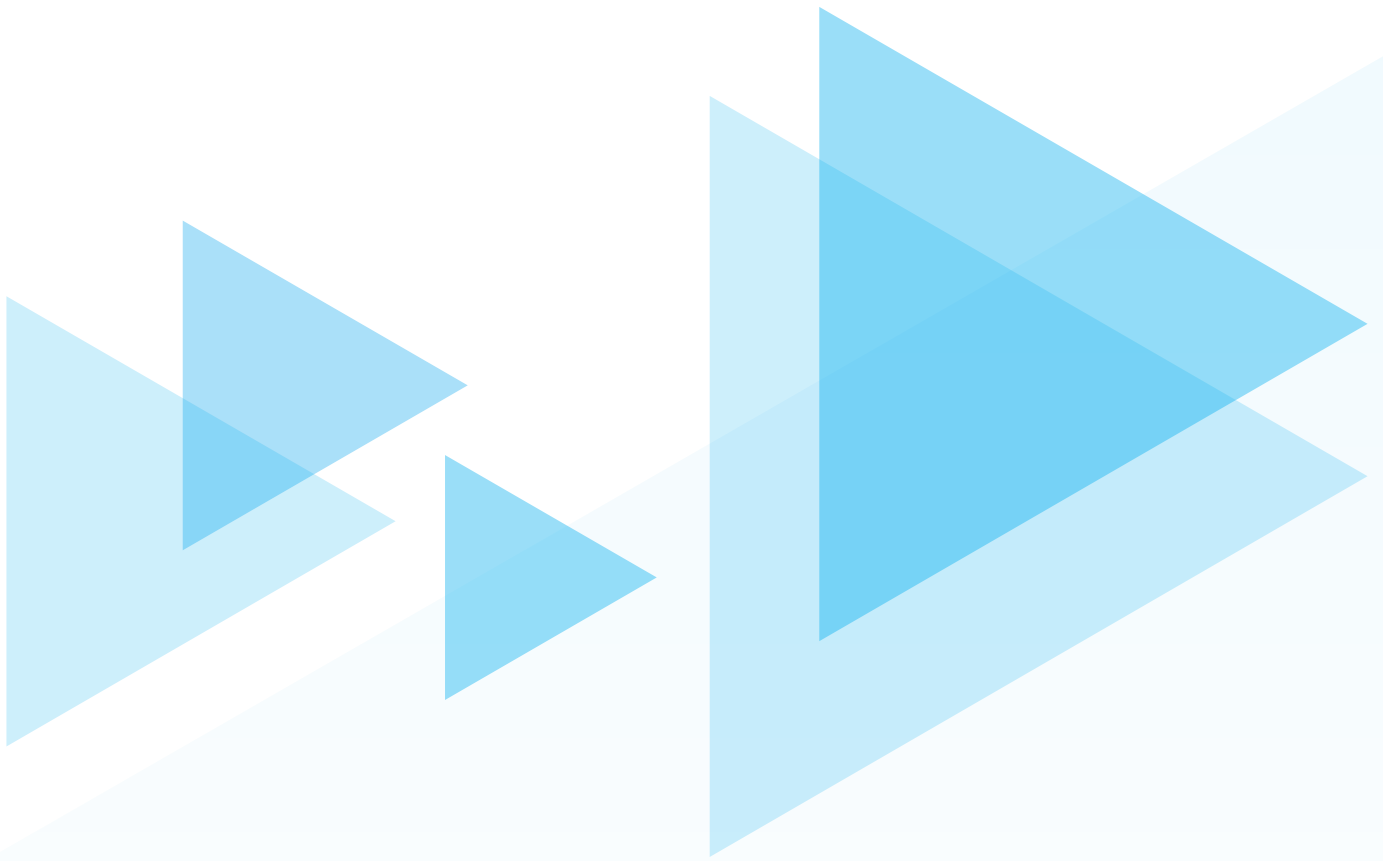


BRAIN HEALTH IN EUROPE

Fostering Innovation, Improving Outcomes

A POLICY ROADMAP



ACKNOWLEDGEMENTS

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CONTENTS

Foreword	2
Executive summary	3
Prioritising brain health	4
The cost of non-action	4
Brain disorders and the global policy debate on non-communicable diseases (NCDs)	5
Fostering research and innovation for brain health	6
Promoting Public-Private Partnerships	7
Enhancing European Reference Networks for brain health	8
Embracing the digital revolution	8
Improving access and outcomes	10
Delivering value to patients and health systems and measuring outcomes	10
Keeping the regulatory environment fit for purpose	11
Conclusion: a call for an integrated approach to brain research and health	13
Key recommendations	14
Case Studies	16
About European Brain Council	21
References	22

FOREWORD

Understanding brain health – and brain disorders – is not only essential, but also now possible. Brain disorders encompass both neurological and mental disorders alike, each with a high individual, social and economic burden. Brain disorders, an umbrella term that encompasses both neurological and psychiatric conditions, are widespread and highly disabling disorders that are often difficult to treat. To this end, when ‘brain health’ and ‘brain disorders’ are mentioned throughout the text, we systematically mean both neurological and mental aspects.

As we enter a new, exciting and potentially revolutionary phase in brain research, where innovative therapeutic solutions become available, improving the health and quality of life of patients should be part of broader research efforts and public health interventions. This requires an integrated and collaborative approach.

Compared to other disease areas, multiple factors hinder faster innovation in brain disorders and explain the lack of attention from policymakers, such as the complexity of the brain itself and variations in levels of funding for brain research across Europe.¹ As a result, the availability of effective treatments and enabling policies for brain disorders remain insufficient.

Increased prioritisation of the brain can only be achieved through the involvement of, and collaboration among, all stakeholders. It is crucial to ensure that collaboration at European and global level enhances brain research in a meaningful way for the benefit of patients and with their involvement.

