

Normal Cognitive Aging in the SIU Longitudinal Cognitive Aging Study

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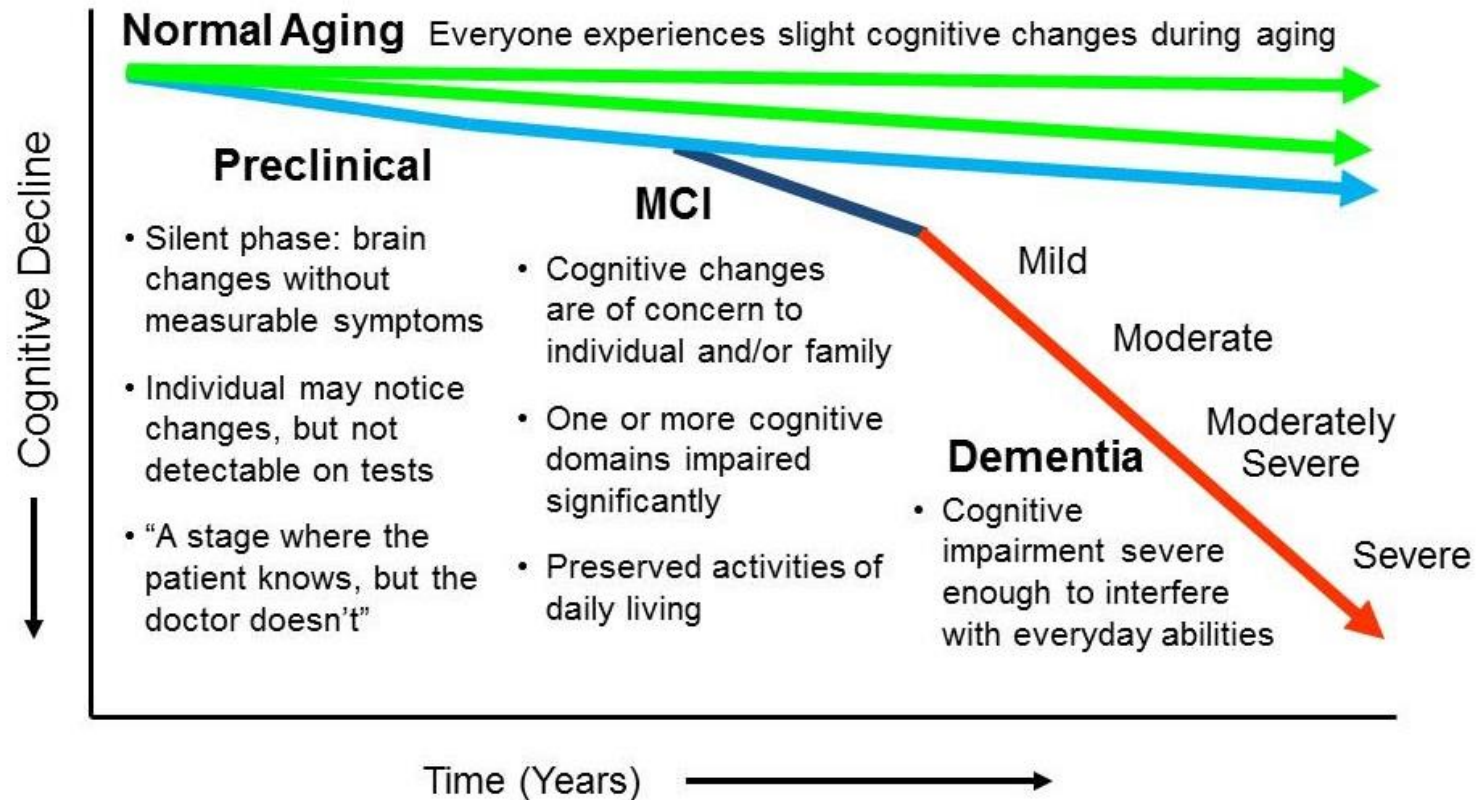
LEARNING OBJECTIVES



- 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



<http://www.mind.uci.edu/alzheimers-disease/what-is-alzheimers/mild-cognitive-impairment>



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.

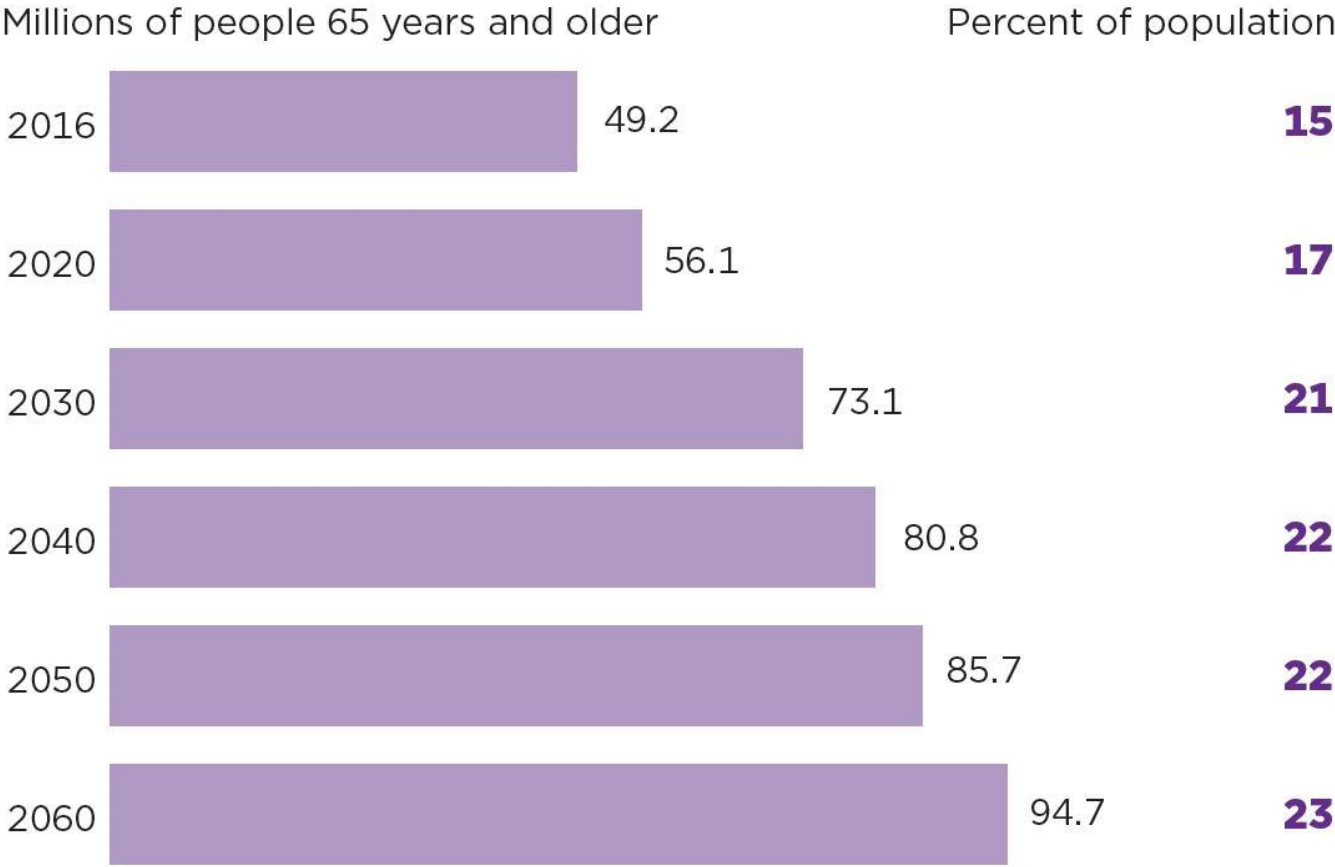


DEMOGRAPHICS OF AGING IN THE UNITED STATES



Projections of the Older Adult Population: 2020 to 2060

By 2060, nearly one in four Americans is projected to be an older adult.



Source: U.S. Census Bureau, 2017 National Population Projections.





DEMOGRAPHICS OF AGING IN THE UNITED STATES

TABLE 1.2 *Becoming an Age Rectangle*

YEAR	UNDER AGE 18	OVER AGE 65
1900	40%	4%
1980	28%	11%
2030	20%	20%





DISABILITY IN OLDER ADULTS

TABLE 1.3 Percentage of Persons Age 65+ With a Disability, 2013

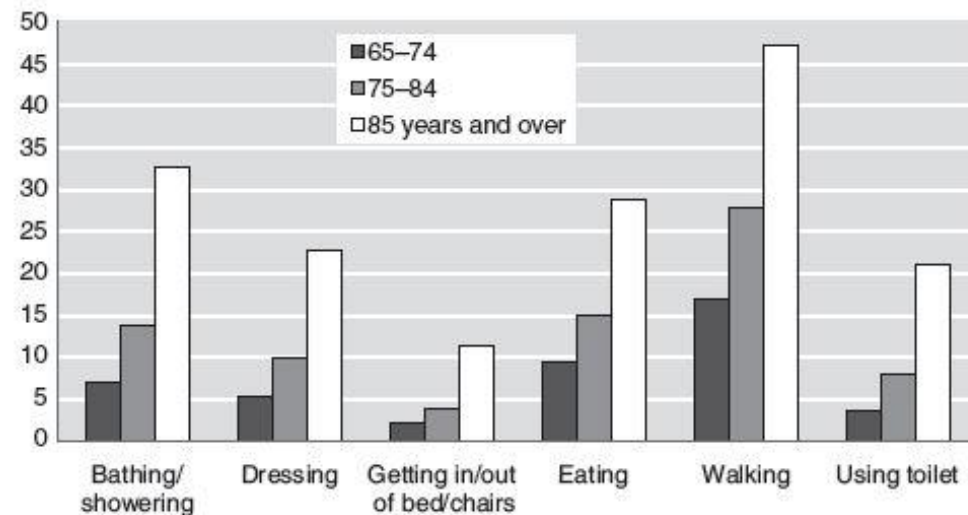
Independent living difficulty	15%
Self-care difficulty	9%
Ambulatory difficulty	23%
Cognitive difficulty	9%
Vision difficulty	7%
Hearing difficulty	15%
Any disability	36%

Source: U.S. Census Bureau, American Community Survey. (2014). *Older Americans with a disability: 2008–2012*. U.S. Department of Commerce.





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



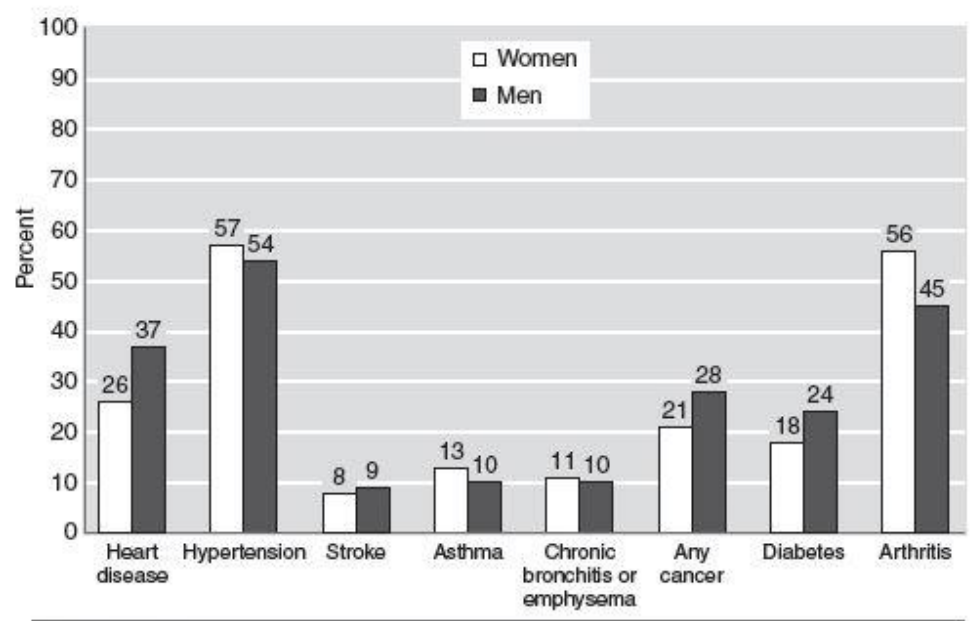
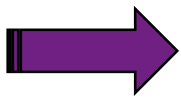
Source: Administration on Aging (AoA). (2011). *A profile of older Americans: 2011*. Retrieved from www.aoa.gov/aoaroot/aging_statistics/Profile/index.aspx





