Co-funded by the European Union

Human Brain Project

# EBRAINS CoCreate Digital Brain Health

# September- October 2022.

*Research and innovation roadmaps with long-term ambitions and visions within brain resilience and disease signatures.*

*Facilitated by EBRAINS Community Building Team*

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### Introducing EBRAINS

EBRAINS is a new digital research infrastructure, created by the EU-funded Human Brain Project, that gathers an extensive range of data and tools for brain related research. EBRAINS will capitalize on the work performed by the Human Brain Project teams in digital neuroscience, brain medicine and brain-inspired technology, and will take it to the next level.

### The EBRAINS ambition

EBRAINS draws on cutting-edge neuroscience, big data, computing, robotics and related technologies to help translate the latest scientific discoveries into innovation in medicine and industry, for the benefit of patients and society. EBRAINS' ambition is to provide the scientific community at large with an open state-of-the-art capability that fosters collaborative brain science, opens the way to ground-breaking discovery and aims to secure Europe's leading position in the dynamically growing field of multidisciplinary brain research and its exploitation.

EBRAINS

# Introduction

**The EBRAINS Community** is being built with and for the people developing, using, supporting, and benefiting from the EBRAINS Research Infrastructure, with an interdisciplinary and inclusive focus. In this context, the **EBRAINS CoCreate** process is a strategic community engagement process, which facilitates multi-actor collaboration on research and innovation roadmaps.

**Research and innovation (R&I)** agendas are generated at many different scales and levels, and by many different bodies, including the European Commission, governments, research agencies, funders, institutions, and individual researchers. A known tendency in this setup is that the scope is often limited by institutional thinking, disciplinary boundaries, or special interests. This leaves a need for defining research agendas across fields and actors, thereby defining more comprehensive and less biased priorities or directions for R&I programmes or projects.

**EBRAINS CoCreate** builds on the method of Open Research Agenda Setting (ORAS) which recognises the benefits of engaging multi-actors including civil society organisations, patient organisations and governance bodies in R&I development alongside scientific and technological experts. The resulting research agendas will in turn include visions or problems that societal actors find important, which strengthens and legitimises the selection of research priorities.

**The EBRAINS CoCreate Digital Brain Health** process is made up of five workshops arranged from early September 2022 to mid-October 2022 with the following set-up:

| Workshop 1: | Workshop 2: | Workshop 3: | Workshop 4: | Workshop 5: |
|---|---|---|---|---|
| Information and visions | Defining challenges and solutions | Initial R&I roadmap identification | Prioritize roadmaps and contribute to Final Report | Realization, lobbying and fundraising |

**The EBRAINS CoCreate Digital Brain Health aims to:**

1) Identify shared long-term ambitions within the areas of brain resilience and disease signatures.
2) Create roadmaps that allow the ambitions to evolve into tangible goals, tracks, and steps.
3) Identify opportunities to realise the R&I roadmaps.

**The origin of the CoCreation theme on Digital Brain Health** was established as a product of cooperation between the EBRAINS Community Building Team and AMU P78 - Aix-Marseille University. This theme covers several topics and aims to have relevance for a broad range of experts and stakeholders within brain health.

# Table of content

# CoCreating Roadmaps on Digital Brain Health – an EBRAINS initiative

*"If a single brain image can tell us a huge amount about one patient with one condition, how much more could we learn if we could compare every image of every patient with that condition?"*

In this EBRAINS CoCreate workshop series focusing on Digital Brain Health, our objective is to create research and innovation roadmaps with long-term ambitions and visions within brain resilience and disease signatures.

With disease signatures researchers hope to find patterns for better diagnostics of brain diseases. This will allow for early diagnosis and treatment of neurological and mental disorders and may even allow us to prevent some diseases.

With brain resilience the hope is that understanding neurobiological mechanisms that contribute to resilience in human brains can lead to improved prevention, prognosis, and adaptation of neurological and mental disorders.

When research projects aim to identify and understand a specific brain disease, they require a lot of data from the brain; data, such as the patient's (epi)-genetic background, cognitive functioning, medical history, socio-economic circumstances, and lifestyle conditions. Although medical researchers can access data at their own hospital relatively easily, access to data in other hospitals is much more difficult, as patient confidentiality, data protection, and the incompatibility of ICT systems are major obstacles.

Therefore, researchers wish to share data with each other!

One such initiative is EBRAINS, a European neuroscience research infrastructure. EBRAINS offers services and ICT solutions which can overcome these constraints, while maintaining the confidentiality that is crucial to the medical profession. Still, international collaboration and sharing health data can be difficult because of different national standards, policies, and cultural norms for data use. Researchers, citizens, and relevant stakeholders therefore need to agree on principles for sharing these personal health data.

The ambition of the EBRAINS services is to allow researchers to exploit medical data, regardless of where it may be stored. Typically, brain diseases have been classified primarily by symptoms. The ability to run experiments using large datasets opens the possibility of applying powerful big data analytical approaches to identify new disease signatures, based on a broad range of factors, from molecular level to whole brain and observable disorders of cognition and behaviour, which should pave the way for improved diagnosis and hence better treatment outcomes as well as early preventions strategies.

The EBRAINS CoCreate Digital Brain Health consists of a workshop series of five workshops, the first and the last held in Marseille and three online. The methodology of each step in the workshop series are elaborated on in the following.

# The CoCreate Journey

## WORKSHOP 1

Gaining common understanding of the main theme 'digital brain health'.

Choosing four topics and group formation in accordance with experience and expertise.

Defining one vision in each group.

Brainstorming on values related to the vision.

*The vision is inspirational and demonstrate a direction - it show us where we want to go, but not how. It can be specific and is informed by values and scenarios.*

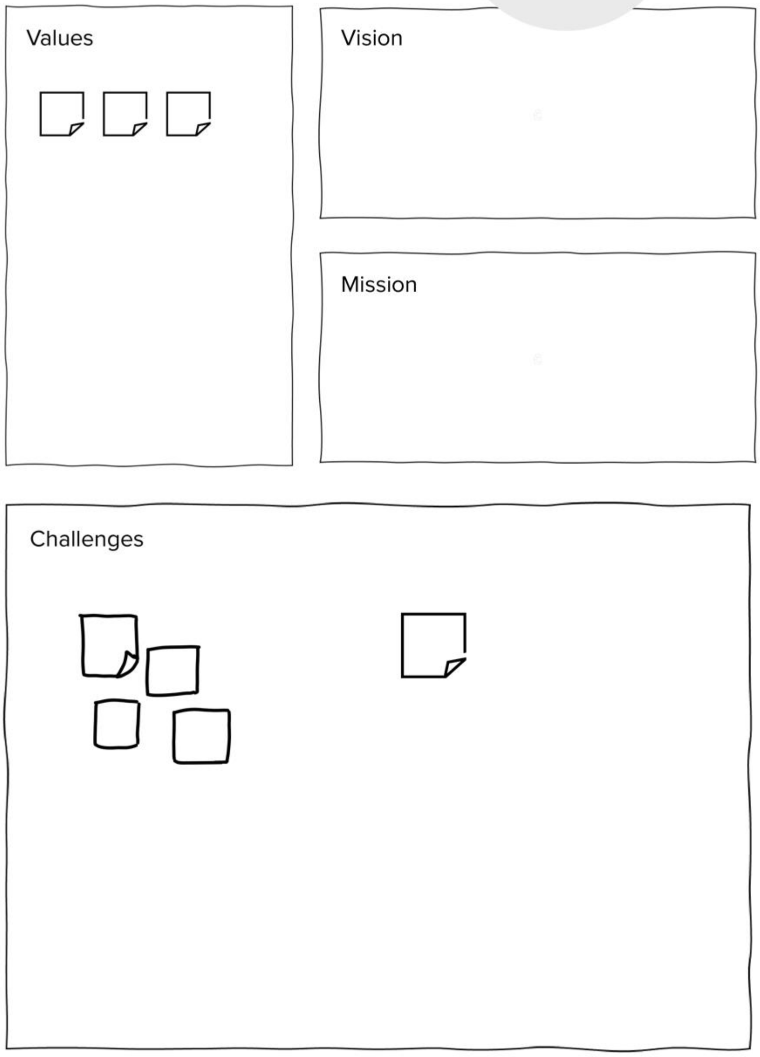

## WORKSHOP 2

Formulation of final definition of the mission.

Definition of the challenges that might arise by executing the mission.

Creating the first sketches of solutions to the challenges.

*Whereas the vision tells us where to go, the mission tells us how to get there*



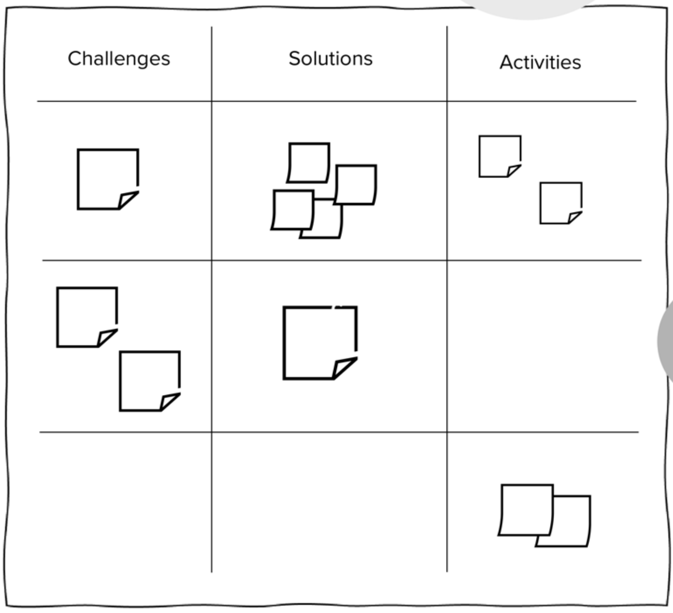
# WORKSHOP 3

Clustering and prioritizing the challenges and identifying realizable solutions to overcome each challenge.

Discussions on necessary activities that is a part of the solutions.

Creation of first sketch of roadmap.

