RÉPUBLIQUE FRANÇAISE
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Inserm
La science pour la santé
From science to health

B cube

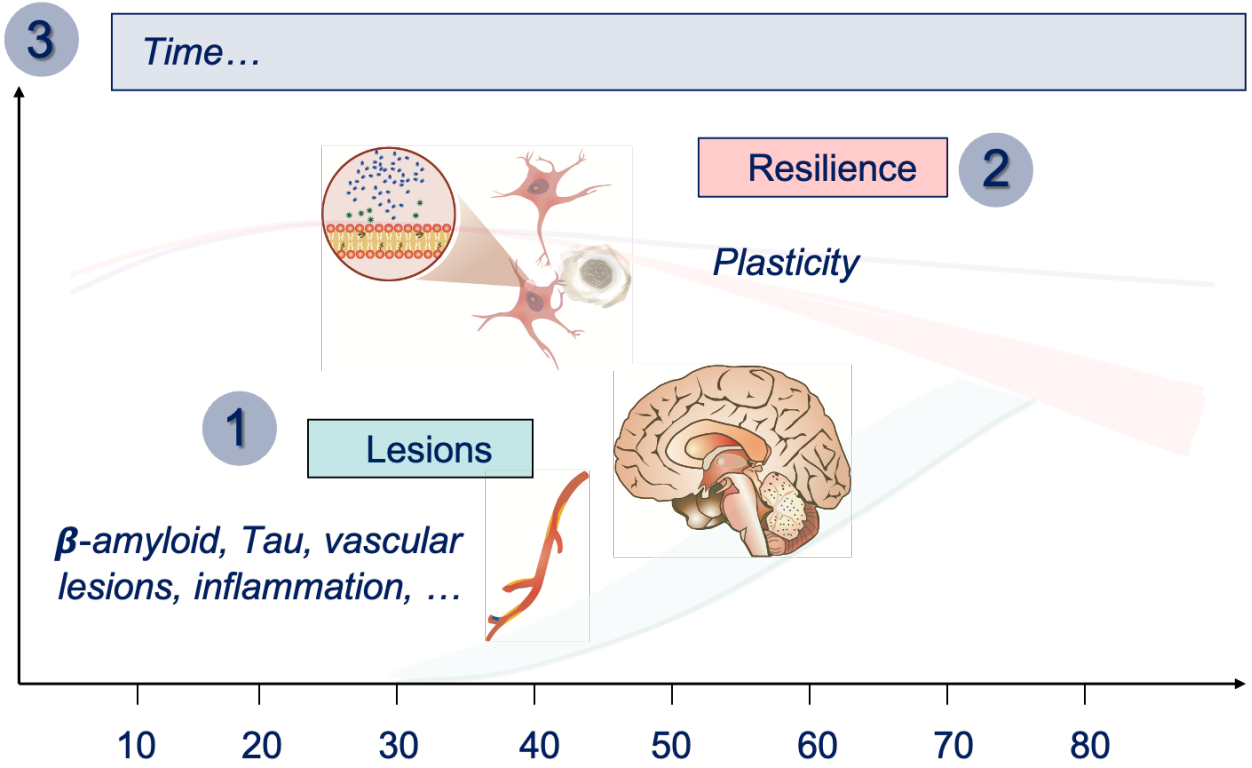
(Biobank and Brain health in Bordeaux)

A novel cohort to study the exposome of brain aging and dementia with high throughput approaches

Cécilia SAMIERI

Codirectrice équipe ELENOR-Bordeaux Population Health (BPH)

