

Why stress is bad for the aging brain and what you can do about it



JC PRUESSNER

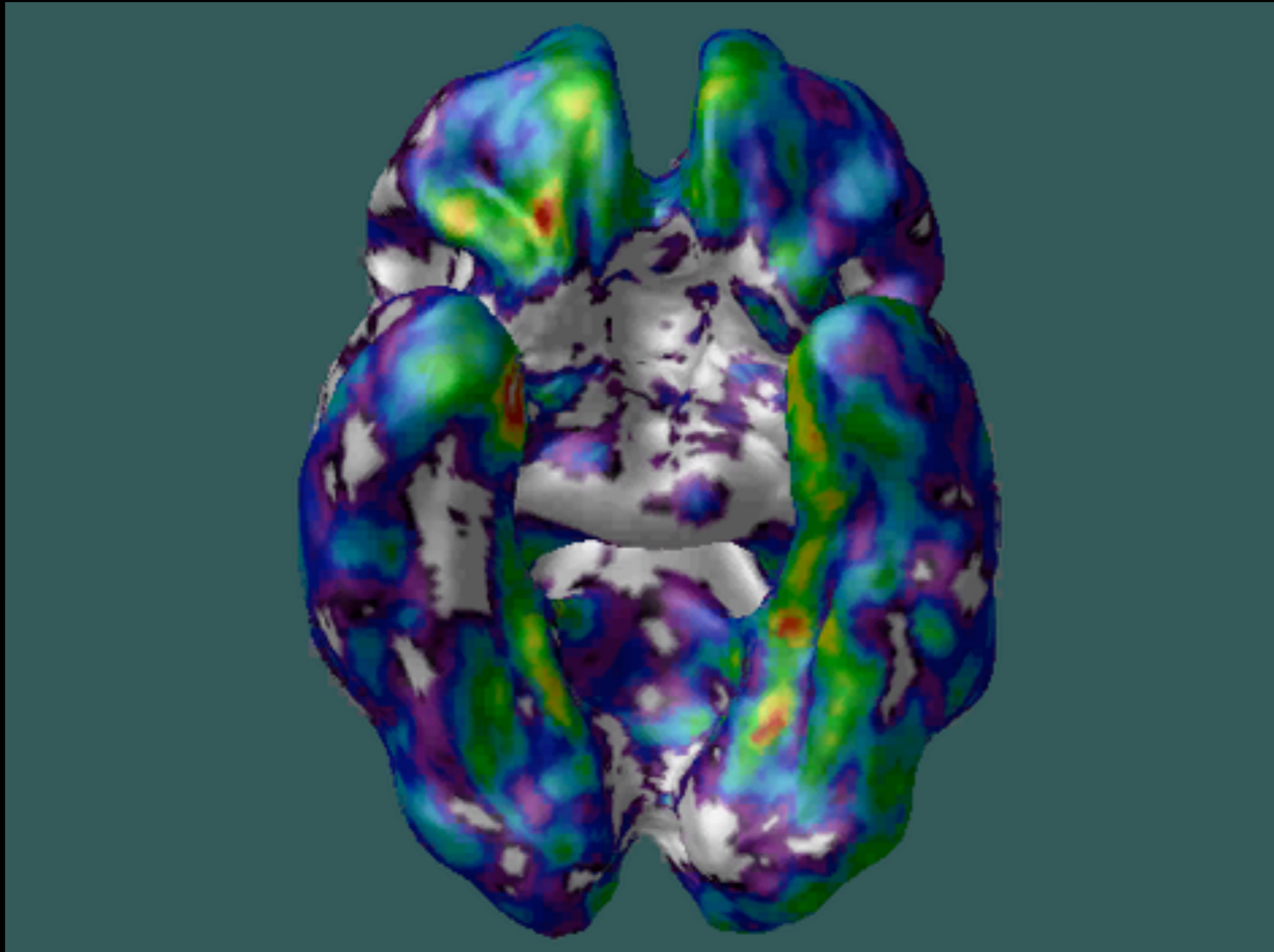


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Aging of the human brain: Global findings

