



# Functional reorganisation of the language system in probable Alzheimer's disease, primary progressive aphasia and cognitive aging

Rik Vandenberghe

# Time course of Alzheimer's disease

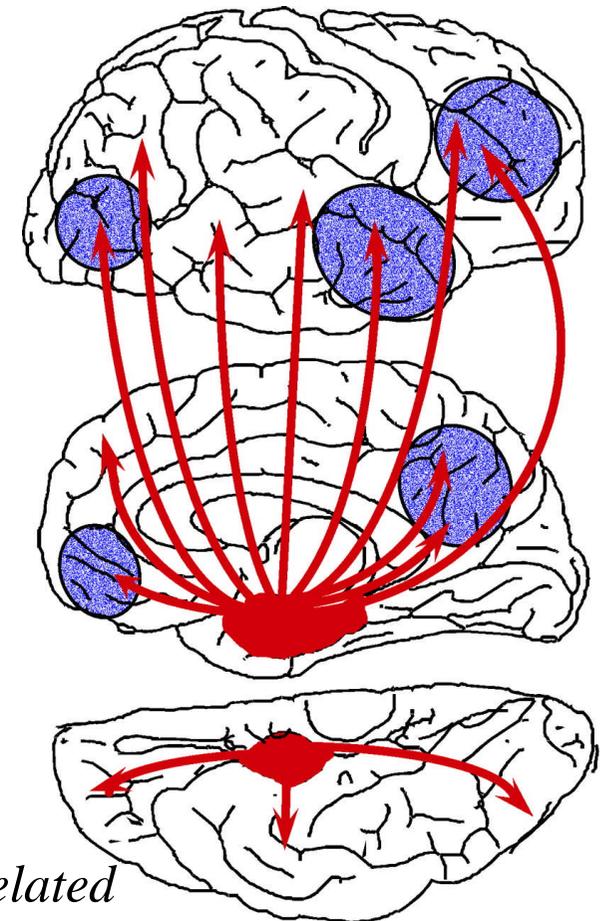
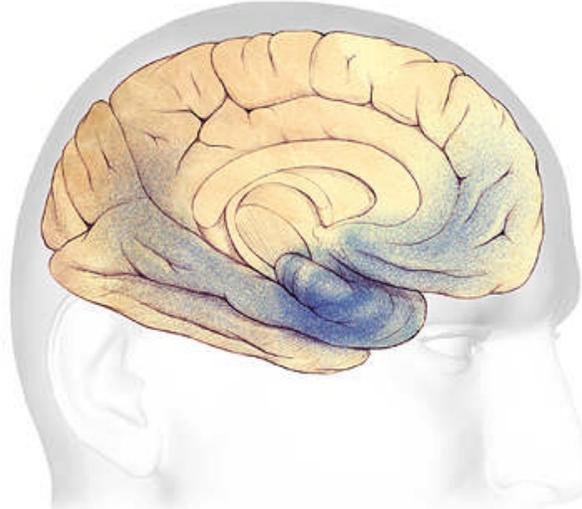
Stage I & II  
Transentorhinal stage



Stage III & IV  
Limbic stage



Stage V & VI  
Isocortical stage



*Braak and Braak, Neuropathological stagein of Alzheimer-related Changes. Acta Neuropathologica, 82, 239-259, 1991*

