Biological stress is 80 years old – after the article of Hans Selye (Nature 1936)

Stress and Alzheimer's disease – new perspectives

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"Neither the prestige of your subjects and

The power of your instruments

Nor the extent of your planning

Can substitute for

The originality of your approach and

The keenness of your observation"

Hans Selye

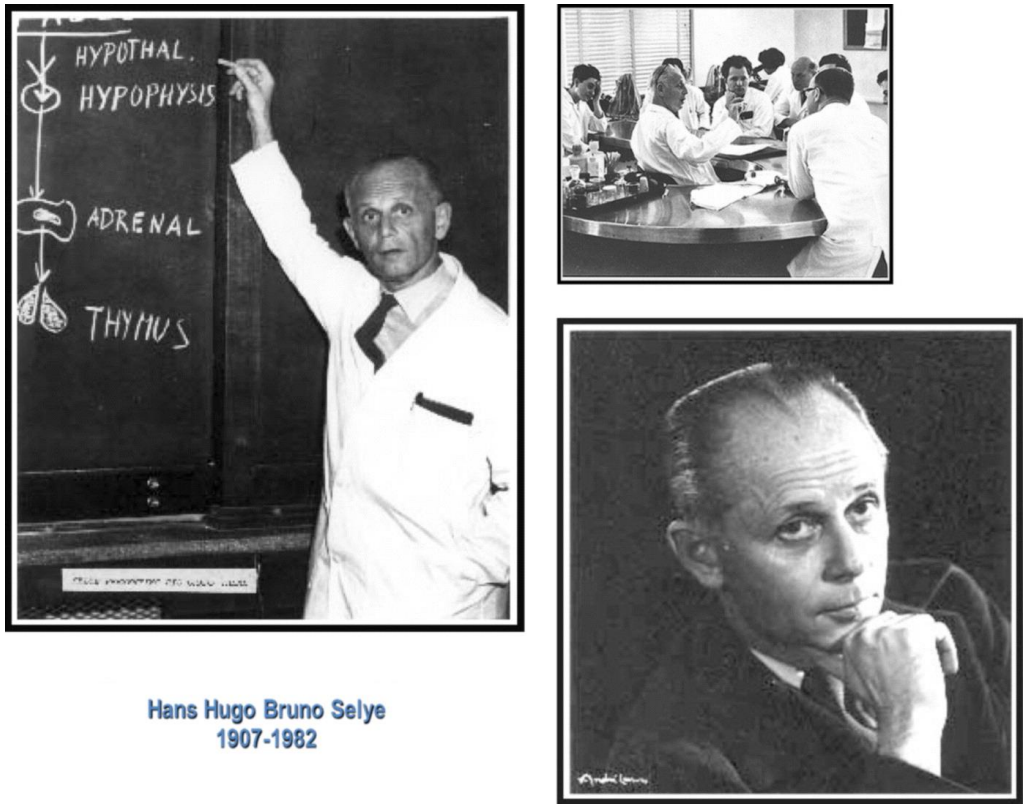


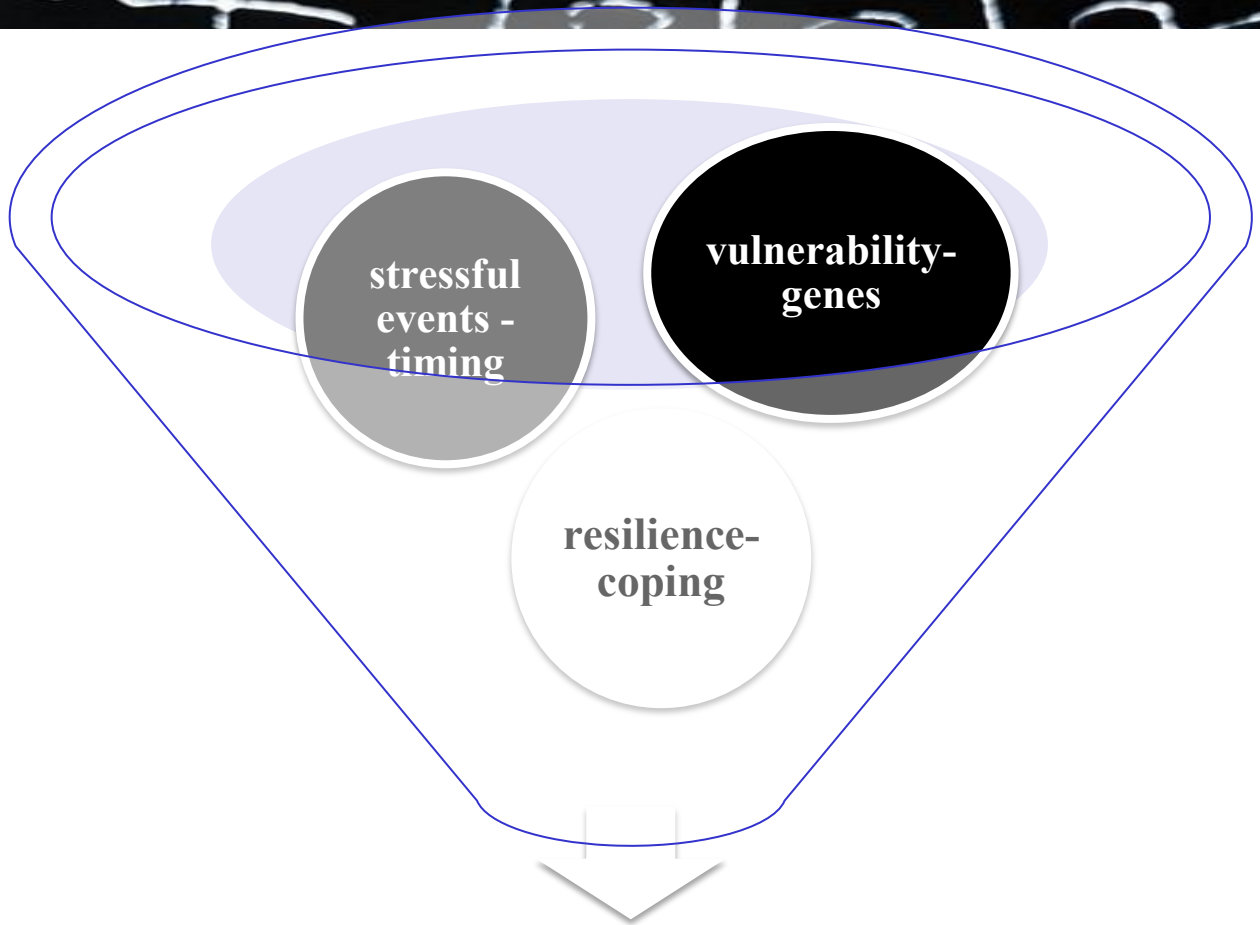
Figure 1. Photographs of Hans Selye from 1950s (left) and 1960s. (Modified from: A personal reminiscence by Dr Istvan Berczi). Selye was born January 26, 1907, Vienna, Austria and died October 16, 1982, Montreal, Canada.

Published in: Sandor Szabo; Yvette Tache; Arpad Somogyi; *Stress* **2012,** 15, 472-478.
DOI: 10.3109/10253890.2012.710919

