

# Foresight Symposium Report 2025 Brain Health European Partnership

“Biological, social and environmental protective and risk factors that protect or threaten brain health across the lifespan”

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## Objective: Preparing the 2026 scientific call for the Brain Health European Partnership

The Foresight Symposium brought together leading scientists, representatives of patient organizations and stakeholders to shape the future research agenda on brain health, with a life-course perspective. Central themes included the key factors influencing brain health over the life course, but also prevention, early detection, resilience, understanding brain disease mechanisms, and advancing therapeutic strategies.

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## Program

9:15 Welcome

Ulrike Busshoff (DLR-PT, Bonn, Germany)

9:15 – 9:30 Introduction

Denis Vivien (Inserm, Paris, France) and Emmanuel Brouillet (CNRS, Paris, France)

9:30 – 10:15 Brain protective and risk factors at all stages of life and the development of disease. General overview

Juan Lerma (CSIC, Madrid, Spain)

10:15 – 10:45 Coffee Break

10:45 – 11:30 Genetics and epigenetic protective and risk factors

Stéphanie Debette (Inserm, Bordeaux, France)

11:30 – 12:15 Environmental and social factors

Andreas Meyer-Lindenberg (CIMH, Mannheim, Germany)

12:15 – 13:15 Lunch break

13:15 – 14:00 Therapeutic Interventions as trajectory modifiers

Urtė Neniškytė (Vilnius University, Lithuania)

14:00 – 14:45 The importance of prevention throughout the whole life course

Tiia Ngandu (Finnish Institute for Health and Welfare, Helsinki, Finland)

14:45 – 15:15 Coffee Break

15:15 – 16:00 Building emotional resilience: intrapersonal, interpersonal and societal approaches

Jennifer Lau (Queen Mary University of London, UK)

16:00 – 16:45 Wrap-up and Future Directions Integrative / Strategies for Lifespan Brain Health

Christophe Bernard (Editor in Chief of eNeuro, Inserm, France),

Masud Husain (Editor-in-Chief of Brain, University of Oxford, UK)

16:45 – 18:00 General discussion (lead by Ulrike Busshoff)



## Introduction to Brain Health Across the Lifespan

### Key Concept

Brain health is influenced by a complex interplay of biological, social, and environmental factors.

### Lifespan Perspective

Brain health evolves from early development through childhood, adulthood, and aging.

### Importance of Study

Understanding protective and risk factors can help guide interventions to enhance brain health and prevent cognitive decline



Ulrike Busshoff (CSA BrainHealth Coordinator)



Denis Vivien (Inserm)



Emmanuel Brouillet (CNRS)

# 1 Speakers & Topics

## 1.1 Juan Lerma (Spain)

Topic: Brain protective and risk factors at all stages of life and the development of disease. General overview.

- Research professor at the Consejo Superior de Investigaciones Científicas
- Vice President of the European Brain Council (EBC) (2022-2024)
- Councilor of the Society for Neuroscience (SfN) (USA) (2023-2024)
- Appointed Member of the Royal Academy of Sciences of Spain (2024)



Publications:

- Unbalanced dendritic inhibition of CA1 neurons drives spatial-memory deficits in the Ts2Cje Down syndrome model. *Nature Communication* (2019).
- Non-canonical Signaling, the Hidden Life of Ligand-Gated Ion Channels. *Neuron* (2016).
- A Role for SNAP25 in Internalization of Kainate Receptors and Synaptic Plasticity. *Neuron* (2009).

## 1.2 Stéphanie Debette (France)

Topic: Genetics and epigenetic protective and risk factors.