*A roadmap is a strategic plan that defines a goal or desired outcome and includes the major steps or milestones needed to reach it.*



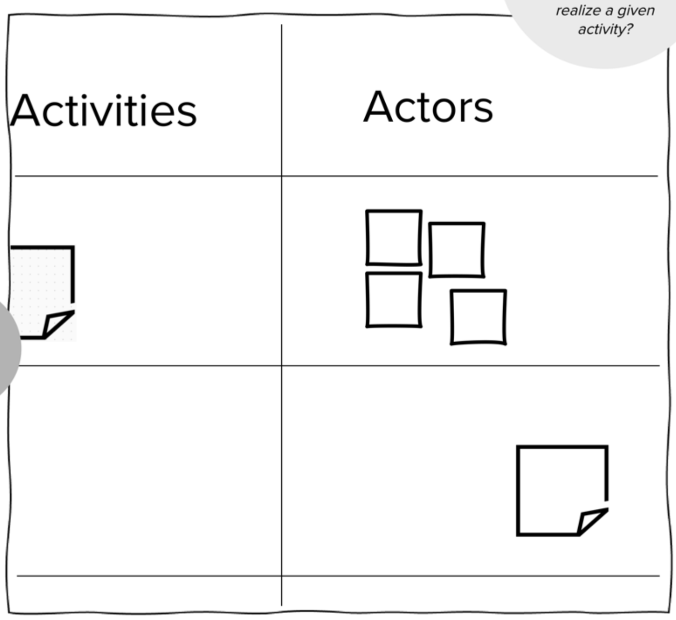

# WORKSHOP 4

Fine-tuning and finalizing the roadmaps followed by discussions on actions to realize them.

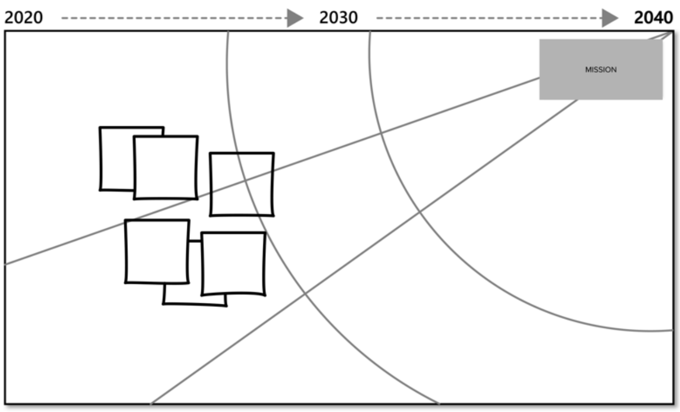
Identification of the needed alliances/actors to get involved in each action.

Starting/continueing writing explanational notes on the topic and roadmap.

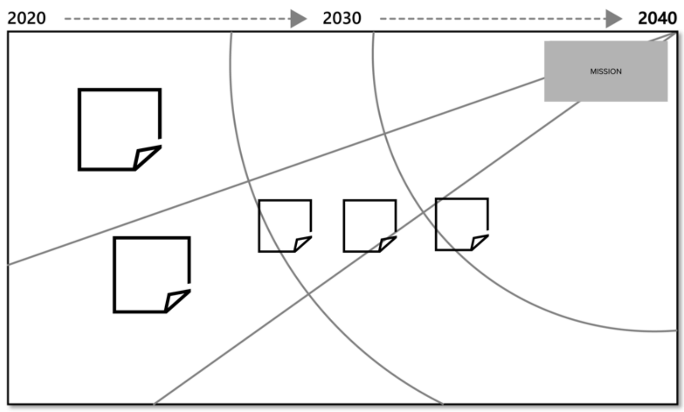
*Which actors must be involved and which alliances must be created to be able to realize a given activity?*




## Roadmap sketch




## Fine-tuned roadmap



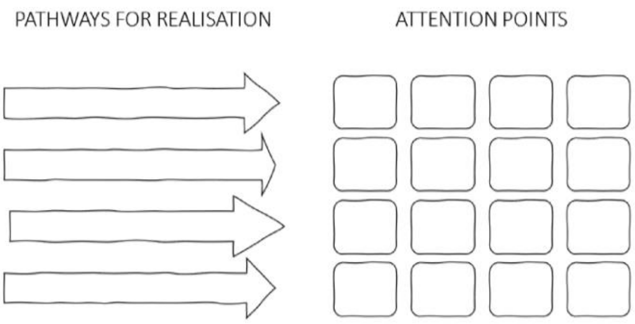
# WORKSHOP 5

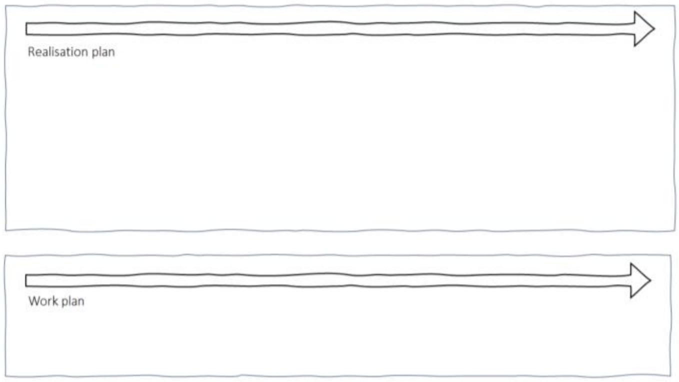
Creating alliances across the four groups.

Making a realisation plan to bring the roadmap into life

Day 1: Dinner brainstorm on realisation pathways

Day 2: Writing down a concrete work plan with to do points on where to go when the workshop is done.




# EBRAINS CoCreate Digital Brain Health – The Roadmaps

A roadmap is a strategic plan that defines a goal or desired outcome and includes the major steps or milestones needed to reach it. The development of roadmaps in EBRAINS CoCreate Digital Brain Health made use of a deliberate wide range of methods including horizon scanning, open brainstorms, ideation, co-creation and online collaborative spaces.

In the following chapters, you will find the four roadmaps developed during EBRAINS CoCreate Digital Brain Health in the fall of 2022. The roadmaps are the result of a deliberation among the participants. Each of the four roadmaps starts with an introduction to the opportunities and challenges, which the roadmap wishes to address, followed by their visions and missions, the envisioned activities and ends with a visualisation of the roadmap, which include the major steps and milestones identified on the research and innovation pathway towards reaching the mission.

## List of roadmaps

- **Longitudinal Data Studies**
  Elucidating multidimensional indicators of individual trajectories in brain health and disease, risk, and resilience, across the lifespan and Europe, to prevent, predict and treat disease, and to promote potential, productivity, wellbeing, and resilience.

- **Healthy Ageing**
  Provide individual citizens with evidence-based information to help them make right decision maintaining brain health.

- **Behavioral Data and Lifestyle Data**
  Personalized medicine: Combination of behavioral and lifestyle in combination with neuroimaging that should lead to better understanding of disorders, stratification of patients, and development of precise and holistic treatment approach.

- **Data Sharing and the Knowledge Graph**
  TRUSTable EBRAINS Community-driven platform with citizens engagement ensuring multilevel stakeholder communication at the service of wellbeing and Digital Brain Health. User-friendly, trustworthy, FAIR, and lawful data sharing infrastructure with sustainable and ecologically friendly software and hardware supported by common ontology and data structures withing Global Health Data Space.

# Roadmap: Longitudinal Data Studies

In this topic, we explore the opportunities for applying longitudinal data to digital brain health. What kind of brain research can be enabled if we have repeated data observations gathered and stored over a longer period of time? What kind of data and data storage possibilities should we explore? Moreover, what are the barriers for making this vision happen and where should we be careful? EBRAINS as a shared digital brain research infrastructure holds the potential to materialize this vision but it requires the input from a network like the EBRAINS Community.

## Introduction

Longitudinal data studies are critical for elucidating how stable, variable, or modifiable effects on (brain) health really are as well as for inferring causality. Cross-sectional designs, while giving important clues, capture inter-individual differences only and are blind to intra-individual dynamics, and thus, cannot stand alone. Critically, results of longitudinal studies have been found to show opposite effects compared to cross-sectional findings. More specifically, we need a longitudinal European (population) neuroscience approach and follow individuals across the lifespan. Such an approach should be complemented with in-depth, interventional, and translational studies.

Longitudinal studies allow for:

- *Identifying multidimensional indicators* predictive of physical (i.e., body) and mental & cognitive (i.e., brain) health and illness, resilience, and potential across the life span.
- *Developing comprehensive predictive models* for ensuring and promoting individual and public physical and mental health, well-being, and productivity by means of evidence based (preventive) public health, educational, social, environmental, and infrastructural policies and programs, personalized medicine, care and education, and industrial and technical innovation.
- *Generating new knowledge* to inform and guide targeted intervention, focussed in-depth and translation studies.
- *Making causal inferences,* in principle

Currently, we are lacking multidimensional indicators, containing information about the individuals' social, physical, and internal environments, their physical & mental health and cognitive reserve, as well as socio-political, economic and cultural dimensions of their lives. These indicators are pivotal for predicting physical (i.e., body) and mental & cognitive (i.e., brain) health and illness, resilience, and potential across the life span. Comprehensive predictive models will allow us to ensure and promote public and individual physical and mental health, wellbeing, and productivity by means of evidence based (preventive) public health, educational, social, environmental, and infrastructural policies and programs, personalized medicine, care and education, and industrial and technical innovation.

We identify four challenges. First, our understanding of human brain and behaviour, and physical and mental health is largely fragmented, and spread over multiple often not interacting research traditions and fields. It does not account for the complex interplay of multi-dimensional factors that emerge on different timescales and drive developmental cascades in individual's brain and body health through the lifespan. Second, the lack of generalizability and replicability of research findings in many research fields hampers our ability to make robust evidence-based predictions. Third, the lack of uniform, robust (but flexible), and easily accessible infrastructural, technical, data analytic, legal, and financial frameworks prevent us to equivalently assess, follow and analyse large representative populations across national borders and time. Fourth, long-term involvement and commitment of essential stakeholders such as individual citizens, and patient, scientific, social, political, (public) health, financial and private actors, institutions, organisations, and initiatives, require consistent, respectful, transparent, evidence-based, and comprehensible communication, discussion, interaction, collaboration, and knowledge transfer, sharing and dissemination.

Contemporary social, political, private, technical, analytic, and scientific landscapes, developments and initiatives favour and pave the way for a longitudinal lifespan (population) neuroscience approach. Here we think of large scale (longitudinal) initiatives, such as ADNI (Alzheimer's Disease Neuroimaging Initiative), HBP (Human Brain Project), ENIGMA, UK biobank, ABCD (Adolescent Brain Cognitive Development), and the EU Lifebrain project as well as initiatives and developments concerning open science and open data collection, curation, standardisation, harmonisation, storing, sharing and analyses tools and platforms (e.g. GitHub, Brain Imaging Data Structure (BIDS), National Institute of Mental Health Data Archive (NDA), Canadian Open Neuroscience Platform (CONP), International Neuroinformatics Coordinating Facility (INCF), EBRAINS Research Infrastructure, etc.), EU funding schemes, block chain and software containerisation technologies etc.

## Our vision

Elucidating multidimensional indicators of individual trajectories in brain health and disease, risk, and resilience, across the lifespan and Europe, to prevent, predict and treat disease, and to promote potential, productivity, wellbeing, and resilience.

