Vestibular loss and cognition in aging adults

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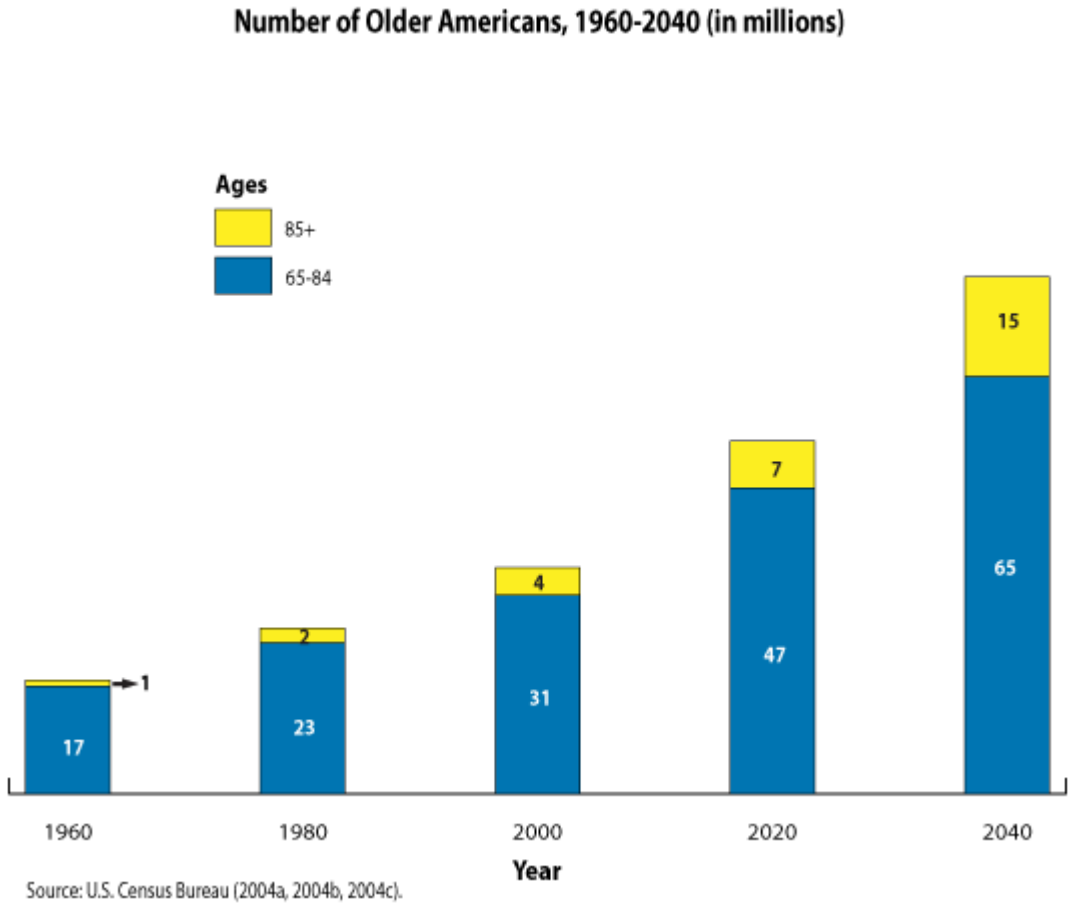
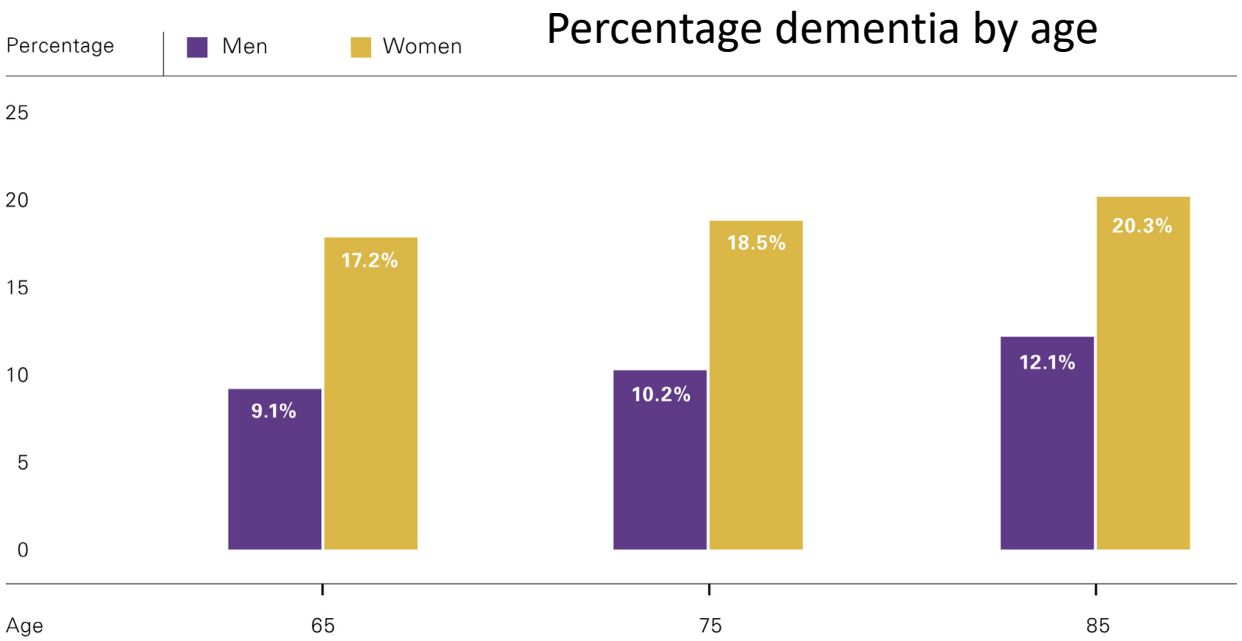
MY JOURNEY

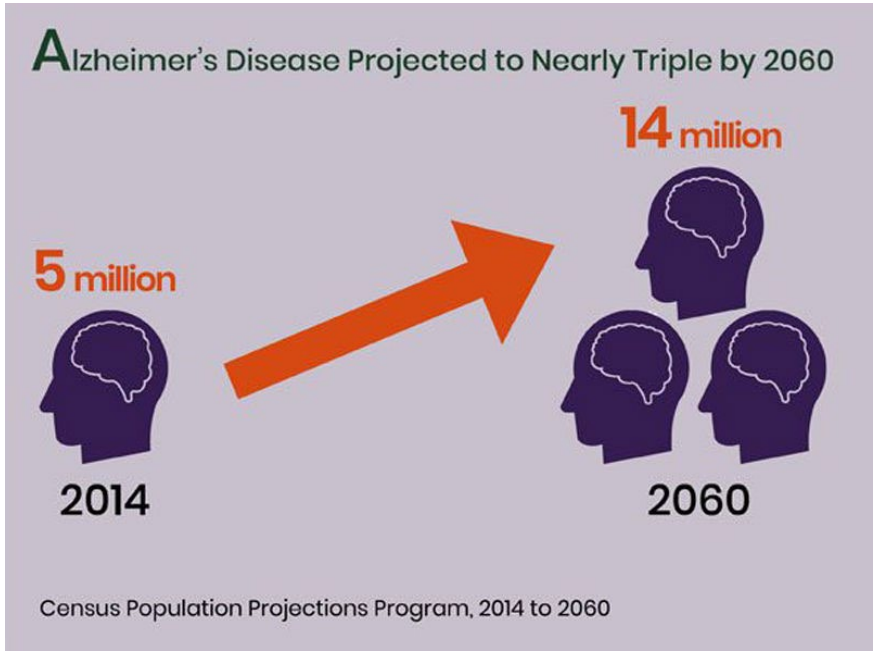
- Matched in **Oto at Hopkins**…discovered the clinical and research (including vestibular) powerhouse as PGY 2!
- **PGY 3:** junior Otology rotation: learning Sheehy principles of chronic otitis media, why do we practice that way?
- **PGY 5:** Learned vestibular physiology writing a chapter, became aware of huge knowledge gaps in aging
- **Fellowship, faculty years**: Spent 1 month with Ugo Fisch's group, built an inter-disciplinary research team, new ideas & questions generated from other disciplines, and from patients.

- Pick a **mentor** who, at any level of career, is looking to the future and striving to be at the forefront of the field.
- Know, but **not necessarily accept**, what has been said, written and accomplished in the past
- Gain **expertise**, keep an eye out for something **new and exciting** and **important** in the field
- Interact and **collaborate** with colleagues and trainees who have skills you don't and with those colleagues and trainees who see or do things from a **different** vantage than yours.
- **Pay it forward!**

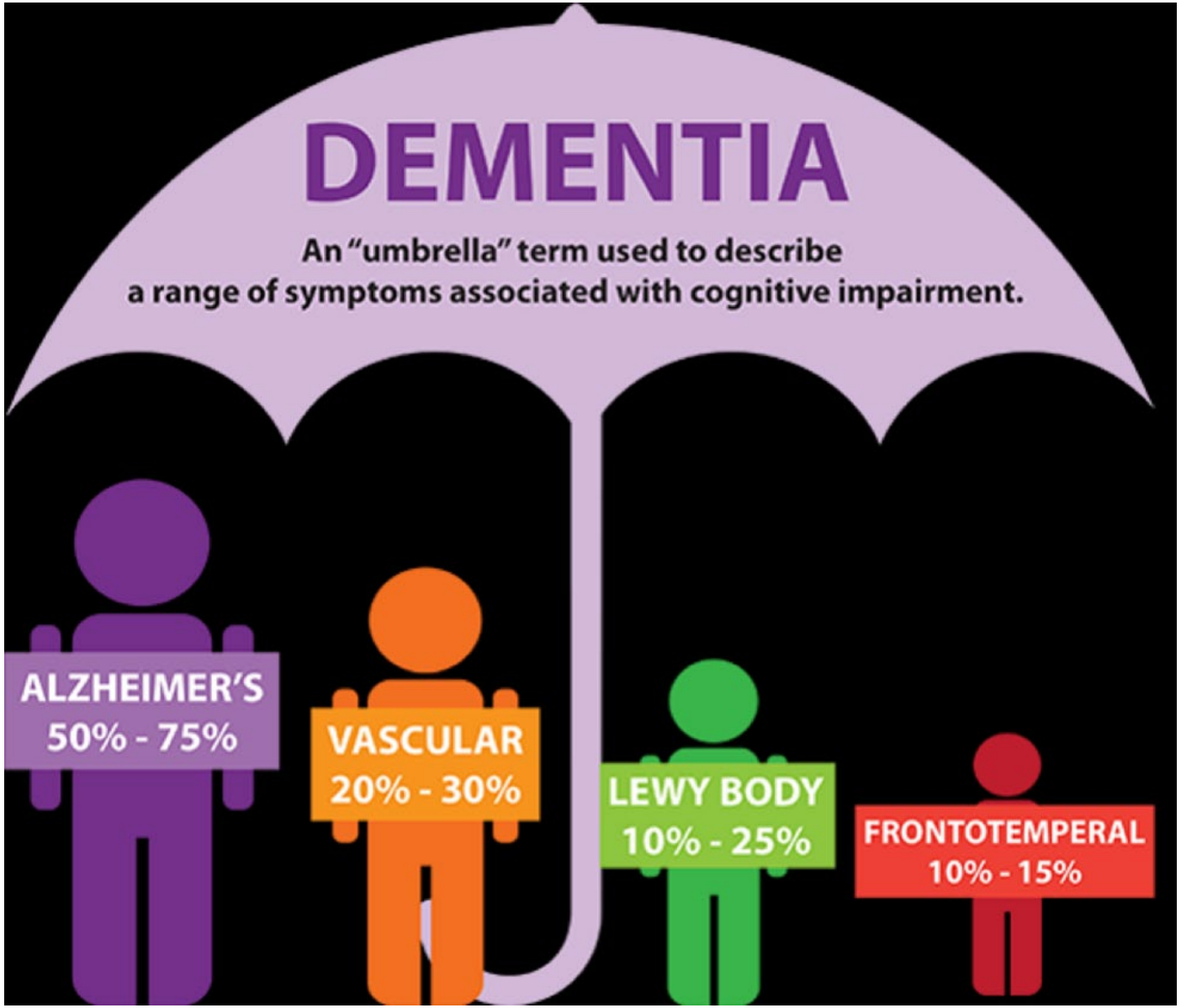
AGING & DEMENTIA



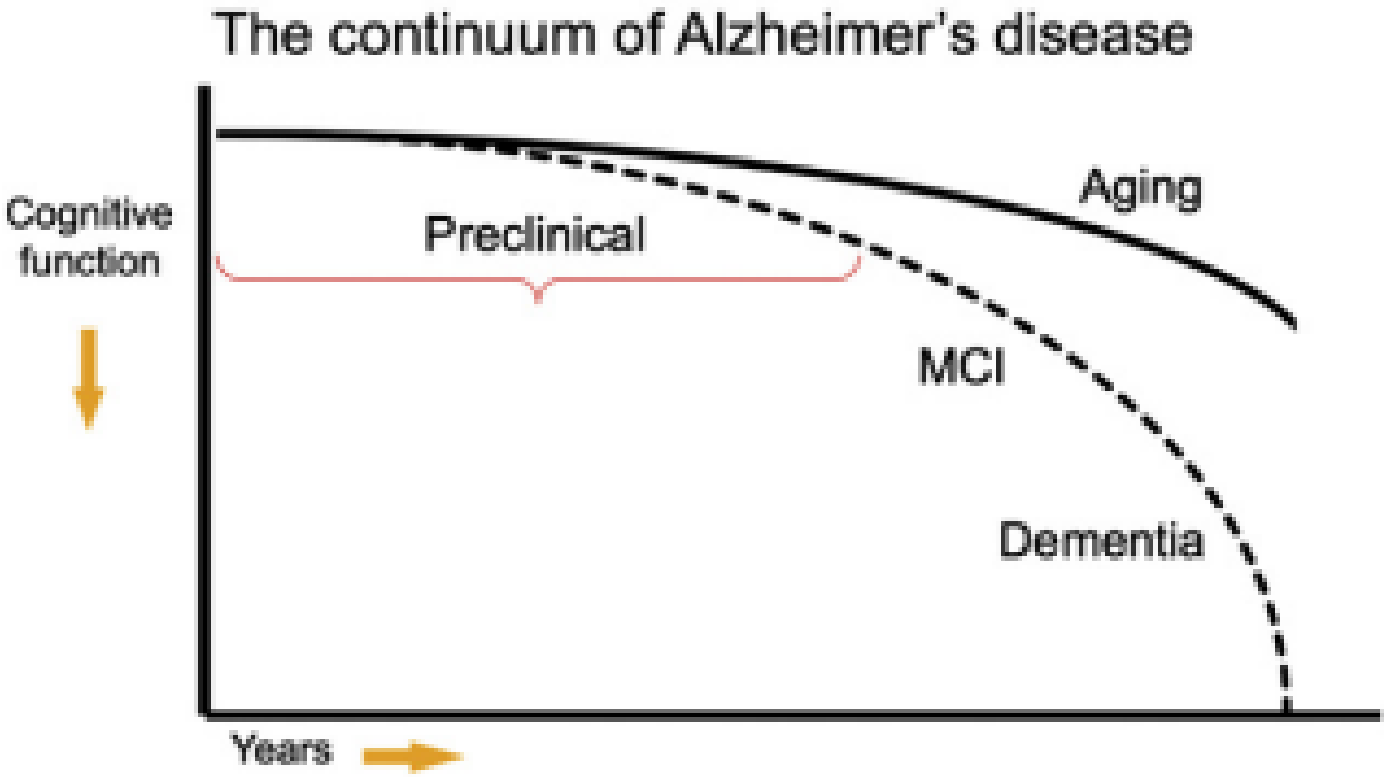




DEMENTIA & ALZHEIMER'S DISEASE (AD)

