

Une cohorte de volontaires sains au Centre IRM-INT

Guillaume AUZIAS & Guillaume MASSON

Cohorte working group: L Velly, R Belzeaux, C Deruelle, N Malfait, JL Anton, J Sein, J Coull, D Meunier ...

Institut de Neurosciences de la Timone

- Pourquoi une telle cohorte ?
- Les enjeux scientifiques, méthodologiques et techniques
- La stratégie de constitution de la cohorte
- Les dimensions
- Le calendrier de mise en oeuvre



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Pourquoi une telle cohorte ?

- **Un constat:** lors de la réflexion autour du renouvellement du scanner, plusieurs manques ont été constatés (CS, CNRS, FLI)
 - Absence de partage de données et de base de données agrégeant près de 10 ans d'activité
 - Pas de grand projet fédérateur autour de l'activité propre du Centre, **en plus** des projets individuels réalisés au Centre
 - Un manque de visibilité du Centre en direction des grandes études multicentriques, des cohortes nationales ou internationales
- **Une révolution en cours:** l'accès à des grandes quantités de données, via des méthodes normalisées de l'acquisition à l'analyse
 - Une augmentation du nombre de participants pour chaque étude (fiabilité statistique, nouvelles méthodes d'analyse type machine learning) qui impose un changement d'échelle du recrutement au data management.
 - Une normalisation des pratiques (de l'acquisition à l'analyse) qui doit être éprouvée localement en lien avec les évolutions internationales (exemple HCP)
 - Contribution à l'OpenScience et aux bases de données multicentriques nationales ou internationales

OpenScience
Data sharing

≠

Putting an archive
on a server !

Reproducibility

Uncontrolled vs uncontrollable effets

Re-usability (ask new question to data)

Every single processing step can be re-run (code sharing)

Which dataset are really re-used and cited ?

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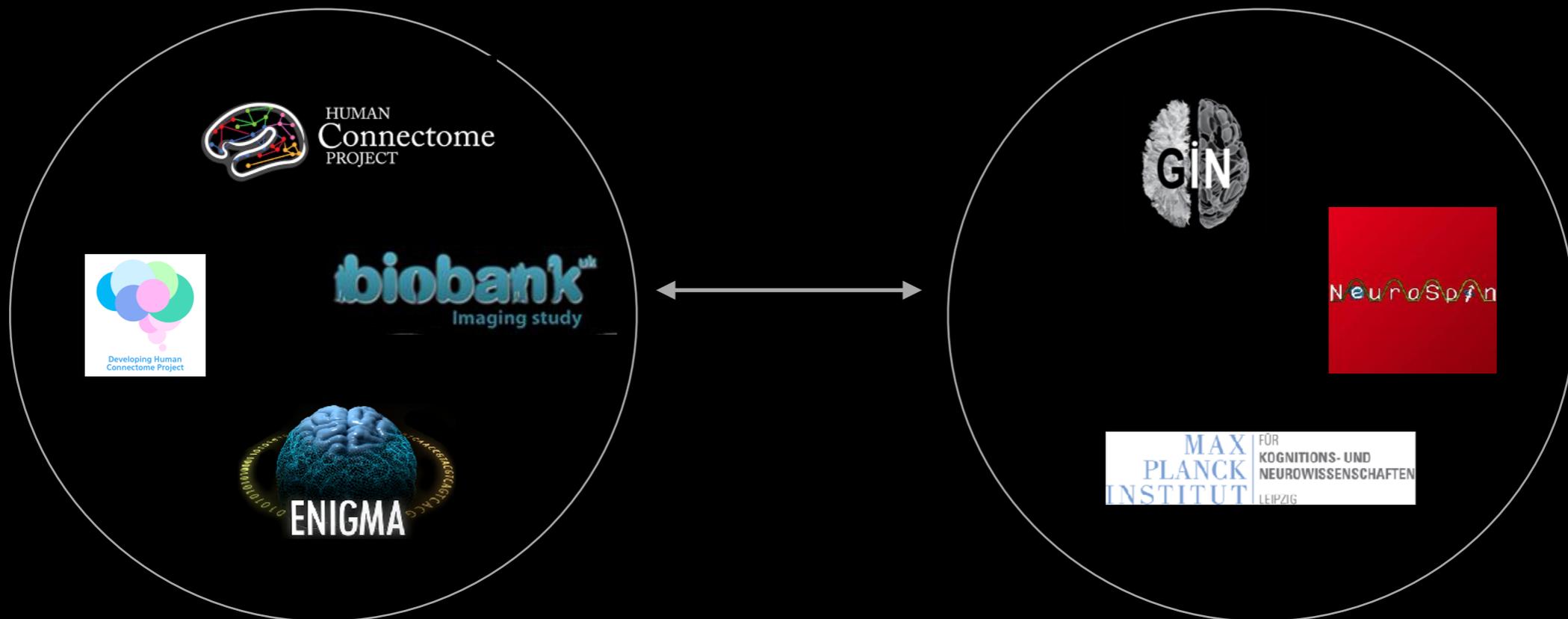
Pourquoi une telle cohorte ?

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- *Cohortes multi ou monocentriques ? Une multiplication des initiatives à différentes échelles*
 - *Pour répondre à des enjeux scientifiques (Human Connectome Project), cliniques (ENIGMA, ABIDE) ou épidémiologique (UKBioBank)*
 - *Pour structurer localement les communautés autour de ces nouveaux enjeux méthodologiques (NeuroSpin, MPG Leipzig...)*

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Pourquoi une telle cohorte ?

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Very large scale (10³-10⁵), multicentric
Big multimodal data set
Heterogeneity (scanner, clinical data..)
Mostly « omics » and data driven

Meso scale (10²-10³), monocentric
Homogeneous(scanner, clinical data..)
Mostly « functional »

We need both data quality and quantity



Depuis 80 ans, nos connaissances
bâtissent de nouveaux mondes

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A few examples of mono Center brain data set

www.nature.com/scientificdata

SCIENTIFIC DATA

OPEN Data Descriptor: A functional connectome phenotyping dataset including cognitive state and personality measures

Received: 27 October 2017
Accepted: 5 November 2018
Published: 12 February 2019

Natacha Mendes¹, Sabine Oligschläger^{1,2,3}, Mark E. Lauckner¹, Johannes Golchert¹, Julia M. Huntenburg^{1,4}, Marcel Falkiewicz¹, Melissa Ellamil¹, Sarah Krause¹, Blazej M. Baczkowski^{1,2,3}, Roberto Cozati¹, Anastasia Osoianu^{1,4}, Deniz Kumral^{7,8}, Jared Pool¹, Laura Golz^{9,10}, Maria Dreyer¹, Philipp Haueis^{1,8}, Rebecca Jost¹, Yelyzaveta Kramarenko¹, Haakon Enger^{11,12}, Katharina Ohmberger^{1,8}, Krzysztof J. Gorgolewski¹³, Nicolas Farrugia¹⁴, Anahit Babayan¹, Andrea Reiter^{7,15}, H. Lina Schaare^{2,7}, Janis Reinelt⁷, Josef Röbbig¹, Marie Uhlig^{2,7}, Miray Erbey⁷, Michael Gaebler^{7,8}, Jonathan Smallwood¹⁶, Arno Villringer^{7,8} & Daniel S. Margulies¹

