

Resilience: Implications for Delirium Onset and Recovery

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Two Faces of Aging

- Geriatric syndromes such as delirium are common, serious, costly, and need more research investment
- Most older adults are productive, high functioning citizens who contribute importantly to the society – and are not an “entitled” segment that is a financial drain on younger generations

Resilience in General:

Definition,

Importance,

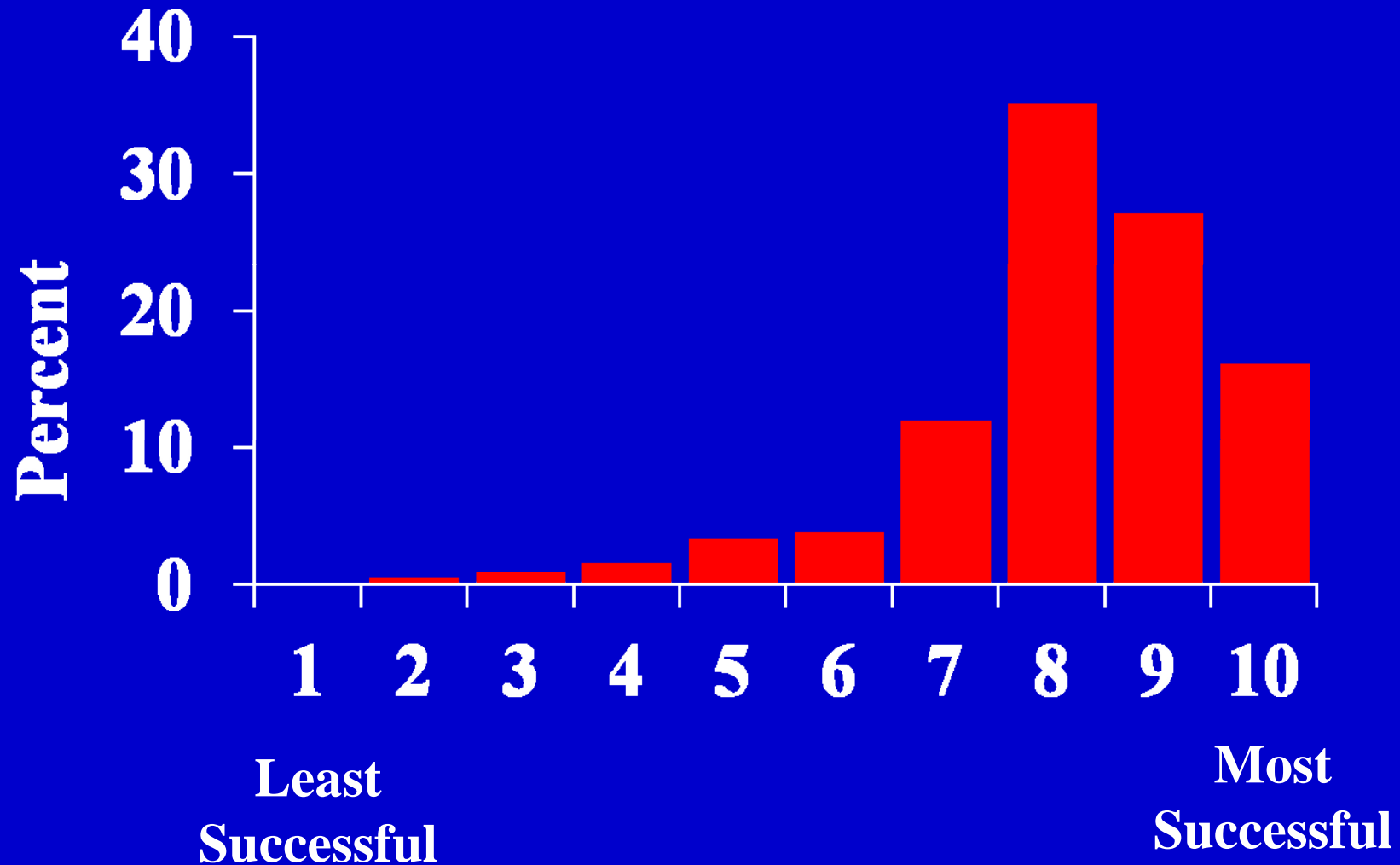
Biology,

Interventions

What is Resilience?