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

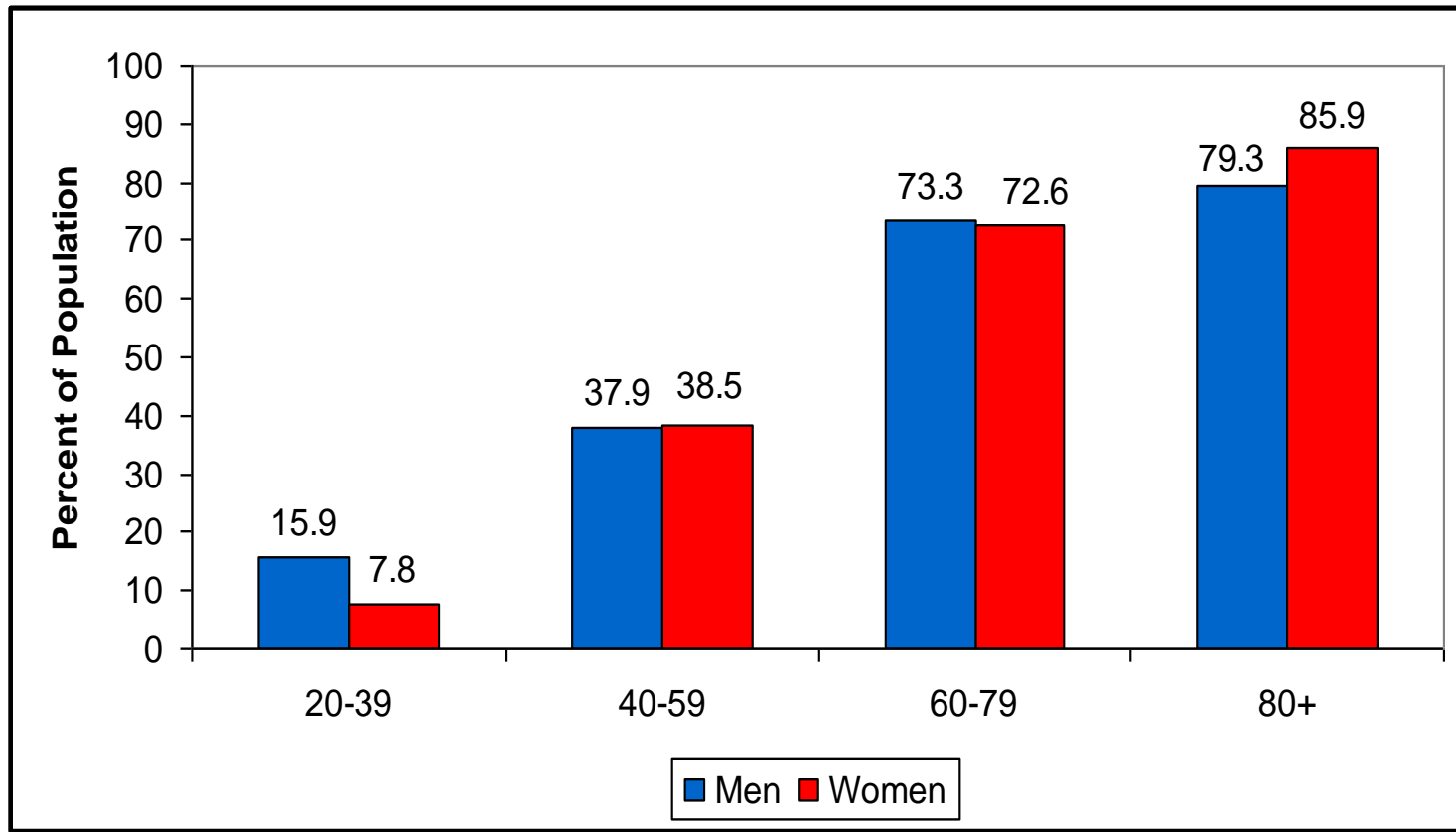
Many of these are risk factors for dementia and are modifiable!



NOTE: Data are based on a two-year average from 2009–2010.
Reference population: These data refer to the civilian noninstitutionalized population.

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

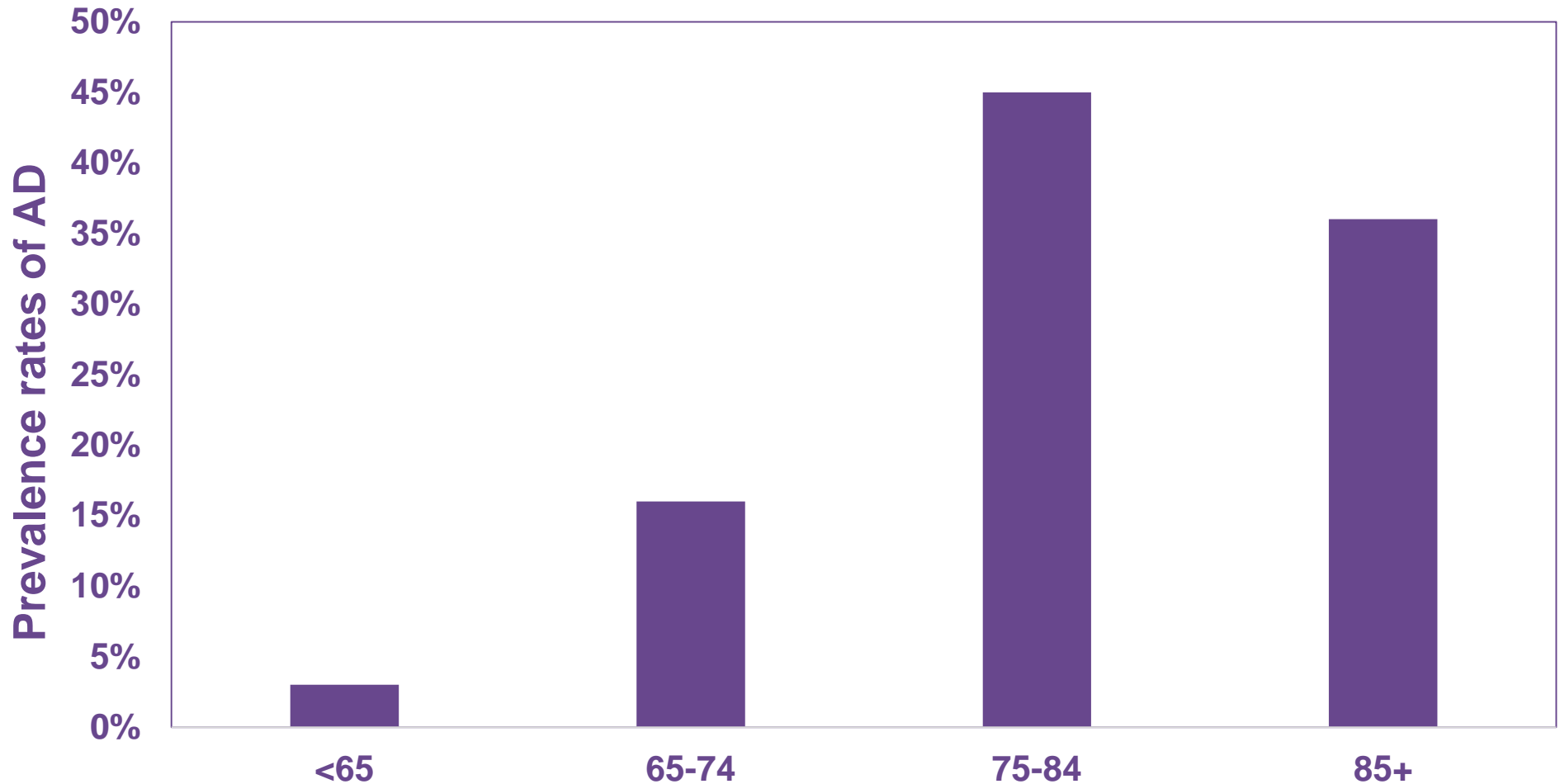




Prevalence of CVD in adults age 20 and older by age and sex (NHANES: 2005-2006). Source: NCHS and NHLBI.

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

INCREASING AGE IS ALSO THE #1 RISK FACTOR FOR LATE-ONSET ALZHEIMER'S DISEASE



adapted Alzheimer's Association Facts and Figures 2019

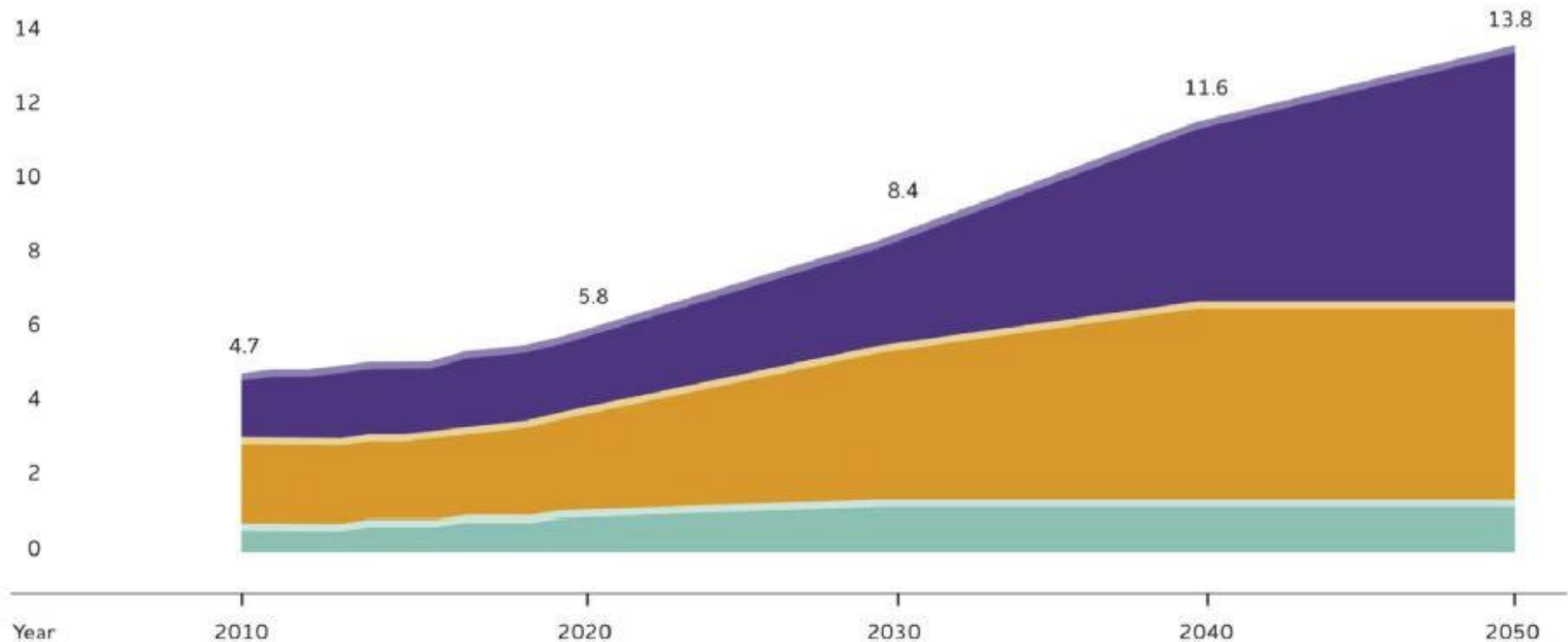
THE PREVALENCE RATES OF ALZHEIMER'S DISEASE TRACK WITH THE INCREASING AGE OF THE UNITED STATES

