Modulating the Aging Brain to Learn

presented by

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Outline

• The Aging Brain
  – What Changes as we age?
  – Functional Neuroimaging Aging Models and testable predictions

• Inter-Individual Differences and Mechanisms
  – Cognitive Reserve
  – Aging Neuronal Gain Control on Cognition (Neurotransmitters)

• Non-invasive Neuromodulations
  – Cognitive Training (Cognitive Reserve)
  – Non-invasive Neurostimulation (Neurotransmitters)
The Aging Brain
- What Changes as we age?
- Functional Neuroimaging **Aging Models** and testable predictions

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What Changes as we age?
Cognitive Performance

Figure 1
Cross-sectional aging data adapted from Park et al. (2002) showing behavioral performance on measures of speed of processing, working memory, long-term memory, and world knowledge. Almost all measures of cognitive function show decline with age, except world knowledge, which may even show some improvement.

Park & Reuter-Lorenz, 2009
What Changes as we age?

Structural Brain Volume

Brain regions that reduce in volume with age.

Brain regions with minimal reduction or stable volume with age.

Figure 2
Cross-sectional and longitudinal aging brain volumes across various brain regions (adapted from Raz et al., 2003). Each pair of line-connected dots represents an individual subject's first and second measurement. The caudate, hippocampal, cerebellar, and frontal regions all show both cross-sectional and longitudinal reduction in volume with age. The entorhinal, parietal, temporal, and occipital regions are relatively preserved with age.

Park & Reuter-Lorenz, 2009
FUNCTIONAL CHANGES IN THE AGING BRAIN
Repetition Helps
(Miyakoshi, Chen et al., Brain Imaging and Behavior, 2012)

- **fMR-adaptation**: Reduction in the magnitude of neural activity as a result of repeated stimuli presentation within functionally relevant cortical areas

- Older adults have reduced FMR-Adaptation

- Extensive stimulus repetition can diminish age-related differences in younger and older adults in **fMR-adaptation**

- fMR-Adaptation is associated with better cognitive performance
Changes in Strategies in Kanji Reading
(Wu et al., 2014)

Fig. 1. The fMRI task paradigm. F: fixation (i.e., rest condition); L: line orientation judgment; H: homophone judgment. Each block lasted for 24 s.

(A) Young adults showed a preference for a semantically mediated pathway from orthographic inputs to the retrieval of phonological representations.

(B) Older adults preferred a direct connection from orthographic inputs to phonological lexicons prior to the activation of semantic representations.

- Older adults preferred a direct connection from orthographic inputs to phonological lexicons prior to the activation of semantic representations.

- The shift in reading pathways accompanied by slowed reaction time for the elderly might suggest age-related decline in the efficiency of network connectivity.
Neural mechanisms for brain function

Compensation
• Recruitment of alternate network by older adults
  – is associated with better performance (e.g. Cabeza, 2002)
  – to maintain performance (e.g. Grady, Maisog & Horwitz, 1994; Madden et al., 1999; Reuter-Lorenz, 2002)

Dedifferentiation
• Decreased in neural specificity with age:
  – broadening of responses for the specific region to a wider array of input as we age (Baltes & Lindenberger, 1997; Lindenberger & Baltes, 1994)
  – due to increased level of noise or decreased levels of functional integration (Li, Lindenberger & Sikstrom, 2001; Rajah & D’Esposito, 2005)
• Is this compensation to maintain performance or failure of compensation?
Adaptation of Brain Functional and Structural Networks in Aging
(Lee et al, PLoSOne, 2015)

- Age-related changes in the functional, structural connectivity between PFC and the posterior brain (controlling for cortical thickness)
- 174 Singapore Chinese adults, 21-80 years, structural, resting-state fMRI, HARDI

Prefrontal Cortex reorganization in aging may be adapted to the need of compensation for resolving less distinctive stimulus information from the posterior brain regions.

Dedifferentiation as an impetus for compensation
Aging Models

**HAROLD:**
Hemispheric Asymmetry Reduction in Older Adults (Roberto Cabeza)

Prefrontal Cortex activity during source Memory was **right lateralized** in Young and Old-Low participants but **bilateral** in Old-High participants. (Cabeza et al. 2002)

**PASA:**
Posterior-Anterior Shift in Aging Compensation:

- Older adults showing less occipital activity had more frontal activity
- Young and older adults were matched on accuracy performance
- Older adults with **greater frontal recruitment** showed **better** cognitive performance


Y: Young; O: Old; M: Memory retrieval; P: visual Perception task
Aging Models

**CRUNCH: Compensation-Related Utilization of Neural Circuits Hypothesis**

(Reuter-Lorenz and Cappell, 2008)

Age-related activation differences should disappear when task difficulty is comparable.