- Age related volume decline starts to occur at the beginning of the third life decade (Jernigan et al., 1990)
- While all brain regions are affected, there are regions more strongly involved in volume reduction (PFC, MTL), and regions less strongly (motor-sensory areas, occipital lobes)
- The reason for these differences in volume reduction is unclear, but it is interesting to find some of the regions more affected by normal aging also to be more strongly implicated in pathological aging (MTL - MCI, AD)

Aging of the human brain: Illustration



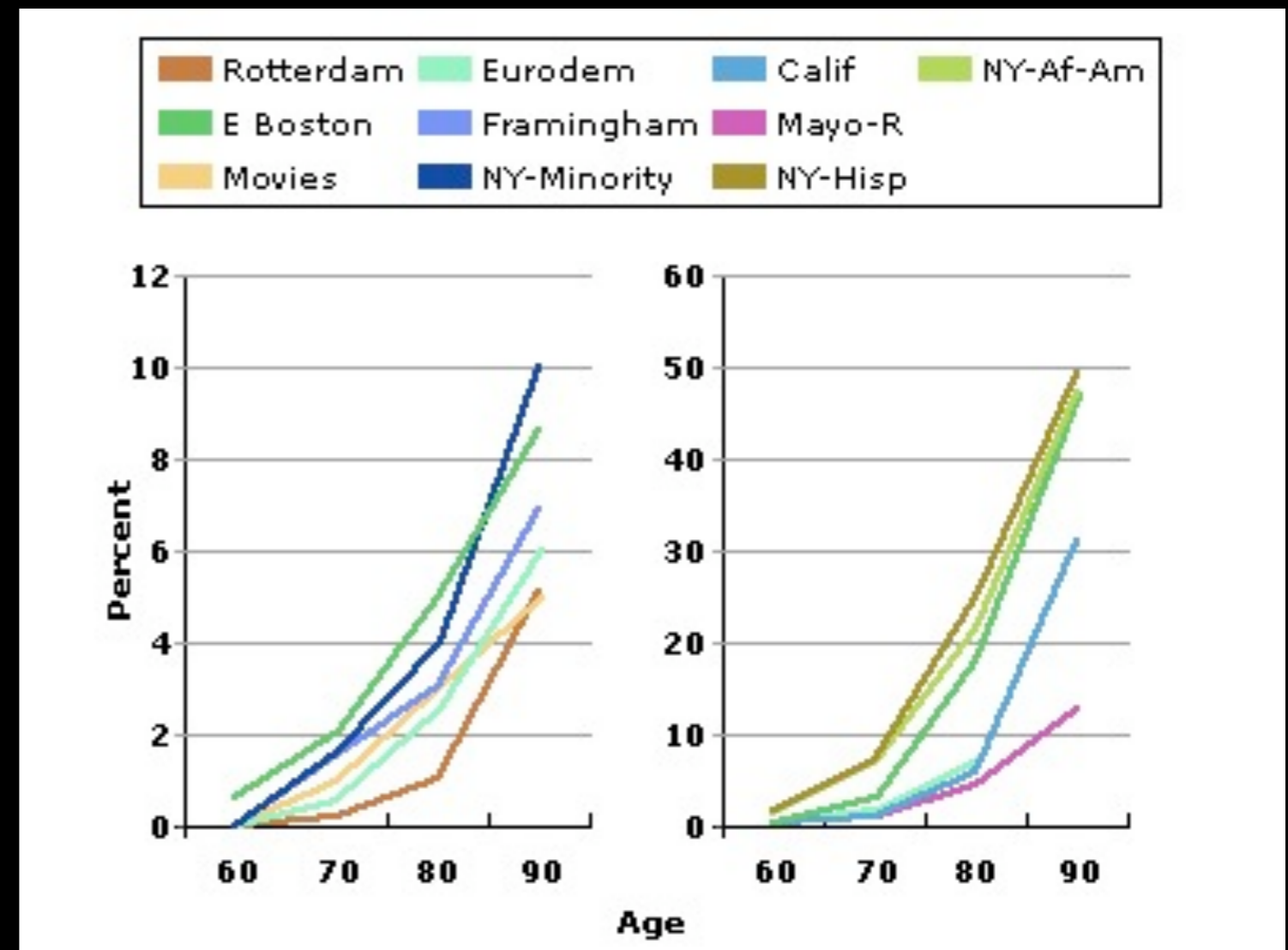
Lerch et al., 2009

Aging of the human brain: Individual differences

- Individual differences in the normal and pathological aging do exist, and are at the focus of continued research efforts
- Revealing the origin of these differences might help to understand general factors impacting the aging of the human brain
- Examples for these individual differences affecting aging include all aspects affecting age-related brain changes

