neuGRID: an online environment for neuroimaging studies

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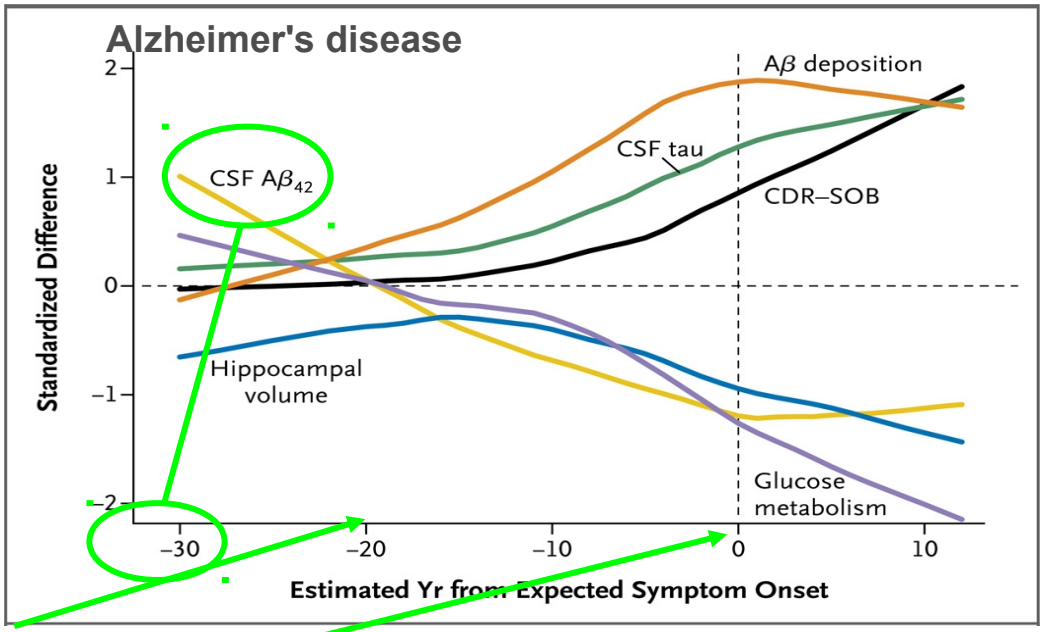
della Malattia di Alzheimer e Malattie Mentali

BACKGROUND

The pathophysiological framework

1. **Converging evidence suggests that the pathophysiological process of Alzheimer's disease begins years, if not decades, prior to the diagnosis of clinical dementia**