Millions of people with Alzheimer's

Ages 65-74

Ages 75-84

Ages 85+



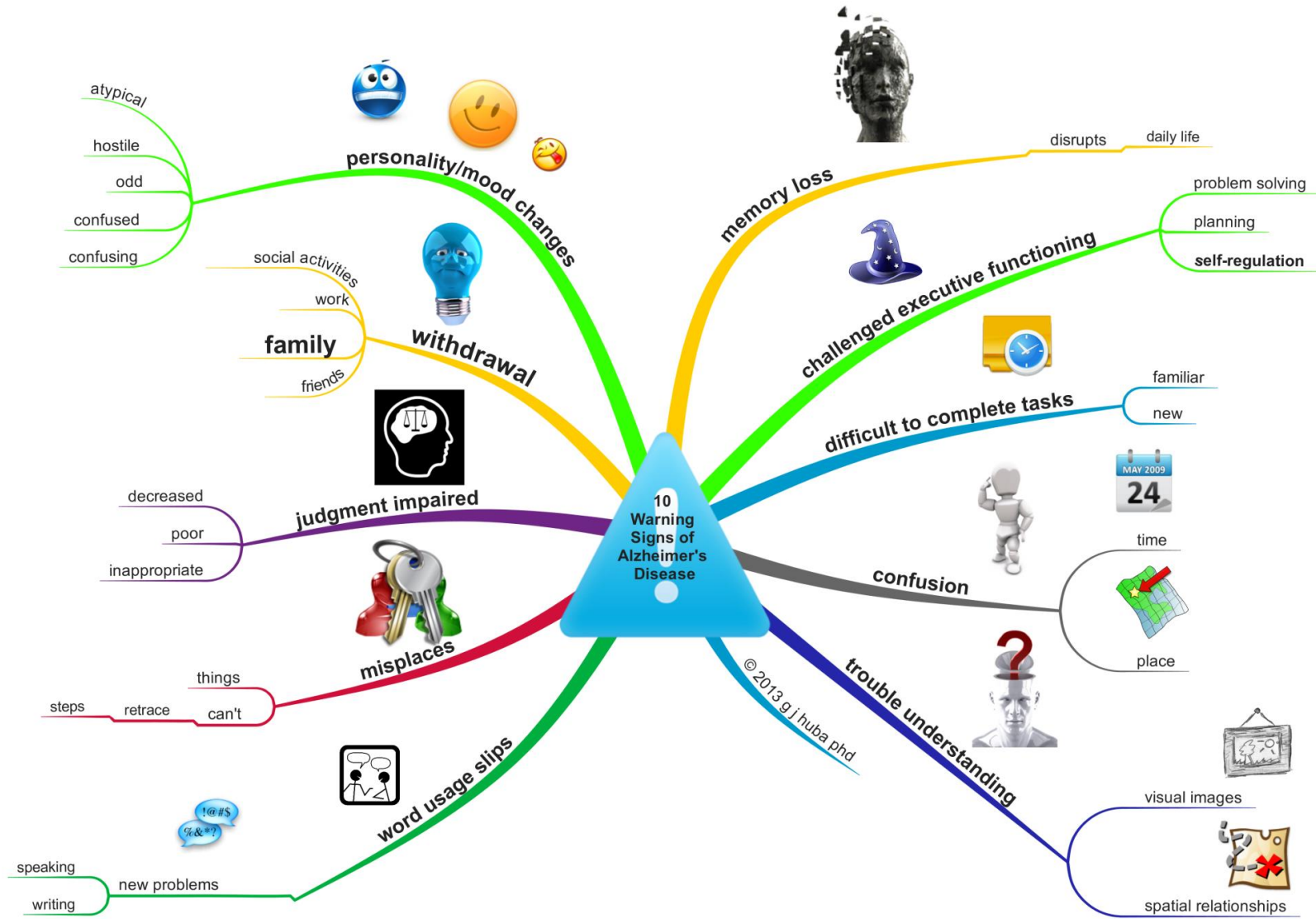
adapted Alzheimer's Association Facts and Figures 2019



- 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.



WARNING SIGNS FOR ALZHEIMER'S DISEASE





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

- Typical
- Standard
- Average
- Not deviating from a norm
- Natural
- In accordance with scientific laws
- 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



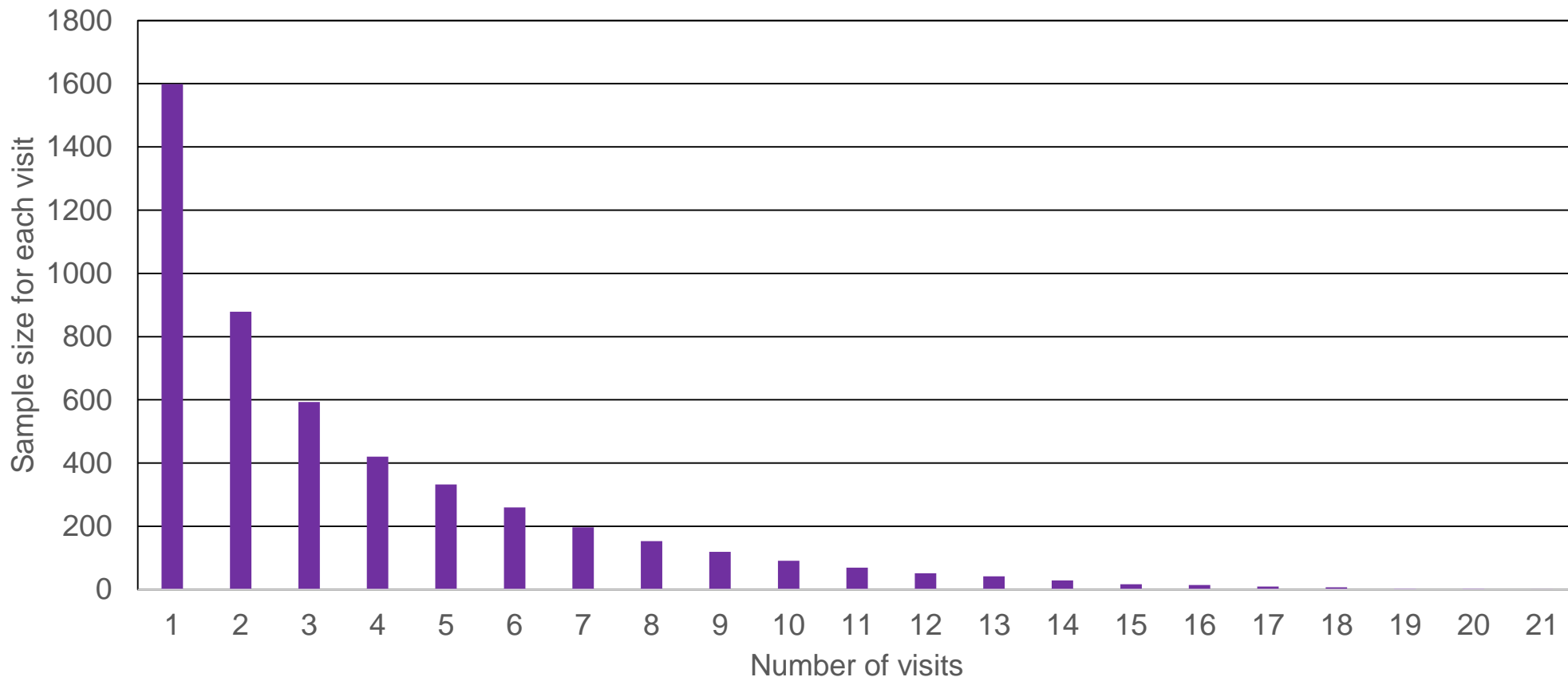
- Individuals must be free of neurological, uncontrolled medical or psychiatric disease at their first visit.
- Preferably, 65+ years of age.
- Approximately 15% of participants met the diagnostic criteria for MCI or AD at baseline or developed these conditions on subsequent visits.
- Particularly interested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



NUMBER OF PARTICIPANTS WITH ONE OR MORE STUDY VISITS



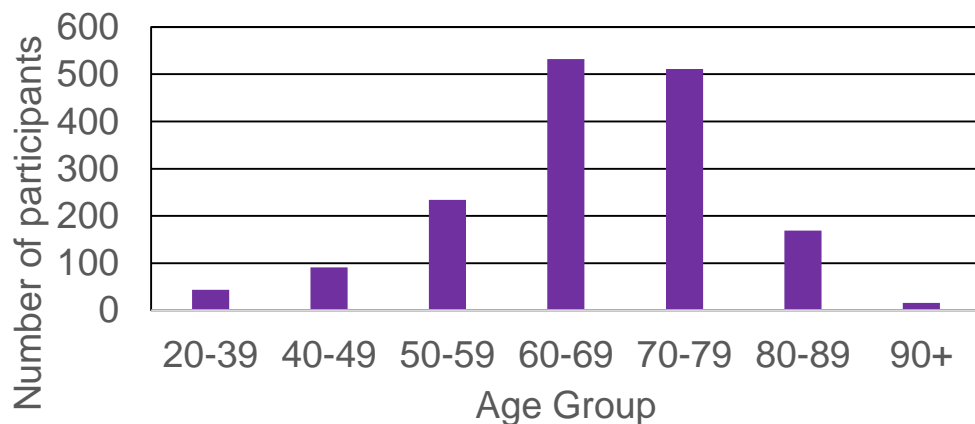
Number of study visits for participants who were cognitively normal at baseline



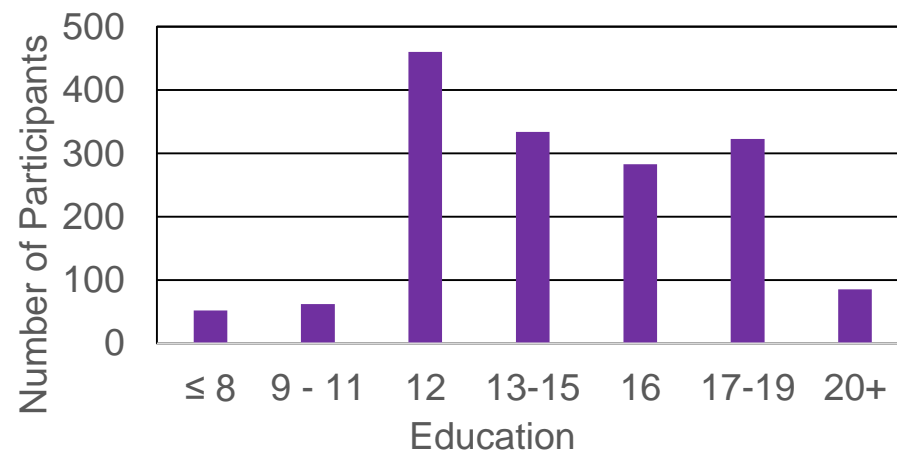
DEMOGRAPHIC DISTRIBUTION OF PARTICIPANTS AT STUDY ENTRY



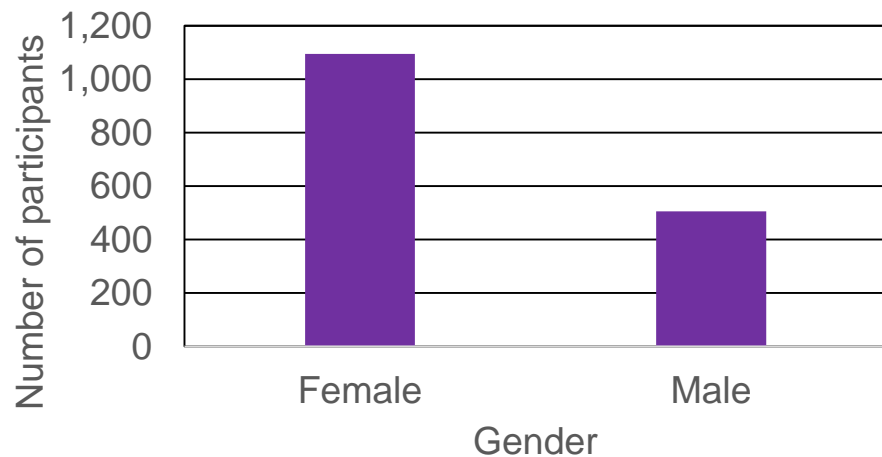
Number of participants per age group at baseline visit



Total years of educational attainment



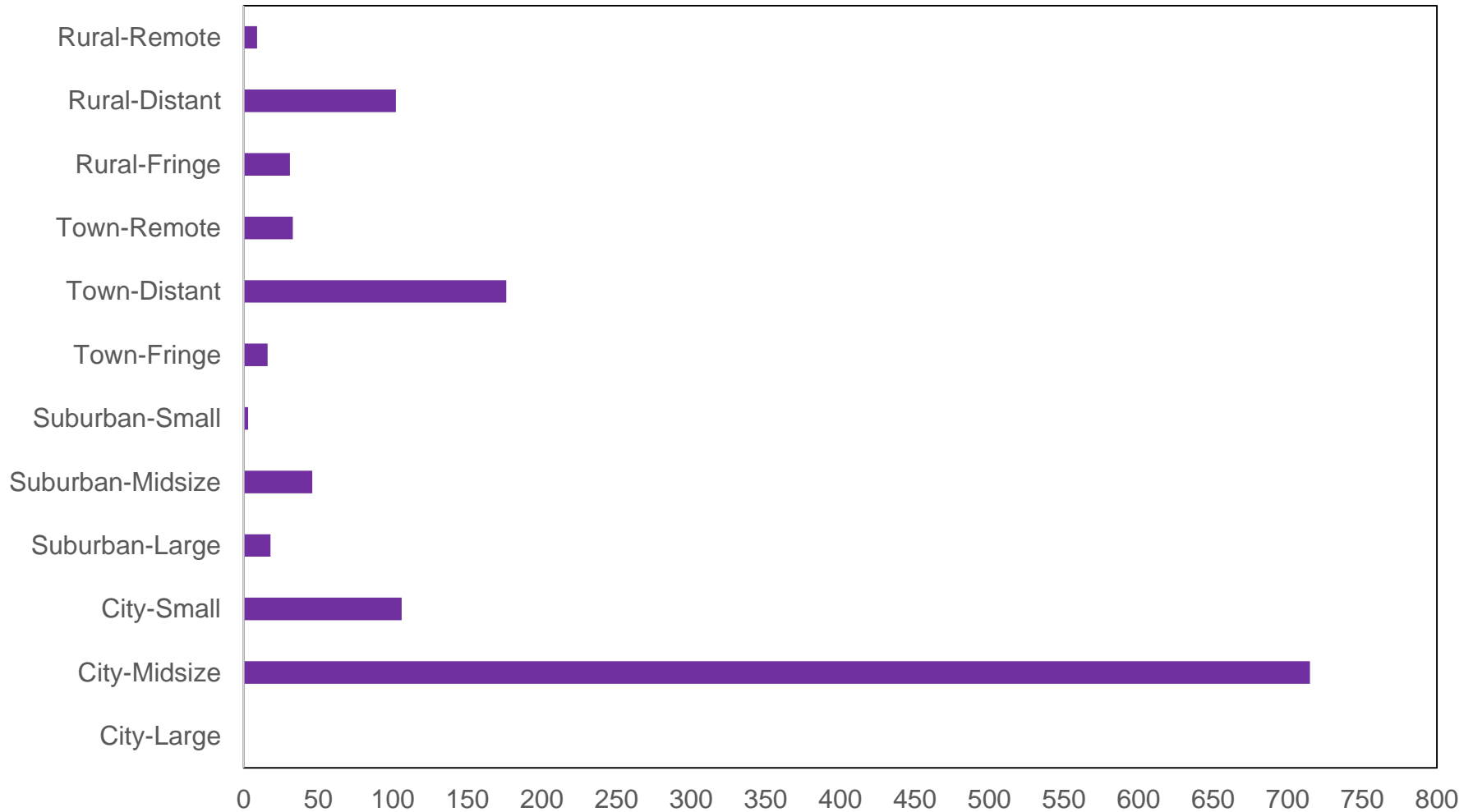
Gender distribution at study entry



WHERE ARE LCAS PARTICIPANTS FROM?



