

Normal Cognitive Aging in the SIU Longitudinal Cognitive Aging Study

Mehul Trivedi, PhD,
Assistant Professor, Department of Psychiatry
SIU School of Medicine, Springfield, IL.
04.May.2022




No Financial Disclosures



ACKNOWLEDGEMENTS

- Ronald Zec, PhD
- Gabriella Weybright, BA
- Benjamin Schulte, BA
- Madison Hollinshead, BA
- Erin Bauer, MS
- Randall Robbs, MBA
- Rebecca Hoffman, MD, MSPH
- Kathleen Schmidt, PhD
- Steve Scaife
- Tom Ala, MD
- Angela Ardoin, MA
- Amber Fifer, PharmD
- Albert Botchway, PhD
- Stephanie Kohrus, BA
- Bruce Monroe
- Dhara Patel
- Pavani Unnam
- Margi Bhatt

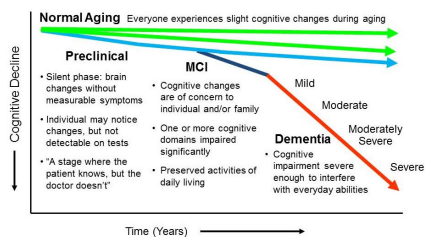
- Countless other students and research staff at the SIU Alzheimer's Center over the years.
- And anyone else who I forgot to include on this list!



LEARNING OBJECTIVES

- Provide information about the neurobiological and neurocognitive effects of normal cognitive aging.
- Provide a description of the demographic characteristics and study methods of the SIU Longitudinal Cognitive Aging Study.
- Provide information about the importance of neuropsychological testing for the diagnosis of neurocognitive disorders versus normal cognitive aging.

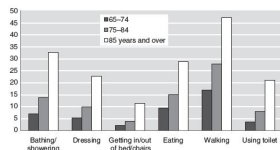
A Continuum of Normal Aging to Dementia



DEMOGRAPHICS OF AGING IN THE UNITED STATES

- In 2016, there were approximately 49.2 million people age 65 or greater.
- By 2060, that number is expected to double to 94.7 million.
- This increase, largely reflects the aging baby boomer population along with improvements in health care.
 - Those individuals born between 1946 and 1964.

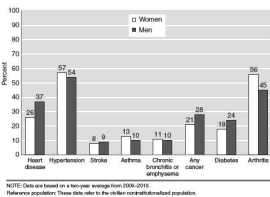
Percentage of persons with limitations in ADL by age group: 2009.



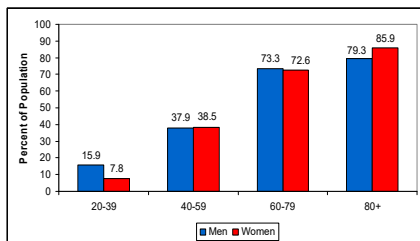
Source: Administration on Aging (AoA). (2011). A profile of older Americans: 2011. Retrieved from www.aoa.gov/aoproof/aging_statistics/Profile/index.aspx

PERCENTAGE OF PEOPLE AGE 65 AND OVER WHO REPORTED HAVING SELECTED CHRONIC HEALTH CONDITIONS, BY GENDER, 2009-2010.

Many of these are risk factors for dementia and are modifiable!