The natural history of pathological changes in autosomal dominant



Bateman et al., NEJM 2013

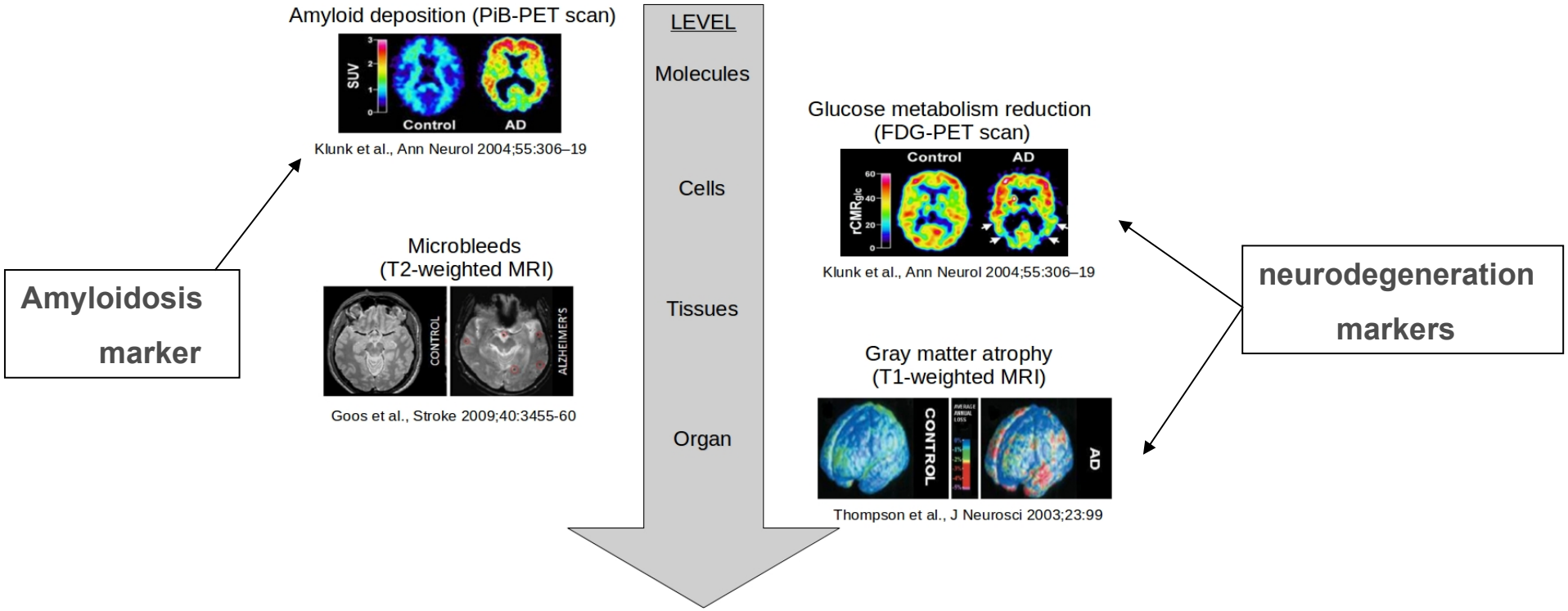
Beginning of amyloid deposition

→ **The long pre-clinical phase of AD provides a critique opportunity to design and test interventions with disease-modifying therapy, and imaging techniques represent an ideal tool for early diagnosis and monitoring of disease progression**