As many chronic diseases, prevention of brain aging pathologies is a challenge



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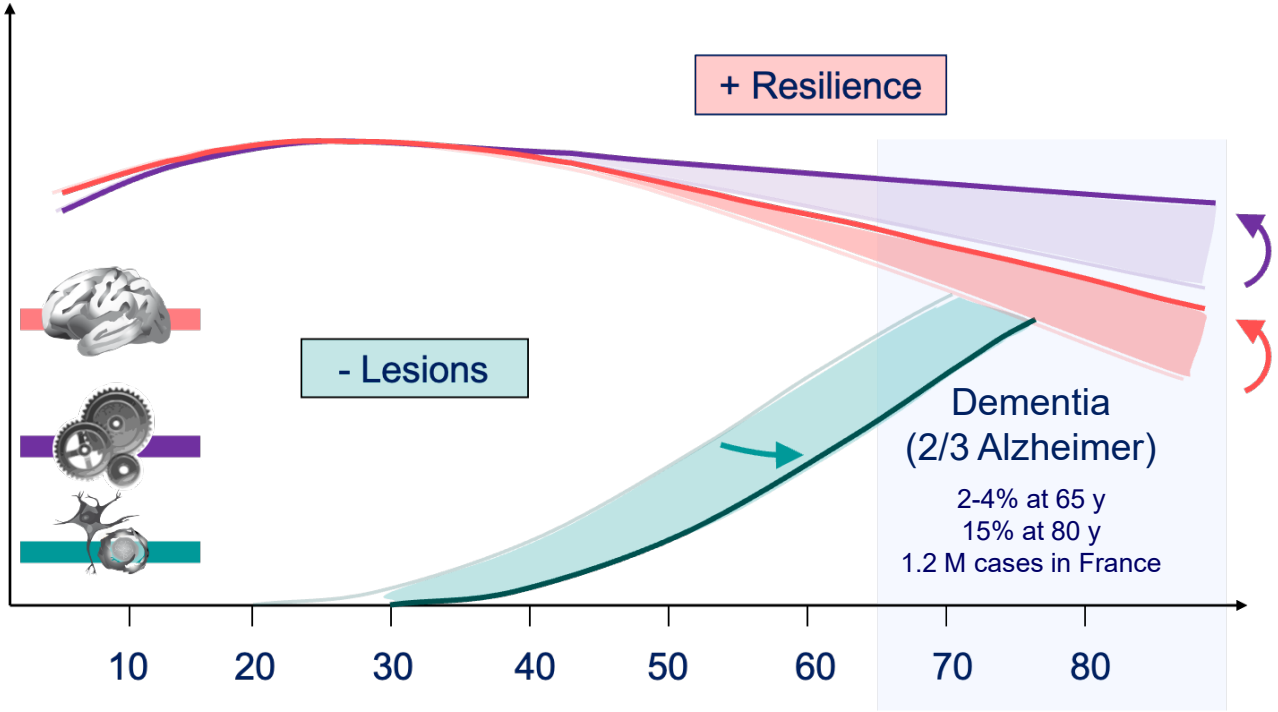
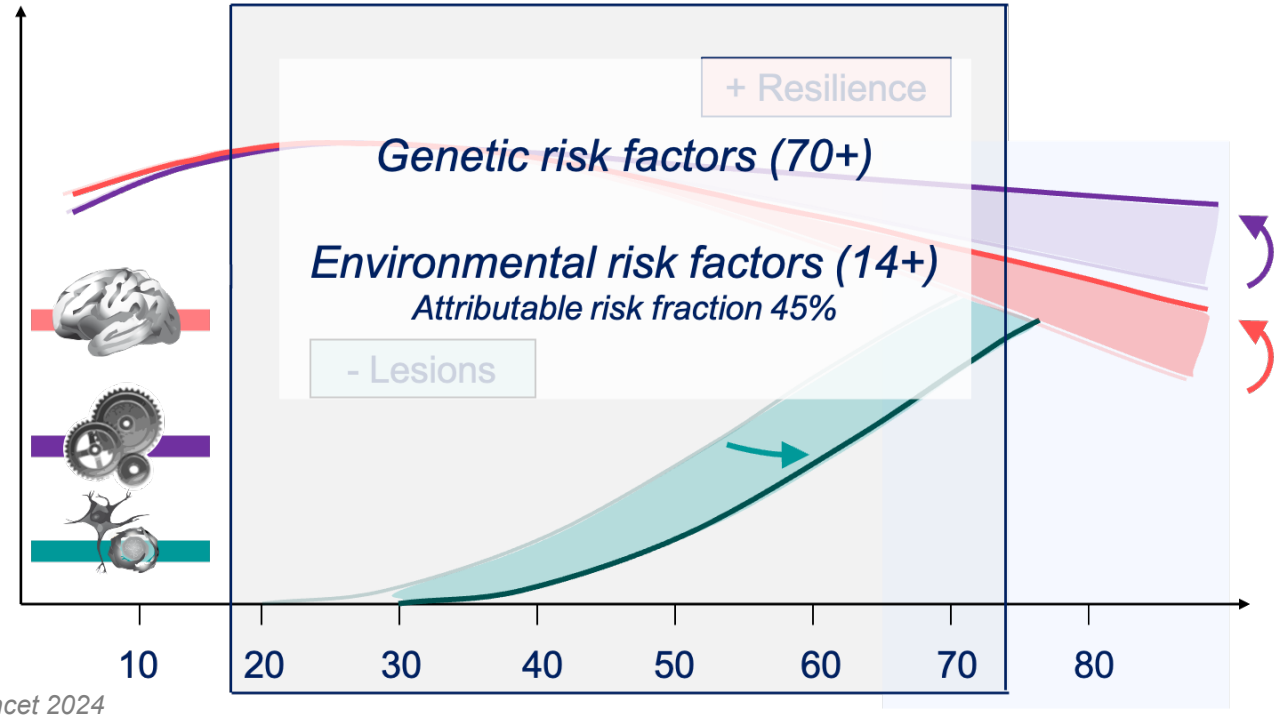


France has been at the forefront of dementia epidemiology since the 80's

- Population-based cohorts:
  - ➔Estimate dementia epidemiology indicators
  - ➔Decipher the natural history in the decades preceding diagnosis
  - ➔Aim to a variability/heterogeneity of exposures/behaviors representative of the general population

- Historical population cohorts:
  - ➔PAQUID (years 1980-xx, 65y+): prevalence, incidence
  - ➔Three-City (3C) (years 2000-xx, 65y+): genetics, biology