The dataset enables exploration of higher-order cognitive faculties, self-generated mental experience, and personality features in relation to the intrinsic functional architecture of the brain. We provide multimodal magnetic resonance imaging (MRI) data and a broad set of state and trait phenotypic assessments: mind-wandering, personality traits, and cognitive abilities. Specifically, 194 healthy participants (between 20 and 75 years of age) filled out 31 questionnaires, performed 7 tasks, and reported 4 probes of in-scanner mind-wandering. The scanning session included four 15.5-min resting-state functional MRI runs using a multiband EPI sequence and a high-resolution structural scan using a 3D MP2RAGE sequence. This dataset constitutes one part of the MPI-Leipzig Mind-Brain-Body database.

MPG Leipzig / Resting state / 300 participants / one session

www.nature.com/scientificdata

SCIENTIFIC DATA

OPEN Data Descriptor: Individual Brain Charting, a high-resolution fMRI dataset for cognitive mapping

Received: 10 November 2017
Accepted: 23 February 2018
Published: 17 June 2018

Ana Luisa Pinho^{1,2,3}, Alexis Amadon², Torsten Ruest^{1,2,3}, Murielle Fabre^{2,3,4,5,6}, Elvis Dohmatob^{1,2,3}, Isabelle Denghien^{2,3,4,5,6}, Chantal Giniesty^{2,7}, Séverine Becuwa-Desmidt^{2,7}, Séverine Roger^{2,7}, Laurence Laurier^{2,7}, Véronique Joly-Testault^{2,7}, Gaëlle Médicuni-Cloarec^{2,7}, Christine Doublet^{1,2,7}, Bernadette Martins^{2,7}, Philippe Pinel¹, Evelyn Eger^{2,3,4,5,6}, Gaël Varocaux^{1,2,3}, Christophe Pallier^{2,3,4,5,6}, Stanislas Dehaene^{2,3,4,5,6,8}, Lucie Hertz-Pannier^{2,5,7,9} & Bertrand Thirion^{1,2,3}

Functional Magnetic Resonance Imaging (fMRI) has furthered brain mapping on perceptual, motor, as well as higher-level cognitive functions. However, to date, no data collection has systematically addressed the functional mapping of cognitive mechanisms at a fine spatial scale. The Individual Brain Charting (IBC) project stands for a high-resolution multi-task fMRI dataset that intends to provide the objective basis toward a comprehensive functional atlas of the human brain. The data refer to a cohort of 12 participants performing many different tasks. The large amount of task-fMRI data on the same subjects yields a precise mapping of the underlying functions, free from both inter-subject and inter-site variability. The present article gives a detailed description of the first release of the IBC dataset. It comprises a dozen of tasks, addressing both low- and high-level cognitive functions. This openly available dataset is thus intended to become a reference for cognitive brain mapping.

NeuroSpin / Cognition / 30 participants / one session

frontiers
in Aging Neuroscience

PROTOCOLS
published: 11 October 2018
doi: 10.3389/fnagi.2018.00321

The Barcelona Brain Health Initiative: A Cohort Study to Define and Promote Determinants of Brain Health

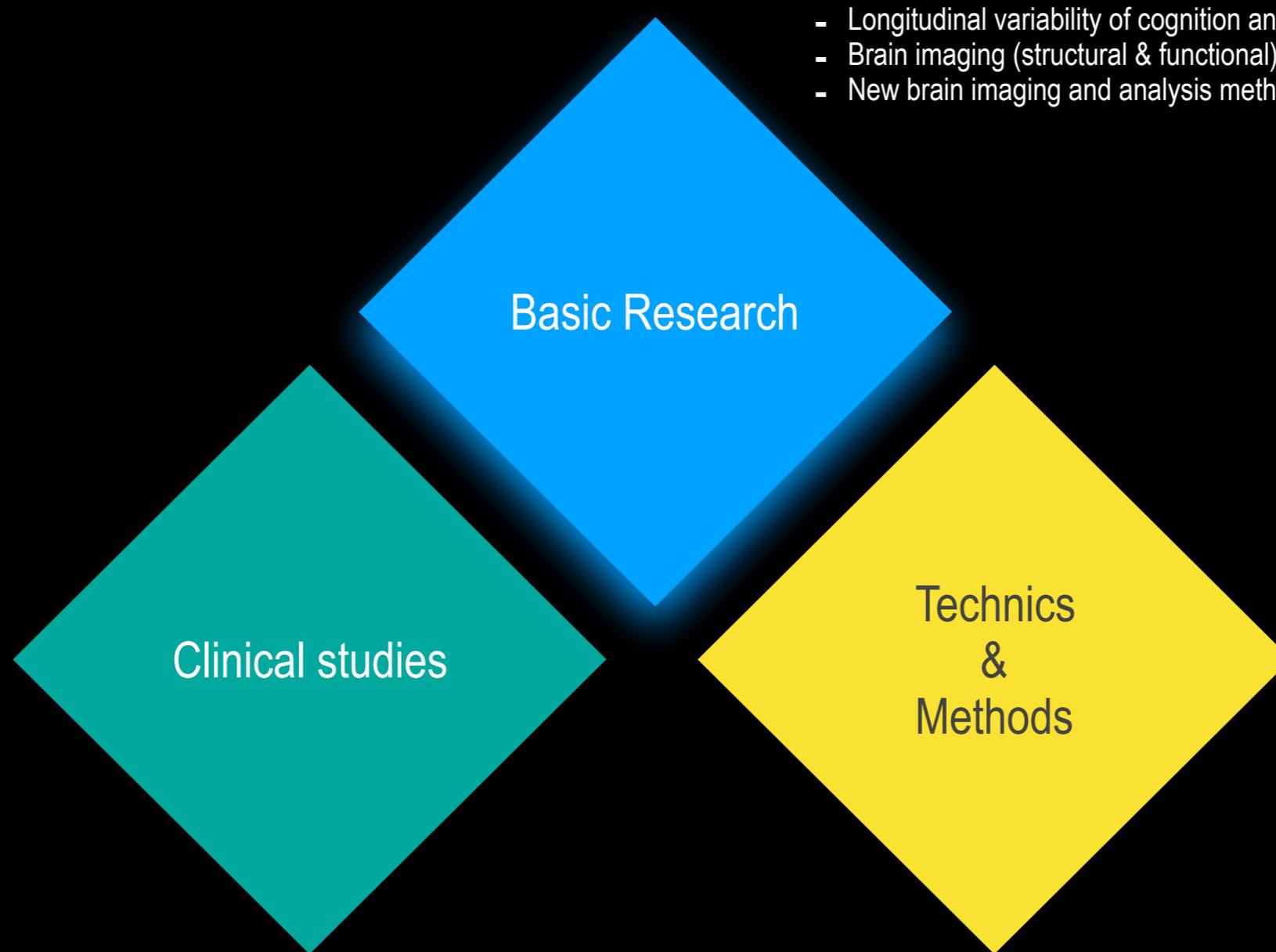
Gabriele Cattaneo^{1,2*}, David Bartrés-Faz^{1,2,3*}, Timothy P. Morris^{1,4,5}, Javier Solana Sánchez^{1,4,5}, Didac Macià^{1,4,5}, Clara Tarrero^{1,4,5}, Josep M. Tormos^{1,4,5} and Alvaro Pascual-Leone^{1,6*}

