

# MRI to Characterize Age-related Cognitive Decline in the Oldest Old

April 27 to 29, 2016

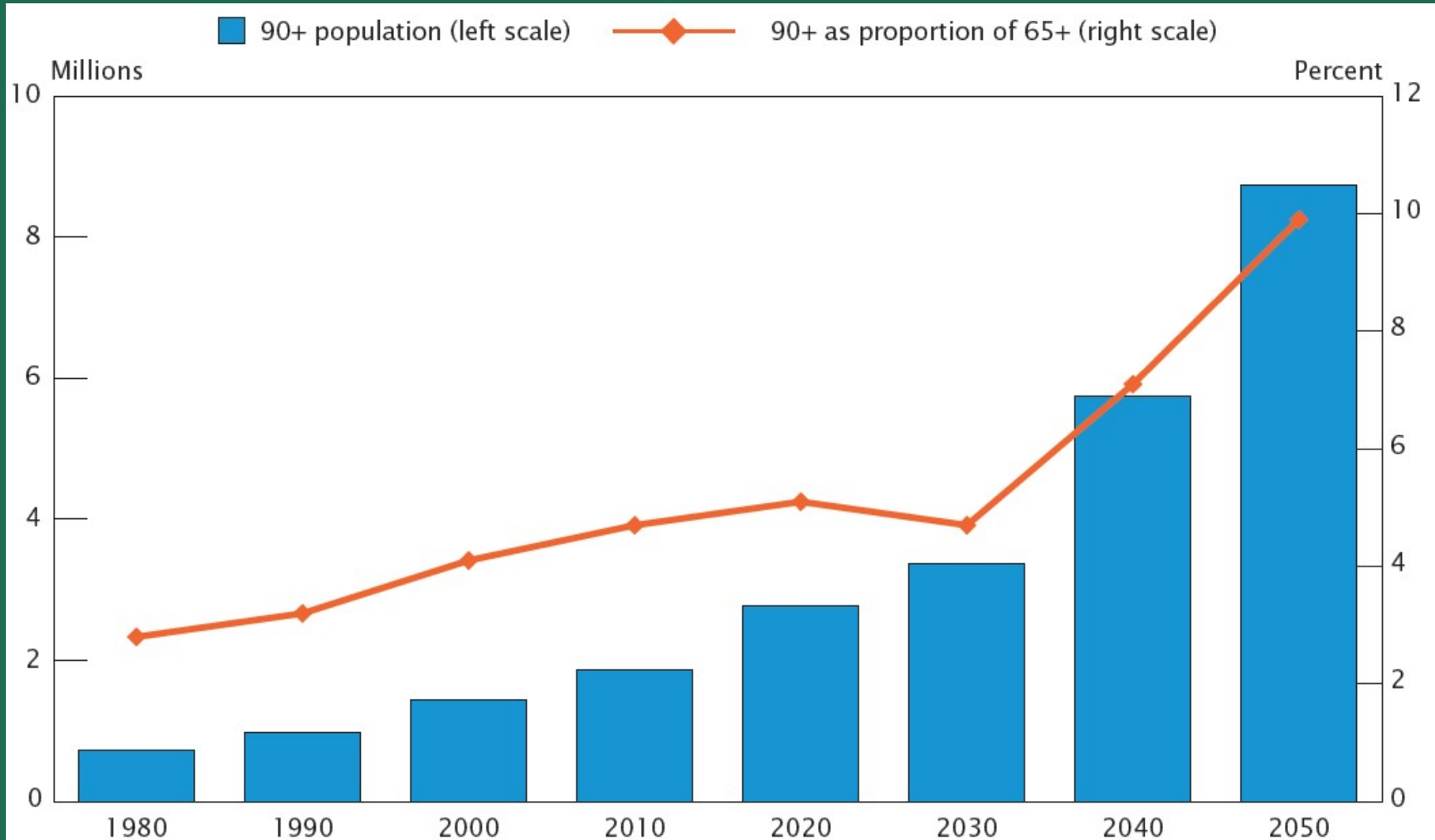
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# Population Aged 90 and Over: 1980 to 2050