## Our mission

- We will establish and maintain the required legal, financial, ethical, and infrastructural frameworks, procedures, and methods to safely collect, curate, integrate and analyse large-scale multimodal health data from multiple sites across Europe.
- We will use the data to develop mechanistic disease and resilience hypotheses and identify predictors of individual health and disease trajectories.
- We will use the framework to test the effectiveness of personalized interventions and public health policies.

## Solutions and activities

Large-scale multimodal, multidimensional, and multinational longitudinal research requires long-term investment and commitment of multiple stakeholders and stable and sustainable physical/IT (e.g., data acquisition, storage, sharing, processing and modelling), analytical, intellectual, legal, socio-political and financial infrastructures. Infrastructures should be scalable and extensible to successfully address future challenges and opportunities. Longitudinal multimodal, multidimensional, and multinational big data requires the development and implementation of adequate data processing, analyses and modelling methods. Moreover, it requires developing and implementing uniform educational, training, career planning and crediting strategies for staff and study personnel.

We propose a longitudinal multinational EU lighthouse project as an ideal. Such a project should strive to longitudinally follow population representative EU cohorts across the lifespan.

We identify five focus areas, which will be elaborated on in the following:

1. Legal, financial, stakeholder and knowledge transfer fundamentals
2. Data infrastructures
3. Data acquisition, curation, standardization, and harmonisation
4. Data analyses
5. Data and knowledge integration: multidimensional predictive indicators

## Legal, financial, stakeholder and knowledge transfer fundamentals

Data privacy and security as defined by the General Data Protection Regulation (GDPR) are core requirements. Multinational longitudinal studies must deal with the considerable heterogeneity in regional and national administrative, ethical, legal, and data protection frameworks, traditions, requirements, and procedures. Furthermore, it is not trivial to ensure consistent long-term commitment and involvement of essential stakeholders i.e., individual citizens, and patient, scientific, social, political, (public) health, financial and private actors, institutions, organisations, and initiatives. Finally, long-term funding, i.e., 10-20 years and beyond, of large scale multinational longitudinal studies is not existing. However, considering that the annual costs for brain disorders amount to approximately 800 billion Euros, one can argue that an annual investment of a small percentage of this amount to ensure evidence based (preventive) public health, educational, social, environmental, and infrastructural policies and programs, personalized medicine, care and education, and industrial and technical innovation, would be well spent.

### Solutions

- Establish uniform implementation of e.g., ethical guidelines and GDPR legal requirements across countries and locally within countries
  - Uniform consent requirements and procedures across countries and locally within countries
  - Streamlining of GDPR compliant data access, data sharing and data processing agreements
- Inform, educate, engage, involve, and interact, collaborate, and consult with stakeholders, and develop and maintain long-term mutual beneficial direct comprehensible communications and networks
- Long-term funding schemes of core infrastructures and personnel

### Actions

- Establish/involve a central expert/knowledge centre to guide and support local and national efforts
- Reach out to, influence, consult with international, EU, National, regional, and private funding agencies
- Reach out to, discuss with, and influence local, national and European policy makers
- Chart and analyse current requirements and procedures. Identify discrepancies, communalities, challenges, and opportunities
  - Chart and analyse current material transfer and data processing agreements. Identify discrepancies, communalities, challenges, and opportunities. Establish common agreement templates
  - Actively engage in influencing and shaping future ethical, data privacy and security regulations and procedures and represent the scientific and longitudinal perspective
- Europe-wide domain-specific certificates (lightweight - based on training) for sensitive data processing
- Build and maintain strong long-lasting collaborations, communication channels & networks, information/knowledge sharing infrastructures & platforms
- Public presence (traditional (mass media, written, visual (documentary), events, digital, information and education activities, knowledge dissemination (academic, policy papers, popular)
- Incorporate infrastructure for longitudinal data studies in infra-roadmaps

### Actors

We identify the following actors that may be approached/involved in all or some of the actions

- Relevant EU, national, regional national) policy makers
- Relevant International, EU, national, regional, and private funding agencies
- Relevant legal organisations (European, National data agencies)
- Existing longitudinal (brain) EU, international initiatives/consortia (UK biobank, PLING, ABCD, Betula, Base, IMAGEN, others)
- European and national brain councils
- Relevant research and scientific stakeholders
- Relevant EU, National patients, and interest groups
- European Big Data Value Association

EBRAINS:

- Relevant EBRAINS workgroups /committees/interest groups (e.g., data governance WG)

## Data infrastructures

Any multinational and longitudinal study must deal with heterogeneity in existing IT systems/platforms and solutions, and their development over time (e.g., end-of-life replacement, new partnering institutions, ...). Long-term stability of the data storage and continuity of the compute environment needs to be ensured. For this, the federated EBRAINS environment must be flexible, scalable, and extensible to address current and future data storage, security, curation, sharing, and analyses needs.

### Solutions

- Platform independent tools (containerisation)
- Federated homogeneous and scalable computing environments available for easy deployment on new systems
- Availability of different flavours of the compute environments for processing sensitive data (batch, cloud, interactive)
- Prioritised maintenance for components involved in the ongoing longitudinal studies. Allocated support for migration to new services if needed.
- User-defined processing steps in a "Common workflow language" (CWL); curation, quality control (QC) sharing between users (open CWL catalogue + curation)

### Actions

- Technical coordination - monitoring longitudinal studies and their requirements.
- Ensure funding and expertise for scalable hardware resources and maintenance
- Federation middleware implementation and maintenance over long periods of time
- Implementation and documentation of development environment
- Define and establish efficient and fast curation process for workflows
    - Provide detailed, comprehensive, and actionable documentation with best practices and user community code libraries/examples. The goal here is to prevent “re-inventing the wheel” and easy and reliable implementation

### Actors

We identify the following actors that may be approached/involved in all or some of the actions

- Current high performance computing providers (FENIX, ICEI)
- Scientific community generating software
- Policy makers
- National research infrastructure providers
- Private data, GDPR compliant, infrastructure providers

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- EBRAINS knowledge graph working group
- EBRAINS Medical Informatics Platform, HIP. Health Data Cloud

## Data acquisition, curation, standardization, and harmonisation

Multinational and longitudinal studies must deal with and minimise heterogeneity in data acquisition methods and procedures, experimental protocols, data measures (e.g., biomarkers, EEG, MRI modalities, questionnaires, lifestyles), and data scoring and analyses practices, as well as account for heterogeneous physical-social-cultural-health-economical-political environments.

### Solutions

- Data standardisation, targeted (depending on question/goals) data harmonisation, uniform experimental protocols, best practices
- Adaptive methods that handle heterogeneous data
- Pro-active (pre-acquisition) data curation

### Actions

- Develop, establish, and implement (best practices for) standardized, multimodal, multidimensional, and multinational longitudinal data acquisitions protocols
    - Implement multicentre standardized data acquisition
- Develop and implement pro-active pre-acquisition data curation procedures to minimize post-acquisition data harmonisation needs
- Involve/Establish a knowledge and expert centre for informing, guiding, and supporting existing and future longitudinal research projects on data standardisation and harmonisation
- Longitudinal data acquisition, curation, and exposition in Knowledge Graphs (KG)

### Actors

We identify the following actors that may be approached/involved in all or some of the actions

- The European Standardisation Organisations (https://single-market-economy.ec.europa.eu/single-market/european-standards/key-players-european-standardisation_en)
- EU (certification, law support)
- Data and metadata standardization communities and interest groups (e.g., BIDS, OpenMINDS, National statistics and health registries, International Neuroinformatics Coordinating Facility (INCF))

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- UNIs members of EBRAINS
- EBRAINS biotech start-ups

## Data analyses

Multimodal, multidimensional, and multinational longitudinal data require the development of reliable, robust, scalable and extensible data processing, modelling and visualization tools, pipelines and frameworks.

### Solutions

- Longitudinal benchmark datasets for development of longitudinal data processing and modelling tools and frameworks
- Longitudinal digital twins: model-driven framework for personalized longitudinal data fusion
- Develop, test, implement, document, and distribute longitudinal data processing and modelling tools, pipelines and frameworks
- End-to-end implementation in EBRAINS

### Actions

- Identify benchmark datasets.
- Develop, evaluate, validate, demonstrate, document, implement and share new longitudinal data analysis tools and frameworks
  - Modality (MRI, EEG, qualitative, sensor, biological) specific
  - Longitudinal meta and mega-analyses
  - Machine learning, decoding, normative modelling, AI solutions, etc
  - Ensure modularity and extensibility
  - Establish testbeds. Reproducibility, quality control, power estimates, simulations, etc
- Ensure continuity in the development, quality control, reproducibility, testing, implementation, documentation, distribution and support of data processing, modelling, and visualisation tools over time
- Software stack QC and continuous integration - focus on preventing biases in results arising from processing data with different versions of involved tools
- Development and implementation of inference technics longitudinal digital twins: model-driven framework for personalized longitudinal data fusion
- Co-design activities to ensure technological and organisational requirements are satisfied
- Integrate longitudinal datasets and tools in EBRAINS

### Actors

We identify the following actors that may be approached/involved in all or some of the actions

- Relevant scientific communities
- Competence centres and research institutes focusing on relevant method development
- Large longitudinal (brain) EU, international initiatives/consortia (UK biobank, Lifebrain, PLING, ABCD, Betula, Base, IMAGEN, others)

EBRAINS

- EBRAINS Facility hubs
- Relevant EBRAINS Partnering projects
- EBRAINS Biotech start-ups

## Data and knowledge integration: multidimensional predictive indicators

Multidimensional predictive indicators should ideally contain longitudinal information about the individuals' social, physical, and internal environments, their physical & mental health and cognitive reserve, as well as socio-political, economic, and cultural dimensions of their lives. However, indicators could also represent a more restricted part of this vast longitudinal multidimensional landscape. Indeed, longitudinal studies will differ with respect to specific research focus, questions and aims, part of lifespan covered, number of assessments, time interval between assessments, included measures, employed analytic methods etc. Critically, to leverage the longitudinal data for development of mechanistic disease and resilience hypotheses and individual predictors of health and disease trajectories, the data on both structural and functional levels must be linked with existing knowledge and theory.

Here it is key to establish the generalizability and replicability of potential predictive indicators and a mechanistic framework allowing for generalizability and consistency of the gained knowledge.