Pre-clinical

Clinical

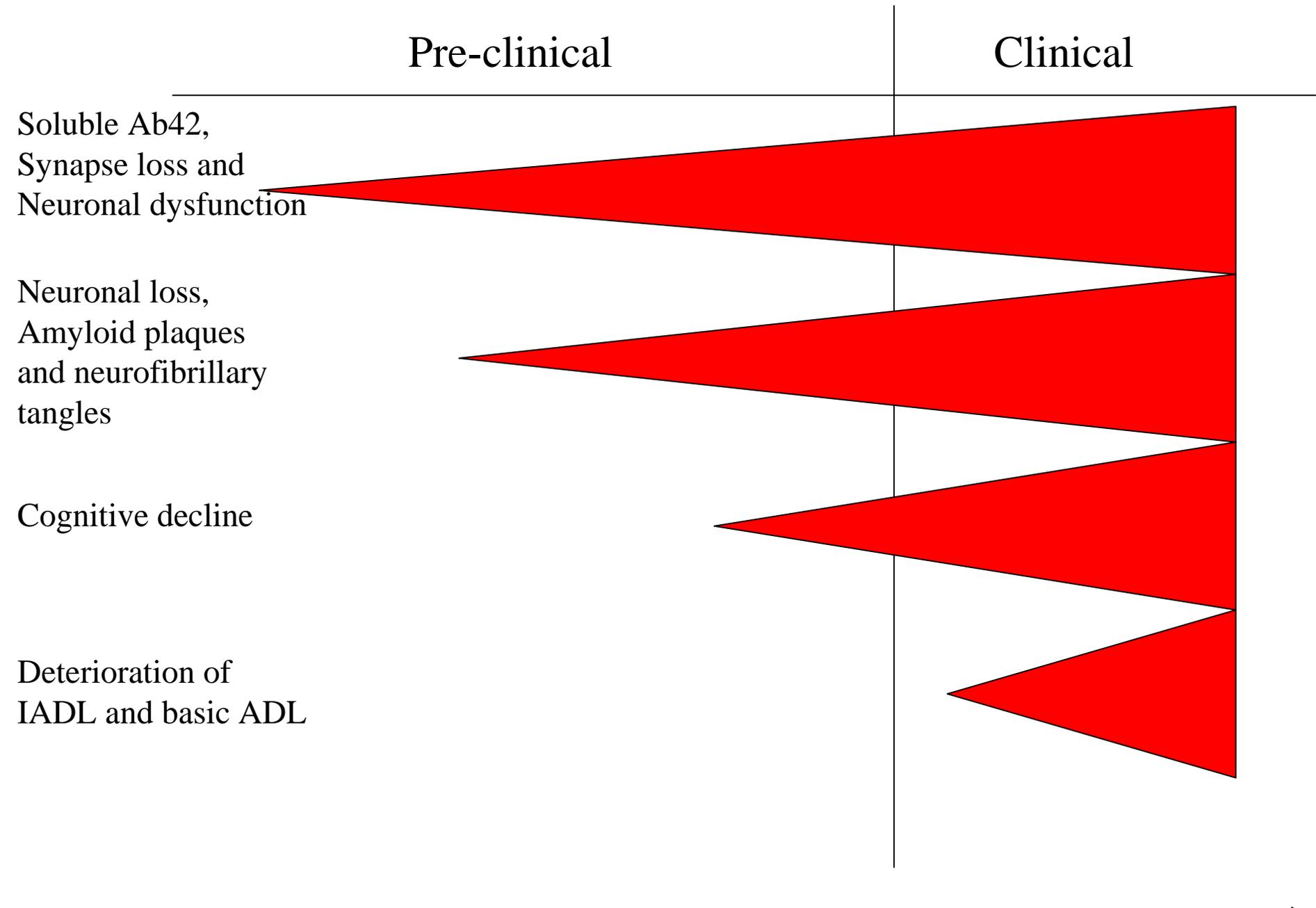
Soluble Ab42,  
Synapse loss and  
Neuronal dysfunction

