Crossroads of Attention and Memory:
Top-down modulation deficit theory of cognitive aging

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My Motivation

- Our population is aging.
- Expectations of what we should be capable of has changed.
- Age-related cognitive deficits cross multiple domains.
- Even mild cognitive deficits decrease quality of life.
- Goal: Identify alterations in fundamental brain mechanisms that underlie the broad spectrum of cognitive aging deficits:
  Top-down modulation

You’re Motivation

- You’re aging.
- Top-down modulation serves at the interface of perceptual, attentional and memory processes.
- Alterations in top-down modulation may underlie cognitive deficits associated with diverse array of neurological and psychiatric diseases.

The crossroads of attention and memory
The crossroads of attention and memory

"The true art of memory is the art of attention.
- No man will read with much advantage, who is not able, at pleasure, to evacuate his mind...
- If the repositories of thought are already full, what can they receive?
- If the mind is employed on the past or future, the book will be held before the eyes in vain."

- Samuel Johnson (1759)
Neurophysiology of Top-down Modulation

Stimulus-Present Modulation
- Perception: Detection, Discrimination
- Memory Encoding

Stimulus-Absent Modulation
- Working Memory Maintenance
- Long-term Memory Recall
- Mental Imagery
- Expectation

Research Program Overview

- How does it work?
- What goes wrong?
- Can we fix it?

- Normal Aging
  - fMRI

- Cognitive Training
  - EEG

- Dementia
  - TMS

- Pharmacology
  - Rx

Top-down Modulation and Aging

Younger participants
- Age = 18 - 30 y.o.
- Education = avg 15 years

Older participants
- Age = 60 - 80 y.o.
- Education = avg 15 years

Older participants reflect the healthy older population

No medications, depression, dementia

Equivalent to age-matched controls on executive & memory testing
Interference

- Internal
  - Intrusions (mind wandering)
  - Diversions (multi-tasking)
- External
  - Distractions (irrelevant stimuli)
  - Interruptions (multi-tasking)

Age-related changes in top-down modulation are selective for deficits in suppression

Younger

Trye 1 2 3

Older

Trye 1 2 3

Scene-selective area

Normal aging is associated with a selective deficit in top-down suppression of irrelevant information (i.e., preserved enhancement).

★ The suppression deficit:
- is associated with working memory impairment.
  - younger adults - Rutman et al. JOCN 2009; Zanto & Gazzaley / Neuroscience 2009
- occurs only in early stages of visual processing (within first 200 ms).
  - Gazzaley et al. PNAS 2008; Zanto et al. Cortex 2010
- occurs whether individuals are prepared or unprepared for distraction.
  - Zanto et al. Cortex 2010
- whether distraction is temporally displaced or concurrent with relevant info.
  - Chadick & Gazzaley (in review)
- diminishes with limited practice (1 hr.), but still persists.
  - Clapp & Gazzaley Neurobiology of Aging 2010
  - younger adults - Berry et al. J Neuroscience 2009
- is associated with changes in prefrontal-visual cortical functional connectivity.
  - Chadick & Gazzaley (in review)
What is the impact of distraction and interruption on working memory in aging?

Clapp & Gazzaley Neurobiology of Aging (2010)

What is the neural basis of the greater impact of distraction and interruption in aging?

Clapp & Gazzaley Neurobiology of Aging (2010)

What is the neural basis of the greater impact of interruption in aging?

Clapp, Rubens & Gazzaley Cerebral Cortex (2010)
What is the neural basis of the greater impact of interruption in aging?

**Impact of Interference on Working Memory in Monkeys**

10 Bonnett Macaques trained on delayed-nonmatch to sample task
5 younger (9-11 y.o.) / 5 older (21-28 y.o)

**Humans**

<table>
<thead>
<tr>
<th>No Interference</th>
<th>Distraction</th>
<th>Interruption</th>
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<tbody>
<tr>
<td>Working Memory Accuracy</td>
<td>90</td>
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**Macaques**

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Courtesy of Carol Barnes and colleagues
Impact of Interference on Perception

Impact of Distraction on Long-Term Memory

Stimulus Absent
Top-down Modulation
Working Memory Maintenance
Long-term Memory Recall
Mental Imagery
Expectation

Impact of Distraction on Long-Term Memory

Study Session
One hour...
Test Session
Hear... “crown”
Press... “3”
(options: 1,2,3,4 or new)

168 novel images

Visual Distraction
Auditory Distraction
Impact of Distraction on Long-Term Memory

fMRI Experiment: Visual Distraction

Wais et al., Journal of Neuroscience (2010)

Neural Mechanisms of Top-down Modulation

- Gazzaley et al., Journal of Cognitive Neuroscience (2005)
- Gazzaley et al., Neuropsychology (2007)
- Rutman et al., Journal of Cognitive Neuroscience (2009)
- Berry et al., Journal of Neurophysiology (2009)
- Zanto & Gazzaley, Journal of Neuroscience (2009)
- Clapp, Rubens & Gazzaley, Cerebral Cortex (2010)
- Zanto, Rubens & Gazzaley, Neuroimage (2010)
- Wais et al., Journal of Neuroscience (2010)
- Bollinger et al., Journal of Neuroscience (2010)
- Wais & Gazzaley, Psychonomic Bulletin and Review (2011)
- Wais, Kim & Gazzaley, Cerebral Cortex (2011)
- Zanto et al., Nature Neuroscience (2011)
- Chadick, & Gazzaley, Nature Neuroscience (2011)

Gazzaley Neuropsychologia (2011)

Age-related Alterations in Top-down modulation

- Gazzaley et al., Neuropsychology (2007)
- Gazzaley et al., PNAS (2008)
- Zanto, et al., Cortex (2010)
- Clapp & Gazzaley, Neurobiology of Aging (2010)
- Zanto, Toy & Gazzaley, Neuropsychologia (2010)
- Anguera & Gazzaley, Clinical Neurophysiology (2011)
- Bollinger et al., Neuropsychologia (2011)
- Wais & Gazzaley, Brain Research (2011)
- Clapp, Rubens & Gazzaley, PNAS (2011)
- Zanto et al., Journal of Neuroscience (2011)
- Zanto et al., Journal of Neuroscience (2011)
- Kalkstein et al., Journal of Neuroscience (2011)

Gazzaley Principles of Frontal Lobe Function (2011)

Top-down modulation deficit in the aging brain: A new theory of cognitive aging

- Both stimulus-present and stimulus-absent top-down modulation are altered in normal aging.
  (e.g., discrimination, memory encoding, maintenance, & recall, mental imagery & object-based and temporal expectation)

- Alterations in top-down modulation are associated with widespread cognitive performance deficits.
  (e.g., working memory, long term memory & perception)

- Age-related changes in prefrontal-sensory cortical networks may underlie impaired top-down modulation and cognitive deficits.

So, where do we go from here?

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