e-INFRASTRUCTURES FOR MEDICAL RESEARCH AND CLINICAL PRAXIS: ACHIEVEMENTS AND THE WAY FORWARD

Roma, Feb 22 2013

IRCCS
CENTRO SAN GIOVANNI DI DIO FATEBENEFRATELLI – BRESCIA
Centro Nazionale per lo Studio e la Cura
della Malattia di Alzheimer e Malattie Mentali

MARKERS OF EFFICACY OF DRUGS FOR NEURODEGENERATIVE DISEASES

DIAGNOSIS OF NEURODEGENERATIVE DISEASES

MODELLING BRAIN FUNCTION AND DYSFUNCTION

MARKERS OF EFFICACY OF DRUGS FOR NEURODEGENERATIVE DISEASES

DIAGNOSIS OF NEURODEGENERATIVE DISEASES

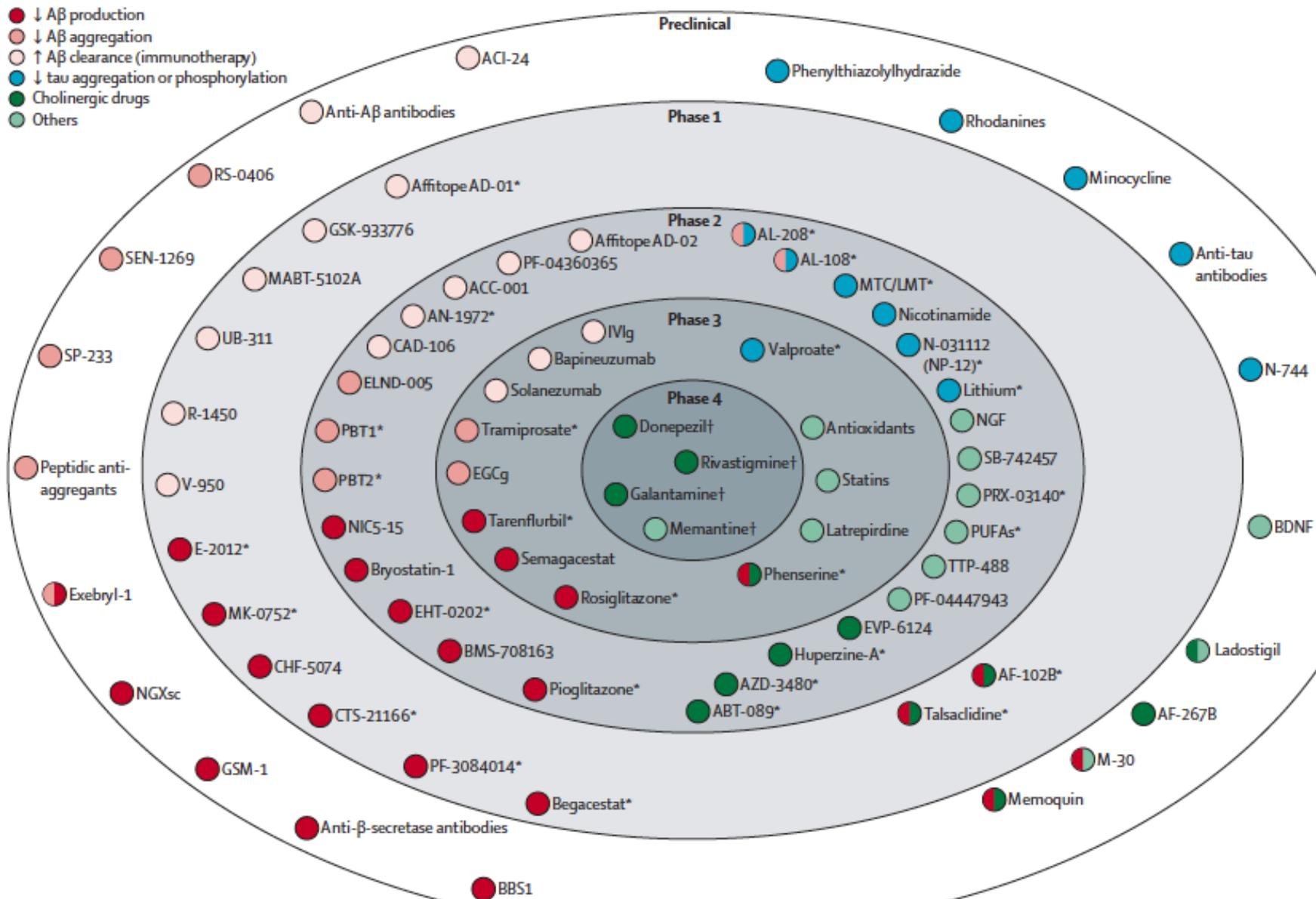**MODELLING BRAIN FUNCTION AND DYSFUNCTION**