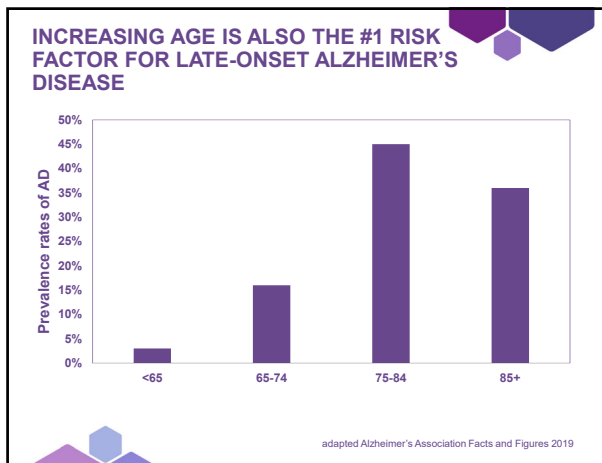


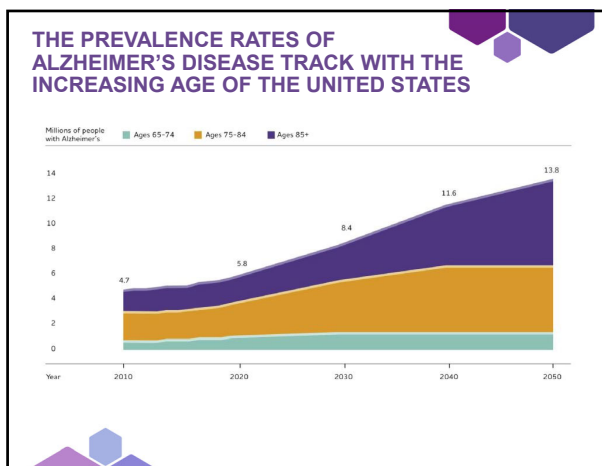
Source: Data from U.S. Census Bureau. Compiled by the Federal Interagency Forum on Aging-Related Statistics—Older Americans 2012: Key Indicators of Well-Being. Retrieved from www.agingstats.gov



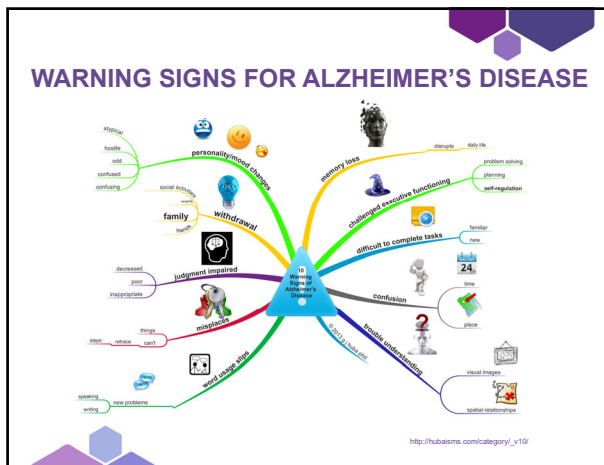
Prevalence of CVD in adults age 20 and older by age and sex (NHANES: 2005-2006). Source: NCHS and NHLBI.

These data include coronary heart disease, heart failure, stroke, and hypertension.





- Declines over time in memory and other cognitive abilities, which are greater than expected for one's age are one of the first obvious symptoms of Alzheimer's disease.
- It is important to understand what normal cognitive aging looks like to be able to better understand what abnormal cognitive aging looks like.



SO "NORMAL" AGING IS ASSOCIATED WITH GREATER DISABILITY, MORE MEDICAL PROBLEMS, AND INCREASED RISK FOR ALZHEIMER'S DISEASE

- What does normal cognitive aging look like?
- What happens to brain structure and function in normal aging?

MANY DEFINITIONS OF WHAT IS NORMAL

<ul style="list-style-type: none"> • Typical • Standard • Average • Not deviating from a norm • Natural • In accordance with scientific laws 	<ul style="list-style-type: none"> • Lacking abnormalities • Not abnormal • Occurring naturally, not because of disease • Free from mental disorder • Balanced, well-integrated functioning
--	--

WHAT DOES NORMAL COGNITIVE AGING LOOK LIKE?