BACKGROUND

Imaging & Alzheimer's pathology

2. Imaging techniques have the ability to detect AD pathology *in vivo*

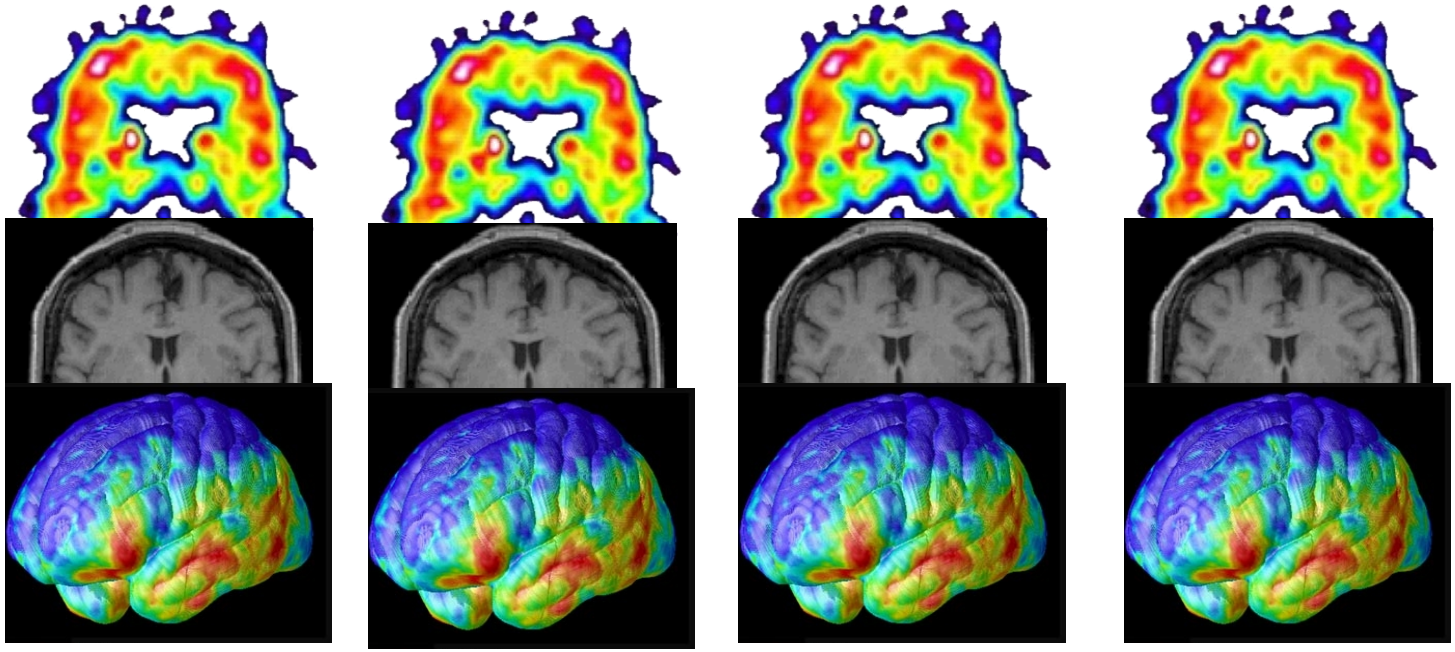


→ **Multi–modal imaging approach**

→ **Need to collect large, serial, datasets**

X-large databases for biomarker discovery & monitoring

ADNI (Alzheimer's Disease Neuroimaging Initiatives)



T0 T6 T12 T18 ...

Subjects: cognitively normal, MCI, and AD

Assessment:
- clinical and nps
- biosamples (blood and CSF)
- multimodal MRI
- molecular PET (FDG- and amyloid-PET)

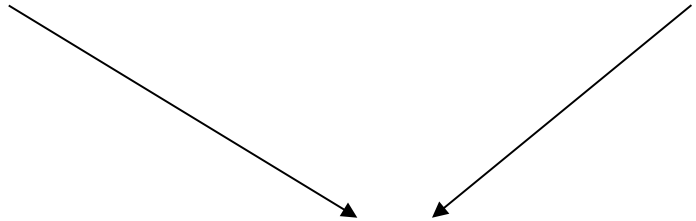
US	ADNI	≈10,000 images
Australian	ADNI (AIBL)	≈ 4,000 images
Japanese	ADNI	(≈ 3,000 images)
European	ADNI (IMI Pharma-cog)	(≈ 1,500 images)

X-large databases for biomarker discovery & monitoring

Challenges

Storage requirements
(large amounts of imaging data)

Data-intensive processing requirements
(serial, multi-modal biomarkers extraction)



Need for infrastructures able to assist the requirements of the neuroscientists to access large image repositories and use computationally intensive algorithms for imaging processing and data mining