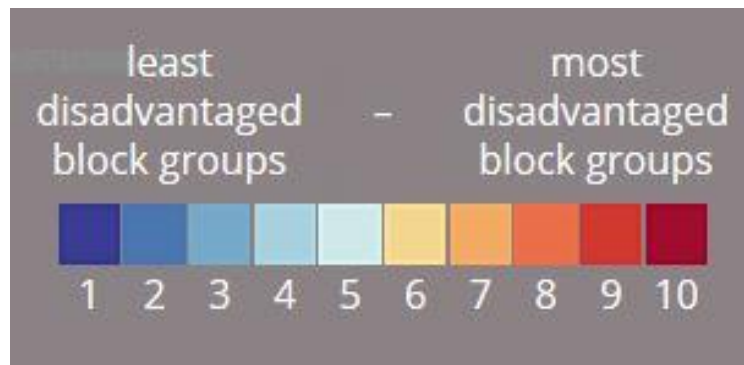
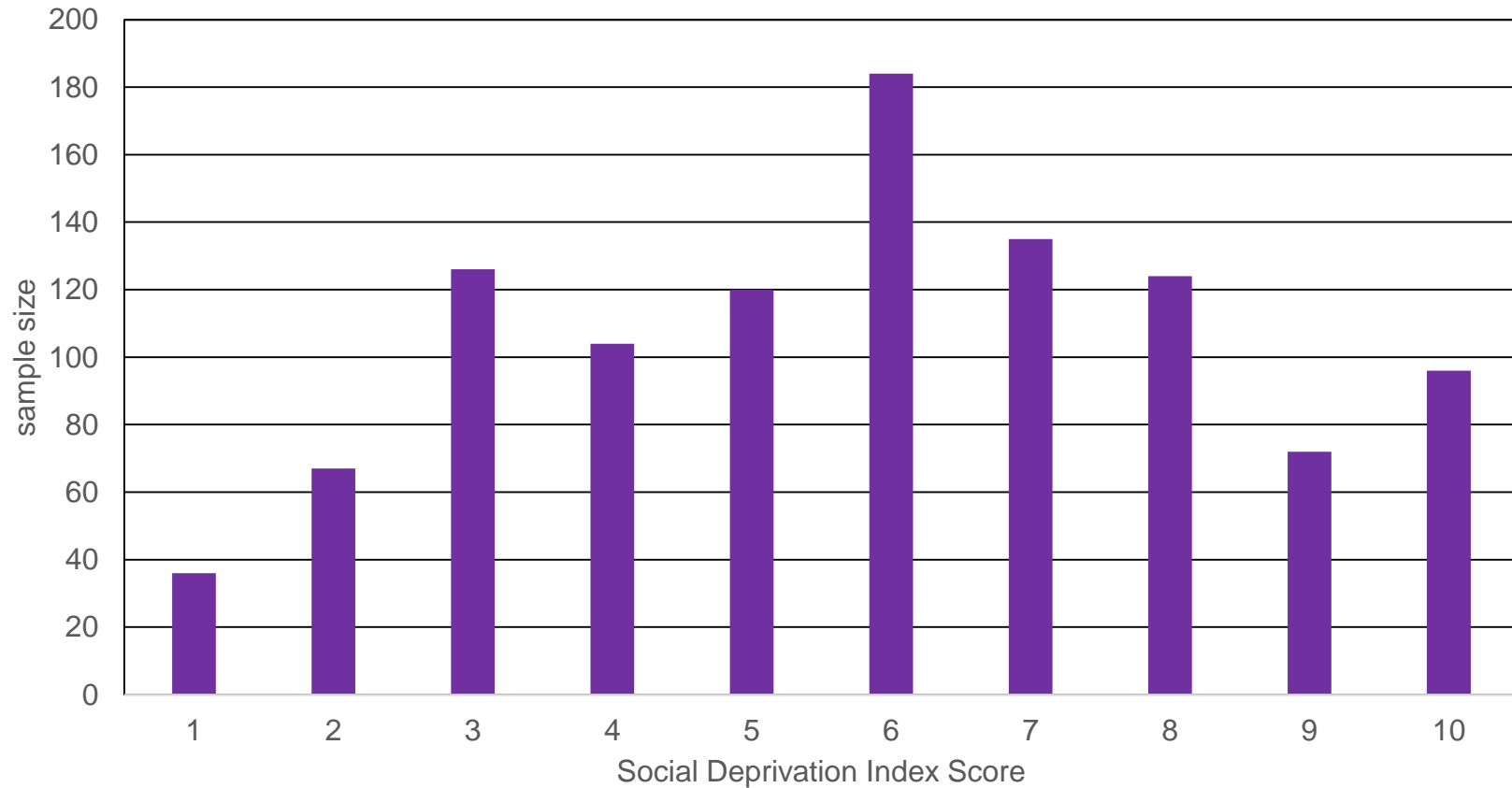
National Center for Education Statistics Geographic distribution of LCAS participants at baseline



WHAT KIND OF COMMUNITIES DO LCAS PARTICIPANTS LIVE IN?



Distribution of Area Deprivation Index Scores at Baseline for LCAS participants



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 reopened in 2018 passed away without their brains being collected.





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



EPISSODIC LEARNING/MEMORY



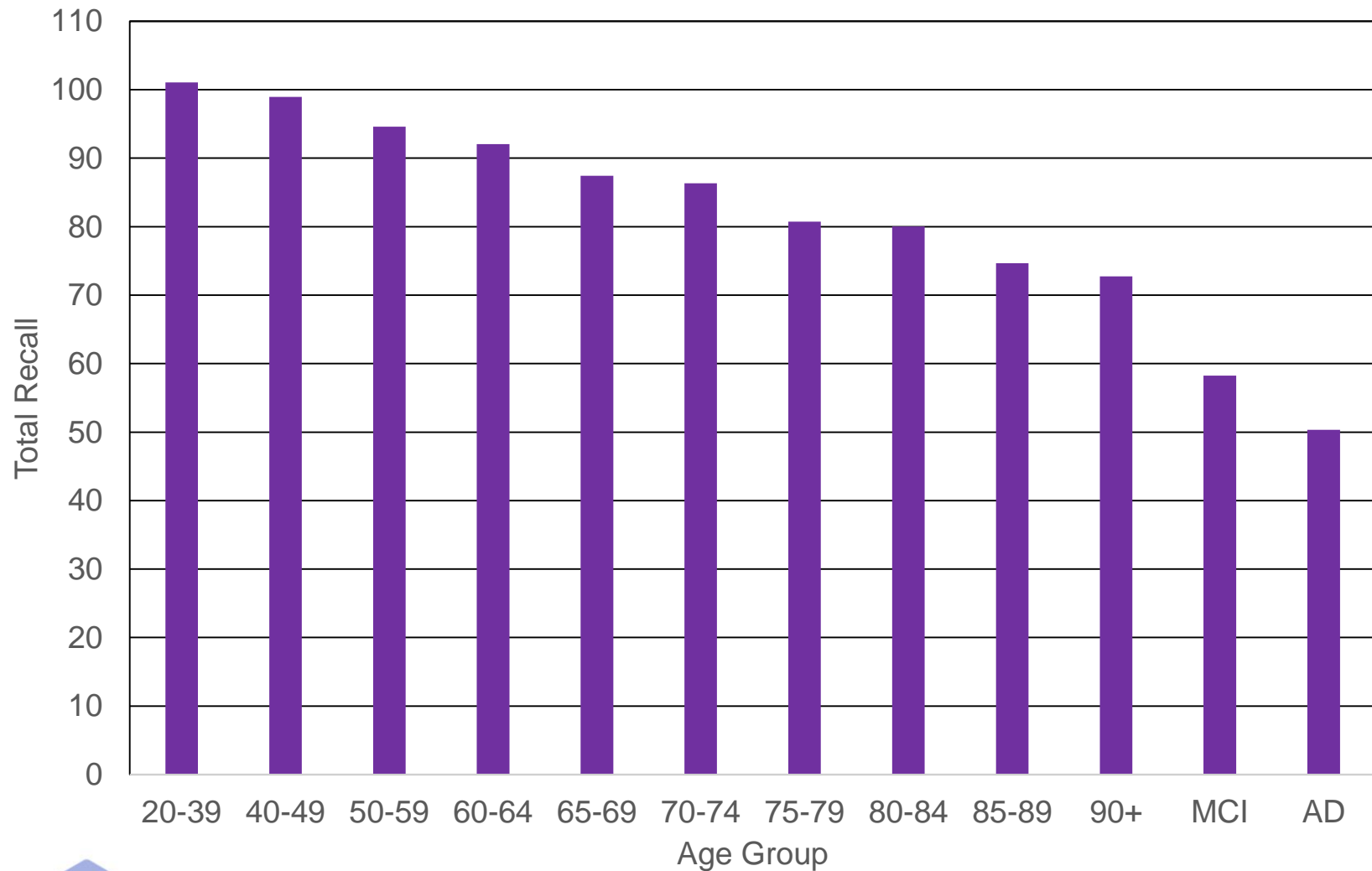
- Word list learning and memory:
 - Repeat the list several times and test free recall after each trial.
 - Test delayed recall for the list (5 and 30 minutes later).
 - Recognition memory.
 - Correctly identify words from the list intermixed with words that were not from the list.
- Story learning and 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)