COVID-19 has severely impacted brain health, with major direct and indirect neurological and mental consequences, ranging from increases in anxious and depressive disorders as a result of social isolation to the neurotropic effect of the virus on the brain.² The dramatic impact of the COVID-19 pandemic has triggered a strong response by international and European institutions, and has shed a light on examples of innovative ways to reconfigure healthcare provision. As a result, the President of the European Commission, Ursula von der Leyen, has called for the EU to become a “global leader” in health.³ Brain disorders need to take a centre stage in the EU’s renewed focus on health policy, to foster research and innovation, and ultimately improve patient health outcomes.

The European Brain Council (EBC) believes that enhanced multi-stakeholder engagement in the brain health ecosystem is needed to foster dialogue, exchange knowledge, facilitate business development, showcase ongoing projects, and – a key concern of this paper – accelerate investment in brain disorders, research and innovation for the benefit of patients.

Better understanding of the human brain takes time, determination and collaboration. Our commitment to, and our trust in research are stronger than ever. The hope for millions of patients affected by brain disorders will continue to be carried by our relentless research efforts. By joining forces and coordinating our efforts we can create a world in which brain disorders are preventable, treatable and manageable by patients and societies alike.

Monica Di Luca

EBC President

EXECUTIVE SUMMARY

Brain disorders are widespread and highly disabling disorders that are often difficult to treat. The case for prioritising brain disorders at a global and European policy level is evident. More than half of the European population (approx. 60%) suffers from a neurological disease,⁴ a number which is set to increase steadily as the population ages. Furthermore, it has been estimated that one in six people across EU countries (17.3%) had a mental health issue in 2016, totalling nearly 84 million people in Europe.⁵ Moreover, depressive disorders are predicted to become the leading cause of burden (DALYs) by 2030.⁶

Brain disorders are also prevalent in children. In 2017 it was estimated that 15 million children in Europe were affected by epilepsy, intellectual disability or a sensory disorder.⁷ In the WHO European Region, depression and anxiety disorders fall into the top 5 causes of overall disease burden among children and adolescents (as measured by disability-adjusted life years).⁸

A European brain health strategy and implementation plan is critical to foster innovation, which is needed to address the high disease burden and to improve the lives of those affected by brain disorders. Innovation should be embedded throughout the pathway that goes from research to care and to patients' quality of life.

It is essential to have a joint approach for all brain disorders. In the past, research and practice within brain disorders were fragmented across disciplines. Today, there is greater awareness of common challenges and opportunities in order to manage brain disorders through a more integrated approach.^{9,10}

This policy roadmap highlights the need to create an enabling environment which promotes brain health in Europe. It captures the perspectives of a range of stakeholders, with experts involved from the outset to provide insights and guidance, and argues the need for political leadership to prioritise brain health policy for improved health outcomes.

The paper's recommendations can be summarised under the following three headings:

- 1** Develop as a matter of priority a **European Brain Plan**, combining research and public health to address brain health in a comprehensive and collaborative way
- 2** Foster the development of **enabling policies and common research platforms** to share data and results of conducted or current research (Knowledge Hubs and Joint Actions), while also **leveraging the European Health Data Space (EHDS)**.¹¹ Embed innovation throughout the pathway that goes from research to care and to patients' quality of life
- 3** **Improve access to treatment and care** and focus on **better health outcomes**, including by ensuring that the EU Pharmaceutical Strategy¹² strikes the right balance between incentives to research and development of new therapies and access to care for all patients across Europe.

PRIORITISING BRAIN HEALTH

Including brain health as a distinct priority on the European Commission's agenda, as well as in the EU4Health programme, is key to make a difference for those living with brain disorders.

Brain disorders have a high global disease burden. Psychiatric conditions such as depression, anxiety disorders and alcohol and drug use disorders, affect more than one in six people across the European Union in any given year.¹³ Meanwhile, neurological disorders alone are the leading cause of *disability-adjusted life years* (DALYs), the loss of the equivalent of one year of full health. In 2017, the total number of DALYs attributable to neurological disorders was 21 million in the EU.¹⁴ Alzheimer's disease and other forms of dementia are now among the top 10 causes of death worldwide.¹⁵

In spite of the above, the work conducted to date in the field of chronic diseases does not address specifically brain disorders.¹⁶ A forward-looking strategic EU approach with tangible actions on brain health is still missing.

Brain disorders are still not given the attention they deserve, whilst their size, impact and cost can hardly be ignored. As many brain disorders tend to be chronically debilitating, they are often viewed as less of an emergency to tackle. The sheer number of brain disorders is underestimated, and they are immensely burdensome to patients and their families, but also costly both in terms of healthcare expenditure and in cost to society. Some brain disorders are well known by policymakers and the public, but many others, such as brain disorders in children, are frequently overlooked and under-resourced.

Additional challenges relate to the difficulty of achieving visible change in the space of a few years, with much longer timeframes required for research and development alongside more risks. This can impact crucial decisions on whether or not to invest in brain research, which often take into account the likely success rate or the estimated time to market a new treatment.

Brain health also constitutes a critical part of post- COVID-19 recovery planning, given the significant disruption of care on brain disorders and impact on patients. Neurological dysfunction is the second most common cause of comorbidity in patients with COVID-19, and dementia and other chronic neurological disorders are associated with an increased risk of mortality. The number of those who are in need of psychiatric help has also increased since the beginning of the pandemic, requiring a reconsideration of the current practices. Moreover, persistent neurological and mental issues are being reported more frequently in patients who have recovered from COVID-19,¹⁷ in what is becoming known as "post-COVID syndrome".

The cost of non-action

The high burden of brain disorders and their socio-economic impact must be urgently recognised by policymakers and an appropriate response must be designed in the same way as for other highly impacting disease areas like cancer and cardiovascular diseases. The cost of brain disorders in Europe amounts to almost €800 billion annually – more than all other major NCDs combined.¹⁸ In 2017 alone, neurological disorders accounted for over 1.1 million deaths in the EU.⁴

A 2020 report from the Stroke Alliance for Europe (SAFE), for instance, shows that if countries continue to fail to invest in stroke prevention, treatments and rehabilitation, the cost of stroke care across Europe could increase to €86 billion by 2040.¹⁹

However, a lack of visibility of brain disorders, combined with the stigma associated with these disorders as well as the great heterogeneity of the field make it difficult to take coordinated action. This makes political leadership all the more necessary to make a difference for those living with brain disorders.

