



Innovative Medicines Initiative

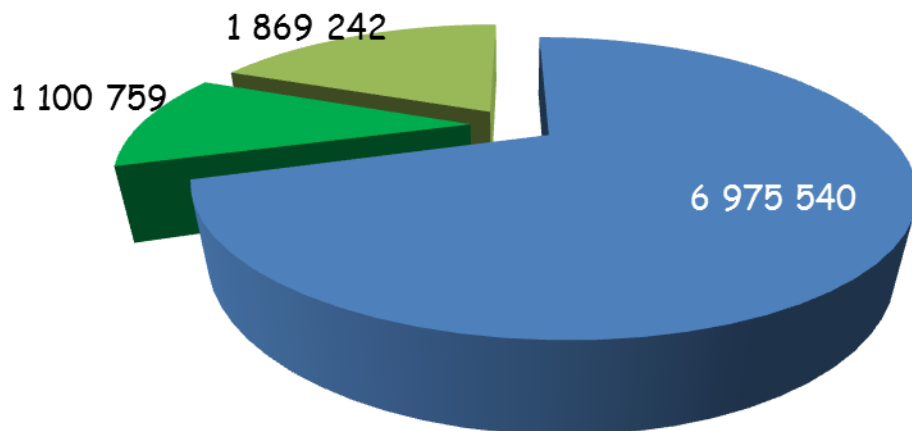
PharmaCog – Alzheimer's Disease

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The issue



People with dementia



■ Western Europe ■ Central Europe
■ Eastern Europe

Total costs	Billions US\$
Western Europe	210.12
Central Europe	14.19
Eastern Europe	14.33

Wimo et al. 2013

- 70% of global societal costs of dementia: USA and Western Europe
- 46% of people with dementia live in high income countries

Current lifetime risk of AD dementia in a 65-year old: 10.5% (*Sperling et al., 2011*)



The issue – 2



- Cognitive impairment
- Disability
- Behavioral & physiological symptoms
- Depression
- Presence of pain
- Physical illness

Early therapeutic intervention can improve:
Cognitive function
Depression, etc. ...
... and delay institutionalization

Acetylcholinesterase inhibitors (AChE-I)

Donepezil (Aricept®)
Galantamine (Reminyl®)
Rivastigmine (Exelon®)

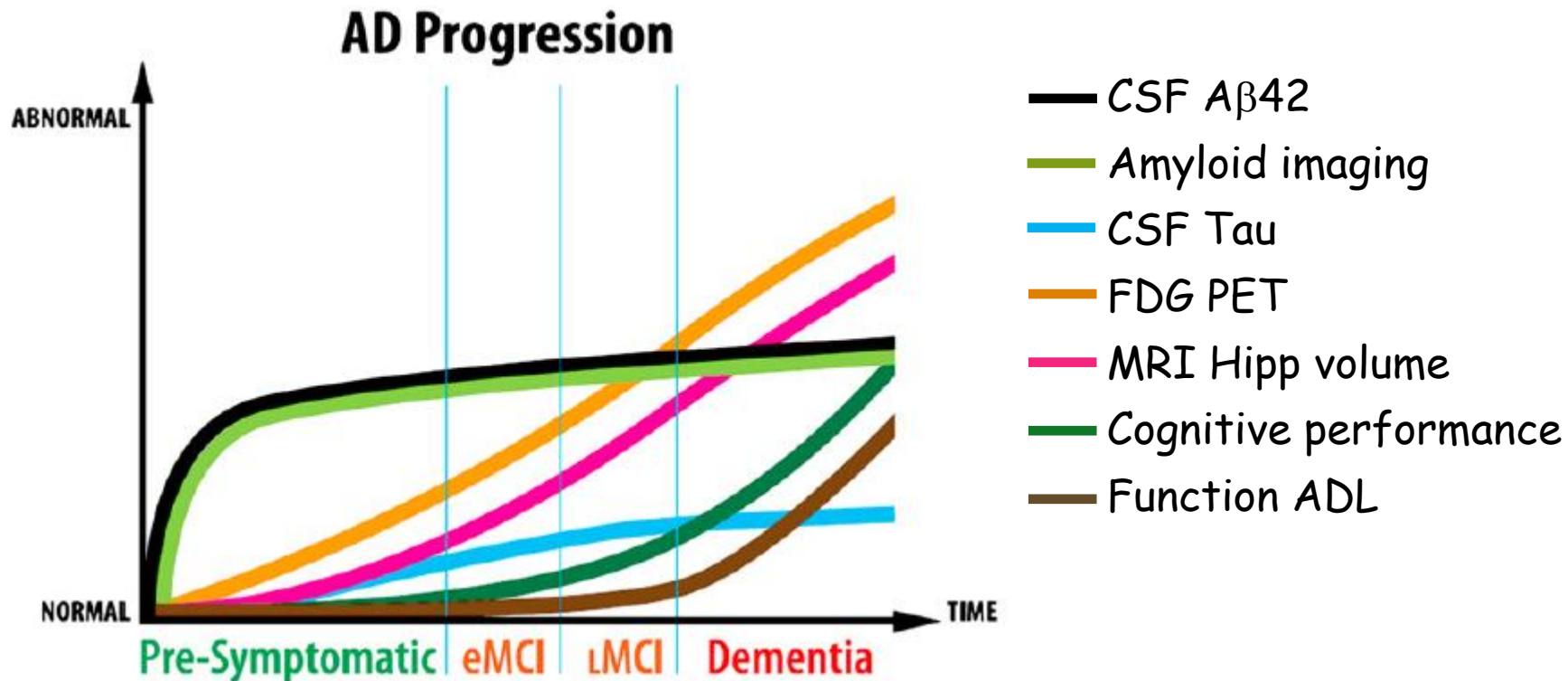
NMDA receptor antagonist
Memantine (Ebixa®)



