The Human Brain Project
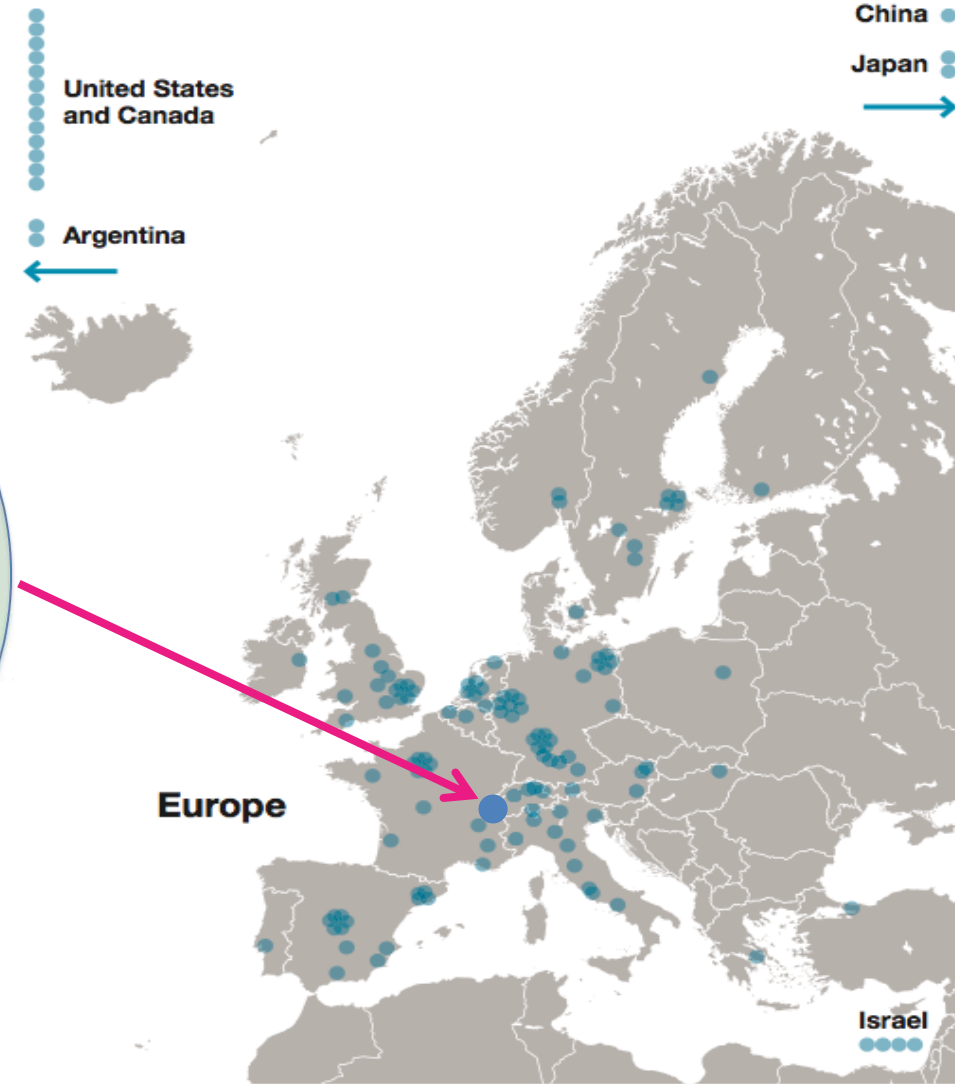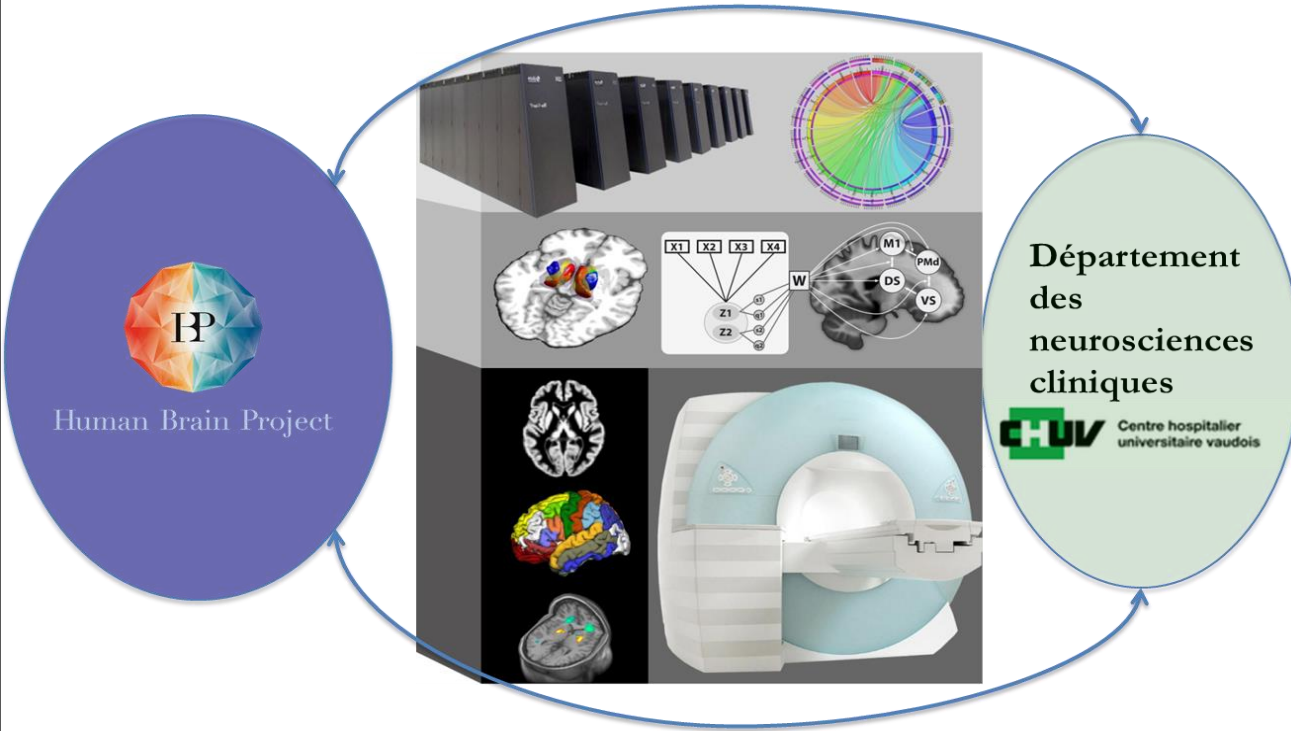# &
- Medical Informatics Platform –

Ferath Kherif
LREN
Département des Neurosciences Cliniques
CHUV

Human Brain Project

EU funded Collaborative project for understanding the human brain
25 Countries
400 Researchers   2013

10 Years

From Data to models of the Brain
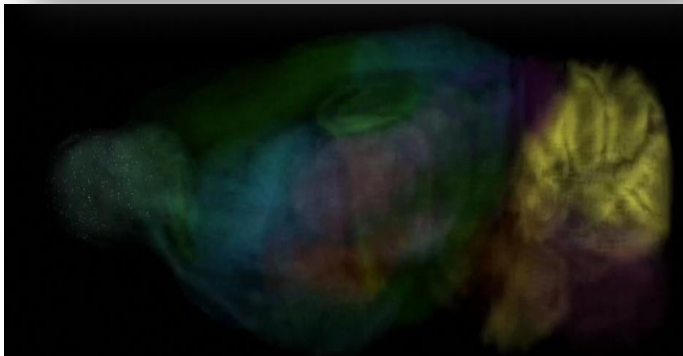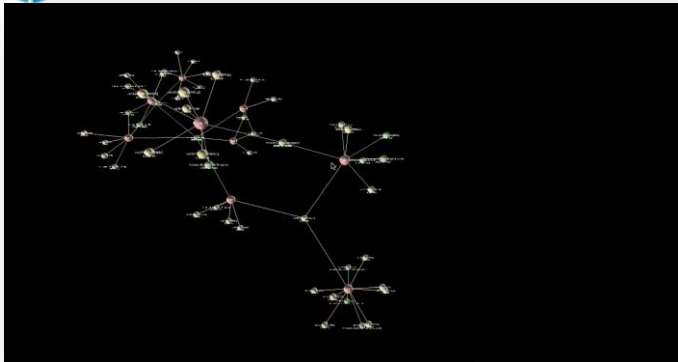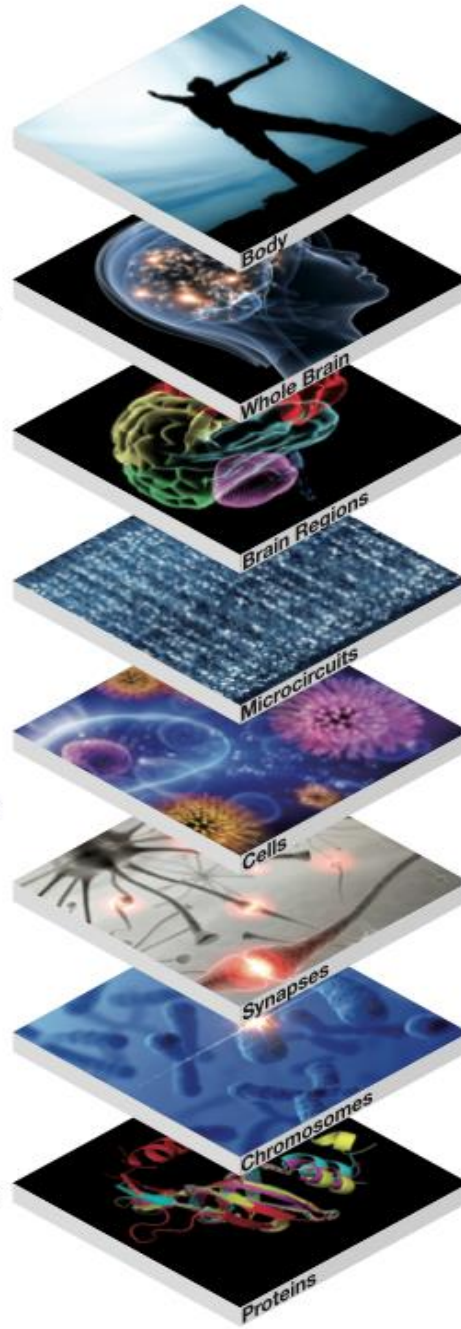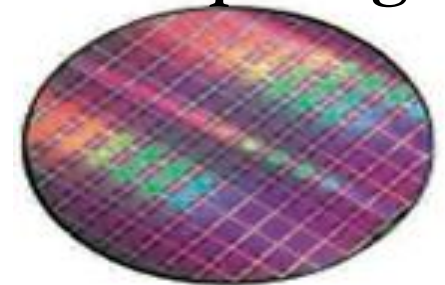