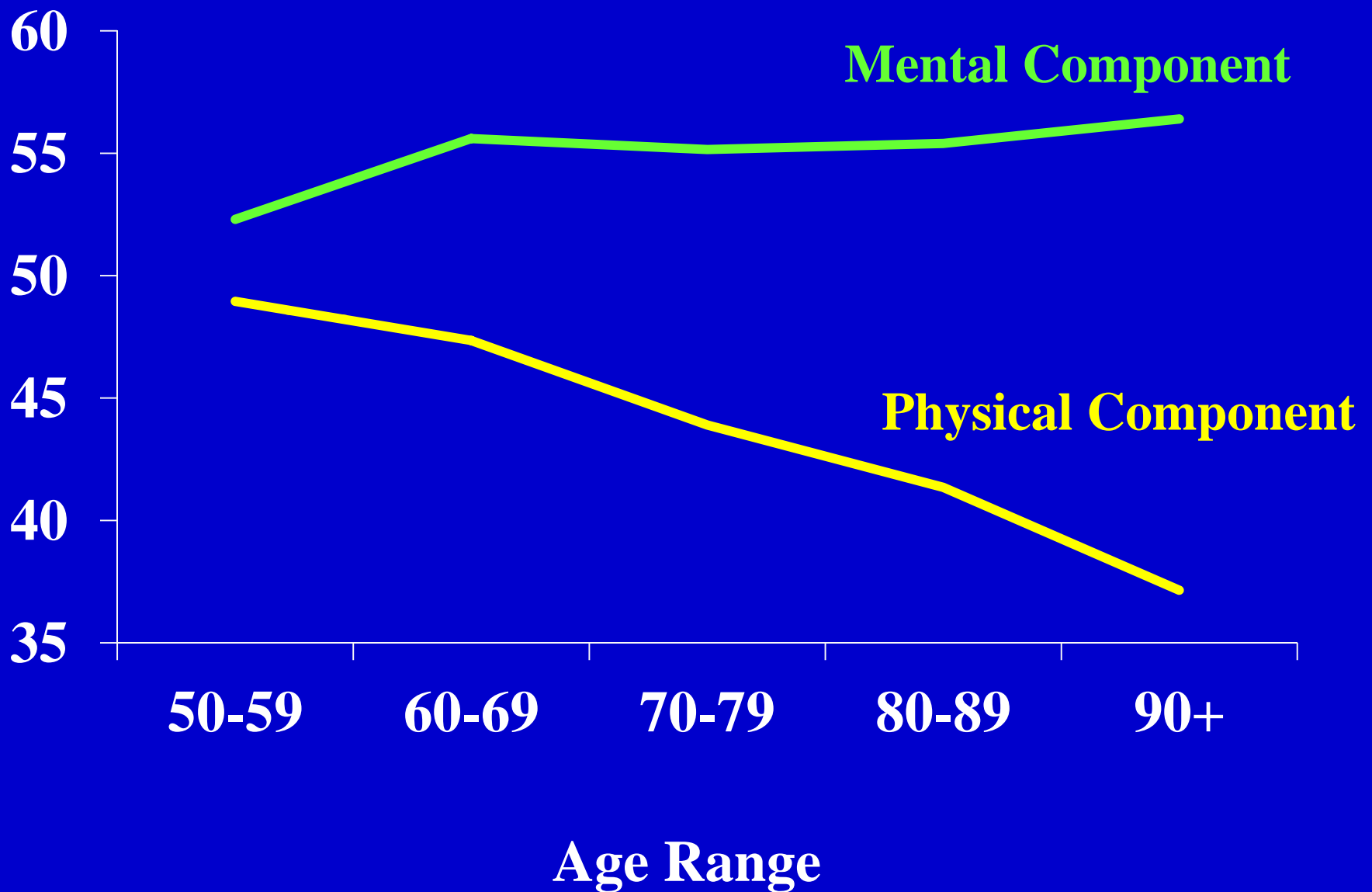
- Trait or Process or Outcome?
- Definition: Ability to adapt positively to adversity, or to recover readily from adversity
- Assessment: Connor-Davidson and other scales
- Different levels:
 - 1. “Survival” after a major adversity
 - 2. Bouncing Back: Return to pre-adversity level
 - 3. Post-traumatic Growth: Becoming stronger after recovering from adversity, to cope with future adversities, and even prevent ones from occurring

Self-Rated Successful Aging Scores in Adults Age 50-99 Years (N=1,105)



(Jeste et al, Am J Psychiatry 170:188-196, 2013)

Health-Related Quality of Life (SF-36)



Why is Resilience Important?

