EXPERT CONSULTATION ON
UNLOCKING GLOBAL COLLABORATION TO ACCELERATE INNOVATION FOR ALZHEIMER’S DISEASE AND DEMENTIA
20-21 June, 2013 - The Harris Manchester College, Oxford, United Kingdom

Fostering Open Access for Alzheimer’s and dementia research

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Neurologist and Deputy Scientific Director, IRCCS Fatebenefratelli,
The National Centre for Alzheimer’s Disease, Brescia, Italy
Summary

Collecting harmonized research data and making them public (ADNIs)

Developing facilities to promote scientific exploitation of data (neuGRID, GAAIN)
Imaging studies in Alzheimer’s disease: Impact on understanding the molecular causes

Brain amyloidosis

Neurodegeneration
Imaging studies in Alzheimer’s disease: What next?

Modelling amyloidosis

Modelling neurodegeneration
Imaging studies in Alzheimer’s disease: Foreseeable impact

Improving diagnosis:
Early diagnosis based on imaging markers

Fostering drug development:
Clinical trials with imaging outcomes
“Data sharing has been **successfully implemented** in initiatives in the biomedical field, such as the **Alzheimer’s Disease Neuroimaging Initiative**”

**EDITORIAL**

The scientific social network

A joint statement from 17 funding agencies urges biomedical researchers to openly share data obtained from population-based studies. Although this will foster more collaboration, new web technologies need to be harnessed, and the attribution of credit must change to facilitate this transition.
What is ADNI:
The Alzheimer’s Disease Neuroimaging Initiative

Genetics – Structural, Diffusion, Rest fMRI – FDG PET – Amyloid PET – CSF & peripheral biomarkers

T0  T6  T12  Tx

NIA Companies (pharma, non pharma)

120M US$
ADNI facts and figures:
The philosophy

Raw and processed data are published on the internet with no embargo
ADNI facts and figures:
The LONI public website

Sharing Alzheimer's Research Data with the World

The Alzheimer's Disease Neuroimaging Initiative (ADNI) unites researchers with study data as they work to define the progression of Alzheimer's disease. ADNI researchers collect, validate and utilize data such as MRI and PET images, genetics, cognitive tests, CSF and blood biomarkers as predictors for the disease. Data from the North American ADNI’s study participants, including Alzheimer’s disease patients, mild cognitive impairment subjects and elderly controls, are available from this site.

Welcome

Returning Users

News
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Total Investigators</td>
<td>3983</td>
</tr>
<tr>
<td>Approved Investigators</td>
<td>3712</td>
</tr>
<tr>
<td>Disapproved Investigators</td>
<td>271</td>
</tr>
</tbody>
</table>

Courtesy of Robert Green
ADNI facts and figures:
Applications by sector

Courtesy of Robert Green
ADNI facts and figures:
Image downloads by year

Courtesy of Robert Green
ADNI facts and figures:
Manuscript submission procedure

- Manuscript submitted to DPC
- Administrative review conducted
- Revised paper re-submitted to DPC
  - Non-Compliant returned to author for revisions
  - Compliant papers sent to individual DPC members for quality review
  - DPC emails author with review results

Courtesy of Robert Green
ADNI facts and figures:
Acknowledgement policy

The ADNI Publication Policy: Commensurate recognition of critical contributors who are not authors

Orest Hurko\textsuperscript{a,*}, Sandra E. Black\textsuperscript{b,1}, Rachelle Doody\textsuperscript{c,2}, P. Murali Doraiswamy\textsuperscript{d}, Anthony Gamst\textsuperscript{e}, Jeffrey Kaye\textsuperscript{f,3}, Thomas O. Obisesan\textsuperscript{f,g,4}, Henry Rusinek\textsuperscript{h}, Doug Scharre\textsuperscript{i,5}, Reisa Sperling\textsuperscript{i,6}, Michael W. Weiner\textsuperscript{k}, Robert C. Green\textsuperscript{l} for the ADNI Data and Publication Committee
Enrichment through biomarkers in clinical trials of Alzheimer’s drugs in patients with mild cognitive impairment


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Translational Medicine, Neuroscience, F. Hoffmann-La Roche Ltd, Basel, Switzerland
Clinical Investigation Centre (CIC-UPCET) and Department of Clinical Pharmacology, UMR-CNRS, 6193 Institute of Cognitive Neurosciences, CHU, Timone, Marseille, France
Neurosciences CEDD, GlaxoSmithKline, Harlow, Essex, UK
AFar Associazione Fatebenefratelli per la Ricerca, Rome, Italy

Received 15 February, 2010; received in revised form 29 April 2010; accepted 29 April 2010
ADNI facts and figures:
Manuscript submission outcome

- 284 manuscripts met acknowledgment criteria
- 322 manuscripts required revision of acknowledgment criteria
- 11 manuscripts were labeled as "Egregiously bad science"

Courtesy of Robert Green
World-wide ADNI initiatives

Worldwide Alzheimer’s Disease Neuroimaging Initiative

Maria C. Carrillo\textsuperscript{a,*}, Lisa J. Bain\textsuperscript{b}, Giovanni B. Frisoni\textsuperscript{c}, Michael W. Weiner\textsuperscript{d,e}

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\textsuperscript{e}Department of Radiology, University of California, San Francisco, CA, USA
World-wide ADNI initiatives
# ADNI-related initiatives in Europe