Figure: Drug development in Alzheimer's disease

Legend:
- ↓ Aβ production
- ↓ Aβ aggregation
- ↑ Aβ clearance (immunotherapy)
- ↓ tau aggregation or phosphorylation
- Cholinergic drugs
- Others

Preclinical: ACI-24, Phenylthiazolylhydrazide, Anti-Aβ antibodies, Rhodanines, RS-0406, Minocycline, SEN-1269, Anti-tau antibodies, SP-233, N-744, R-1450, Peptidic anti-aggregants, BDNF, Exebryl-1, MK-0752*, NGXsc, Ladostigil, CHF-5074, AF-267B, CTS-21166*, M-30, GSM-1, Memoquin, PF-3084014*, Anti-β-secretase antibodies, BBS1

Phase 1: Affitope AD-01*, GSK-933776, MABT-5102A, UB-311, V-950, E-2012*, BMS-708163, Pioglitazone*, AZD-3480*, ABT-089*, Talsaclidine*, AF-102B*

Phase 2: Affitope AD-02, AL-208*, AL-108*, PF-04360365, MTC/LMT*, ACC-001, Nicotinamide, AN-1972*, N-031112 (NP-12)*, CAD-106, Lithium*, ELND-005, NGF, PBT1*, SB-742457, PBT2*, PRX-03140*, NIC5-15, PUFAs*, Bryostatin-1, TTP-488, EHT-0202*, PF-04447943, Tarenflurbil*, EVP-6124, Semagacestat, Huperzine-A*, Rosiglitazone*, Phenserine*

Phase 3: IVlg, Bapineuzumab, Solanezumab, Tramiprosate*, EGCg, Valproate*, Antioxidants, Statins, Latrepirdine

Phase 4: Donepezil†, Rivastigmine†, Galantamine†, Memantine†
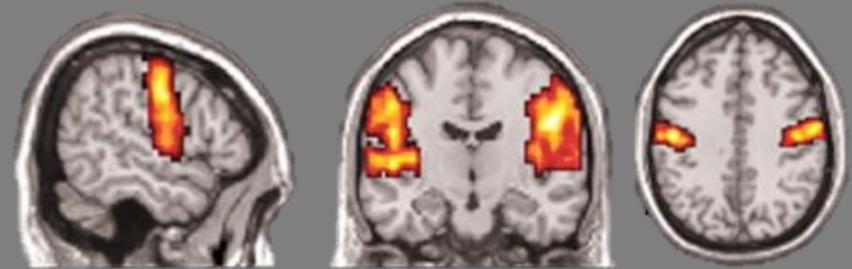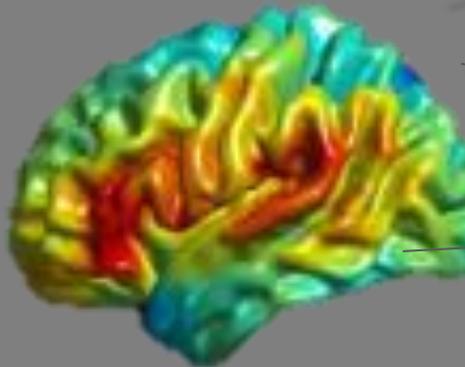
Advanced biomarkers

STRUCTURAL (GM damage)
MR Cortical thickness mapping
MR Automated segmentation
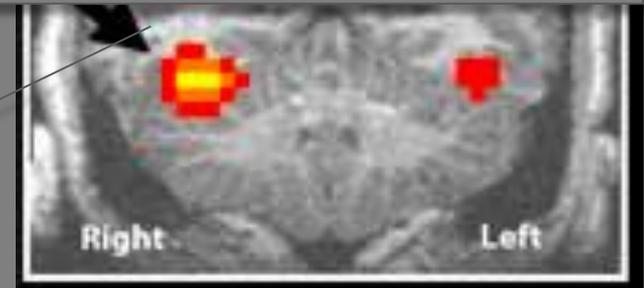MR Voxel-based statistics

