Principles in the Study of Brain Health and Aging

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Introduction

- From its early days, neuroimaging has been used to study brain changes due to both disease and aging.
- Most research has focused on pathological changes due to diseases like Alzheimer’s.
- A large number of studies have also examined brain changes in “normal” or “healthy” aging.
- A smaller, but growing emphasis has been placed on individual differences among older individuals in terms of cognition and emotion.
Outline

- Structure of the aging brain
- Relationship of structural changes to cognitive and emotional changes
- Brain function in old age
- Relationship of functional patterns to cognitive and emotional abilities
- Strategies to maintain brain health
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Structural Imaging

- Used for visualization and morphometric measurement of brain anatomy
- Primarily developed for detection of abnormalities by visual inspection (radiology)
- Co-opted for morphometric analyses of brain structures and tissue-types
Magnetic Resonance Imaging (MRI)

- Originally called NMR because capitalizes on nuclear magnetic resonance
- Earliest clinical uses in early 1980s
- Subject placed in strong static magnetic field which causes alignment of atomic nuclei
- Radiofrequency pulse applied that introduces phase coherence in random spins
- This coherence results in a magnetic signal whose decay varies depending on tissue type, which is detected by the MR scanner
MRI Scanner

Source: Mark Cohen’s slides
T1 Weighted MRI Images

CSF is dark
Grey matter is grey
White matter is light
Bone is white

Schizophrenia Patient  Same Age Healthy Control
Structural Changes in Old Age

- Many structures get smaller with age; fluid filled spaces get larger
- The amygdala, a structure important for emotional processing, may not change as much with age

Fjell et al, 2013
Structural Changes in Old Age

- The cortex thins with age, particularly in prefrontal and middle temporal regions
- Parts of prefrontal cortex important for emotional regulation are relatively preserved or may even thicken

Fjell et al, 2009
Diffusion Tensor Imaging (DTI)

- MR-based method first used in early 90’s
- Brownian motion of water molecules in the brain is constrained within fibers (anisotropic diffusion) and attenuates MR signal
- Tensor characterizes direction and magnitude of diffusion
- Can produce images and measurements of white matter connections
Tractography

Source: LOCI
White Matter Integrity & Aging

- Connections between parts of the brain weaken with age
- These changes are most pronounced in anterior regions of the brain and for measures affected by myelination

Davis et al, 2008
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Cognitive Performance

Salthouse, 2000, 2003
Variable decline & preserved domains

Working Memory

Word Knowledge

Wilson, 2002
In general, bigger structures and stronger connections are better (83% of the 50 reviewed studies).

Most evidence for this in medial temporal lobe and prefrontal cortex.

Not clear whether this is only true in older adults or may also be true in younger adults.

Fjell et al (2006) found that those seniors with the best cognitive performance had thicker cortex than young adults in some regions.
Thicker Cingulate and Subcallosal Gyrus in High Performing Elders Compared to Young Participants

Fjell et al, 2006
Relationship to Stress

Lupien et al, 1998
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Functional MRI (fMRI)

- Introduced in early 90’s
- Blood oxygenation level dependent (BOLD)
  - More oxygen delivered to active regions than can easily be consumed, so excess O₂ in these areas
  - De-oxygenated hemoglobin (Hb) is paramagnetic (disruptive to magnetic signal)
  - So, in active areas with more oxygenated Hb, the MR signal is more intense
- Arterial spin labelling (ASL)
  - Images perfusion / blood flow directly
  - May be closer to neurons than BOLD
Raw BOLD Image

T1 Weighted

T2* Weighted

Source: Robert Cox’s web slides
Processed BOLD Images
Resting State Default Mode Connectivity

Fox & Greicius, 2010
ASL Perfusion Image

Source: Scheffler website
Functional Changes in Old Age

- **Resting blood flow / metabolism**
  - Decreases with age, particularly frontal
  - Less coordination of low-level fluctuations in BOLD signals in particular networks (at rest or during a task)

- **Altered task-related response**
  - Posterior to anterior shift in aging (PASA)
  - Hemispheric asymmetry reduction in older adults (HAROLD)
  - Ventral to dorsal shift in prefrontal activity
Default mode changes

Jones et al, 2011
Brain function during a learning task

- 9 young (avg age = 27); 10 old (avg age = 75) scanned with FMRI
- Studied face-name pairs
- Recognition task after scanning: pick correct name for the face
- Brain response during encoding of successfully remembered face-name pairs compared between groups

Bangen et al, 2012
Age-related brain response changes

Hemispheric Asymmetry Reduction in OLDer Adults (HAROLD)

Posterior to Anterior Shift of Activation (PASA)
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Greater Right Prefrontal Response during Learning in Older Good Learners
In general, results suggest that PASA and HAROLD pattern are most apparent in those with the best cognitive performance → compensation

Evidence for compensation is most pronounced in the frontal cortex
Positivity and aging

- Negative emotions decline with age while positive emotions stay the same – relative positivity
- Older people pay attention to and remember positive events more than negative events

Carstensen et al, 2000
Optimism, attitudes, and aging

- Optimists are more resilient, less depression, have greater social support, live longer, and are healthier
- Older individuals are more optimistic (Lennings, 2000)
- Positive attitudes towards aging are related to better cognitive performance (Hertzog & Hultsch, 2000)
- Activating negative stereotypes makes age-related cognitive deficits worse (Hess et al, 2003)
Brain Response in Older Optimists

- 16 older adults (avg age=78) who ranged in optimism scores from average to very optimistic
- fMRI imaging during processing of fearful faces
Response to fearful faces

Dorsal Medial PFC (\(\eta^2 = 0.17\))

Ventral Medial PFC (NonSig)

Amygdala (\(\eta^2 = 0.14\))
Optimistic brains less active when processing fearful faces

Bangen et al, JNCN, 2013
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"I was wrong...you can teach an old dog new tricks."
Videogame cognitive enhancement

- Working memory and sustained attention were also improved after the multi-task training

Anguera et al., Nature, 2013
Videogame brain enhancement

Anguera et al., Nature, 2013
Six months of aerobic exercise increased brain volume in older adults

Colcombe et al, 2006
11 Hours of Meditation (Integrative Body-Mind Training) Increased Fiber Integrity in Left Ant. Corona Radiata

Tang et al., PNAS, 2010
- Calorie restriction (Okinawa diet – nutrient rich, low calorie diet)
- Physical exercise
- Optimizing stress
- “Super foods”: broccoli, vitamin E, curcumin
- Psychosocially stimulating environment
- Positive attitude
- Learning new skills
- It is never too early nor too late to start
Thank you for your attention!

Questions?