**Table 1**

<table>
<thead>
<tr>
<th>ADNI-related initiatives in Europe or led by EU scientists</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Funding agency</strong></td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Data collection</td>
</tr>
<tr>
<td>AddNeuroMed</td>
</tr>
<tr>
<td>Pharma-Cog Workpackage 5 (E-ADNI)</td>
</tr>
<tr>
<td>Swedish ADNI</td>
</tr>
<tr>
<td>Italian ADNI</td>
</tr>
</tbody>
</table>

**Development of standard operational procedures**

<table>
<thead>
<tr>
<th><strong>Funding agency</strong></th>
<th><strong>Budget</strong></th>
<th><strong>Duration</strong></th>
<th><strong>Timelines</strong></th>
<th><strong>Principal investigators</strong></th>
<th><strong>Countries</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer Association</td>
<td>$800k</td>
<td>4 yr</td>
<td>Started 2009, ongoing</td>
<td>Blennow</td>
<td>40 Labs (EU, US, Japan, Australia, Brazil)</td>
</tr>
<tr>
<td>Lilly—Wyeth</td>
<td>€70k</td>
<td>2 yr</td>
<td>Closing 2012</td>
<td>Frisoni-Jack</td>
<td>24 centres in EU, US, Canada, and Australia</td>
</tr>
</tbody>
</table>

**Infrastructure development**

<table>
<thead>
<tr>
<th><strong>Funding agency</strong></th>
<th><strong>Budget</strong></th>
<th><strong>Duration</strong></th>
<th><strong>Timelines</strong></th>
<th><strong>Principal investigators</strong></th>
<th><strong>Countries</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>FP7</td>
<td>€2.7 M</td>
<td>3 yr</td>
<td>Closing Jan 2011</td>
<td>Frisoni</td>
<td>IT, FR, SP, CH, UK, SW</td>
</tr>
<tr>
<td>FP7</td>
<td>€440 K</td>
<td>2 yr</td>
<td>Closing Dec 2011</td>
<td>Frisoni-Toga-Evans</td>
<td>IT, FR, UK, US, CD</td>
</tr>
<tr>
<td>French National Foundation on AD and RD</td>
<td>€3 M+</td>
<td>3 yr</td>
<td>Starting 2010</td>
<td>Mangin-Lehericy</td>
<td>FR</td>
</tr>
</tbody>
</table>

Abbreviations: ADNI, Alzheimer’s Disease Neuroimaging Initiative; EC, European Commission; IMI, Innovative Medicines Initiatives; NHS, National Health System; EADC, European Alzheimer’s Disease Consortium; FP7, 7th Framework Programme; AD and RD, Alzheimer’s disease and related diseases.

Frisoni GB, Alzheimers Dement 2010
Imaging markers of neurodegeneration

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

**MICROSTRUCTURAL (WM damage)**
- MR Tensor-based morphometry
- MR Tract-based spatial statistics

**FUNCTIONAL (network damage)**
- MR Activation fMRI (with task)
- MR Rest fMRI network extraction

neuGRID: a grid-based image analysis environment

Algorithm pipelines for marker extraction

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

Vast computational resources

<table>
<thead>
<tr>
<th>Node</th>
<th>Storage (MB)</th>
<th>CPUs (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>3,557</td>
<td>40</td>
</tr>
<tr>
<td>Italy</td>
<td>3,170</td>
<td>40</td>
</tr>
<tr>
<td>France</td>
<td>4,095</td>
<td>2,600</td>
</tr>
<tr>
<td>Maat</td>
<td>1,268</td>
<td>8</td>
</tr>
<tr>
<td>Brazil</td>
<td>0</td>
<td>128</td>
</tr>
<tr>
<td>EGI</td>
<td>71,793</td>
<td>1,912</td>
</tr>
<tr>
<td>TOTAL</td>
<td>83,883</td>
<td>4,728</td>
</tr>
</tbody>
</table>
**Proof-of-concept of neuGRID:**
Tracking Alzheimer’s disease progression on 3500 MR scans

| Analyzed data                  | MR Scans          | 6,500 ADNI       |
|                               | Images            | ~1,300,000       |
|                               | Voxels            | ~9,352,500,000   |
| Algorithm                     |                   | MNI’s CIVET      |
| Experiment duration on the Grid |                   | < 2 Weeks        |
| Experiment duration on single computer |             | > 5 Years        |
| Total mining operations       |                   | 286,810          |
| Max # of processing cores in parallel |             | 184              |
| Number of countries involved  |                   | 4                |
| Volume of output data produced |                   | 1 TB             |
| Success rate                  |                   | 93%              |
Proof-of-concept of neuGRID: Tracking Alzheimer’s disease progression on 3500 MR scans
GAAIN
Global Alzheimer’s Association Interactive Network
GAAIN:
What is that?

- Global network of committed investigators
- Vast network of data and computational resources
- Ontologies and metadata standards provide semantic framework
- Analytic tools for comparison of data across studies
GAAIN data federation:
Leave data with the scientist, move around metadata

Courtesy of Arthur Toga and Maria Carrillo
Challenges to opportunities of open data sharing in the life sciences

- Technical issues, e.g. grid certificates for grid computing
- Incompletely established standards for biomedical data
- Uncertain business model
- Discontinuous commitment of funding agencies
Opportunities

- Foster drug development for socially impactful diseases
- Harnessing the power of the Cloud to share data and applications
- Expansion of the base of scientists with access to sophisticated scientific facilities
- Extension of top class science to disadvantaged and underdeveloped world regions