MICROS
MR Tens
MR Trac

FUNCTI
MR Activ
MR Res

Sensorimotor network

Default mode network

Right   Left

Ashburner, Frisoni, et al. Lancet Neurol 2003

Large multimodal multicentre datasets (n. scans)

STUDY	Sequence					
	sMR	*dMR*	*rest fMRI*	*EEG*	*FDG-PET*	*Amy PET*
Pharmacog/E-ADNI (IMI)	900	900	900	900	---	---
ADNI / ADNI-GO / ADNI2	13'500	1'550	3'950	---	3'750	250
J-ADNI	3'500	---	---	---	1'000	500
AddNeuroMed (IMI)	3'500	---	---	---	---	---
AIBL/Au-ADNI	1'800	1'800	---	---	300	450
1000 connectomes	---	1350	700	---	---	---
OASIS	2'000	---	---	---	---	---
LADIS (5th FP)	1'200	---	---	---	---	---
EMIF-AD (IMI)	15'000	5'000	5'000	---	2'000	1'000
AD Without Borders	3'000	---	---	---	200	---

neuGRID
N4U (neuGRID for you)

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Highlights

Video

▶A new application is now available. This
application is a terminal which allows you to get

International Science Grid this Week-
SUBSCRIBE!

neuGRID:
a cloud-based image analysis environment

neuGRID
N4U (neuGRID for you)

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Large image datasets

OASIS
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LADIS
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ADDNEUROMED
Read More »
The AddNeuroMed Study

ADNI
Read More »

Algorithm pipe-lines for marker extraction

$$\left(\frac{d^3 y}{dx^3}\right)^4 + 2\,\frac{dy}{dx} = \sin\ x$$

Pipeline	Biological phenomenon
CIVET — Available for processing in neuGRID	Cortical thickness
FreeSurfer — Available for processing in neuGRID	Cortical/subcortical anatomy
FSL — Available for processing in neuGRID	Structure (sMRI), microstructure (diff MR), function (fMRI)

Vast compu-tational resources

Node	Storage (MB)	CPUs (n)
Sweden	3,557	40
Italy	3,170	40
France	4,095	2,600
Maat	1,268	8
Brazil	0	128
EGI	71,793	1,912
TOTAL	**83,883**	**4,728**

Help & Training

LEARN

help desk

Home Progetti Aiuto

neuGRID4you Help Desk

Panoramica **Attività** Segnalazioni

Attività

Da 27-11-2012 a 26-12-2012

21-12-2012

23:18 Support #797: desktop fusio
*If you have openjdk, try to put the on...
Try to start FF from a termina...*
Jérôme Revillard

21:29 Support #797: desktop fusio
*Hi Jerome,
both gateways. But it's not a problem...*
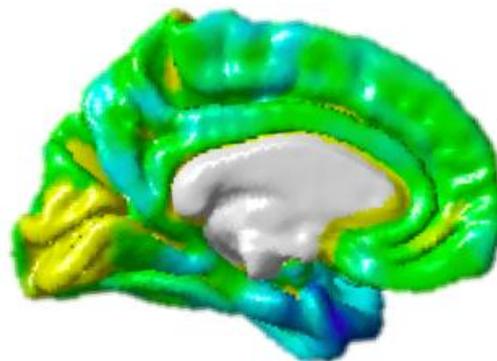Luigi Antelmi