Neuroscience

Unify

Medicine

Classify

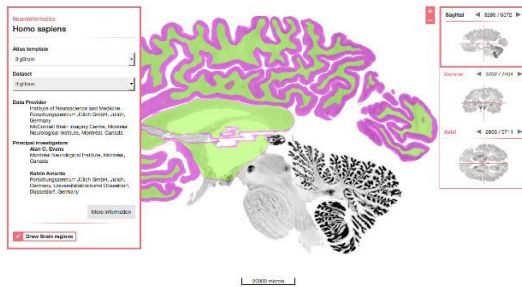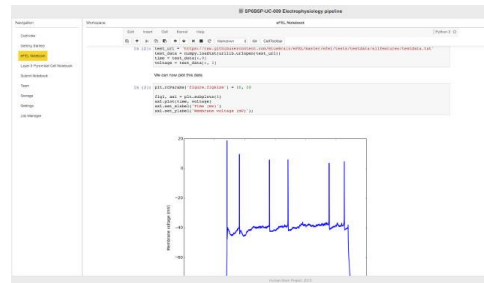**Computing**

Produce

Accessing the HBP Platform Ecosystem

The HBP Platforms provide strategic tools in:

Neuroinformatics
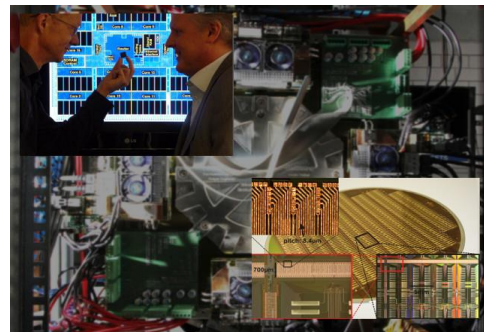

Brain Simulation

Medical Informatics

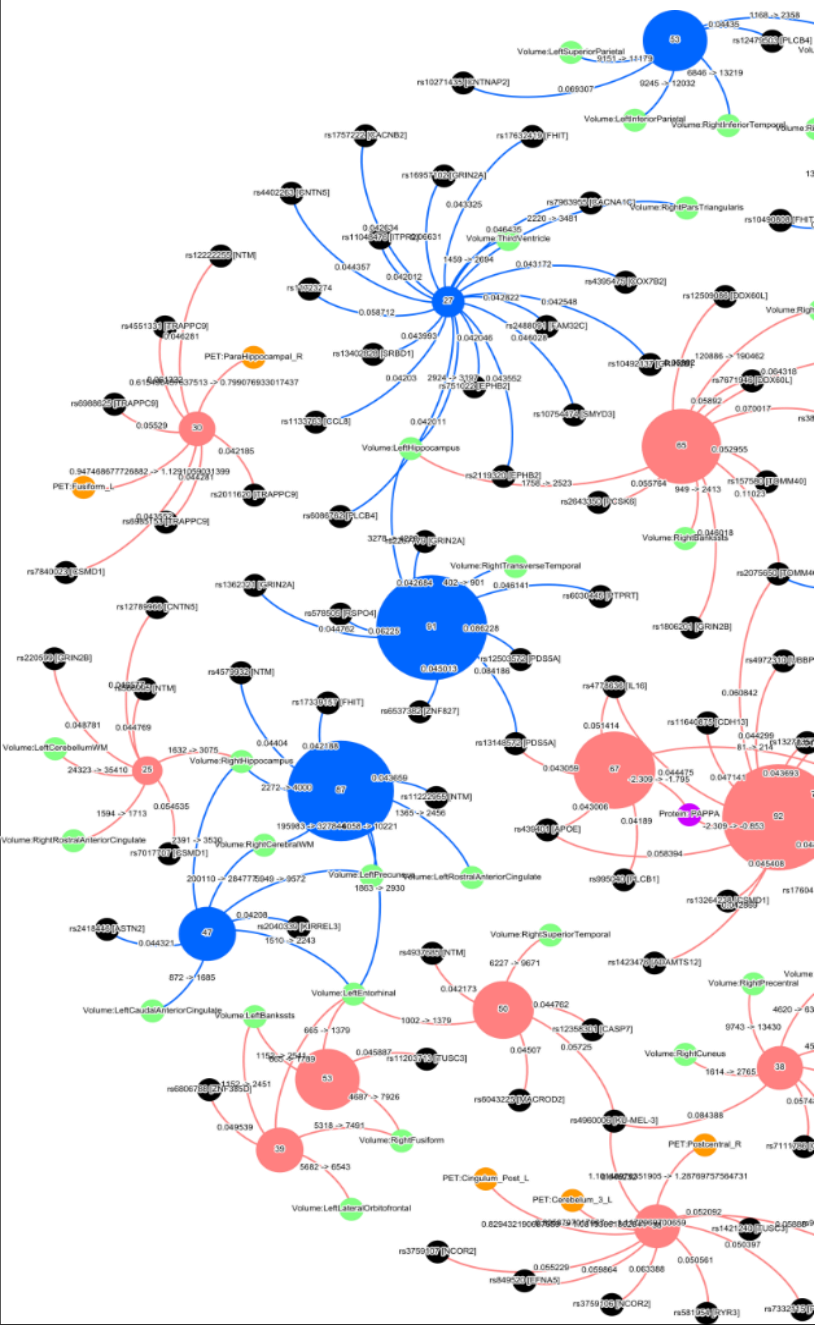*High Performance Analytics and Computing (HPAC)*

Neuromorphic Computing

Neurorobotics

1. Establish a framework for federating clinical data – all diseases, many hospitals

2. Develop federated query technology that respect anonymity requirements

3. Develop machine learning algorithms

4. Derive biological signatures of brain disease

- Athens University of Economics and Business (AUEB)

- University College London (UCL)

- Bordeaux University (UBO),

- Uppsala University (UU)

- Centro San Giovanni di Dio Fatebenefratelli (FBF)

- McGill University (MCGILL)

- University of Southern California (USC)

- University of Edinburgh (ED)

- Centre Hospitalier Universitaire Vaudois (CHUV)

- Ecole Polytechnique Fédérale de Lausanne (EPFL)

- Tel Aviv University (TAU)

- Josef Stefan Institute (JSI)

- University Medical Centre of Leids (LUMC)

- Geneva University Hospital (HUG)

- Athens University (UoA)

Evidence based medicine

Facilitate Knowledge exchange between medical informatics Communities
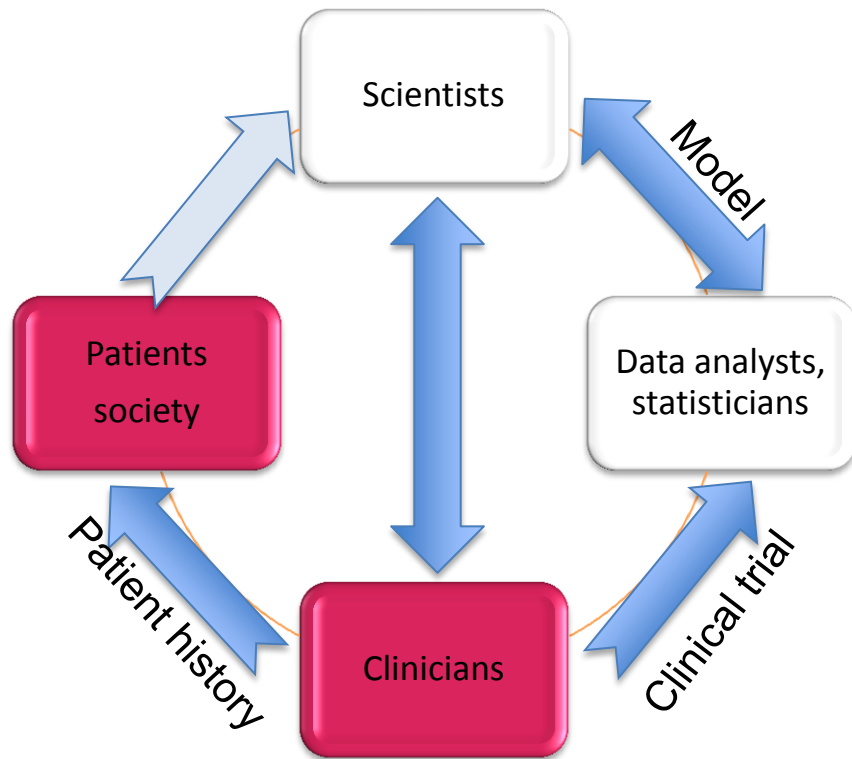
Facilitate the integration of life science research Clinical research and patients care

Research : data analyses, hypotheses testing and **model building**

Clinic: data analyses, hypotheses testing and **decision support**

Developers: Create and **deploy apps**

General public: engagement, information **contribution** to small crowdsourcing task (curation)