While taking action on brain disorders cannot be delayed, further studies are needed to build evidence on the economic cost of non-action, how to improve the efficiency of brain health and care pathways, prevent avoidable deaths and implement cost-effective solutions. Brain health advocates, health systems and policymakers need good data to further understand the burden of disease.

Brain disorders and the global policy debate on non-communicable diseases (NCDs)

Brain disorders should be fully integrated into the global NCD agenda. As the global momentum to address the threat posed by brain disorders is increasing, it is crucial to recognise the full burden of brain disorders globally, also in relation to existing high-level commitments such as the Sustainable Development Goals (SDGs),²⁰ the WHO's dedicated brain health department and the United Nations (UN) Political Declaration on Universal Health Coverage, which call for the scaling up of comprehensive and integrated services for prevention, as well as treatment for people with mental disorders and other mental health conditions as well as neurological disorders.²¹ In 2020, WHO Member States endorsed a resolution that would lead to a 10-year WHO Intersectoral Global Action Plan on Epilepsy and other neurological disorders.²²

However, brain disorders have not yet received the political global priority they require. For example, only 24% of countries worldwide have stand-alone neurological health policies.²³ Strategic links to these high-level global commitments thus need to be strengthened, laying a strong foundation for an integrated approach to brain disorders.

RECOMMENDATIONS

- ▶ **Promote holistic EU action on brain health:** an EU Vision and Mission on brain health should be embedded in a strategic plan on a European Health Union and aligned with any existing international resolutions. It should address the full spectrum of brain-related disorders throughout the life span
- ▶ **Address COVID-19-related impact on brain health:** brain health should be included in the health-related recovery planning and receive the appropriate level of support and resources
- ▶ **Raise awareness on the cost of non-action:** new policy research should be promoted to illustrate the socio-economic impact of brain disorders and the value of effective and efficient investments
- ▶ **Advocate for the expansion of NCDs to include brain health:** both mental and neurological disorders should be coherently addressed and fully integrated within the NCD agenda in Europe and globally

FOSTERING RESEARCH AND INNOVATION FOR BRAIN HEALTH

A strategic research and innovation agenda that ensures coordination and collaboration at European and global level is a critical objective that cannot be overstated.

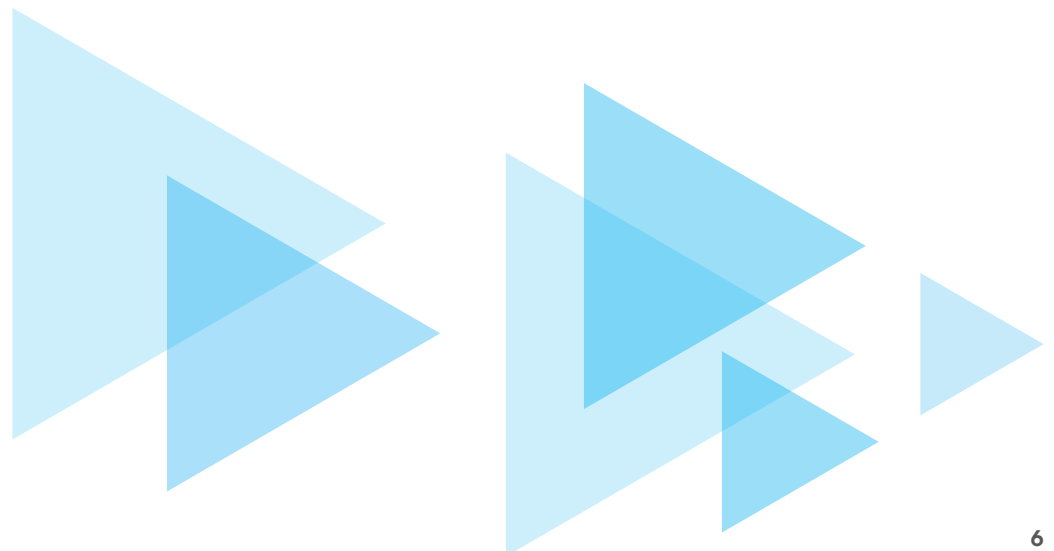
Brain research has been characterised by significant progress over the past years. Breakthroughs in the understanding of the brain are imminent, and recent advances offered by enabling tools such as artificial intelligence (AI), biomarkers and big data will further benefit neuroscience and accelerate the discovery of innovative therapeutic solutions for unmet needs.^{24,25}

The EU has undertaken some important steps to boost brain research initiatives with partners around the world, including through the EU Joint Programme on Neurodegenerative Diseases (JPND),²⁶ the ERA-NET Neuron Network²⁷ and the Human Brain Project,²⁸ to mention a few. It has allocated an increasing amount of financial resources to such research over the past decade, for instance by financing the €1.5 billion Human Brain Project.

However, advances in brain research are often hindered by regulatory obstacles, for instance due to concerns around data safety and protection, animal research, the appropriate use of gene technology and long approval processes for innovative solutions.

EU support for brain research spans across various European Commission funding mechanisms, from Horizon 2020²⁹ (followed by Horizon Europe³⁰) to the industry co-supported Innovative Medicines Initiative (IMI),³¹ the European Research Council (ERC)³² and the Future and Emerging Technologies (FET) programme.³³ Furthermore, the EU-funded European Brain Research Area (EBRA)³⁴ project is helping to develop a shared agenda for brain research and new strategic international initiatives. In doing so, EBRA is enhancing synergies among partners and research communities, breaking down silos, and avoiding fragmentation and the duplication of efforts in brain research. It also enhances the EU's voice in global research.