- Professor of Epidemiology
- Centre Bordeaux Population Health Research Inserm UMR1219, Bordeaux
- 2025 Paris Brain Institute director
- Visiting professor position at Kyoto University Center for Genomic Medicine



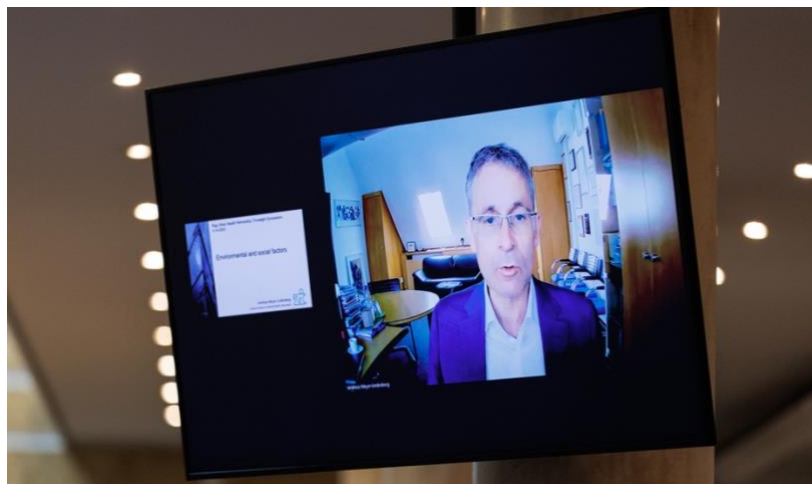
Publications:

- Sargurupremraj, M. et al. Genetic Complexities of Cerebral Small Vessel Disease, Blood Pressure, and Dementia. JAMA Netw (2024).
- Mishra, A. et al. Stroke genetics informs drug discovery and risk prediction across ancestries. Nature (2022).
- Malik, R. et al. Multiancestry genome-wide association study of 520,000 subjects identifies 32 loci associated with stroke and stroke subtypes. Nat Genet (2018).

### 1.3 Andreas Meyer-Lindenberg (Germany)

**Topic: Environmental and social factors.**

- Director Central Institute of Mental Health, Mannheim
- Chairman of the Executive Board
- Medical Director of the Department of Psychiatry and Psychotherapy
- Professor of Psychiatry and Psychotherapy, Heidelberg University



Publications:

- The non-ergodic nature of mental health and psychiatric disorders: implications for biomarker and diagnostic research. Meyer-Lindenberg A. (2023) World Psychiatry
- Ventral Striatal-Hippocampus Coupling During Reward Processing as a Stratification Biomarker for Psychotic Disorders. Schwarz K, (...) Meyer-Lindenberg A. (2022) Biol Psychiatry
- Identifying multimodal signatures underlying the somatic comorbidity of psychosis: the COMMITMENT roadmap. Schwarz E, (...) Meyer-Lindenberg A. (2021) Mol Psychiatry

## 1.4 Urtė Neniškytė (Lithuania)

**Topic: Therapeutic Interventions as trajectory modifiers.**

- Professor at Vilnius University, Research Team Leader
- Lab Scientific Director
- Member of the Board of Lithuanian Neuroscience Association
- Member of the Young IBRO Committee of the International Brain Research Organization



Publications:

- Bujanauskiene D,(...) Neniskyte U. Integrity assay for messenger RNA in mouse and human brain samples and synaptosomal preparations. (2024) iScience.
- Neniskyte U, et al. Phospholipid scramblase Xkr8 is required for developmental axon pruning via phosphatidylserine exposure. (2023 ) EMBO J.
- Paolicelli RC, et al. Microglia states and nomenclature: A field at its crossroads. (2022) Neuron.

## 1.5 Tiia Ngandu (Finland)

**Topic:** The importance of prevention throughout the whole life course.

- Affiliated to Research, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, 2022-2025
- Finnish Institute for Health and Welfare (Finland)



### Publications:

- Dementia prevention: The potential long-term cost-effectiveness of the FINGER prevention program, (2023) Alzheimer & dementia.
- The role of brain integrity in the association between occupational complexity and cognitive performance in subjects with increased risk of dementia, (2023) Gerontology.
- Occupational complexity and cognition in the FINGER multidomain intervention trial, (2022) Alzheimer & dementia.

## 1.6 Jennifer Lau (UK)

Topic: Building emotional resilience: intrapersonal, interpersonal and societal approaches

- Associate Professor, King's College London
- Co-Director of the Youth Resilience Unit at Queen Mary, University of London
- She previously taught at the University of Oxford, and has been a post-doctoral fellow at NIMH.