Neuronal loss,  
Amyloid plaques  
and neurofibrillary  
tangles

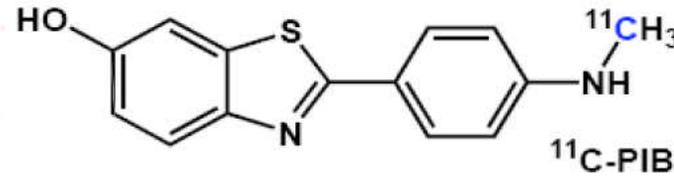
Cognitive decline

Deterioration of  
IADL and basic ADL

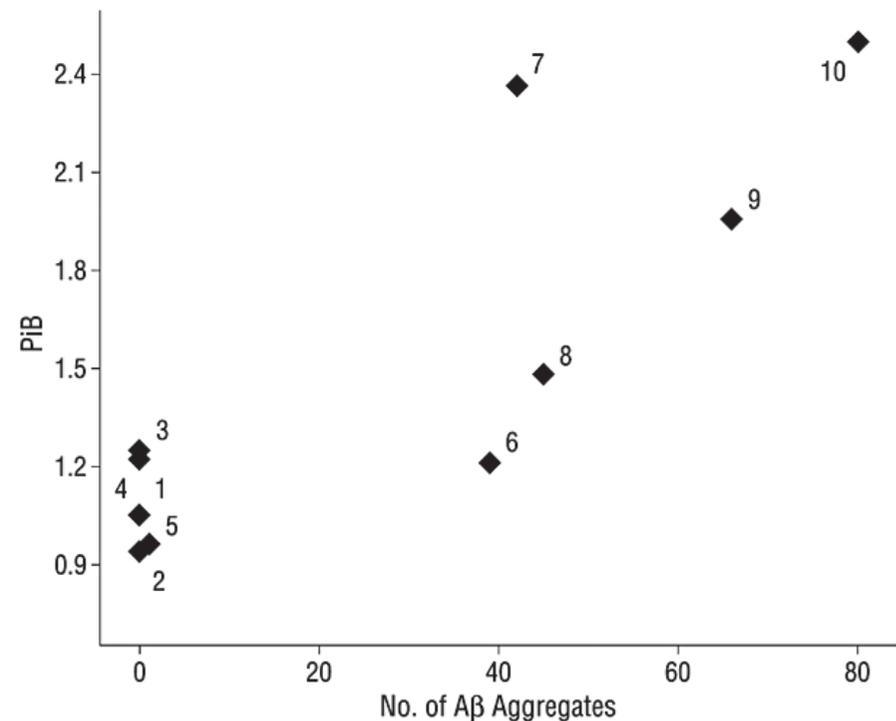
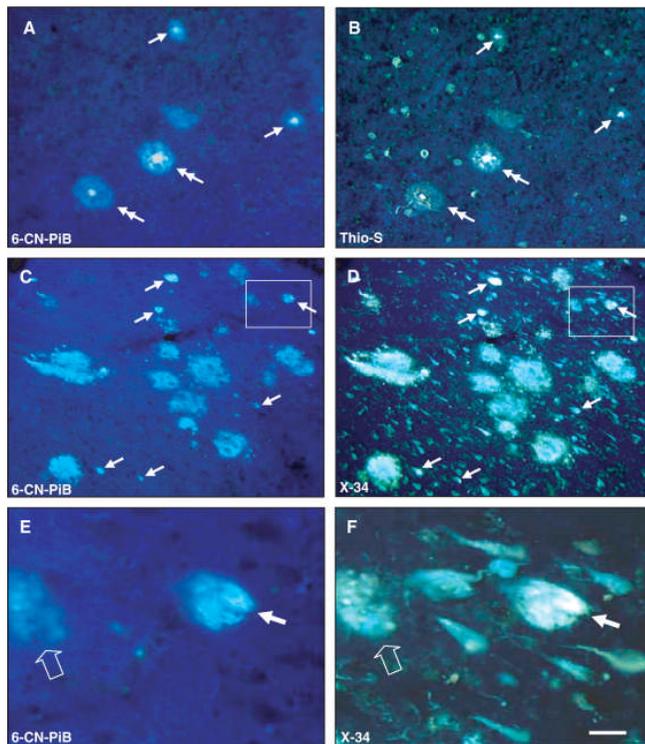
Time (in years)



# In vivo imaging of A $\beta$ amyloid in the human brain



Correlation between neuropathological A $\beta$  aggregates and in vivo  $^{11}\text{C-PIB}$  uptake