Horizon Europe, the EU's research and innovation programme for 2021-2027, has a dedicated Health Cluster which aims to improve the understanding of health and diseases, to develop innovative methodological and technological solutions to better manage them and to design sustainable approaches for the digital transformation and delivery of integrated, person-centred and equitable health and care services. However, there is still no recognition of the need to give more importance to brain disorders within the programme's calls, which the research community sees as a worrying oversight.³⁵



The EBC has repeatedly stressed the need for improved recognition of brain research and for its support within the scope of Horizon Europe.³⁵ This is a key requisite for improving human health and decreasing the overall burden of disease on European citizens. In order to further improve the programme, there are a number of points that should be considered:

- ▶ The need to address the full spectrum of brain-related diseases
- ▶ The importance of increased collaboration and coordination in the brain research space
- ▶ An increased focus on supporting basic as well as translational research
- ▶ Narrowing the scope of work programmes

Alongside Horizon Europe, and in the context of the post-COVID-19 recovery plan, new health funding programmes such as EU4Health must not only strengthen health security and crisis preparedness, but should also look at investing in areas with significant unmet needs, including brain health. The EU has the opportunity to demonstrate leadership and vision by introducing a comprehensive plan that includes targets and expected outcomes aimed at accelerating brain research, reducing the burden of brain disorders, enhancing early diagnosis, advancing knowledge about the human brain and preventing brain disorders.

The creation of a **Brain Health Partnership** could improve alignment and synergies across European initiatives to intensify scientific collaborations, identify gaps in knowledge, improve data sharing and facilitate access to infrastructure. With many flagship projects ending in 2023, including JPND and the Human Brain Project, there is the need for a new coordinated programme in the field of neurodegeneration research in the EU. As a previous proposal by France to create such a partnership did not receive sufficient support, the challenge of getting Member States and national funding councils to commit to long-term partnerships remains.

Promoting Public Private Partnerships

Public Private Partnerships can significantly boost brain research by linking academic, clinical and industry research agendas.³⁶

The new European Partnership for Health Innovation³⁷ will see the scope of joint research between industry, academics and SMEs expand beyond pharmaceuticals, to include medical technology, biotech, digital health and vaccines.³⁸ This new programme should continue to invest in brain research. Its predecessor, the Innovative Medicines Initiative (IMI), was launched in 2008 and subsequently renewed as IMI2 in 2012. Considered the world's largest public private research programmes in health, the two initiatives have invested a total of €5.6 billion to plug the gaps in Europe's system for translating its world-leading biomedical science into new drugs. In the past decade, IMI has supported important research projects, including in the brain health field (such as the Neuronet³⁹ and NeuroDeRisk⁴⁰ initiatives), and its achievements should be recognised more openly by policymakers and considered as a positive model for further action.



Enhancing European Reference Networks for brain health

European Reference Networks (ERNs) aim to facilitate sharing of knowledge and data as well as discussion on complex or rare diseases and conditions, including brain disorders, that require highly specialised treatment, and concentrated knowledge and resources.⁴¹

The ERN model provides added value. The model can also be used for acute or complex conditions or patient populations who, while not rare, can benefit from exchange of good practices. Any initiative to promote collaboration across institutes, countries and disease areas represents an achievement for brain health research.

The sharing of health data, in close cooperation with **patient organisations** and **connected clinical and research networks**, has the strong potential to transform care delivery and drive research and innovation, including in brain health. ERNs bring together these elements and provide a major opportunity to improve health outcomes and the lives of people living with a complex or rare condition.⁴²

Embracing the digital revolution

New digital technologies can accelerate brain research and the development of new therapies, as well as improve quality of life. Digital health is changing the scenario for healthcare professionals, industry and – most importantly – patients: from facilitating diagnosis through innovative technologies to the management of chronic diseases, exchange of data and remote support for patients through telemedicine, to drug discovery and post-marketing studies.

For example, a digital pill for schizophrenia represents the first FDA-approved software-based therapy.⁴³ Within the EU, there are a number of innovative projects underway where digital technologies are used to further understand the human brain.⁴⁴

New long-term integrated digital healthcare approaches, including rehabilitation, are warranted to address concerns related to the increasing number of chronic brain disorders. Studies indicate that a telemedicine-based approach is both feasible and efficient.^{45,46} Increasing and maintaining participation as well as autonomy in daily routine are promising findings that open up scenarios for the continuity of care at home through digital solutions.⁴⁷

The digital revolution is not without challenges. Access and exchange of data across Europe is often to be reconciled with the General Data Protection Regulation (GDPR) which, while having the best intentions in terms of safeguarding privacy, imposes limitations on how data can be shared and therefore on how health data can be exploited for brain research.

The proposed **European Health Data Space (EHDS)** is a welcomed step. Its focus on interoperability will be an important accelerator in improving brain research and data collection by providing the infrastructure to find solutions more quickly by sharing data across borders.

Brain research could provide a best practice case study for the digital transformation of healthcare due to the high potential that digital has in this field. The COVID-19 pandemic is a prime example, with neurology maintaining an acceptable level of service provision thanks to its adaptability to digital health solutions, for instance, telemedicine and remote monitoring systems. Digital solutions can revolutionise care delivery, provided that digital literacy (for patients and healthcare professionals) and a robust infrastructure are considered priorities in the strategic planning.

RECOMMENDATIONS

- ▶ **Strengthen Horizon Europe and Public Private Partnerships (PPPs):** allocate appropriate level of resources to brain research. Strengthen Public Private Partnerships since they can boost, and connect, basic and translational research
- ▶ **Build on EBRA's collaborative model:** ensure continued investment in brain research to enhance synergies among partners to avoid fragmentation and duplication
- ▶ **Implement a monitoring and evaluation (M&E) framework:** define indicators for countries to consider in each domain and area of the brain research framework
- ▶ **Promote stronger European Reference Networks (ERNs):** provide value for rare and complex neurological diseases and can provide added value by opening up the benefit from exchange of good practices to more common disease areas
- ▶ **Ensure safe use and exchange of quality data in the European Health Data Space (EHDS):** improve data collection and sharing to accelerate brain research

IMPROVING ACCESS AND OUTCOMES

Scientific and medical innovation becomes particularly meaningful when it addresses an unmet need, is accessible to patients and ultimately improves health outcomes.