Dementia and sporadic Alzheimer's disease are multifactorial

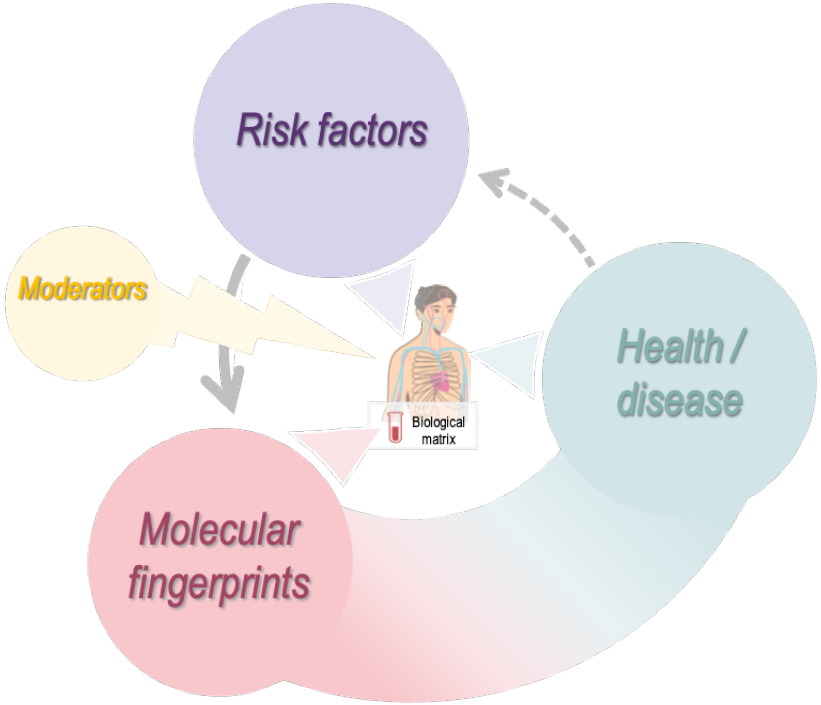


Livingston et al., Lancet 2024

Many questions remain on prevention, that call for more knowledge on etiology and mechanisms

- Which modifiable factors are causal?
- Which factors act on specific neuropathology pathways and which more generally on biological aging homeostasis?
- Which combination of modifiable factors to recommend?
- In which optimal time-windows?
- Are there some sensitive groups? By genetic background, biological aging level (microbiome and gut homeostasis, immunosenescence, inflammaging)…
- How about emerging factors, eg pollutants, infections, …?