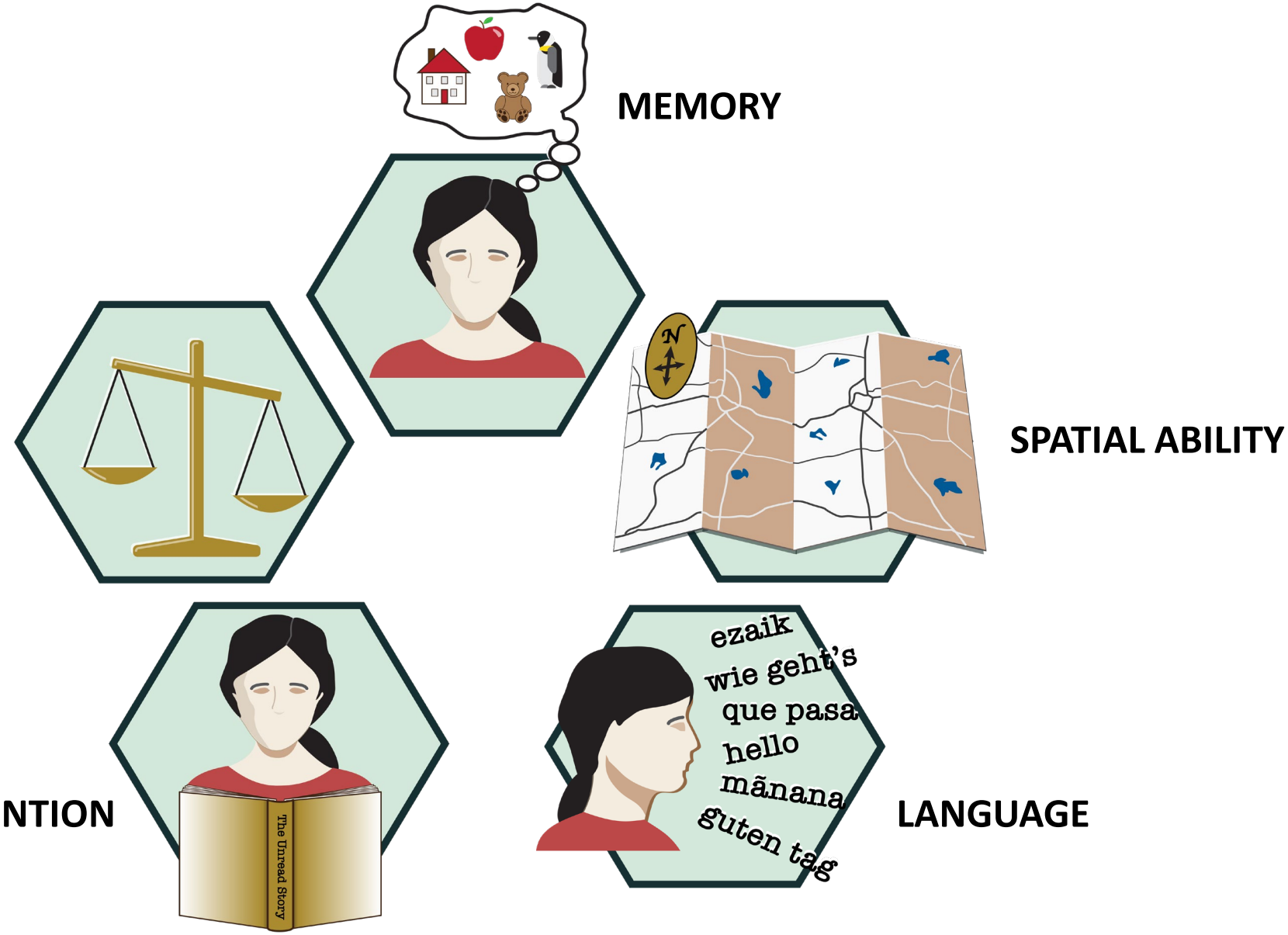


ALZHEIMER'S DISEASE

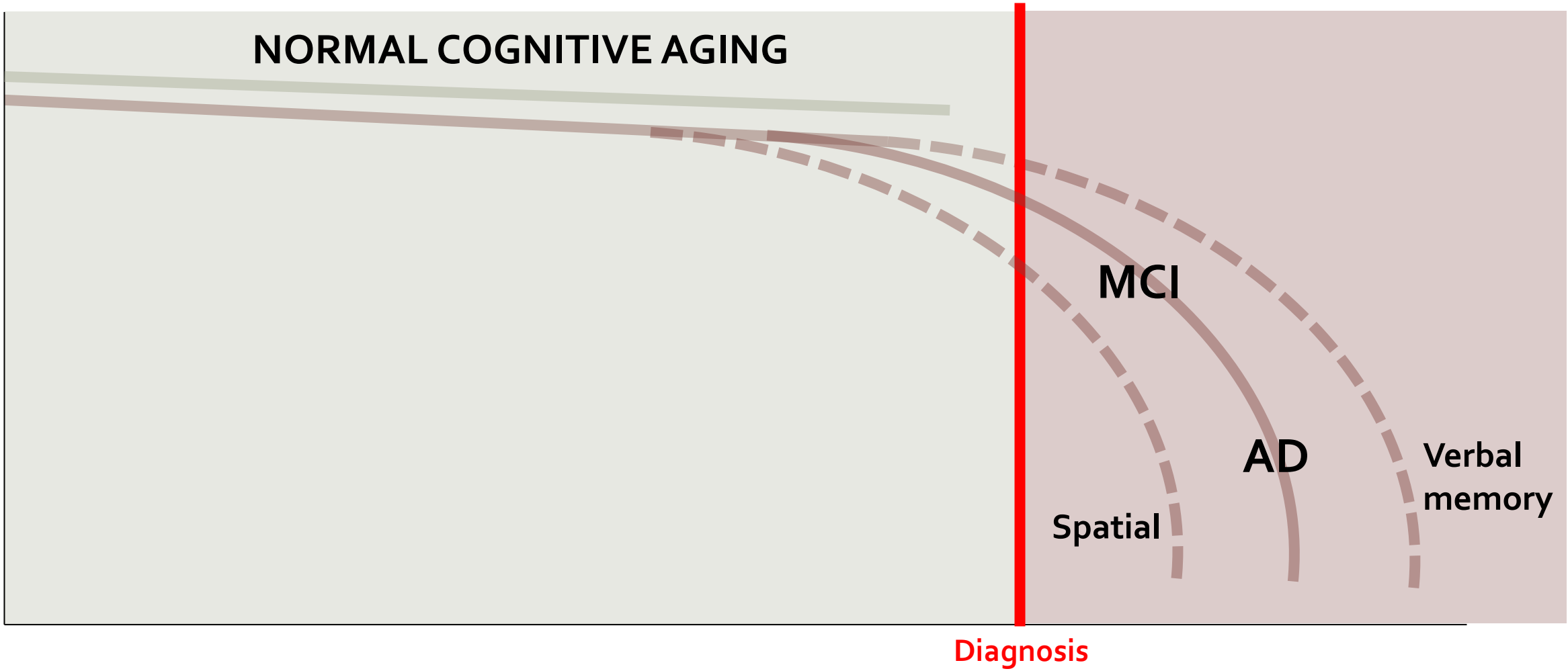


Sperling et al, Alzheimers Dementia 2011

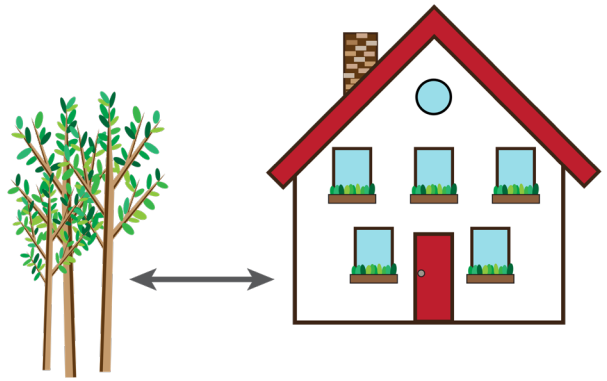
DOMAINS OF COGNITIVE FUNCTION



COGNITIVE AGING AND IMPAIRMENT



DECLINE IN SPATIAL SKILLS

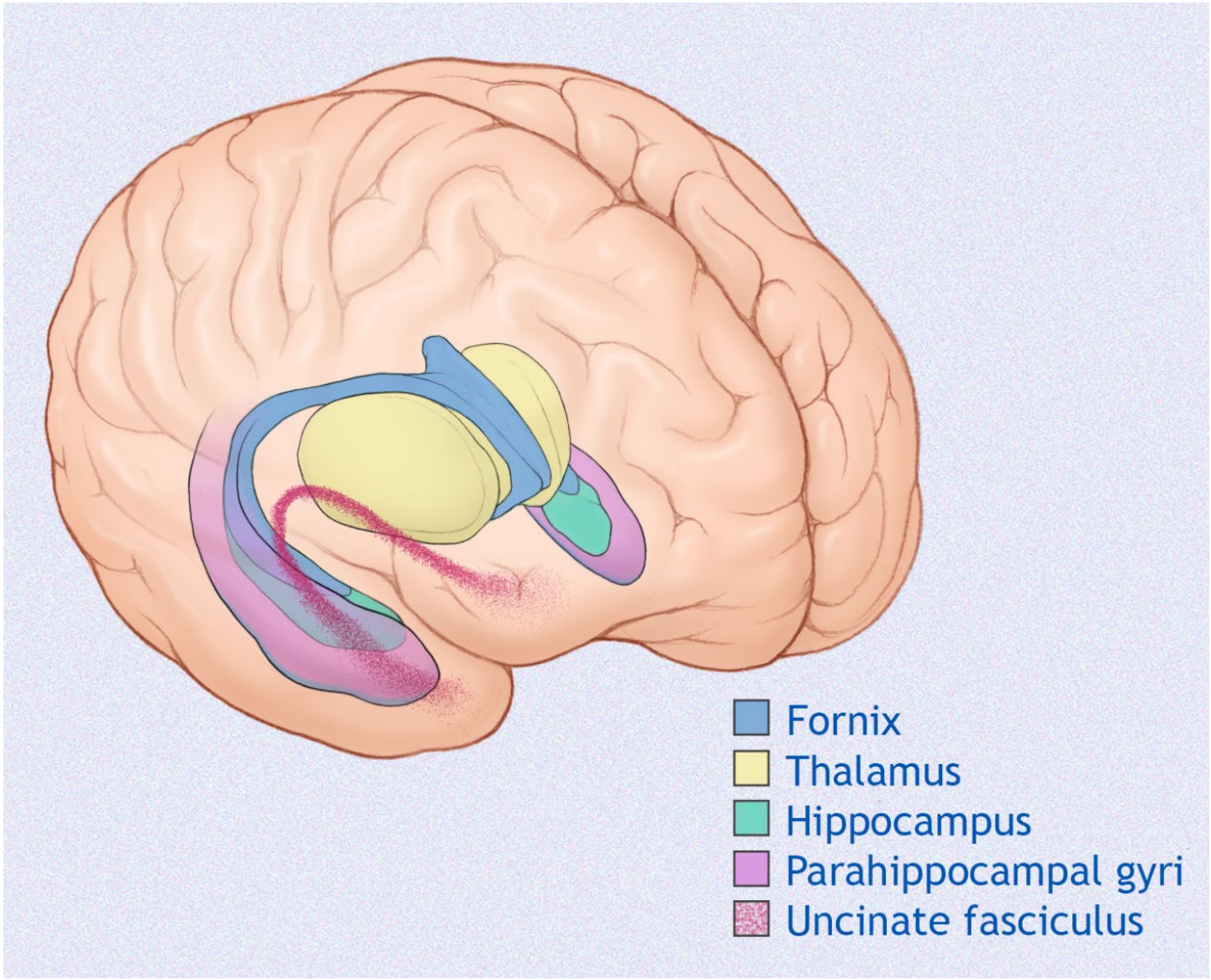


SPATIAL MEMORY

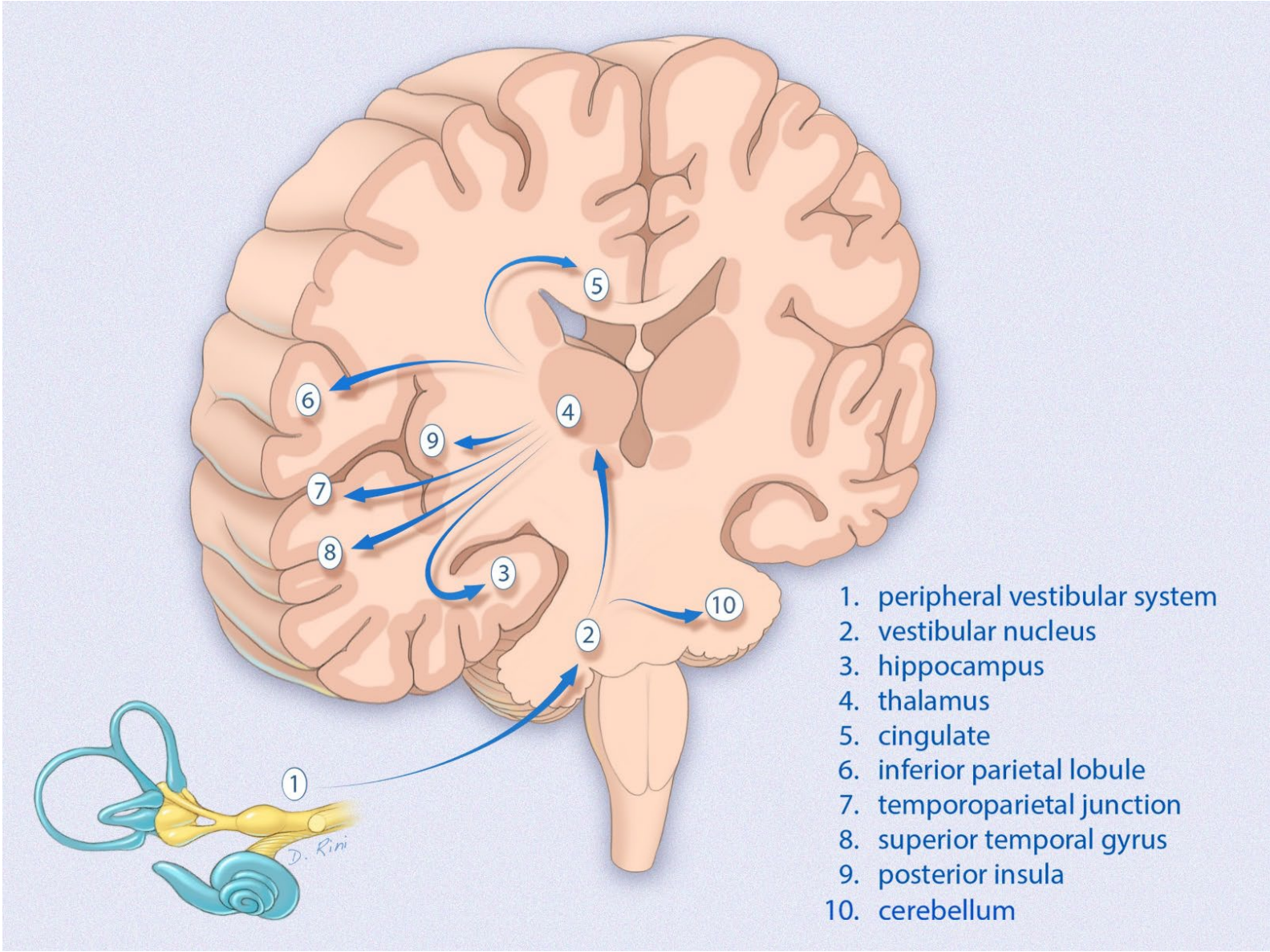
SPATIAL NAVIGATION/ WAYFINDING

WANDERING

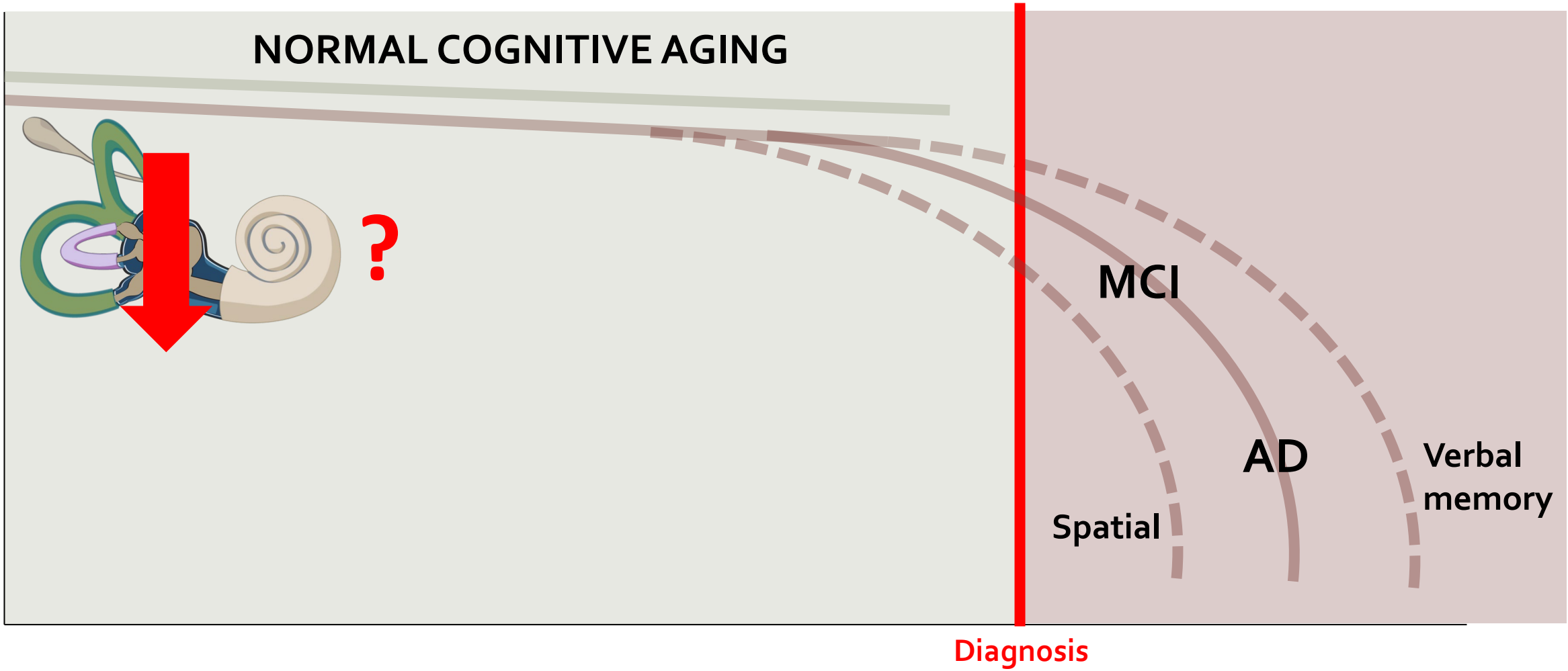
SPATIAL COGNITION BRAIN STRUCTURES



SPATIAL BRAIN STRUCTURES RECEIVE VESTIBULAR INPUT

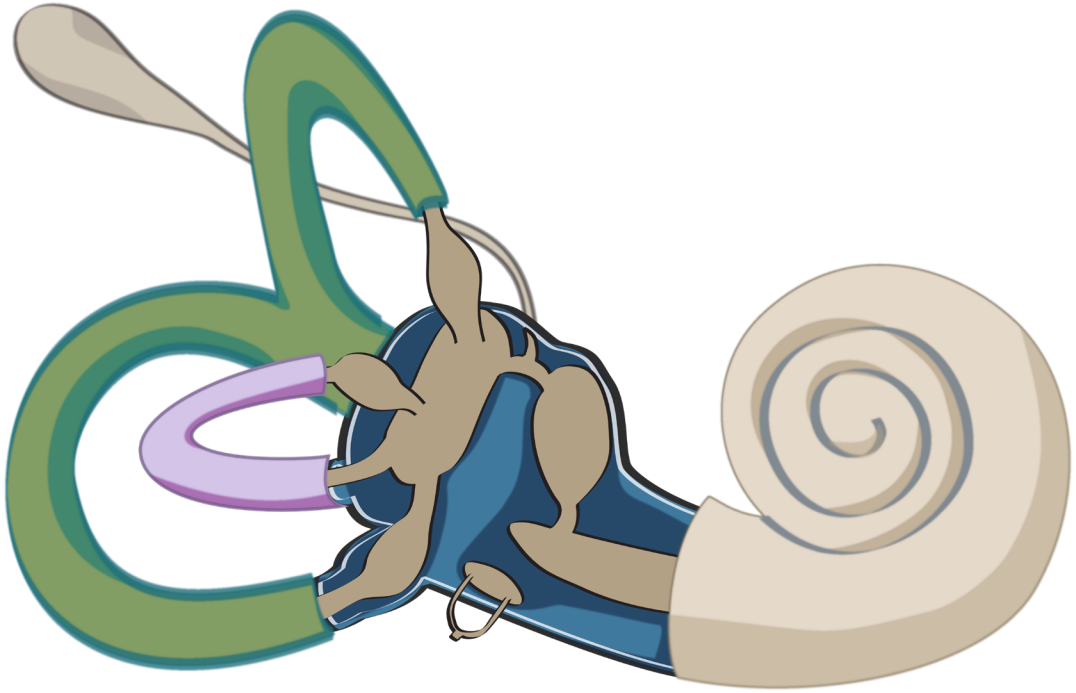


VESTIBULAR LOSS AND COGNITION

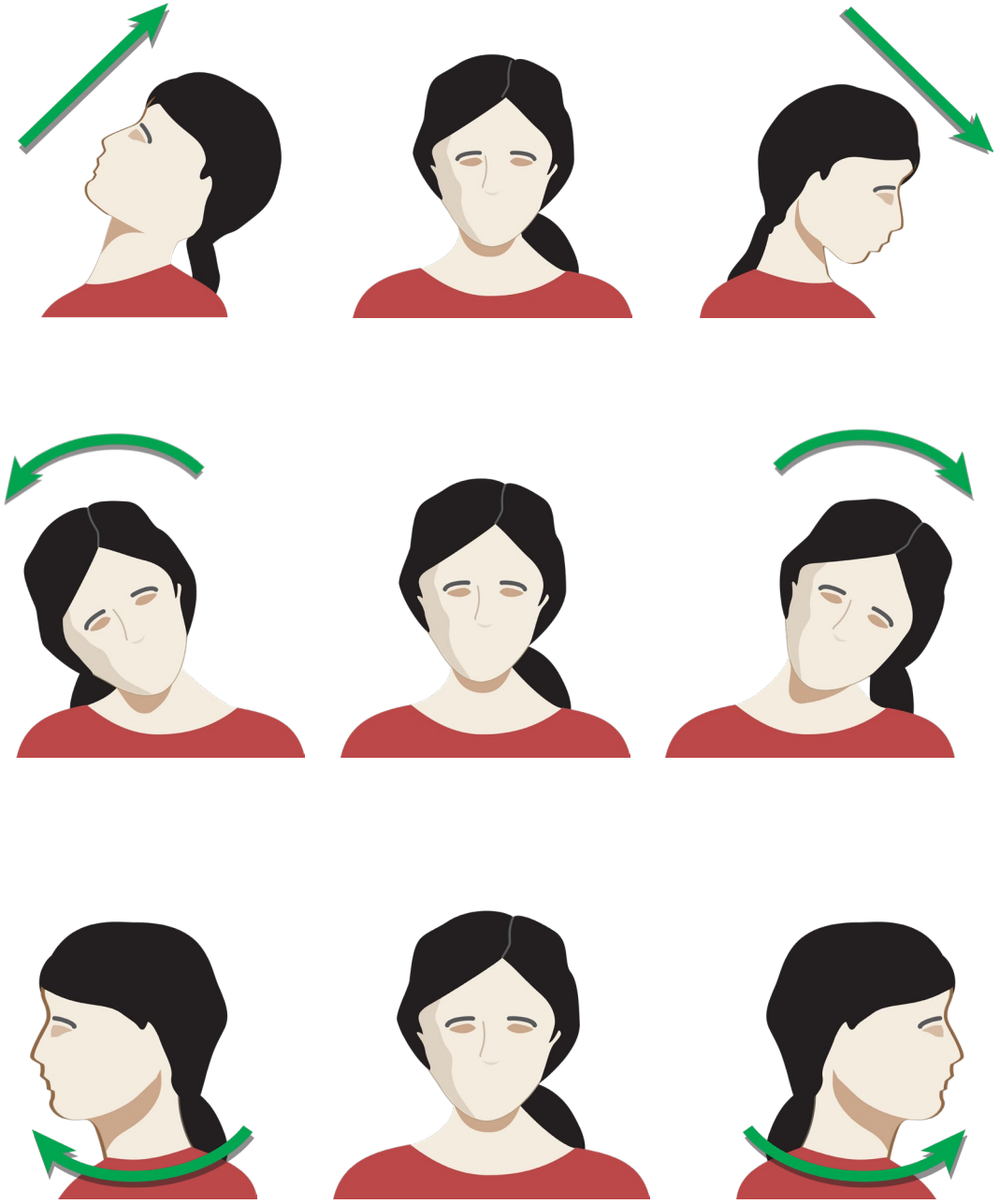


VESTIBULAR SYSTEM & SPATIAL FUNCTION