This requires a continuous focus on value for patients and equitable access to quality care, in addition to a careful assessment of the efficiency and adaptability of healthcare systems and the associated regulatory framework.

It also requires more, and better, data on the burden of disease, including data on indirect costs and across the entire health and social care system. Furthermore, while social inequality factors such as gender, ethnicity, educational or socioeconomic setting have been recognised as important to understanding inequalities in access and outcomes, we still are lacking sufficient data on how to address these inequalities sufficiently.

The commitment to *'leave no one behind'* is a core principle of the 2030 Agenda for Sustainable Development.⁴⁸ However, according to the World Health Organization, access to services and support, including essential medicines for brain disorders, remains insufficient, especially in low and middle-income countries.⁴⁹

Significant variations remain in access to care across Europe,⁵⁰ and therefore must remain a priority issue. Differences in access are visible across the entire patient pathway, from screening and early diagnosis, to treatment and post-treatment due to the heterogeneity of Europe's population and the unequal burden of disease. Similarly, unequal patient access to clinical research remains a significant barrier to patients.⁵¹ The causes are multi-factorial, including late market access assessments, duplicative evidence requirements, and national pricing and reimbursement policies.

Delivering value to patients and health systems and measuring outcomes

In order to deliver real value to patients, a shift from disease-oriented to outcome-oriented care is crucial. Patient reported outcome measures (PROMs) and patient reported experience measures (PREMs) are essential tools to evaluate and improve healthcare results by putting patients and what matters most to them at the center.⁵² Brain health is a great example for this approach given the nature of chronic brain disorders, where overall functionality and quality of life is often more important than short term symptomatic improvement.

Despite considerable progress in symptom control, prevention of relapse and rehabilitation, unfortunately, there is still no cure for most brain disorders.

Primary and secondary prevention strategies remain essential, such as diagnostic tools for brain disorders, encouraging healthier lifestyles and routine screening for conditions such as dementia, autism and depression. Early detection and intervention with the necessary psychosocial support is also crucial to prevent the development of more severe conditions, which reduces the burden on carers and on the healthcare system (for example, by delaying the need for institutionalisation).⁹

Up-to-date real-world evidence (RWE) and the creation of registries and of mechanisms for rapid and safe information exchange should be integrated into decision-making. Collecting harmonised RWE on brain disorders at European level, for example, through the European Reference Networks, is a concrete example of how existing initiatives can be leveraged to develop European biobanks. Accelerating the development of more efficient patient care pathways, which can be monitored and measured, is an effort that should be supported by the entire brain health community.

Value-based healthcare has been considered as a potential solution to enable better patient outcomes.⁵³ This holistic approach towards seamless care models critically intertwines wider patient and societal outcomes with efficient spending of resources. Doing this should lead to both a more sustainable framework for payers, and improved care for patients. However, many brain disorders are rare and might never be assessed as 'cost effective' or bringing 'value'.

There are often discrepancies between the burden of disease and willingness of payers to fund certain therapies. Incremental innovation is critical to providing gradual and yet meaningful improvements to existing solutions.²⁷ It is essential to develop regulatory and reimbursement processes, as well as healthcare systems and services, that work to support the implementation of both incremental innovation and personalised healthcare for brain disorders.

Keeping the regulatory environment fit for purpose

In order to ensure access and better outcomes for brain disorders, the regulatory environment needs to be kept fit for purpose.

As the new **EU Pharmaceutical Strategy** takes shape, appropriate incentives, commitments and accountability of the industry should be balanced in support of brain health research. A new R&D paradigm would be welcome which focuses on unmet need and a patient-centric agenda, including greater patient involvement in clinical development and outcomes research.⁵⁴

In order to foster innovation, different types of incentives are required, which address the different challenges existing in each field. The concept of '**de-risking**' research, by helping public and private sectors sit together, becomes critical: this could be as simple as facilitating and enhancing access to data, to funding, providing IP-related mechanisms or defining an enabling regulatory framework. Academia currently takes the largest part of the risk, whereas industry is often perceived as becoming increasingly risk-averse. As the gap between the two actors is growing, EU and national authorities have an important role to play in bridging this gap – for the benefit of research overall.

EU regulatory guidelines for **clinical trials** should be continuously updated to ensure sufficient patient involvement and to ensure they are fit for purpose. For example, the European Medicines Agency's guidelines on the treatment of schizophrenia⁵⁵ are based on measurement scales used in clinical trials in the 1970s and 1980s. Therefore, they could be considered outdated or no longer clinically fit for purpose, yet they remain part of the regulatory process. COVID-19 has shown that, with sufficient political leadership, hurdles in trial design can be overcome and flexibility inserted into the regulatory process. Increased regulatory flexibility should also be considered for brain disorders.

The **repurposing of established medicines** or active substances can allow the marketing of existing medicines for a new indication, therefore contributing to better access to medicines for patients.⁵⁶ Repurposing older drugs in areas of unmet medical needs could lead to faster development times, reduced costs and less risk for industry, as medicine repurposing commonly starts with compounds that have already been tested in humans and many have demonstrated an acceptable level of safety and tolerability. A number of regulatory incentives for the repurposing of established medicines exist, including for paediatric use marketing authorisations (PUMA).⁵⁷

Brain disorders are prime targets for precision medicine. Whereas the slow progression and heterogeneity of adult genetic brain disorders pose challenges for early diagnosis, they provide an opportunity for early intervention.⁵⁸ In addition, a high proportion of childhood onset neurological disorders are genetic in nature and are important targets for precision therapy. Improving outcomes in these developmental disorders will provide lifelong benefits for the individual and society. In general, targeted therapies that match patients' genomic information can improve health outcomes and further facilitate the medicine development process.⁵⁹

Health Technology Assessment (HTA) can play a key role in rewarding and prioritising valuable innovation, allowing sustainable healthcare systems to provide an optimal level of quality care. However, current HTA models do not sufficiently account for early intervention, which is key for many brain disorders and need to evolve further in order to appropriately recognise the full benefit of early intervention. Moreover, better coordination of HTA for key technologies could improve timely access to innovative technologies.⁶⁰ The ongoing efforts on the legislative proposal for an EU HTA Regulation should be seen as a tool to ensure greater access and availability of therapies for brain disorders – for the benefit of patients and carers.