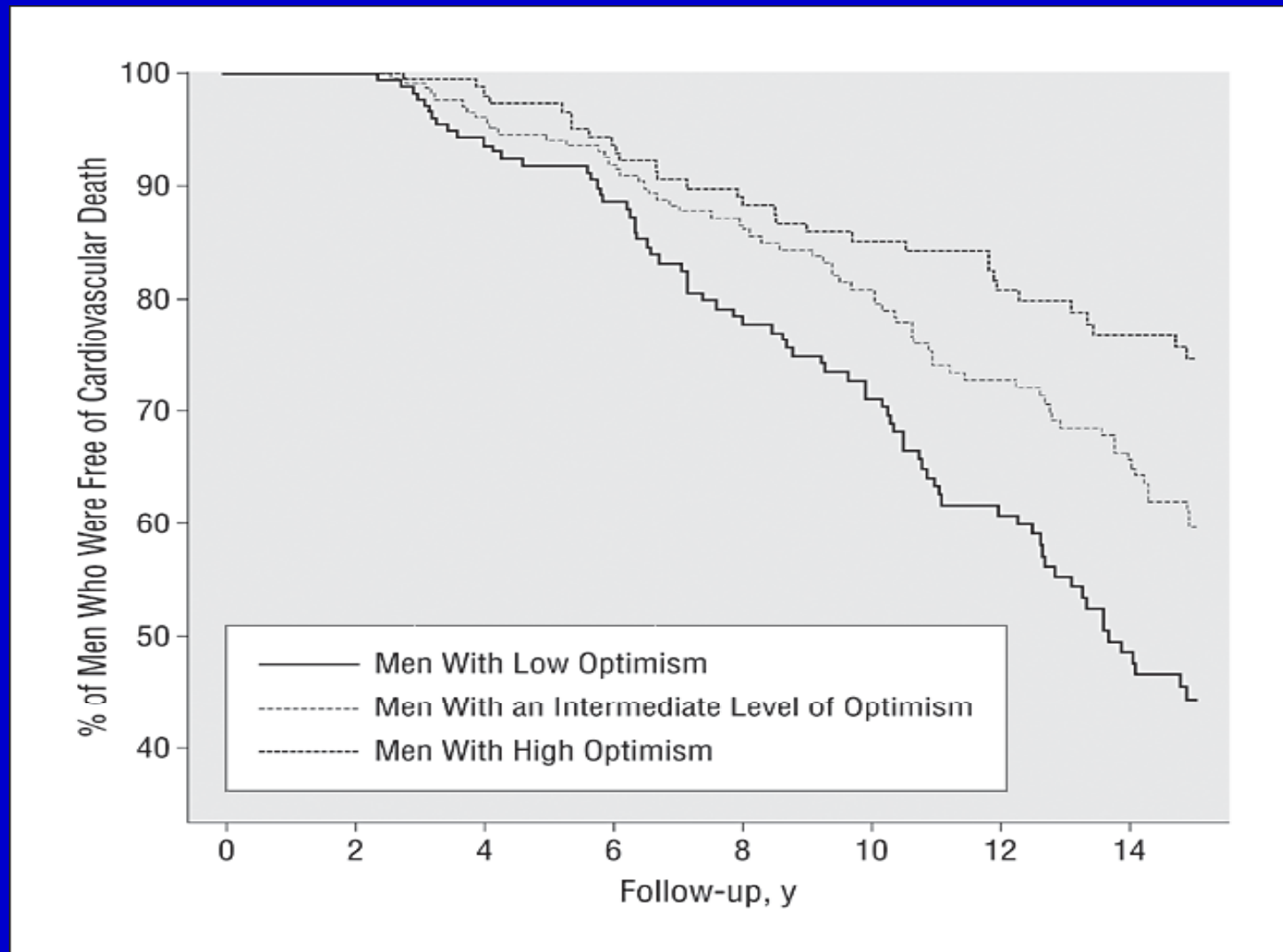
- Greater optimism, social engagement, etc.
- In physically ill patients, resilience is associated with medically desirable behaviors (self-care, treatment, & exercise adherence), and better health outcomes (emotional health & well-being, less pain, and improved physical health)
- People in their 90s, who endorsed higher levels of resilience, had a 43% higher likelihood of living to 100 years compared to their peers