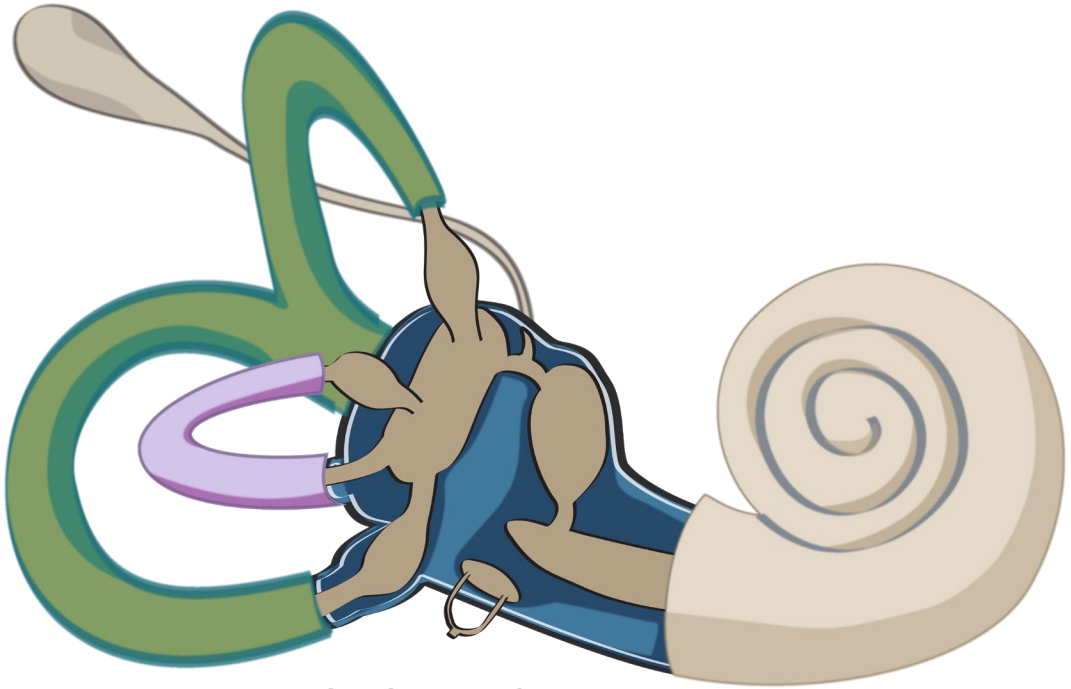
VESTIBULAR SYSTEM



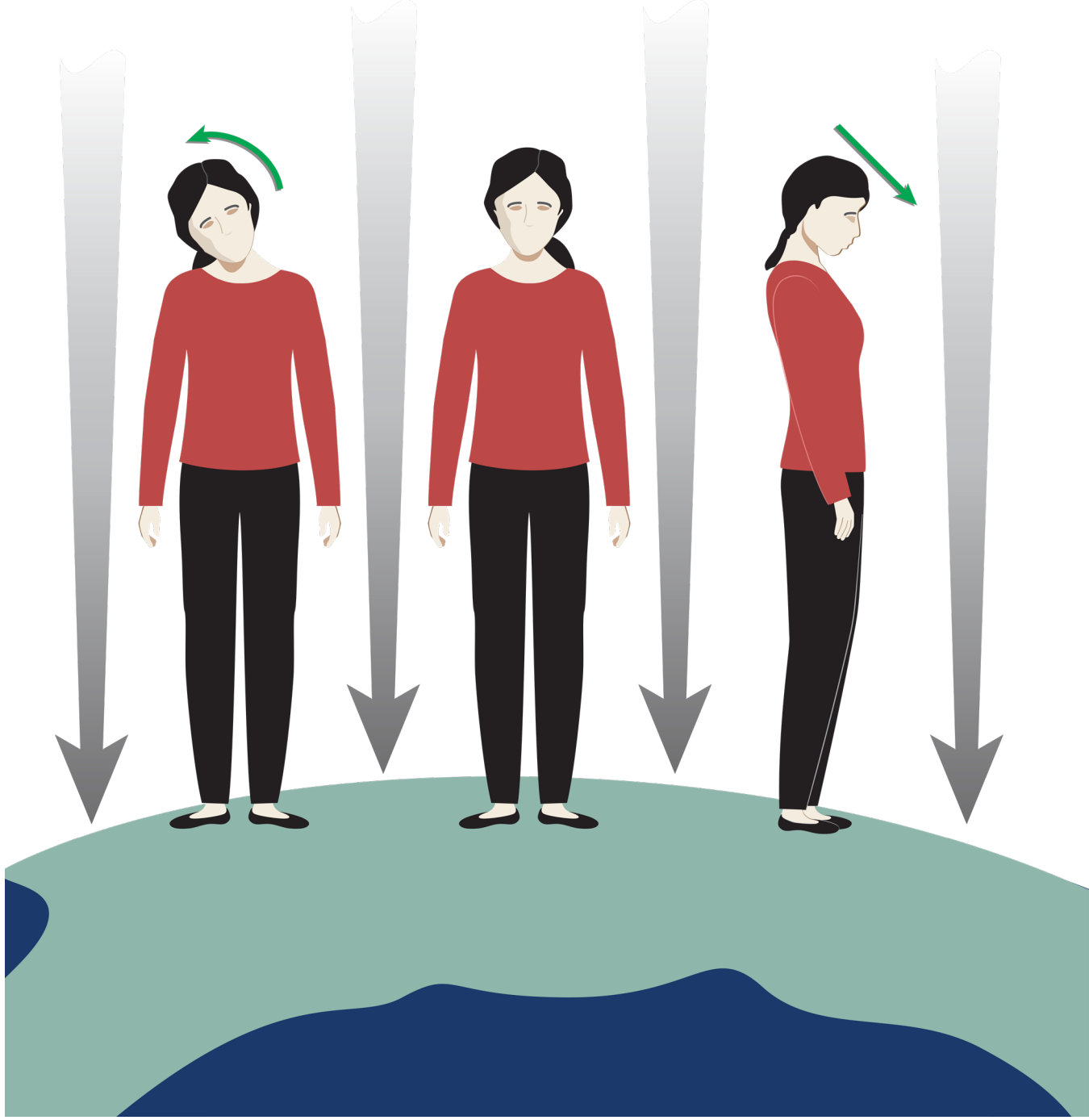
SEMICIRCULAR CANALS



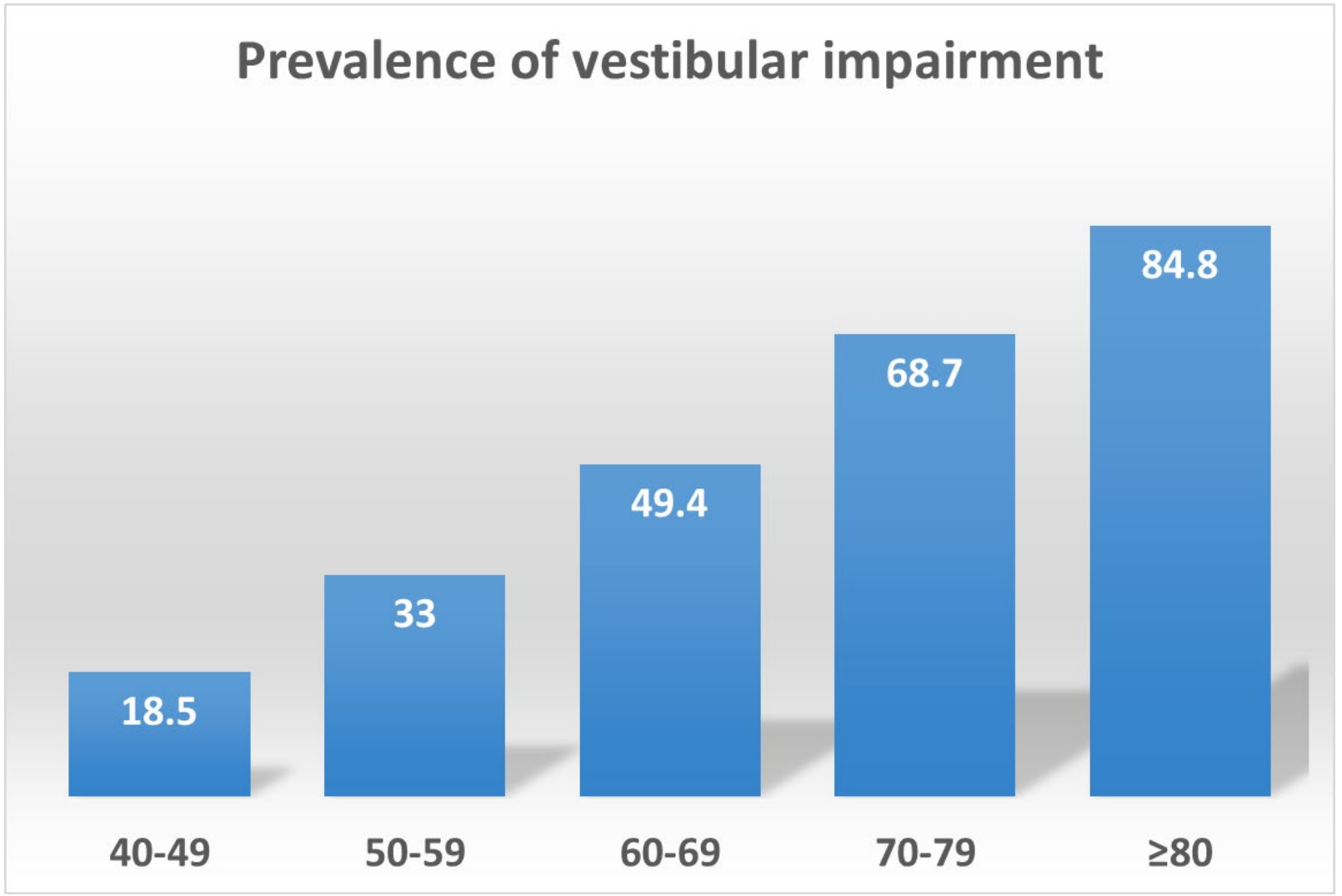
VESTIBULAR SYSTEM



OTOLITHS
(SACCULE, UTRICLE)



VESTIBULAR IMPAIRMENT INCREASES WITH AGE



Agrawal et al Arch Int Med 2009

LEVELS OF EVIDENCE

Animal studies

Human studies

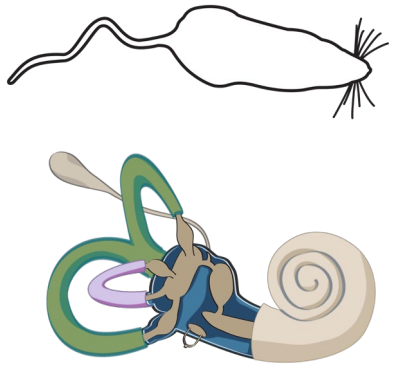
Design:
Clinical (patients, small N)
Epidemiologic (populations, large N)
Clinical trials

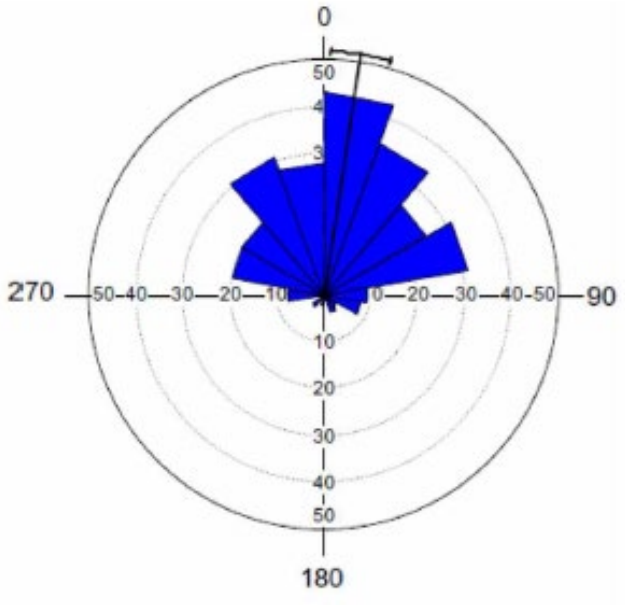
Cognitive/brain outcomes:
Cognitive tests
Brain structure & function
Behavior

EVIDENCE FROM ANIMAL STUDIES

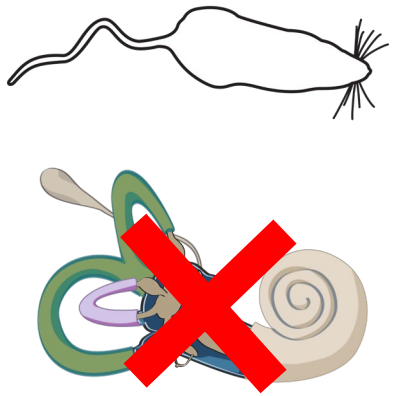
VESTIBULAR INPUT NEEDED FOR SPATIAL NAVIGATION