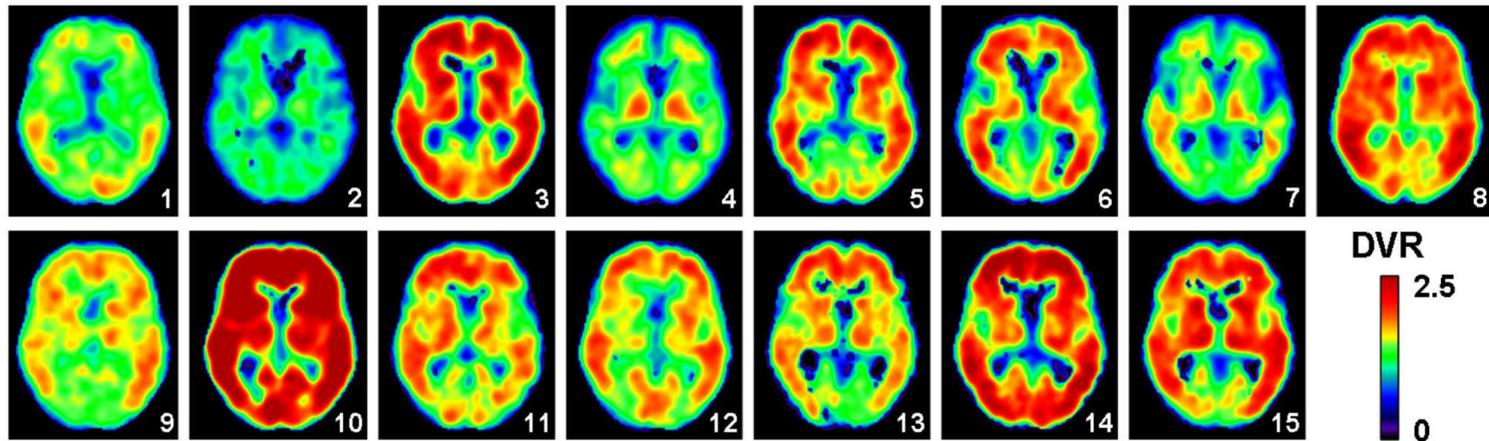


Ikonomovic et al., Brain, 131, 1630-1645, 2008

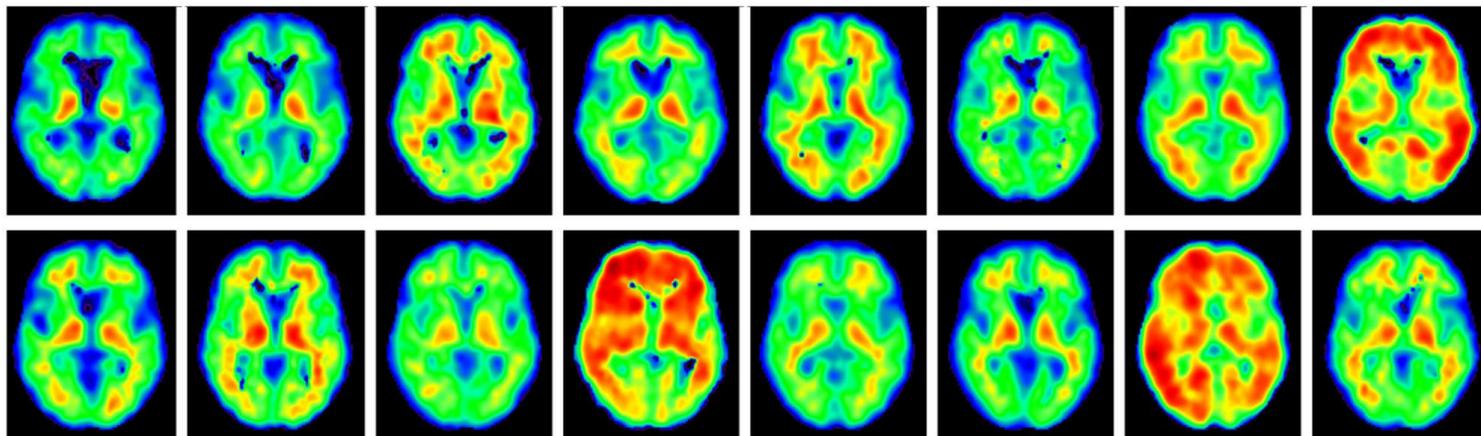
Leinonen et al., Arch Neurol 65, 1304-1309, 2008

# $^{11}\text{C}$ -PIB in AD and healthy controls

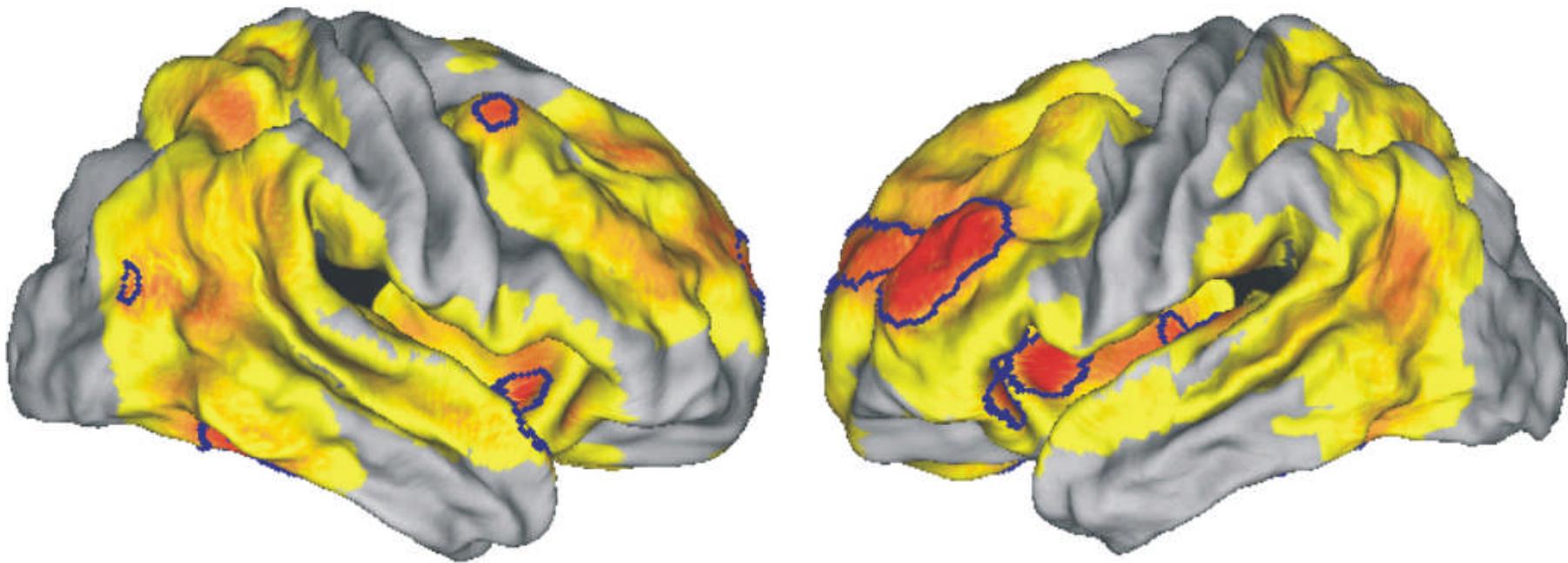
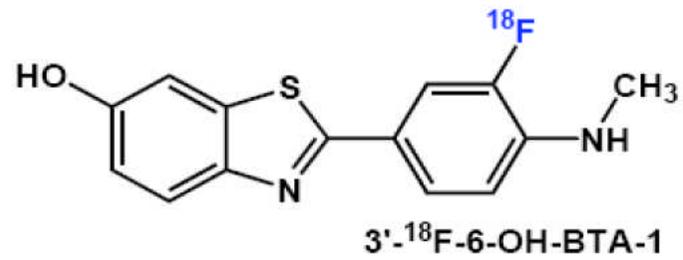
*15 early stage clinically probable AD patients*