Epidemiology has deepened with technological advances



Epidemiology has deepened with technological advances

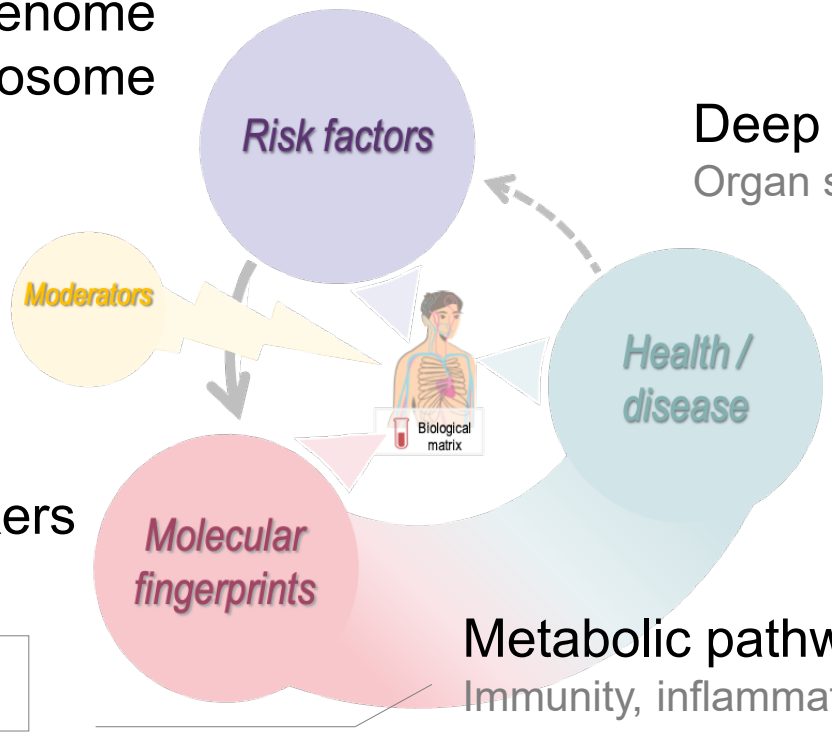
Genome
Exposome

Genomics
Real-time exposure measurements,
GIS, EHR, …

Socio-environmental disparities, …

Exposure biomarkers

Omics in tissues / biofluids

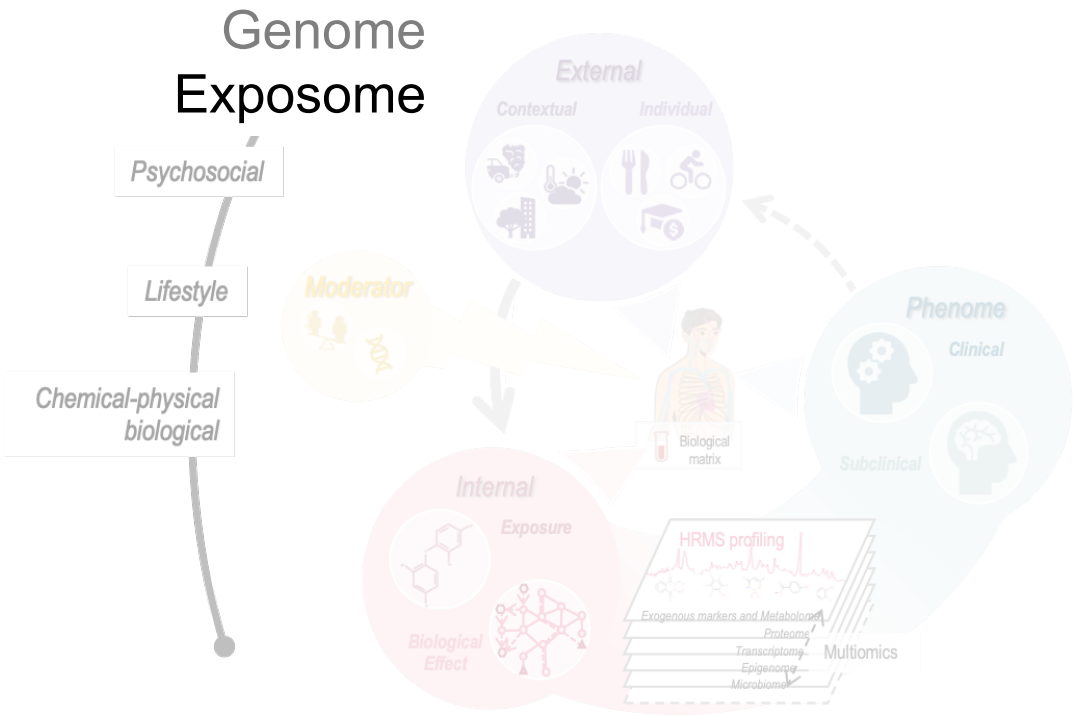


Deep phenotyping
Organ structure/function/pathology

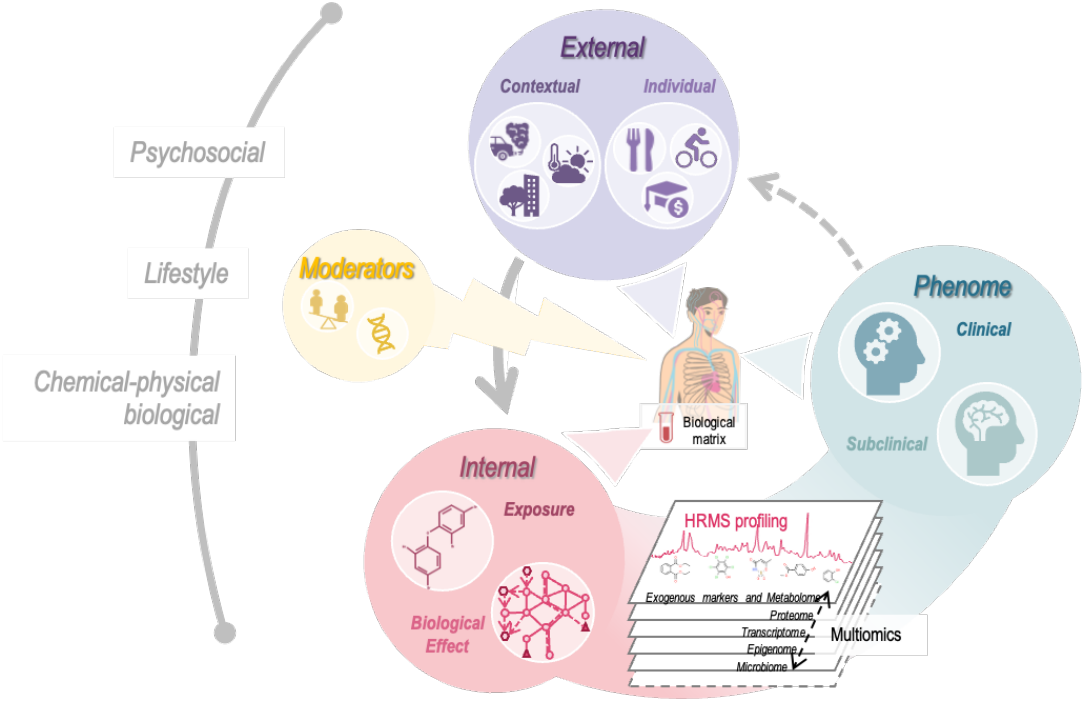
Radiomics,
Real-time clinical measurements,
EHR, …

Metabolic pathways
Immunity, inflammation, lipid metabolism, …

The exposome concept can advance etiological knowledge and prevention of brain aging pathologies



The exposome concept can advance etiological knowledge and prevention of brain aging pathologies



Exposomics can advance etiological knowledge and prevention of brain aging pathologies

nature neuroscience

Perspective

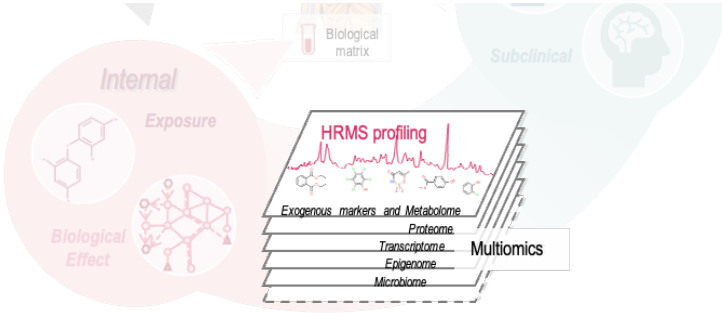
https://doi.org/10.1038/s41593-024-01627-1

Assessing the contribution of the chemical exposome to neurodegenerative disease

Received: 6 June 2023

Accepted: 21 March 2024

S. Lefèvre-Arbogast[1,2,5], J. Chaker[2,5], F. Mercier[2], R. Barouki[3], X. Coumoul[3], G. W. Miller[4], A. David[2,6] & C. Samieri[1,6]