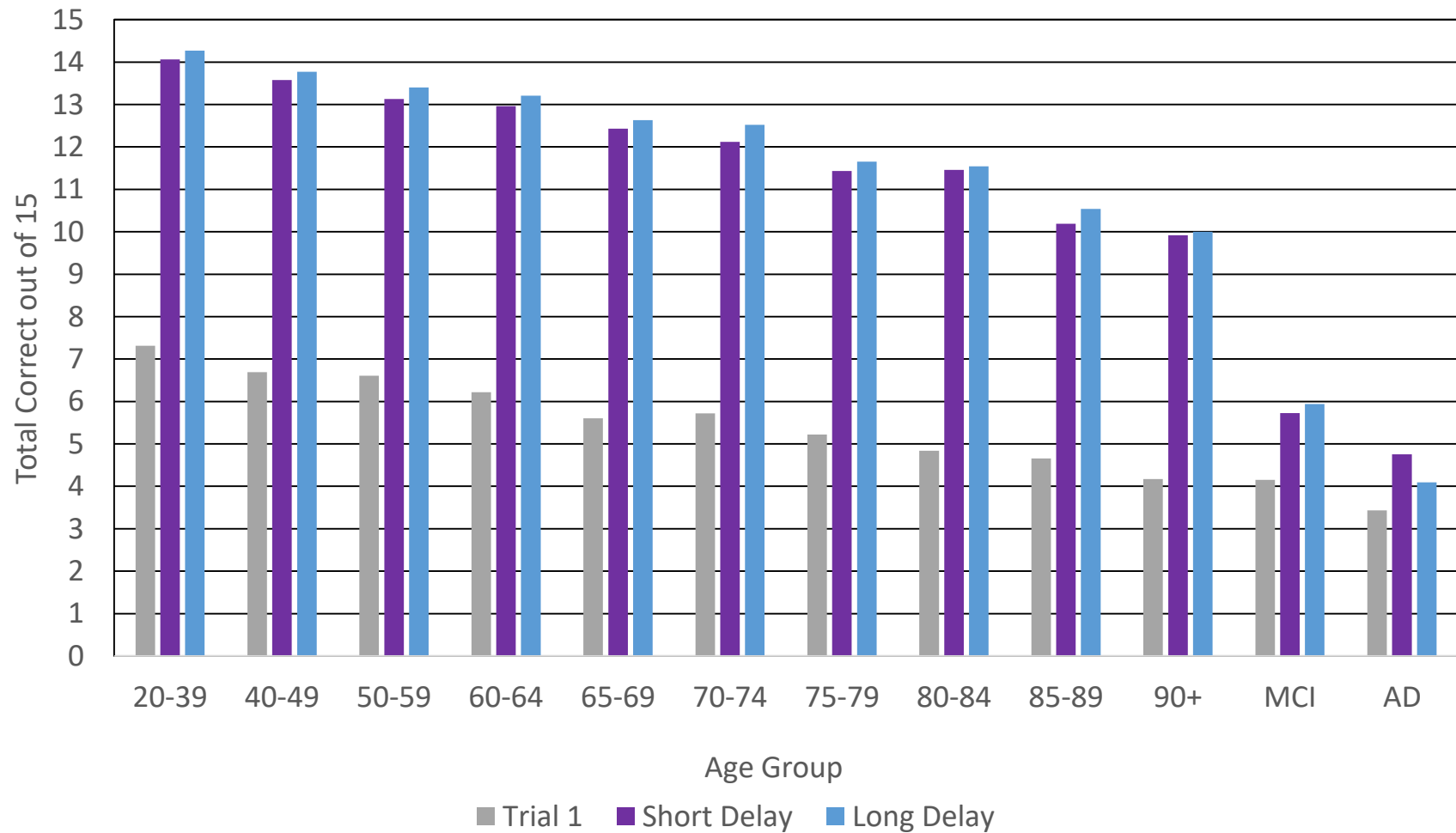
RAVLT Total Recall Across 8 Trials



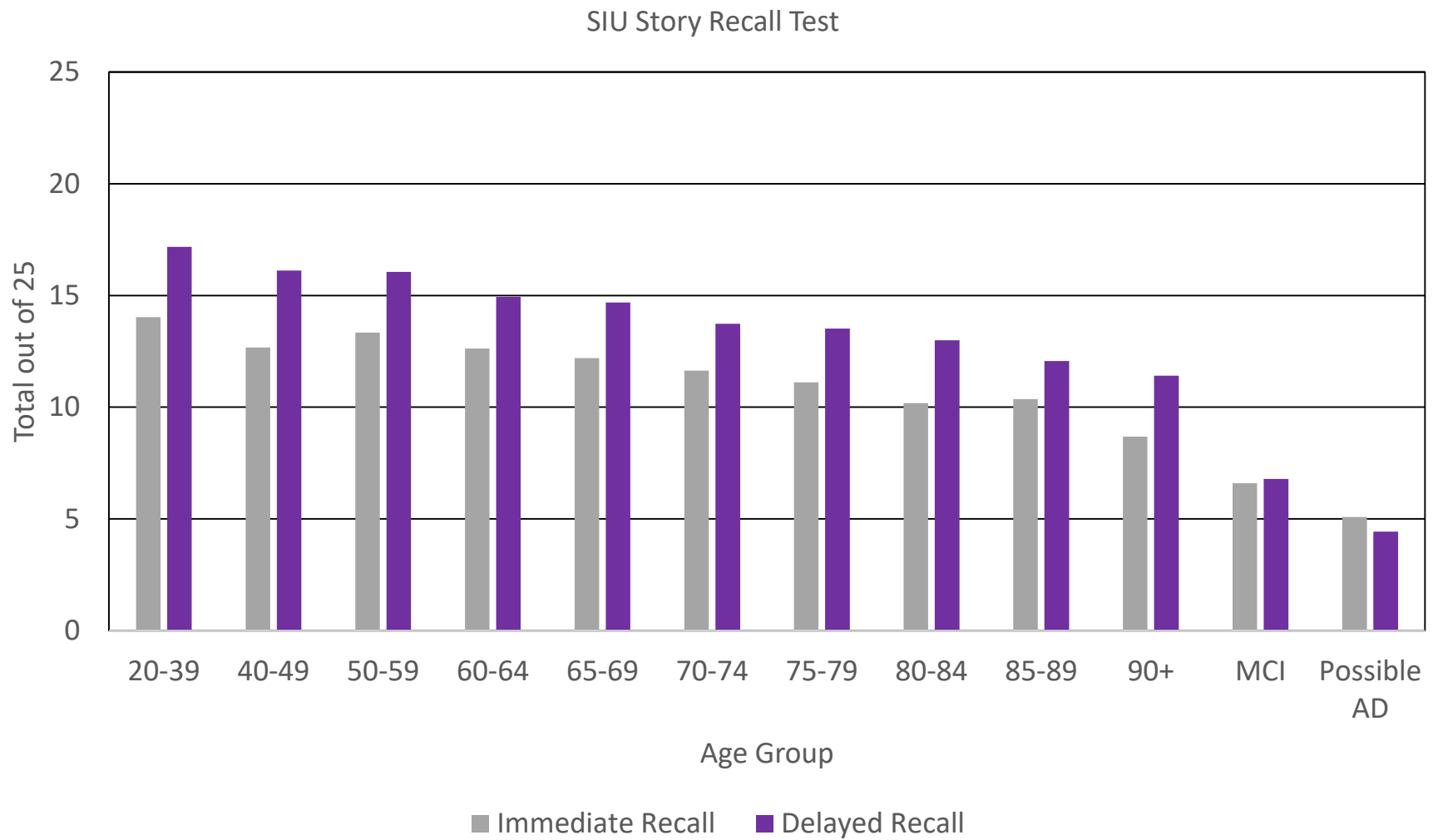
AGING EFFECTS ON A WORD LIST LEARNING/MEMORY TEST (RAVLT)



RAVLT total words recalled over 8 trials

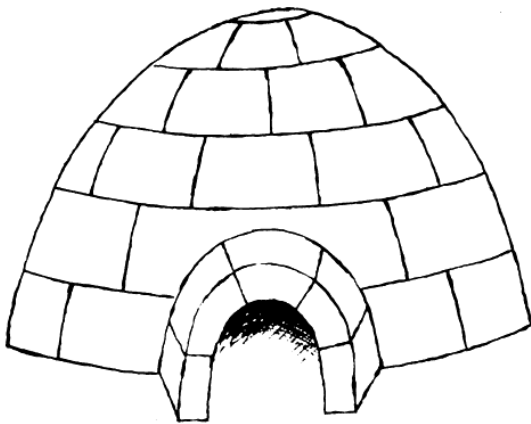


AGING EFFECTS ON THE SIU STORY RECALL TEST

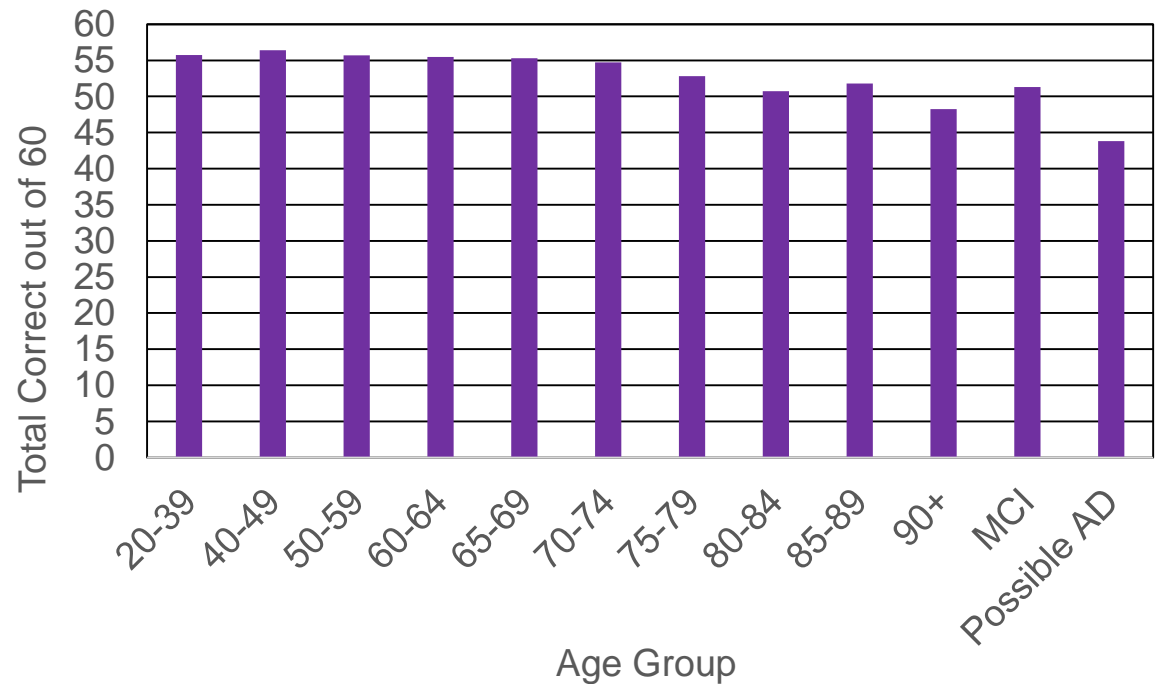


Aging effects on Language skills: Naming of Line drawings

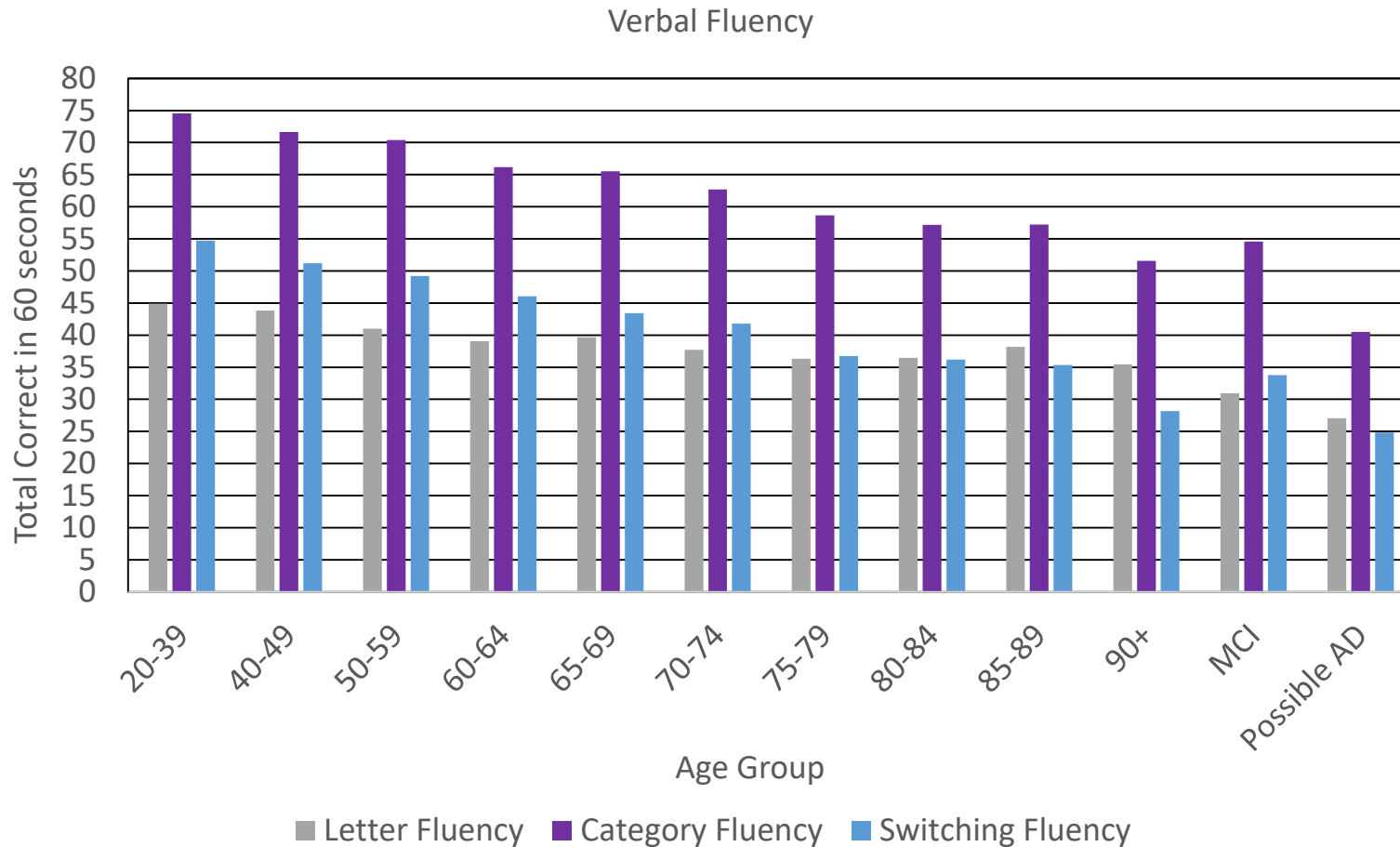
What is this called?