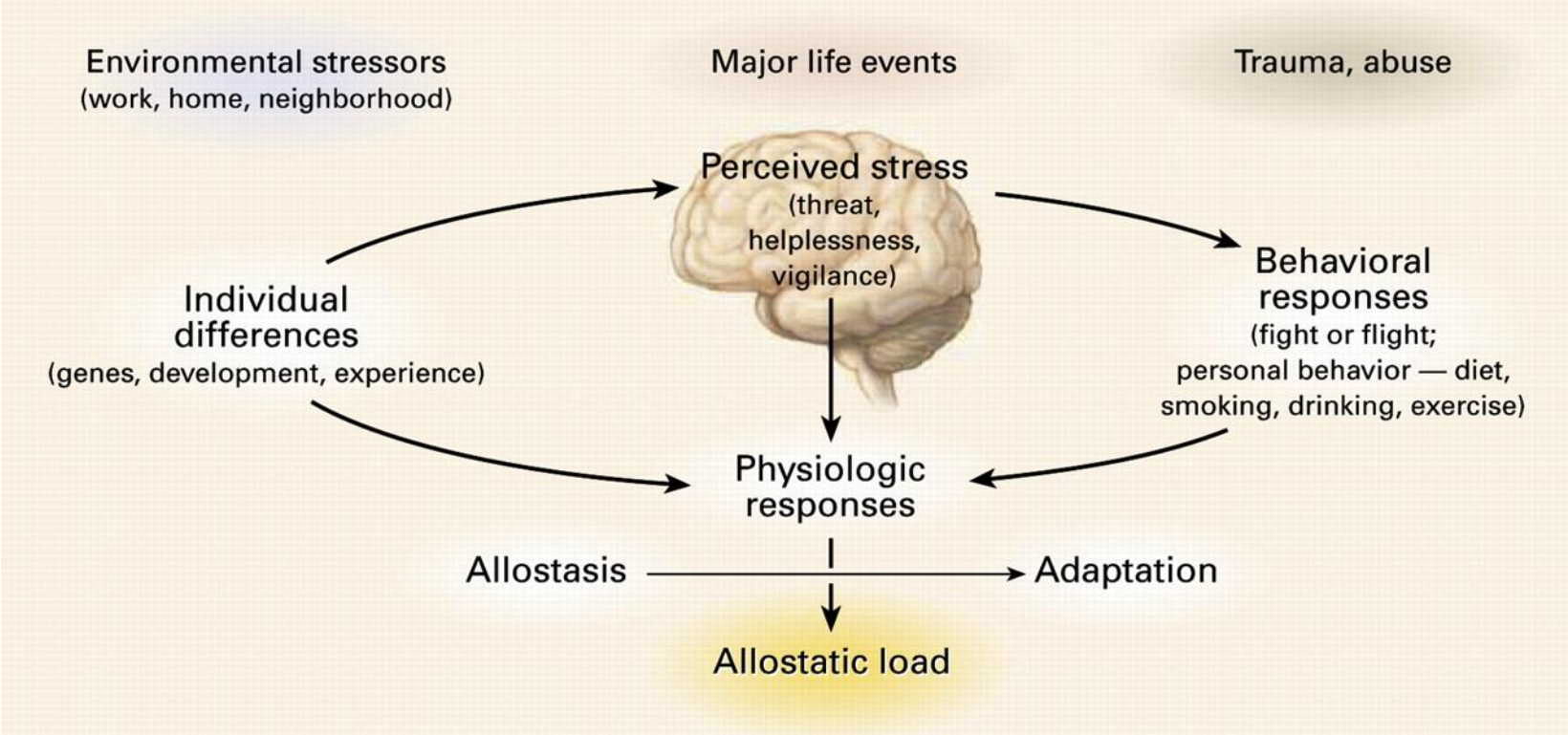
The legacy of Hans Selye and the origins of stress research: A retrospective 75 years after his landmark brief "Letter" to the Editor[#] of Nature

Sandor Szabo, Yvette Tache & Arpad Somogyi

Questions of interest…

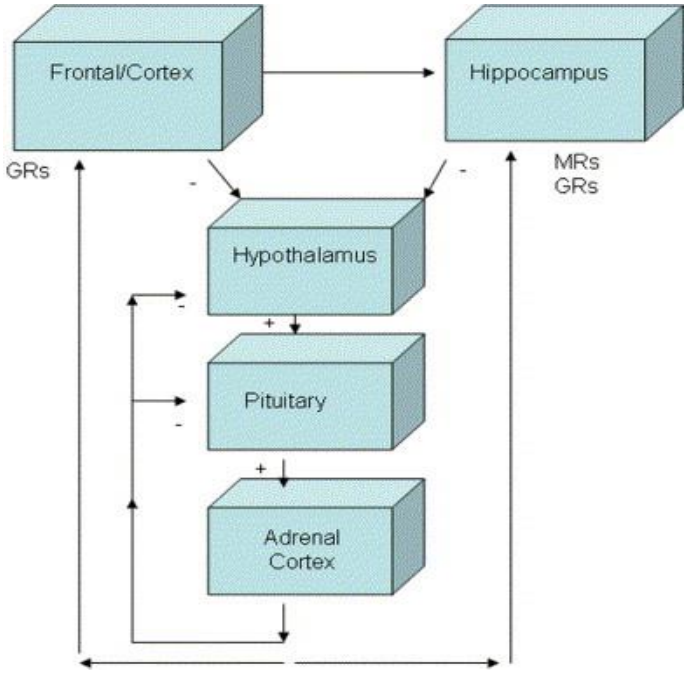


Central role of the brain in allostasis and the behavioral and physiological response to stressors. [From McEwen (211), copyright 1998 Massachusetts Medical Society.]. – increased levels of glucocorticoids

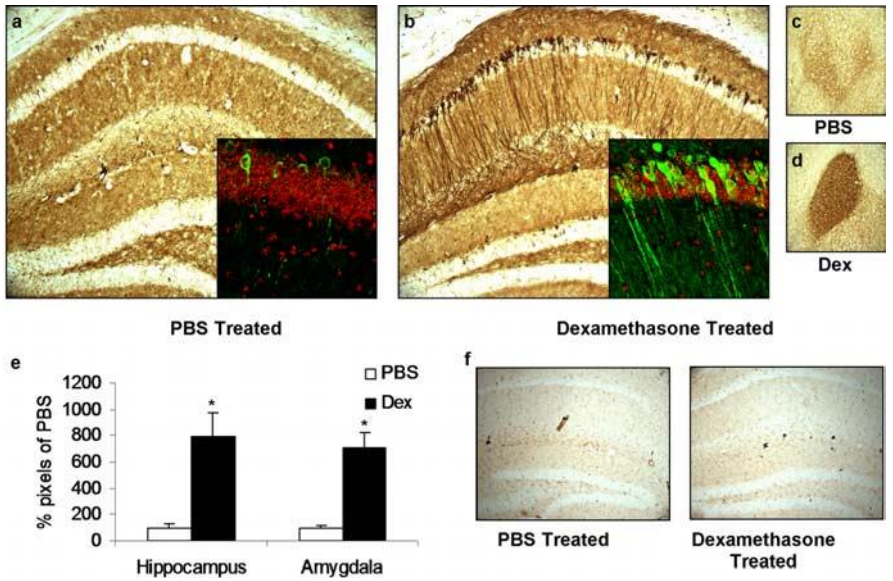


Bruce S. McEwen Physiol Rev 2007;87:873-904

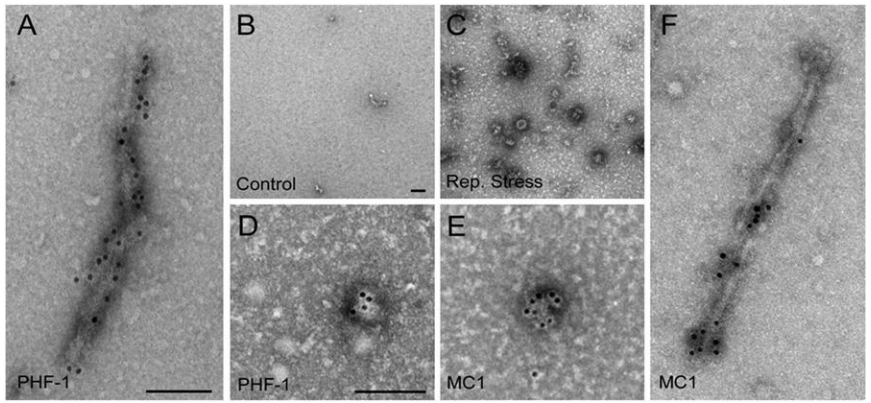
Physiological Reviews

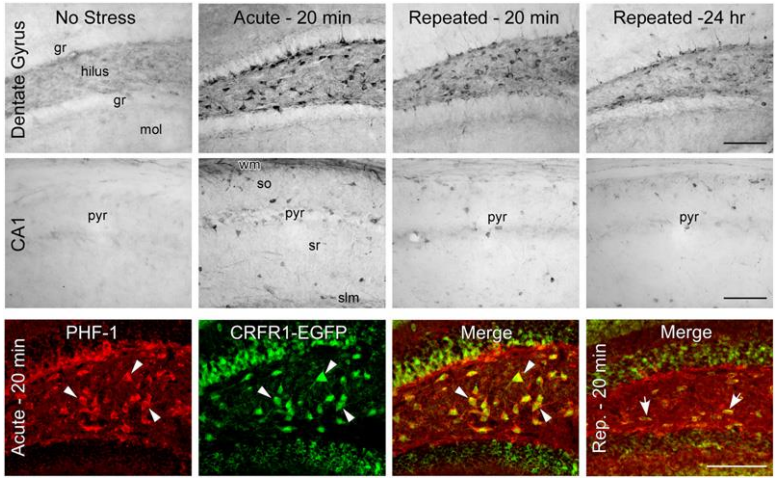


Glucocorticoids Increase Amyloid-beta and Tau Pathology in a Mouse Model of Alzheimer's Disease
(Green et al., 2006)