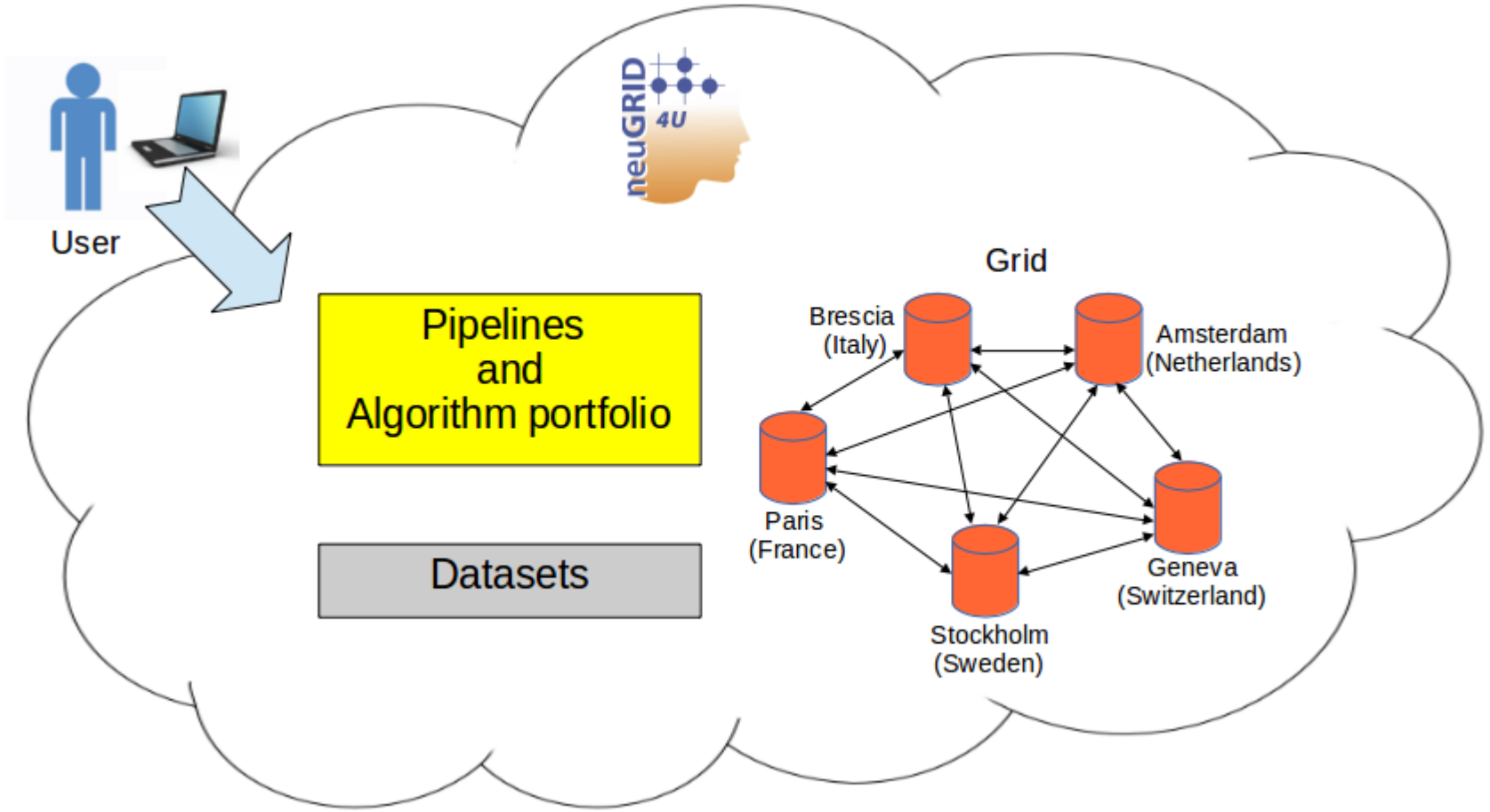
neuGRID for computer-assisted extraction of imaging biomarkers & data mining

- neuGRID is a FP7 EU-funded project aimed to enable neuroscientists to perform sophisticated neuroimaging processing and data mining through an intuitive, web-based, grid/cloud enabled platform

- neuGRID aims to bring the brain image analysis center “home” to the user, avoiding the need to locally configure hardware & software, and the need for Instructional Technology Centers (ITCs) technicians

- Can perform analyses that, up to 10 years ago, were exclusively performed at large brain imaging centers

neuGRID's platform structure



neuGrid leverages the pan-European Internet network for Education and Research (high-bandwidth connection among the computing nodes of the platform)