Evidence based medicine

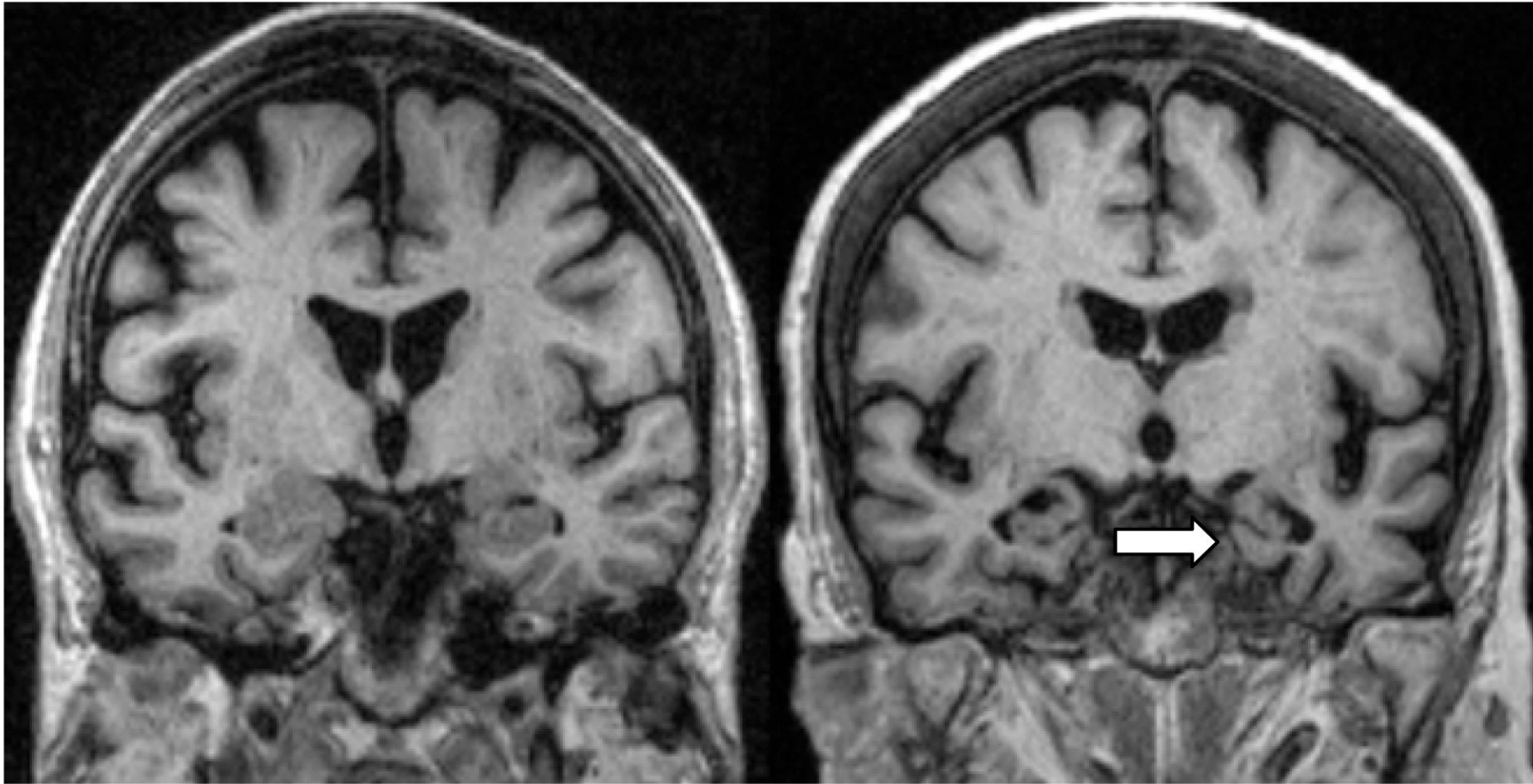Going beyond symptoms based medicine : symptoms are not discriminative.

How big data can help: **Bradford Hil (1965)**

Inferring causality from observational data

1. **Strength** : effect size
2. **Consistency** : multiple evidence
3. **Specificity** : multiple disease
4. **Temporality** : Causality
5. **Biological gradient:** multiscale
6. **Biological Plausibility :** knowledge
7. **Coherence** replicability
8. **Experiment** Clinical trial
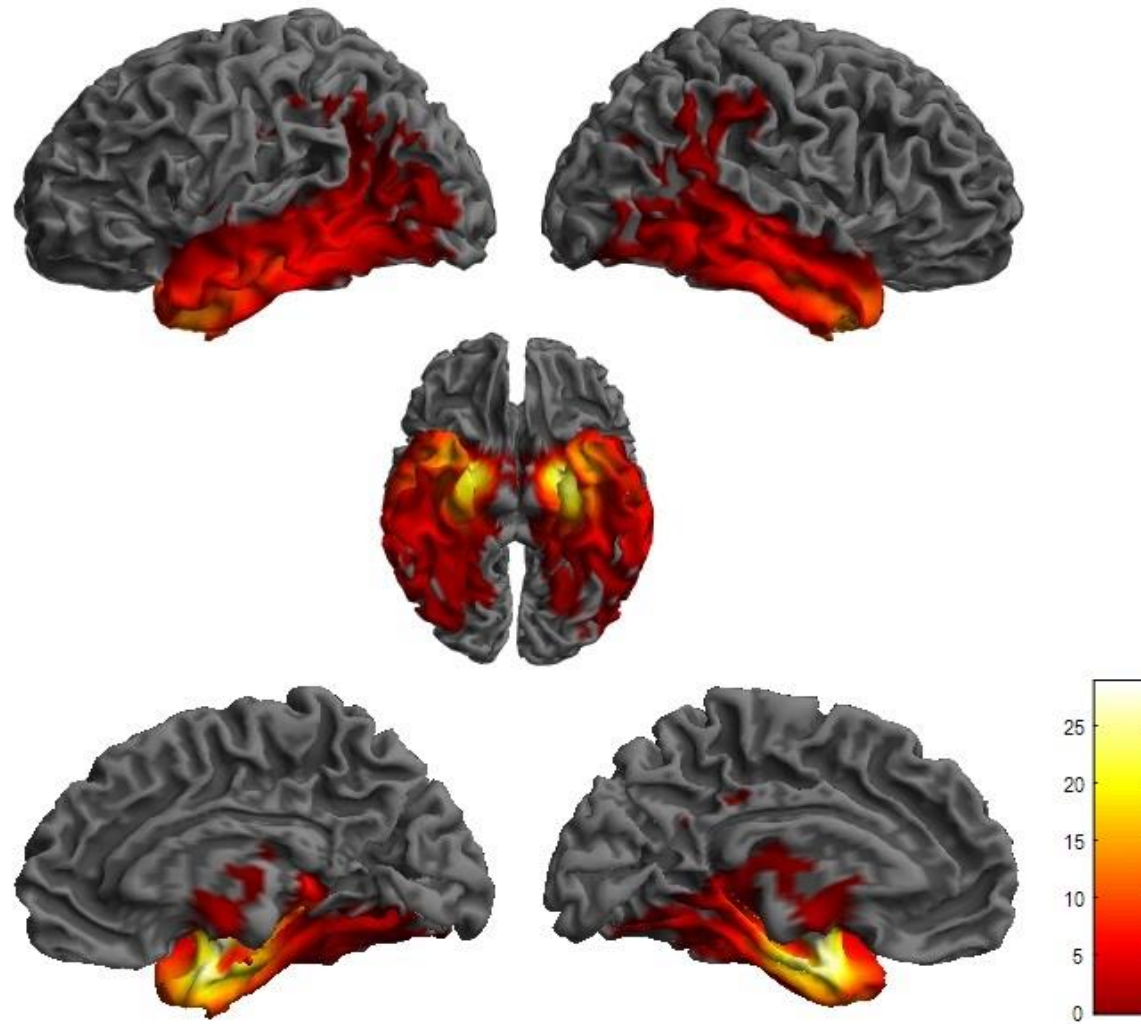9. **Analogy** Alternative models