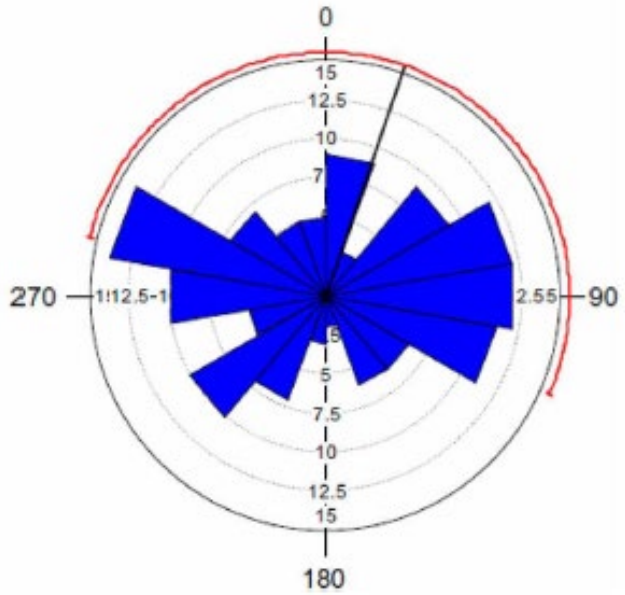
CONTROL





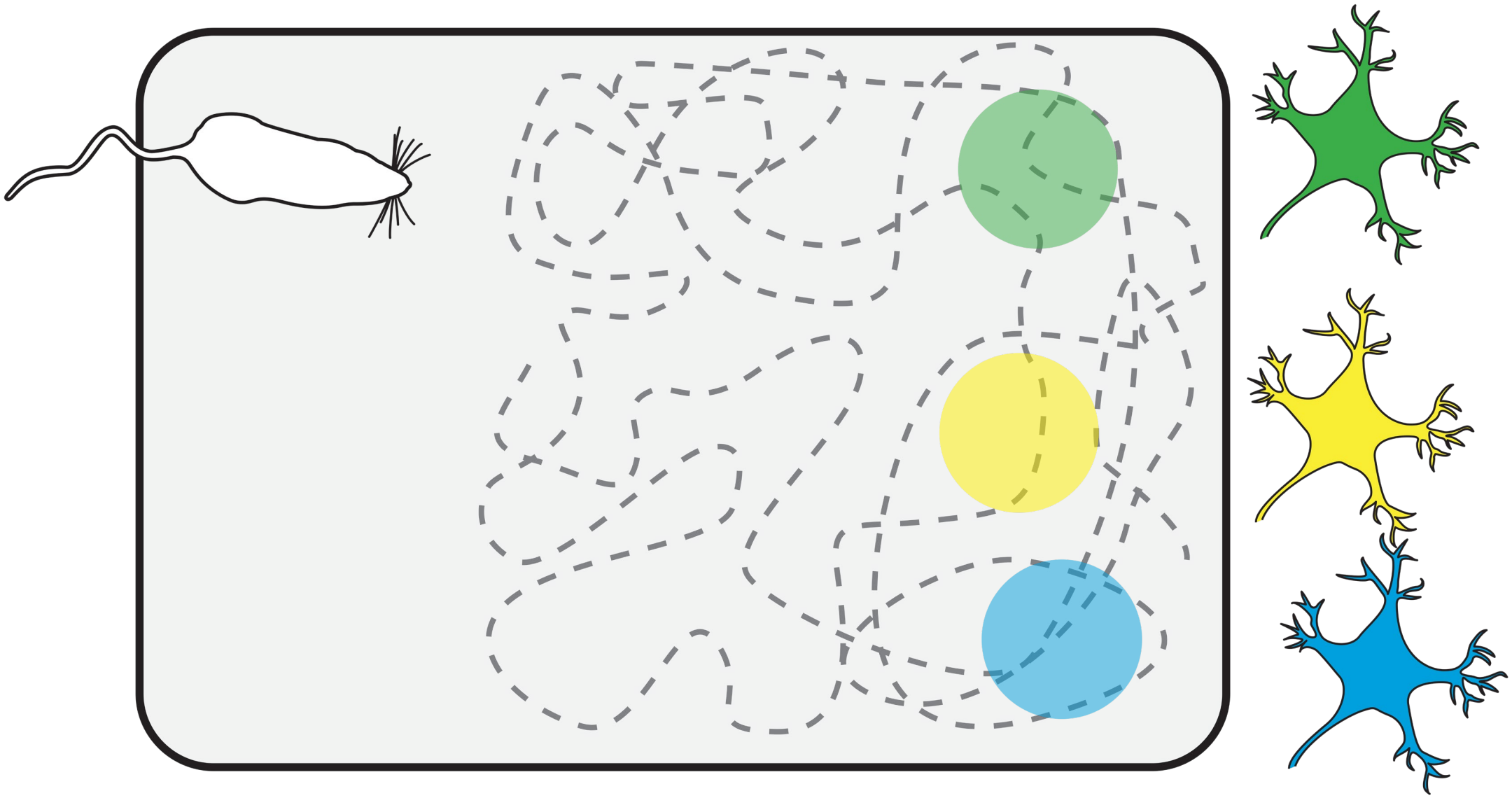
BILATERAL VESTIBULAR LOSS



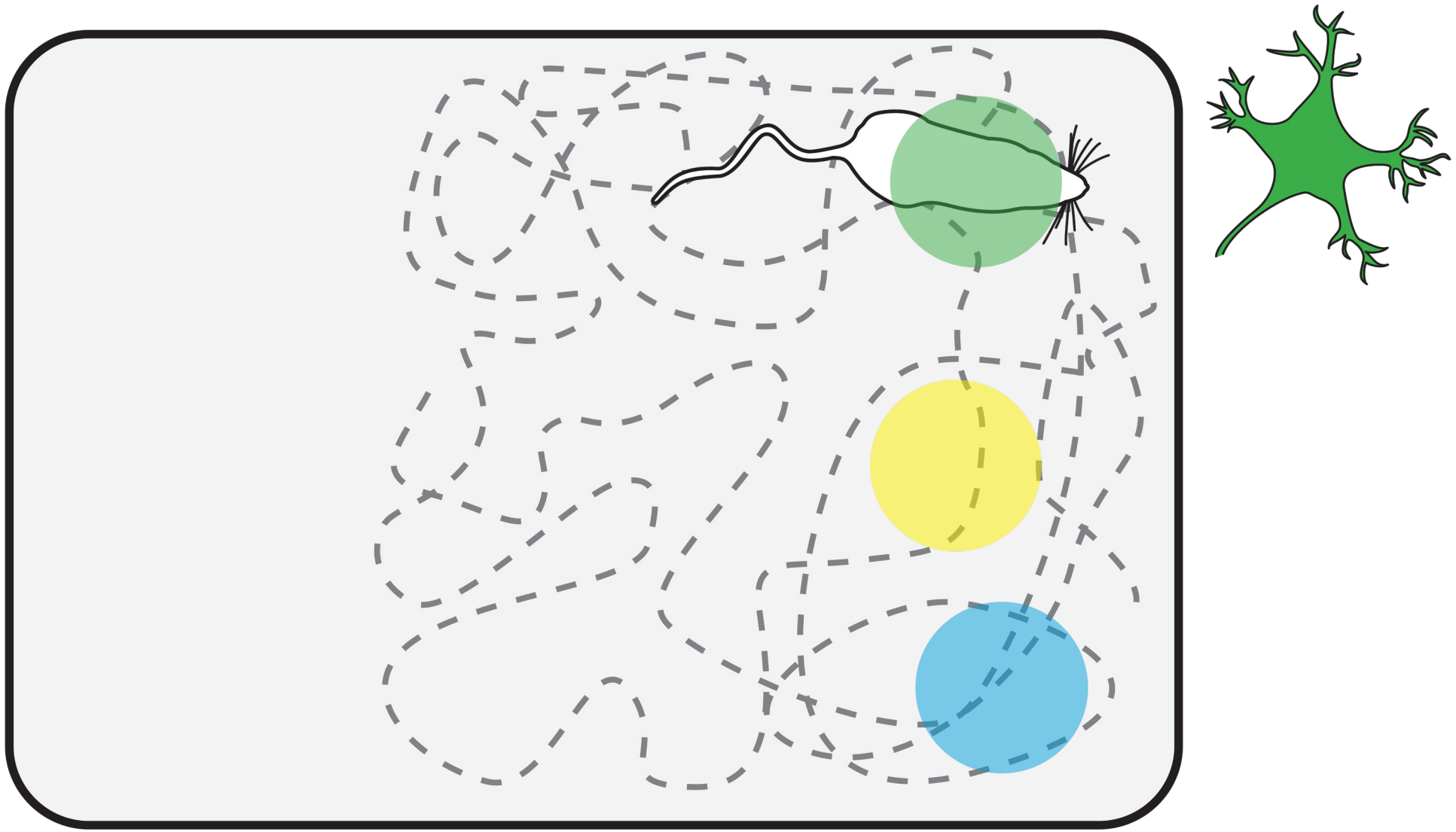


Baek Zheng, Darlington, Smith, Neurobiol Learn Mem 2010

HIPPOCAMPAL PLACE CELLS



HIPPOCAMPAL PLACE CELLS



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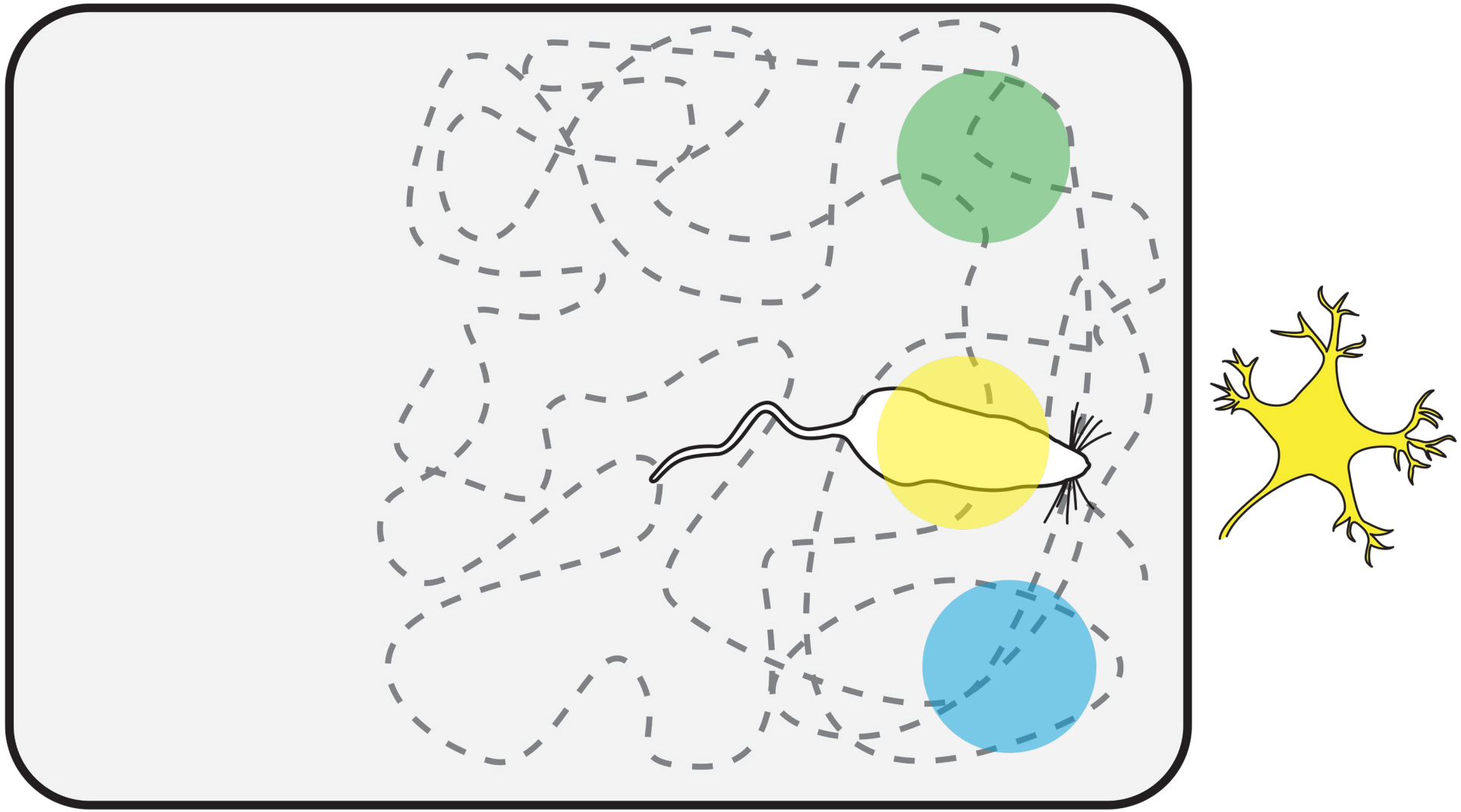

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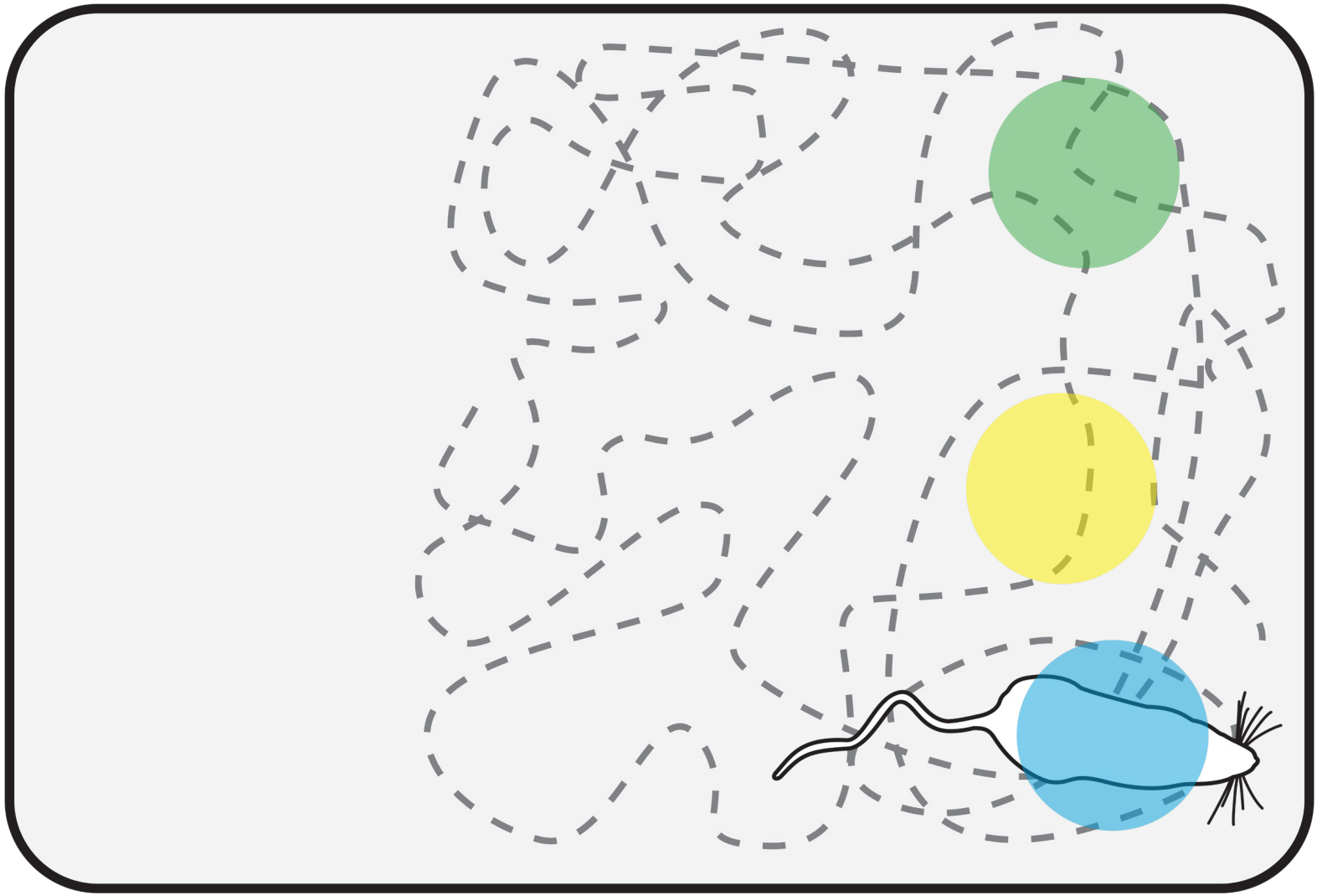