RECOMMENDATIONS

- ▶ Advocate for **equal patient access to care across Europe**
- ▶ **Upgrade strategic and regulatory policy framework:** implement a Pharmaceutical Strategy that fosters innovation and recognises meaningful incremental steps, while ensuring access to therapies
- ▶ Collaborate with the European Medicines Agency (EMA) in the review and development of relevant **clinical guidelines** (including new scales based on PROMs) and ensure sufficient patient involvement
- ▶ **Advance research on RWE:** collect RWE on brain disorders on EU level and promote greater use of RWE in regulatory processes
- ▶ **Support joint clinical assessments:** challenge the current fragmentation of HTA for greater access and availability of medical technologies to all patients
- ▶ **Raise awareness on the value of precision medicine:** present the heterogeneity of brain diseases to ensure the right treatment or therapy based on appropriate diagnosis

CONCLUSION

A CALL FOR AN INTEGRATED APPROACH TO BRAIN RESEARCH AND HEALTH

The European Brain Council urges the European Commission to come forward with a clear plan to tackle brain health in a collaborative, integrated and forward-looking manner in Europe and to further support EU Member States and associated countries in their efforts to combat the impact of brain disorders.

The European Brain Council calls upon the EU Member States and associated countries to implement, and where appropriate create, public health programmes addressing brain health in a systematic and comprehensive way, making the best possible use of available resources in order to stimulate more and better coordinated research and to foster strategies for prevention, early detection, diagnosis and adequate treatment.⁶¹

“Neurodevelopmental disorders are growing, and a much deeper knowledge of the brain is necessary. Scientific and technological research, from molecular to behavioural levels, have been carried out in many different places but they have not been developed in a really interdisciplinary way. Research should be based on the convergence of different interconnected scientific sectors, not in isolation...”

World Health Organization⁶²

An integrated, holistic European approach to brain research and brain health is overdue in order to maximise impact and improve outcomes in brain health through coordinated action.⁶³

National Brain Councils and comprehensive **National Brain Plans** in EU Member States and associated countries, for example, the 2017 Norwegian National Brain Health Strategy,⁶⁴ will continue to be essential for driving the brain health agenda. However, a comprehensive European strategy, supported by adequate funding, would not only better connect national efforts, but significantly accelerate them by creating synergies and overcoming silos.

As previously elaborated in the EBC Value of Treatment reports,⁹ the following three dimensions require urgent attention by decision-makers:

- ▶ Investments in more basic and clinical as well as translational neuroscientific research
- ▶ Steps to increase brain disease awareness, patient empowerment and training for health care providers at all levels of care
- ▶ Prevention, timely intervention and health care services delivery so as to support clear patient pathways fostering seamless care through validated models of care

KEY RECOMMENDATIONS

In Europe, in order to address these issues, it will be essential to:

1

Develop an EU-wide research and public health combined Brain Plan to address brain health in a comprehensive and collaborative way, strategically connecting National Brain Plans

- ▶ **Promote holistic EU action on brain health:** an EU Vision and Mission on brain health should be embedded in a strategic plan on a European Health Union and aligned with any existing international resolutions. It should address the full spectrum of brain-related disorders throughout the life span
- ▶ **Address COVID-19-related impact on brain health:** brain health should be included in the health-related recovery planning and receive the appropriate level of support and resources
- ▶ **Raise awareness and invest in generating evidence on the cost of non-action:** new policy research should be promoted to illustrate the socio-economic impact of brain disorders and the value of effective and efficient investments
- ▶ **Advocate for the expansion of NCDs to include brain health:** both mental and neurological disorders should be coherently addressed and fully integrated within the NCD agenda in Europe and globally

2

Promote the development of common research platforms to share data and results of conducted or current research (Knowledge Hubs and Joint Actions), while also leveraging the **European Health Data Space (EHDS)**

- ▶ **Strengthen Horizon Europe and Public Private Partnerships (PPPs):** allocate appropriate level of resources to brain research. Strengthen Public Private Partnerships since they can boost, and connect, basic and translational research
- ▶ **Build on EBRA's collaborative model:** ensure continued investment in brain research to enhance synergies among partners to avoid fragmentation and duplication
- ▶ **Implement a monitoring and evaluation (M&E) framework:** define indicators for countries to consider in each domain and area of the brain research framework
- ▶ **Promote stronger European Reference Networks (ERNs):** provide value for rare and complex neurological diseases and can provide added value by opening up the benefit from exchange of good practices to more common disease areas
- ▶ **Ensure safe use and exchange of quality data in the European Health Data Space (EHDS):** improve data collection and sharing to accelerate brain research

3

Ensure that the EU Pharmaceutical Strategy strikes the right balance between incentives to research and development of new therapies and access to care for all patients across Europe

- ▶ Advocate for **equal patient access to care across Europe**
- ▶ **Upgrade strategic and regulatory policy framework:** implement a Pharmaceutical Strategy that fosters innovation and recognises meaningful incremental steps, while ensuring access to therapies
- ▶ Collaborate with the European Medicines Agency (EMA) in the review and development of **relevant clinical guidelines** (including new scales based on PROMs) and ensure sufficient patient involvement
- ▶ **Advance research on RWE:** collect RWE on brain disorders on EU level and promote greater use of RWE in regulatory processes
- ▶ **Support joint clinical assessments:** challenge the current fragmentation of HTA for greater access and availability of medical technologies to all patients
- ▶ **Raise awareness on the value of precision medicine:** present the heterogeneity of brain diseases to ensure the right treatment or therapy based on appropriate diagnosis

Enhancing global collaboration on research and innovation, with a key leadership role from the EU, is key to effectively addressing today's societal challenges and improving the health and well-being of citizens. The European brain research community is focused, committed and highly competent. We urge policymakers to support our work in order to accelerate innovation in brain health for the benefit of those who need it most – patients.