*16 cognitively intact healthy controls*



*Nelissen N, et al., A $\beta$  amyloid deposition in the language system and how the brain responds, Brain, 130, 2055-2069, 2007*

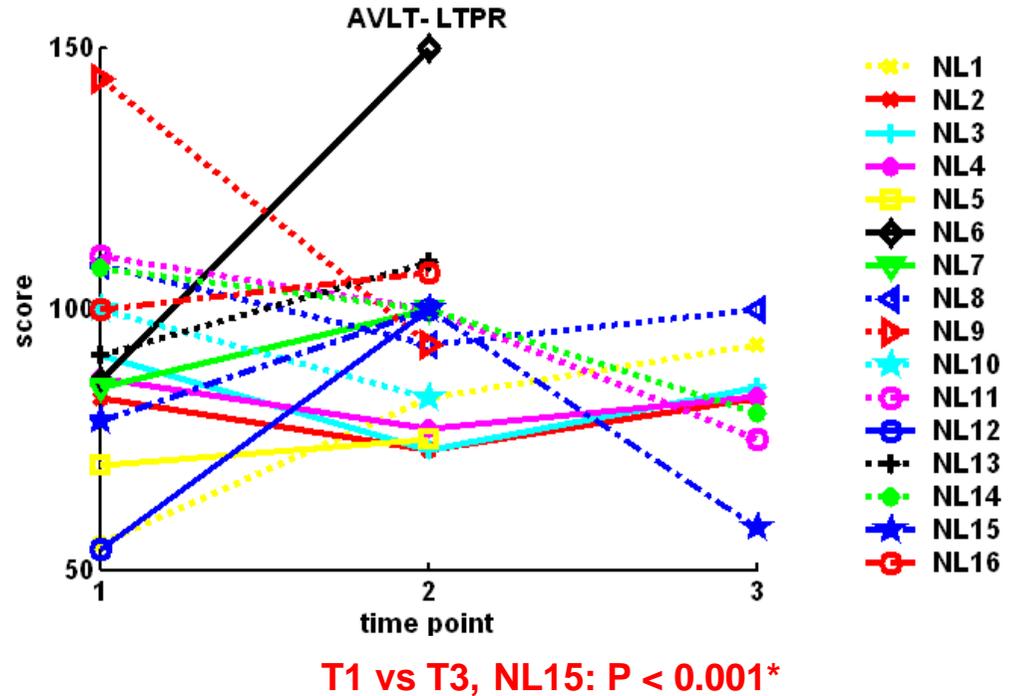
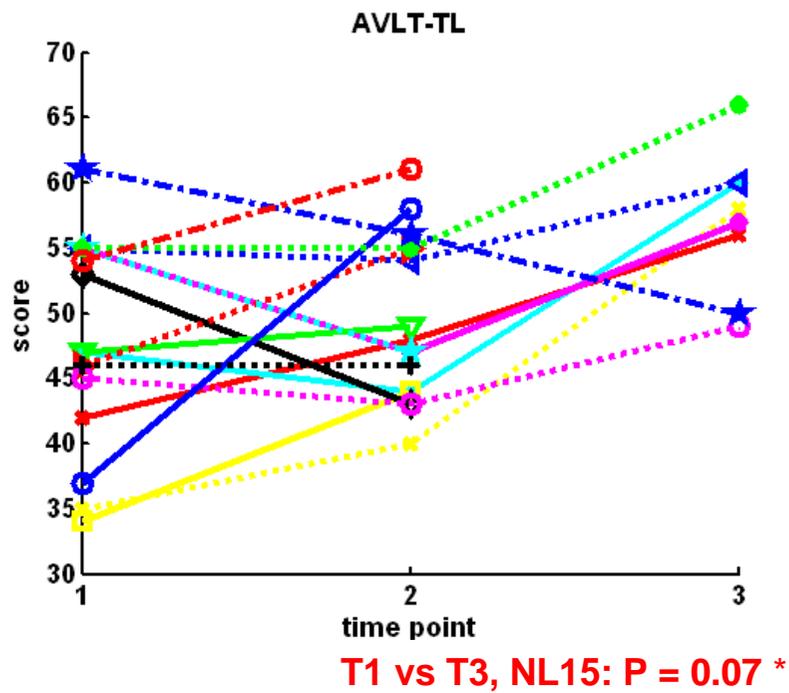
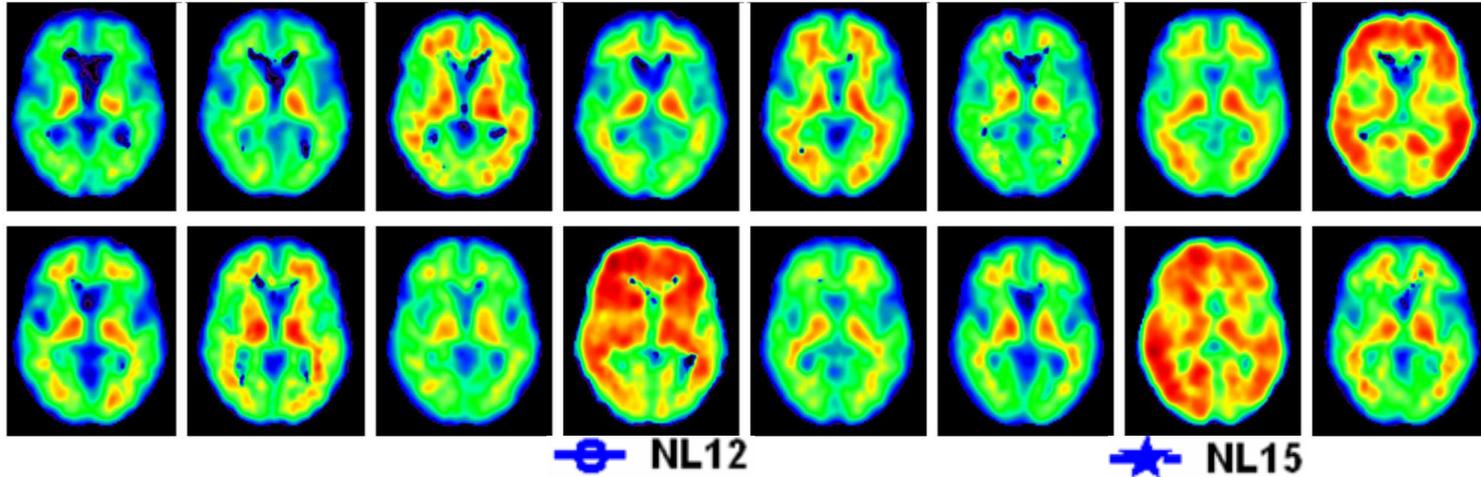