Boston Naming Test



Aging effects on Language Skills: Verbal Fluency

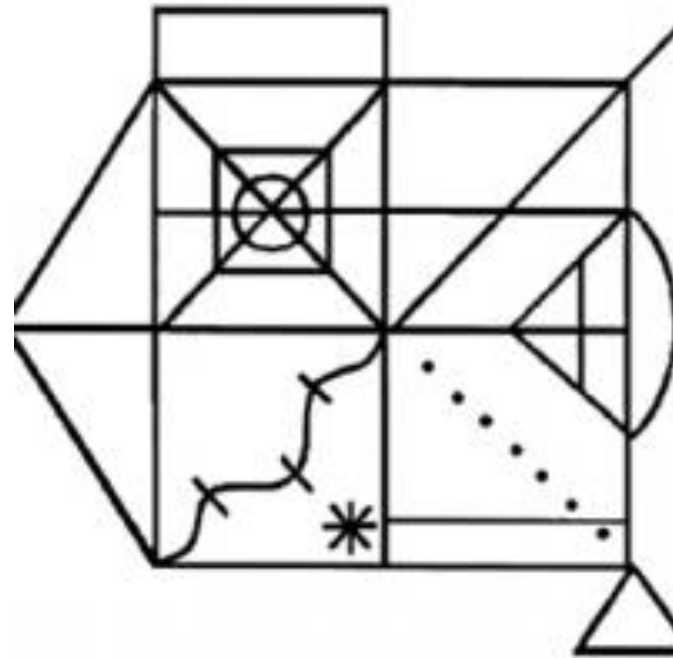
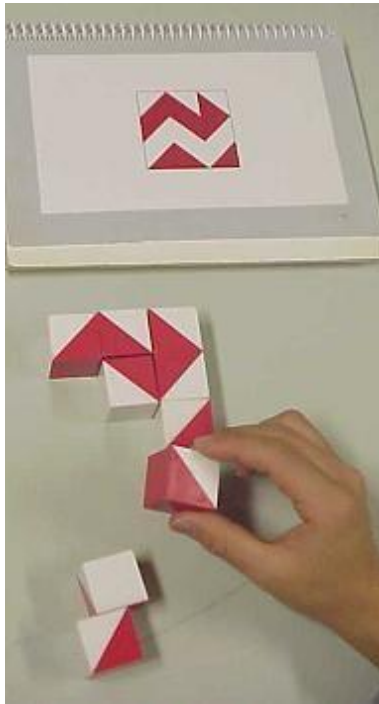


- Letter fluency: Tell me as many words as you can that begin with the letters 'F, A, S' but do not say any words that start with capital letters or numbers.
- Category fluency: Name as many unique animals, boys names, and states as you can.
- Switching fluency: Switch back and forth between saying occupations/colors,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

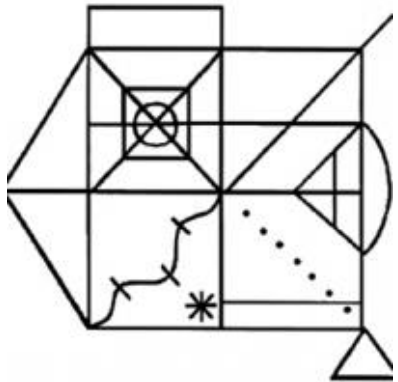


VISUOSPATIAL SKILLS

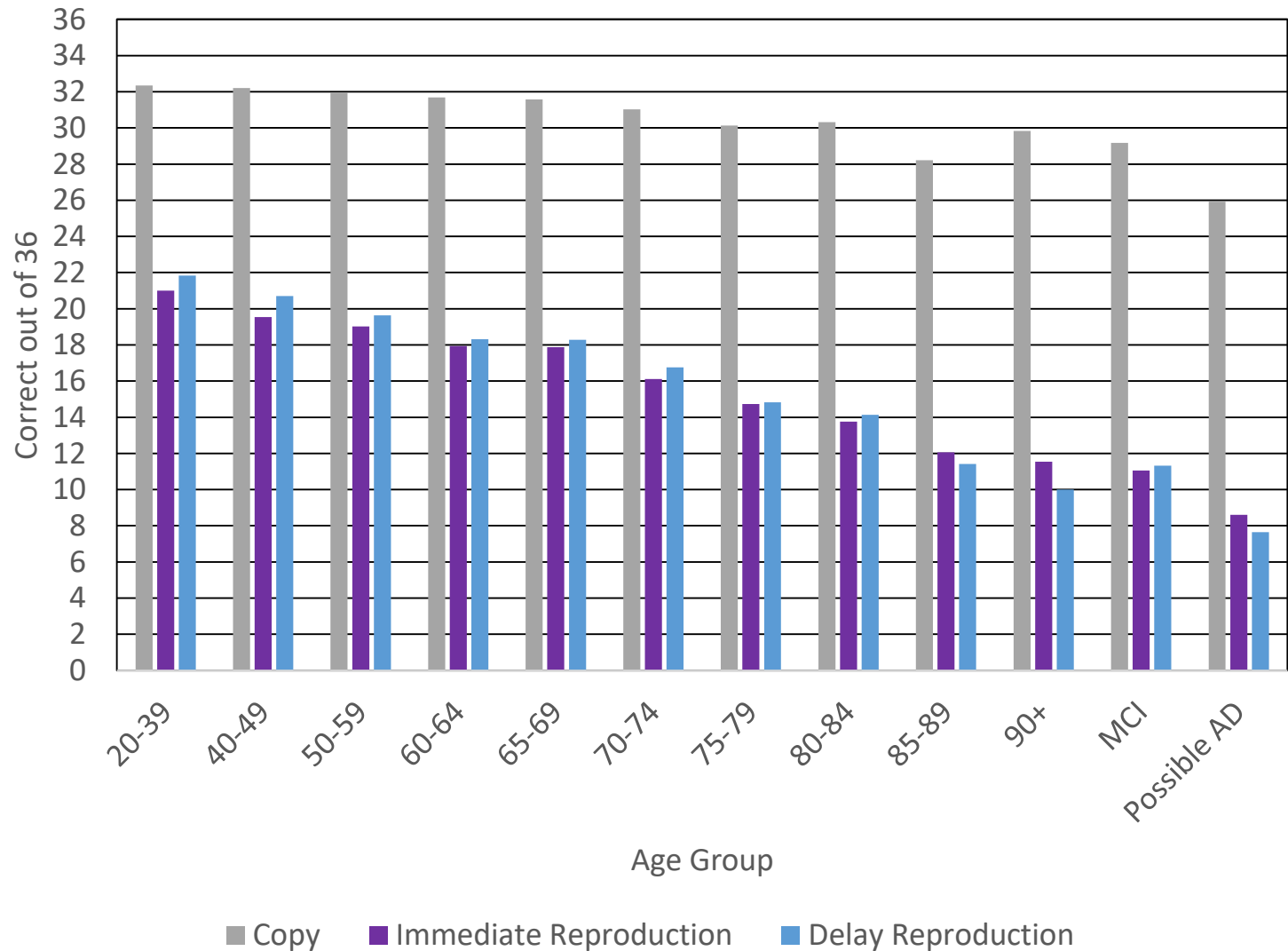
- Complex Figure Copy with immediate and delayed recall
- Spatial Reasoning



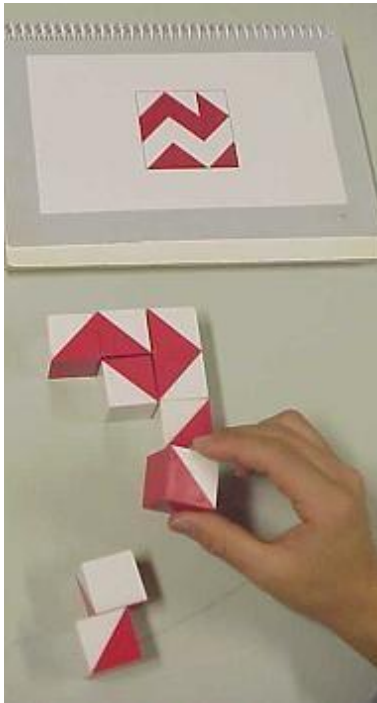
RO-CFT COPY, IMMEDIATE RECALL, AND DELAYED RECALL TRIALS



