Strategies for Successful Brain Aging

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How does cognition change with age?

- Harder to learn new things
- Harder to multitask
- Harder to recall ‘when’ and ‘where’
- Harder to make and remember associations e.g. faces and names
- Not everyone changes.
- Up to 20% of older adults perform as well as young adults on memory tests.
Different cognitive aging trajectories

Development 0-24
Adult life 25-65
Older age 65+

Cognitive Function

Age

Individual Differences

Cognitive impairment threshold
How does the brain change with age?

- Cortical mass shrinks particularly in the **hippocampus** (memory) and the **frontal lobes** (higher cognitive function)

- **Synapses and dendrites** are reduced (NOT **cell death**)!

- **Chemical messengers** (neurotransmitters) reduced

- **Connections** (white matter) more sluggish

- **Vascular** pathologies accumulate
Pick a card, any card

Concentrate... remember your card...

Now your card is gone...
Memory only for the gist

You have a limited capacity and your long-term memory held only the gist.
A little test of your memory
Which one of the pair did you see?
Which one of the pair did you see?
Memory is pretty darn good...

Almost 90% accurate!

Standing (1973)
It’s also pretty automatic

- **Automatically** and **incidentally encodes information** without intention or specifically attending to it.

- Exploration is learning. Want proof? Have you seen this picture before?
But it’s far from perfect

- Which of these two pictures did you see?
Distinguishing similar memories

Young adults

Old
Similar
New

Proportion of response

Novel
Similar Lure
Repetition

Older adults

Old
Similar
New

Proportion of response

Novel
Similar Lure
Repetition

Yassa et al. (2010)
Different aging trajectories

- Young Adults
- High Performing Older Adults
- Low Performing Older Adults

Individual Differences

Yassa et al. (2010)
Supplementation

- Antioxidants
- Vitamin E
- Coenzyme Q10 (idebenone)
- Vitamin B 12
- Coconut oil
Resveratrol

• Present in skins and seeds of red grapes.

• Some evidence in animal models that resveratrol **clears amyloid beta peptides** (Alzheimer’s pathology)

• So far, one trial suggests that it can be used in AD patients to **slow down decline** but still too early

• Typical doses used in clinical trials are ~1000 mg a day.
Curcumin

• Curcumin (in the Indian spice turmeric) shows promise.

• In animals, it reduces damage from oxidative stress, lowers brain beta-amyloid, and enhances cognition.

• Recent evidence that it may clear amyloid and tau pathology in humans and enhances cognition.

• More clinical trials underway!
The Mediterranean Diet
The Mediterranean Diet

- Rich in “good” fats, multicolored fruits and vegetables, and protein from fish sources
- Reduces risk of metabolic syndrome and mortality risk from all causes
- May reduce risk for cognitive decline
- Among those with AD it is associated with lower mortality
Blueberries

• Blueberry supplementation reduces oxidative stress and inhibits acetylcholinesterase, the enzyme that breaks down acetylcholine

• Improves memory in healthy older adults

• Bioactives in blueberries improve insulin sensitivity in obese, insulin-resistant men and women

• More trials underway
Hyperglycemia and diabetes

- Hyperglycemia is a risk factor for **premature cognitive decline**, even in the absence of diabetes.

- **Fasting insulin levels** correlated with cognitive decline in women without diabetes.

- Diabetes **doubles the risk** of developing Alzheimer’s disease.

- Alzheimer’s – Type 3 diabetes? Insulin resistance?

- Intranasal insulin for treatment of MCI and early AD? **Currently underway**
Caffeine and cognitive decline

• Improves **long-term memory**

• Is associated with **increased longevity** in 90+ adults

• Improves **cognition** and reduces the **formation of β-amyloid** in mouse models

• A study of nearly 700 elderly men over a 10-year period found that consuming 3 cups of coffee was associated with a **4-fold slower rate of cognitive decline**

• Caffeine **reduces tau deposits** and pro inflammatory and oxidative stress markers and enhances spatial memory in AD mice
Physical exercise

• Physical activity linked to **reduced risk for AD** in epidemiological studies

• Small benefits in clinical trials, most notably in **memory and executive function**

• **Aerobic** as well as **strength training** show positive effects

• Sessions between **30 minutes and an hour** show larger effects than shorter sessions and no significant benefit of longer sessions.
Social and leisure activities

• Engaging in **mentally stimulating activities** such as reading, playing board games, playing musical instruments, knitting, gardening, and dancing lower dementia risk

• Maintaining a **larger social network** has protective effects.