Publications:

- Lau, J. Y. F., Shariff, R., & Meehan, A. J. Are biased interpretations of ambiguous social and nonsocial situations a precursor, consequence or maintenance factor of youth loneliness? (2021) Behaviour Research and Therapy
- Bang, D., Haller, S., Bahrami, B. & Lau, J.Y. Group decision-making is optimal in adolescence. (2018) Scientific Reports
- Cohen Kadosh, K., Linden, D. E.J. & Lau, J. Y. Plasticity during childhood and adolescence: innovative approaches to investigating neurocognitive development. (2013) Developmental Science

## 1.7 Christophe Bernard (France)

Topic: **Wrap-up and Future Directions Integrative & Strategies for Lifespan Brain Health**

- Editor in Chief eNeuro
- Director of research at INSERM U1106 in the Institute of Systems Neuroscience



Publications:

- Design, Characterization, and In Vivo Application of Multi-Conductive Layer Organic Electrocorticography Probes. (2023) ACS Applied materials & interfaces
- Convergence of adenosine and GABA signaling for synapse stabilization during development. Gomez-Castro, F; Zappettini, S; (...); Bernard, C ; Lévi, S. (2021) Science
- The circadian dynamics of the hippocampal transcriptome and proteome is altered in experimental temporal lobe epilepsy. Debski, KJ; Ceglia, N; (...); Bernard, C. (2020) Science Advances

## 1.8 Masud Husain (UK)

Topic: Wrap-up and Future Directions Integrative & Strategies for Lifespan Brain Health

- Editor-in-Chief, Brain
- Professor of Neurology & Cognitive Neuroscience
- Professorial Fellow, New College
- Co-lead, Dementia Theme, Oxford Health NIHR Biomedical Research Centre
- Co-lead, Dementia Research Oxford



Publications:

- The computational cost of active information sampling before decision-making under uncertainty. (2021) Nat Hum Behav
- 2. Cerebrovascular risk factors impact frontoparietal network integrity and executive function in healthy ageing. (2020) Nature Communications
- 3. Neuroscience of apathy and anhedonia: a transdiagnostic approach. (2018) Nature Reviews Neuroscience

## 2 Key Scientific Insights

### 2.1 Lifespan Approach to Brain Health

Brain health is influenced by a continuum of factors such as genetics, education, parental care, physical and mental activities, sleep, diet and drug or alcohol use, social interactions, trauma history and cardiovascular profiles, socioeconomic environment and ecosystem (e.g. urbanicity versus countryside, exposure to nature). It was stressed that these factors are important throughout life, even at prenatal state, but that a particularly critical period is the one during which the brain is extremely plastic and vulnerable and still in the maturation phase (until the theoretical age of 21). This phase of early life-experience is decisive. Insights from animal studies (e.g., maternal care's impact on epigenetics and brain health) as models for human development, follow up of cohorts using various types of data (from biofluids, neuroimaging to environment experiences) were discussed.

### 2.2 Mechanisms, Biomarkers, and Omics

A core theme was moving "from risk to disease" by focusing on causal mechanisms. Identification of the causal mechanisms underlying brain health alteration (cognitive decline, dementia, degeneration, stress, multigenic risk factors etc.) is necessary. Redefining brain diseases as biological pathways has also been suggested. Because early actions could delay onset of brain diseases, targeting these biological pathways offers promising routes for personalized intervention, if optimal time window for intervention could be precisely defined. It should be kept in mind, however, that correlations are not causal demonstrations, which often require the use of cellular and animal models. Furthermore, biomarker discovery, setting up of multi-domains and longitudinal life-course studies in diverse or specific (with extreme phenotypes) populations worldwide looking at socio-environmental exposures and integrating biobank and multi-omics data (genomics, transcriptomics, etc.) are essential. The importance of capturing temporal changes in cell-specific gene expression was highlighted. More collaboration is also needed between clinical and preclinical research groups. The organisation and sharing of data within common infrastructures are essential for brain research.

## 2.3 Drug Development and Repositioning

Current drug development pipelines are inefficient: only 9% of drugs entering Phase I reach market approval, often due to a poor understanding of underlying biology. There has been significant support for repurposing existing drugs (e.g., Ketamine for depression, VCAM-1 inhibitors for stroke, Psychedelics (LSD, etc..) for mental disorders) and improving translational models, including organoids and iPSCs. The challenges of finding potent new therapeutic drugs for brain diseases (muscarinic agents for schizophrenia for example) and knowing how to deliver them to the brain are persistent.