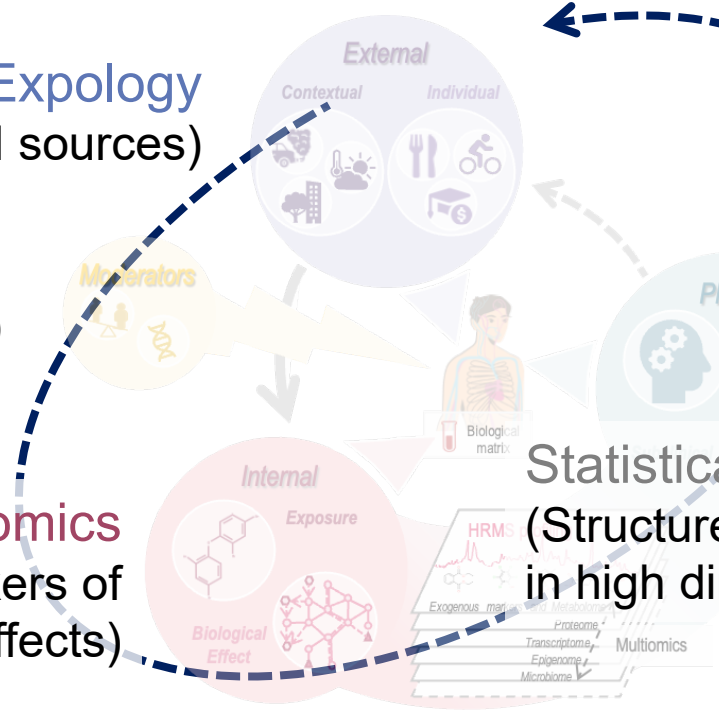


We need a cohort with novel tools to operationalize the concept and capture early signs of neuropathology

Expology
(Environmental sources)

(Susceptibility factors)

Exposomics
(Biomarkers of exposures and effects)

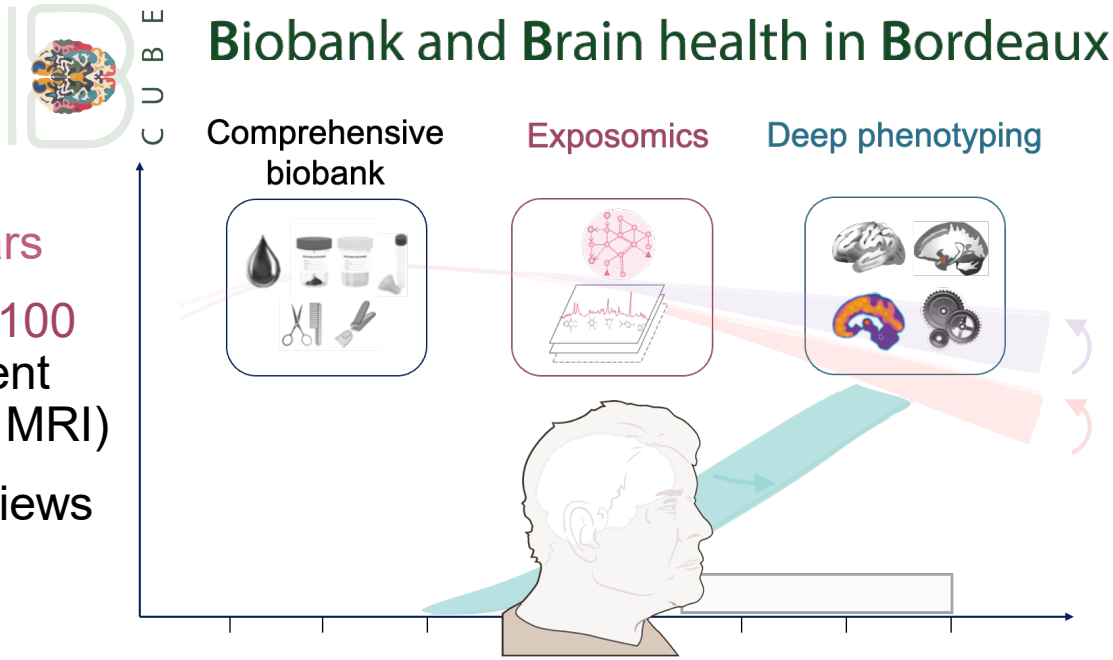


Deep molecular and imaging-based phenotyping
(Clinicobiological markers of the brain aging continuum)

Statistical methods
(Structure, dynamics and causality in high dimension context)

A new population-based study to decipher the exposome of brain aging in early stages