• High educational level and occupational attainment (**high cognitive reserve**) associated with decreased dementia incidence.
Cognitive and brain training examples

- Lots of brain-training exercises and games online
- Taking different routes back home or to work
- Playing chess and strategy games
- Reading
- Free mobile apps for memory
- Learn a new language
- Learn a new programming language
- Tutor schoolchildren
Sleep strengthens memories

Computerized sequential finger tapping task:

**Trial**
- Tapping 30s
- Rest 30s

**Training**
- x12 Trials

**Retest**
- x3 Trials

**Outcome Measures**

- **Speed** = No. correct sequences per trial
- **Accuracy** = No. errors / sequence
Sleep strengthens memories

Stickgold and Walker (2005)
Sleep deprivation impairs memory

- 36 hours of sleep deprivation
- Word-pair test

Walker (2006)
How does sleep affect memory?

• Replay memories during sleep

Same sequence
But much faster
Sleep stages and changes with age

Aging is associated with **decreased** total sleep, **reduced** stage 4 sleep, and sleep **fragmentation**.
Sleep and Alzheimer’s disease

• There is a link between sleep disturbances and **cognitive decline** in older adults

• Shorter sleep duration and poor sleep quality are associated with **higher amyloid burden** measured using C11-PiB PET scans

Spira et al. JAMA Neurology 2013
Sleep and glymphatic clearance

• The **glymphatic system** clears garbage in the nervous system and gets rid of amyloid while we sleep.

• Sleep changes the cellular structure of the brain and makes it possible to clear waste. This is a possible mechanism by which **sleep disturbances may make it difficult for the brain to get rid of metabolic waste.**

• In one study (Xie et al. (2013) researchers showed that asleep mice cleared TWICE as much amyloid from their brains as awake mice.
General good sleeping habits

- Regular schedule
- Avoiding stimulants
- Bedroom comfort
- Calming routines
- No screens
- Limit light exposure
- No big meals
- No napping
Lifelong learning and cognitive reserve

What is **Cognitive Reserve**?

Individual differences in cognitive performance based on **effective compensation** or coping with brain pathology.

Measures of reserve:

- Education and IQ
- Occupation
- Socioeconomic status
- Leisure activity
Adult plasticity – juggling?

- ~60 year olds, never juggled, 2 groups:
  - Learned to juggle 3 balls (3 months training)
  - No juggling training

- Functional MRI scans:
  - Before training
  - Right after 3m training
  - After 3m without juggling

Boyke et al. (2008)
Adult plasticity – juggling?

• Participants
  • 24 trained
  • 24 untrained

• DTI and structural scans
  • Before training
  • At end of 6w training
  • After 4w w/o juggling

Scholtz et al. (2009)
Prevention - A lifespan approach

Development 0-24: Prenatal health, early childhood environment, activity, education, nutrition

Adult life 25-65: Prevent or reduce cardiovascular risk, maintain physical activity, healthy sleep and social engagement

Older age 65+: Maintain physical activity, cognitive and social engagement, healthy sleep, and manage chronic illness

Cognitive impairment threshold

Prevention

Age

Cognitive Function
Successful aging is absolutely possible!

Jeanne Louise Calment
1875-1997 (122)

Edna Parker
1893-2008
Age 115

Tomoji Tanabe
1895-2009
Age 112

Maria de Jesus
1893-2009
Age 115
Strategies for aging success

• Maintain **heart health** – avoid anything that’s bad for your heart

• Eat heart-healthy **balanced meals** – no deficiencies

• Make sure your get **restful sleep** (quantity and quality)

• Consume **alcohol** and **caffeine** only in moderation

• Engage in **physical** and **mental exercise**

• Maintain an active **social** and **leisure network**

• Keep coming to **seminars**!
UCI Center for the Neurobiology of Learning & Memory
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Distinguished Professor of Neuroscience
Duke University

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"As long as our brain is a mystery, the universe will also be a mystery."

- Santiago Ramón y Cajal