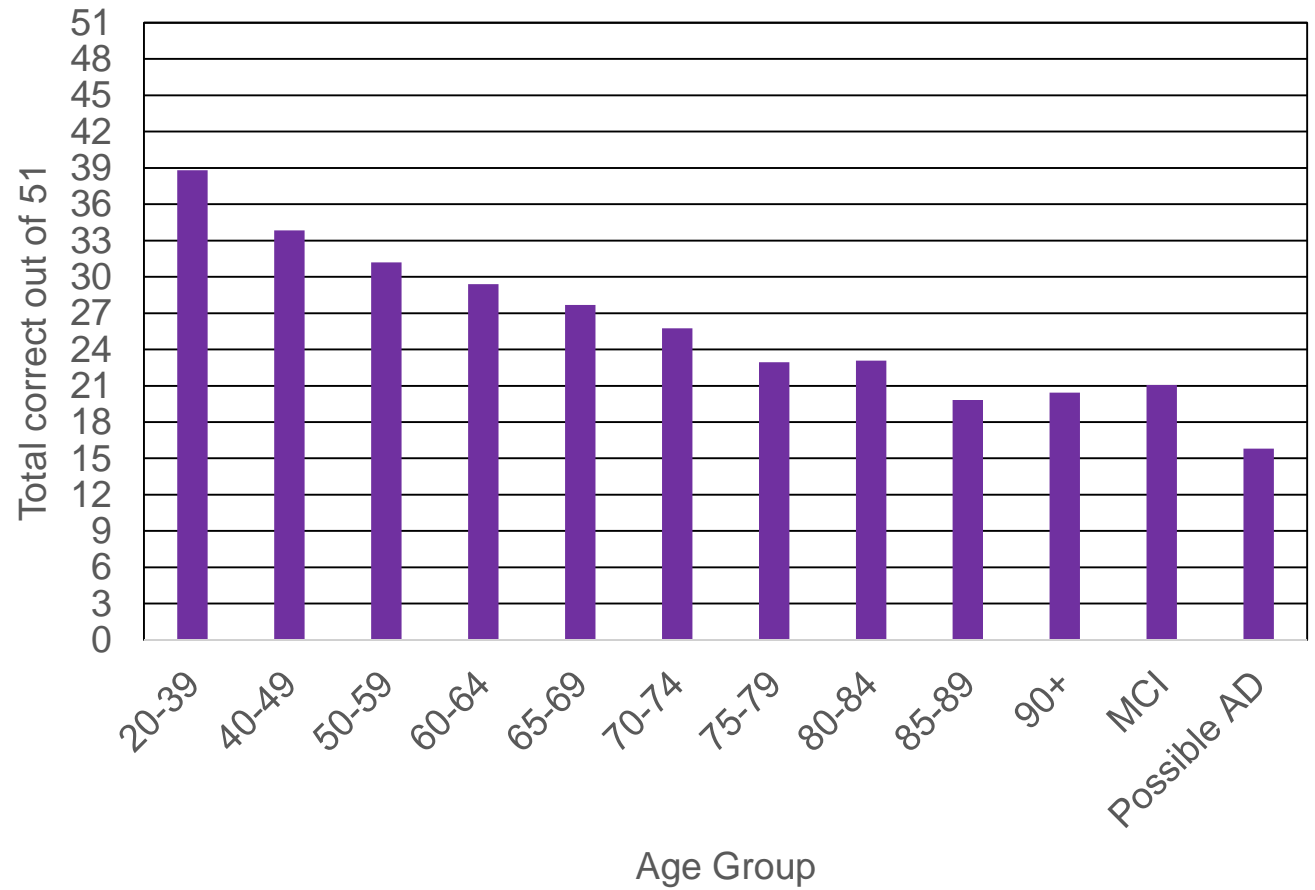
Rey Osterrieth Complex Figure Test



SPATIAL PROBLEM SOLVING



WAIS-R Block Design Raw Score



EXECUTIVE FUNCTIONS

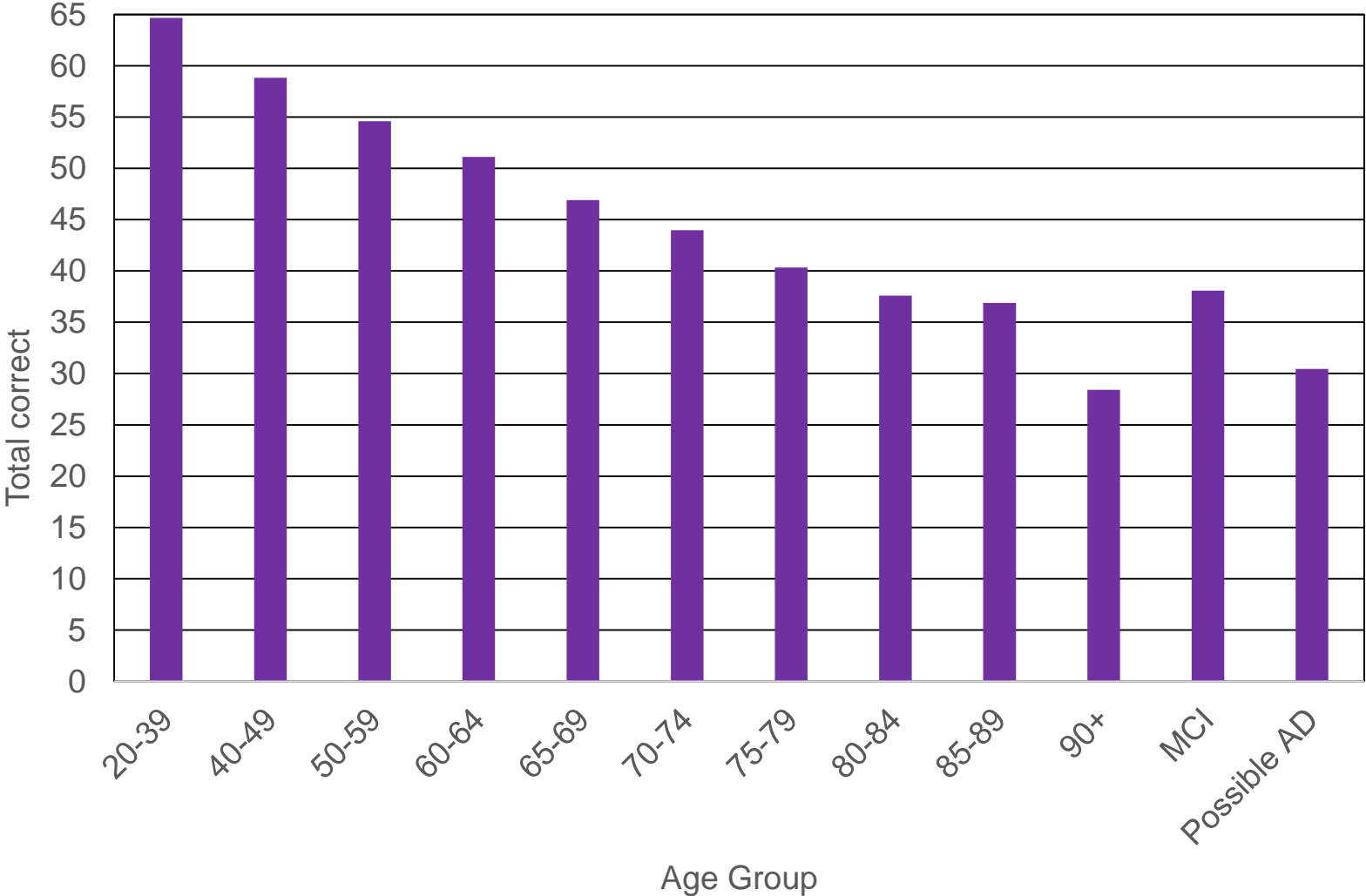
- “Frontal lobe functions”
- A set of cognitive processes that include:
 - Attentional control
 - Inhibitory control
 - Working memory
 - Cognitive flexibility
 - Multitasking
 - Reasoning
 - Problem solving
 - Planning/Organization
 - Set-Shifting



PROCESSING SPEED



WAIS-R Digit Symbol Raw Score



KEY

C	F	T	Γ	⊥	>	+	⊃	⊥
1	2	3	4	5	6	7	8	9

C F T Γ ⊥ > + ⊃ ⊥
 Γ > C F ⊥ > T Γ C F > ⊥ Γ T ⊃
 Γ ⊥ + ⊃ C T + Γ ⊃ ⊥ T ⊥ Γ +
 T Γ ⊥ C > Γ C ⊥ > + ⊥ ⊃ T > Γ
 ⊥ ⊥ ⊃ T > + Γ ⊥ T T + ⊥ T ⊃ C
 > ⊥ + T T > Γ ⊥ C + T ⊥ > ⊃ Γ
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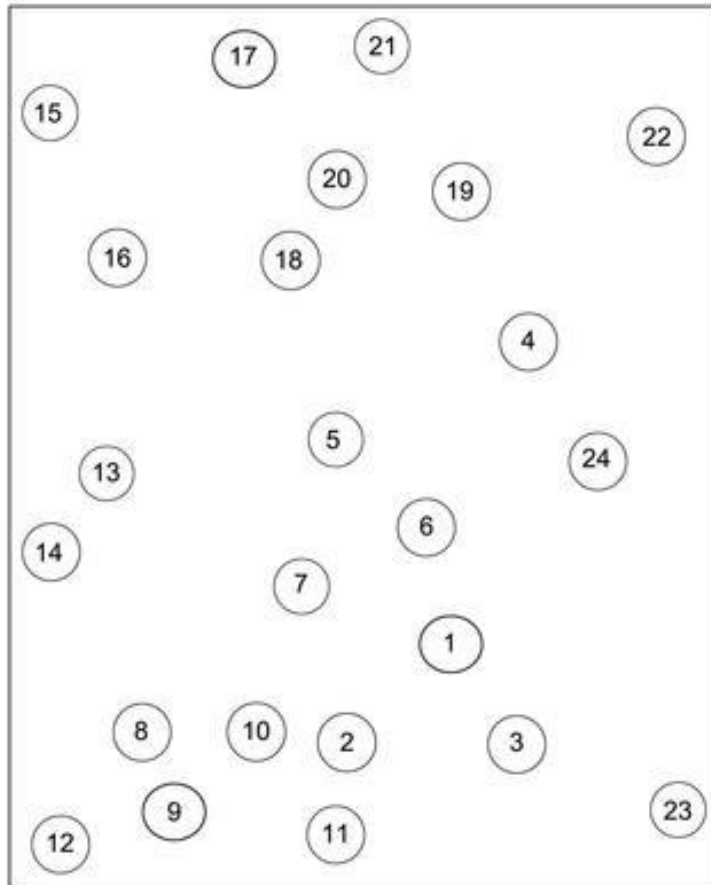


PROCESSING SPEED AND EXECUTIVE FUNCTION



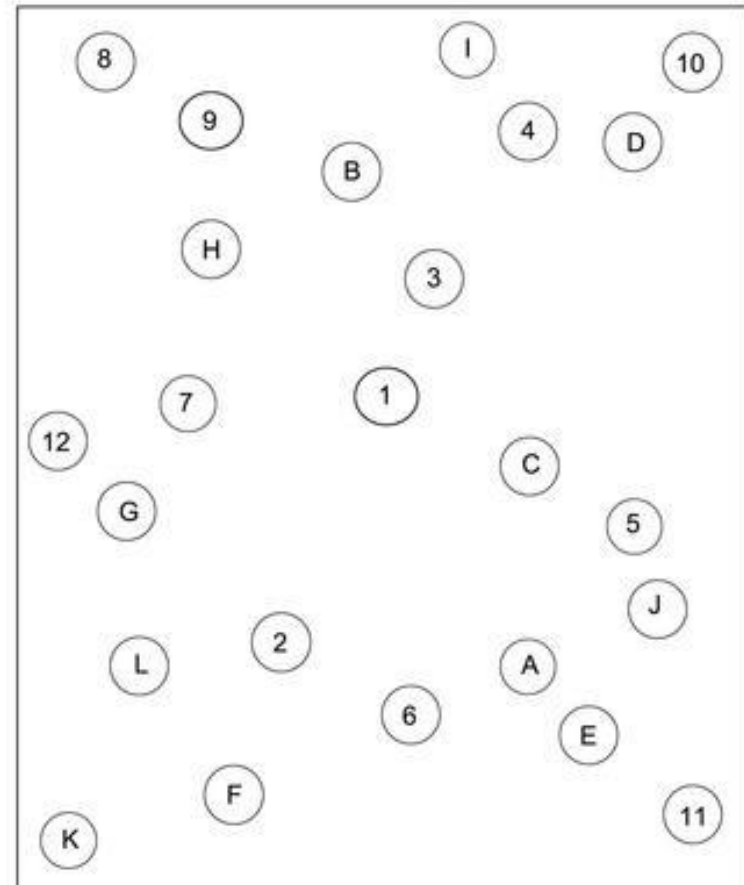
Trail making test A

Patientens navn: _____ Personnummer: _____ Datum: _____

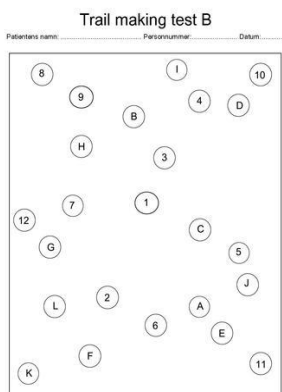
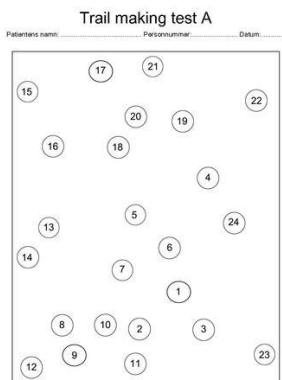


Trail making test B

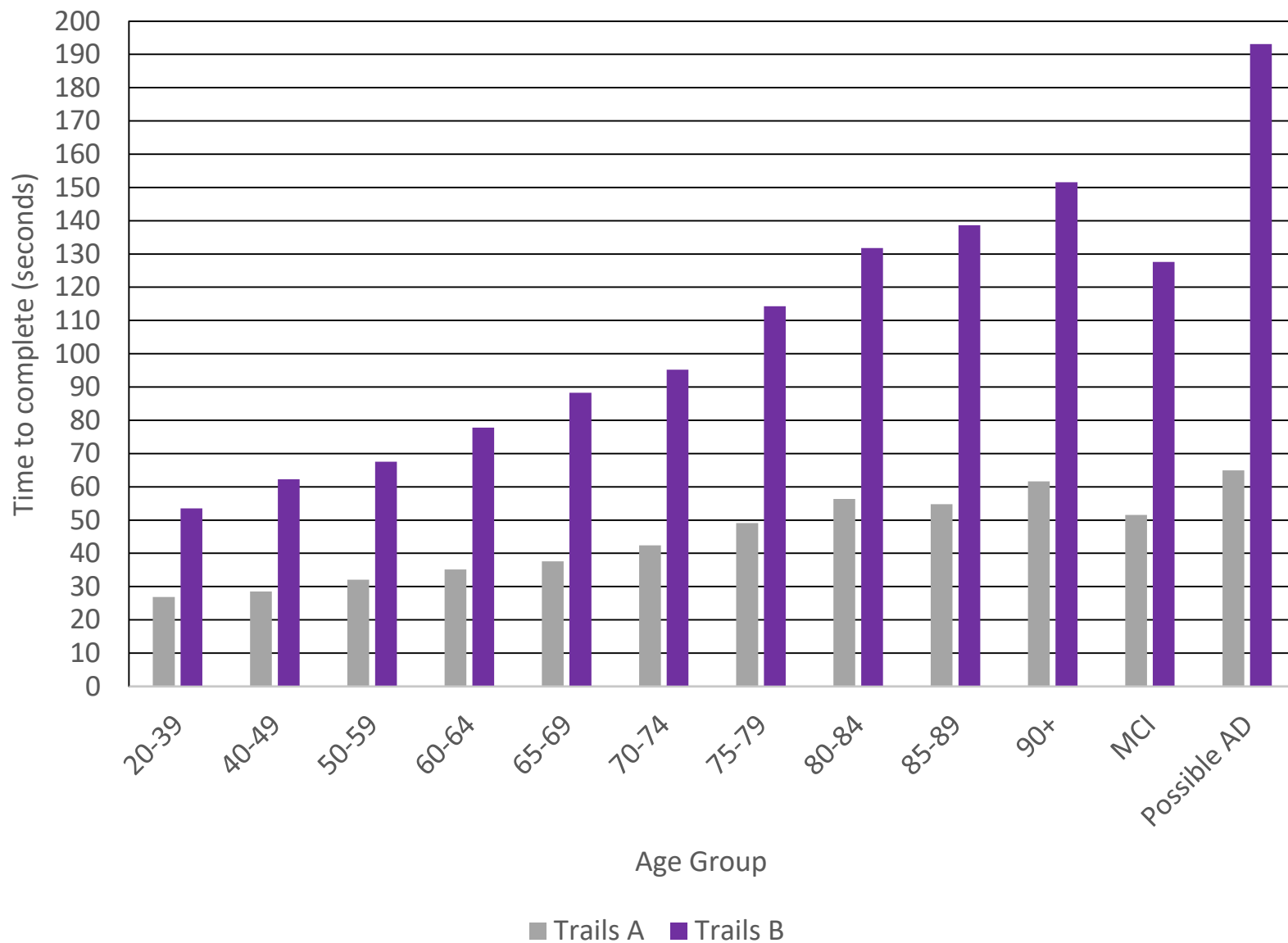
Patientens navn: _____ Personnummer: _____ Datum: _____