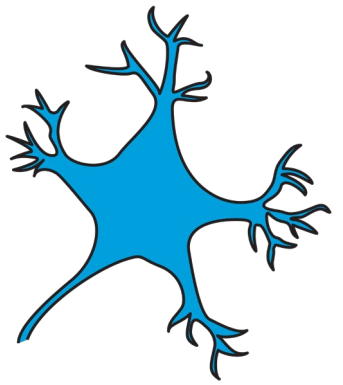
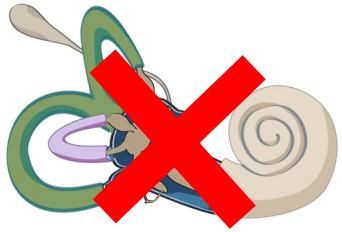
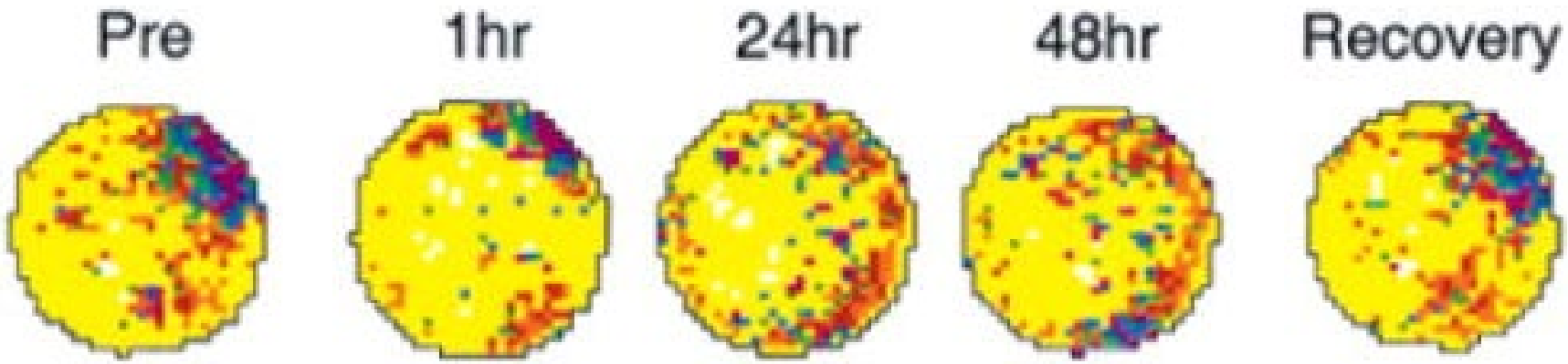




VESTIBULAR INPUT NEEDED FOR PLACE CELL FUNCTION

BILATERAL VESTIBULAR LOSS

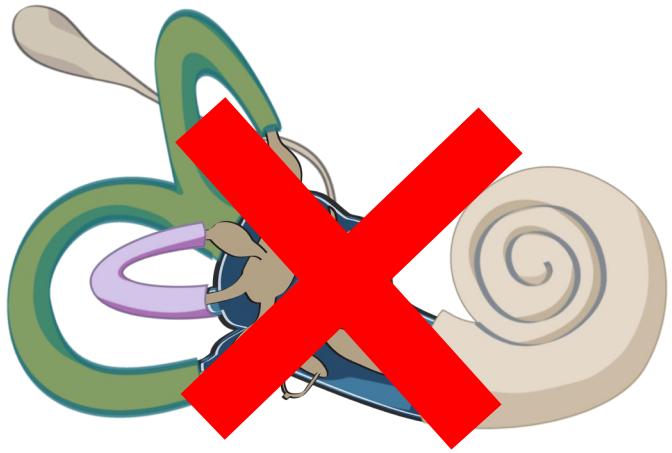


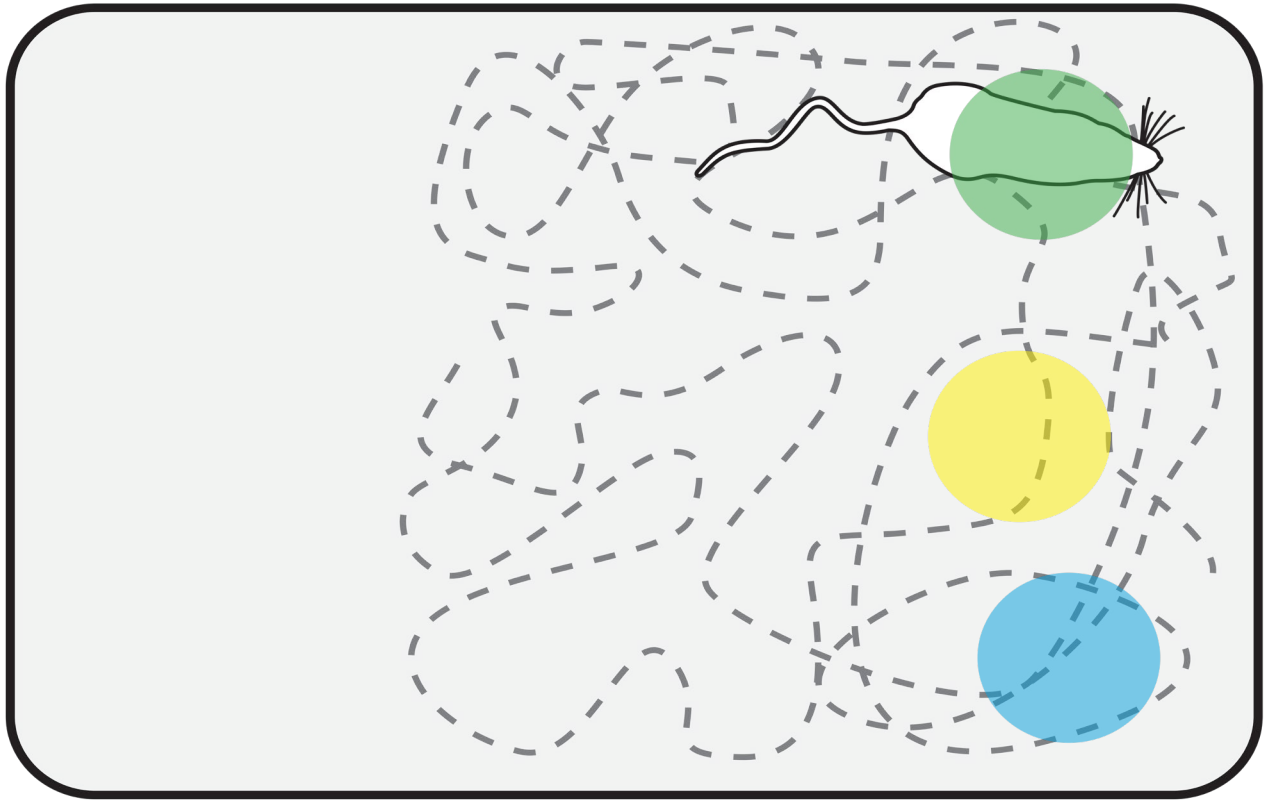


BILATERAL VESTIBULAR LOSS

Stackman and Taube,
Hippocampus 2002

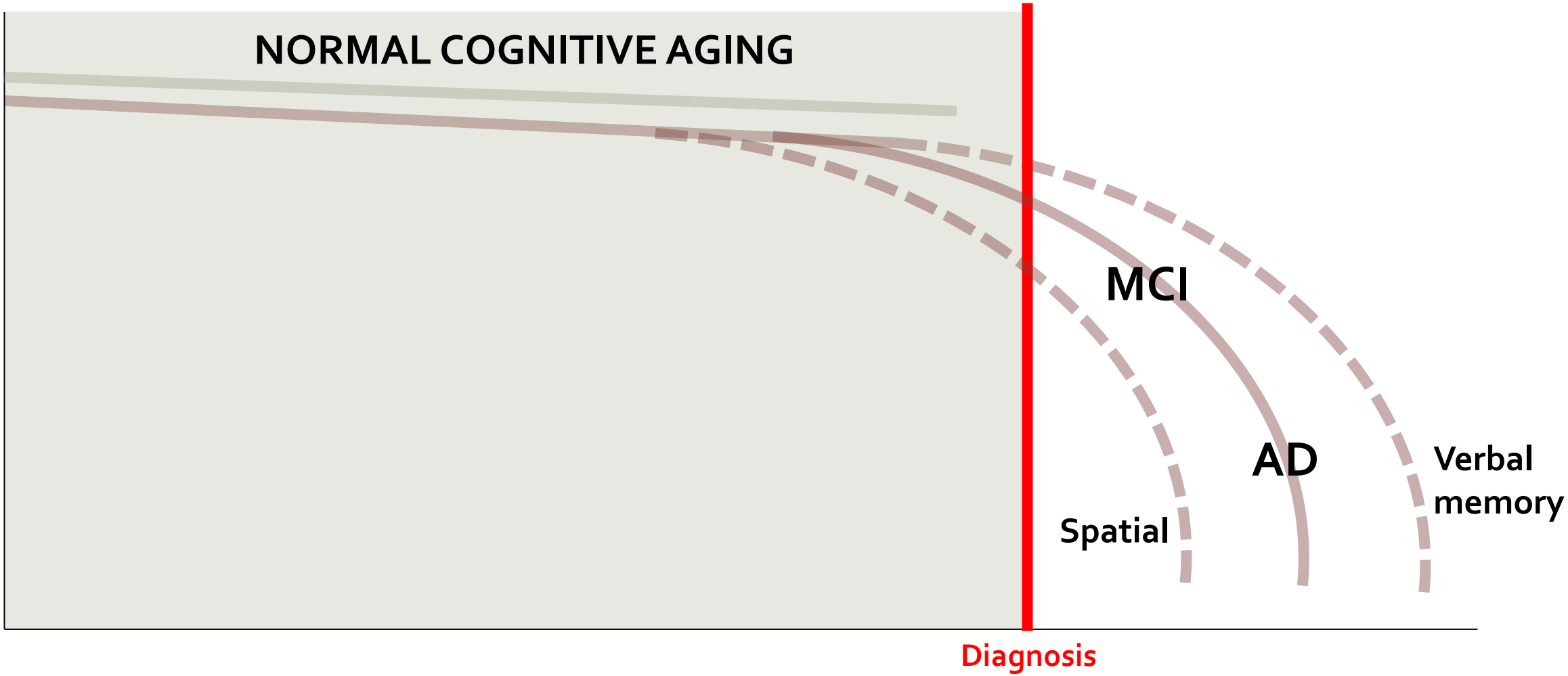
VESTIBULAR INPUT NEEDED FOR PLACE CELL FUNCTION