Nelissen N, Van Laere K, Thurfjell L, Owenius R, Vandenberghe R, Koole M, Bormans G, Brooks D, Vandenberghe R, *Journal of Nuclear Medicine*, 2009

# I. Amyloid imaging and the pre-clinical phase of AD

16 cognitively intact healthy controls

← NL8



- NL1
- NL2
- NL3
- NL4
- NL5
- NL6
- NL7
- NL8
- NL9
- NL10
- NL11
- NL12
- NL13
- NL14
- NL15
- NL16

\*Crawford and Garthwaite. *Neuropsychology*, 2007;21:611-620.

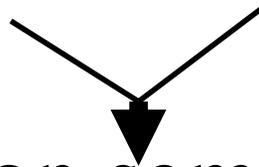
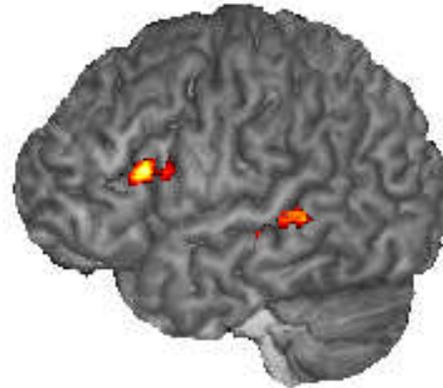
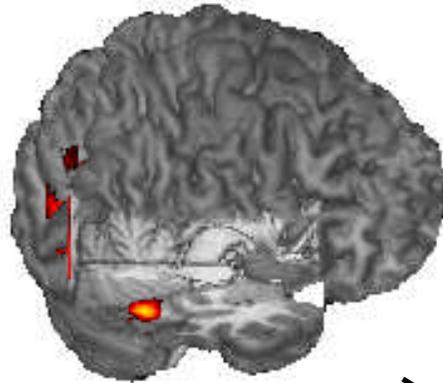
- There is a huge interest in the pre-clinical phase of AD.
- Novel disease-modifying therapy will probably be most effective if it can be administered as early as possible in the disease course, even prior to clinical disease manifestations