### Solutions

- Provide computational modelling and simulation to link between structure and function and their interplay along the longitudinal axis
- Develop mechanistic disease and resilience hypotheses and identify predictors of individual health and disease trajectories
- Develop the methods to test the hypotheses and to realize predictors
- Test the effectiveness of personalized interventions and public health policies

### Actions

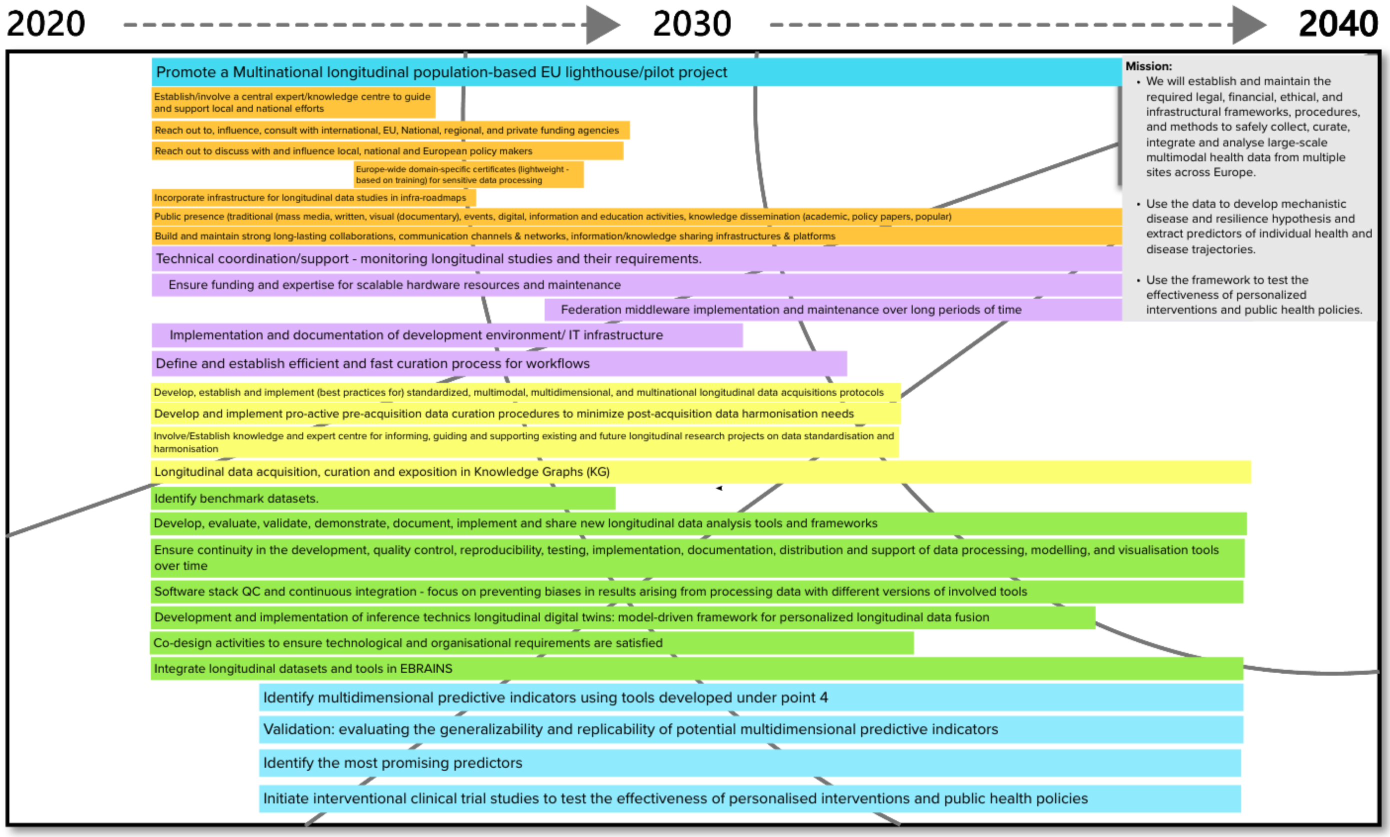
- Identify multidimensional predictive indicators using tools developed under point 4
- Validation: develop consensus strategies, guidelines, best practices, testbeds for evaluating the generalizability and replicability of potential multidimensional predictive indicators
- Identify the most promising predictors
- Initiate interventional clinical trial studies to test the effectiveness of personalized interventions and public health policies

### Actors

We identify the following actors that may be approached/involved in all or some of the actions

- Scientific community
- Patient organisations
- Clinical stakeholders/institutions
- Public health institutions
- (Public health) policy makers
- International, EU, national and private funding agencies

# Roadmap Illustration



| Activities - Longitudinal Data Studies | |
|---|---|
| 0 | Promote a longitudinal multinational population-based EU lighthouse project |
| 1 | Legal, financial, stakeholder and knowledge transfer fundamentals |
| 1.1 | Establish/involve a central expert/knowledge centre to guide and support local and national efforts |
| 1.2 | Reach out to, influence, consult with international, EU, National, regional, and private funding agencies<br>• Chart and analyse current requirements and procedures. Identify discrepancies, communalities, challenges, and opportunities<br>• Chart and analyse current material transfer and data processing agreements. Identify discrepancies, communalities, challenges, and opportunities. Establish common agreement templates<br>• Actively engage in influencing and shaping future ethical, data privacy and security regulations and procedures and represent the scientific and longitudinal perspective |
| 1.3 | Europe-wide domain-specific certificates (lightweight - based on training) for sensitive data processing |
| 1.4 | Build and maintain strong long-lasting collaborations, communication channels & networks, information/knowledge sharing infrastructures & platforms |
| 1.5 | Public presence (traditional (mass media, written, visual (documentary), events, digital, information and education activities, knowledge dissemination (academic, policy papers, popular) |
| 1.6 | Incorporate infrastructure for longitudinal data studies in infra-roadmaps |
| 2 | Data infrastructures |
| 2.1 | Technical coordination - monitoring longitudinal studies and their requirements. |
| 2.2 | Ensure funding and expertise for scalable hardware resources and maintenance |
| 2.3 | Federation middleware implementation and maintenance over long periods of time |
| 2.4 | Implementation and documentation of development environment |
| 3 | Data acquisition, curation, standardization, and harmonisation |
| 3.1 | Develop, establish, and implement (best practices for) standardized, multimodal, multidimensional, and multinational longitudinal data acquisitions protocols<br>• Implement multicentre standardized data acquisition |
| 3.2 | Develop and implement pro-active pre-acquisition data curation procedures to minimize post-acquisition data harmonisation needs |
| 3.3 | Involve/Establish a knowledge and expert centre for informing, guiding, and supporting existing and future longitudinal research projects on data standardisation and harmonisation |
| 3.4 | Longitudinal data acquisition, curation, and exposition in Knowledge Graphs (KG) |
| 4 | Data analyses |
| 4.1 | Identify benchmark datasets. |
| 4.2 | Develop, evaluate, validate, demonstrate, document, implement and share new longitudinal data analysis tools and frameworks<br>• Modality (MRI, EEG, qualitative, sensor, biological) specific<br>• Longitudinal meta and mega-analyses<br>• Machine learning, decoding, normative modelling, AI solutions<br>• Ensure modularity and extensibility<br>• Establish testbeds. Reproducibility, quality control, power estimates, simulations, etc |
| 4.3 | Ensure continuity in the development, quality control, reproducibility, testing, implementation, documentation, distribution and support of data processing, modelling, and visualisation tools over time |
| 4.4 | Software stack QC and continuous integration - focus on preventing biases in results arising from processing data with different versions of involved tools |
| 4.5 | Co-design activities to ensure technological and organisational requirements are satisfied |
| 4.6 | Integrate longitudinal datasets and tools in EBRAINS |
| 5 | Data and knowledge integration: multidimensional predictive indicators |
| 5.1 | Identify multidimensional predictive indicators using tools developed under point 4 |
| 5.2 | Validation: develop consensus strategies, guidelines, best practices, testbeds for evaluating the generalizability and replicability of potential multidimensional predictive indicators |
| 5.3 | Identify the most promising predictors |
| 5.4 | Initiate interventional clinical trial studies to test the effectiveness of personalized interventions and public health policies |

# Roadmap: Healthy Ageing

In this topic, we attend to the area of healthy ageing of the brain. We know there can be great individual variability within cognitive ageing trajectories. What kind of research is then necessary to understand why and how these variabilities occurs? Which risk factors should we focus on and what are the possible impacts of a shift in focus? Moreover, how we can best interpret the age-related changes and differences in brain structure, activation, and functional connectivity? With this topic we hope to strengthen both the visions for research within healthy ageing and to engage the communities focusing on brain resilience and healthy brain trajectories.

## Introduction

As life expectancy continues to rise in the world, populations and society turn toward science in order to break the dependence between seniority – an older age in which one could remain relatively healthy and active – and dependency – an old age declining towards death. Understanding and being able to predict individual brain health trajectories is a paramount challenge for the society, which science tries to address. Being able to advance the prognosis of neuro-degenerative disease by only 5 years, would decrease the societal and economic burden by 50%, by earlier treatments. Many challenges are present in the effort to simulate such trajectories and make predictions, but a major one among them is the high inter-individual variability, which does not allow for a universal solution, but requires a personalized treatment.

In the context of EBRAINS, the scope of building around Healthy Ageing ranged from identifying the challenges regarding research, technology, ethics, and public engagement, to bringing solutions that come with corresponding activities and actors. All of this, with the **vision** of *providing individual citizens with evidence-based information to help them make the right decisions for maintaining brain health.*

Mission

Towards democratization (equal access, transparence) of longitudinal temporal interactive acquisition of neuronal signals, generation of multimodal quantitative metrics of risk and resilience states, driving informed measures for maintaining brain health or preventing brain diseases.

Hereby, we identified three challenging aspects: data acquisition, data understanding and last, applications.

### Data acquisition

But what kind of data? The first priority is to get multi-modal data from the existing literature and accessible cohorts. Longitudinal data collection is very important for developmental and aging studies. Data gaps must get identified and eventually bridged. Can AI help with filling these gaps? This also raises a point for new data acquisition, coming from collaboration between labs, with the aim of targeting different parts of age-related features. Moreover, behavioral and lifestyle data can be of great importance; but is there a coherent way to merge them with the rest of data? In parallel, we must look at the ethical standards for the collection and use of data for personalized analysis. What features of the data must be ignored to block the linkage back to the individuals? Are these features important for healthy ageing analysis?

Solutions

The EBRAINS platform enables depositing different kinds of data and simultaneously giving access to the researchers and eventually to the public. For this to happen, the security requirements (GDPR platform) must be satisfied. That could also eventually enable people to deposit lifestyle and behavioral data that were individually collected.
In this regard, the data standards need to be defined, which also concerns population-based multi-modal and big data.
Missing gaps can be identified based on the literature, but also machine learning can play an important role in this quest.

Activities

Network based or driven activities (inspiration from EU COST or EU IHI).