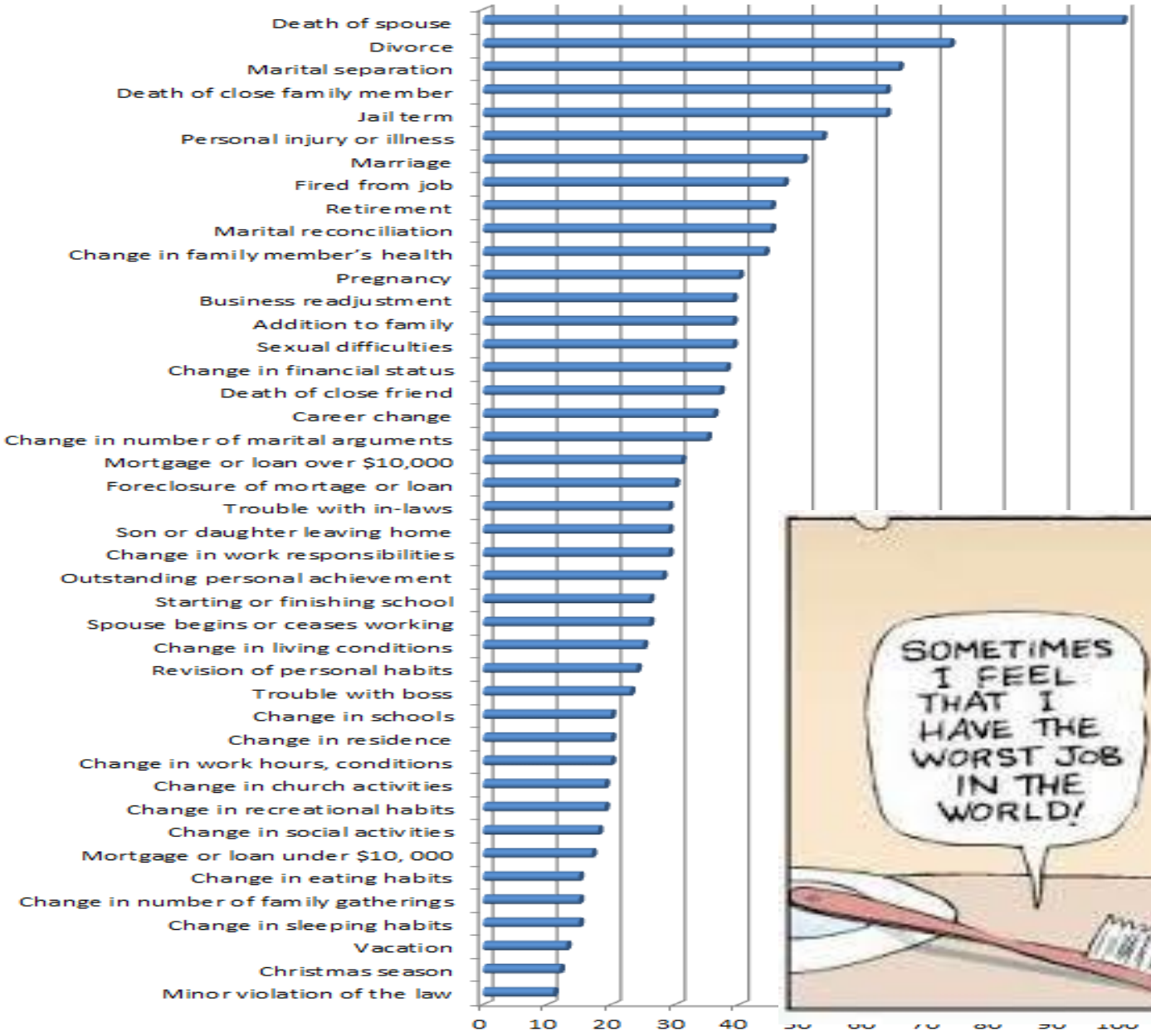


Corticotropin-releasing factor receptor-dependent effects of repeated stress on tau phosphorylation, solubility, and aggregation
(Rissman et al., 2011)

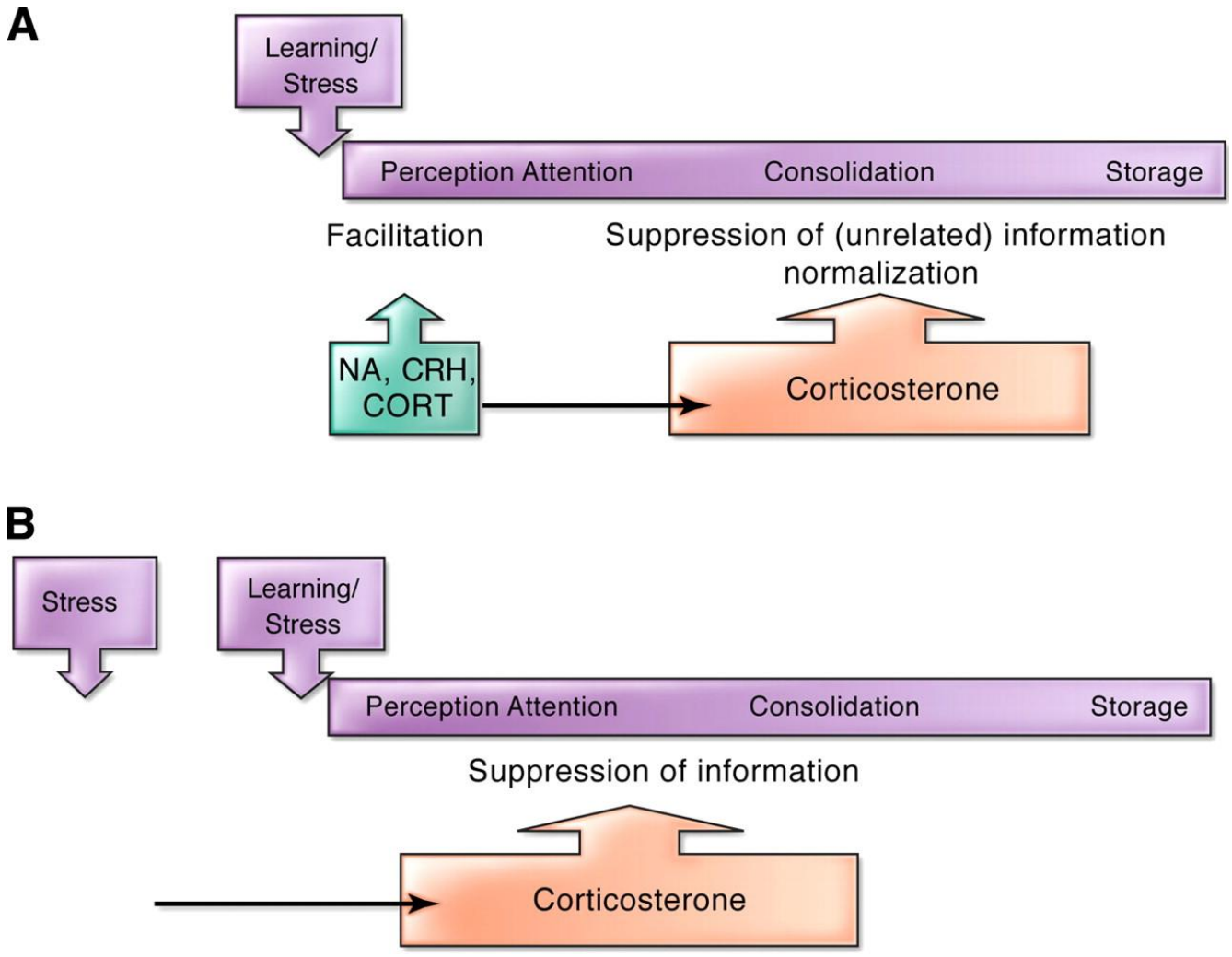




Life Stressors (from Holmes & Rahe, 1967)



Opposing effects of stress on learning depend on the timing of the events.