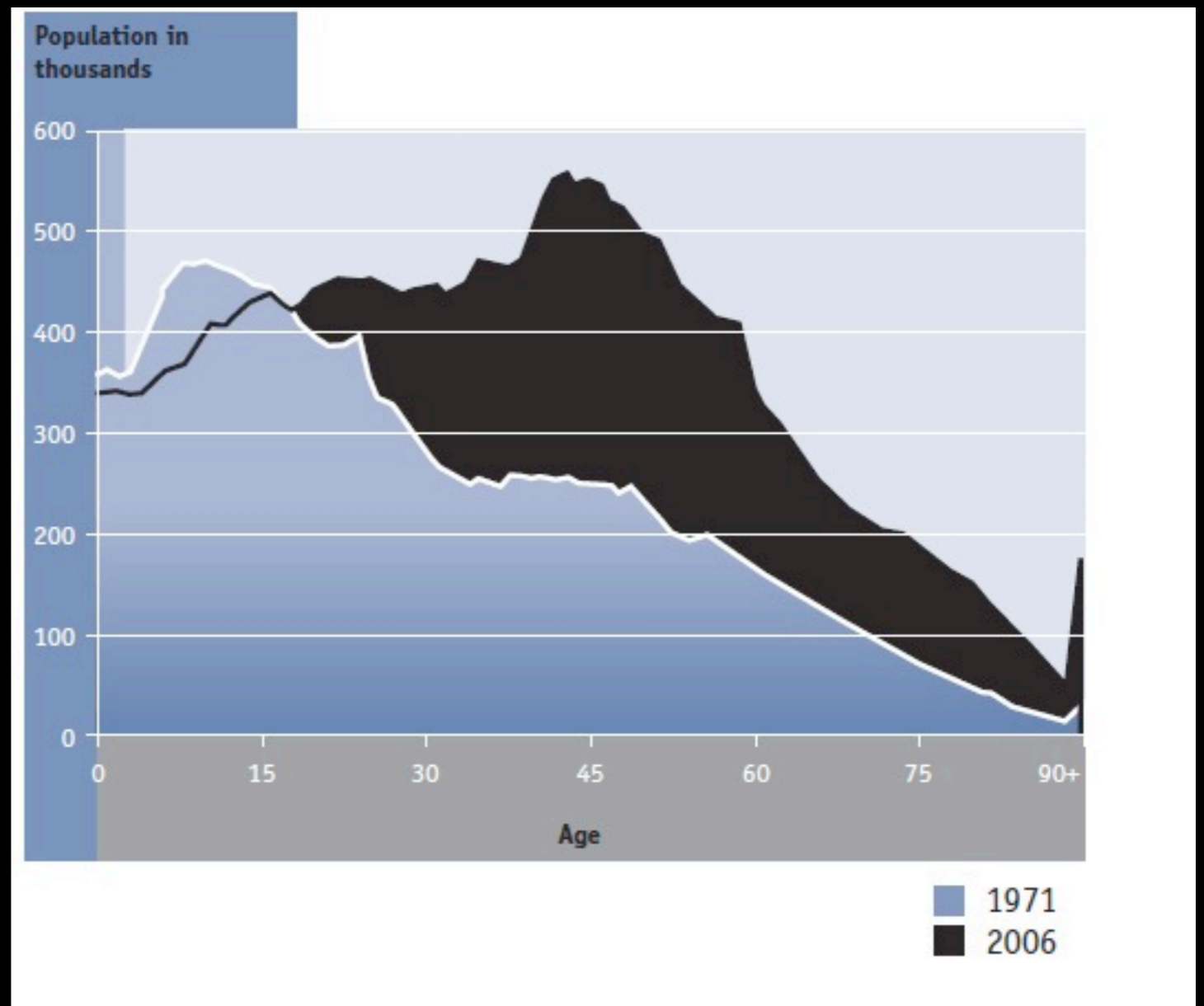
The aging brain: Dementia

- Risk to fall ill from Alzheimer's disease
- 1 : 13 (ages 65 - 74)
- 1:9 (ages 75 -84)
- 1 : 4 (ages 85 and up)



Old age in Canada

- Elderly in Canadian Society fastest growing population segment
- Number of centenarians doubles every nine years



Consequences for age-related brain disease

- 35 Million AD cases, 450,000 in Canada
- will triple by 2050
- Current annual cost of \$315 Billion worldwide, and \$5.5 Billion in Canada alone

Factors affecting the aging brain: What do we know?