EVIDENCE FROM HUMAN STUDIES

HUMAN STUDIES: NORMAL COGNITIVE AGING

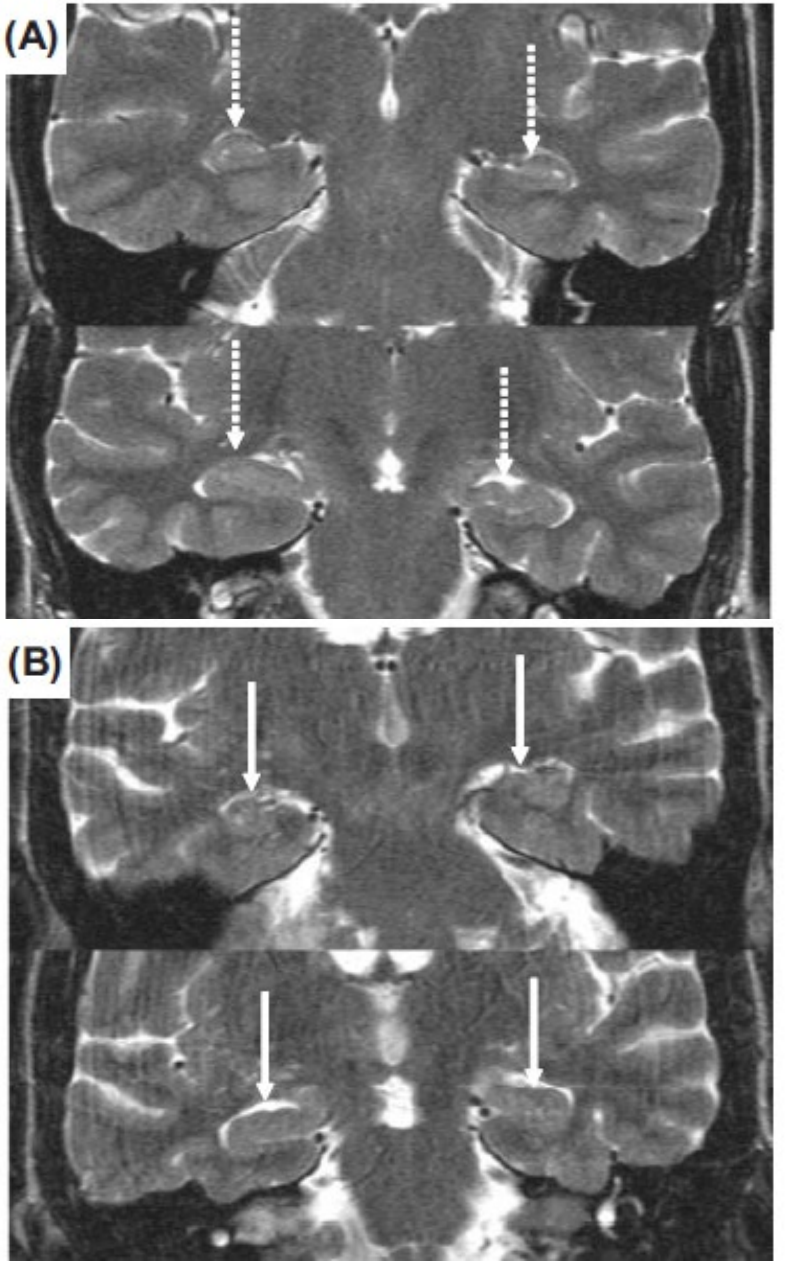


CLINICAL STUDIES: BRAIN STRUCTURE & BEHAVIOR

N=10 patients with bilateral vestibular nerve section

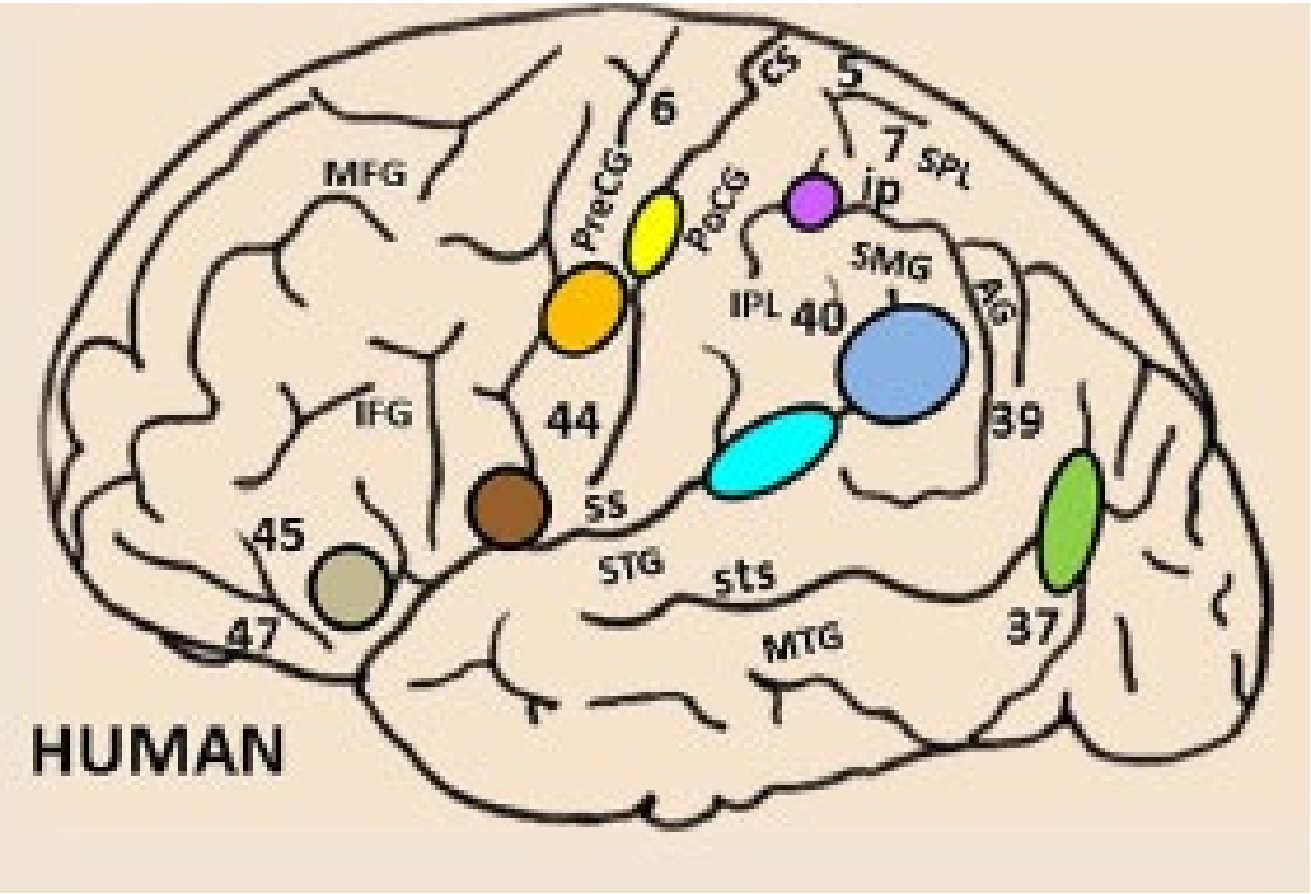
Brain structure

Behavior



Brandt et al Brain 2005

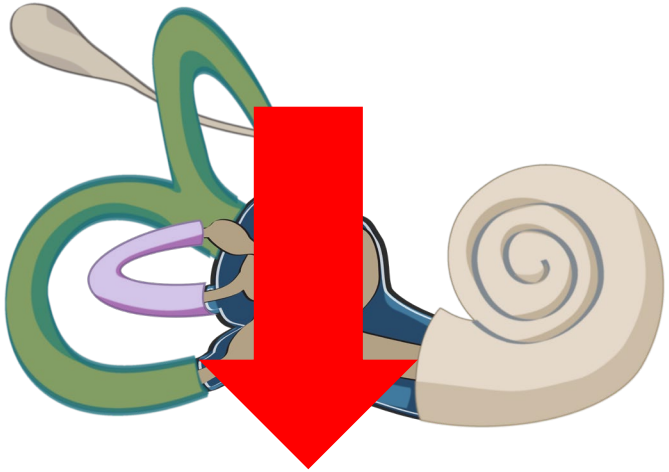
CLINICAL STUDIES: BRAIN FUNCTION



- Galvanic vestibular stimulation in healthy subjects activates a number of cortical regions:
  - Hippocampus (place cells)
  - Temporo-parietal junction
  - Insular cortex
  - Anterior dorsal thalamus (head direction cells)

Dieterich and Brandt, Brain 2008

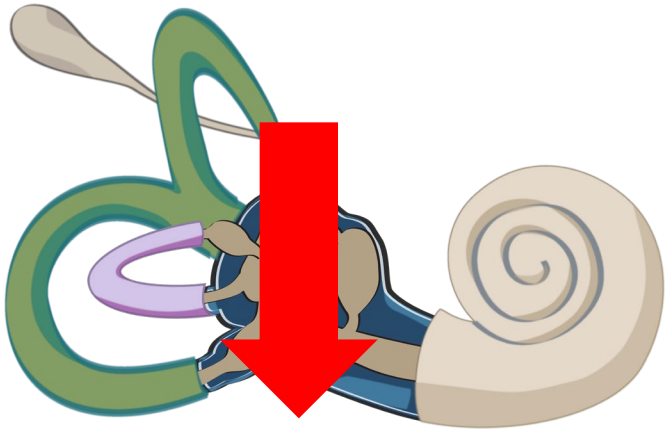
THREE EPIDEMIOLOGIC/POPULATION-BASED STUDIES

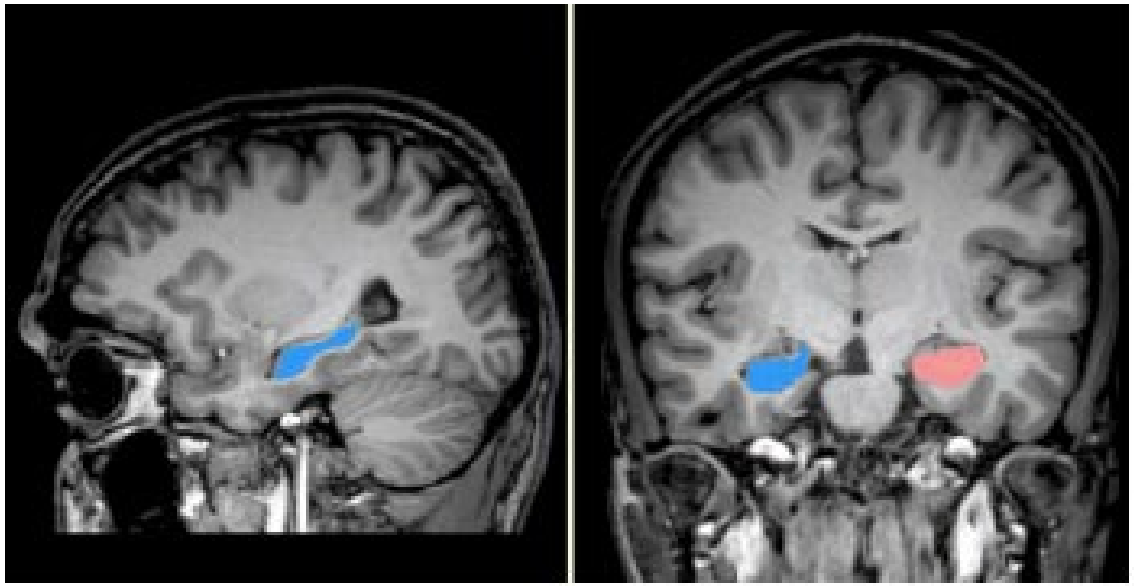


BLSA (N=183) *Bigelow et al JAGS 2015*
NHANES (N=1303) *Semenov et al JGMS 2015*
NHIS (N=20,950) *Bigelow et al JNNP 2015*