(Lamond et al, J Psychiatr Res 43:148-154, 2008;

Shen & Zeng, Demogr Res 23:105-116, 2010;

Stewart & Yuen, Psychosomatics 52:199-209, 2011)

Kaplan-Meier Survival Analysis According to Tertiles of Dispositional Optimism



(Giltay EJ et al, Arch Intern Med 166:431-436, 2006)

2 Meta-analyses

- 83 Studies of Optimism: Association with cardiovascular outcomes, physiological markers (including immune function), cancer outcomes, outcomes related to pregnancy, physical symptoms, pain, and mortality (all $p < .001$)
- 148 Studies of Social Engagement (N > 300,000): 50% increased likelihood of survival among participants with strong (vs. weak) social relationships, across different groups

(Rasmussen et al, Ann Behav Med 37:239-256, 2009;
Holt-Lunstad et al, PLoS Med 7:e1000316, 2010)

Biology of Stress Resilience

Genes

1. HPA axis
2. Others

Early Life Stresses

Stress Sensitization vs.
Stress Inoculation



Epigenetics



Response to Stress:
Maladaptive vs. Resilient

(Russo et al, Nat Neurosci 15:1475-84 2012)

Neurobiology of Resilience

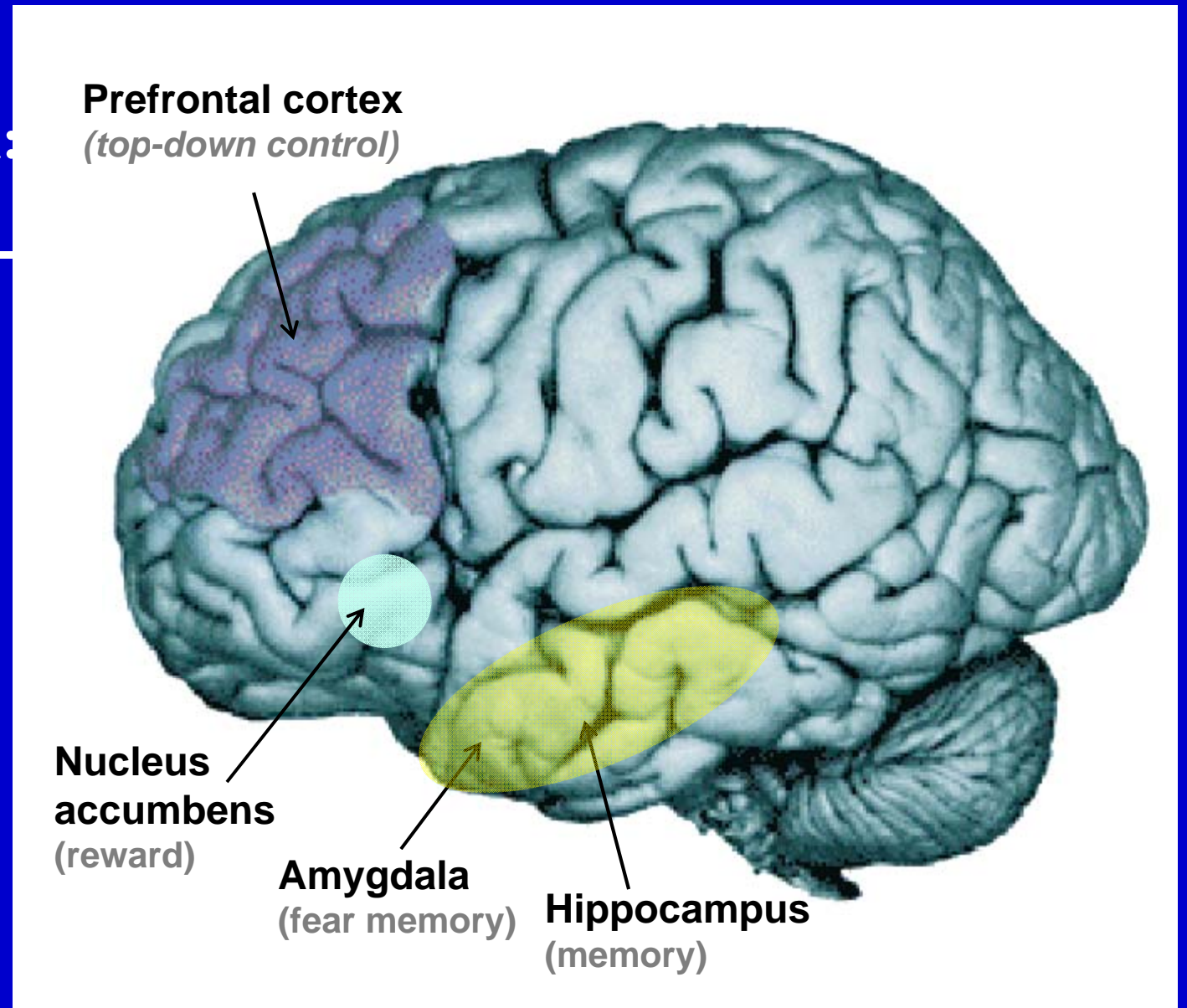
1. Heritable; Reported candidate genes: *MAO-A*, *IL10*, *FGG*, *CRHR1*, *FKBP5*, *COMT*, *5-HTTLPR*, *NPY*, *BDNF*, *NGFI-A*
2. Adaptive functioning of social behavior circuits of the brain (responsible for fear, reward, emotional regulation) involving prefrontal cortex, nucleus accumbens, amygdala, and hippocampus
3. Animal models