¹ Institut Guttmann, Institut Universitari de Neurorehabilitació adscrit a la UAB, Badalona, Spain, ² Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain, ³ Departament de Medicina, Facultat de Medicina i Ciències de la Salut, Universitat de Barcelona, Barcelona, Spain, ⁴ Universitat Autònoma de Barcelona, Barcelona, Spain, ⁵ Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Spain, ⁶ Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, United States

UAB/ Cognition- ageing / 1000 participants / longitudinal

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Les enjeux scientifiques et techniques



- Longitudinal variability of cognition and brain imaging (anatomical, functional)
- Brain imaging (structural & functional) reproducibility
- New brain imaging and analysis methods (quantitative imaging)

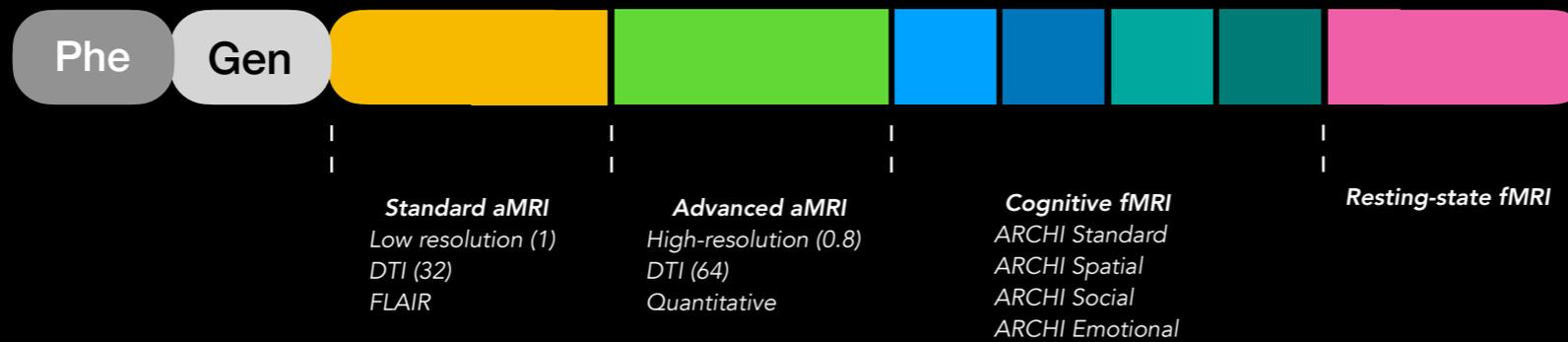
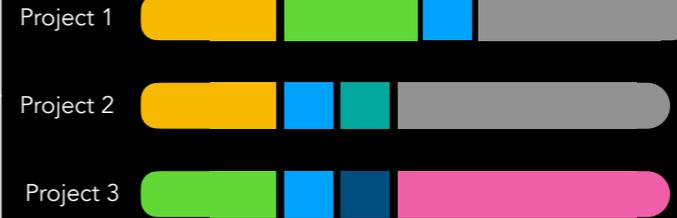
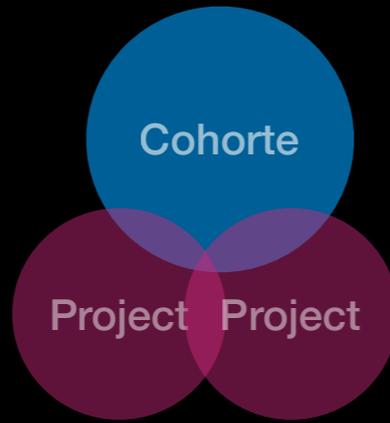
- Attracting clinical studies (Prisma 3T scanner, long-term infrastructure..)
- Control adult participants for clinical studies (neurology, psychiatry..)
- Control children for clinical studies (atypical brain development)

- Data management workflow and multimodal integration
- Ethics and Regulations
- Diffusion (OpenScience, contribution to larger cohortes..)

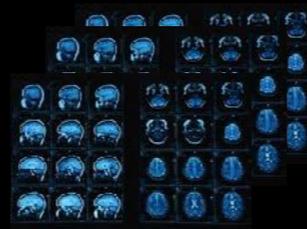
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Le rationnel de la cohorte

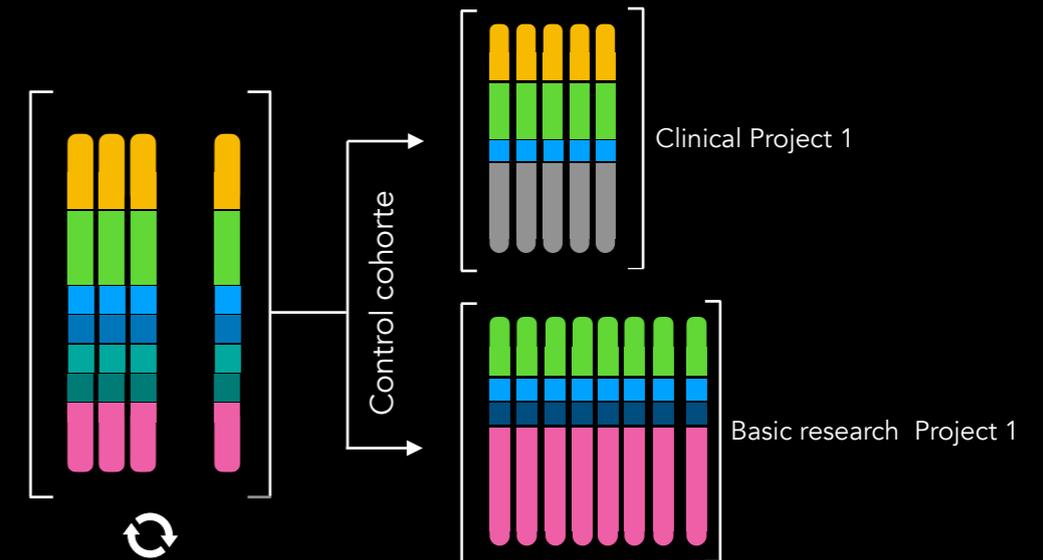
Aggregate
(after PI agreement)