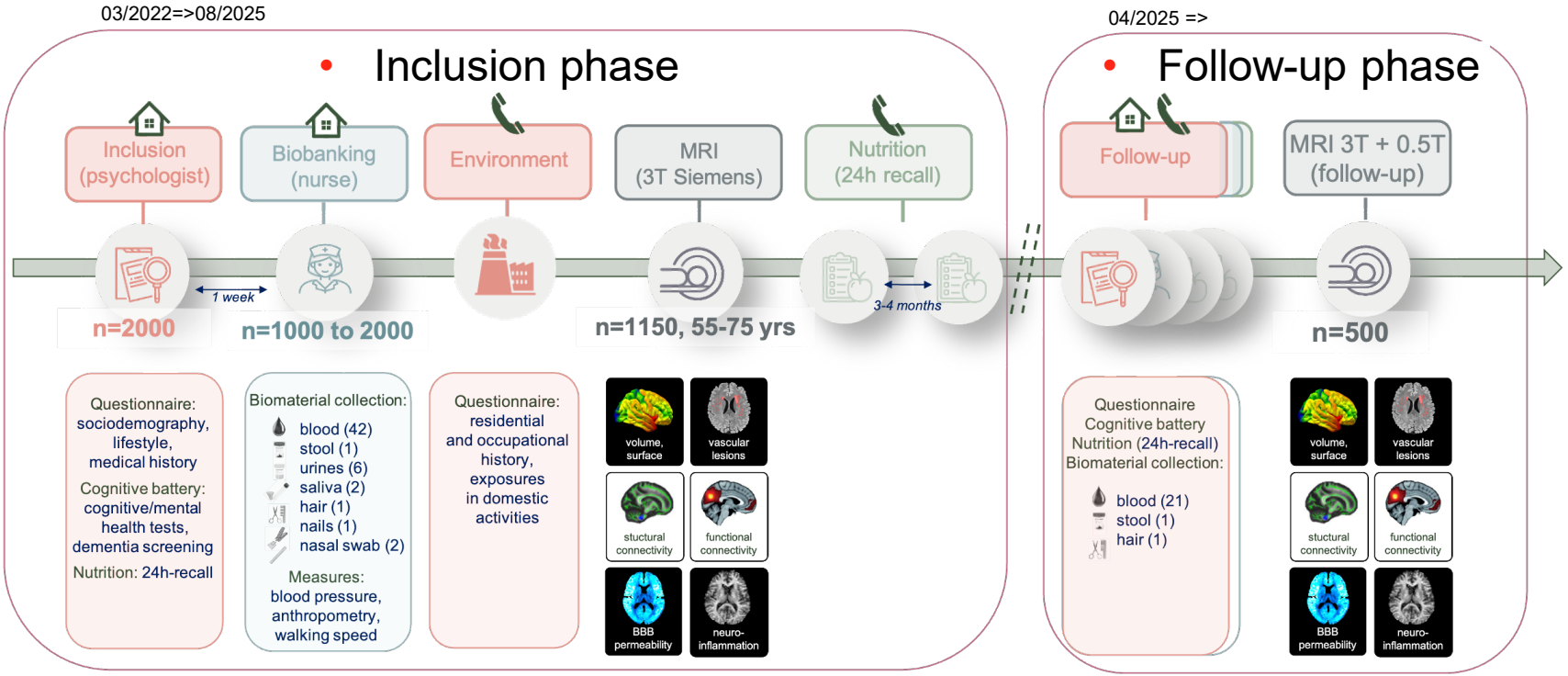
- **55**-80 years
- n=2000, >1100 MRI (current n=1660, 600 MRI)
- Home interviews



- Molecular signatures of brain aging
- Epidemiological platform

This project benefits from support from the French government operated by BPI France under the program "Investissements d'Avenir"

A new population-based study to decipher the exposome of brain aging in early stages



… which adresses unique questions within the Bordeaux's site pole of expertise on brain aging (and internationally)

VBHI Vascular Brain Health Institute BORDEAUX

GOUVERNEMENT
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FRANCE 2030

L'institut VBHI a bénéficié d'une aide de l'État gérée par l'Agence Nationale de la Recherche au titre de France 2030 portant la référence « ANR-23-IAHU-0001 ».

Soutenu par : université de BORDEAUX, CHU BDX Centre Hospitalier Universitaire Bordeaux, Inserm, Inria, Région Nouvelle-Aquitaine, Fondation Bordeaux Université

En partenariat avec : Assistance Publique Hôpitaux de Paris, cnrs, IRD Institut de Recherche pour le Développement

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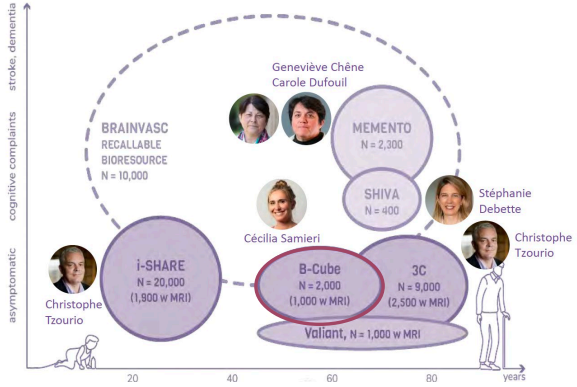
VBHI Vascular Brain Health Institute BORDEAUX