20:57 Support #797: desktop fusio

Proof-of-concept of neuGRID:
validation of popular cortical thickness extraction algorithms on 3500 ADNI MR scans
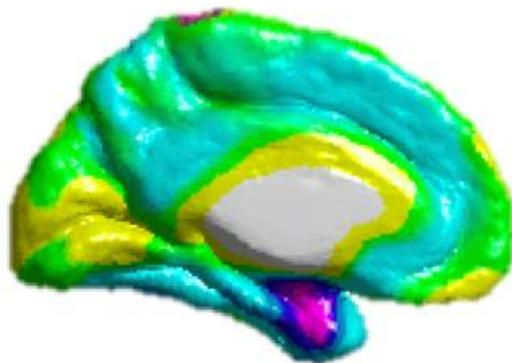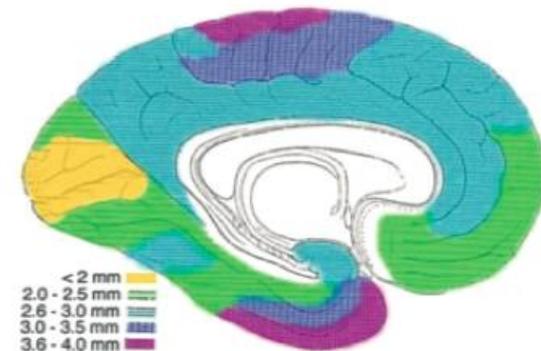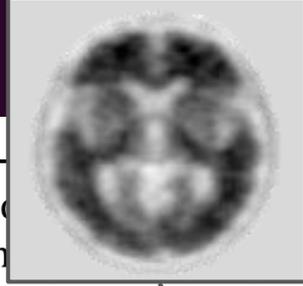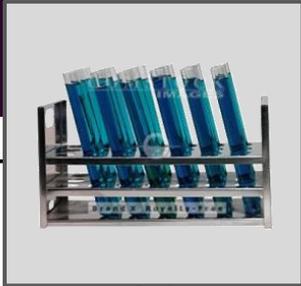

**Redolfi et al., NeuroImage submitted

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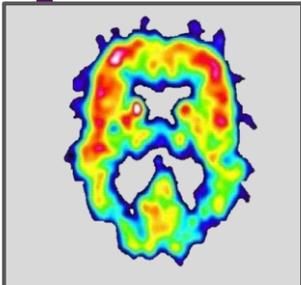**MODELLING BRAIN FUNCTION AND DYSFUNCTION**

Core Alzheimer's biomarkers

...rs of ...ease pathophysiology in the revised NINDS-AA diagnostic ...eim... Asterisks denote markers included in an early proposal for revised criteria by Dubois and colleagues [2].
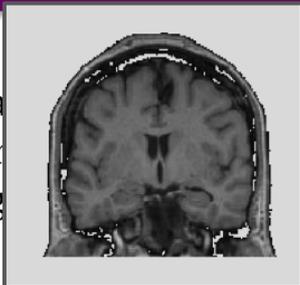
Biomarkers of brain β-amyloidosis	• Increased uptake on amyloid imaging with PET (*) • Decreased CSF Ab42 (*)
Biomarkers of neuronal injury (synaptic dysfunction and neuronal loss)	• Temporoparietal hypometabolism on 18F-FDG PET (*) • Medial temporal (hippocampal) atrophy (*) • Increased CSF tau/phospho-tau (*) • Temporoparietal hypoperfusion on SPECT
...ida... ...ion ...nag... biomarkers	• fMRI activation studies, resting BOLD functional connectivity, MRI ...ectroscopy, diffusion tensor imaging • Infla... ...nes) and oxidative stress biomarkers (isop... • Rate...

Frisoni et al., Lancet Neurol 2011

Local implementation of core AD biomarkers

Biomarker-based diagnosis in the Memory Clinic in Brescia

Frisoni et al., Alzheimers Dement 2009
**Galluzzi et al., J Neurol 2010

Development of diagnostic markers

Validation in pilot diagnostic studies
Translational Outpatient Memory Clinic

Diagnostic biomarkers into clinical reports

MMSE 27/30

Npsy tests

Aspecific cortical atrophy

Hippocampal volume <99th %

No subcort vasc dis (ARWMC 0/36)

Abnormal Abeta42 and tau

Bilat TP hypometab T-sum 55.679
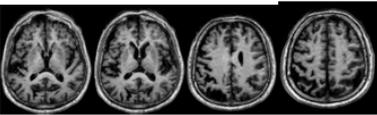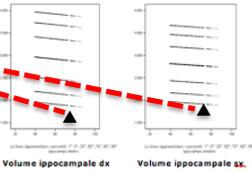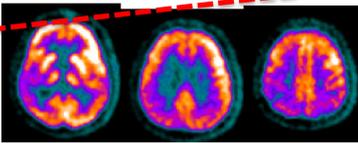
Implementing Alzheimer's biomarkers in the clinic for the diagnosis of prodromal and atypical cases: the Italian inter-societal approach to clinical, organizational, and ethical issues