Evidence based medicine

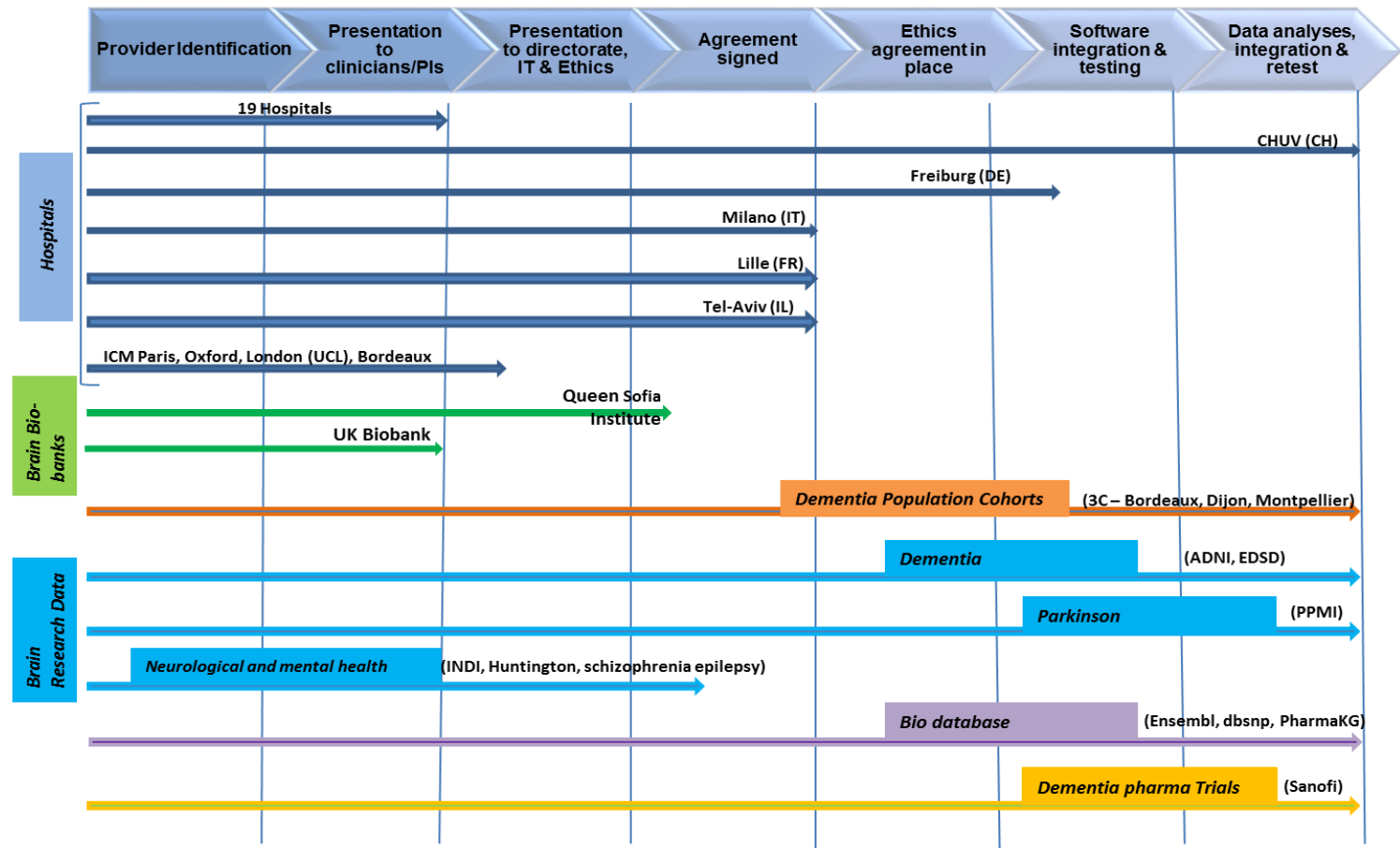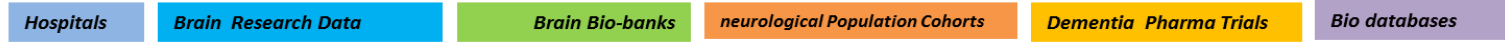Going beyond symptoms based medicine : symptoms are not discriminative.

Evidence based medicine

Going beyond symptoms based medicine : symptoms are not discriminative.

Multiple Sources of data/evidence:

| Hospitals | Brain Research Data | Brain Bio-banks | neurological Population Cohorts | Dementia Pharma Trials | Bio databases |

Process flow (left to right):
Provider Identification → Presentation to clinicians/PIs → Presentation to directorate, IT & Ethics → Agreement signed → Ethics agreement in place → Software integration & testing → Data analyses, integration & retest

Hospitals
- 19 Hospitals
- CHUV (CH)
- Freiburg (DE)
- Milano (IT)
- Lille (FR)
- Tel-Aviv (IL)
- ICM Paris, Oxford, London (UCL), Bordeaux

Brain Bio-banks
- Queen Sofia Institute
- UK Biobank

- Dementia Population Cohorts (3C – Bordeaux, Dijon, Montpellier)

Brain Research Data
- Dementia (ADNI, EDSD)
- Parkinson (PPMI)
- Neurological and mental health (INDI, Huntington, schizophrenia epilepsy)
- Bio database (Ensembl, dbsnp, PharmaKG)
- Dementia pharma Trials (Sanofi)

Objective: Multiscale Disease Signatures

The MIP provides methods to analyse federated data from hospitals, research centres and biobanks and aim to federate the different communities of users from these different locations.
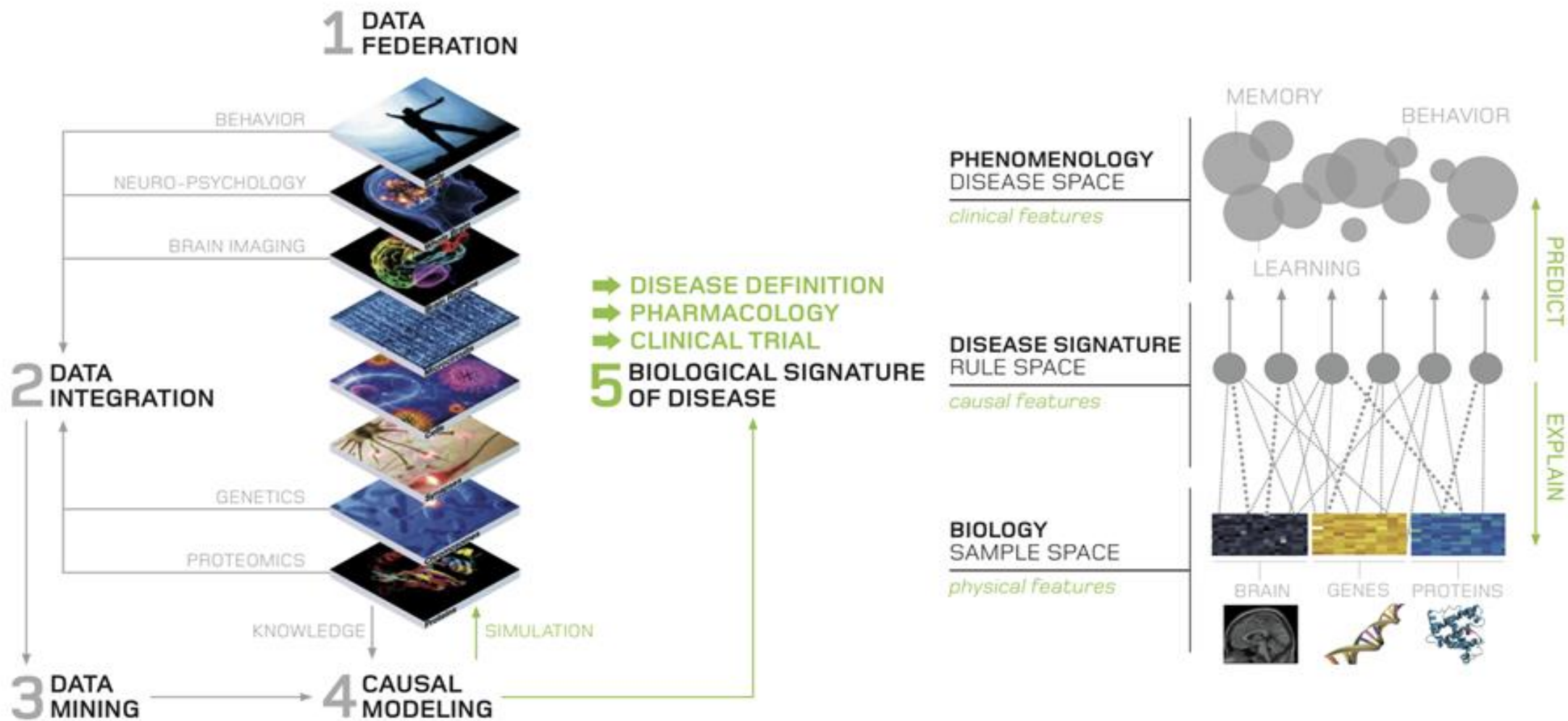
Roadmap New Use Cases

First Disease Signatures from Hospital Data

Demonstrate how clinicians and researchers can use the Platform to build models that can be applied to clinical practice.

- o develop an objective, biologically grounded model of neurological and psychiatric diseases based on multi-level clinical data
- o establish a first proof-of-concept for personalised medicine for neurology and psychiatry.

Cross-Cutting Multi-Scale Studies Using the MIP Capabilities

Demonstrate the interaction of SP8 with other SPs to generate deeper knowledge about brain disease mechanisms.

- o use biological signatures of disease to provide the data required for high-fidelity reconstructions and simulations of disease
- o create a brain disease atlas that can be used to map, classify and diagnose brain diseases.

Operating the Platform for the Community

Demonstrate how the clinical research community and other medical initiatives can use the Platform

- o add new functionalities to the MIP
- o Create via the Collaboratory new communities supported by the MIP.