neuGRID's portfolio – available tools

Tool	Description
CIVET	Cortical thickness extraction from MRI data
FREESURFER	a set of automated tools for reconstruction of the brain's cortical surface and other brain structures from MRI data;
FSL	a library of image analysis for MRI, functional MRI and diffusion tensor imaging (DTI) brain imaging data
BRAINVISA	Software platform that hosts heterogeneous tools. The main toolboxes are dedicates to T1-weighted MRI, sulci identification and morphometry, cortical surface analysis, diffusion tensor imaging and tractography, functional MRI and nuclear imaging
SPM	a statistical tool for examining differences in brain activity recorded during neuroimaging experiments using fMRI or PET scans
ITK	an open-source, cross-platform system that provides developers with an extensive suite of software tools for image analysis.
VTK	an open-source, freely available software system for 3D computer graphics, image processing and visualization
R and OCTAVE	free software environments for statistical computing and graphics
MNI LIBRARIES	a set of packages that allow the management, conversion and visualization of different file formats;
3DSlicer	a free, open source software package for visualization and image analysis
MRICRON	an image viewer supporting different image file format. It can load multiple layers of images, generate volume renderings and draw volumes of interest

Example: data challenge 1 (2010)

Extracting Alzheimer's disease cortical thickness measures on 7500 MR scans

3 different cortical thickness extraction pipelines CIVET, FREESURFER, BRAINVISA

Experiment duration using neuGRID	< 3 months
Experiment duration on a single computer	> 100 years
Number of patients	800
Number of MR brain scans	7.500
Total processing operations	700.000
Number of CPU cores involved	1.300
Number of nodes involved	6
Volume of generated data	2.2 TB

Outcomes

-Assessing robustness of the most common algorithms and pipelines

-Evaluate which are more sensitive to specific patterns (in this case atrophy patterns in Alzheimer's disease at mild stages)

-New patterns discoveries and clustering thank to high statistical power

Example: data challenge 2

Extracting hippocampus measures of 800 subjects and assessment of algorithms reproducibility

7 hippocampus segmentation algorithms

Algorithm	CPU core hours per subject	Total CPU core hours (800 subjects)
FSL / FIRST	12 - 24	10.000 - 20.000
FreeSurfer / Hippocampus	150	120.000
MAPS-HBSI / Hippocampus	150	120.000
AdaBoost	6	5.000
FSL / SIENA	5	4.000
FSL / VIENA	5	4.000

Outcomes

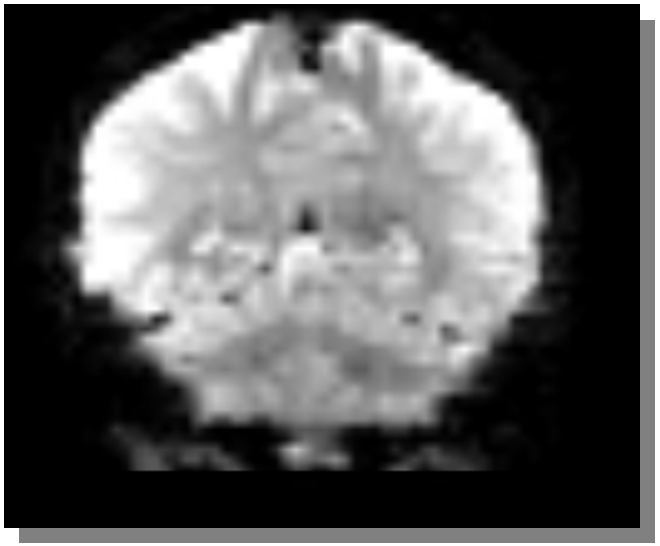
-Assessing robustness of the most common hippocampus segmentations tools

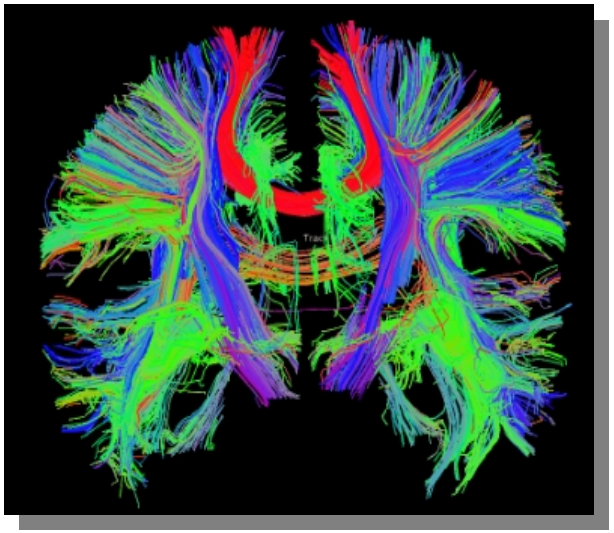
-Evaluate which are more sensitive in cohorts discrimination

-Generate normative distributions for single subject comparisons.