## II. Functional reorganisation of cognitive brain circuits in early-stage Alzheimer's disease and cognitive aging

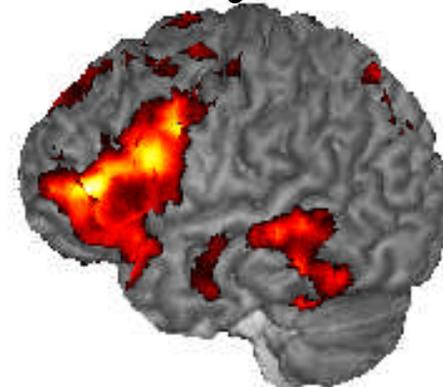
# Input-modality specific gates of entry

Input modality: **Pictures**

Input modality: **Words**



The “common semantic system”

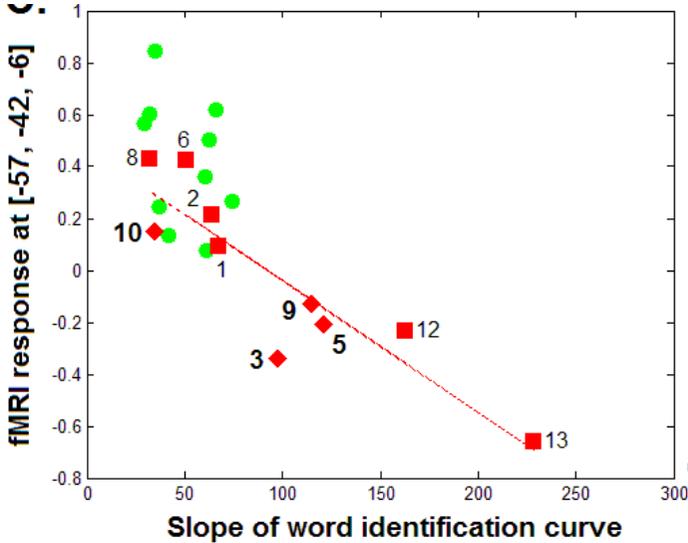
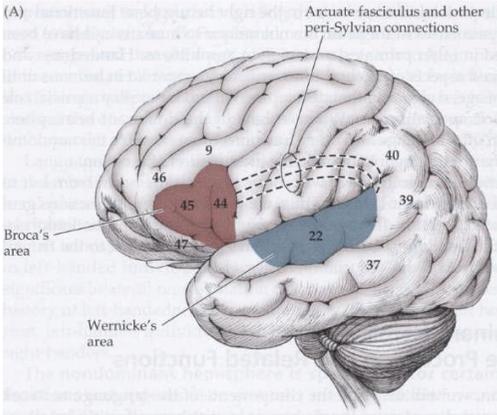
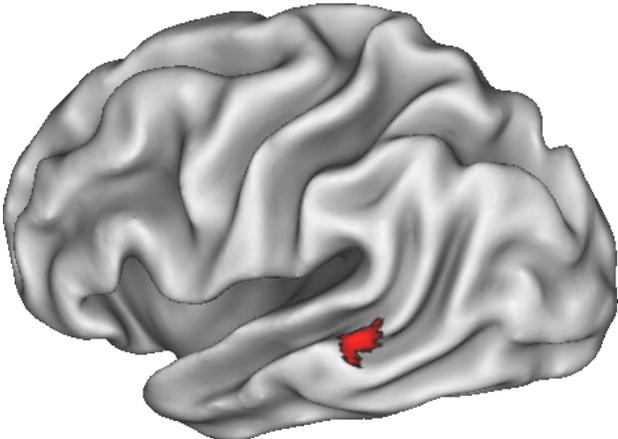


*Vandenberghe et al., Nature, 383, 254-256, 1996; Vandenberghe et al., Ann. Neurol. 2005, Nat. Neurosci. 2006, Cereb. Cortex 2008*