The Medical Informatics platform

DATA
- **8'305 CHUV patients – 9'601 data points**

- **Clinical data – 58'028 diagnostic labels**

Clinical outreach: Computer-based diagnosis

VISUALISATION	ANALYSIS	DIAGNOSTIC

USER'S INTERFACE & QUERIES

DATA MINING SERVERS

RULE-BASED ALGORITHMS

PUBLIC DATABASES

RESEARCH DATA

HBP BRAIN MODELS

Provide bridge
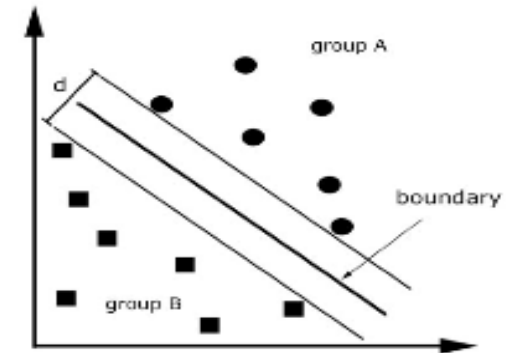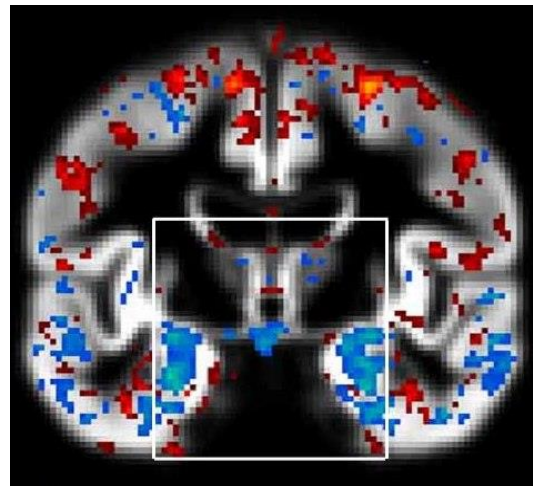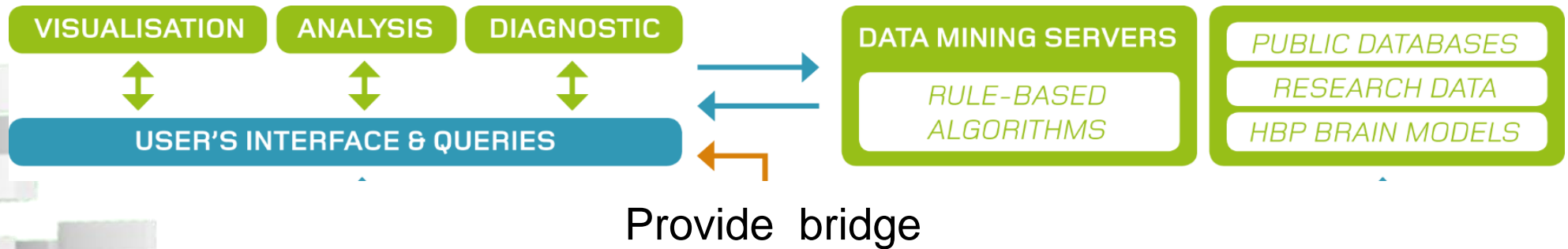
Medical informatics community to explore the genomic and proteomic data for disease understanding.

Use case: Study replication

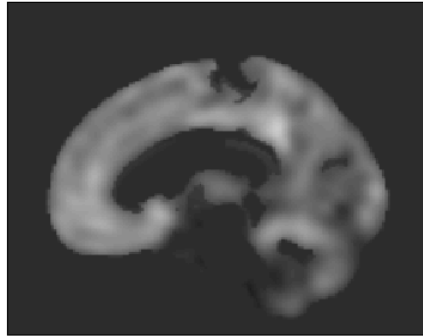Mapping the effects of ApoE4, age and cognitive status on 18F-florbetapir PET measured regional cortical patterns of beta-amyloid density and growth.
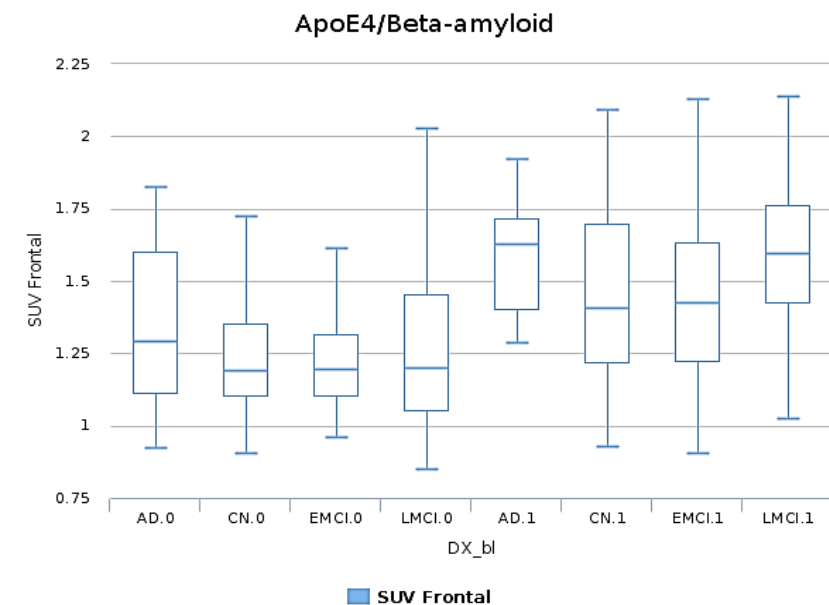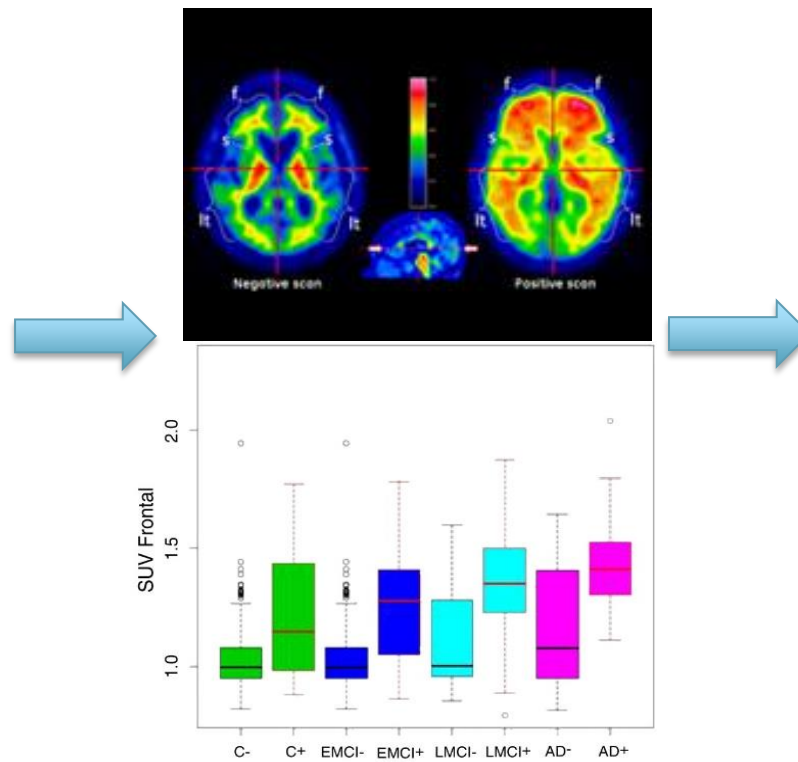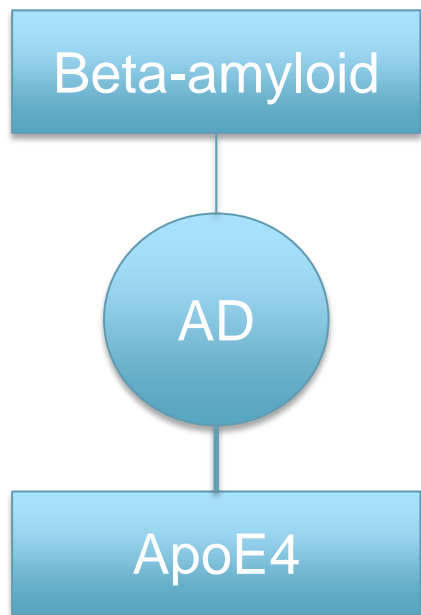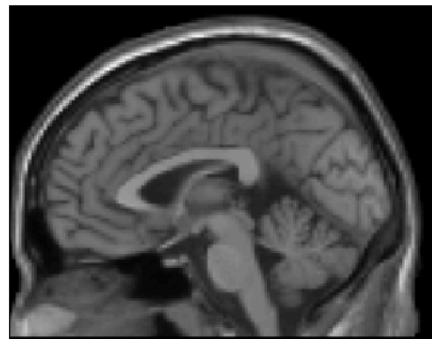

Murphy KR et al *(NeuroImage 78 (2013) 474–480)*

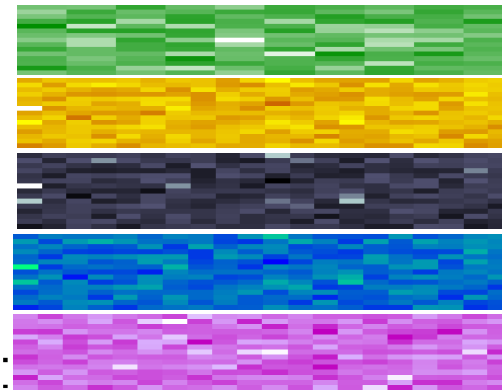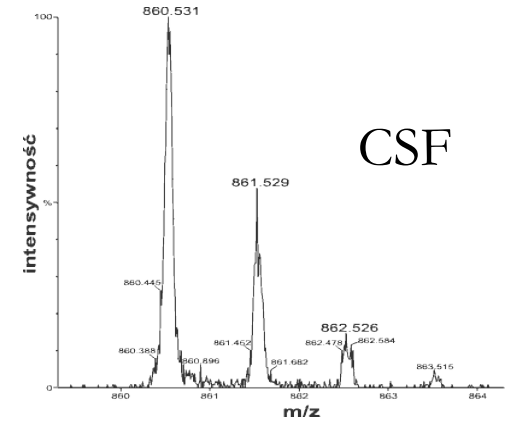# Proof of Concept