Diffusion & Usage

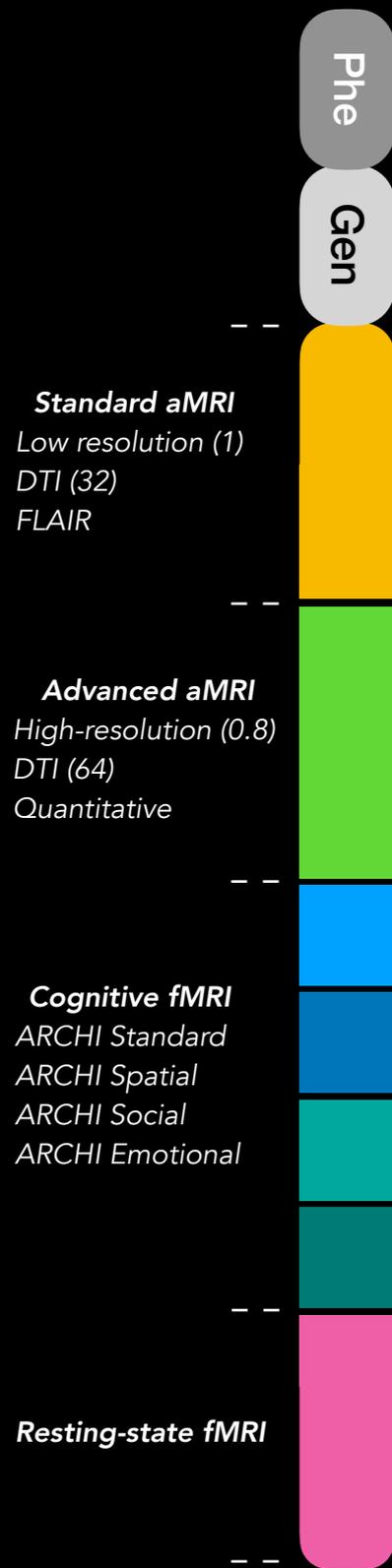


Multimodal Database

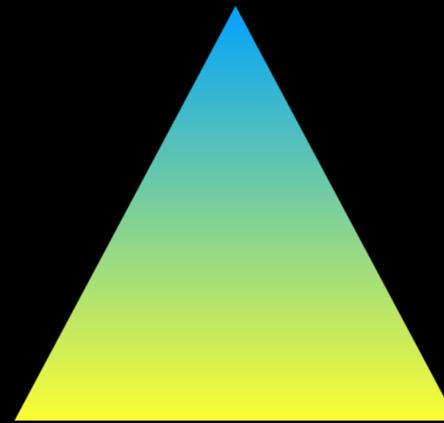


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Le rationnel de la cohorte



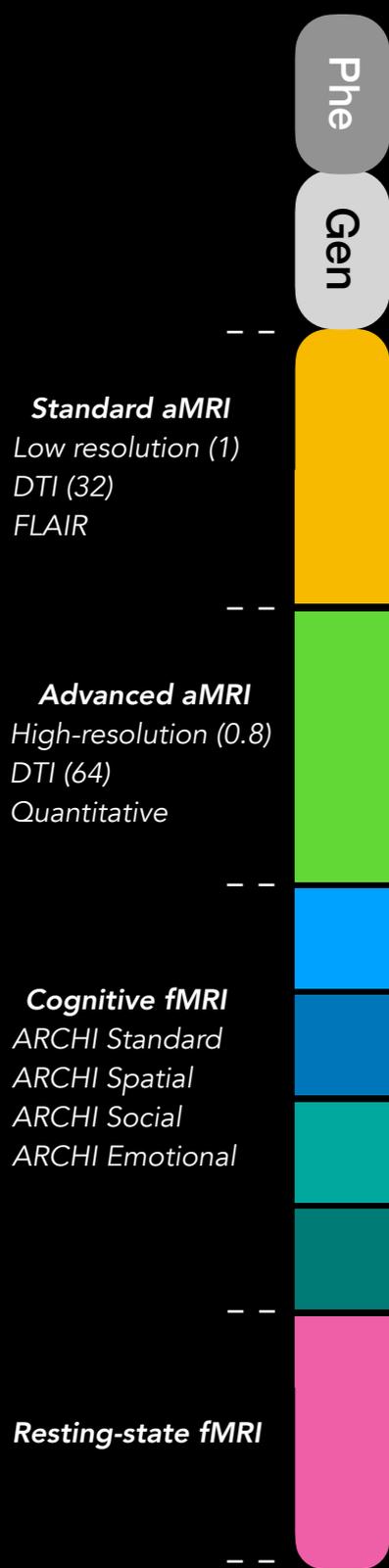
*Behavioural (Cognitive)
Phenotyping*



*Genomics &
Biomarkers*

*Brain Imaging
(anatomical & functional)*

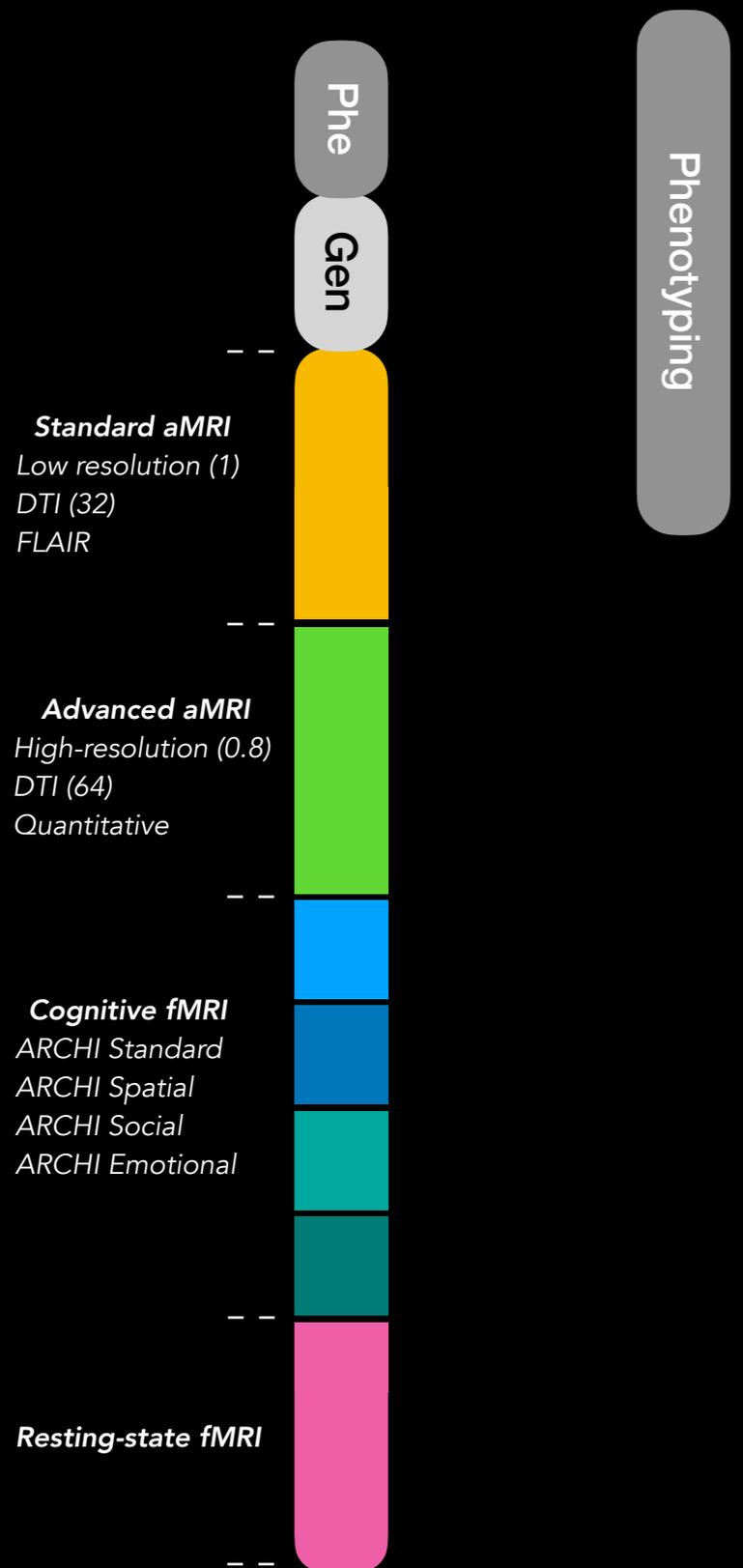
- We cannot be exhaustive but rather having a rationale based on
 - One scientific question: longitudinal cognitive/psychopathological assessment across lifespan
 - Which cognitive and neuropsychological dimensions ?
 - Which functional brain imaging ? Resting state, basic cognitive functions
 - The needs of clinical studies
 - Anatomical (structural, DTI) markers
 - Quantitative MRI
 - Resting states
 - Others ?



- Biographic and biometric data (age, height/weight)
- Clinical record
- Neuropsychological assessment (IQ, handedness...)
- Neuropsychiatric assessment
- Cognitive assessment (**which dimensions ?**)

- Blood and tissue sampling
- Genomics and transcriptomics (RNA, miRNA..)
- Neuroinflammation biomarkers

Example of questionnaires lists used in other brain imaging datasets
(Max Planck Leipzig, oriented towards resting states in healthy volunteers
1-2Hrs/participant)



Abbreviation	Behavioral Measure	N
<i>Personality and Habitual Behaviors</i>		
AMAS	Abbreviated Math Anxiety Scale ²	145
ASR	Adult Self Report adapted from ¹³	213
BDI	Beck Depression Inventar-II ^{14, 15, 16}	210
BIS/BAS	Behavioral Inhibition and Approach System ^{17, 18, 19, 20}	288
BCQ	Body Consciousness Questionnaire ²¹	79
BP	Boredom Proneness Scale ²²	209
SCS	Brief Self-Control Scale ^{23, 24}	214
ESS	Epworth Sleepiness Scale ^{25, 26}	210
FBI	Facebook Intensity Scale ²⁷	180
Gold-MSI	Goldsmiths Musical Sophistication Index ^{28, 29}	214
HADS	Hospital Anxiety and Depression Scale ^{30, 31}	210
IAT	Internet Addiction Test ³²	214
IMIS	Involuntary Musical Imagery Scale ³³	214
MPU	Mobile Phone Usage	210