Example: data challenge 3

Extracting functional and structural connectomes in psychiatric diseases





<u>Processing</u>

-Brain spatial normalization

-Brain parcellation in Region of interests

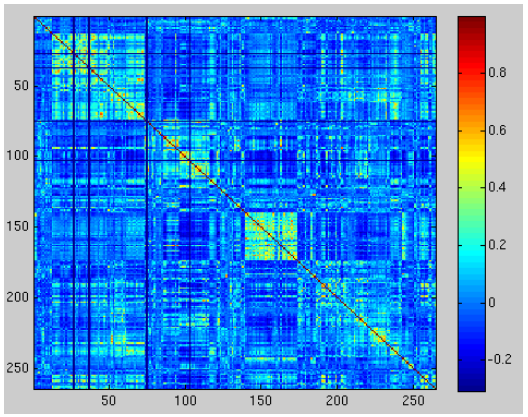
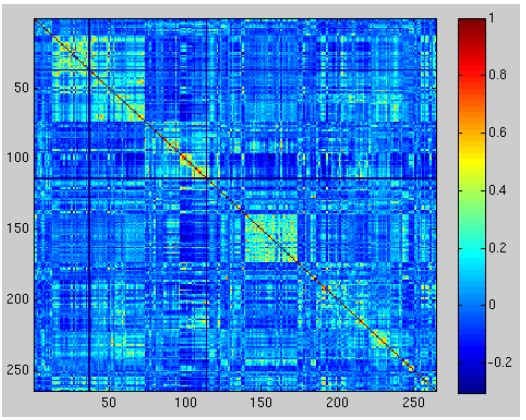
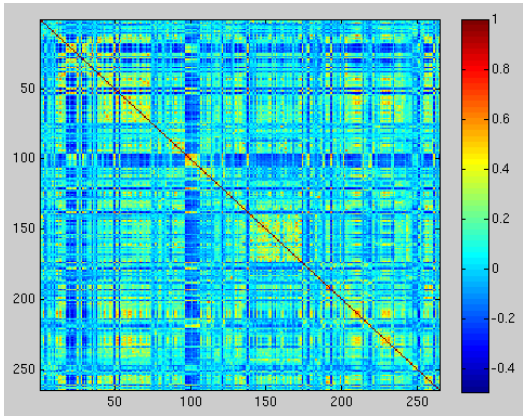
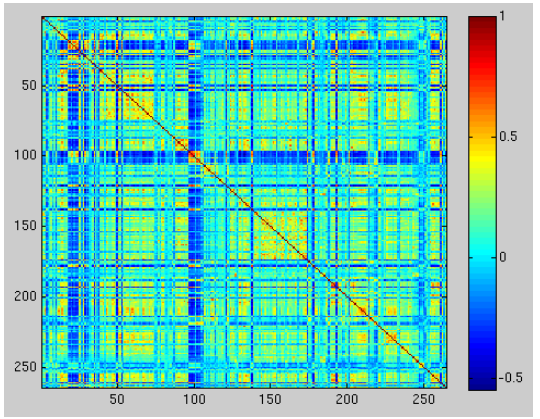
-Intensity correlation between ROIs (functional connectivity)

-Fiber tracking between ROIs (structural connectivity)

- Results: 4 TB (3’875 subjects)
- PSY subjects: CTR, SCHIZO, ASD, ADHD, PTSD
- Connectomics extracted: 2’960 matrices
- Algorithms used: FCP-CPAC, UMCP; Camino, DTK, MRtrix