CASE STUDIES

CASE STUDY 1

CAJAL Advanced Neuroscience Training Programme

The CAJAL Advanced Neuroscience Training Programme is a high-level hands-on neuroscience training hub in Europe, supported by funding from the Federation of European Neuroscience Societies (FENS), the International Brain Research Organization (IBRO) and the Gatsby Charitable Foundation. Since 2015, CAJAL courses have been held in two host venues known for their cutting-edge neuroscience research, the Bordeaux School of Neuroscience in France and the Champalimaud Centre for the Unknown in Lisbon. There are now over 500 international scientists who have benefited from the Programme's training opportunities, establishing an even stronger network of scientists who are able to contribute top neuroscience research in Europe and abroad. Course topics have included computational neuroscience, ageing cognition, advanced imaging techniques, bioenergetics for brain function, electrophysiology and other subject areas translatable and beneficial also to clinicians, industry and other key stakeholders. The Programme provides an excellent example of how partnerships in support of advanced training and research can foster growth in the brain sciences and improve understanding and treatment of human health conditions.

CASE STUDY 2

EANcore COVID-19 Initiative

The European Academy of Neurology (EAN) set-up a dedicated taskforce in March 2020 in response to the COVID-19 pandemic. Since then, this task force has set up the EANcore COVID-19 online resource centre to provide key resources to neurologists: updates on important publications and research, guidance in the form of consensus statements and surveys, and reports from clinicians in countries experiencing major outbreaks. In addition, a retrospective and prospective registry to collect data on the neurological manifestations of COVID-19 has been launched. To date, the EAN Neuro-COVID Registry (ENERGY) has collected data on about 700 patients across 18 countries, while also partnering with major ongoing national registries in Norway, Spain, Portugal, UK, US, Latin and Central America.

CASE STUDY 3**ECNP Networks and Thematic Working Groups (TWGs)**

The ECNP Networks are a unique scientific initiative, bringing together researchers from across European academia and industry in translational neuroscience, to form multi-disciplinary clusters to collect and aggregate clinical data and stimulate the sharing of ideas, discoveries and practices.

As well as providing a platform for European-wide collaboration, the Networks also leverage Europe's rich but dispersed resource base in clinical data, to open up new research horizons in brain science and facilitate the development of new and better methods of diagnosis and treatment. Fifteen Networks cover a matrix of diseases and methodologies, with an additional five Thematic Working Groups oriented towards emergent transnosological themes and technologies.

The strength and potential of the Networks and TWGs have made them powerful springboards for European grants; networks-based consortia currently run some of Europe's largest neuroscience research projects, as well as being the catalysts for several European Brain Research Area (EBRA) clusters.

ECNP supports the infrastructure of the Networks and TWG programme, including funding for meetings, data storage, grant application preparation, administrative assistance and communications.



CASE STUDY 4

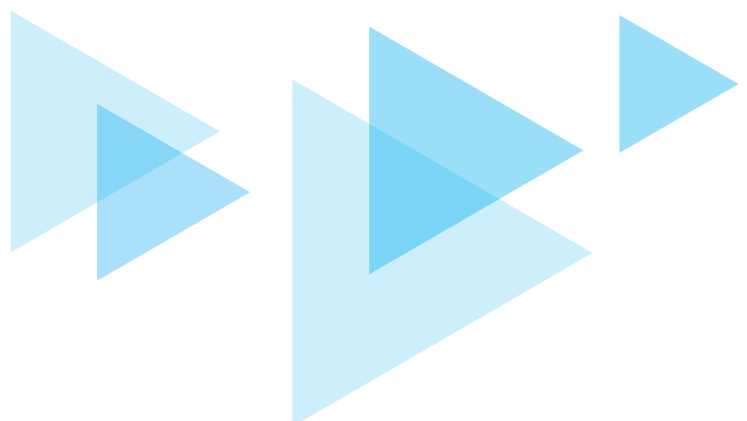
European Brain Research Area (EBRA)

Launched on 1 November 2018, this EBC-coordinated EU project was designed to respond to the Horizon 2020 call on 'coordinating European brain research and developing global initiatives'. The EBRA project was created as a catalysing platform for brain research stakeholders (researchers, clinicians, patients, governments, funders and public institutions) to streamline and better co-ordinate brain research across Europe while fostering global initiatives. It aims at reducing the fragmentation and duplication of research efforts and at fostering synergies through enhanced coordination of brain research efforts at the EU and global level.

The Shared European Brain Research Agenda (SEBRA) in particular, focuses on research opportunities and research and innovation gaps to be addressed in the field, priorities for action in the short and long term and research areas that would benefit most from cross-collaboration. SEBRA will be used to provide recommendations on future areas of innovative and translational research.

EBRA brings together the following partners:

- **European Brain Council**
- **Human Brain Project (HBP):** the 10-year project began in 2013 and directly employs 500 scientists at more than 100 universities, teaching hospitals and research centres across Europe. As one of the two largest scientific projects ever funded by the EU, the HBP is building a research infrastructure to help advance neuroscience, medicine and computing
- **EU Joint Programme on Neurodegenerative Disease Research (JPND):** the largest global research initiative aimed at tackling the challenge of neurodegenerative diseases. JPND aims to increase coordinated investment between participating countries in research aimed at finding causes, developing cures, and identifying appropriate ways to care for those with neurodegenerative diseases
- **ERA-NET Neuron:** the initiative supports basic, clinical and translational research in the diverse fields of disease-related neuroscience. Ministries and funding organisations across Europe, Israel, Turkey and Canada have joined forces to conquer diseases of the brain and the nervous system. It aims to support research directed at a better understanding of brain diseases and their progression, to pave the way for new or improved routes for diagnosis and therapy.