Bruce S. McEwen Physiol Rev 2007;87:873-904

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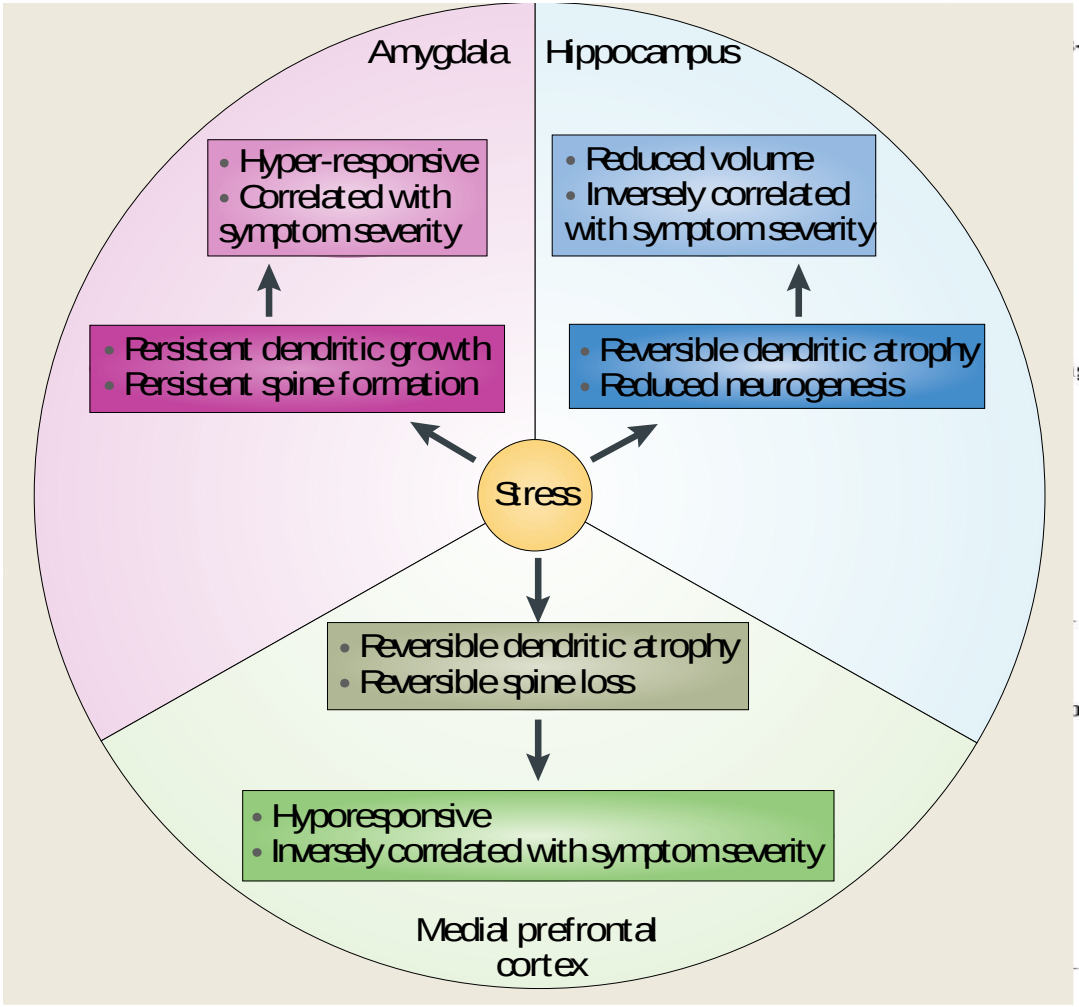
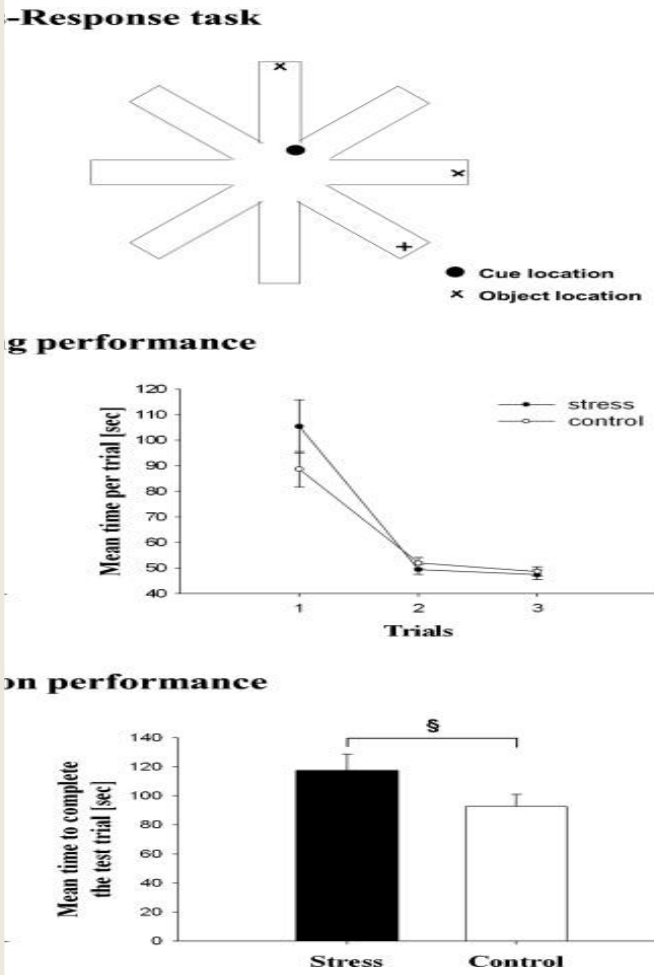
Stress disrupts cognitive processes

(Roozendaal et al., Nature Reviews, Focus on Stress, 2009)





Guenzel et al., 2012

BRAIN
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Midlife psychological stress and risk of dementia: a 35-year longitudinal population study

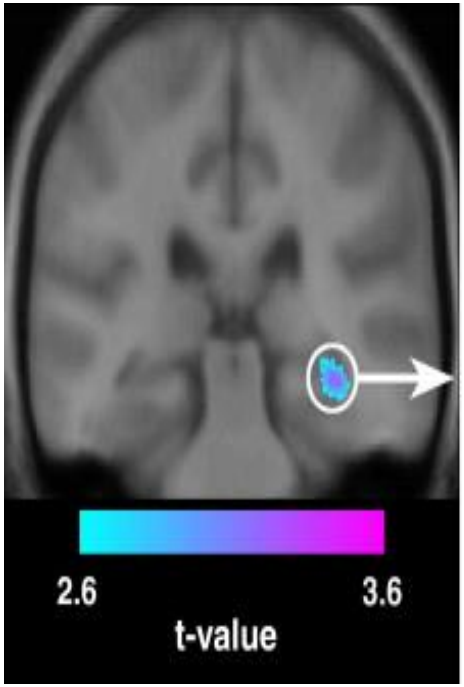
Lena Johansson,[1] Xinxin Guo,[1] Margda Waern,[1] Svante Östling,[1] Deborah Gustafson,[1,2] Calle Bengtsson[3] and Ingmar Skoog[1]

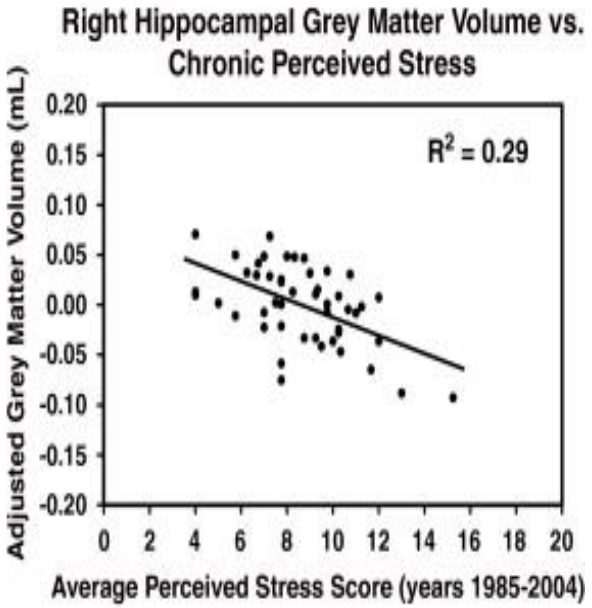
To conclude, we found an association between psychological stress in middle-aged women and development of dementia, especially Alzheimer's disease. More studies are needed to confirm our findings and to study potential neurobiological mechanisms of these associations.

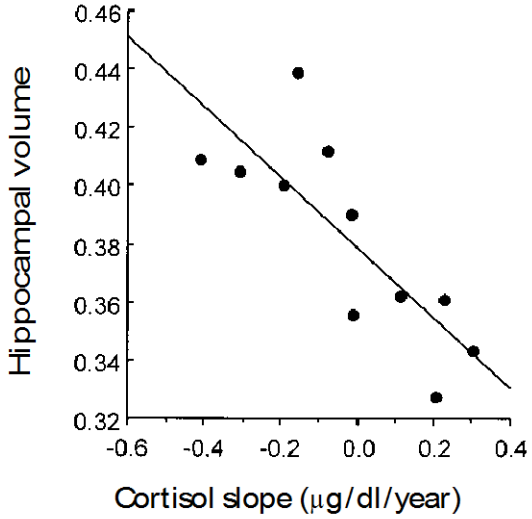
- Framingham study
  - more severe events – higher rate of cognitive decline – PTSD?
- Alzheimer's Disease Neuroimaging Initiative (ADNI)
  - chronic stress – better cognitive function
  - ApoE e4 carriers – stronger association (Comijs et al., 2011)

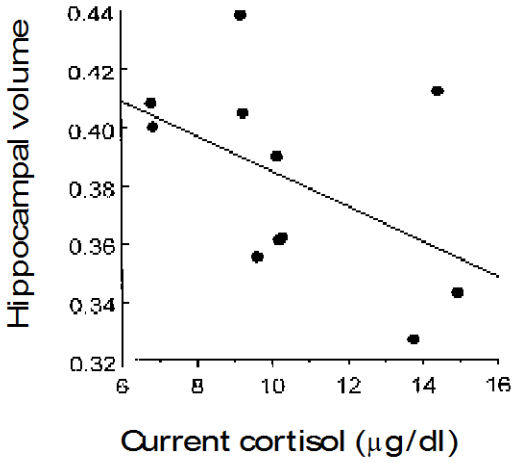
Stress, cortisol and the hippocampal volume