**HAROLD is a special case of CRUNCH**

(Berlinger et al. 2013)

The differences are due to processing capacity.

(Schneider-Garces et al., JOCN 2009, 22(4)655-669)
Aging Models: STAC

- Scaffolding Theory of Aging and Cognition (Park and Reuter-Lorenz, 2009)
Testable Predictions from STAC

• Is there a **direct relationship** between brain degradation and degree of scaffolding?

• Does **compensatory scaffolding** at a younger age predict cognitive vulnerability in later adulthood?

• What **lifestyle activities** promotes scaffolding (brain health)?

• How much do specific types of **cognitive training (neuromodulation)** change the brain?
  – What type is most effective in sustaining cognitive health?
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Explaining Individual Differences

COGNITIVE RESERVE

Premorbid Intelligence

Education

Literacy, Occupational complexity, leisure activities, cohesion of social networks, personality variables
What is Cognitive Reserve?

Individual’s ability to make flexible and efficient use of available brain reserve when performing task to compensate for age-related effects or pathology.

Models of Task related neural activity versus task demands

Mechanistic Roles of Cognitive Reserve (Steffener & Stern, 2012)
PET receptor imaging studies showing age-related declines in receptor binding potentials in DA, 5-HT and ACTH systems.

NEUROTRANSMITTERS AND AGING NEURONAL GAIN CONTROL ON COGNITION
Decline in DA neuromodulation by stochastic attenuation of the gain (G) parameter with the sigmoidal activation function, that models presynaptic to postsynaptic input-response transfer

Li & Rieckmann, 2014

Neuronal Gain Control Model: captures aging-related decline in dopaminergic neuromodulation
Aging Models: STAC

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**Neural Challenges**
- Shrinkage
- White Matter Changes
- Cortical Thinning
- Dopamine Depletion

**Compensatory Scaffolding**
- Frontal Recruitment
- Neurogenesis
- Distributed Processing
- Bilaterality

**Scaffolding Enhancement**
- New Learning
- Engagement
- Exercise
- Cognitive Training
- Non-invasive neurostimulation

**Level of Cognitive Function**

**Cognitive Reserve**

**Neuronal Gain Control**

**Functional Deterioration**
- Dedifferentiation of Ventral Visual Area
- Decreased Medial Temporal Recruitment
- Increased Default Activity
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Cognitive Training
(Karback & Kray, Dev Science, 12:6, 2009)

- Training in Executive control in task-switching in near and far transfer

- Suggested training in executive attention had far transfer to other executive tasks and fluid intelligence

- Jaeggi et al, PNAS (2008) and Rudeback et al, PLOSOne, (2012) supported transfer to fluid intelligence with demanding WM task via intensive training
Cognitive Training
(Karr et al, Neuropsychology 2014)

Meta-analysis of cognitive training and physical exercise studies on executive functions in older adults over the last 50 years

- mental stimulation, physical exercise and social engagement
Non-Invasive Brain Stimulation

• Repetitive Transcranial Magnetic Stimulation (rTMS)

• Transcranial Direct Current Stimulation (tDCS)
Modulation by Non-invasive Brain Stimulation (NIBS)
(Brunelin & Fecteau, Brains Stimulation, 2015)

NIBS to enhance neuronal gain control in aging
NIBS Research in Aging is still limited

- **tDCS of right DLPFC increased older adults’ conscious awareness of error commission** (Harty et al. J Neurosci, 2014)

- **Delayed effect**: tDCS over temporoparietal cortex had no immediate effect of learning of objects and locations, improvement only seen after 1 week (Flöel et al, Neurobiol. Aging, 2012)

- **Differences** comparing results across age groups
  - tDCS stimulation of anterior temporal lobes improved face recall greater in older than younger adults (Ross et al, 2011)
  - Disproportionately benefit older adults’ learning of motor sequences (Zimerman et al, 2013)
  - Young adults’ memory performance improves with tDCS of left or right hemisphere, but older adults only improve with left hemisphere stimulation (Manenti et al, 2013)
  - Older adults with **higher education benefited** from tDCS during working memory task, but not older adults with lower education (Berryhill et al, 2012)

**Anodal tDCS (atDCS) stimulation**: older adults’ number of errors on a word generation task is reduced from their performance under sham stimulation and reaches the level of young adults (Meinzer et al. J. Neurosci, 2013)
Considerations for Future Directions for Neuromodulation (in older adults)

- **Maintenance**: What is the time period over which effects can persist?

- Is cognitive training **necessary** to elicit long-term changes?

- Is neurostimulation more effective for some networks or regions than others?

- Cognitive training with neurofeedback vs external stimulation

- Combining cognitive with neurostimulation to enhance effects?

- How does aging affect which regions to be targeted, in isolation or as part of a network?
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