CASE STUDY 5**European Reference Networks:
EpiCARE and Rare Neurological Diseases (ERN-RND)**

European Reference Networks (ERNs) are virtual networks involving healthcare providers across Europe. They aim to facilitate discussion on complex or rare diseases and conditions that require highly specialised treatment, and concentrated knowledge and resources.

EpiCARE brings together highly specialised health centres (28 full members and 15 affiliated partners) in 24 European countries with expertise in rare and complex epilepsies. The centres closely collaborate with scientific societies (ILAE, EAN, EPNS, Epilepsy Alliance Europe) and a number of other epilepsy teams in the EU with expertise in specific domains. EpiCARE offers a coordinated approach for epilepsy diagnostics and treatment by using e-tools and cross-country e-consultancy.

ERN-RND aims to address the unmet needs of more than 500,000 people living with RNDs in Europe. Through coordination and knowledge transfer, ERN-RND is a patient-centred network to address the needs of RND patients of all age groups, with or without a definite diagnosis, by implementing an infrastructure for diagnosis, evidence-based management, treatment and collection of patient data.

CASE STUDY 6**IT4Anxiety Project**

IT4Anxiety project is an EU-funded research project in which GAMIAN-Europe is actively participating, particularly through assistance with result dissemination and inclusion of the patient voice throughout the different steps of the project.

The IT4Anxiety project aims to support the development and implementation of innovative solutions, particularly in relation to digital technologies, to help people affected by anxiety disorders. The project places an emphasis on targeting anxiety that results from brain and mental health disorders, such as anxiety caused by neurodegenerative disorders like Alzheimer's, or from PTSD.

The project brings together a wide range of stakeholders, including mental health professionals, startups specializing in the mental health and neuroscience fields, universities, higher education establishments and public bodies. The goal of the project is to collaborate with 15 startups to develop 10 technological solutions to anxiety that can complement conventional medical protocols.

CASE STUDY 7**The transformation of adult cells into pluripotent embryonic cells opens a way to study human brain diseases mechanisms, find new treatments, and replace damaged brain cells**

The recent discovery of simple ways to “dedifferentiate” adult body cells into induced pluripotent stem cells (iPSCs) opens fascinating possibilities for brain diseases. iPSCs are similar to the cells of the early embryo that generate all the cells of an adult animal, including the nervous system. Scientists can derive neurons from iPSCs or generate tiny 3D-structures (“mini-brains” or brain organoids) that reproduce the complexity of small pieces of the developing nervous system. These allow for the first time to study the early development of the human nervous system and its alterations. By studying cells derived from patients suffering from neurological or psychiatric disorders, it becomes possible to identify the mechanisms leading to their degeneration or malfunction and to perform initial screening for new medicines. Similarly, the toxic effects of environmental factors (e.g. pollutants) and their interactions with genetic factors can be initially assessed on these cells.

Until then, regenerative medicine approaches based on the grafting of cells into the brain to replace defective ones, was hampered by the limited access to human nerve cells and immunocompatibility problems. The first evaluation of iPSC-derived neurons to replace degenerating neurons was recently started in Parkinsonian patients. Importantly, the cells can be derived from the patients themselves. Research in this field is progressing very fast. While still at a very early stage and requiring scrupulous evaluation, this technology holds great potential for rare disorders as well as more common neurodegenerative diseases of the brain or the eye, and possibly, in the future, some psychiatric diseases.

CASE STUDY 8**Training Initiatives for Neurology Advocates (TINA)**

In 2016, EFNA launched its Training Initiatives for Neurology Advocates (TINA). EFNA is eager to ensure that these training activities are targeted to the neurology sector and the specific obstacles faced therein. Working with other stakeholders in the field (e.g. neuroscientists, neurologists, industry, regulators and payers) is an essential part of the approach.

Many of these workshops have focussed on equipping patients with the knowledge and skills they need to understand and engage in discussions on topics related to pharmaceutical policy – pricing, access and reimbursement. Workshops have also been held on themes such as patient involvement in neuroscience research and development, and science for advocates.

Under TINA, EFNA has been running 2-3 workshops annually for neurology patient advocates at both a pan-European and national level, creating a pool of empowered patient representatives who are available to participate actively in R&D and the associated decision-making processes. During the COVID-19 pandemic, TINA has been transformed into a series of e-learning modules. The latest series will focus on precision medicines and personalised healthcare.



ABOUT THE EUROPEAN BRAIN COUNCIL

The European Brain Council (EBC) is a network of major stakeholders in the area of brain health, with a membership encompassing scientific societies, patient organisations, professional societies and industry partners. Its main mission is to promote brain research with the ultimate goal of improving the lives of Europeans living with brain conditions. To find out more about the work of the European Brain Council, please visit our website www.braincouncil.eu

EBC has been promoting all the work being done to improve brain health and prevent and treat brain disorders in Europe. Different organisations, researchers, patients and carers are working on different conditions – Stroke, Multiple Sclerosis, Traumatic Brain Injury, Epilepsy, Cerebral Palsy, Mental Illness are only a few examples. We believe that by bringing together the very diverse activities which are all considered brain disorders, we can all benefit.

In order to ensure a bottom-up and top-down approach, thereby ensuring optimal key stakeholder management on both national and EU level, EBC realises that the best results are created in close alignment with National Brain Councils (NBCs). NBCs are independent and multidisciplinary councils that unite scientific organisations of neuroscientists, psychiatrists, neurologists, neurosurgeons, patients' associations, as well as the pharmaceutical and medical device industry, in order to speak with one strong voice on behalf of the whole of the "brain space".

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