(Lupien et al. 1998, Apostolova et al. 2010)

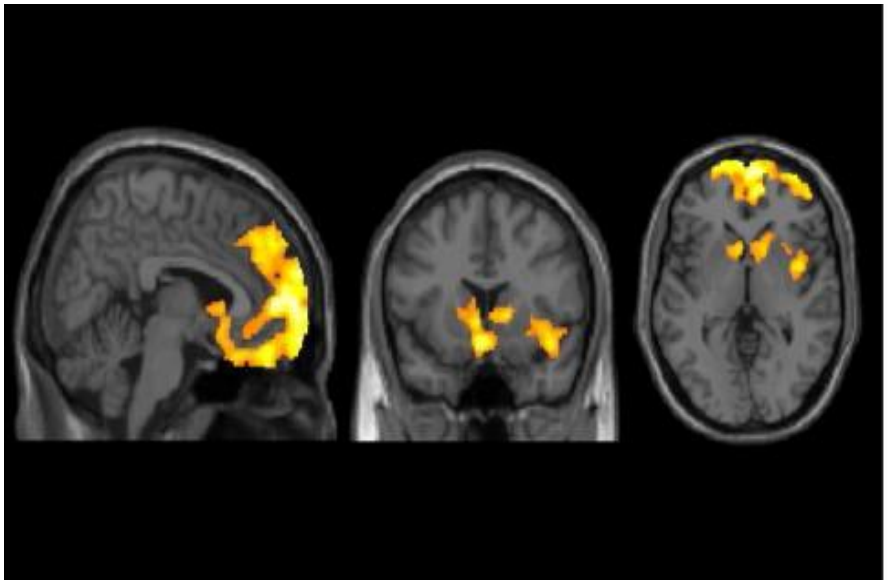


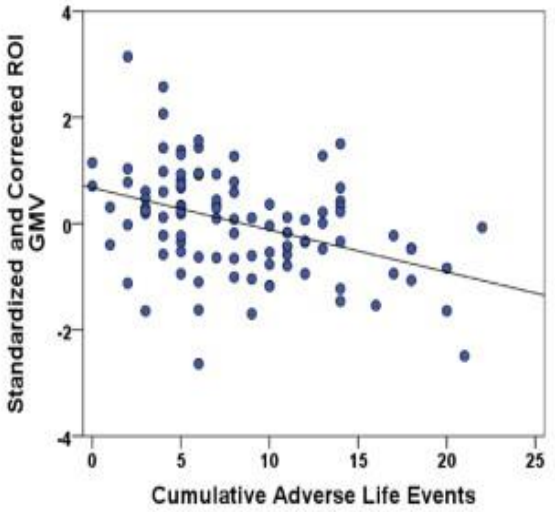


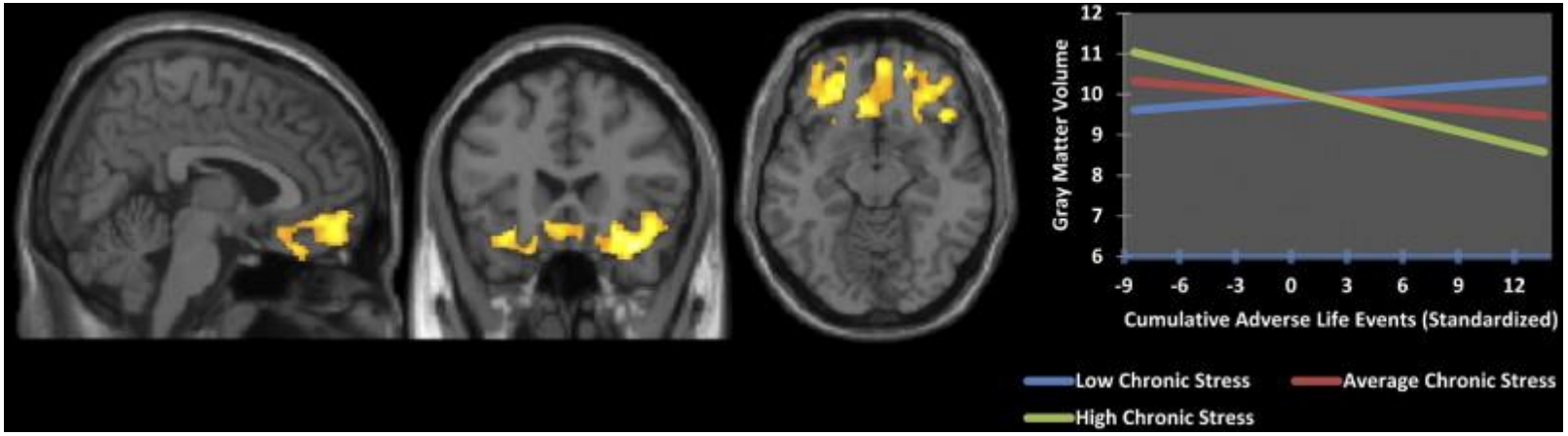




Cumulative Adversity and Smaller Gray Matter Volume in Medial Prefrontal, Anterior Cingulate, and Insula Regions. (Ansell et al., 2012)