(Feder et al, Nat Rev Neurosci 10:446-457, 2009;
Rana et al, 2013)

Brain Imaging Studies of Resilience

Resilience is associated with:

- Increased top-down control over emotions;
- Decreased bottom-up reaction to fear;
- Increased bottom-up reward



Neuroplasticity of Adulthood

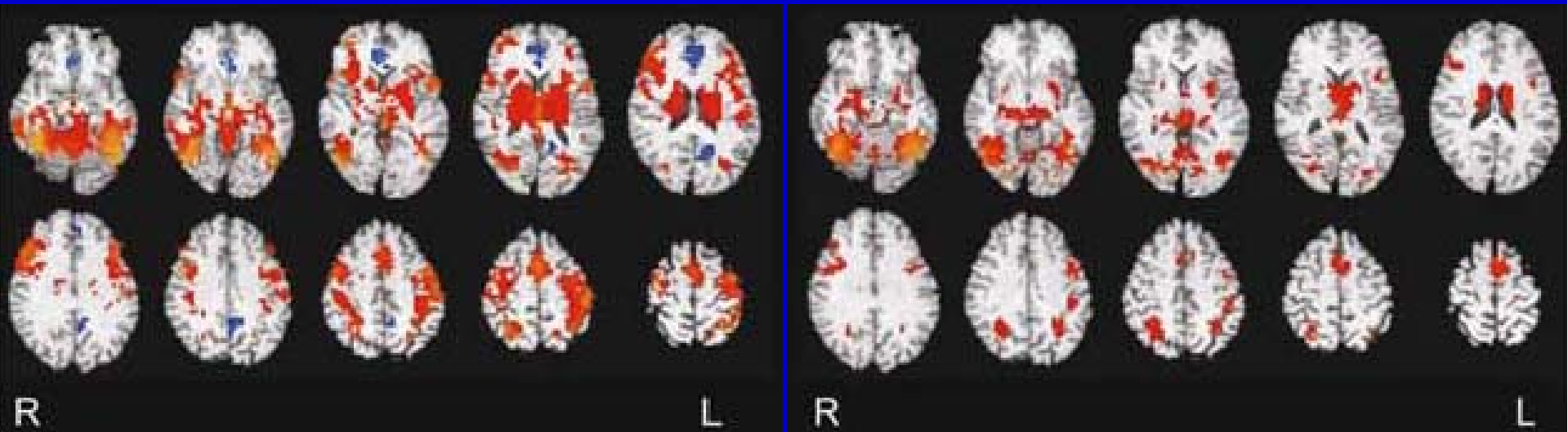
- Compensation for Neurodegeneration: Enhanced ability to recruit alternate brain networks &/or more efficient utilization of those networks, especially in prefrontal region
- Synaptogenesis & Selective Neurogenesis, if stimulated by physical & psychosocial activity
- “Sociostatic” Changes (Adaptive shifts in emotional regulation): Reduced amygdala and frontostriatal activation while viewing negative pictures or with regret, respectively