- Vascular factors
- Physical activity
- Cognitive activity
- Social engagement
- Diet
- Depression

Vascular factors

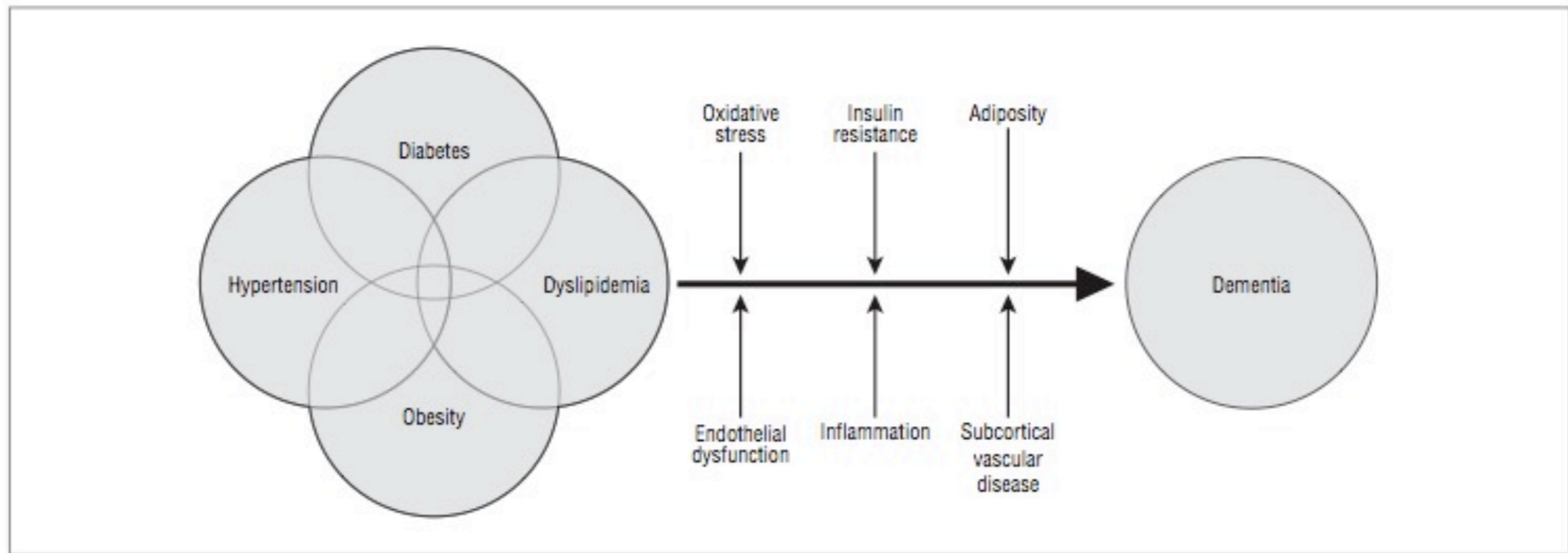


Figure. Possible mechanisms that may explain the association between vascular risk factors and an increased risk of developing dementia.

Physical activity

- Physical activity usually declines in old age
- High physical activity associated with reduced incidence of AD in old age
- mechanisms complex and multifactorial (effect via vascular system, neurotrophic factors?)

Cognitive activity

- both the exposure to cognitive challenges as well as the ability to resolve complex cognitive tasks is reduced with age
- however, not all areas are affected: example of fluid vs. crystallized intelligence
- cognitive activity in elderly leads to reduced symptoms of dementia even in the presence of neuropathology (cognitive reserve)

Cognitive activity

- benefit of cognitive training is domain specific, however
 - ★ memory
 - ★ reasoning
 - ★ mental processing speed

Social engagement

- Social engagement is typically declining throughout late adulthood
- However, in persons that maintain high social engagement a lower incidence of dementia can be observed
- interaction with cognitive and physical activity?