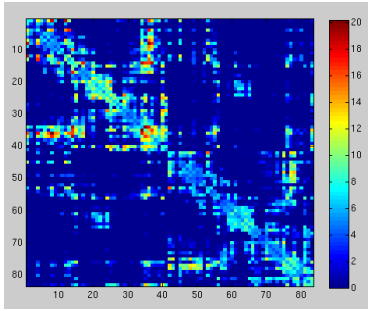
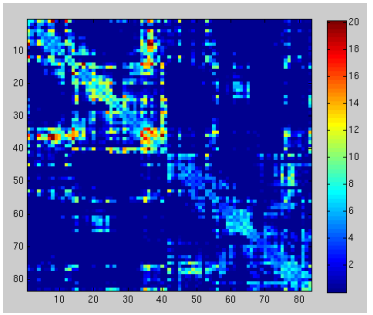
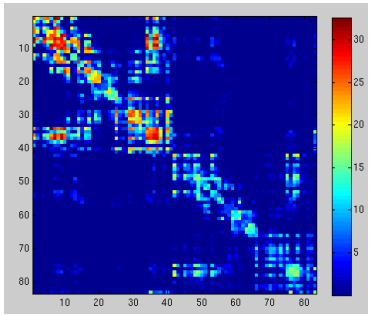
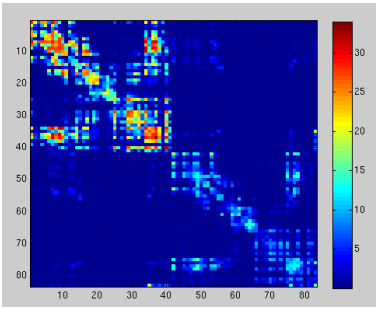
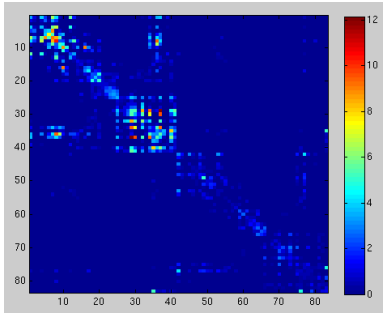
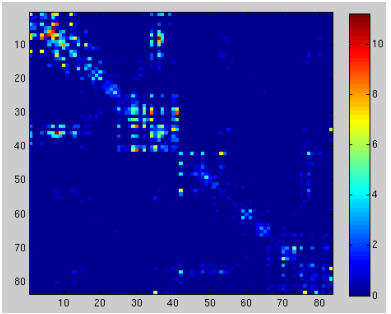
Example: data challenge 3