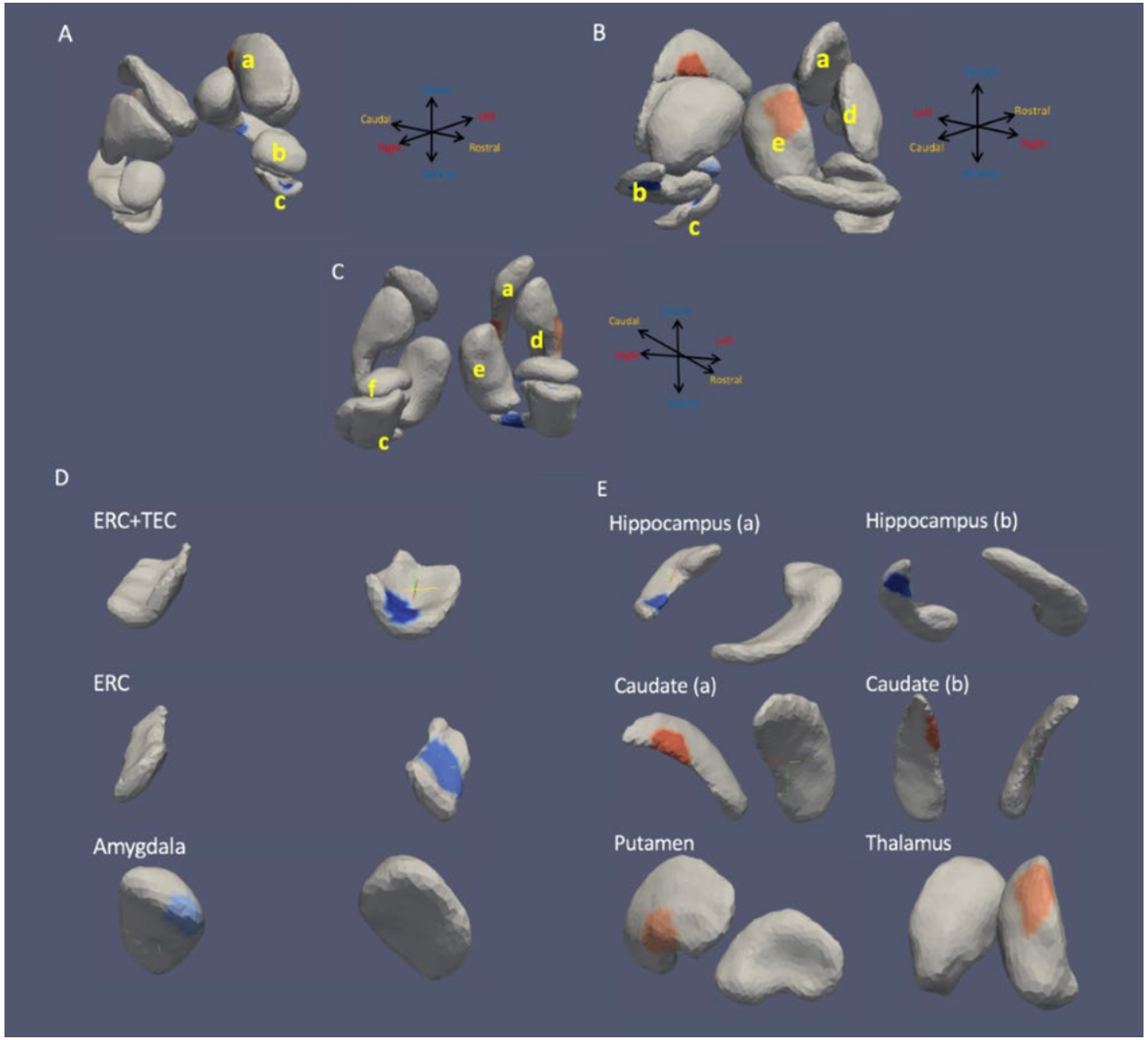
COGNITIVE TESTS

EPIDEMIOLOGIC STUDY: BRAIN STRUCTURE



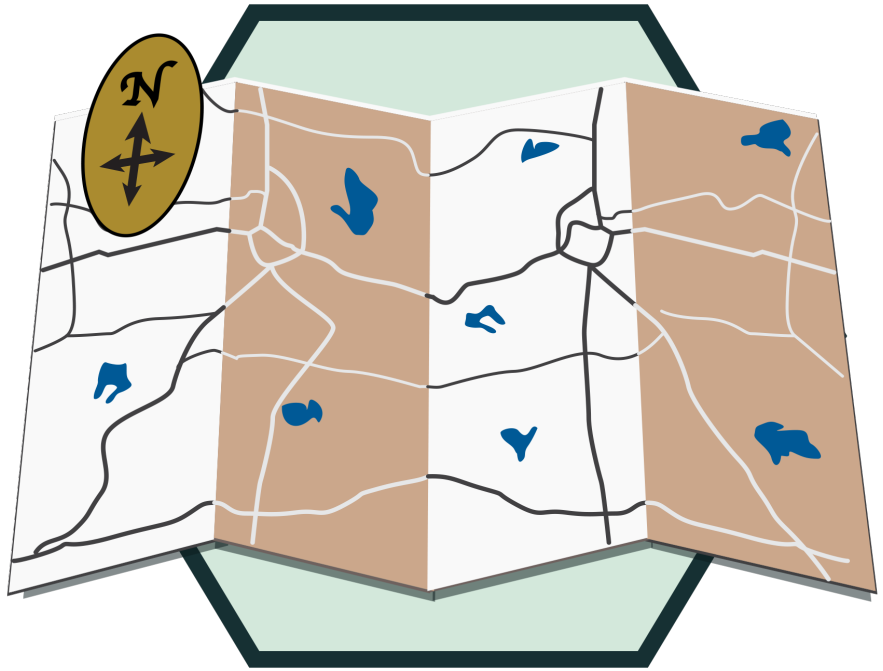


Kamil et al Otol Neurotol 2018



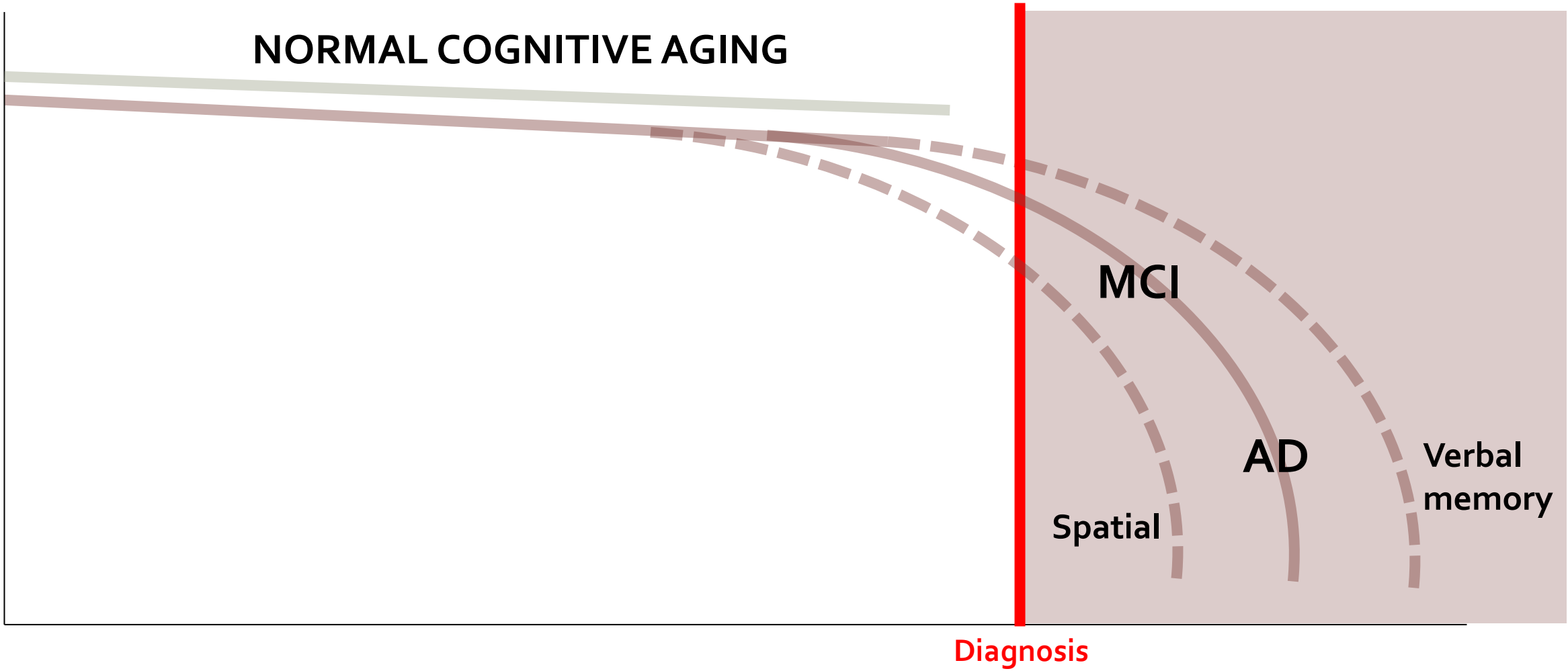
Jacob et al Heliyon 2020

EPIDEMIOLOGIC STUDIES: BEHAVIOR



- **NHANES** *Wei et al Front Neurol 2017*
- **NHIS** *Wei et al Ear and Hearing 2018*

HUMAN STUDIES: COGNITIVE IMPAIRMENT



AD IS HETEROGENEOUS

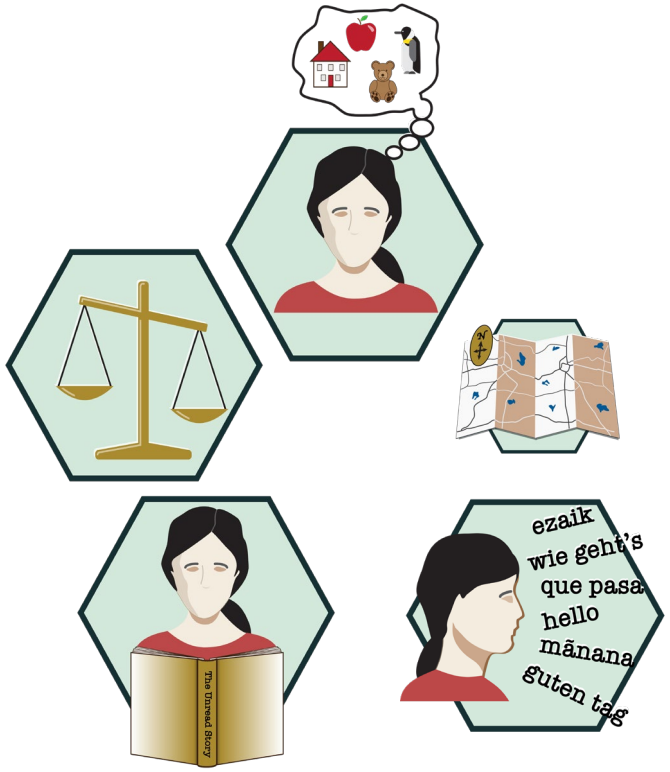
AD IS HETEROGENEOUS: SOME PATIENTS HAVE MORE SPATIAL SUBTYPE