Giovanni B Frisoni, IRCCS Fatebenefratelli, Brescia
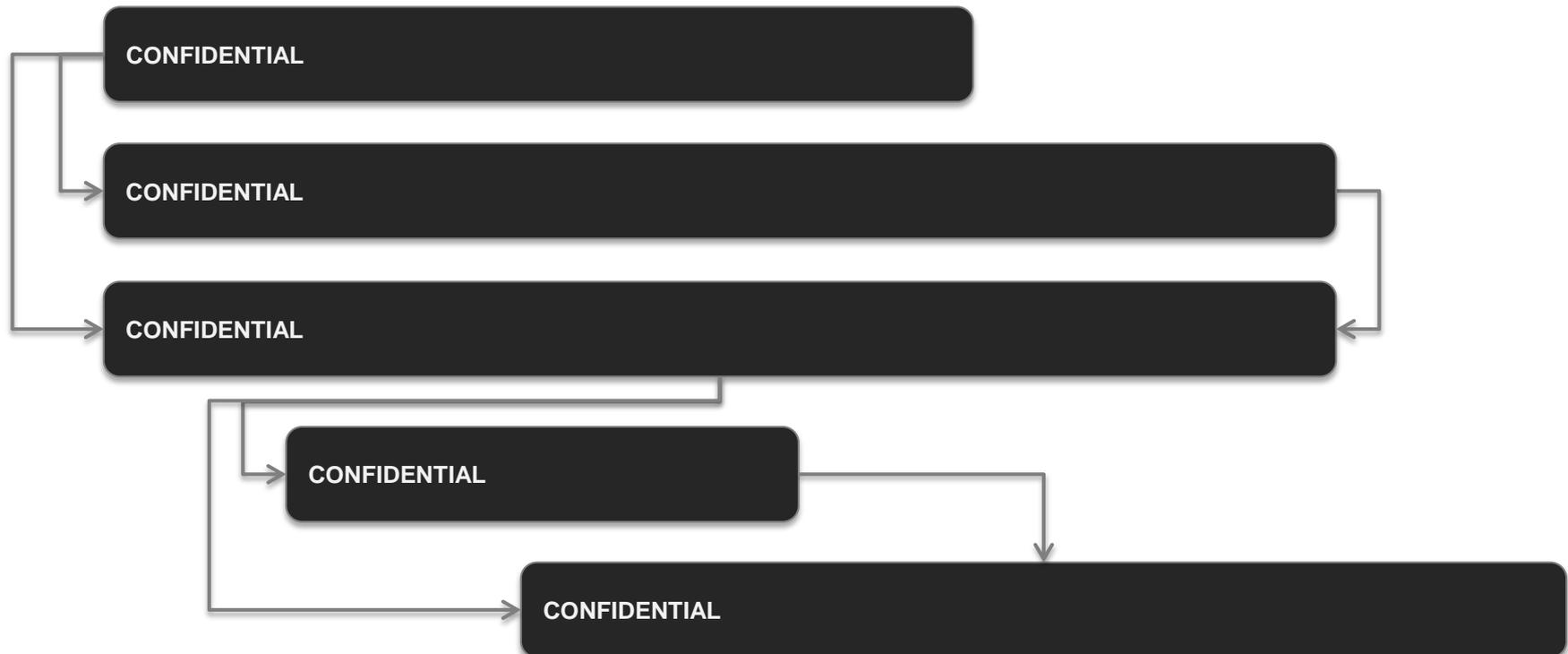Stefano Bastianello, Italian Association of Neuroradiology
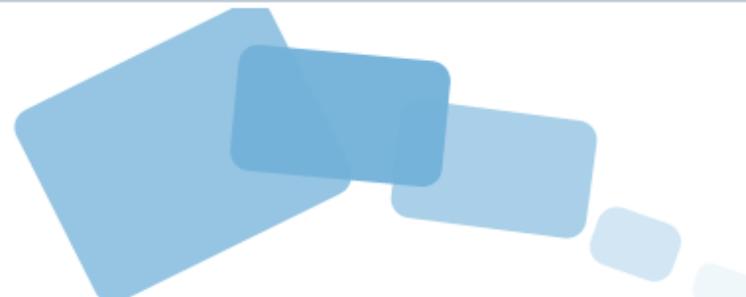Gaetano Bernardi, Italian Society of Laboratory Medicine
Daniela Perani, Italian Association of Nuclear Medicine
Corinna Porteri, Study Group of Bioethics of the Italian Neurol Society
Marco Trabucchi, Italian Psychogeriatrics Association
Alessandro Padovani, SINDEM, Italian Neurological Society