Vulnerable Processes

- Fluid IQ
- Reaction time
- Psychomotor speed
- Working memory
- Executive function
- Episodic learning/memory
- Complex visual processing

(Relatively) Preserved Processes

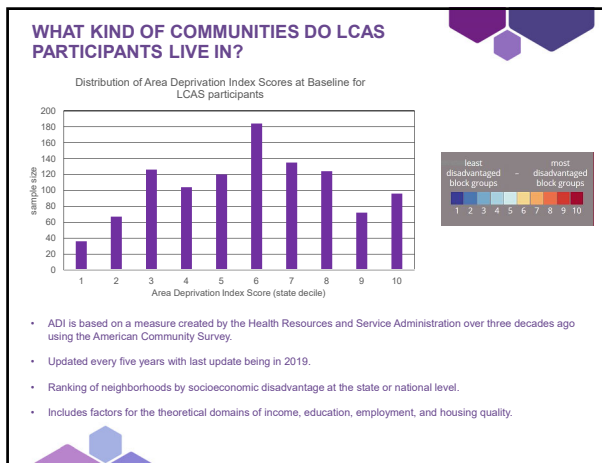
- Crystallized IQ
- Word reading
- Simple attention span
- Vocabulary
- Priming
- Semantic memory
- Procedural memory
- Long-term autobiographical memory.

THE SIU LONGITUDINAL COGNITIVE AGING STUDY (LCAS)

- LCAS is a community-based, longitudinal cohort study of the incidence of neurocognitive disorders such as AD in predominantly older adults who reside in Springfield and the surrounding communities.
- The study was started by Dr. Ronald Zec, PhD in 1984 with a focus on improving the sensitivity of neuropsychological testing to the diagnosis of mild cognitive impairment and dementia.
- The study was closed in 2016 and reopened in 2018.
- Over 1,600 (mostly older) adults (age range: 18-90+). Participants complete:
 - Serial cognitive testing (2.5 hours), every effort is made to see participants on a yearly basis.
 - 95% of participants in the cohort are white/Not-Hispanic and over 70% are female.
- Currently following over 150 participants, some of whom have been in the study for over 30 years!
- Over 100 sisters from Saint Francis, Sacred Heart, and Ursuline convents in the Springfield area have participated in the study.
- Participants are recruited from the community via newspaper advertisement, word-of-mouth, and community presentations.
- Sample is enriched for persons with a family history of AD (children, siblings, other relatives).
- 960 participants have passed away.

SIU LCAS INCLUSION AND EXCLUSION CRITERIA

- Individuals must be free of neurological, uncontrolled medical or psychiatric disease at their first visit.
- Preferably, 65+ years of age.
- Approximately 15% of participants met the diagnostic criteria for MCI or AD at baseline or developed these conditions on subsequent visits.
- Particularly interested in individuals with a family history of AD, minority groups, and individuals who reside in rural communities.



- ### CURRENT NEUROPSYCHOLOGICAL TEST BATTERY ASSESSES:
- Orientation and Mental Status
 - Learning and Memory
 - Language
 - Visuospatial skills
 - Processing Speed and Executive Function

- ### CURRENT QUESTIONNAIRES
- Assess personality, subjective cognitive activities and complaints, mood, and anxiety.
 - Assess lifestyle factors:
 - Independent living skills
 - Social activity
 - Diet
 - Physical Activity
 - Detailed medical history inventory:
 - Information regarding personal medical and psychosocial histories,
 - family medical and psychosocial histories
 - Current medications.

OPTIONAL BRAIN DONATION PROGRAM

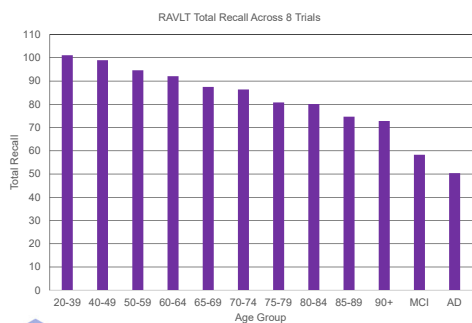
- 26 participants have died, donated their brain, and had an autopsy.
 - 17 were diagnosed with AD.
- 38 controls signed the intent to donate form and passed away without their brains being collected for unknown reasons.
- Of the participants we are currently following, around 60 have completed the intent to donate forms.
 - 2 participants who completed the intent-to-donate form after the study re-opened in 2018 passed away without their brains being collected.