Key research challenges



Diagnosis



Aisen et al., 2010



The need for a PPP



- Building an AD network between EFPIA, academia and biotech to foster future collaboration, access technological expertise and to establish 'harmonised' clinical centres for drug studies
- Enabling early interactions with regulators (FDA/EMA) on AD biomarkers
- Raising issues in AD translational research to budget holders, e.g. EU Parliament
- Delivery of a unique database on the effect of AD drugs on a matrix of biomarker



Headline achievements



Novel Disease Markers in Development by SMEs

AlzProtect Platelets: APP metabolites namely 55 kD and 25 kD fragments determined by Western blots

Exonhit (now Diaxonhit)

Lymphocytes: about 150 RNA transcripts including transcripts related to Abeta pathway, to inflammatory pathway and to immune mechanism determined by microarray

Innovative Health Diagnostics (IHD)

Red blood cells: binding of Abeta1-42 on cellular membrane and change in PKC conformation in red blood cells, determined by specific fluorescent probes

Innovative Concept in Drug Development (ICDD)

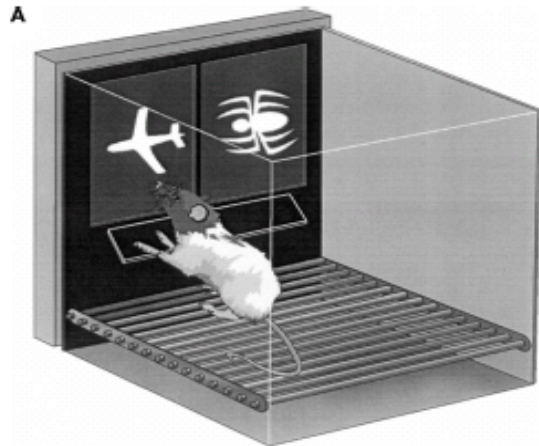
Red blood cells: panel of inflammatory markers



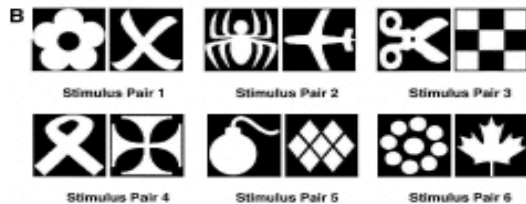
Headline achievements



- ❖ **Touchscreen technology in mice:** cross-validation study to assess reliability of the touchscreens - visual discrimination task
- ❖ **Validation for testing pharmacological agents:** in transgenic mice