CONFIDENTIAL

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DECIDE

Diagnostic Enhancement of Confidence by an International Distributed Environment

DECIDE Science Gateway

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This Includes the possibility to access the Science Gateway from within the Social Network page.

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Welcome

Welcome to the DECIDE Science Gateway. If you do not yet have an account, find below the instructions to register and sign in.

1) Register

(If you have already registered an account on the DECIDE Science Gateway go directly to step 2)

In order to create an account on the DECIDE Science Gateway you have to click on the "Register" link which appears on the top right of this page.

Once you are in the registration page, fill the form with all the required information. If you already belong to any of the Identity Federations supported, please select it in the list which appears in the form. Otherwise, leave it blank and choose & confirm a password in the relative box; you will be enrolled in the IDPCT Identity Provider of the GrIDP Identity Federation. Please, do not forget to specify the application you would like to use and the role you would like to have. When complete, submit the web form and confirm your request of registration following the link which appears in the email that you will receive by the portal at the address you have indicated in the web form.

2) Sign In

(If you do not have yet an account on the DECIDE Science Gateway go back to step 1).

Once you receive the email informing you that your request of registration to the DECIDE Science Gateway has been accepted by the administrators of the portal, you are ready to sign in. To do so, you can either click on "Sign In", at the top right of this page, or follow this link. You will directed to the Identity Federations' discovery service. There you have to specify the Federation and the Organisation you belong to. If you did not indicate any in the registration phase, please select "GrIDP" as Federation and "Identity Provider Catania (IDPCT)" as Organisation which are our "catch-all" services. Once you are done, do not forget to Sign Out clicking on the button which will appear on the right of the top panel in the browser.

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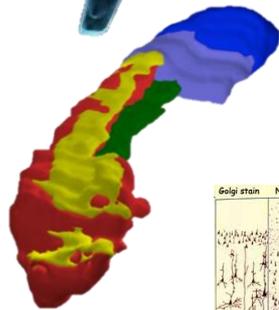**MODELLING BRAIN FUNCTION AND DYSFUNCTION**

The
Human
Brain
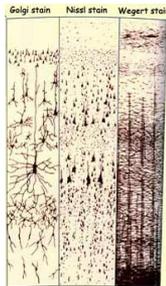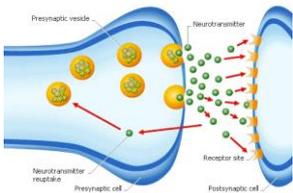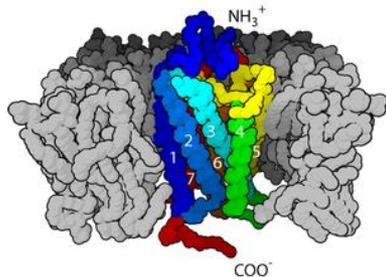**Project**

http://www.youtube.com/watch?v=jAOUrsnt8CA

ORGAN

CORTICAL AREAS &
SUBCORT STRUCTURES

NEURAL COLUMNS

SYNAPTIC FUNCTION

NEUROTRANSMITTER-
RECEPTOR

Obama Seeking to Boost Study of Human Brain

By JOHN MARKOFF

Published: February 17, 2013

The Obama administration is planning a decade-long scientific effort to examine the workings of the human brain and build a comprehensive map of its activity, seeking to do for the brain what the Human Genome Project did for genetics.