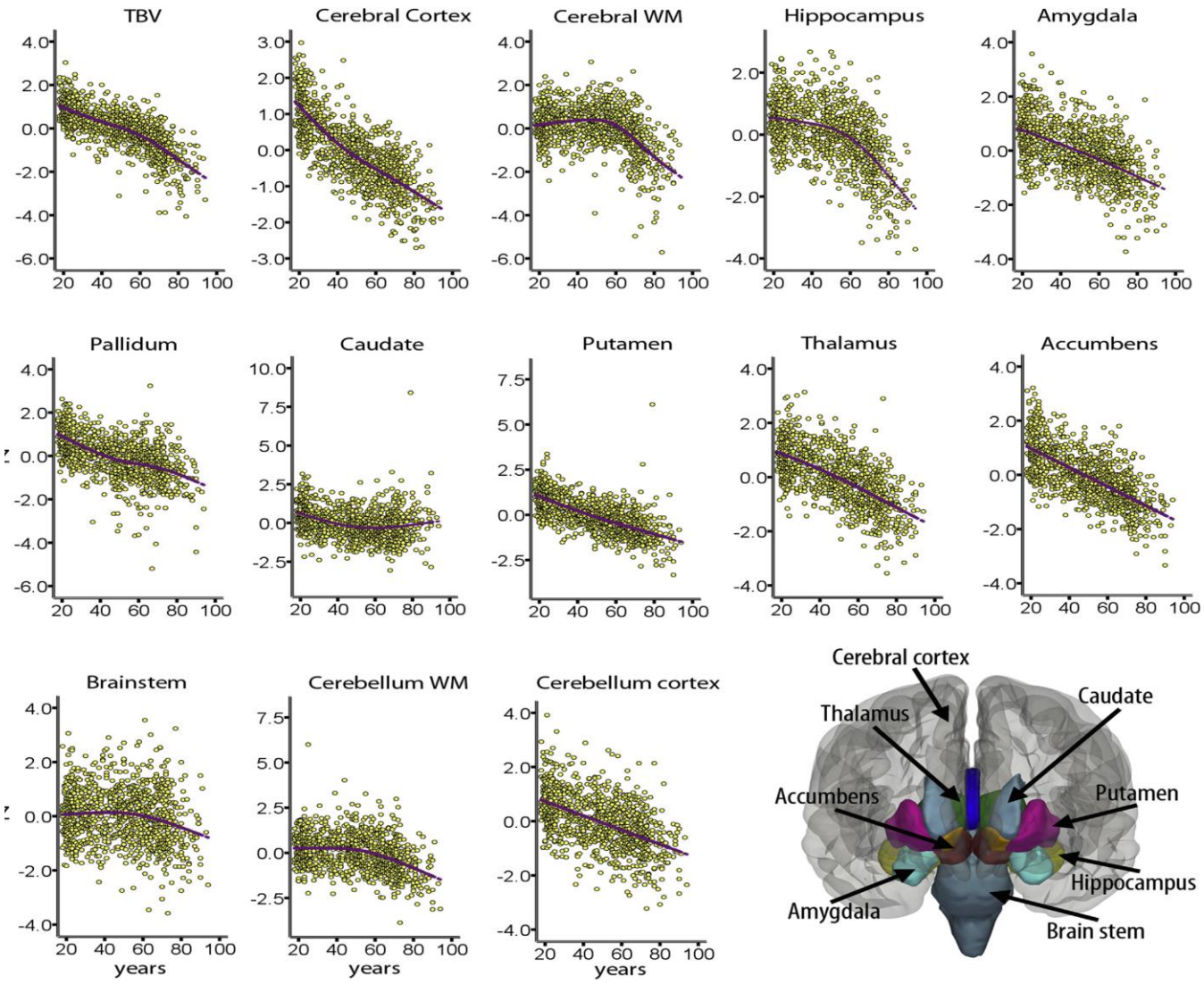




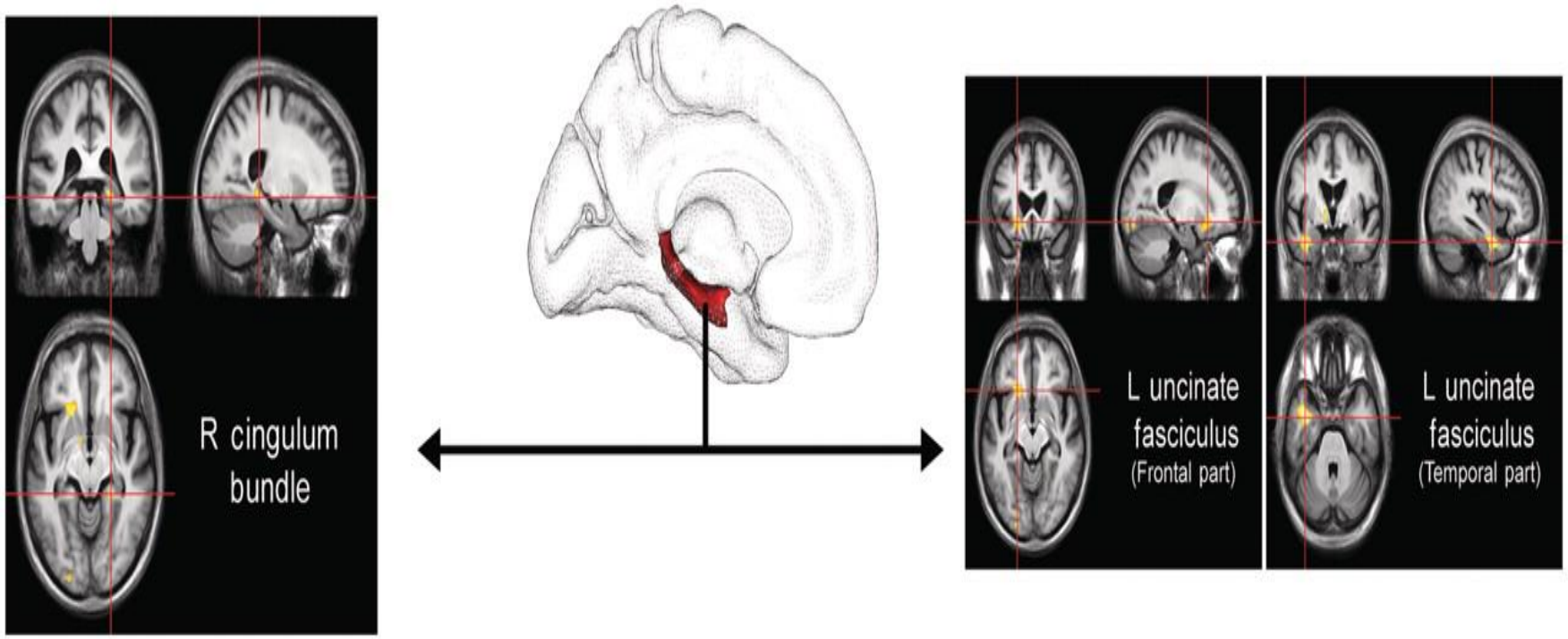


Critical periods – nonlinear subcortical aging (Fjell et al., 2013)

A.M. Fjell et al. / Neurobiology of Aging 34 (2013) 2239–2247



Relationship between baseline hippocampal atrophy and white matter–MRI percent change maps.



Nicolas Villain et al. Brain 2010;133:3301-3314

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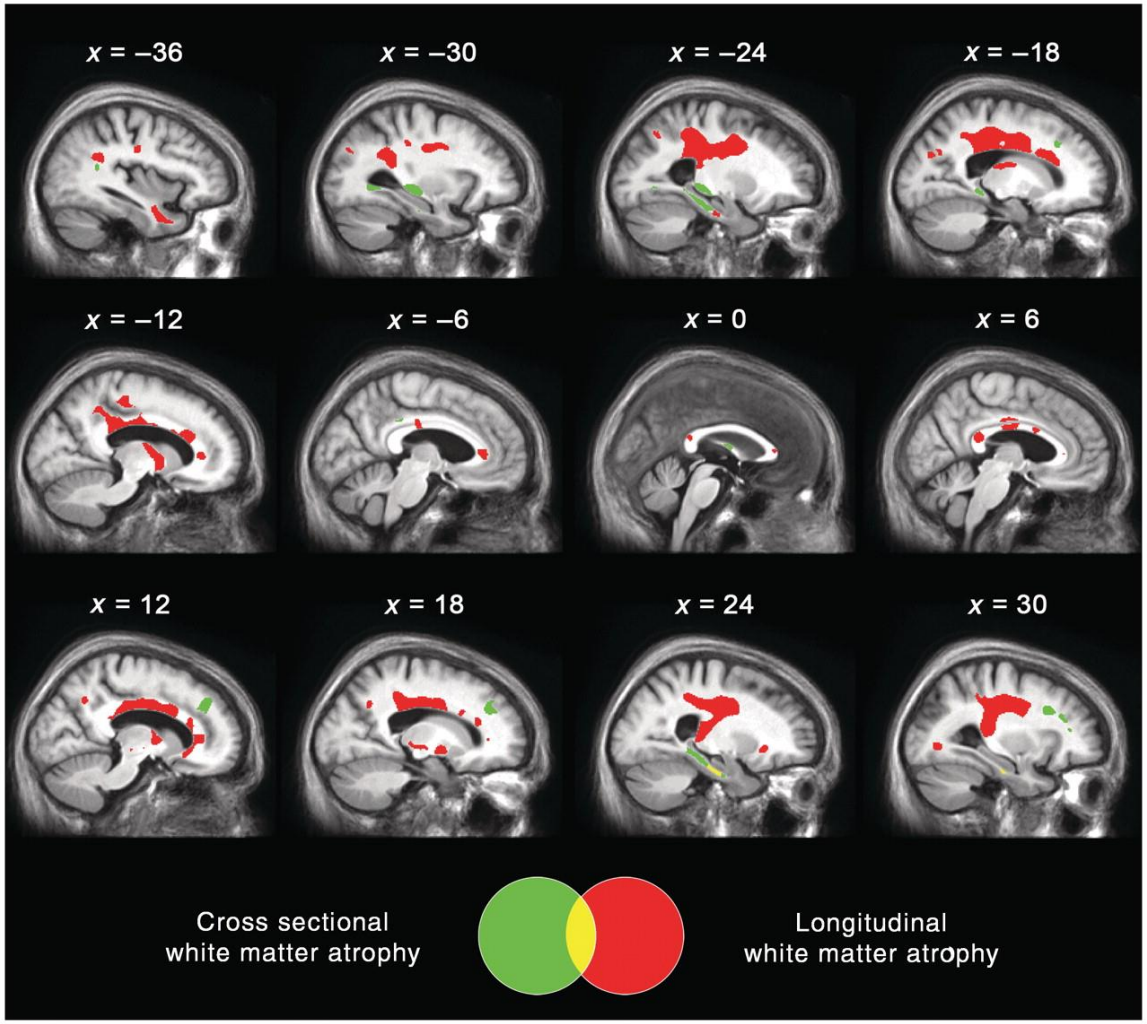
Illustration of white matter alterations.