# Language, cognitive aging and cortical neurodegenerative disease

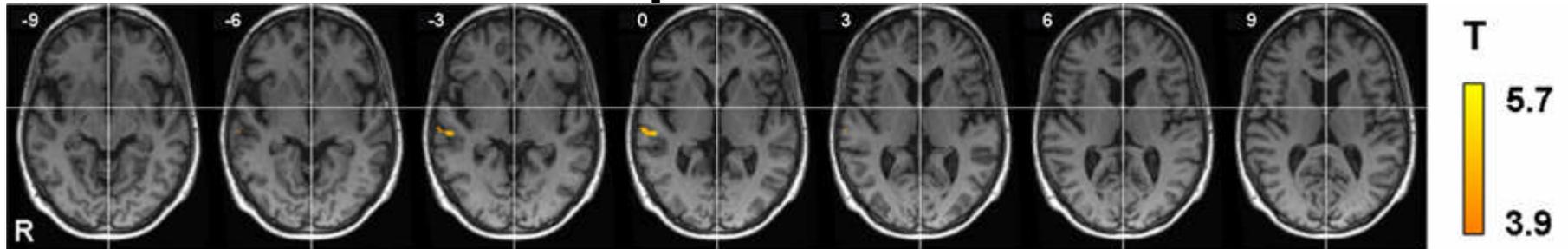
- How does the language system change in
  - Cognitive aging
  - Predementia stage of Alzheimer's disease
    - Vandenberg et al., Cereb Cortex, 2008
  - Early stage of Alzheimer's disease
    - Nelissen et al. Brain, 2007
  - Frontotemporal degeneration (primary progressive aphasia)
    - Vandenberg et al., Ann Neurol 2005

# The earliest language area affected in AD

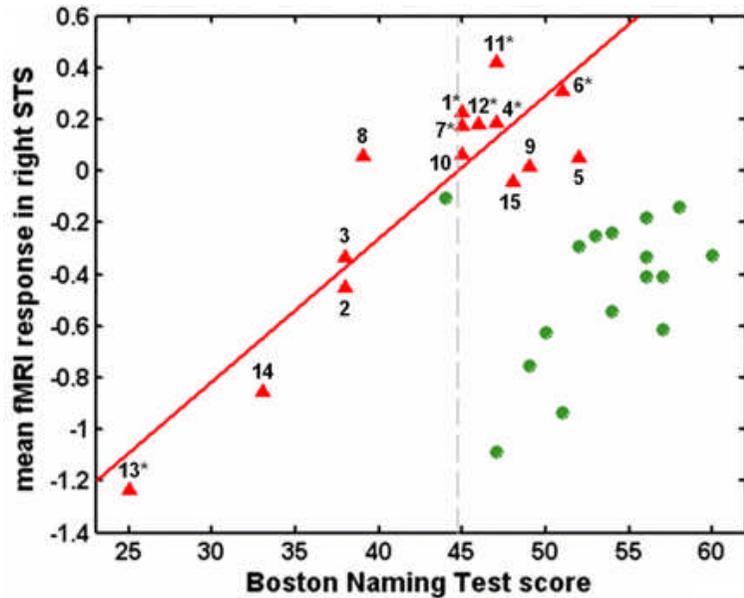


Vandenbulcke et al., *Cerebral Cortex* 2007; 17, 542-551, 2007

# Recruitment of the right hemisphere in AD

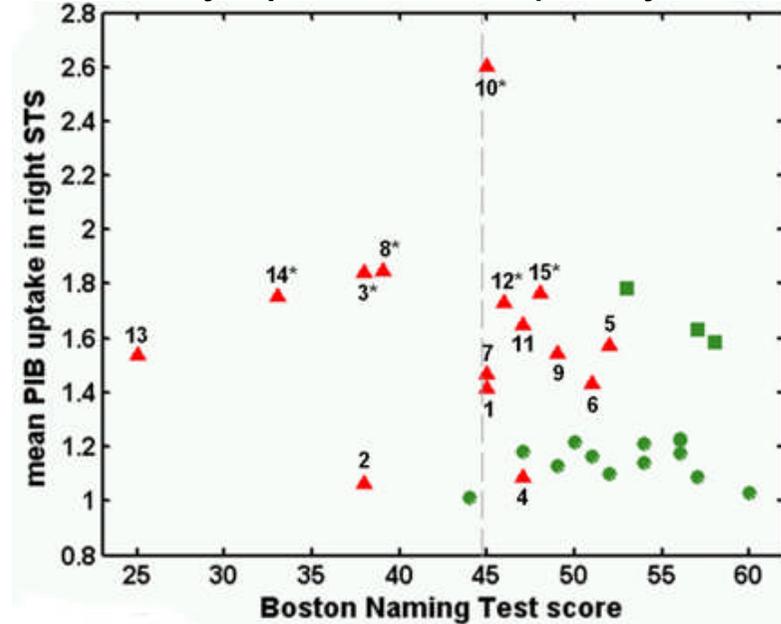


*Naming is preserved if right-sided STS is activated*



**51,-9,-15, Z 4.53, r = 0.90**

*No quantitative relationship between clinical symptoms and A $\beta$  amyloid load*



*Nelissen N et al.  $\beta$ amyloid deposition in the language network and how the brain responds, Brain, 130, 2055-2069, 2007*

# Conclusion

- Pre-clinical stage of Alzheimer's disease
  - Predictive value of  $^{18}\text{F}$  amyloid scan
- Early-stage Alzheimer's disease
  - Role of functional reorganisation of cognitive brain systems in response to  $\text{A}\beta$  related injury

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