Extracting functional and structural connectomes in psychiatric diseases

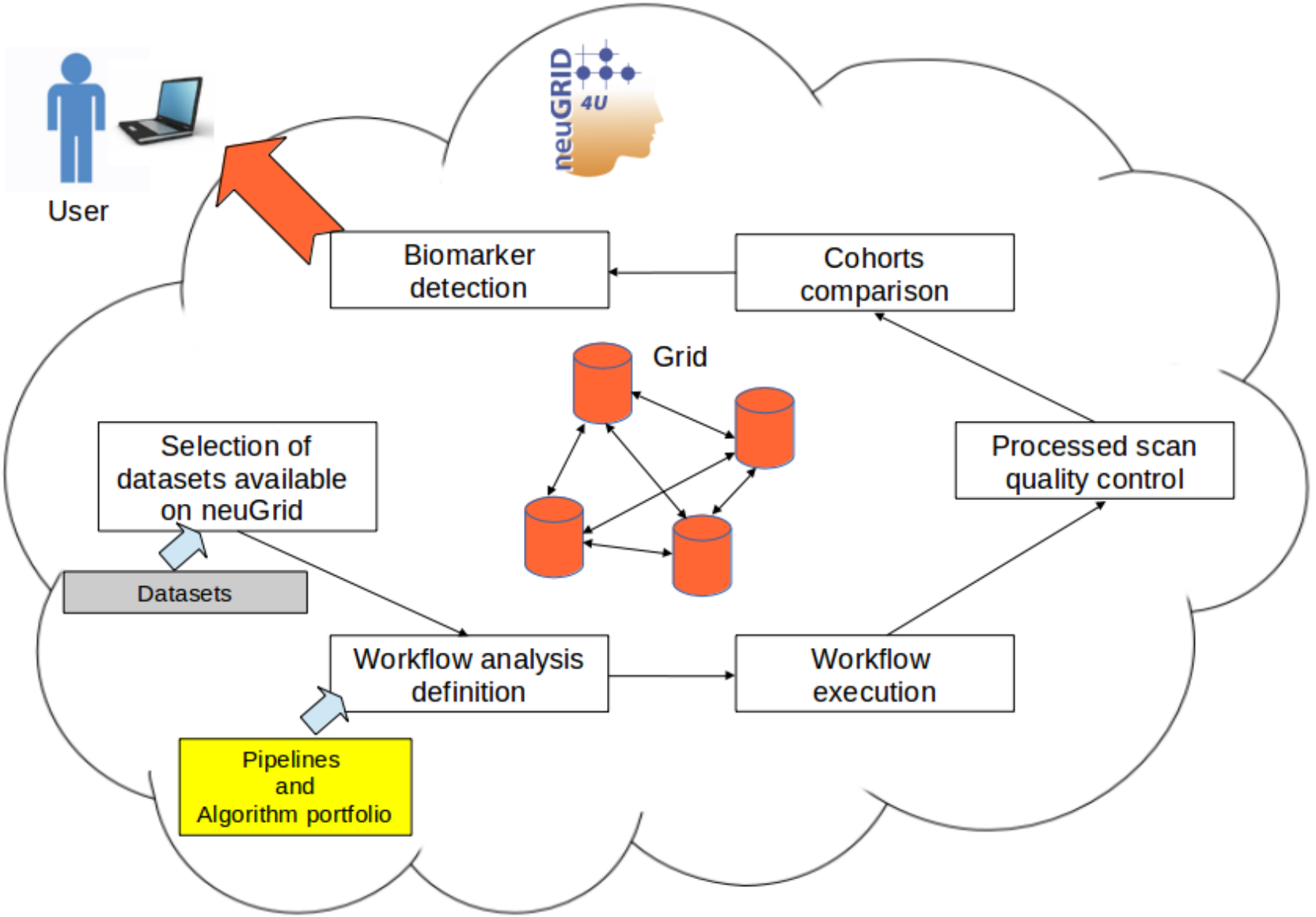
	CTR	SCHIZO	SVM (LOO)
FCP-CPAC			functional 96 %
UMCP			74%

Example: data challenge 3

Extracting functional and structural connectomes in psychiatric diseases

	CTR	SCHIZO	SVM (LOO)
Camino			Structural 71 %
DTK			80 %
MRtrix			77 %

neuGRID for novel biomarkers discovery & drug development



neuGRID for novel biomarkers discovery & drug development

Advantages for neuroscientists:

- high calculation performances, thanks to grid/cloud distributed computational elements

- availability of clinical data: vast imaging datasets can be integrated in order to assure significant statistical basis in the research of novel biomarkers meanwhile relieving the neuroscientist from the burden of collecting many data for normative dataset construction

- easiness and flexibility: neuroscientist can access and assemble workflows/pipelines through a simple web interface

Timesaving: data browsing and queries make subset studies feasible without new processing

security and privacy: data are protected through anonymization and encryption during web transmission

Opportunities of infrastructures for the exploitation of data in the life sciences

Opportunities:

- Improving diagnosis: early diagnosis based on imaging markers
- Fostering drug development for socially impactful diseases: clinical trials with imaging outcomes
- Expansion of the base of scientists with access to sophisticated scientific facilities
- Extension of top class science to disadvantaged and underdeveloped world regions

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neuGRID partners

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