Diet

- Relatively independent from age, but the effects of a bad diet are amplified in old age
- Diet influences other risk factors (obesity, hypertension, diabetes, inflammation)
- positive factors: fish, fruit, vegetables, red wine, green tea, certain herbs (mediterranean diet)
- mediated by antioxidants and polyunsaturated fatty acids?

Summary

- Normal and pathological aging is associated with a wide variety of changes in the body and the brain
- A number of factors have been shown to induce interindividual variability
- vascular factors, physical and cognitive activity, social engagement, diet and absence of depression

The promise of prevention

- Primary prevention: Reduce number of new cases (who show onset of symptoms)
- Secondary prevention: Reduce the duration of illness
- Tertiary prevention: Reduce the functional (negative) consequences of the illness

Primary prevention in AD

- Five year delay in onset -> reduce incidence by half
- Ten year delay in onset -> reduce by more than two-thirds
- Ten year delay would save more than \$4 Billion per year in Canada

What defines the onset of Dementia?

- According to Reisberg's Global Deterioration Scale (1982):
- Stage 1: No complaints, subject is mentally fit
- Stage 2: Subjective complaints, very mild cognitive decline, usually not detectable with cognitive assessments
- Stage 3: mild cognitive decline: like stage 2, but very careful cognitive screening begins to detect first changes
- Transition between stages takes >10 years ('silent disease')
- thus, disease is progressing for a long time before symptoms start to become apparent

Consequences and Challenges for Prevention

- Programs and Interventions need to start in the absence of symptoms
- People must be motivated to engage in prevention even it is unclear whether they are affected
- Best possible outcome of prevention: Not getting ill!
(As compared to getting cured from a disease)
- Difficulties in recruitment and attrition
- Very cost-intensive

Challenges and opportunities of Prevention Programs

- Challenges: Strain on society, policy makers, health care system
- Opportunities: Not all preventive factors with regards to dementia have probably been identified (Inherent difficulty of identifying factors that didn't make you sick; i.e. that did not do anything)
- One of the prevention targets: Stress

So what's stress got to do with it?

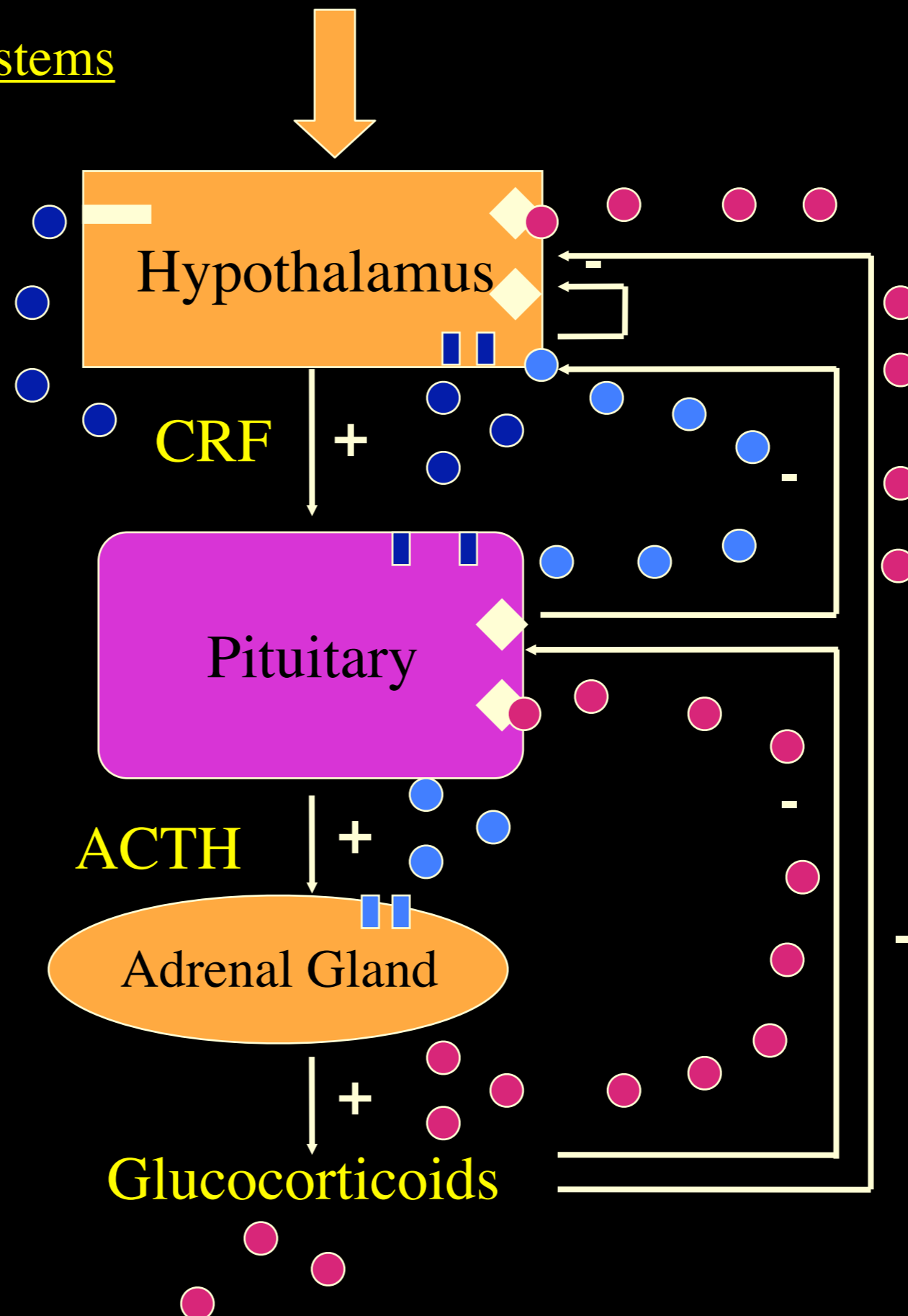
- Stress influences many of the known risk factors associated with pathological aging
- Exercise, CVD, Nutrition, Cognitive Aging
- WHO: Stress will be the second leading cause of disease by 2020
- How is stress doing that?

