AddNeuroMed Imaging Update
WW-ADNI : July 2013

Andy Simmons, Simon Lovestone
for the AddNeuroMed Group

European Federation of Pharmaceutical Industries and Associations, Pharmidex Pharmaceutical Services, Capsant Neurotechnologies LTD, Università degli Studi di Perugia, Aristotle University of Thessaloniki, Roskilde University, AstraZeneca, Kungl Tekniska Högskolan, Karolinska Institutet, King's College, London, Centre Hospitalier Universitaire de Toulouse, GlaxoSmithKline Research & Development Ltd, Proteome Sciences PLC, University College London, University of Southampton, Hunter Fleming Limited, BioWisdom, Cerebricon Ltd.
AddNeuroMed Study

- Six European sites
- 385 subjects with MRI (of total > 700 subjects)
  - 133 AD, 134 MCI, 118 Controls
- All subjects
  - Clinical / cognitive assessments
  - Blood / plasma / RNA
  - 1.5 T structural MRI
- Imaging time points
  - Baseline, 3 months, 1 year
- Approximately 40 papers to date
AddNeuroMed Study

- Diagnostic markers
- Progression markers
- Surrogate markers for use in trials
- Proteomics
- Lipidomics
- Genomics
- Metabonomics
- Intelligence networks
- Bioinformatics

Case control sample
Long term follow-on sample
Short term follow-on sample
Imaging database

385 AddNeuroMed
- 0, 3, 12m

821 ADNI 1
- 0, 6, 12, 18, 24, 36, 48m
ADNI-2/GO
- Currently uploading

288 AIBL
- 0, 18,
250 London cohort
- 0, 12, 24, 36m

750 London memory clinic
- 0m

2000 Young controls
- 0m
Imaging Database

- New database design in progress
- Scalable to tens of thousands of subjects
- Flexible integration with imaging pipelines
- Automated data upload
- Upload from multiple centres
1150 subjects in total

- Freesurfer regional volumes/cortical thickness
- MNI Civet regional volumes/cortical thickness
- Scheltens MTL atrophy
- Manual hippocampal measures
- Range of automated hippocampal measures
- Automated WMH measures – in progress
- Fazekas scale – in progress
A critical issue for visual MTA assessment is the cut-off score that determines deviance from normality.

**Age-dependent MTA cutoff**: 
- < 75 years, a MTA score of ≥ 2 is considered abnormal; 
- > 75 years, a MTA score of ≥ 3 is considered abnormal.

**MTA ≥ 1.5 cutoff**: 
- based on average of MTA ratings of both hemispheres, ≥ 1.5 is considered abnormal.
Influence of Age, Disease Onset and ApoE4 on Visual Medial Temporal Atrophy cut-offs in 1150 subjects

- Significant MTA differences between ApoE4 and non-ApoE4 using both ≥ 1.5 and age-dependent cut-offs in younger AD patients.
- Both cut-offs influenced by increasing age

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>≥ 1.5 cut-off</th>
<th>Age cut-off</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AD-like</td>
<td>CTR-like</td>
</tr>
<tr>
<td>Age range 50 - 69</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>AD patients</td>
<td>63</td>
<td>42 (66.7%)</td>
<td>21 (33.3%)</td>
</tr>
<tr>
<td>CTR</td>
<td>45</td>
<td>7 (15.6%)</td>
<td>38 (84.4%)</td>
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<tr>
<td>Age range 70 - 79</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>AD patients</td>
<td>165</td>
<td>146 (88.5%)</td>
<td>19 (11.5%)</td>
</tr>
<tr>
<td>CTR</td>
<td>241</td>
<td>67 (27.8%)</td>
<td>174 (72.2%)</td>
</tr>
<tr>
<td>Age range 80 - 90</td>
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<td></td>
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<tr>
<td>AD patients</td>
<td>94</td>
<td>84 (88.4%)</td>
<td>10 (10.6%)</td>
</tr>
<tr>
<td>CTR</td>
<td>59</td>
<td>36 (61.0%)</td>
<td>23 (39%)</td>
</tr>
</tbody>
</table>
Impact of ApoE4 and ApoE2 on Hippocampal Volume in > 1400 European 14 year olds

- European IMAGEN study carried out at 11 European sites
- 3T ADNI-1 MPRAGE
- GWAS available
- Imaging at baseline (complete) and 4 year follow up (in progress)
Impact of ApoE4 and ApoE2 on Hippocampal Volume in > 1400 European 14 year olds

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<table>
<thead>
<tr>
<th></th>
<th>ApoE E4 carriers (n= 343)</th>
<th>ApoE E4 non-carriers (n=1069)</th>
<th>t-value</th>
<th>p</th>
<th>ApoE E2 carriers (n= 212)</th>
<th>ApoE E2 non-carriers (n=1200)</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>14.44 ± 0.40</td>
<td>14.45 ± 0.41</td>
<td>-0.104</td>
<td>0.917</td>
<td>14.41 ± 0.39</td>
<td>14.45 ± 0.41</td>
<td>-1.248</td>
<td>0.212</td>
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<tr>
<td>Gender (Male/Female)</td>
<td>165/174</td>
<td>534/535</td>
<td>--</td>
<td>0.852</td>
<td>114/98</td>
<td>589/611</td>
<td>--</td>
<td>0.233</td>
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<tr>
<td>BMI</td>
<td>20.86 ± 3.27</td>
<td>20.71 ± 3.56</td>
<td>0.673</td>
<td>0.501</td>
<td>20.72 ± 3.26</td>
<td>20.75 ± 3.53</td>
<td>-0.126</td>
<td>0.906</td>
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<tr>
<td>Verbal IQ</td>
<td>111.29 ± 14.84</td>
<td>111.29 ± 15.51</td>
<td>-0.003</td>
<td>0.997</td>
<td>110.26 ± 15.56</td>
<td>111.48 ± 15.31</td>
<td>-1.06</td>
<td>0.289</td>
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<td>Performance IQ</td>
<td>107.84 ± 13.93</td>
<td>107.54 ± 14.47</td>
<td>0.336</td>
<td>0.737</td>
<td>106.89 ± 14.58</td>
<td>107.74 ± 14.30</td>
<td>-0.80</td>
<td>0.424</td>
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<tr>
<td>CANTAB SWM strategy</td>
<td>31.10 ± 5.41</td>
<td>31.22 ± 5.42</td>
<td>-0.336</td>
<td>0.737</td>
<td>31.36 ± 5.20</td>
<td>31.16 ± 5.46</td>
<td>0.490</td>
<td>0.367</td>
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<tr>
<td>Normalised R Hippocampus*</td>
<td>4351.8 ± 436.9</td>
<td>4305.1 ± 474.4</td>
<td>--</td>
<td>0.289</td>
<td>4332.4 ± 504.9</td>
<td>4313.6 ± 458.8</td>
<td>--</td>
<td>0.103</td>
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<tr>
<td>Normalised L Hippocampus*</td>
<td>4226.0 ± 504.1</td>
<td>4224.2 ± 475.3</td>
<td>--</td>
<td>0.406</td>
<td>4232.4 ± 518.2</td>
<td>4234.7 ± 476.3</td>
<td>--</td>
<td>0.357</td>
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</tbody>
</table>
Sharing AddNeuroMed data

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