### Actors

- Neurotech companies, e.g. Neuroelectrics, Artinis, g.tech, Kernel
- EU bodies-politicians
- Data standards stewards
- Potential researchers collaborating with HBP
- Hospitals, University Medical Centres

## Data understanding

Multimodal data come from different imaging techniques which give measures for different spatial scales. Common but also complementary features must be extracted for the purpose of understanding and integrating them. Even harder challenges apply to lifestyle and behavioural data if we want to make use of it for enhancing our analysis. Longitudinal data can give pictures for different ways of development regarding plasticity and dynamics. Can the developmental pathways be understood and quantified probabilistically? Is it possible to describe the ageing trajectory with some low dimensional representation and thus study its potential dynamics? If yes, can we create a model that gives rise to such behaviours or what are the limitations of modelling such systems? For personalized treatment and analysis, it is necessary to incorporate machine learning tools and build up AI algorithms that can produce automatic personalized modelling and predictions.

### Solutions

The solution to understanding the data lies in bringing together biophysical modeling and data driven AI approaches. More specifically, we need:

- Developing more data informed (biophysical) models to allow integration/expression of the data features
- Co-simulation of models on different spatial scales
- AI tools for model inversion and better predictions (even with data driven approaches) and validation on longitudinal datasets.
- Trying to group different approaches (data driven vs model based)
- Integration of tools and data
- Easy and intuitive access to data

### Activities

- Testing different hypotheses for the mechanisms linking structure with the relevant functional data features
- Combining bottom-up and top-down modelling approaches
- Identifying limitations and complementarities between the models

For the community:

- Raise awareness in the scientific community
- Facilitating researchers access to training sessions
- Facilitating researchers' participation in and use of EBRAINS
- Scaling interfaces to EBRAINS (from simple to advanced)
- Hosting training sessions in accessing and using data

### Actors

- Potential researchers collaborating with HBP
- AI community, e.g., ECMLPKDD, ICML, Neurips

For the community:

- EBRAINS education and training team

## Applications

In the end, what is needed to maintain brain health, i.e., to keep the individual on a healthy aging trajectory and prevent the onset of diseases? Should the output of our analysis get translated to actions or negations for each individual? And even if our analysis and predictions are well-grounded what are the challenges for engaging the public? How can we raise public awareness? Citizens are expected to be familiar with the technology required for our purposes and also be increasingly self-sufficient; but this is a challenge that also addresses appropriate health literacy and education. But also, what about the different systems of care for different countries? How restricted can our applications get based on that factor?

### Solutions/Activities

Healthy aging is one of the major concerns for any society that seeks productivity and fruitfulness from its human resources. For this reason, sectors, politicians, and stakeholders must be engaged to address the vision. But the EBRAINS platform must be able to give beneficial and constructive output in a readable and intuitive form. Interfaces should get developed for practitioners and patients; general condition and patient specific dashboards and apps should be ready to be provided. At the same time, public awareness must be raised. Health and scientific literacy should be developed. Moreover, especially for the elderly population, ICT interactions should get developed and facilitated.

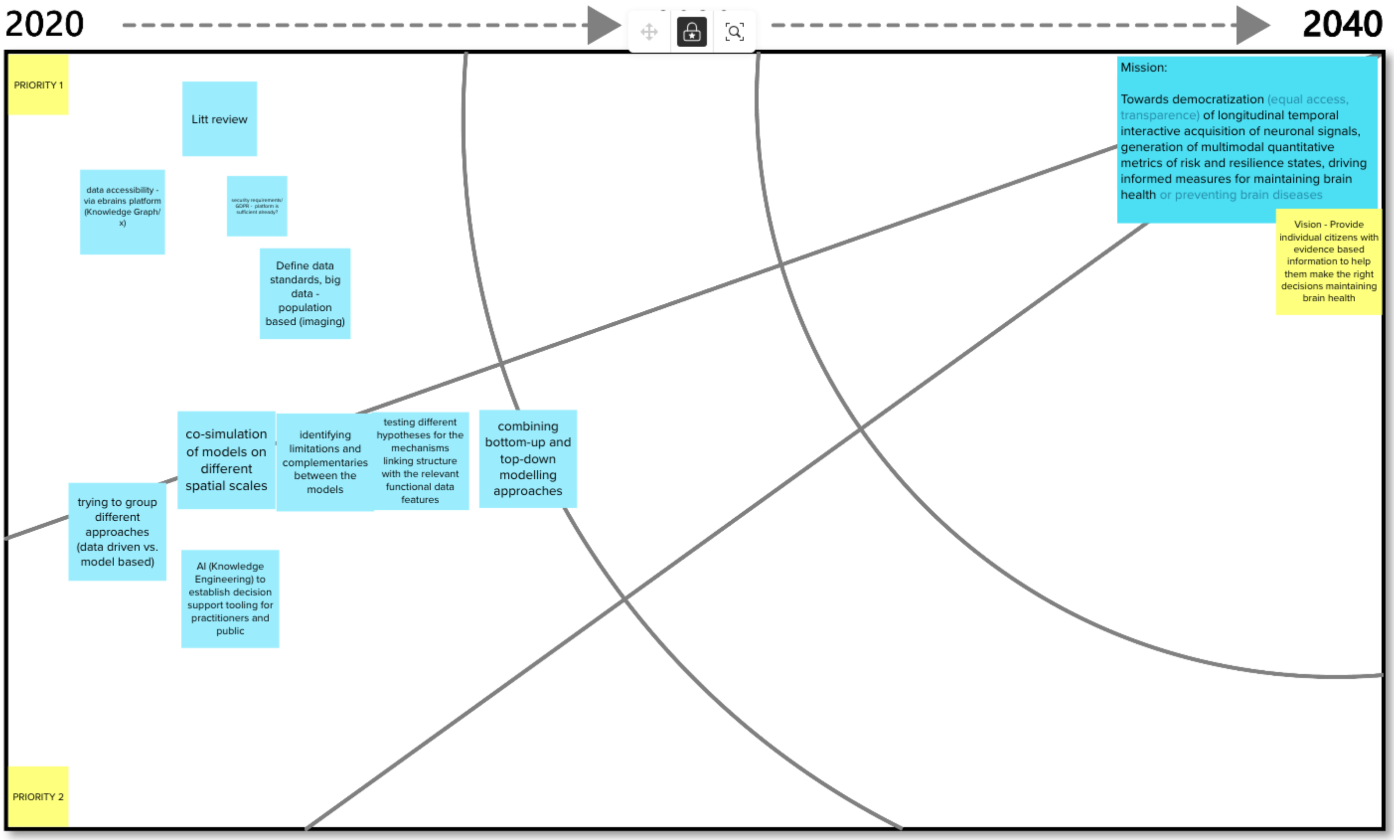
### Actors

- App developers
- Healthcare practitioners
- EBRAINS developers
- Departments of Health-communications

Other:

- Approach politicians
- Organize workshops (EBRAINS)
- Setting up more events for discussion and realization

## Roadmap Illustration




## Activities – Healthy Ageing

| | |
|---|---|
| 1 | Data accessibility - via EBRAINS platform (Knowledge Graph/x) |
| 2 | Security requirements/GDPR |
| 3 | Define data standards, big data - population based (imaging) |
| 4 | Trying to group different approaches (data driven vs. model based) |
| 5 | AI (Knowledge Engineering) to establish decision support tooling for practitioners and public |
| 6 | Co-simulation of models on different spatial scales |
| 6.1 | Identifying limitations and complementariness between the models |
| 6.2 | Testing different hypotheses for the mechanisms linking structure with the relevant functional data features |
| 6.3 | Combining bottom-up and top-down modelling approaches |

# Roadmap: Behavioral Data and Lifestyle Data

In this topic, we focus on the possibilities for incorporating behavioral data and lifestyle data to digital brain health. Our lifestyles and habits impact our brain health and our cognitive and mental wellbeing, but much more research is needed to understand the forces behind these impacts. How can we best integrate behavioral data and lifestyle data in studies of the brain? Which sources and possible collaborations should we approach? And what are the possible pitfalls of connecting clinical brain data with nonclinical brain data? At this EBRAINS CoCreate series, we aim to bring together various experts who can contribute to this topic from different views.

## Introduction

The development of personalised medicine and treatments requires a holistic approach to health, disease, and illness. It requires an understanding of the complex processes that can result in illness and disease, and these include accounting for the personal behaviour and lifestyle of an individual. The focus of this roadmap is to identify broad strategies when developing personalized treatment that recognises the impact of environmental factors on well-being and quality of life.

The roadmap for Behavioural Data and Lifestyle Date in Neuroscience recognises the impact of external actions by the individual on the body and brain and therefore the solutions to internal changes should engage with these triggers. For example, Alzheimer's disease causes changes in the brain which result in neurons ceasing to be able to function. Whilst much research has focused on the correlation between high levels of certain proteins and cell death and the development of medications to reduce cell death a broader focus is emerging. By altering behaviour such as eliminating some factors such as smoking or increasing other lifestyle factors involving diet and physical exercise, evidence suggests individuals can reduce their risk of developing Alzheimer's Disease. To create a roadmap that incorporates behavioural data and lifestyle data, requires the cooperation and collaboration of multiple actors with varied skills and knowledge. Whilst much of the data may have already been made available, creating a coherent synthesis which can be translated into actionable research will be a challenge. Not only does it have to provide research which accounts for all aspects of the multi-disciplinary approaches, it also must arrive at a point whereby clinicians and health professions can provide treatments that change the course or reduce the likelihood of developing poor health outcomes. To this end, individuals will make health focused decisions to limit poor health, researchers and health professions will develop new strategies to cooperate and create tools to facilitate this and broader community and government bodies will provide an environment which is safe to do so to improve the health of local and global populations.

The development of a lifestyle data and behavioural data approach in the neuroscience has a broad range of challenges. From our roadmap, we have identified involving four separate areas, namely the study population, the scientific investigations, the infrastructure, and governance.

Firstly, identifying the study population involves determining both the behaviours and lifestyle variables to be considered in the context of neuroscience, and it also requires careful consideration of who will be selected to be included in a representative sample. In part, this will be influenced by the research interests of the multi-disciplinary actors involved. Thus, behaviour and lifestyle should be accounted for within the context of culture and ethnicity. This is in addition to defining what would fall within the domain of "normal" and what would be considered "pathological" in terms of behaviour and lifestyle in relation to specific aspects of brain health.

Secondly, the scientific investigations will involve challenges when addressing issues related to behaviour and lifestyle in neuroscience. Identifying biomarkers which can be used in neuroscience research has been an ongoing issue as these are limited. For example, neuroimaging has few proven biomarkers for identifying links between behaviour and brain activity. For behaviour linked to lifestyle the use of living human participants is essential. The availability of biomarkers is further reduced if there is a preference for non-invasive biomarkers.