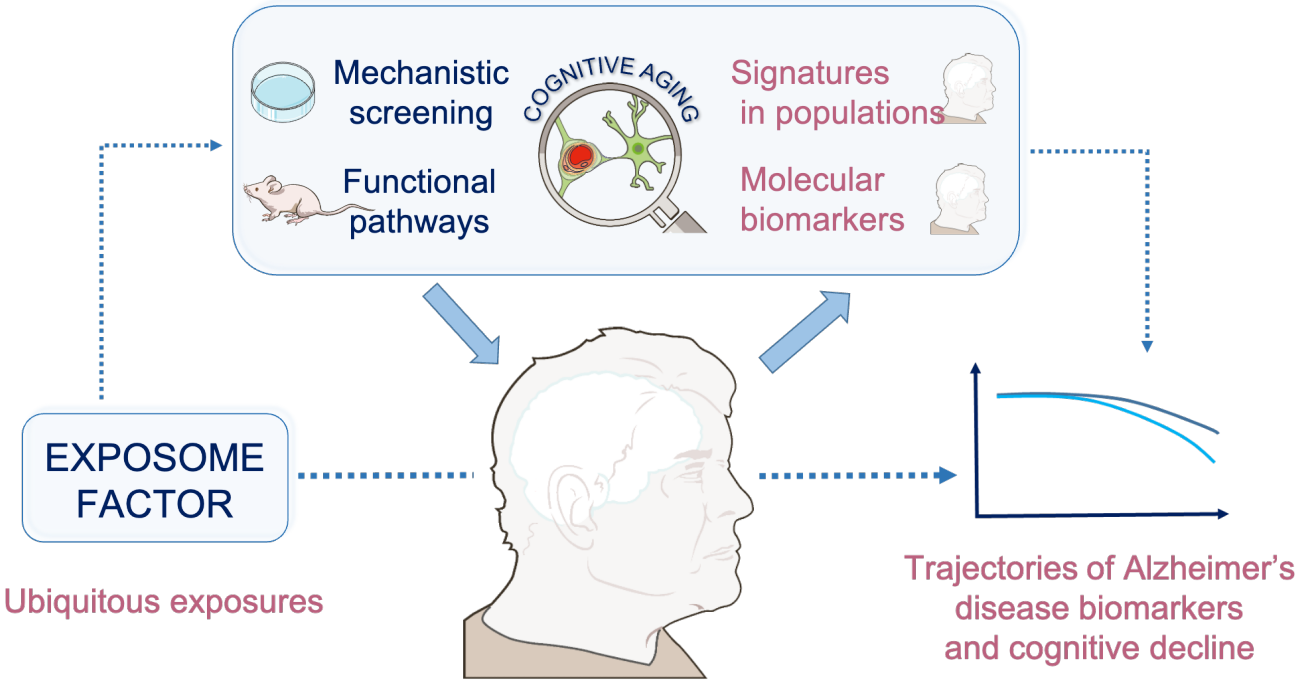
- Cohorts



- Programs

T1.3.2 « Next-generation etiological research on the exposome of VBD across the lifespan »

Translational projects with an exposome approach leveraging molecular epidemiology cohorts

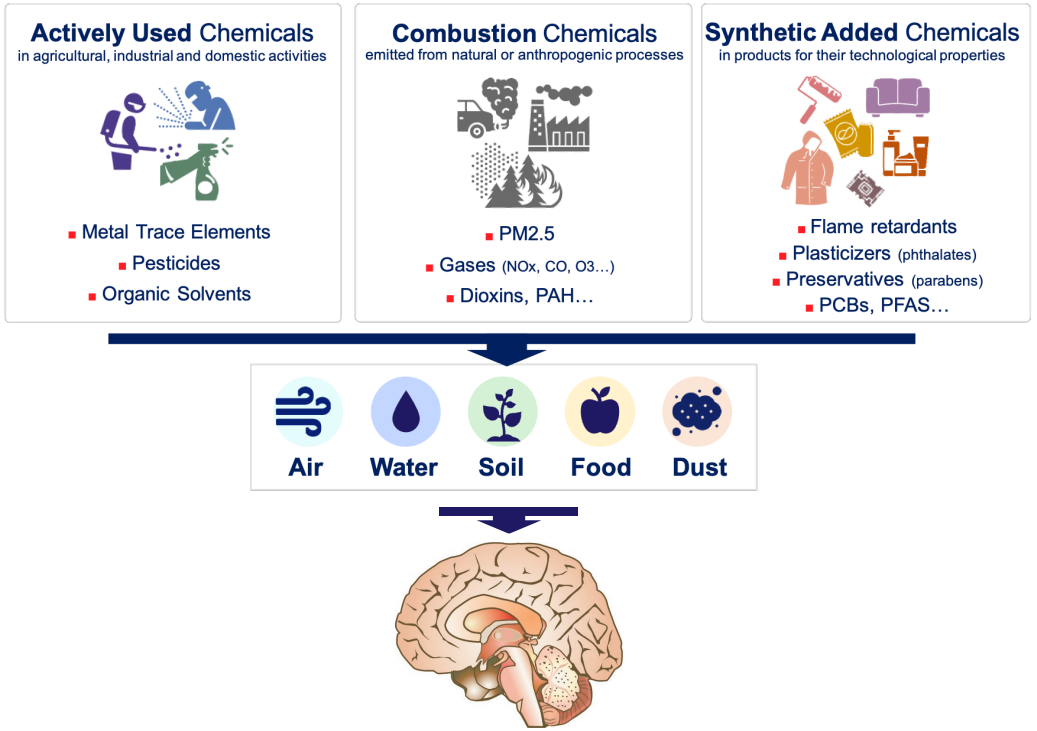


Translational projects with an exposome approach: B cube

- Food metabolome
- Chemical exposome — Exposomics
- Infectious exposome / microbiota-gut-brain axis — Microbiomics
- Exposome methods
- …

The chemical exposome of brain aging

- >300,000 chemicals are on the market, yet the extent of the chemical exposome is unknown
- We hypothesize that the chemical exposome holds etiological clues to accelerated brain aging and related diseases



The chemical exposome of brain aging: promises of exposomics science

- Challenge:

/!\ chemical space is

➔Highly variable

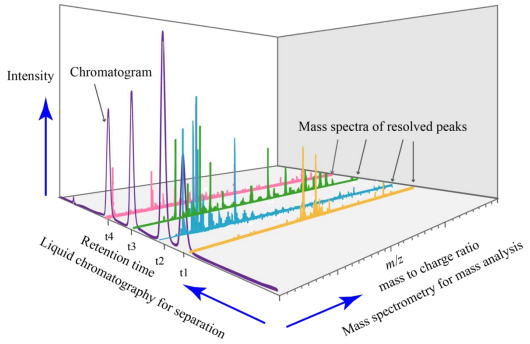
➔Diverse in nature (wide range of physicochemical properties – polarity, mass…)

➔Heterogeneous in concentration levels (trace substances)

➔Dynamic

- Opportunities:

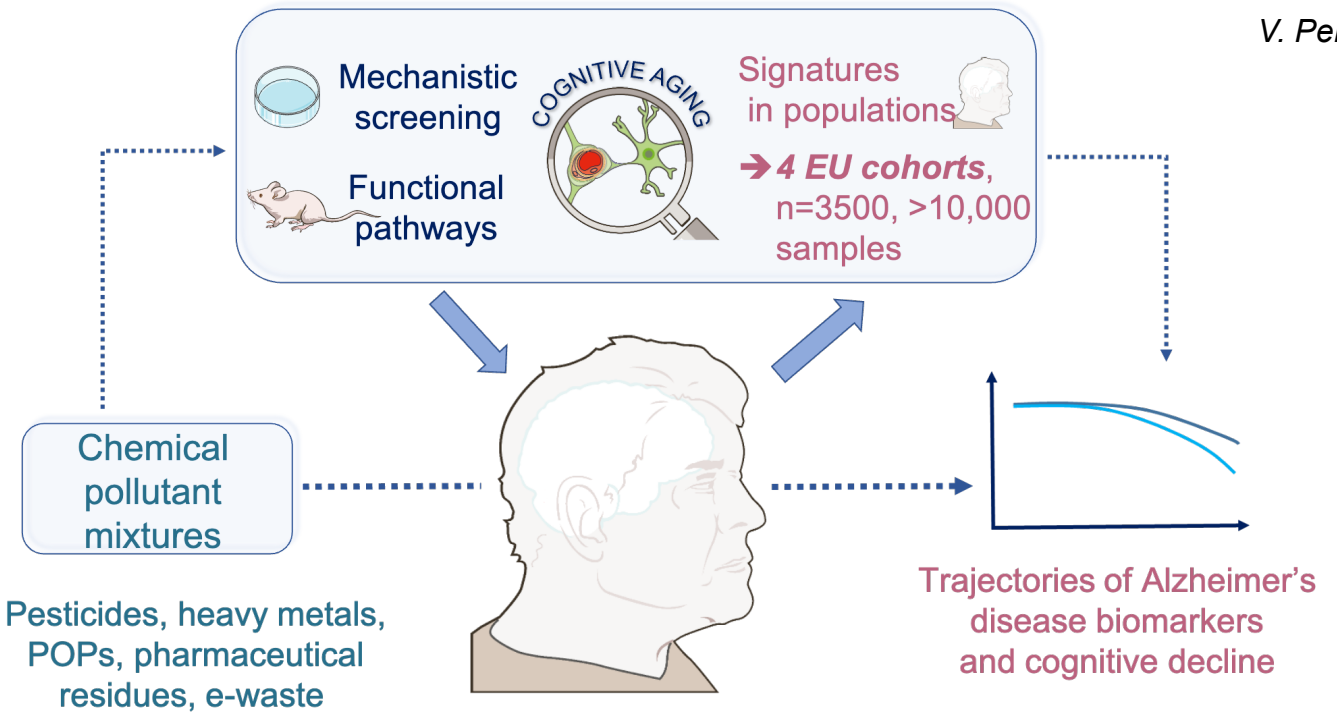
➔HRMS-based chemical profiling to capture both exogenous and endogenous chemicals

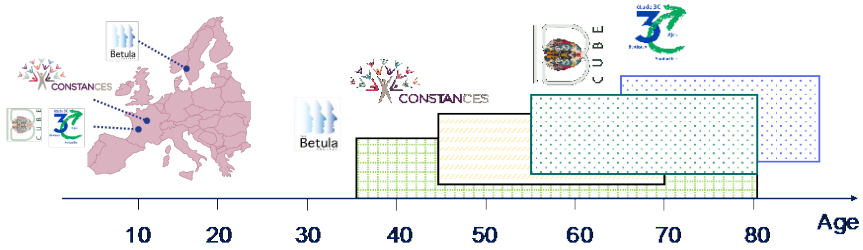


Lefèvre-Arbogast et al, Nat Neurosci 2024

Exposomics to discover chemical pollutant signatures of brain aging pathologies : Horizon Europe EXPOSIGALZ

Coordinator
V. Perrier, U Montpellier





Epidemiology workflow

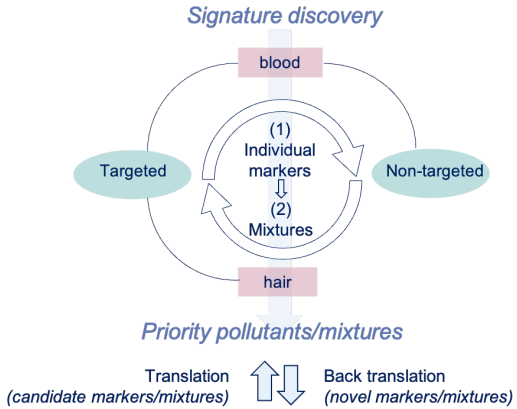
14 metals (ICP-MS)

44 POPs (GC-MS/MS)

OC pesticides, brominated flame retardants, PCBs

>160 markers (LC and GC-MS/MS)

PFAS, PCBs, PBDEs, non-persistent OP pesticides, pyrethroids, neonicotinoids, anilinopyrimidines, bisphenols, phthalates, nicotine-cotinine, …



>100 000 untargeted signals, >150 priority suspects (LC-HRMS)

Preclinical work packages

Thank you!

BORDEAUX POPULATION HEALTH Research Center - U1219

ELEANOR

LEHA

Vascular Brain Health Institute BORDEAUX

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Margot Berland, Research assistant


Deborah Jullien, Research assistant

Collaborative teams

EPICENE

ACTIVE

BIOSTAT

SISTM

Chez Christian et Renée, Alzheimer n'est pas invitée !