Acute stress: the effects

Acute effects of stress - hormonal changes in brain and periphery

Hormonal Feedback Systems

The Hypothalamic-Pituitary-Adrenal (HPA) axis



Target Cells

- CRF: increase or decrease appetite, reduce regenerative functions, increase alertness
- Cortisol: increase gluconeogenesis from the liver, increase blood pressure, increase fat storage, increase glucose uptake from the periphery, increase metabolic activity, decrease hippocampal activation, impair memory

Net effect of stress: provide energy

- Acutely, the primary effect of stress is an increase of energy... to be able to better cope with the task at hand...
- .. by fighting or flighting
- throughout evolution, a stressful situation typically involved a physical threat



Stress today

- However, typical stressors in today's society are different:
- coping with the loss of a loved one
- adapting to changes in environment, and responsibilities
- dealing with time pressure
- facing social threats, embarrassments (at work, or at home)
- in fact, the best known stressor used for investigating stress in the laboratory is:

Public speaking!



Acute Stress effects often contraindicated

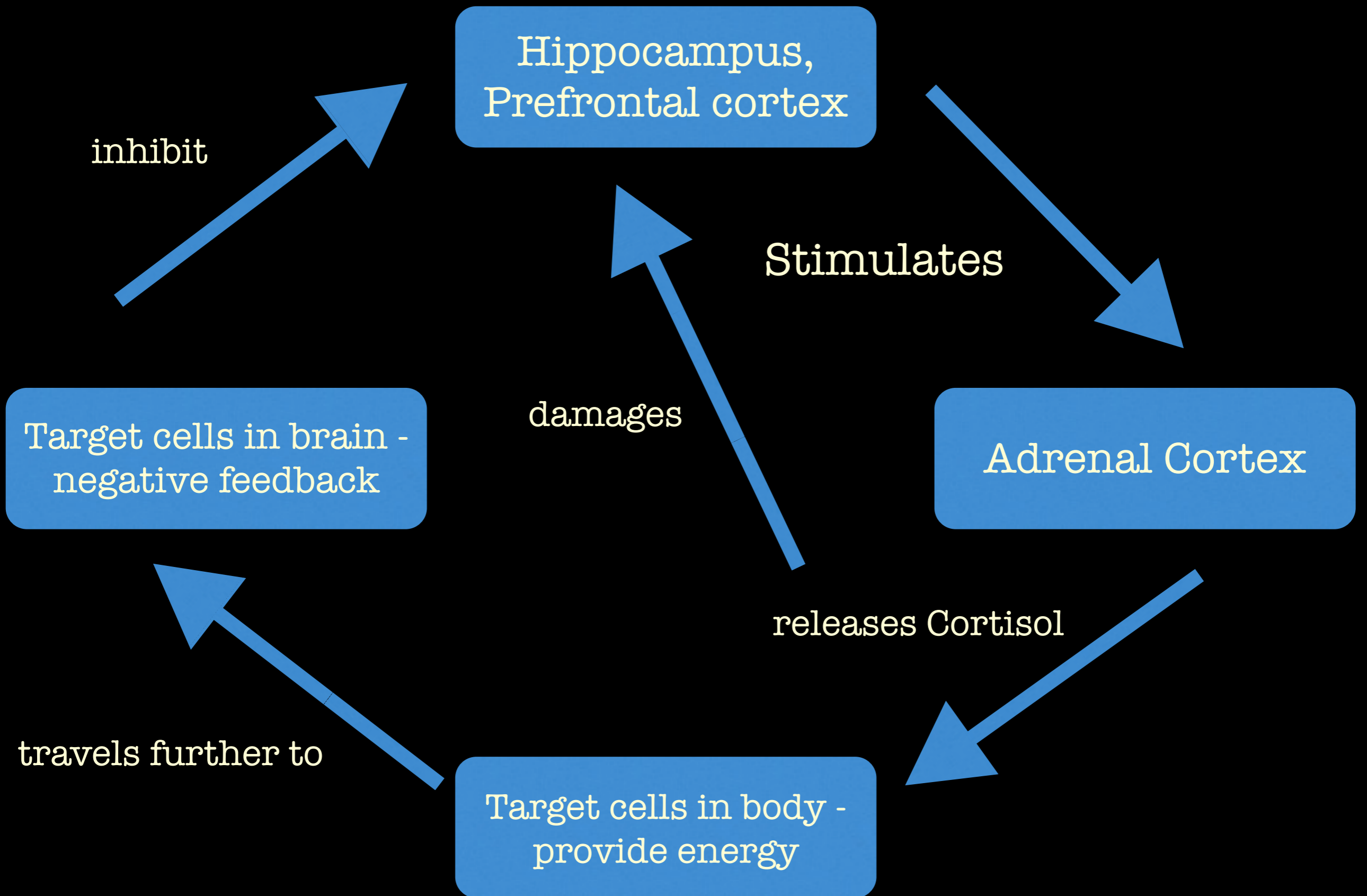
- it provides energy but energy isn't needed (optimal stage of arousal will be surpassed)
- it impairs memory but memory is needed
- it promotes fat storage but fat storage is not desirable