MGIQ	Multi-Gender Identity Questionnaire ³⁴	159
MMI	Multimedia Multitasking Index ³⁵	209
NEO PI-R	NEO Personality Inventory-Revised ^{10, 11, 12}	169
PSSI	Personality Style and Disorder Inventory ³⁶	209
SE	Self-Esteem Scale ³⁸	214
SD3	Short Dark Triad ³⁹	213
SDS	Social Desirability Scale-17 ^{40, 46}	214
TPS	Tuckman Procrastination Scale ⁴¹	214
UPPS-P	UPPS-P Impulsive Behavior Scale ^{42, 43, cf. 44}	214
<i>Mind-Wandering and Mindfulness</i>		
FFMQ	Five Facets of Mindfulness Questionnaire ⁴⁵	79
MCQ-30	Metacognition Questionnaire ^{46, 47}	79
NYC-Q_posttasks	New York Cognition Questionnaire ⁴⁸	202
NYC-Q_postscan		188
NYC-Q		
Short-NYC-Q_inscan1	Short Version of the New York Cognition Questionnaire ⁸	175
Short-NYC-Q_inscan2		174
Short-NYC-Q_inscan3		174
Short-NYC-Q_inscan4		170
Short-NYC-Q_postETS		181
Short-NYC-Q_prescan		159
S-D-MW	Spontaneous and Deliberate Mind-Wandering ^{51, cf. 44}	214
VISQ	Varieties of Inner Speech Questionnaire ⁵²	214
<i>Synesthesia</i>		
SYN	Synesthesia Color Picker Test (synesthete.org) ⁵³	73
<i>Cognitive Control and Sustained Attention</i>		
Oddball	Adaptive Visual and Auditory Oddball Target Detection Task e.g., ^{54, cf. 55}	137
ACS	Attention Control Scale ⁵⁶	210
CCPT	Conjunctive Continuous Performance Task ⁵⁰	169
ETS	Emotional Task Switching ^{49, see 57}	189
<i>Creativity</i>		
AUT	Alternative Uses Task ^{58, 59}	77
CAQ	Creative Achievement Questionnaire ⁶⁰	79
RAT	Remote Associates Test cf. ^{61, 62}	77
TCIA	Test of Creative Imagery Abilities ⁶³	77

Phe

Gen

Standard aMRI
Low resolution (1)
DTI (32)
FLAIR

Advanced aMRI
High-resolution (0.8)
DTI (64)
Quantitative

Cognitive fMRI
ARCHI Standard
ARCHI Spatial
ARCHI Social
ARCHI Emotional

Resting-state fMRI

Standard aMRI

Advanced aMRI

- Standard aMRI
 - Structural T1w, T2w: 1mm
 - FLAIR 2D / FLAIR 3D
 - ASL clinique
 - diffusion: DTI (32 directions)

~15min

- Advanced aMRI
 - Structural T1w, T2w: 0.8mm
 - diffusion: DTI (100 directions, 1.8mm)
 - Quantitative MRI (T1, T2*, PD, MT..)