Nicolas Villain et al. Brain 2010;133:3301-3314

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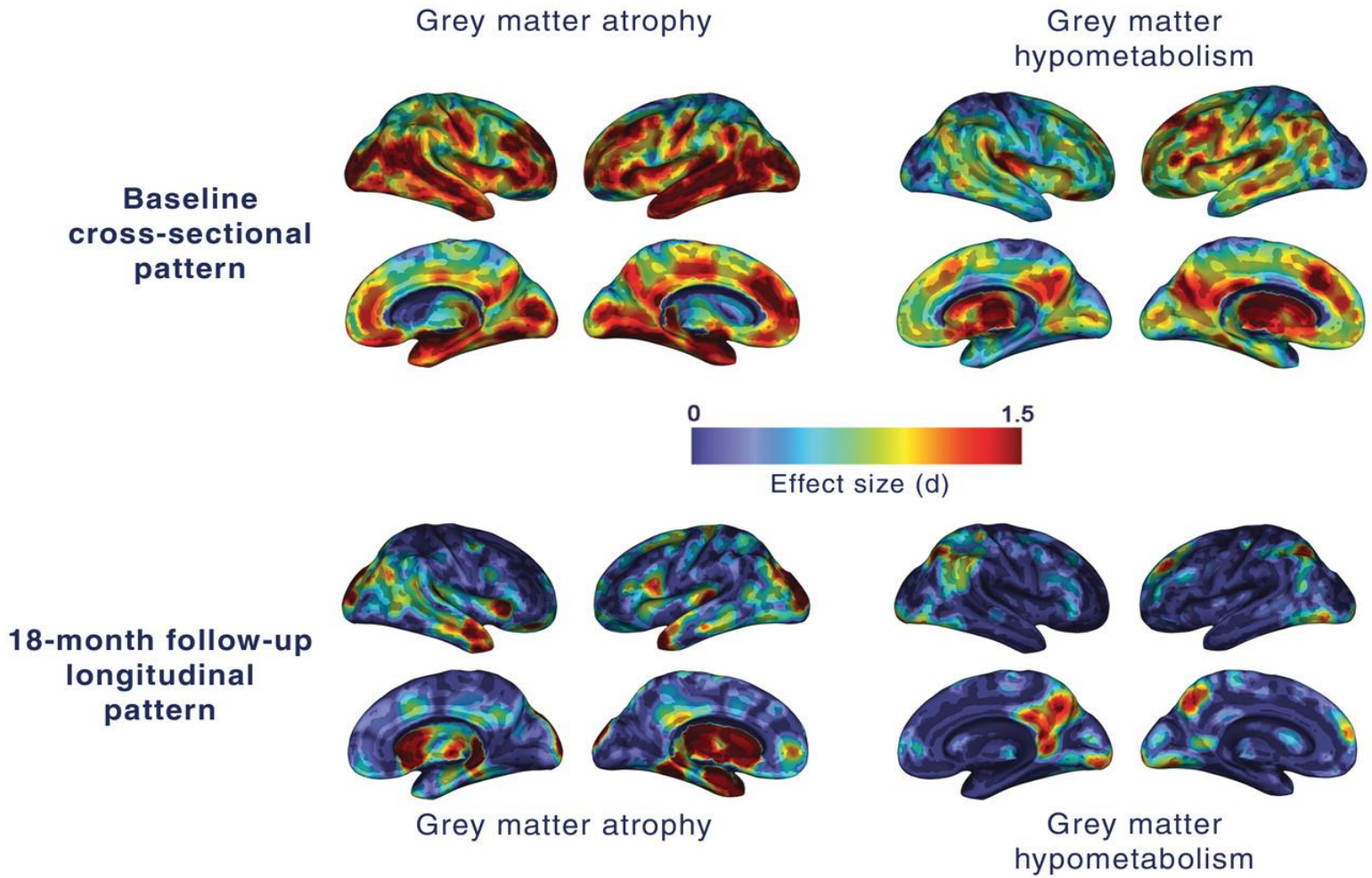
Brain patterns of grey matter atrophy and 18FDG-PET hypometabolism in amnestic MCI. Profiles of brain alterations in patients with amnestic MCI at baseline compared with healthy elderly (top) and over the 18-month follow-up period (bottom).



Nicolas Villain et al. Brain 2010;133:3301-3314

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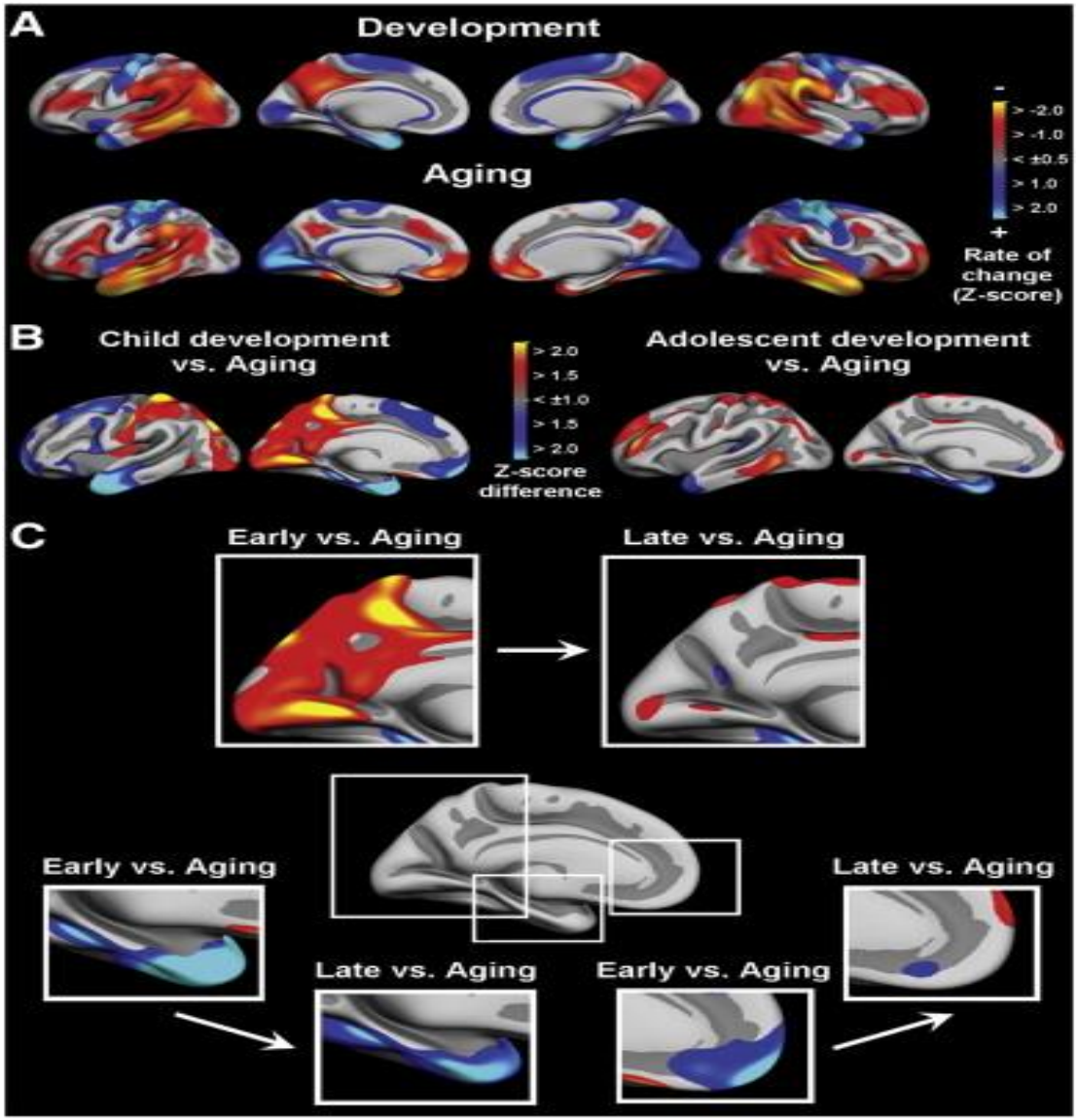
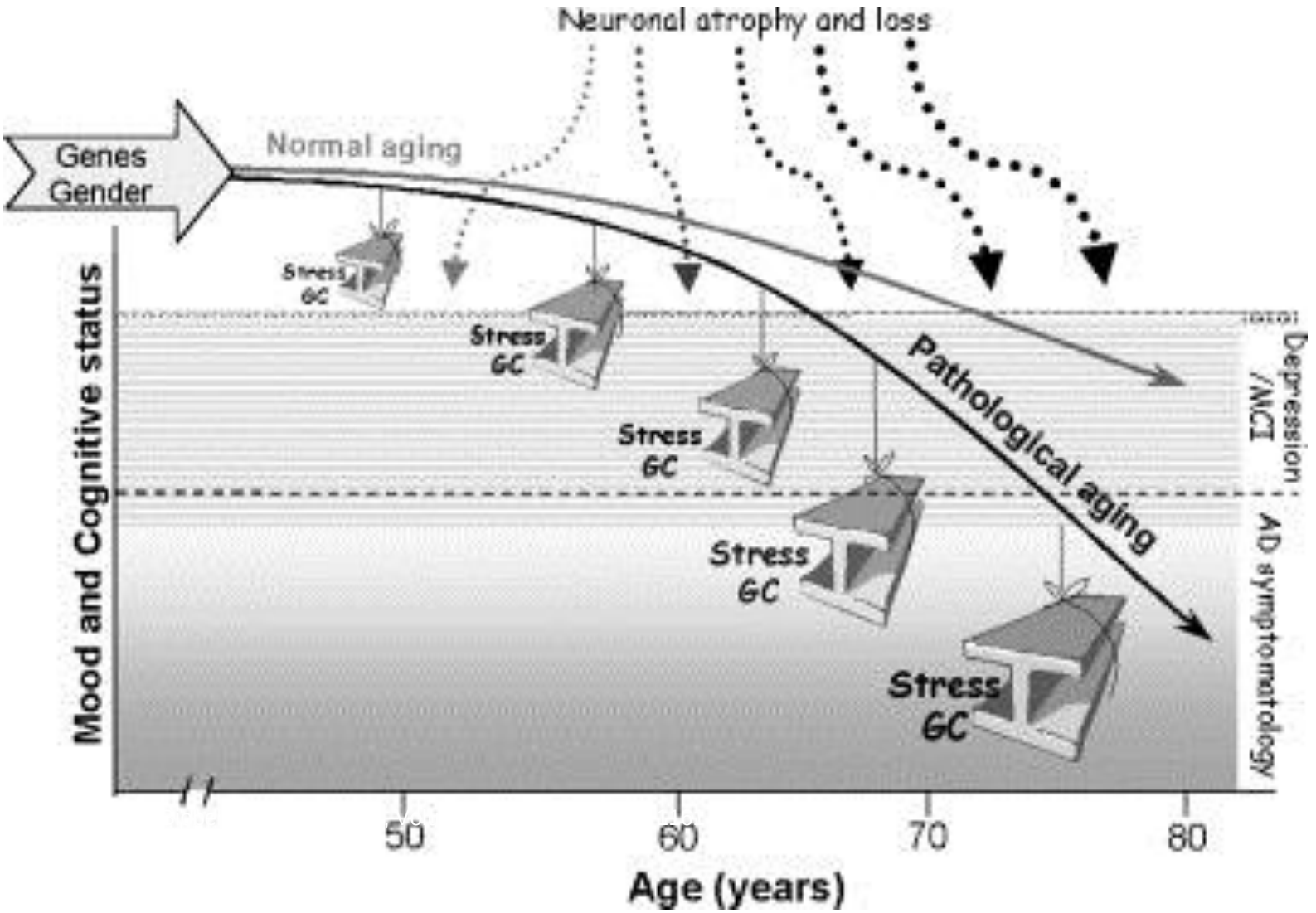
Brain development and aging: Overlapping and unique patterns of change. Tamnes et al., 2013.