Thirdly, infrastructure is a challenge for developing neuroscience which incorporates behaviour and lifestyle influences on the brain is setting up the infrastructure. The development of the infrastructure relates to data collection and creating partnerships with groups to facilitate innovative insights into the broader agenda of how people live and brain health.

Finally, governance for such a research programme should be comprehensive. There is the potential for identifiable data on individual persons because behaviour and lifestyle are more overt aspects of life. In addition, depending on the type of lifestyles being identified, situating personal characteristics such as this within the context of culture further allows for persons to be identified.

## Identify risk factors for neuro psychiatric diseases in existing scientific knowledge or to rephrase this:

Review legacy data in scientific journals in relation to behaviours and lifestyles, and risk factors for specific diseases, an example could be neuro-psychiatric disease.

### Solutions

Identify what and who should be the subject of the investigation. The who could include cultural groups, socio economic groups, or various subgroups of a society. Identify a behaviour within the research community, where there are some meaningful outcomes, even if that is contradictory. Define what would be an appropriate behaviour to be researched in relation to neuroscience and how it can be determined to be “normal” or “pathological”.

### Activities

Develop or identify a machine learning (ML) program to complete the literature review that will review across disciplines and beyond neuroscience. Determine which type of ML would be the most appropriate. The key component of the research is that a behaviour can be identified (e.g., there are biomarkers), and there is some knowledge about the risk factors and there are neuroscientific tools that can assess this.

### Rationale

Identify what is possible for this initial research approach to behaviours/lifestyle and neuroscience. In terms of behaviours and lifestyles, the assumption is that behaviours imprint within the body/mind which impacts the brain. The lifestyle is external to the body/mind and so is directly observable within the context of culture and community. Behaviours can also be observed external to the body and the outcome of the behaviours is evidenced within the body/mind. The brain/behaviour link is internal and requires biomarkers for detection.

## Scientific: find common knowledge on behaviours in the scientific community

### Solutions

To identify an appropriate behaviour to research given current neuroscience tools and biomarkers and identify common knowledge on this behaviour within the scientific and more specifically the neuroscience community. Alzheimer’s Disease (AD) is used to illustrate this point. Relevant to behaviour data and lifestyles data in neuroscience, is personality and the risk of dementia[1], in particular AD. Higher levels of anxiety, anger, hostility, depression and being vulnerable to stress, that is, neuroticism facets have been associated with persons later developing AD or other dementias. At the same time, they are less likely to score higher on conscientiousness facets, such as, competence, order, dutifulness, and self-discipline.

### Activities

Develop a community of researchers and stakeholders to identify an appropriate behaviour that can be researched with current or newly created biomarkers and neuroscientific tools. Undertake a pilot study to identify what combination of tools and biomarkers would complement each other in a study i.e., triangulation.

### Rationale

Research behavioural and lifestyle as indicators of personality to examine AD biomarkers. Changes in behaviours and lifestyle may reduce the impact of personality and increase resilience against neuropathology to forestall the emergence of clinical dementia. For example, in AD, Sea Hero Quest (a serious game) can identify changes in spatial navigational skills up to 20 years before symptoms occur. So, there is a biomarker that identifies changes in the brain. Whilst not the earliest sign of change, some investigations are still pre-clinical. Blood and CSF can detect changes in Amyloid and Tau as well as, amyloid PET (positron emission tomography) imaging. This provides triangulation for the biomarkers related to the development of AD. The scientific community could discuss this considering behaviours, personality, and lifestyle in relation to AD.

The ability to diagnose persons in the pre-clinical symptom at risk stage would be the initial step in developing other biomarkers and methods to link behaviours and changes in the brain. In turn, this could provide more knowledge about AD and the development of environmental as well as pharmaceutical approaches.

## Infrastructure: use existing monitoring solutions or build new cohort with novel measures

### Solutions

The use of ML will enhance the existing analysis of behavioural data and lifestyle data within the neurosciences. It may also improve data on the body to identify biomarkers which can link data from the body and the brain. For example, if looking at the neuroticism facets such as anxiety, then this should be reflected in blood pressure reading. In relation to behaviours and AD, for example, can meaningful links be made between these events? In addition, regarding the conscientiousness facets, such as, competence, order, dutifulness, and self-discipline can some aspects be linked to the later development of AD.

### Activities

Review the behaviour and lifestyle data with the use of ML to identify and explore further neuroticism and conscientiousness. Is there a link between neuroticism and self-isolation? Do the facets of conscientiousness have associations with other elements of AD development? If there are any promising associations this could then be followed up with new research.

### Rationale

Aspects of Neuroticism, conscientiousness, behaviours, and lifestyle all have been associated with the later development of AD. All of these lend themselves to developing non-pharmaceutical solutions to address behaviours and lifestyle which lead to reduction in disease and well-being.

## Governance: actively seek advice on privacy in relation to personal data

### Solutions

By operating within the EBRAIN co-creating space this will reduce fragmentation[2] of the research and develop an innovation ecosystem and limit duplication. This could provide an environment which can better control how personal data is used and improve privacy.

Activities

use research infrastructures for science collaboration to address common problems and build partnerships to reduce the risk of privacy breeches. Consider using a combination of cloud-based storage and locally based storage of online data.

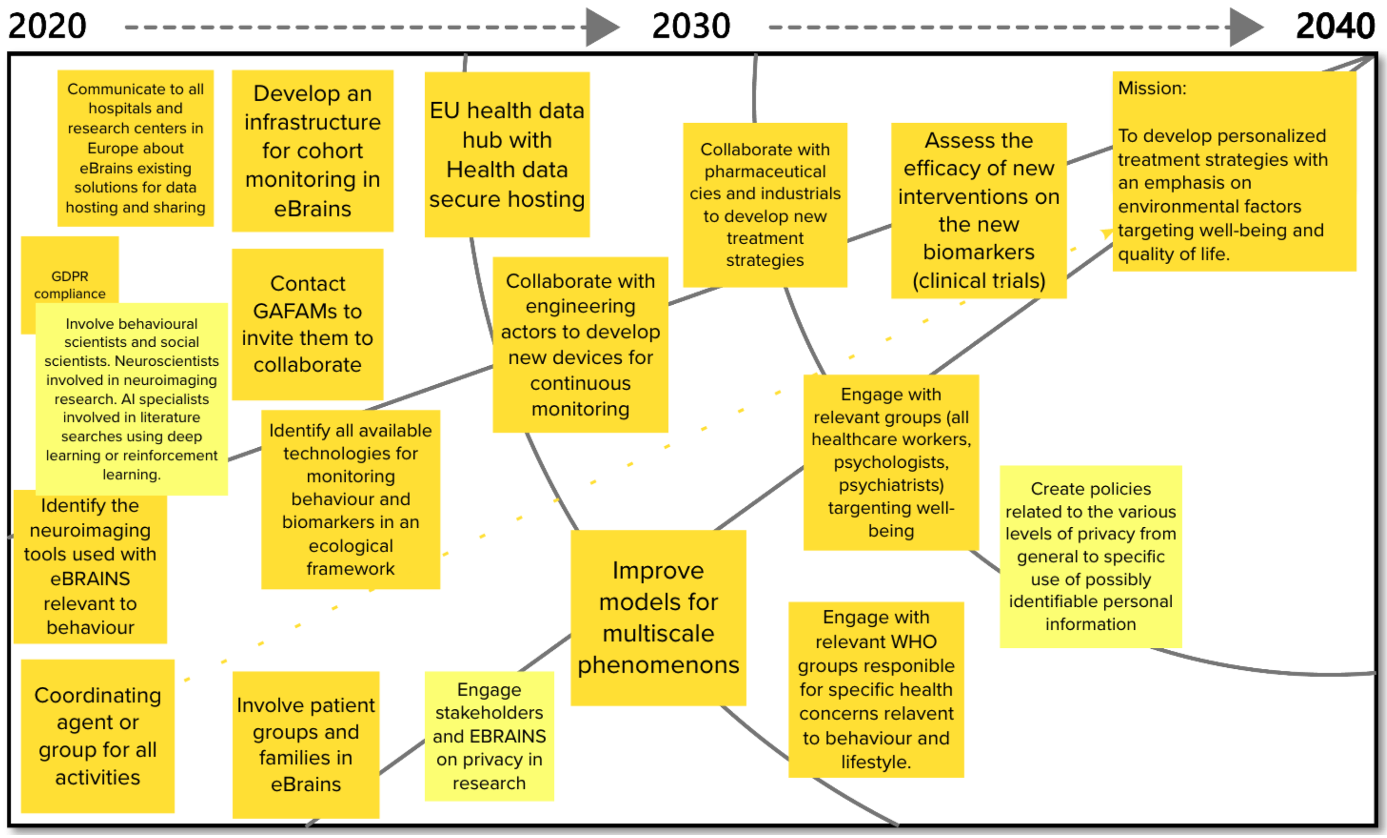
Rationale

ML and the broadening of the use of personal data brings new knowledge and requires further improves in security.

[1] Terracciano A et al, Personality Change in the Preclinical Phase of Alzheimer Disease. JAMA Psychiatry. 2017 Dec; 74(12): 1259–1265.

[2] https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/european-research-infrastructures_en

## Roadmap Illustration




## Activities - Behavioral Data and Lifestyle Data

| | |
|---|---|
| 1 | **Mission:** to develop personalised treatment strategies with an emphasis on environmental factors targeting well-being and quality of life |
| 2 | **Requirements:** Identify the neuroimaging tools used with EBRAINS relevant to behaviour |
| 3 | **Stakeholder:** Involve scientists from behavioural science, neuroscience, IT, etc |
| 5 | **Stakeholder:** Notify hospitals & research centres of EBRAINS data sharing and hosting. |
| 6 | **Requirements (secondary):** Develop an infrastructure for cohort monitoring in EBRAINS |
| 7 | **Requirements (secondary):** Create an EU health data hub with Health data secure hosting |
| 8 | **Stakeholder:** Invite GAFAMs to collaborate |
| 9 | **Requirements:** Identify all available technologies for monitoring behaviour and biomarkers in an ecological framework |
| 10 | **Stakeholder:** Involve patients and families in EBRAINS |
| 12 | **Stakeholder:** Collaborate with engineers to develop new devices for continuous monitoring, Engage stake-holders and EBRAINS on privacy in research |
| 13 | **Requirements (secondary):** Improve models for multiscale phenomenon |
| 14 | **Stakeholder:** Collaborate with pharmaceuticals & industries to develop treatment strategies |
| 15 | **Stakeholder:** Engage with relevant WHO groups responsible for specific health concerns relevant to behav-iour and lifestyle |
| 16 | **Regulations Policy:** create policies related to the various levels of privacy from general to specific use of possibly identifiable personal information -> Ensure GDPR compliance |
| 17 | **Stakeholder:** create a coordinating agent/group fort all activities |

# Roadmap: Data Sharing and the Knowledge Graph

In this topic, we explore the EBRAINS Knowledge Graph. With this Knowledge Graph it is possible to acquire and share the data researchers need to make their next discovery. It also enables researchers to connect to the software and hardware tools needed to analyze the data. However, brain research data can often be sensitive. So how do we preserve the possibilities to maximize on each other's knowledge by opening the access to shared data? How do we secure the curation and sharing of brain data in the EBRAINS Knowledge Graph in a sustainable way? Together we can cocreate how to shape the future for the EBRAINS knowledge graph.