~30min

~40min

Phe
Gen

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Low resolution (1)
DTI (32)
FLAIR

Advanced aMRI
High-resolution (0.8)
DTI (64)
Quantitative

Cognitive fMRI
ARCHI Standard
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Resting-state fMRI

Resting State fMRI

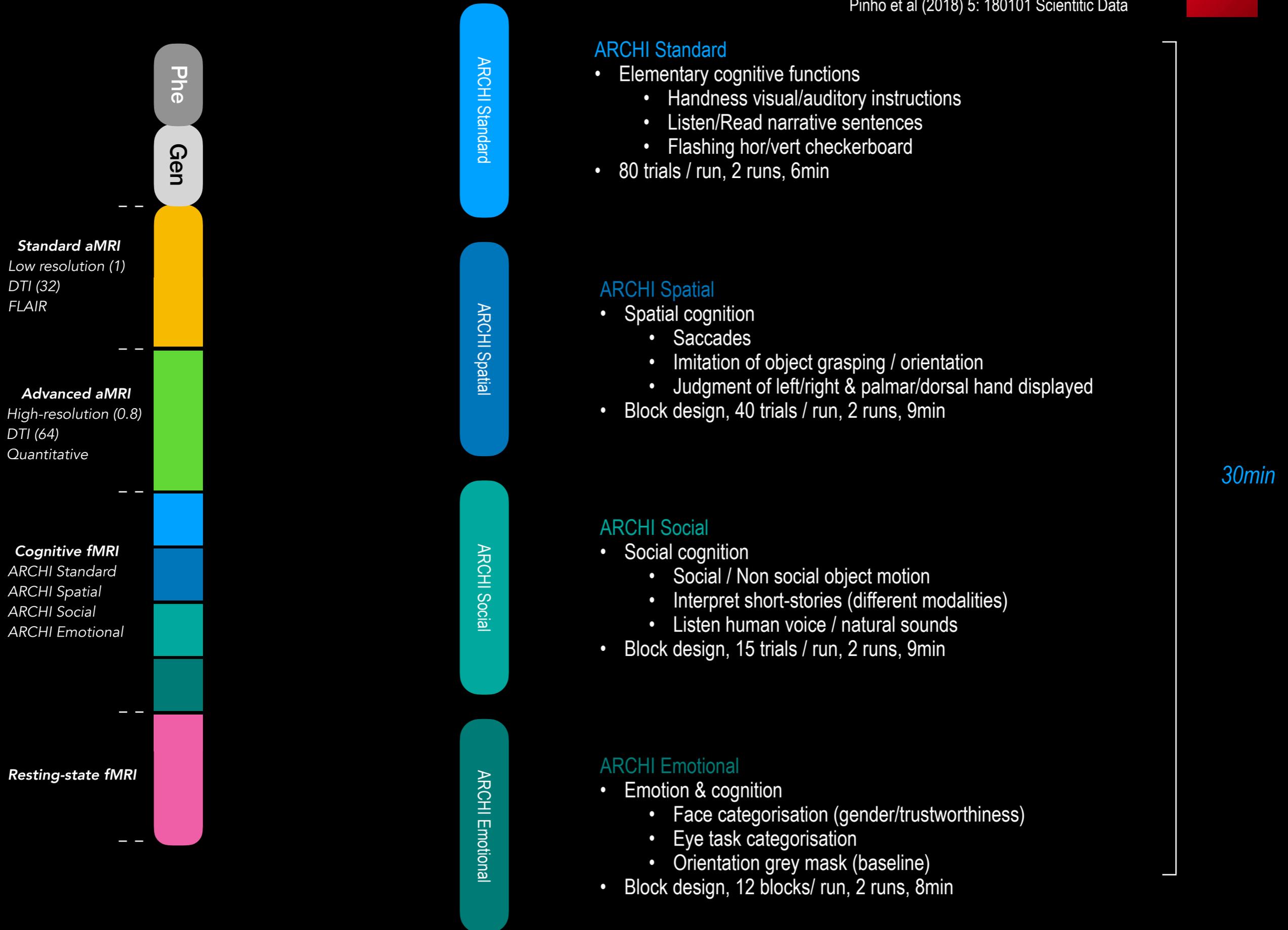
- 2D EPI, resolution spatiale 2.5mm, résolution temporelle 1.2s
- No activity, darkness
- Q: do we need to assess mind wandering offline ?

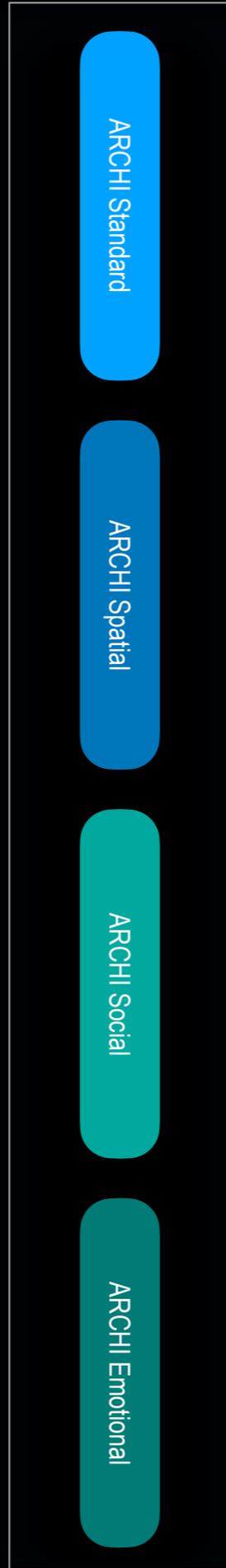
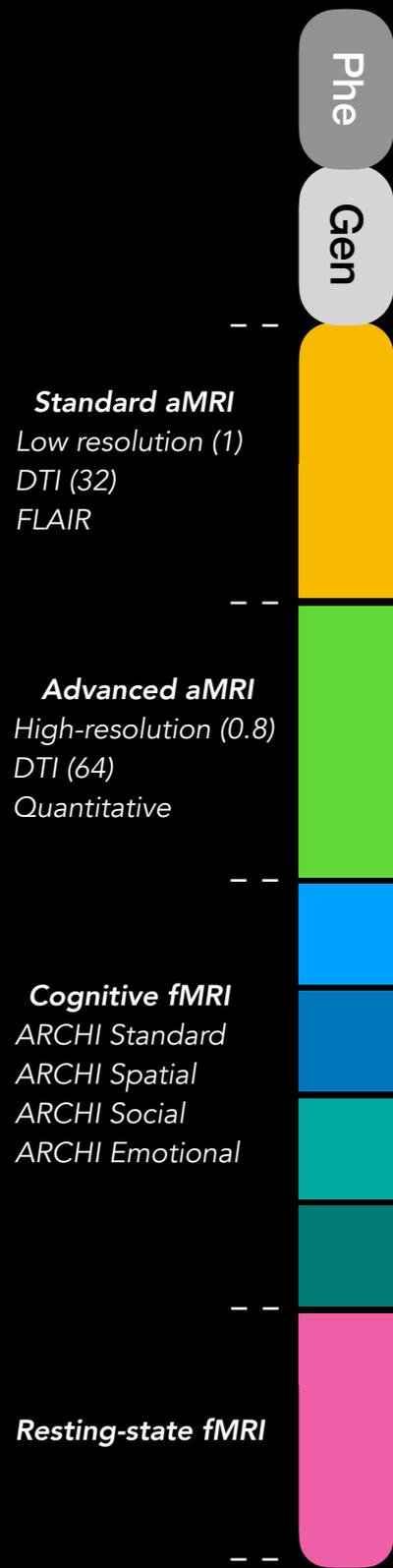
10min