So what does normal cognitive aging look like in this cohort?

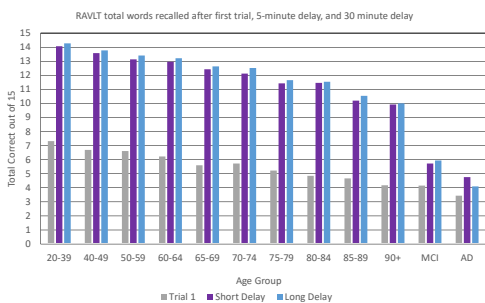
EPISODIC LEARNING/MEMORY

- Word list learning and memory:
 - Repeat the list several times and test free recall after each trial.
 - Test delayed recall for the list (5 and 30 minutes later).
 - Recognition memory.
 - Correctly identify words from the list intermixed with words that were not from the list.
- Story learning and memory:
 - Examinee is read a short story and asked to recall the story immediately after hearing it and then again 20 minutes later

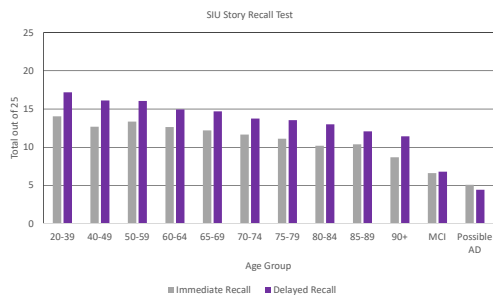
AGING EFFECTS ON A WORD LIST LEARNING/MEMORY TEST (RAVLT)



AGING EFFECTS ON A WORD LIST LEARNING/MEMORY TEST (RAVLT)

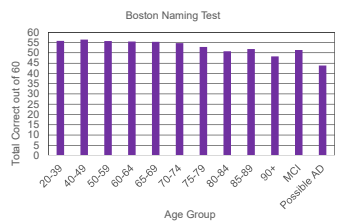
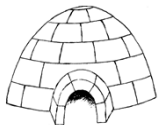


AGING EFFECTS ON THE SIU STORY RECALL TEST

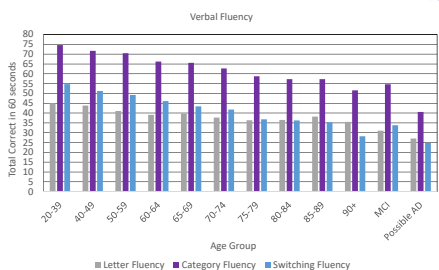


Aging effects on Language skills: Naming of Line drawings

What is this called?



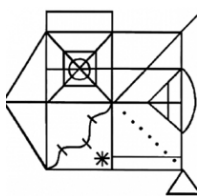
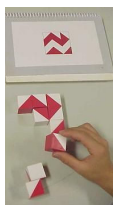
Aging effects on Language Skills: Verbal Fluency



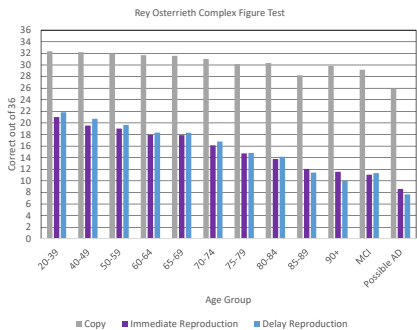
- Letter fluency: Tell me as many words as you can that begin with the letters 'F, A, S' but do not say any words that start with capital letters or numbers.
- Category fluency: Name as many unique animals, boys names, and states as you can.
- Switching fluency: Switch back and forth between saying occupations/colors, states of the United States and animals, and the letters C and P