Chronic Stress: Peripheral effects

- Carbohydrate craving
- Trunk obesity
- Arteriosclerosis and High blood pressure

Chronic Stress: Brain effects

- Glucocorticoid cascade hypothesis
- The vicious cycle of circulating stress hormones



Long-term effects of stress

- peripherally and centrally, stress affects
- diet
- arteriosclerosis
- CVD

So is there something you can do about it?

- goes back to the definitions of stress
- stress in environment and individual
- both can be addressed
- Some suggestions:

The psychology of stress

- term derived from physics
- identifying the pressure necessary to break an object
- both related to object and environment

Stress in the literature

- Mason, 1968
- Biondi & Picardi, 1999
- Dickerson & Kemeny, 2004
- Lazarus: Demand vs. Resources

Key factors

- uncontrollability
- unpredictability
- novelty
- ego-involvement
- negative consequences
- distress
- tension
- irritability
- impatience

Overarching theories: Lazarus

- primary and secondary appraisal
- comparison of demand vs. resources
- if resources $>$ demand \rightarrow challenge
- if demand $>$ resources \rightarrow threat, stress

Conclusions: What can you do about it?

- In yourself: improve on resources, autonomy, self-concept (self-help groups, environmental structure)
- Around you: change the environment where necessary, adjust goals, withdraw from unattainable expectations