The ARCHI functional MRI set is well correlated with major HCP tasks

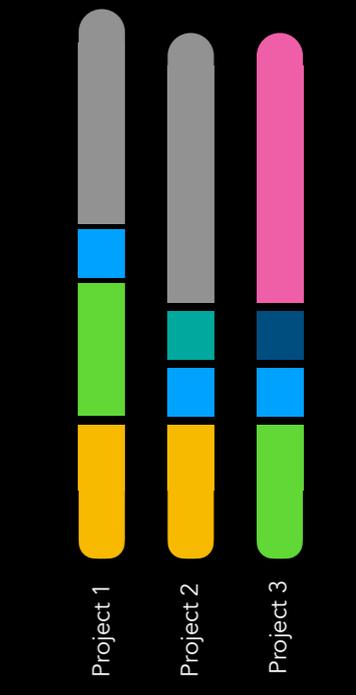
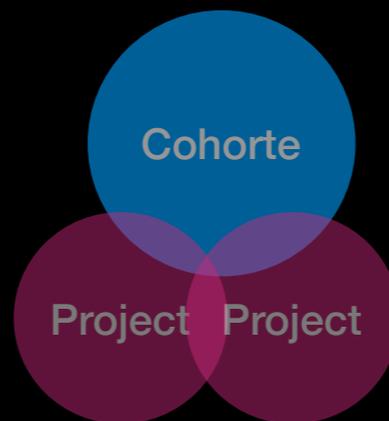


Pinho et al (2018) 5: 180101 Scientific Data





- **Modular design** around main cognitive dimensions, in line with neuropsychological assessment
- A module can be inserted in any fMRI session to **aggregate** the database and/or be used in clinical studies
- The **exact content of each module** could be customised according to the specific needs of scientific project in Marseille



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Data collection workflow

Population:

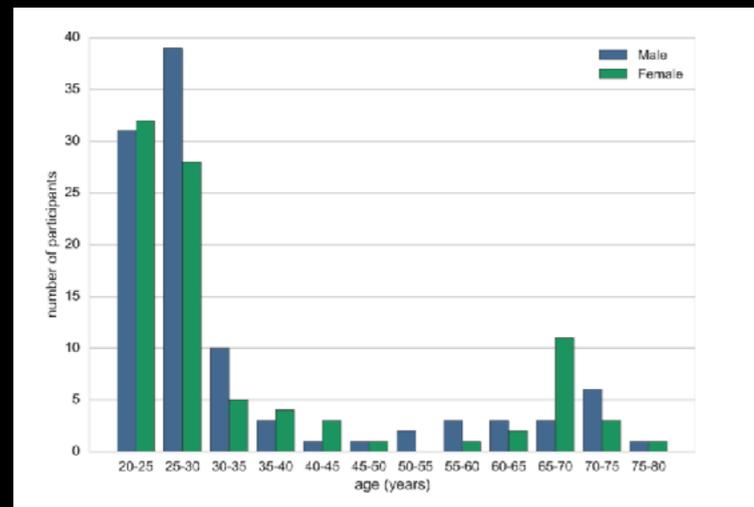
- 300 healthy volunteers (children/adults/elderly) over 7 years (*which distribution ?*)
- Each participant has one phenotype/clinical examination per year, one brain imaging session every 2 years
- A small subgroup of young adults has 4 consecutive MRI sessions (over 2-3weeks) for the reproducibility study

Monocentric studies

- Very few longitudinal survey
- Highly documented behavioural/cognitive evaluation
- Population demographic is most often skewed or dedicated to a sub-population (when large numbers > 1000, epidemiology)

Reproducibility studies

- Quantification of measurement errors
- Quantification of noise / uncontrollable variables
- What is the minimal error in my measurement ?
- What is the most subtle variation I can estimate ?



MaxPlanck Leipzig Mind-Brain Data Set

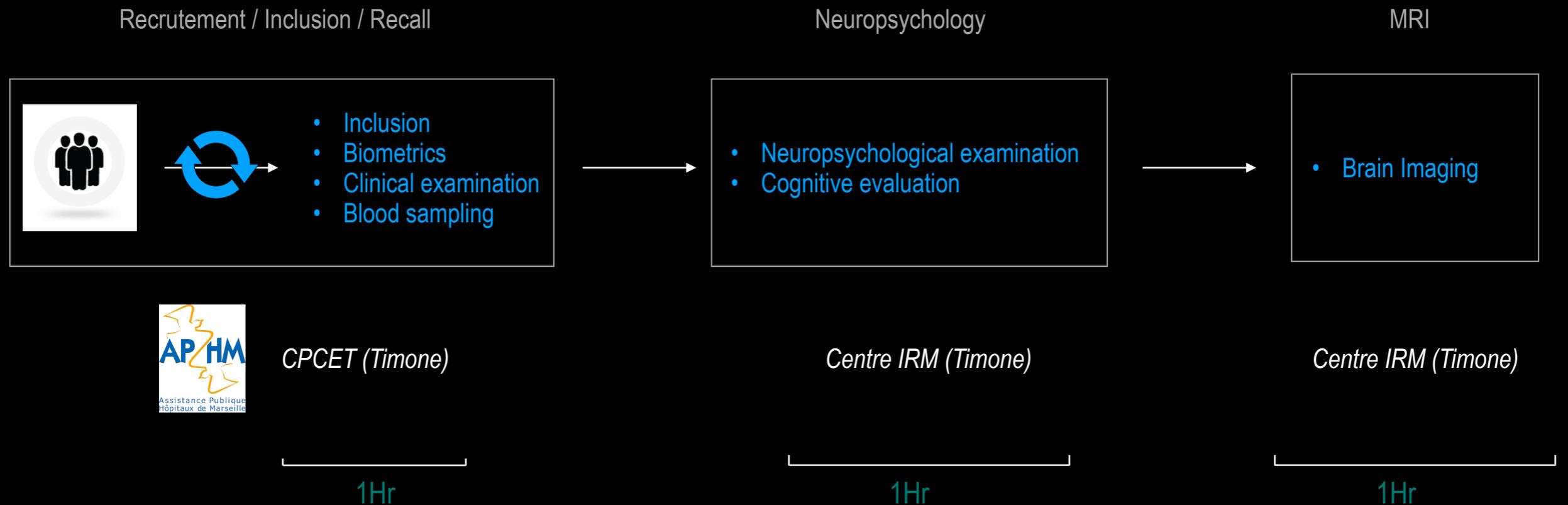
- 2 test-retest sessions is really a minimum
- OASIS : n=20
- KKI : n=19
- HCP: n=40
- CORR: n:1000 but multi centric and bad quality