912 Alzheimer's patients
5566 Healthy controls

BRAIN IMAGING

MRI data

PET data

Gene data

CSF data

Protein data

PET

MRI

CSF
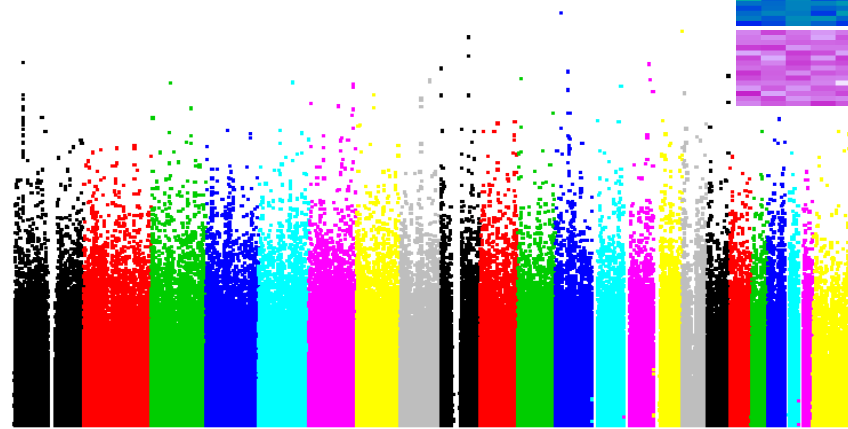
Organising
Tabulating
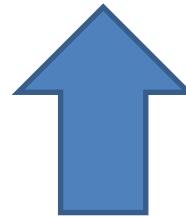
Processing...
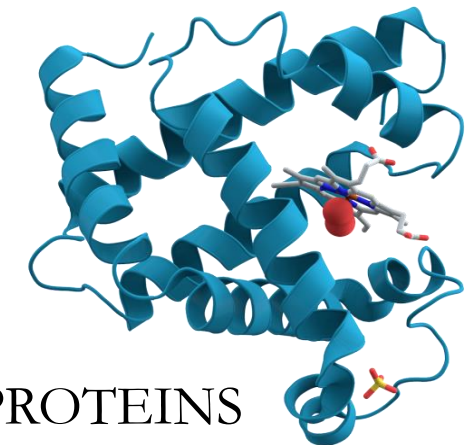
**CLINICAL SCALES
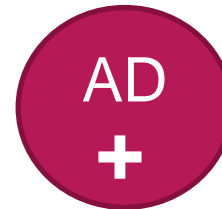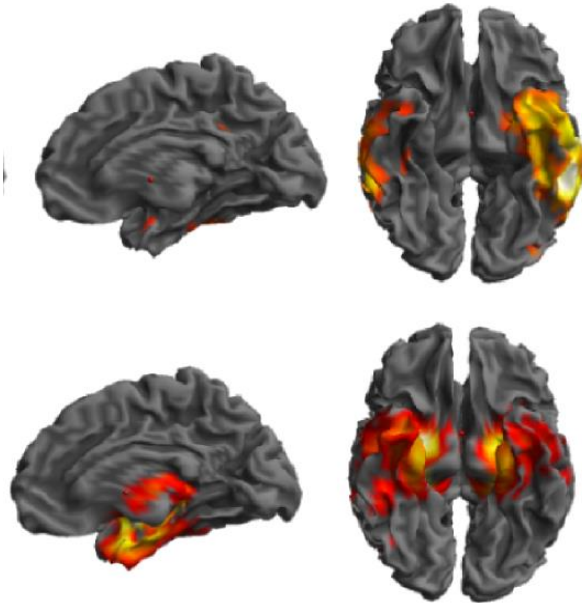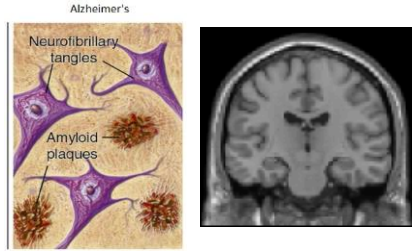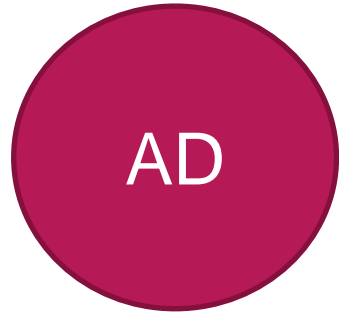& MEASUREMENTS**

GENES

PROTEINS

Methods

- **Phenotype-led Semi-supervised clustering**
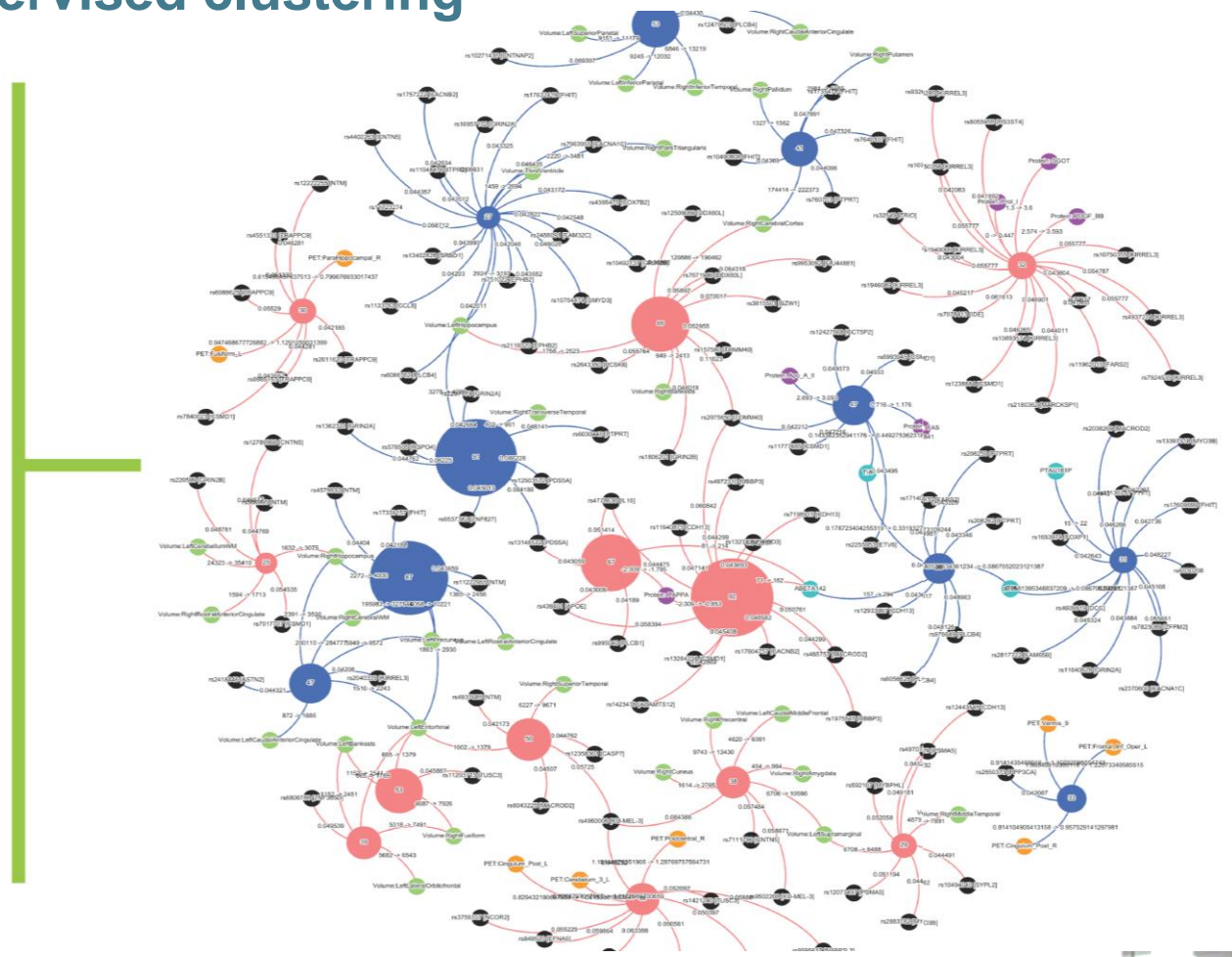
- **Derived model of genetic, proteomic variables to underline the subgroups of Alzheimer's disease and healthy controls.**