- 1) Visual discrimination & cognitive flexibility
- 2) Visuo-spatial associative learning
- 3) Sustained attention



CANTAB battery - humans

Non-verbal tests sensitive to pharmacological agents



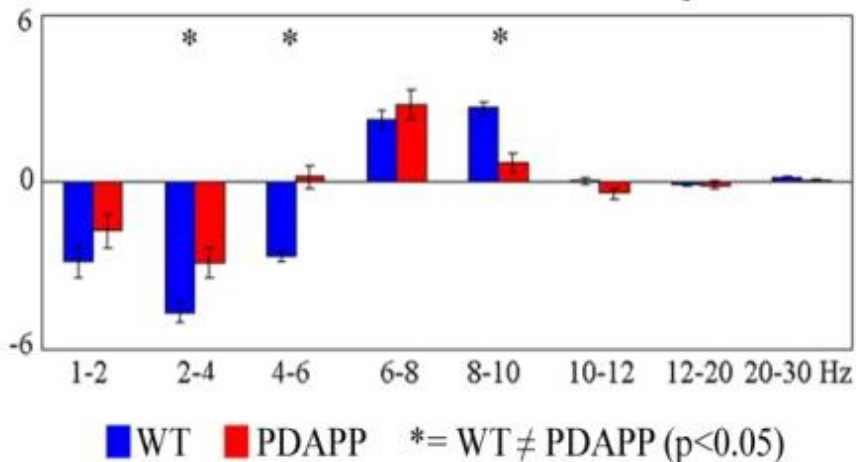
Headline achievements



Pathological cortical neural synchronization in PDAPP and TASTPM mice

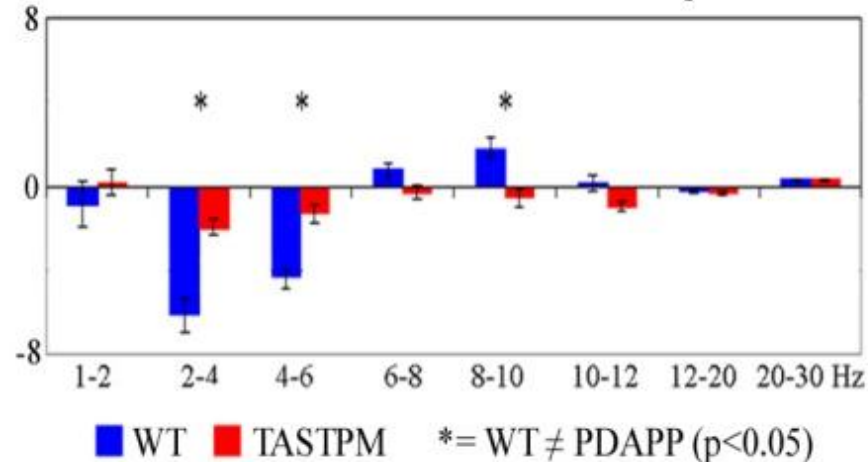
WT vs. PDAPP mice

Statistical ANOVA interaction between Group and Band



WT vs. TASTPM mice

Statistical ANOVA interaction between Group and Band



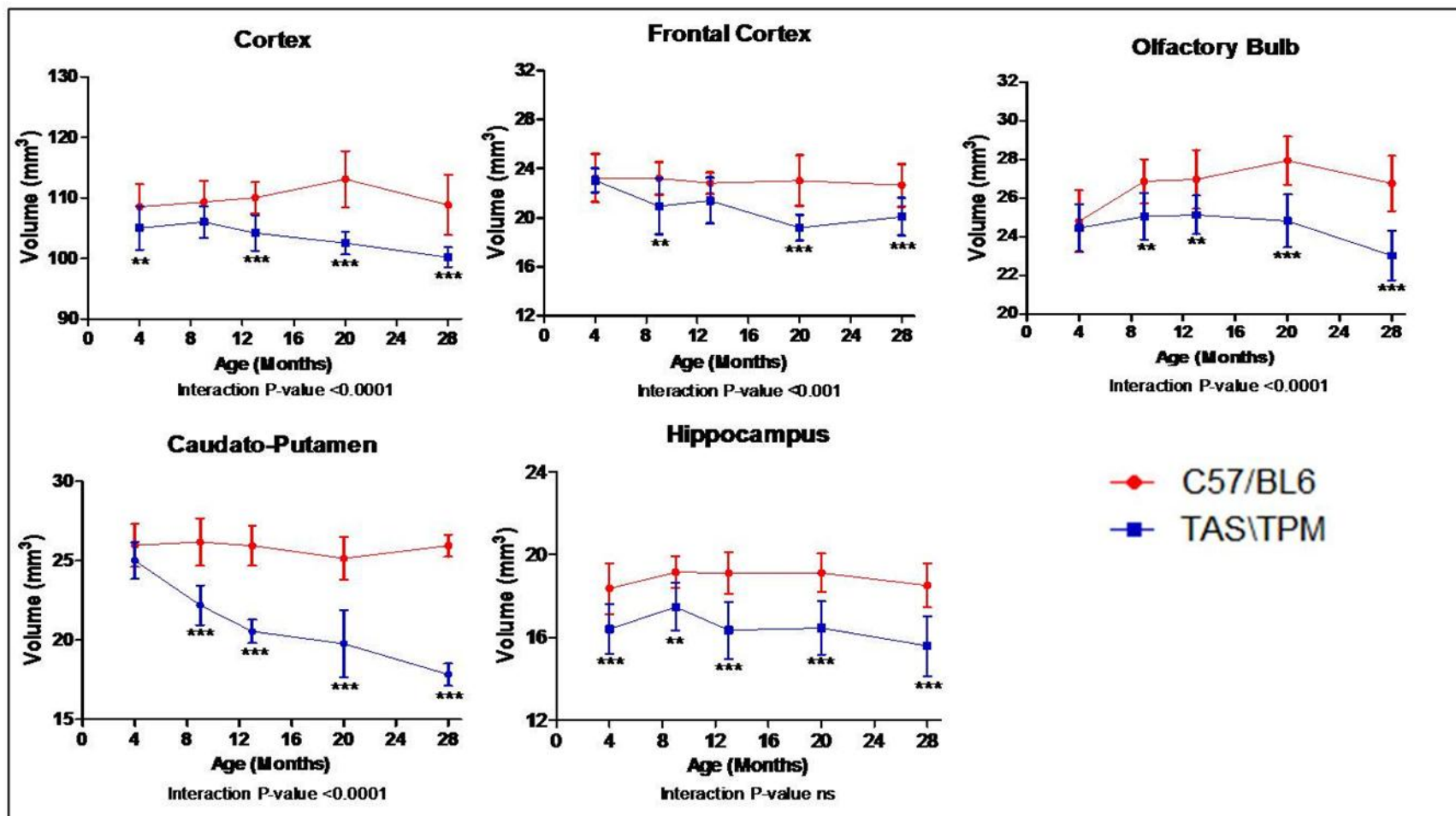
Normalized EEG power density - wake active minus passive behavioral state
The grand average of the EEG power density for all frequency bands of interest is reported for WT vs. PDAPP mice and WT vs. TASTPM mice



Headline achievements



Structural MRI in 3 transgenic mouse strains, e.g. TASTPM (APP/PS1)



What next?



- Longitudinal studies in transgenic mice using novel disease modifiers
- Testing the biomarker battery with novel symptomatic treatments
- Backtranslate from clinical ongoing studies
- Modelisation of efficacious dose using PK/PD analyses in rodents and humans



Remaining challenges



Treatment, symptomatic & disease modifying

Better, earlier diagnosis

Better understanding of the disease



Thank you



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- **Yves Lamberty**, UCB
- **Jill Richardson**, GlaxoSmithKline R&D Ltd
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- **Marina Bentivoglio**, University of Verona
- **Philippe Verwaerde**, Alzprotect
- **Lee Dawson**, Eisai





www.alzheimer-europe.org