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Data collection workflow

Population:

- 200 healthy volunteers (children/adults/elderly) over 7 years
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- A small subgroup of young adults has 5 consecutive MRI sessions (over 2-3)



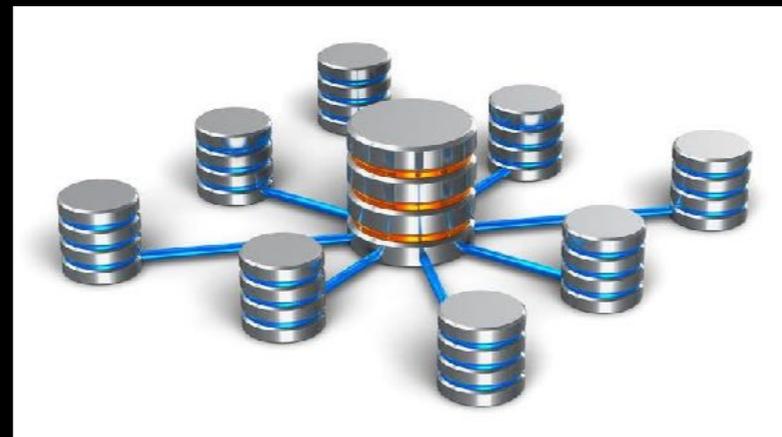
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Data workflow & Data management plan



Phe Gen Imagerie multi-modale

Data structuring
INT multi-modal databases



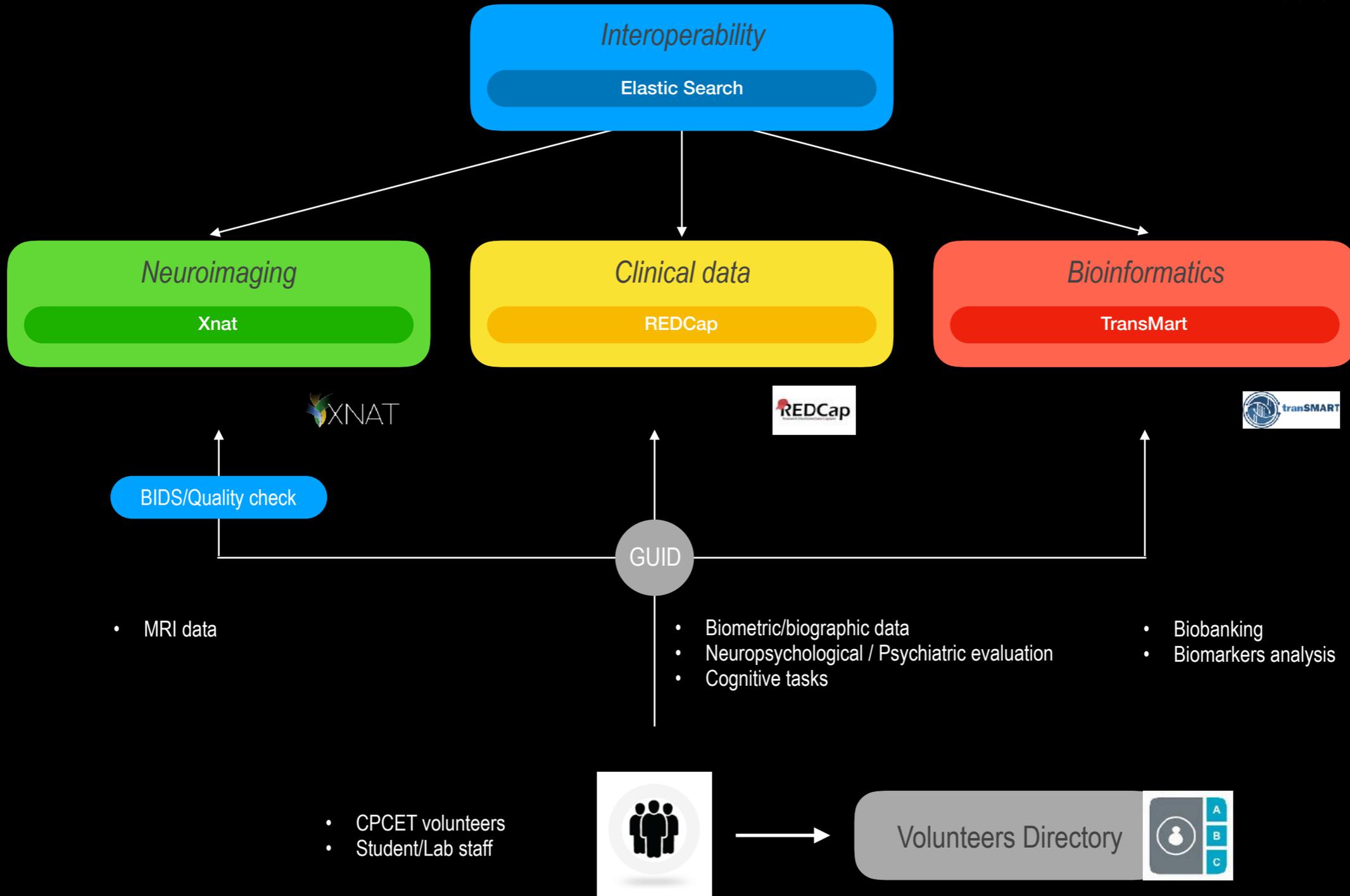
OpenScience



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Data workflow & Data management plan

NIT Platfom (INT)
 S Takerkart
 O Coulon
 D Meunier
 D Bachar



Une cohorte de volontaires sains au Centre IRM-INT

Study design and management

A group was formed at INT to discuss and build the project

- G Auzias, J Sein, JL Anton, J Coull, N Malfait, R Belzeaux, C Deruelle, P Pomietto and others
- Volunteers are welcome to join and participate in the design and implementation phases
- A project management team must be set rapidly

Final Project definition

- Precise definition of clinical and cognitive tasks/evaluations
- Precise definition of the cohorte demographics (size, age range, distribution...)
- Structuring of the MRI data workflow (quality checks, BIDS, Data flow to INT Computing Center and Databases)

Finances, Promotion, Ethics & Régulation

- Economy of the project: external costs (CPCET, CRB, neuropsychologist) and internal costs (scan, biology, data management...)
- Financing Centre IRM, INT and partners to be found (ILCB)
- CNRS agreed on being the Promoteur
- Data management plan needs to be checked (CNRS, AMU..)
- CPP proposal to be sent in September 2019

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Time line