Methods

- **Biology-led classfication**

AD

HC

Alzheimer's
Neurofibrillary tangles
Amyloid plaques

AD + Symptoms + Pathology

AD − Symptoms NO Pathology

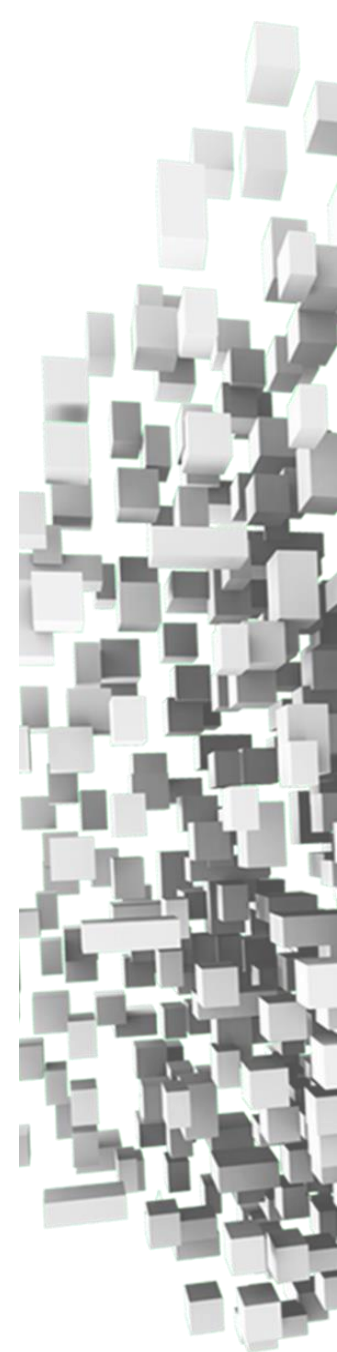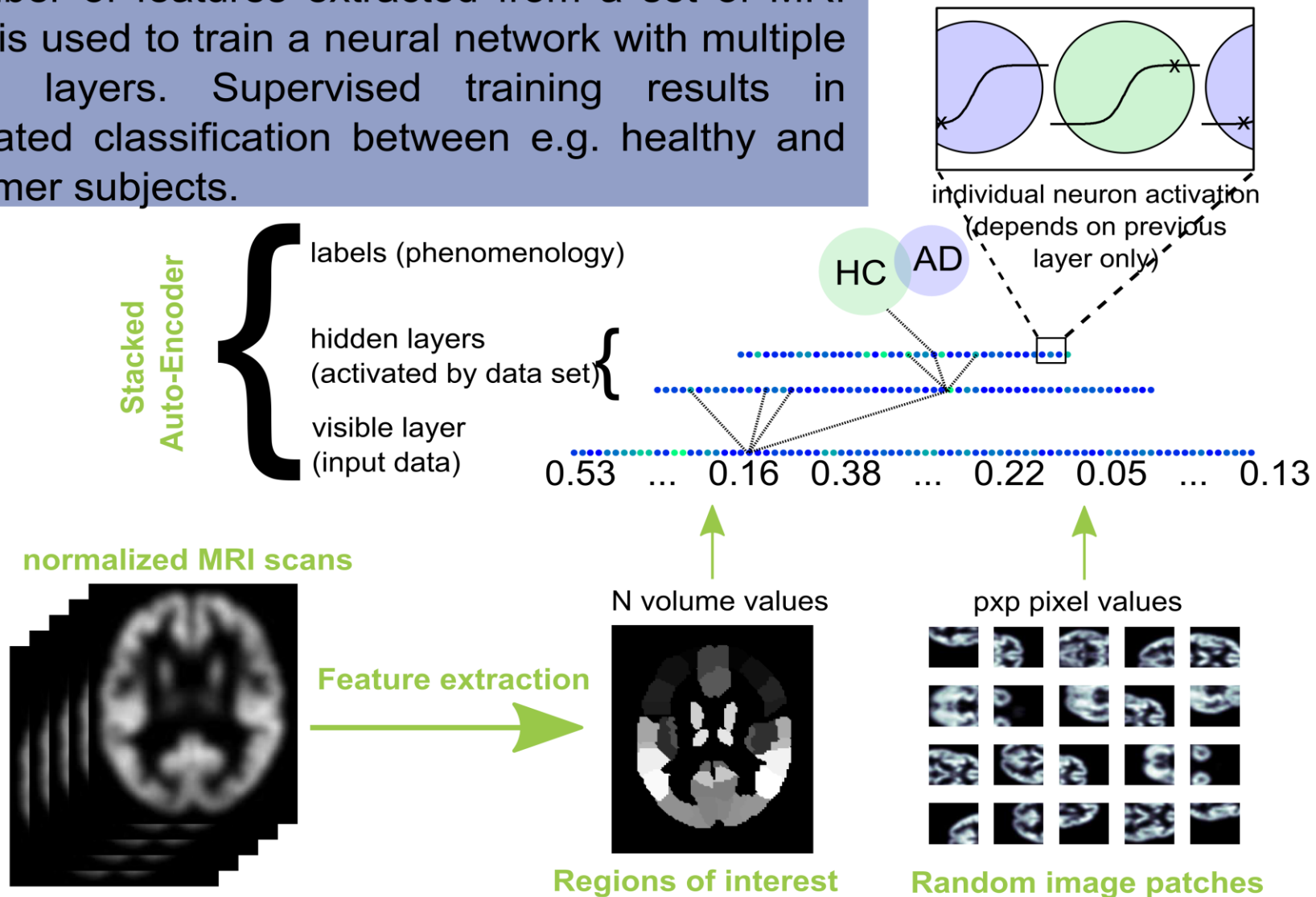**HC +** NO Symptoms + Pathology

HC − NO Symptoms NO Pathology

- **Intermediate phenotype of disease with**

- **Automated Diagnostic based on pathology**

Methods

DEEP LEARNING ALGORITHM

A number of features extracted from a set of MRI scans is used to train a neural network with multiple hidden layers. Supervised training results in automated classification between e.g. healthy and Alzheimer subjects.

individual neuron activation (depends on previous layer only)

HC AD

Stacked Auto-Encoder

labels (phenomenology)

hidden layers (activated by data set)

visible layer (input data)

0.53 ... 0.16 0.38 ... 0.22 0.05 ... 0.13

normalized MRI scans

Feature extraction

N volume values

pxp pixel values

Regions of interest

Random image patches

Proof of Concept
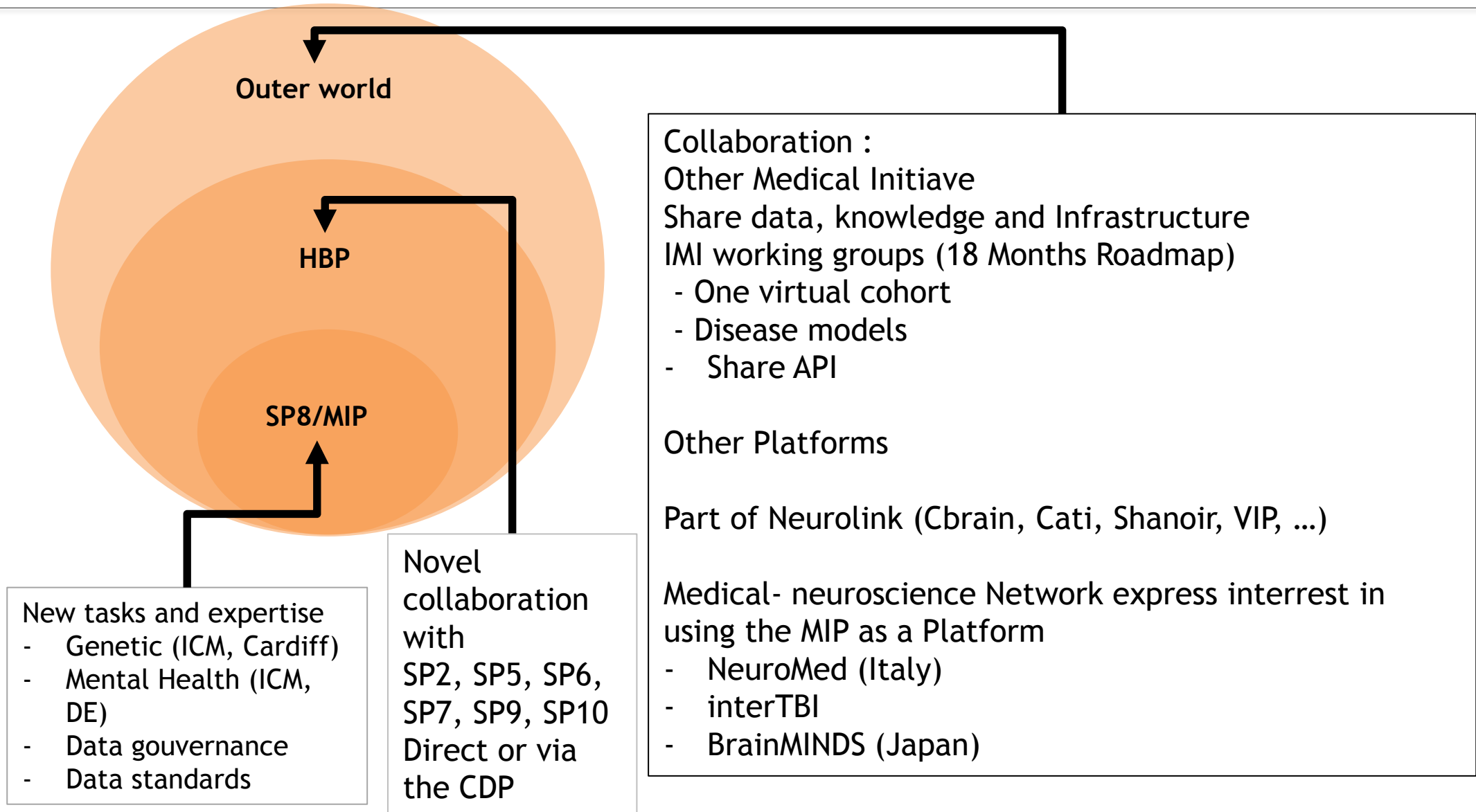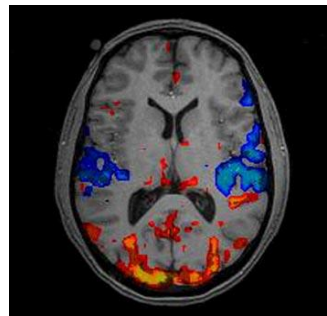