VISUOSPATIAL SKILLS

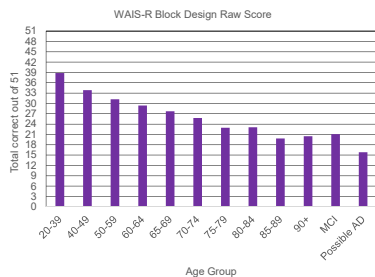
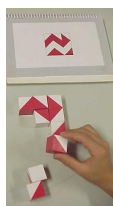
- Complex Figure Copy with immediate and delayed recall
- Spatial Reasoning



COPY, IMMEDIATE RECALL, AND DELAYED RECALL TRIALS



SPATIAL PROBLEM SOLVING



PROCESSING SPEED

KEY

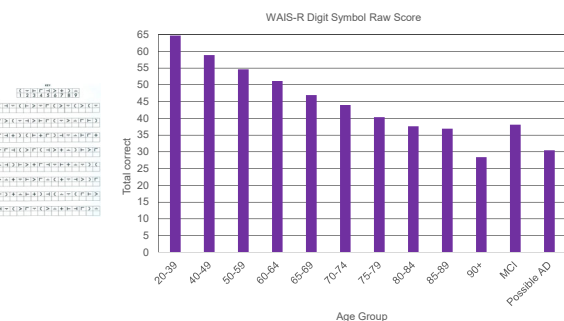
C	+	F	>	+	>	+	>	
1	2	3	4	5	6	7	8	9

C	+	F	>	F	>	F	>	C	>	C	+
F	>	C	+	F	>	F	>	C	+	F	>
F	+	+	>	C	+	F	>	F	>	+	+
+	+	+	>	F	>	C	+	+	+	>	F
+	+	>	F	>	+	+	+	+	+	>	C
>	+	+	+	+	+	F	>	C	+	+	+
+	+	+	+	+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+	+	+	+	+

EXECUTIVE FUNCTIONS

- “Frontal lobe functions”
- A set of cognitive processes that include:
 - Attentional control
 - Inhibitory control
 - Working memory
 - Cognitive flexibility
 - Multitasking
 - Reasoning
 - Problem solving
 - Planning/Organization
 - Set-Shifting

PROCESSING SPEED



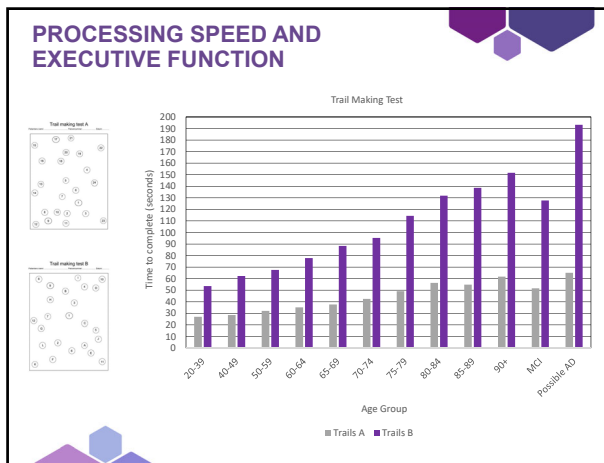
PROCESSING SPEED AND EXECUTIVE FUNCTION

Trail making test A

Patient's name: _____ Page number: _____ Date: _____

Trail making test B

Patient's name: _____ Page number: _____ Date: _____



PROCESSING SPEED AND EXECUTIVE FUNCTION

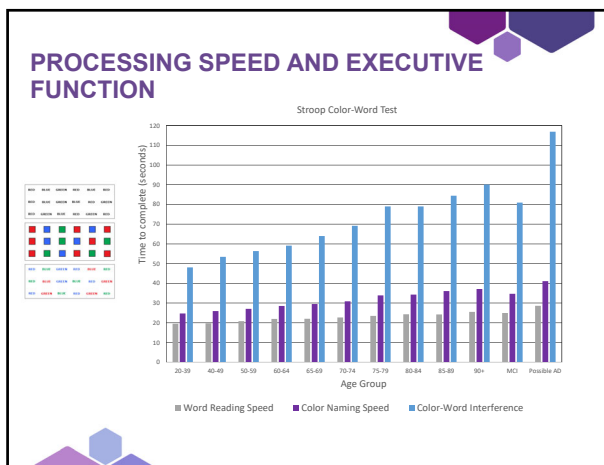
Read the words as quickly as you can across each line until the end of the last line