PROCESSING SPEED AND EXECUTIVE FUNCTION



Trail Making Test





















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

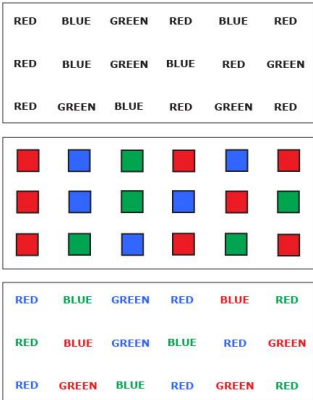
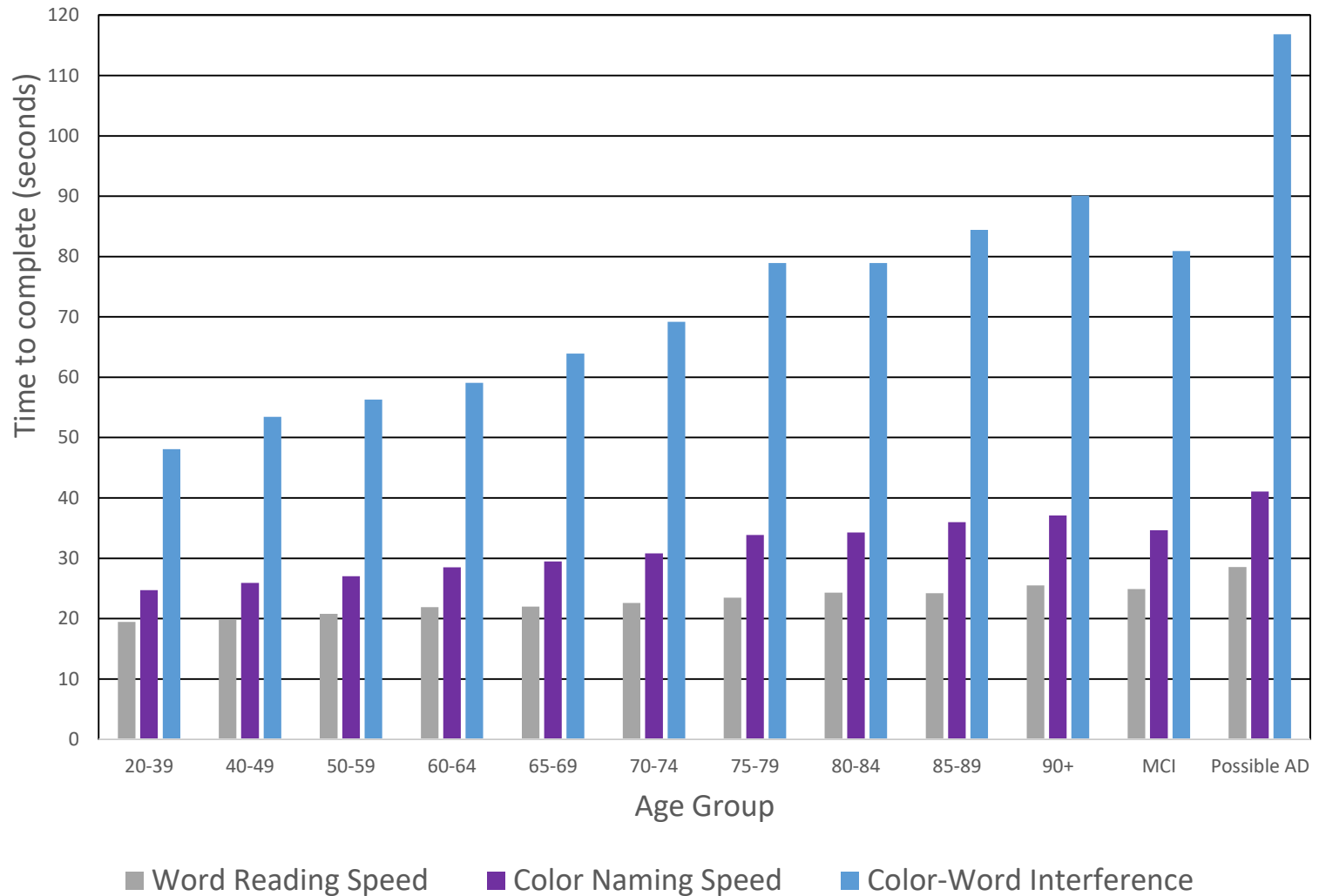
					
					
					

Name the color of the ink the words are printed in but do not read the words

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

PROCESSING SPEED AND EXECUTIVE FUNCTION

Stroop Color-Word Test





WHAT BRAIN CHANGES ARE HAPPENING IN NORMAL AGING?



SHRINKAGE!



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

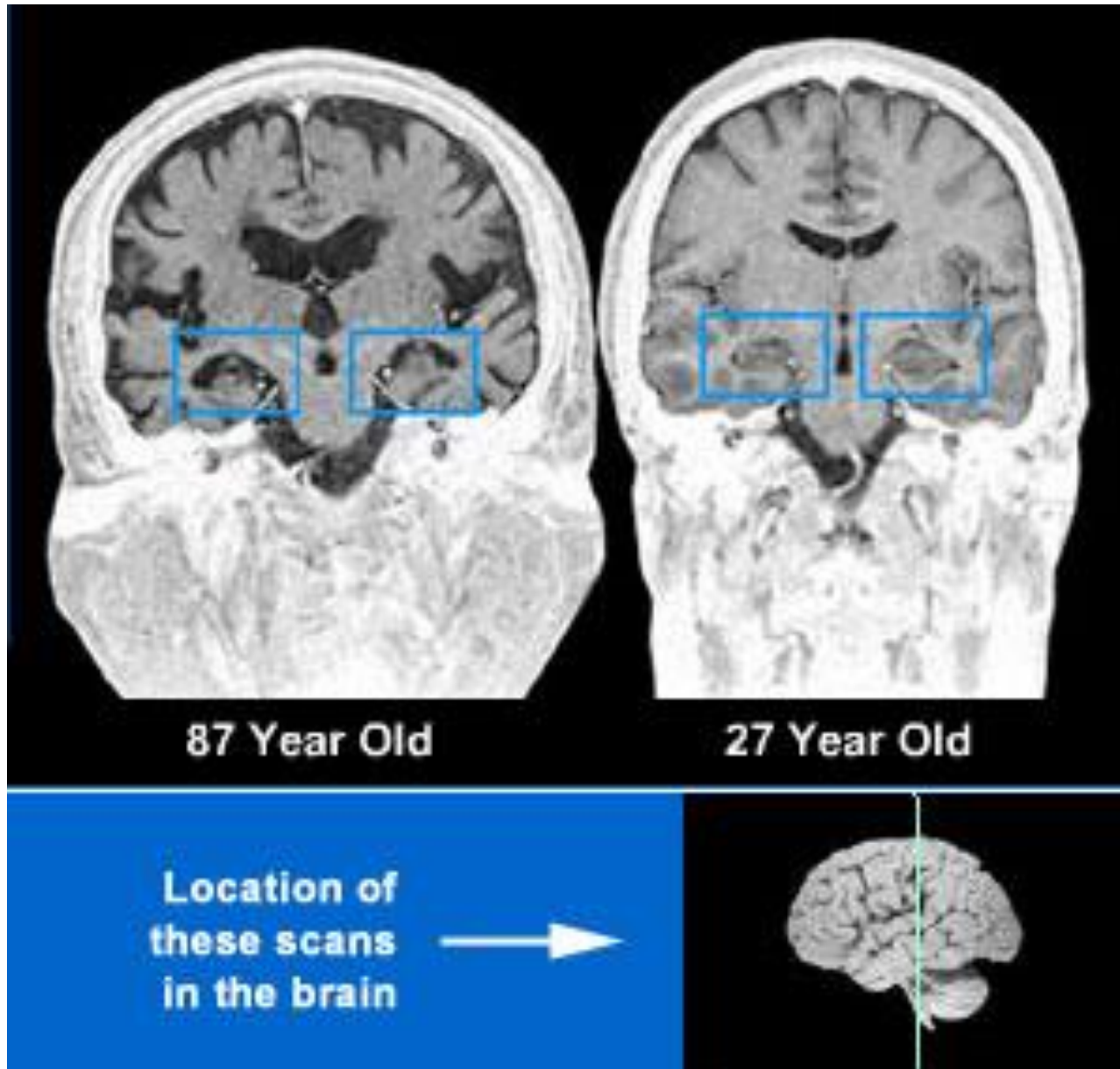
BRAIN VOLUME



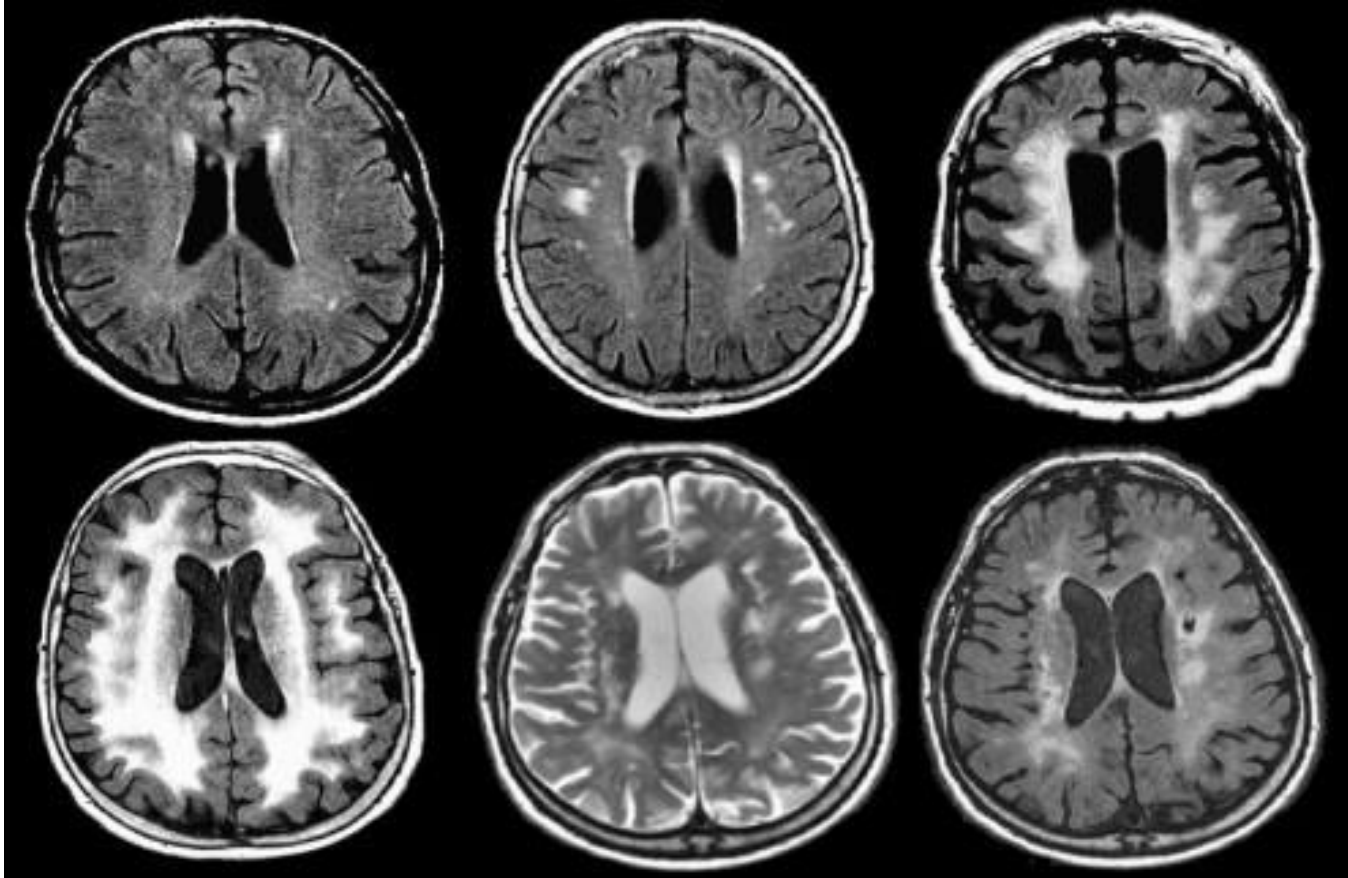
- Brain volume ↓ with age at a rate of ~2% per decade beginning in early adulthood.
- CSF volume ↑ with age
- The percentage of brain volume loss correlates with declines in cognitive function in both normal aging and AD.
- Conflicting reports in the literature about which parts of the brain sustain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