"Every dollar we invested to map the human genome returned $140 to our economy — every dollar," he said. "Today our scientists are mapping the human brain to unlock the answers to Alzheimer's. They're developing drugs to regenerate damaged organs, devising new materials to make batteries 10 times more powerful. Now is not the time to gut these job-creating investments in science and innovation."
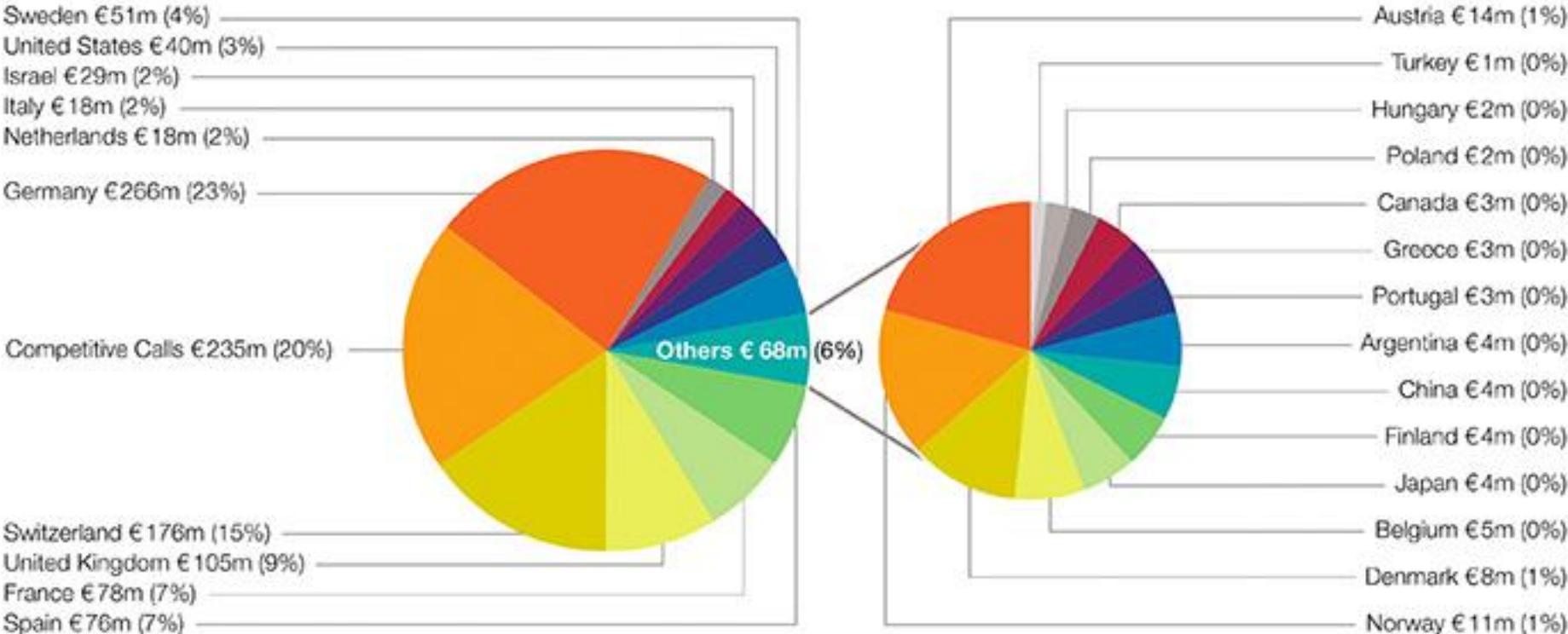
Budget by country

Sweden €51m (4%)
United States €40m (3%)
Israel €29m (2%)
Italy €18m (2%)
Netherlands €18m (2%)
Germany €266m (23%)
Competitive Calls €235m (20%)
Switzerland €176m (15%)
United Kingdom €105m (9%)
France €78m (7%)
Spain €76m (7%)
Others € 68m (6%)

Austria €14m (1%)
Turkey €1m (0%)
Hungary €2m (0%)
Poland €2m (0%)
Canada €3m (0%)
Greece €3m (0%)
Portugal €3m (0%)
Argentina €4m (0%)
China €4m (0%)
Finland €4m (0%)
Japan €4m (0%)
Belgium €5m (0%)
Denmark €8m (1%)
Norway €11m (1%)

Figure 42: Cost breakdown by country for the whole flagship

WHAT PART WILL ITALY PLAY?