RED BLUE GREEN RED BLUE RED
 RED BLUE GREEN BLUE RED GREEN
 RED GREEN BLUE RED GREEN RED

Name the colors as quickly as you can across each line until the end of the last line

Name the color of the ink the words are printed in but do not read the words

RED BLUE GREEN RED BLUE RED
 RED BLUE GREEN BLUE RED GREEN
 RED GREEN BLUE RED GREEN RED



WHAT BRAIN CHANGES ARE HAPPENING IN NORMAL AGING?



SHRINKAGE!

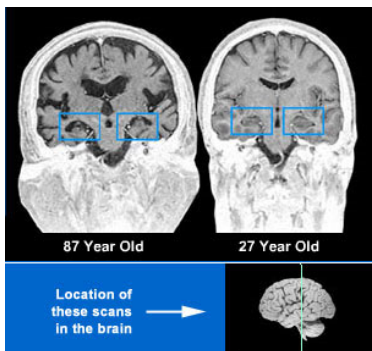


I was in the pool! I was in the pool!

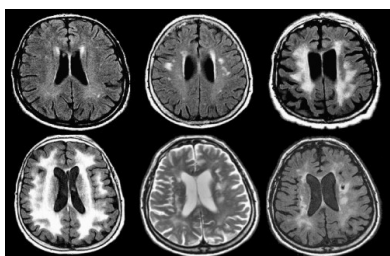
BRAIN VOLUME

- Brain volume ↓ with age at a rate of ~2% per decade beginning in early adulthood.
- CSF volume ↑ with age
- The percentage of brain volume loss correlates with declines in cognitive function in both normal aging and AD.
- Conflicting reports in the literature about which parts of the brain sustain greatest volume loss
 - Frontal vs. Temporal vs. Parietal vs. Occipital

THE AGING BRAIN



MICROVASCULAR CHANGES ON MRI



The spectrum of small vessel disease-related brain changes in MRI: white matter lesions ranging from punctate foci (*upper left*) to extensive confluent abnormalities (*lower left*) and lacunar infarcts (*lower right*).

MICROVASCULAR CHANGES IN NORMAL AGING

- More prominent white matter ischemia as age ↑.
- ↓ white matter integrity in normal aging.
- Speed of information processing along white matter tracts ↓ in normal aging
 - Critical for the processing and integration of complex information.
- Myelin breakdown in white matter contributes to the cognitive declines associated with normal aging.

AGING AND NEUROCHEMISTRY

- ↓ Dopamine
- ↓ Acetylcholine
- ↓ Norepinephrine
- ↓ Serotonin
- ↓ NMDA receptors
- ↓ Cholinergic receptors

THE AGING BRAIN: FUNCTIONAL CHANGES

- **Single-unit recordings**
 - Diminished neuronal firing rate/alteration in firing pattern
- **Sensory evoked potentials**
 - Diminished and delayed
- **Blood flow (SPECT)**
 - Diminished perfusion in select cortical regions
- **Metabolic activity (PET)**
 - Diminished uptake in select cortical regions
- **fMRI**
 - Changes in task-related activation

SUMMARY

- Aging is associated with increased prevalence of chronic medical conditions, disability, and dementia.
- The SIU LCAS study is but one of many large studies across the world that are examining neurobiological, neuropsychological, and psychosocial factors that are associated with both normal and abnormal aging.
- Normal Aging is associated with changes in brain structure/function, which correlates with age-related declines in cognitive function.
- Normal Aging is associated with declines in some (but not all) cognitive abilities.
 - These changes are less extensive than observed in individuals who go on to develop dementia.

Thank You for your attention!

Questions?