## 2.4 Prevention and Resilience

Prevention strategies must target early and prodromal stages of brain diseases. The issue of social isolation or loneliness (experienced during COVID-19 pandemic for example) is very important in terms of prevention. A link has been highlighted between loneliness and addictions for example. Societal action to avoid loneliness could produce immediate impact. We also discussed the possibility that improving emotional resilience—across childhood, adolescence, and adulthood—could be achieved through higher exposure to nature starting from the unquestionable observation that increased urbanicity, decreased biodiversity and dramatic climate changes have dramatic consequences for brain health. However, mechanisms underpinning resilience remain poorly understood, with a lack of longitudinal data to explore developmental trajectories. There is a need to pursue these efforts with multimodal cohort studies.

# 3 Technological Dimensions

## 3.1 Digital tools

Sustainable and ethical digital tools for the daily follow up of cohorts. For example, multimodal cohort studies (e.g., 1.5 million participants) are being designed to assess how urban environments, social interaction (tracked via mobile sensors), and green spaces impact brain function and mental health.

## 3.2 NeuroImaging and “omics”

The strategic importance of using neuroimaging in combination with genetic/epigenetic/proteomic datasets to pinpoint key molecular mechanisms of psychiatric and neurological disorders has been underscored. One key point is the necessity to facilitate the re-use of data generated in cohort studies (availability of dataset, interoperability, etc.) assuring the best ethical, regulatory, reliability, and security practices. In this context, it appears essential to make the best use of pan-european infrastructures such as EBRAINS that can develop, improve and deliver powerful and standardized methods for the analysis of multidimensional data.

## 3.3 Digital Twins and In Vitro Models

New digital and biological tools, including digital twins and BBB/organoid models, were recognized as necessary to bridge preclinical and clinical research.

# 4 Strategic Directions for the Call

## 4.1 3P Framework

Protect, Prevent, and Preserve brain health across the lifespan.

## 4.2 Cross-Sector Collaboration

Facilitate partnerships between academia, patients’ organizations, biotech, and regulatory bodies.

## 4.3 Stratified Approaches

Emphasize biomarker-based stratification considering age, gender, and comorbidities. Interdisciplinary and data sharing / standardization are needed.

## 4.4 Focus Topics

Genetic/Epigenetic mechanisms, drug repurposing, urban environment effects, social cognition, digital monitoring, and resilience-building interventions.

This meeting reaffirmed the importance of an integrated, multidimensional and large-scale, and translational approach to addressing brain health challenges in Europe.

## 5 Conclusion

In conclusion, we have heard excellent scientific presentations which all emphasise the fact that we need to include all these different biological, social and environmental factors on brain health, but even more importantly at all stages of life. We need preclinical studies to demonstrate the causality of the mechanisms involved in brain disorders. We also need longitudinal clinical studies involving large cohorts, to look at the different phases of life. In these studies, it is important to take age into account, but also gender. Another aspect that was highlighted was the need to really strengthen the bridges between pre-clinical and clinical research, and also to strengthen interdisciplinary research, because all disciplines need to be involved in the service of brain health. Biological factors are important, but environmental factors are becoming increasingly so as a result of climate change and the upheaval of our societies. We need the biological sciences as a whole, but we also need the human and social sciences. Biological factors are important, environmental factors are becoming increasingly so, due to climate change but also to the upheaval in our societies, and social factors are essential and have repercussions on our mental health. It was agreed that all these biological, social and environmental factors should be taken into account when it comes to brain health, throughout the different phases of life and also in their transition.

## 6 Feedback

"Thanks very much for elaborating this report. Great job! Congratulations."

Juan Lerma

"Fine with me, thanks!"

Andreas Meyer-Lindenberg

"The report looks great!"

Tiia Ngandu

"Thank you, the report looks great!"

Urte Neniškytė

"Thank you very much for this report and for your efforts."

Catherine Marquer