# Introduction

## Vison

TRUSTable EBRAINS Community-driven platform with citizens engagement ensuring multilevel all stakeholders communication at the service of wellbeing and Digital Brain Health. User-friendly, trustworthy, FAIR, and lawful data sharing infrastructure with sustainable and ecologically friendly software and hardware supported by common ontology and data structures withing Global Health Data Space.

## Mission

Co-create, co-evaluate standardized but adaptive Open and FAIR Digital Brain Health solutions and training on all possible levels supported and harmonized by common ontology to facilitate Prevention, Diagnostics, Prognosis, and Adaptation of neurological disorders inferring multiscale mechanisms of disease signatures and brain resilience.

The brain is the most complex object in the existing universe. Integration of multimodal data is crucial to understand the multiscale structure and function of the brain in health and disease. Thus, the ambition of EBRAINS is to apply analysis using large and representative datasets with common data structures and ontology-based metadata annotation to effectively explore new disease signatures and pathological pathways. Data sharing via EBRAINS could increase the discoverability of the research as well as its reuse facilitating new findings. According to FAIR principle (Findability, Accessibility, Interoperability, and Reusability), data sharing can advance the efficiency of neuroscientific research and tackle the lack of reproducibility and replicability.

However, data sharing can compromise the privacy of study participants. A possible issue could be a conflict between open science and GDPR (General Data Protection Regulation). Brain-related data is sensitive data that could be used for re-identification compromising participants' privacy. Neuroscientists should take all precautions in their practice including data minimization, de-identification, anonymization, and pseudonymization. There are different data sharing standards across countries with variations in policies, laws, recommendations, and cultural perceptions. Hence, multi-level stakeholder communication and collaboration should be established ensuring involvement of citizens in Digital Brain Health roadmaps. **TRUSTable EBRAINS services could provide a background for Global Health Data Space** improving global health and well-being to achieve **Universal Health Coverage (UHC) 2030** as a part of The Sustainable Development Goals (SDG) within United Nations (UN) The 2030 Agenda for Sustainable Development.

## EBRAINS TRUSTable Digital Brain Health Services

The Initial issue to consider is the trust of patients and research participants. Without consent, we cannot consider sharing data. Thus, neuroscientists and medical doctors should transparently demonstrate their intent and virtue to share data and explain measures to retain privacy and security.

### Solutions

Designing "Living Lab" Strategy
Cultivate "Open Brain Consent" to share brain-related data.
Ensure safe, sustainable, and eco-friendly software and hardware

### Activities

**Human Brain Project Internal Meeting** 13-14 October

"EBRAINS TRUSTable integrated services for the discovery of multi-scale disease mechanisms"

Chair: Petra Ritter, Charité - Universitätsmedizin Berlin

**Global Health Summit 2022** 16-18 October "How to Achieve a Global Health Data Space"

Chair: Petra Ritter, Charité - Universitätsmedizin Berlin, Speaker: Paweł Świeboda Human Brain Project Director-General

Create inclusive and TRUSTable Digital Brain Health services accessible to the general public and individuals with different levels of literacy. Training and services with human communication if needed.

Development of inclusive, trustable, and explainable EBRAINS patient consent form for data sharing.

Identify and measure the environmental impact of hardware and software development

Info-meetings for Digital Brain Health stakeholders on a commitment to reduce the ecological footprint.

Mapping of activity in relation to the complex adaptive system of The Sustainable Development Goals (SDG) within United Nations (UN) The 2030 Agenda for Sustainable Development to achieve **Universal Health Coverage (UHC) 2030**

## International, national, and institutional Open Neuroscience guidelines with curation on the early stage of project planning (before the experiment).

### Solutions

FAIR training, infrastructure, software, and data. Guidelines for experiments with FAIR principles and integration by design and default. Implement Open Science guidelines based on standards and best practices and disseminate them together with relevant tools. In parallel with research articles neuroscientists should also be focused on Data Articles and for example BIDS README files including structured consistent ways to describe data itself, experiments details, triggers, scales, exclusions, and missing data.

### Activity

Develop and provide training on WEB-BASED user-friendly Data Curation ecosystem: electronic experimental data capture fitted for BIDS and openMINDS tools helping for future curation and increased interoperability.

Distribute multilevel guidelines including EBRAINS patient consent form for data sharing.

Implementation of EBRAINS National Nodes and institutional level curations with established data curation workflows within a web-based curation ecosystem reusable by other platforms and institutions.

## Address interoperability and harmonization of data, tools, and platforms

How can we address the interoperability of data, tools and platforms? how do we keep including new technology, data, tools, and ontologies, without 'breaking' anything and still have a stable environment?

### Solutions

Harmonization, the balance between maintaining and developing. Co-Creation, Co-evaluation. EBRAINS interacting with other platforms (e.g. CONP) and/or data searches (Google data sets).

### Activity

Harmonization cross platforms working groups (e.g., The International Neuroinformatics Coordinating Facility (INCF)).
Create interface and Interoperability between BIDS and openMINDS.
OpenMINDS and Neuro Imaging Data Model (NIMD) common ontology development.
Design Global Health Data Space with EBRAINS Digital Brain Health TRUSTable integrated services.

## Data Sharing and Knowledge graph CoCreate Roadmap integration and adaptation alliances with all other Collaborators

### Solutions

Adapt "Data Sharing and Knowledge Graph" for common needs and goals of "Longitudinal Data Studies", "Healthy Aging", "Behavioral and lifestyle studies" and "Public Perceptions on: EBRAINS Data Sharing to facilitate Prevention, Diagnostics, Prognosis, and Adaptation of neurological disorders.

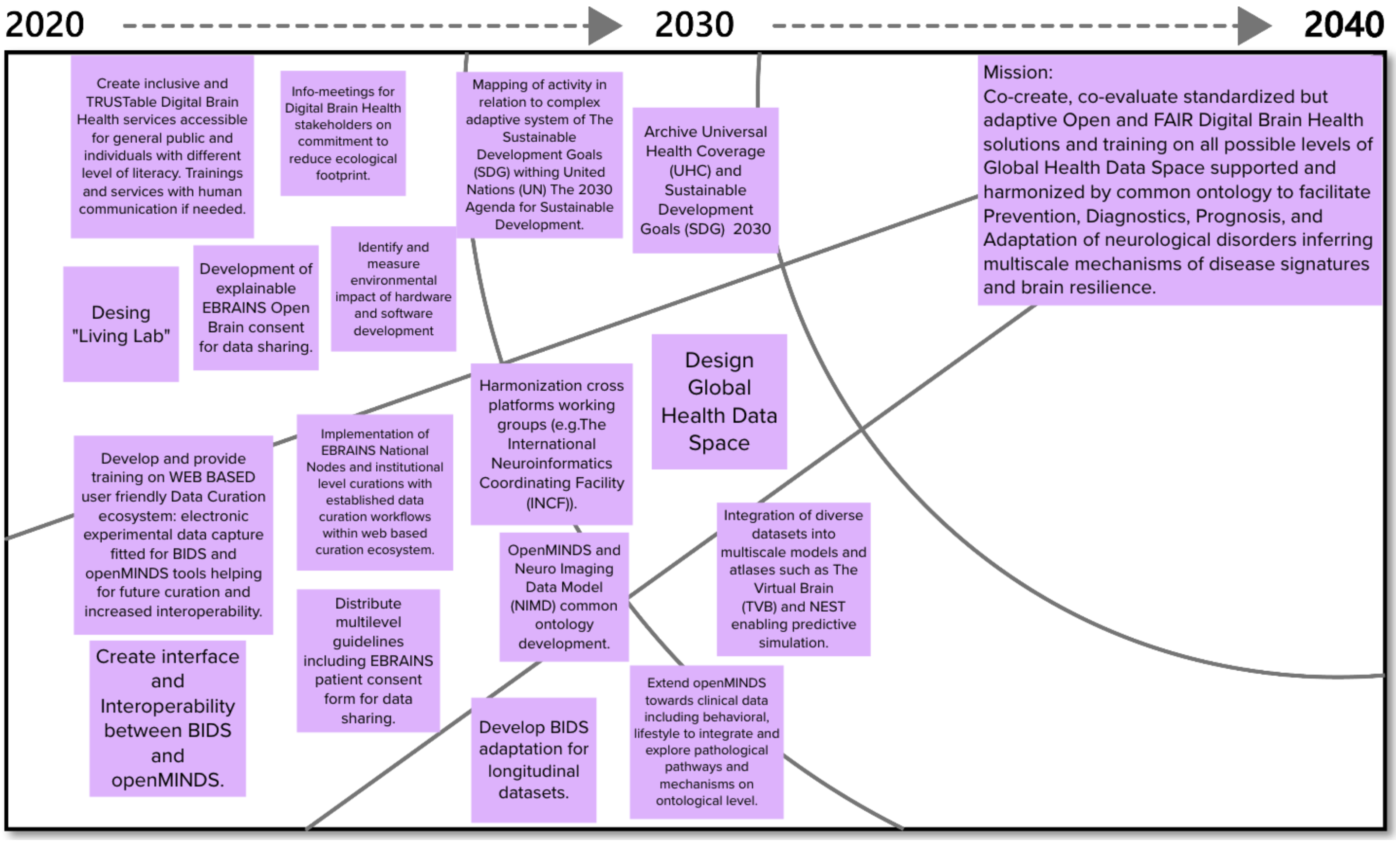
### Activity

**Develop BIDS adaptation for longitudinal datasets.**

Extend openMINDS towards clinical data including behavioral, and lifestyle to integrate and explore pathological pathways and mechanisms on ontological level.