(Mather, 2004; Bangen et al, J Int Neuropsychol Soc 18:402-13, 2012; Bangen et al, J Neuropsychiatry Clin Neurosci Nov 26, 2013; St Jacques et al, J Int Neuropsychol Soc 15:819-25, 2009; Brassens et al, Science 336:612-4, 2012; Gage et al J Neurosci 22:612-3, 2002; Dennis & Cabeza, 2008; Eyler et al Biol Psychiatry 70:115-22, 2011)

fMRI Study: Whole Brain Response to Remembered Face-Name Pairs in High-Performing Older & Younger Adults

Older Adults

Young Adults



(Bangen et al, J Int Neuropsychol Soc 18:402-13, 2012)

Interventions to Enhance Resilience

- **Master Resilience Training for the armed forces**
- **Stress Management and Resilience Training (SMART)**
- **Mindfulness-Based Stress Reduction**
- **Novel Biological interventions such as Training to modulate one's own brain activity with real-time fMRI-based neurofeedback**

(Loprinzi et al, Clin Breast Cancer 11:364-8, 2011; Rose et al, 2013; Creswell et al, 2012; Caria et al, 2007)

Resilience in the Context of

Delirium:

Neurocognitive Reserve,

Psychosocial / Behavioral

Reserve,

Interventions

Neurocognitive Reserve

- **Brain Reserve (passive, fixed):** neural reserve and neural compensation
- **Cognitive Reserve (active, dynamic, modifiable):** access to complex cognitive networks
- **Neurocognitive Reserve: Education, Executive function, Complexity of occupational work, and Complexity of lifetime & leisure activities**

(Greene et al, 2009; Stern 2009; Sachdev and Valenzuela 2009; Willis et al, 2008; Kolanowski et al, 2010)

Education and Delirium

- **Samples of 491 & 461 hospitalized patients: Controlling for the effects of age, gender, dementia, comorbidity, and severity of illness, each year of completed education was associated with a 0.91 lower odds of delirium (Jones et al., 2006)**
- **779 newly hospitalized patients over age 70: Lower education was associated with development of delirium (odds ratio =0.92), and activity mediated the relationship between education and risk for delirium**

(Yang et al, 2008)

Psychosocial / Behavioral Reserve

- **Depression vs. Resilience**
- **Intelligence, Optimism, (Wisdom)**
- **Coping strategies, Spirituality**
- **Social engagement and Social support**
- **Mentally stimulating physical activity (e.g., Video-Exercise games such as Nintendo's Wii)**

(Jones et al, 2010; Wald et al, 2006; Rosenberg et al, Am J Geriatr Psychiatry 18:221-6, 2010)

Depression and Delirium

- **416 newly hospitalized patients: 2 depressive symptoms (dysphoric mood and hopelessness) predicted of incident delirium, controlling for physical & mental health (McAvay, et al., 2007)**
- **998 patients screened for postoperative delirium: Pre-operative depressive symptoms, especially combined with executive dysfunction, predicted post-operative delirium (Smith, et al. 2009)**
- **100 pre-operative patients age >50: Depressive symptoms (and executive dysfunction) predicted post-operative delirium (Greene et al, 2009)**

Intervention to Enhance Reserve for Preventing Delirium in Dementia

- **Cognitive training via stimulating activities is reported to evoke cognitive processing and facilitate plasticity in dementia**
- **30-minute sessions of tailored cognitively stimulating recreational activities for up to 30 days are hypothesized to decrease severity and duration of delirium and improve physical & cognitive function in a cost-effective way**

(Kolanowski et al 2010, 2011)

A Call for a New Positive Psychiatry

- **A new model of Positive Psychiatry that would focus on recovery, promotion of successful aging, neuroplasticity, prevention, and interventions to enhance positive psychological traits such as resilience, optimism, and social engagement**
- **Clinical, neurobiological, and intervention research in this area is clearly warranted**

(Jeste & Palmer, Br J Psychiatry 202:81-83, 2013)

Specific Needs for Research

- **Defining the construct of resilience in the context of delirium: neurocognitive as well as psychosocial / behavioral reserve**
- **Developing validated and practical measurement tools for these reserves**
- **Longitudinally examining bidirectional relationship between delirium and the reserves**
- **Testing pragmatic and cost-effective multi-domain prevention and intervention strategies to enhance the reserves**

SUMMARY

- **Resilience in older people is underestimated and understudied**
- **Psychosocial / Behavioral Reserve is likely to be enhance Neurocognitive Reserve**
- **Resilience, partially genetically determined, is modifiable through environment and behavior**
- **Enhancing positive traits such as resilience through behavioral or biological interventions will become a key component of medical care**