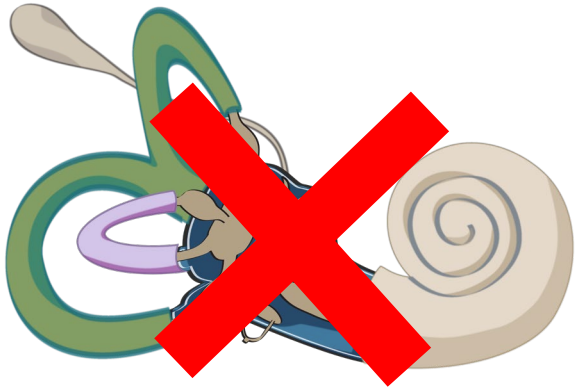
Spatial disorientation

Wandering: occurs in ~50% of individuals with severe dementia

Falls

AD PATIENTS WITH SPATIAL SUBTYPE HAVE VESTIBULAR LOSS

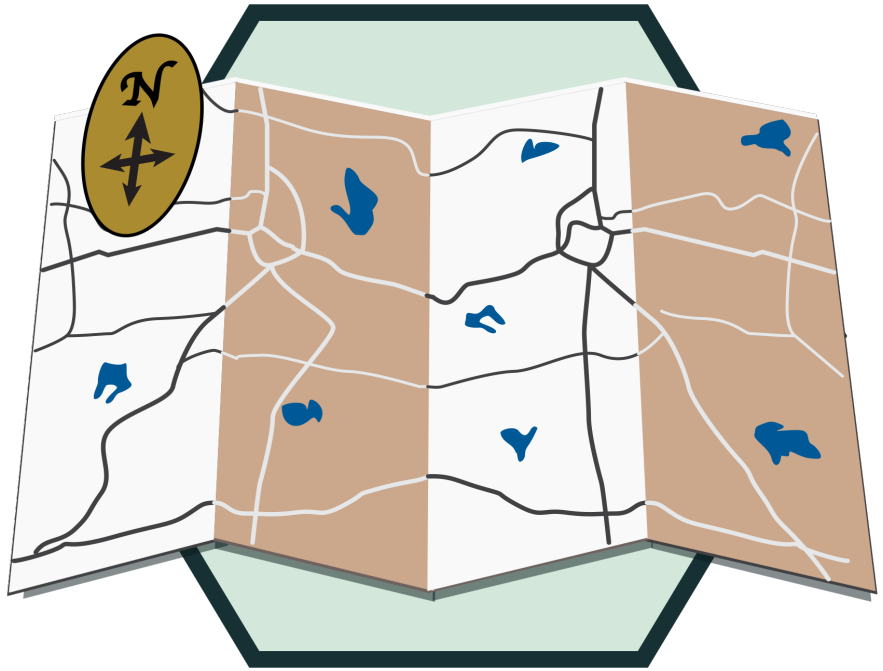




25%

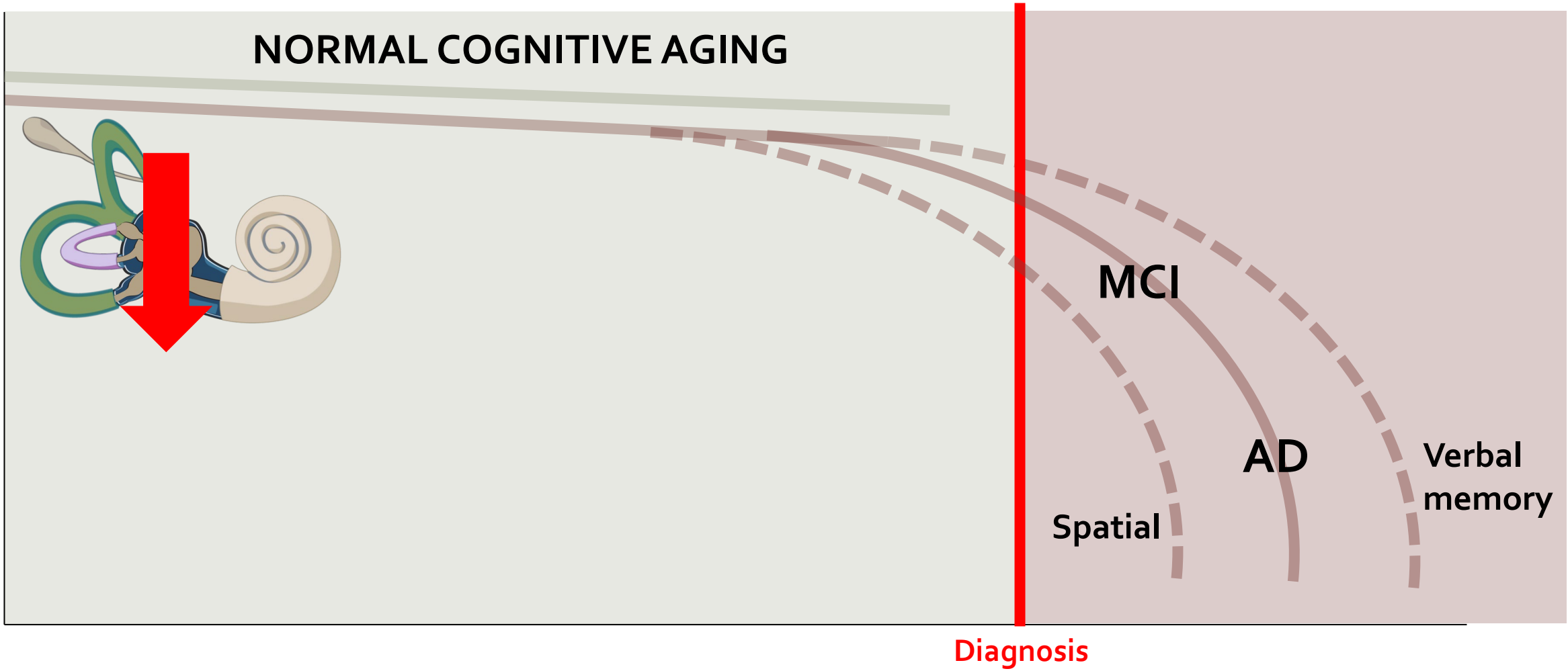
95%

AD CLINICAL STUDY: BEHAVIOR

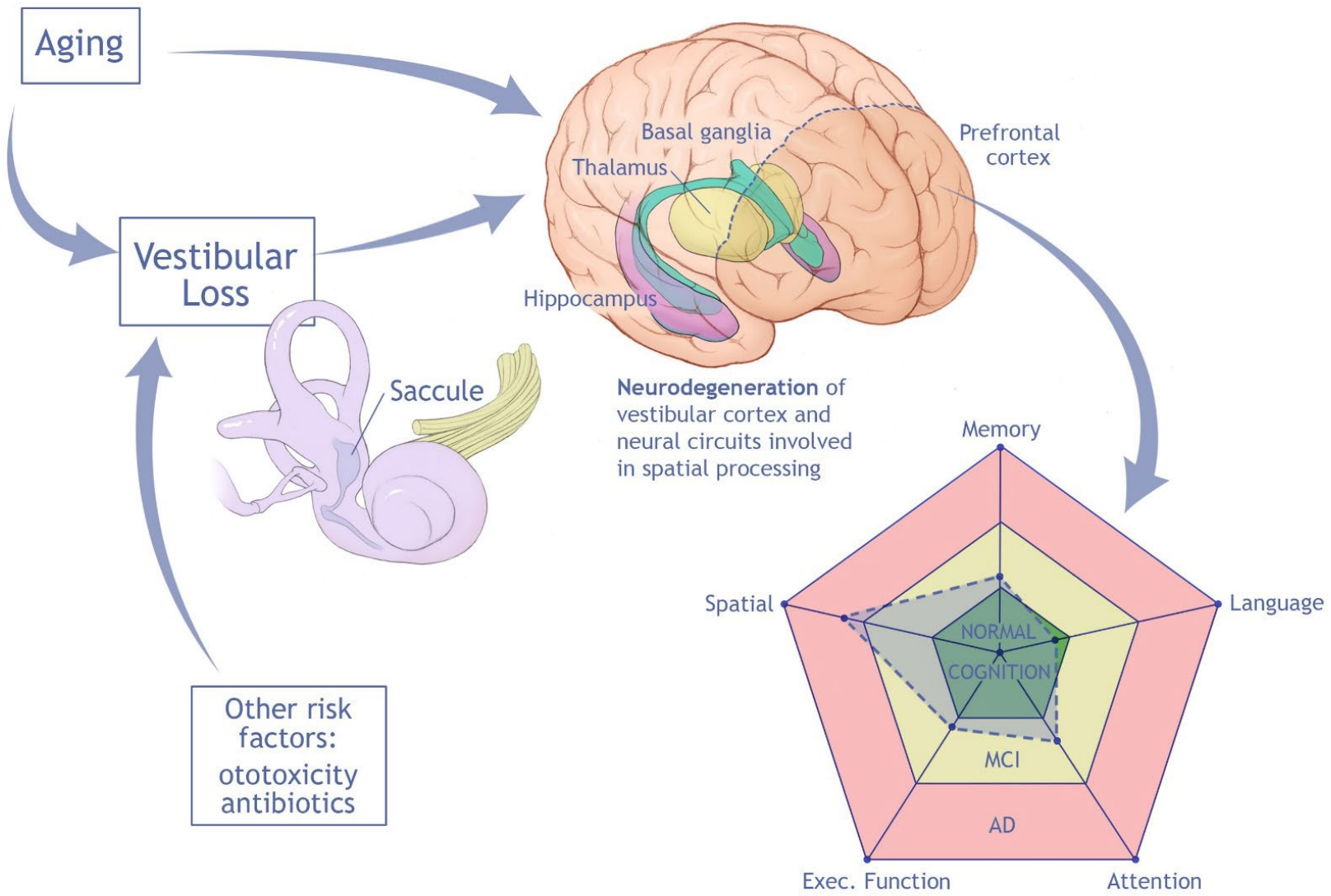


AD Clinical Study *Wei et al Dement Geriatr Cogn Dis 2017*

VESTIBULAR LOSS AND COGNITION



VESTIBULAR LOSS & COGNITION: CONCEPTUAL MODEL



Agrawal et al Aging Ment Hlth 2019

CURRENT STUDIES

Establish causal relationships

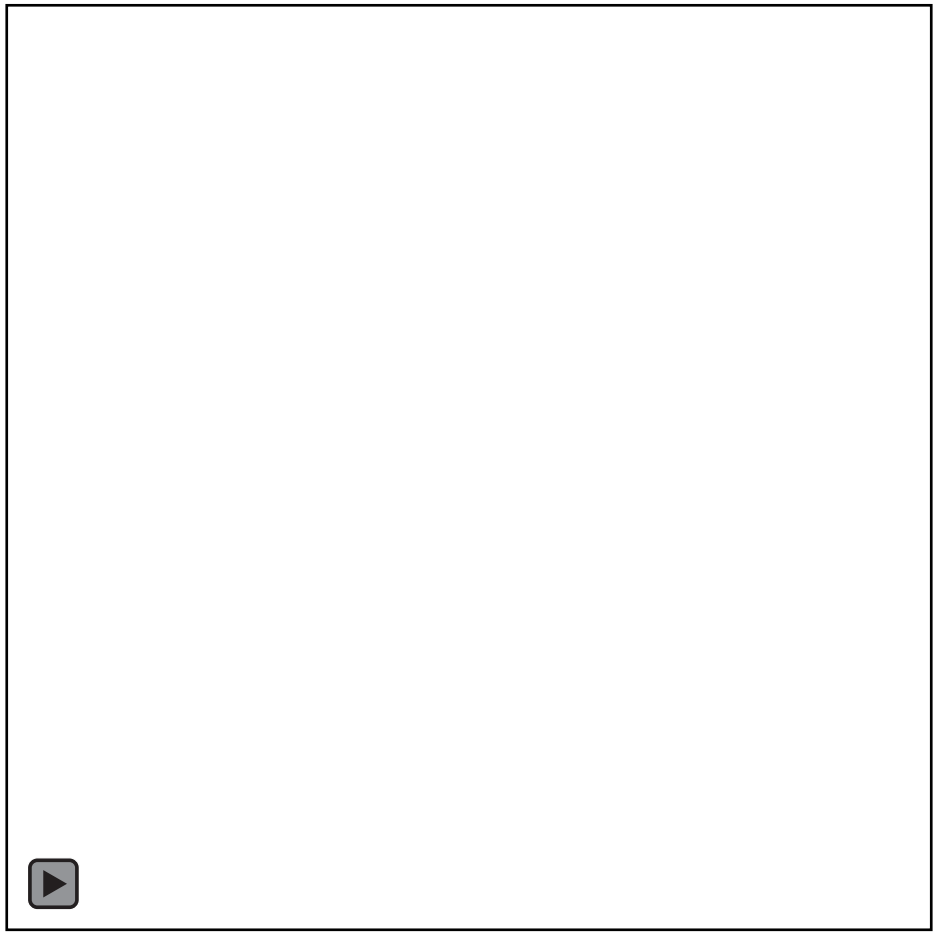
Longitudinal studies, clinical trials

Does prevention/treatment of vestibular loss improve cognitive outcomes?

Vestibular therapy: preliminary evidence

Vestibular implant, regeneration

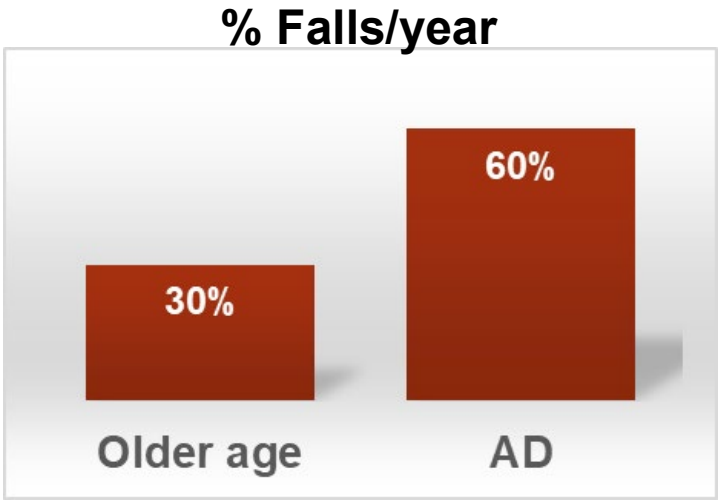
FULL CIRCLE

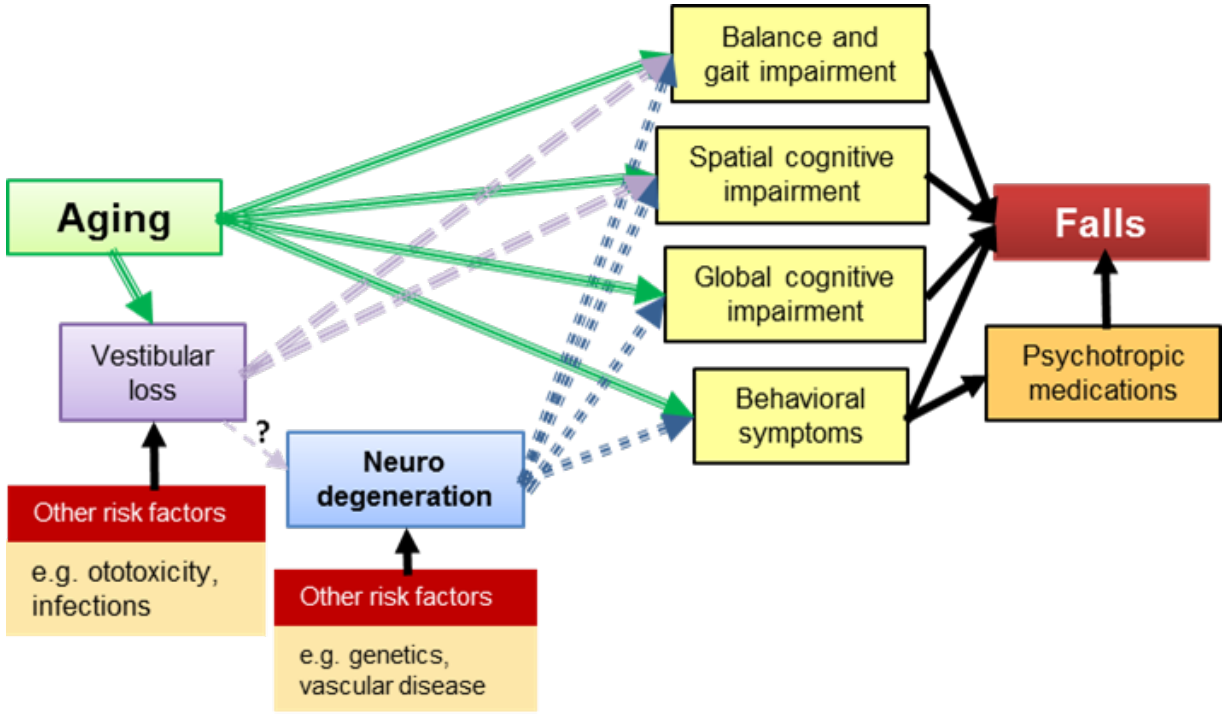


ALZHEIMER'S DISEASE AND FALLS

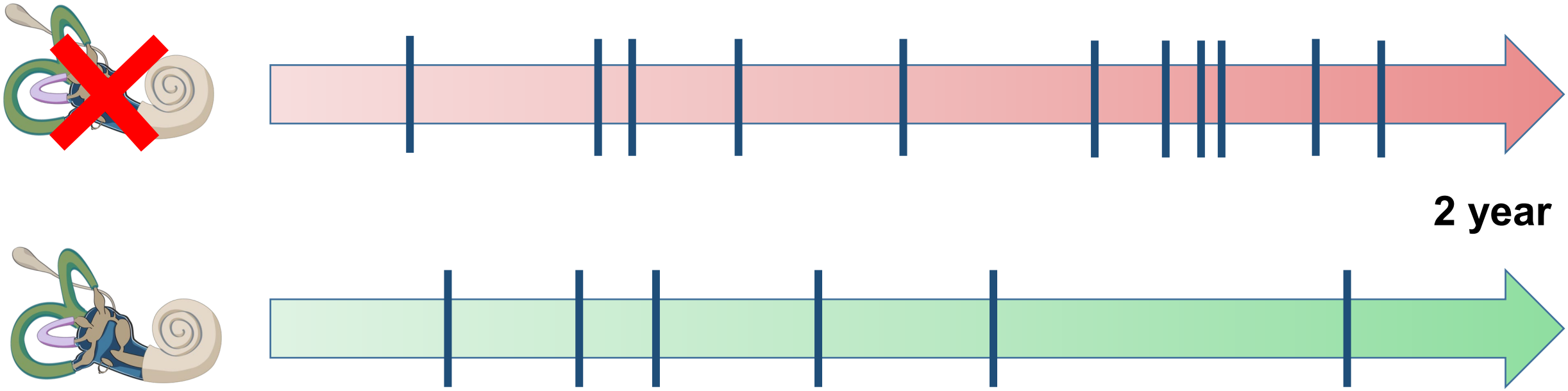
Heart disease
Cancer
COPD
Stroke
Unintentional injuries
Alzheimer's disease
Diabetes
Kidney disease
Pneumonia
Suicide

Alzheimer's is the only disease in the top 10 causes of death in the U.S. that cannot be prevented, slowed, or cured





ALZHEIMER'S DISEASE AND FALLS



Vestibular loss increases hazard of falls by 50%.

Biju et al *Journal of Alzheimer's Disease* 2022

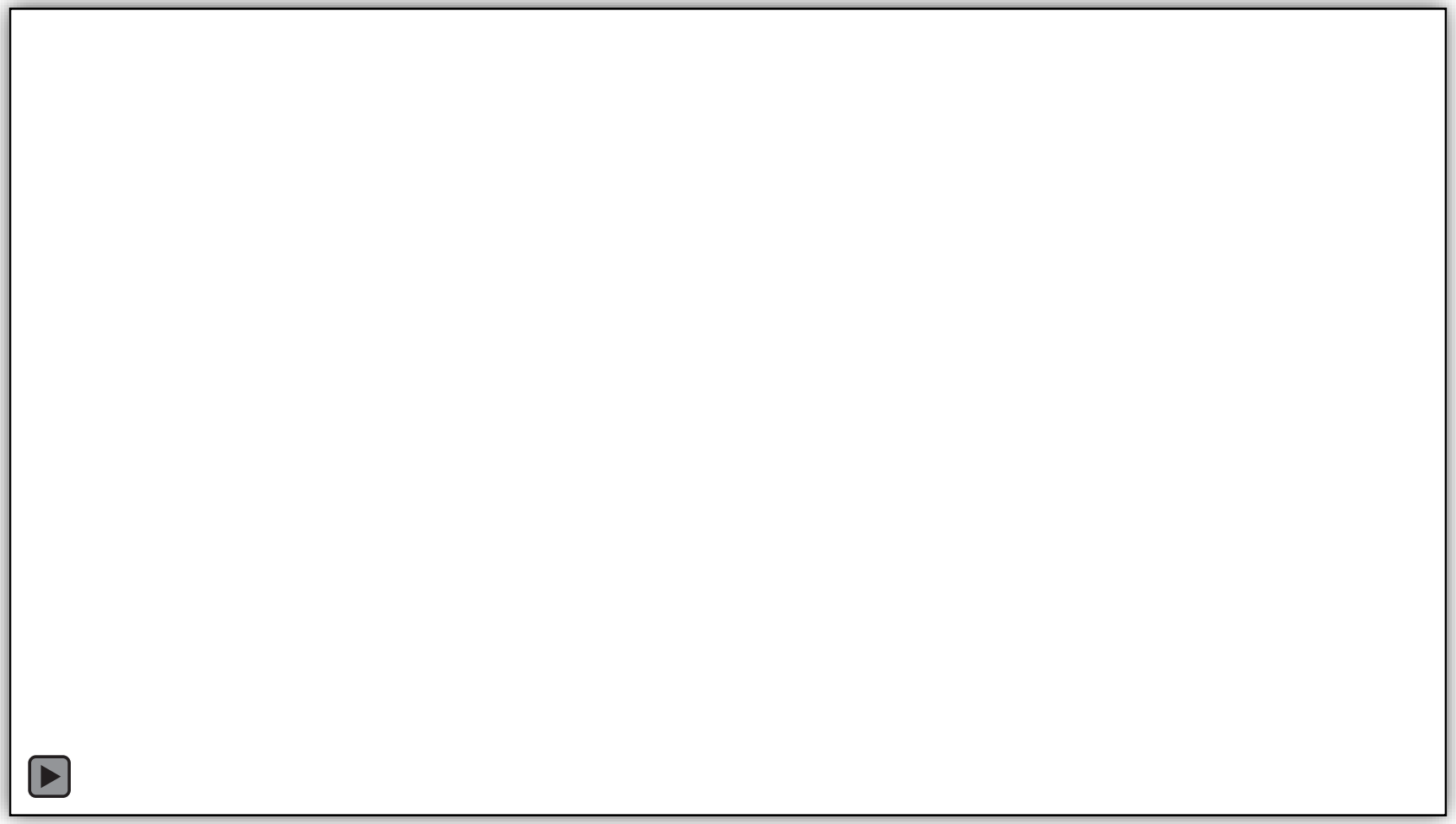
CLINICAL TRIAL OF VESTIBULAR THERAPY IN AD

Klatt et al J Neuro PT 2019

CLINICAL TRIAL OF VESTIBULAR THERAPY IN AD

So et al Laryng Inv Oto 2023

CLINICAL TRIAL OF VESTIBULAR THERAPY IN AD



Demonstration of the smooth pursuit exercise for the control group

TAKE-HOME POINTS

- Vestibular system linked to cognition, specifically spatial cognition, in healthy adults and in Alzheimer's disease
- Vestibular loss increases risk of falls in Alzheimer's disease (mechanism unknown – balance? spatial cognition?)
- Ongoing clinical trial of vestibular therapy to reduce falls in Alzheimer's disease

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Collaborators

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Tim McNamara, PhD
Paul Smith, PhD

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NIH R01AG073115

THANK YOU!

QUESTIONS?