Integration of diverse datasets into multiscale models and atlases such as The Virtual Brain (TVB) and NEST enabling predictive simulation (e. g. The Swedish National Facility for Magnetoencephalography Parkinson's Disease Dataset (NatMEG PD) on EBRAINS)

## Roadmap Illustration



| Activities - Data Sharing and the Knowledge Graph | |
|---|---|
| 1. | **EBRAINS TRUSTable Digital Brain Health Services** |
| 1.1 | **Human Brain Project Internal Meeting** 13-14 October: "EBRAINS TRUSTable integrated services for the discovery of multi-scale disease mechanisms" – Chair: Petra Ritter, Charité - Universitätsmedizin Berlin. |
| 1.2 | **Global Health Summit 2022** 16-18 October: "How to Achieve a Global Health Data Space" – Chair: Petra Ritter, Charité - Universitätsmedizin Berlin – Speaker: Paweł Świeboda Human Brain Project Director-General. |
| 1.3 | Design "Living Lab" strategy. |
| 1.4 | Create inclusive and TRUSTable Digital Brain Health services accessible to the general public and individuals with different levels of literacy. Training and services with human communication if needed. |
| 1.5 | Development of inclusive, trustable, and explainable EBRAINS patient consent form for data sharing. |
| 1.6 | Mapping of activity in relation to the complex adaptive system of The Sustainable Development Goals (SDG) within United Nations (UN) The 2030 Agenda for Sustainable Development to achieve U**niversal Health Coverage (UHC) 2030.** |
| 1.7 | Info-meetings for Digital Brain Health stakeholders on a commitment to reduce the ecological footprint. |
| 1.8 | Identify and measure the environmental impact of hardware and software development. |
| 1.9 | Achive Universal Health Coverage (UHC) and Sustainable Development Goals (SDG) 2030. |
| 2 | **International, national, and institutional Open Neuroscience guidelines with curation on the early stage of project planning** |
| 2.1 | Develop and provide training on WEB-BASED user-friendly Data Curation ecosystem: electronic experimental data capture fitted for BIDS and openMINDS tools helping for future curation and increased interoperability. |
| 2.2 | Distribute multilevel guidelines including EBRAINS patient consent form for data sharing. |
| 2.3 | Implementation of EBRAINS National Nodes and institutional level curations with established data curation workflows within a web-based curation ecosystem reusable and adaptive for other platforms and institutions. |
| 3 | **Interoperability and harmonization of data, tools, and platforms** |
| 3.1 | Harmonization cross platforms working groups (e.g., The International Neuroinformatics Coordinating Facility (INCF)). |
| 3.2 | Create interface and Interoperability between BIDS and openMINDS. |
| 3.3 | OpenMINDS and Neuro Imaging Data Model (NIMD) harmonized ontology development. |
| 3.4 | Design Global Health Data Space with EBRAINS Digital Brain Health TRUSTable integrated services. |
| 4 | **Integration of EBRAINS CoCreate Digital Brain Health roadmaps** |
| 4.1 | Adapt "Data Sharing and Knowledge Graph" for common needs and goals of "Longitudinal Data Studies", "Healthy Aging", "Behavioural and lifestyle studies" and "Public Perceptions on: EBRAINS Data Sharing. |
| 4.2 | Integration of diverse datasets into multiscale models and atlases such as The Virtual Brain (TVB) and NEST enabling predictive simulation (e. g. The Swedish National Facility for Magnetoencephalography Parkinson's Disease Dataset (NatMEG PD) on EBRAINS). |
| 4.3 | Extend openMINDS towards clinical data including behavioural, and lifestyle to integrate and explore pathological pathways and mechanisms on ontological level. |
| 4.4 | Integration of EBRAINS Co Create Artificial Intelligence and Digital Brain Health. |

# EBRAINS CoCreate Digital Brain Health - Bringing the roadmaps into life

In the fifth and final workshop, the groups brainstormed and designed actionable points for actors to act upon for how to realise their visions, missions, and roadmaps. Here, the participants were able to form new groups and deliver joint outcomes. In the following, you will find the considerations the participants made about the outcomes of our workshops.

# Recommendations for EBRAINS

1. Overall recommendations
    1.1. Provide **positive feedback** on what is going well in EBRAINS.
    1.2. Identify **what is missing** and what should be done.
    1.3. Make it part of **EBRAINS mandate** to steer research prioritization in Europe (with the help of National Nodes).
    1.4. **EBRAINS to take lead** in supporting longitudinal studies on a European level through lobbying, infrastructure support, harmonization of data, coordination of initiatives.
    1.5. EBRAINS as an expert knowledge and infrastructure hub.
    1.6. EBRAINS expertise in e.g., data management planning, data curation, data sharing, data analyses, and quality assessment, is a corner stone of research reproducibility.
    1.7. Enhance **awareness in community** that EBRAINS is uniquely positioned to support longitudinal studies by the following actions.
2. Recommendations to EBRAINS about Longitudinal Data Studies
    2.1. *Top-down:* Develop a narrative by EBRAINS leaders to be included in their presentations and interactions with e.g., scientific, funding, political, public, public health, and private stakeholders.
    2.2. *Bottom-up:* Establish a **longitudinal studies EBRAINS sub-community** to coordinate and guide the development and implementation of longitudinal (multicenter) capabilities in EBRAINS.
    2.3. Raise **awareness within patient associations** of importance of longitudinal studies in EBRAINS and gather their support for European prioritization.
    2.4. Longitudinal studies provide ***the only means to track and map individual trajectories*** of brain health, risk and resilience, disease development and progression, and elucidate the impact of e.g., biological, environmental, social, cultural factors, interventions, practices, lifestyle, and other quality-of-life determining factors.
3. Recommendations to EBRAINS about Epidemiology
    3.1. Epidemiology in brain diseases is still poorly understood. We first need to be able to sketch a plan for improving this.
    3.2. EBRAINS can be used to **set up some organization to continue this process**. This group can then expand to include national health institutes. Foundations of the pharmaceutical companies should be also interested in this, but also organisms such as Alzheimer UK for example.
    3.3. Analysis of **steps in scientific research to achieve a better epidemiology for brain health**. For example, to get more awareness of the importance of the study of causality, not only data driven research. We need to specify what kinds of research needs to be strengthened through education. One example is epidemiological/societal impact on brain health.
    3.4. **Better communication** is needed. Maybe EBRAINS to be used as a platform, but to take an example from the industry, where a lot of effort is put in better communication.
    3.5. **Reaching to the companies and improving collaboration** with them. For example, NVIDIA have been very eager to sponsor and help projects in HPC and AI in general. This can be very helpful for computational resources.
4. Lighthouse project
    4.1. EBRAINS initiate and support a **European wide multicenter population based longitudinal multimodal and multidimensional lighthouse project** with a life span perspective. Such a project could focus on healthy aging.
    4.2. EBRAINS to **lead the way** and lobby for EU political support and governmental funding.
    4.3. EBRAINS to **engage and mobilize** scientific, public health, clinical, patient, and private stakeholders.
    4.4. EBRAINS to **establish pro-active standardization** of data acquisition, curation, sharing, and harmonization protocols and procedures – Longitudinal data knowledge graph.
    4.5. EBRAINS to **attract, develop, validate**, and **implement** longitudinal (hypothesis and data driven) data analysis and modelling tools and frameworks.

## EBRAINS Community Space Actions

1. Establish sub-community
    1.1. Establish a **longitudinal studies EBRAINS sub-community** to coordinate and guide the development and implementation of longitudinal (multicenter) capabilities.
2. Awareness
    2.1. Enhance **awareness in community** that EBRAINS is uniquely positioned to support longitudinal studies.
    2.2. Write an **opinion paper or community statement** (led by Lars, Francisca, Augusta, Aske).
    2.3. **Organize courses, co-create workshops** with relevant scientific, legal, clinical, public, and patient stakeholders, raise public awareness by means of e.g., public lectures, and visibility on social and traditional media platforms.
    2.4. **Attract** existing (multicenter,) multimodal and multidimensional longitudinal studies to the EBRAINS platform. Such spearhead studies would drive the development and implementation of longitudinal data capabilities (e.g., legal support, data sharing/curation/harmonization, data analyses and modelling workflows and quality metrics, etc.).
    2.5. EBRAINS should **devote resources** to such ”paving the way” endeavours. Existing projects generally have well established e.g., legal, data curation, data analysis, data sharing, and computational frameworks and thus need to be *convinced* that EBRAINS is worth their time and investment → Reward of participation.
3. EBRAINS Community meeting Call Proposal for realization of roadmaps
    3.1. Use case from Swedish EBRAINS National Node.
    3.2. EBRAINS-compatible and INCF-powered Center for Imaging Research (CIR) at Karolinska Institute.
4. Current agenda
    4.1. Developing a supporting E-infrastructure.
    4.2. Developing and harmonizing CIR data collection, computation (HPC), and analysis methods.
    4.3. Increasing the access to and utilization of rare CIR imaging instruments and novel AI-based analysis methods.
    4.4. Increasing and improving CIR training and support services.

## Policy Recommendations

1. Policy as priority one
    1.1. Even if only 10% of the people would follow health policy recommendations, it would already have a **significant impact** for the society. However, evidence-based health recommendations require that we identify highly dynamic and dimensional patterns of associations from the data to begin with, and for that we need the data to be accessible! Subsequently, we can study mechanisms.
    1.2. Main roadblock are the national regulations – health care data is nationally owned in most of the cases!
    1.3. European medical standard record (a new norm) would ensure critical data usability. For example, in France, medical records are currently structured differently in each hospital.
    1.4. We should implement working examples and best practices. For example, for data acquisition protocols and pro-active data harmonization. Nobody should start from scratch and re-invent the wheel again.
    1.5. In the long term, data from private companies should be also made available if it can improve the public health.

# List of Participants

| | | |
|---|---|---|
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EBRAINS Community

This CoCreation event on Digital Brain Health is organized by the EBRAINS Community Building Team. EBRAINS Community is a growing online community within neuroscience, brain medicine, and brain-related technology. Whether you are looking for other EBRAINS users, would like to engage in research facilitated by the EBRAINS services and tools, or find elements of neuroscience and brain-related technology interesting, the odds are you will find like-minded in the EBRAINS Community.

# Sign up for EBRAINS Community

Follow the link below and you will be sent directly to the first destination of your journey, the sign-up page. Simply sign-up with your EBRAINS Account or with your e-mail and click 'Sign up as Member'. The next step is then to verify your e-mail address through an e-mail that will be sent directly to your e-mail inbox. Give it a few minutes and remember to check your spam folder!

When you have signed up as a member and logged in, it is time for you to start building your personal profile. You simply follow the steps that you will be presented when you access your profile:

1. First name
2. Surname
3. Choose a minimum of one field of interest

Now press 'Publish to EBRAINS' and start using the features and functions! You can always access your profile at a later time to fill in additional information or edit your profile.

Join the EBRAINS community here:

community.ebrains.eu

Human Brain Project

## Behind EBRAINS CoCreate

EBRAINS CoCreate Digital Brain Health is run by
The Danish Board of Technology,
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