Legend:
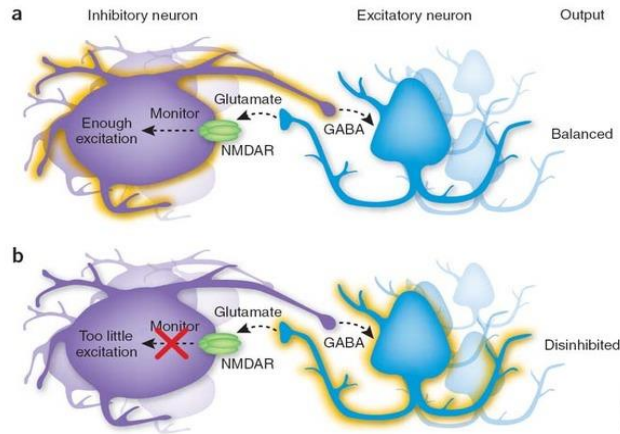- AD Rule
- NL Rule
- MRI Data
- PET Data
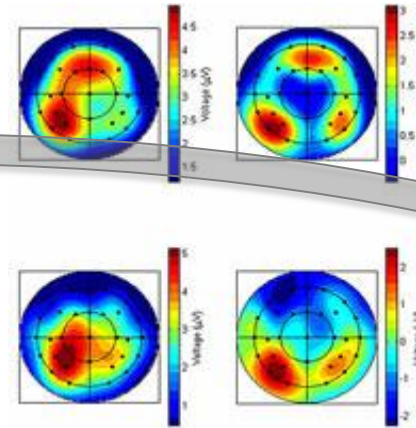- Proteomics
- CSF
- Genetics
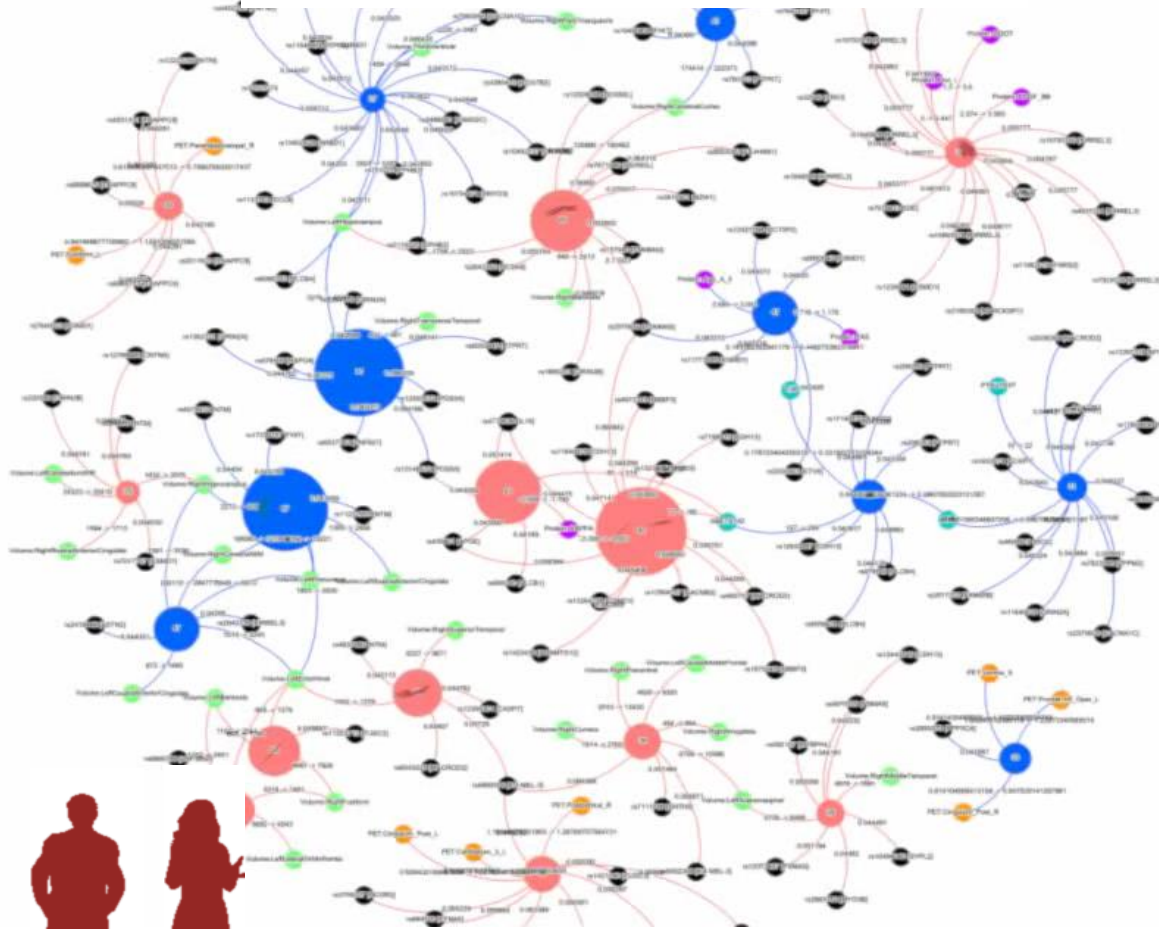
Foster Collaboration and Exchange

Outer world

HBP

SP8/MIP

Collaboration :
Other Medical Initiave
Share data, knowledge and Infrastructure
IMI working groups (18 Months Roadmap)
 - One virtual cohort
 - Disease models
 -   Share API

Other Platforms

Part of Neurolink (Cbrain, Cati, Shanoir, VIP, …)

Medical- neuroscience Network express interrest in using the MIP as a Platform
-   NeuroMed (Italy)
-   interTBI
-   BrainMINDS (Japan)

New tasks and expertise
-   Genetic (ICM, Cardiff)
-   Mental Health (ICM, DE)
-   Data gouvernance
-   Data standards

Novel collaboration with SP2, SP5, SP6, SP7, SP9, SP10 Direct or via the CDP
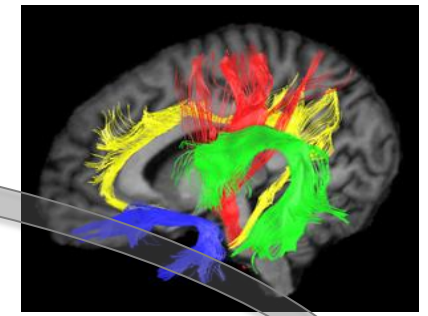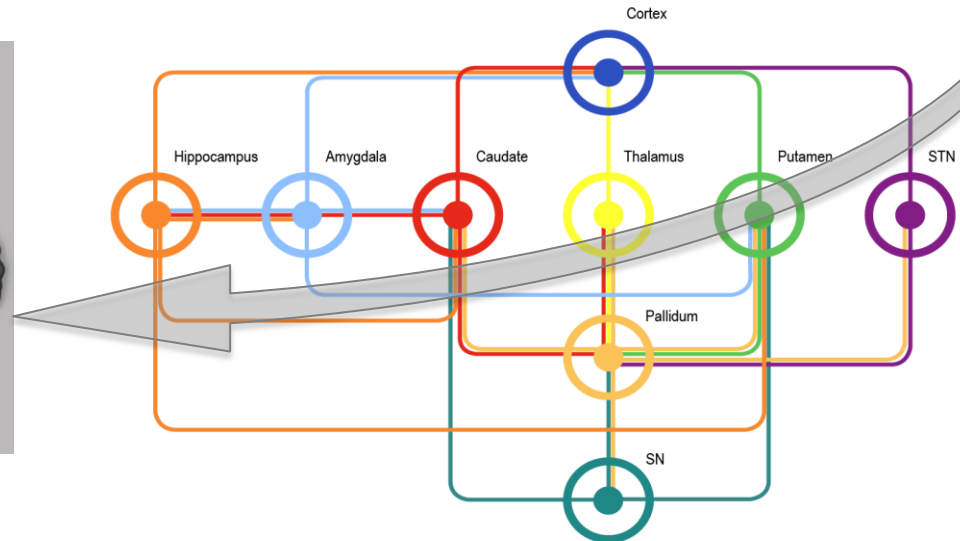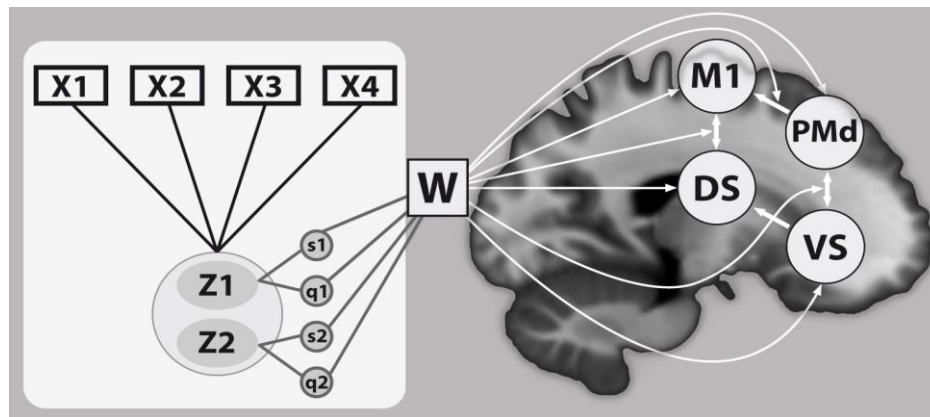
Disease Modeling

fMRI

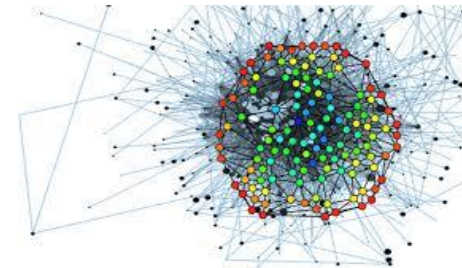EEG

DTI

"MIP as a Service".

The strategy is designed to be viable long term and ensure self-sustainability of the MIP, encouraging new data centres and hospitals to join the MIP community themselves and so participate to with data.
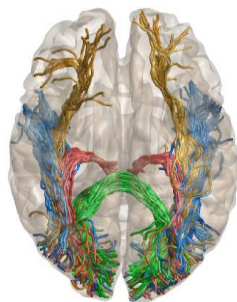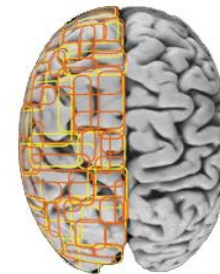

CLINICAL & RESEARCH DATA

DATA MINING

BIOLOGICAL SIGNATURES OF DISEASE

FEATURE EXTRACTION

CLINICAL NEUROSCIENCE

LREN, Laboratoire de Recherche en Neuroimagerie,
Département de Neurosciences Clinique ,
CHUV - Université de Lausanne, Switzerland

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Claudia Modenato
Borja Hernandez
Sara Lorio
Remi Castella
Lester Garcia-Melier
Sandra Martin
Ettore Accolla
Ludovic Sautel

Renaud Marquis
Richard Frackowiak
David Slater
Maria Knyazeva
Anne Ruef
Antoine Lutti
Marzia der Lucia
Valerie Beaud
Melissa Saenz
Yohan Boillat
Elham Barzegharan
Sandrine Muller
Athina Tzovara

Alzheimer's disease: advancing research through collaboration

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