Depression and mood status: effects on cognition

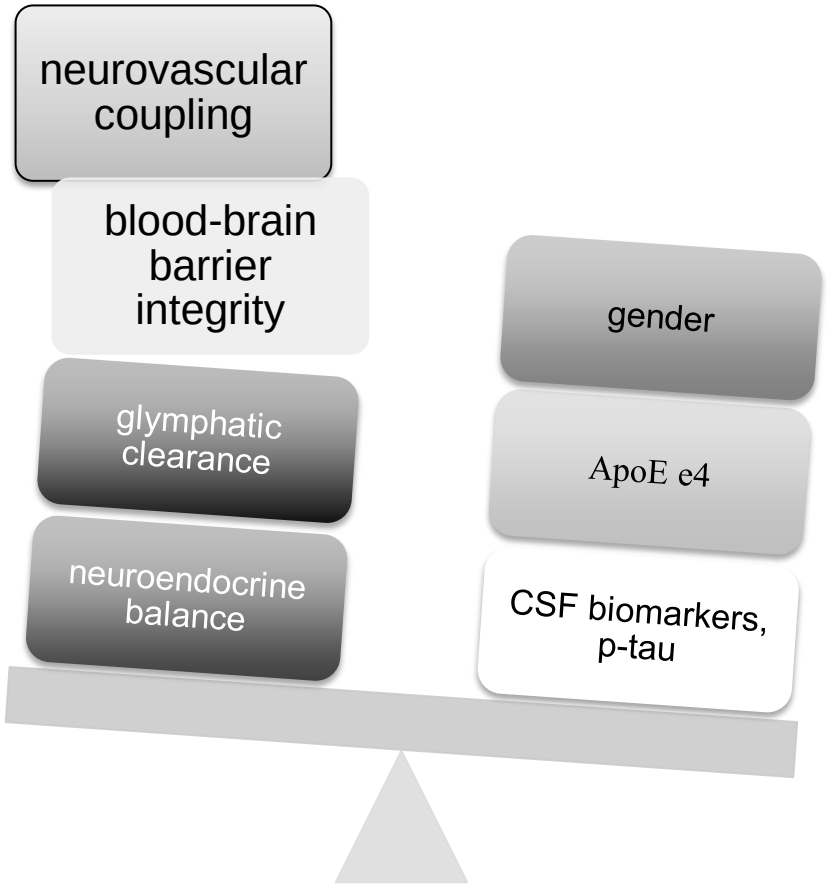


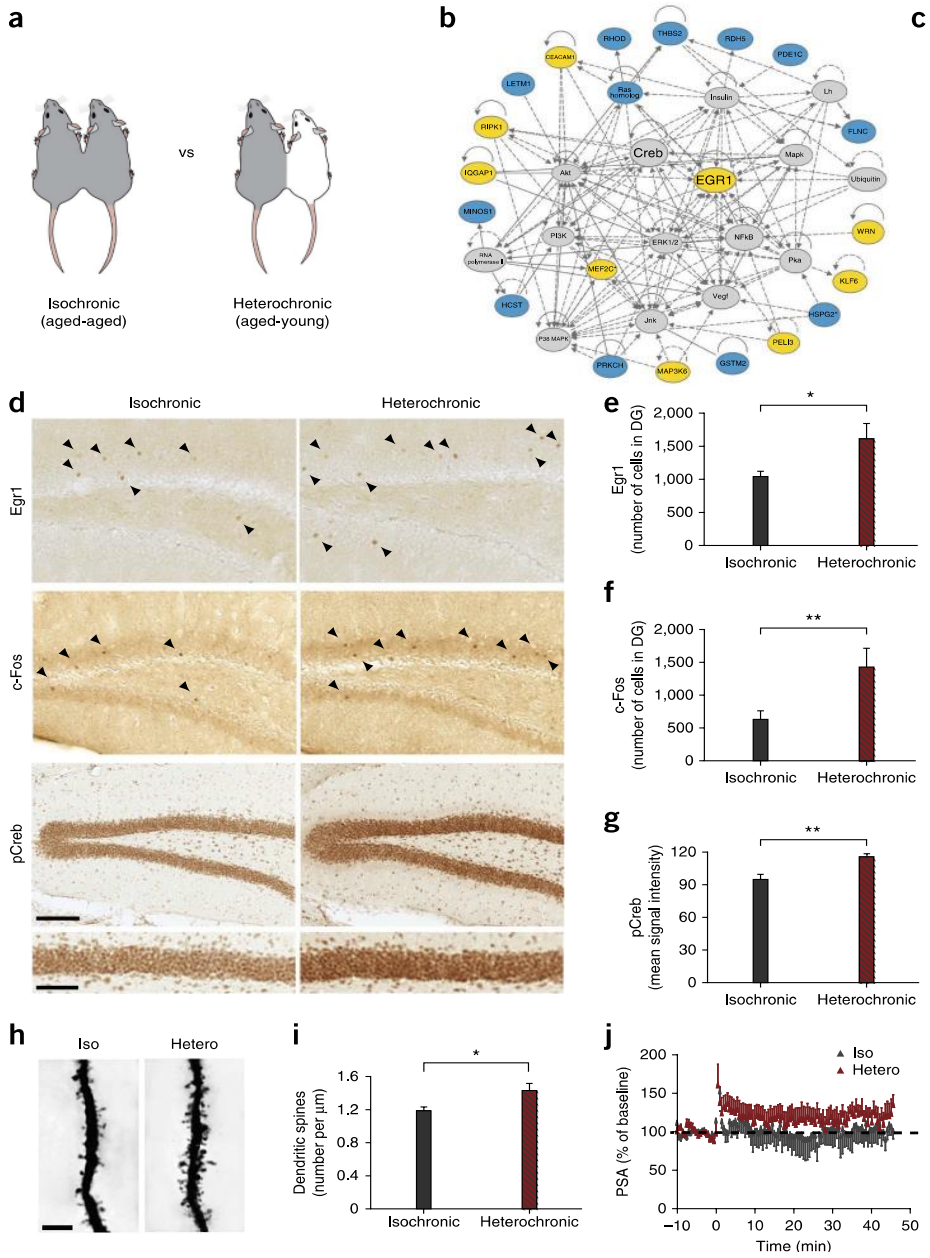
I. Sotiropoulos et al. / Neuroscience and Biobehavioral Reviews (2008)

Delicate balance

(Recent Developments in Understanding Brain Aging: Implications for Alzheimer's Disease and Vascular Cognitive Impairment, Deak et al., 2015)

Treatment vs prevention dilemma





Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice

(Villeda et al., Nature Medicine 2014)

- heterochronic parabiosis: joining blood supply between young and old animals
- ‘rejuvenated phenotype’:

beta-2-microglobulin decrease

synaptic plasticity related transcriptional changes in hippocampus- dentritic spine density improved

cognitive performance improved

Thank you very much for your attention