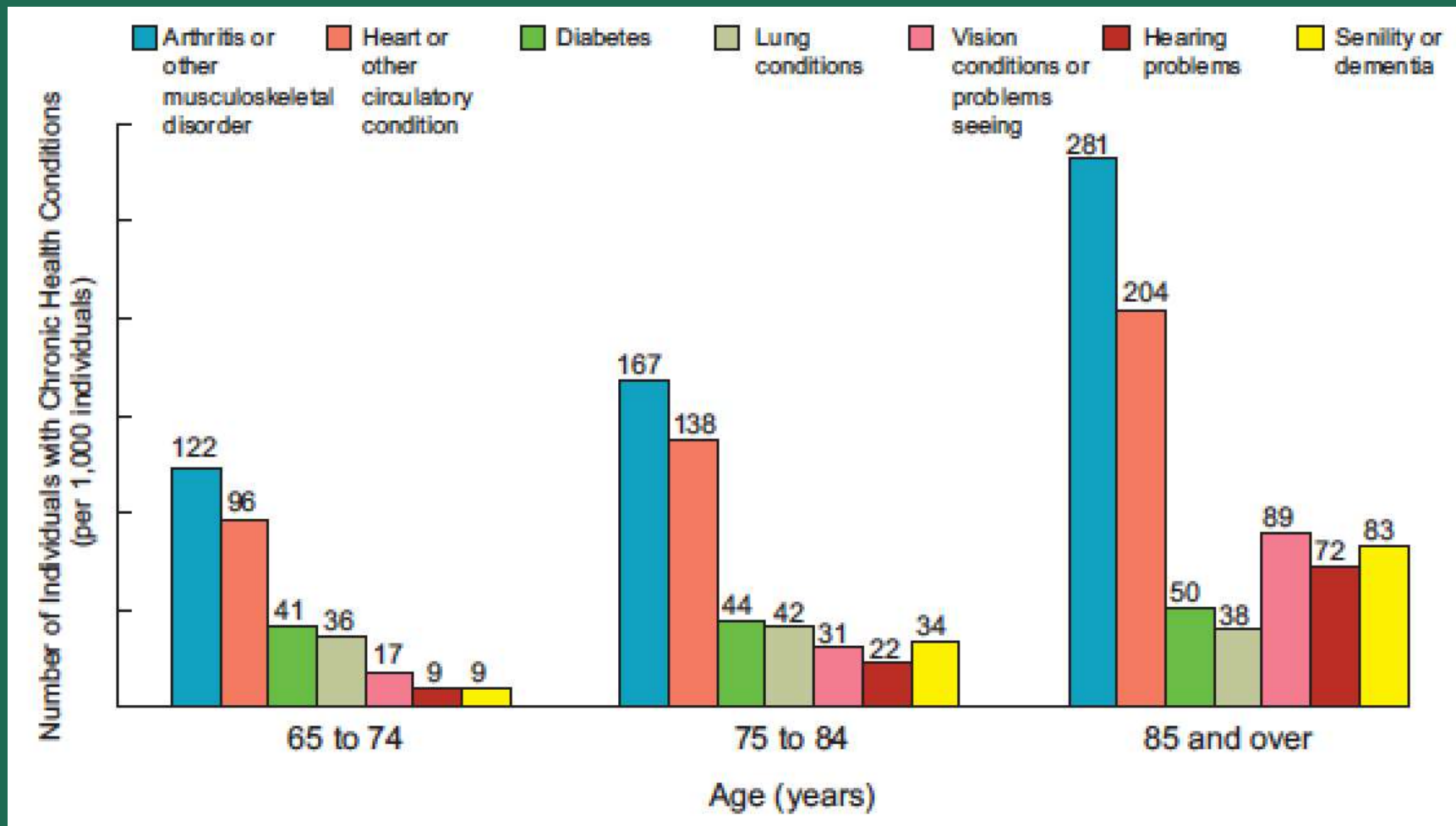


Note: The projections originate with a base population from Census 2000 and are not based on data from the 2010 Census.

Sources: U.S. Census Bureau. 1980: 1980 Census of Population, PC80-1-B1, Table 41; 1990: 1990 Census of Population, CP-1-1, Table 13; 2000: Census 2000, Summary File 2, PCT3; 2010: 2010 Census, Summary File 1, PCT12; 2020–2050: 2008 National Population Projections, Table 12.

# Our Aging Population (and its effects)

IOM Report: “Most older adults have at least one chronic disease or condition that requires ongoing care.”



# Prevalence of dementia in studies of centenarians

**Table 2** | Prevalence of dementia in representative studies of centenarians

Study	Total number of participants (% female)	Diagnostic criteria	Age range (mean years $\pm$ SD)	Prevalence of dementia (%)			Participants with normal cognition (%)
				Total	Female	Male	
Swedish Centenarian Study <sup>29</sup>	100 (82)	DSM-III-R	100	27 (42)*	30	16	34
Georgia Centenarian Study <sup>9</sup>	244 (84.8)	GDS >3	98–108 (100.60 $\pm$ 2.04)	52.3	54.5	41.9	22.5 <sup>†</sup> (22.7 female; 20.9 male)
Northern Italy Centenarian Study <sup>30</sup>	92 (59)	DSM-IV	100–107 (101.8 $\pm$ 1.6)	61.9	69.6	50	20.6 <sup>†</sup> (16.1 female; 30.6 male)
Tokyo Centenarian Study <sup>31</sup>	304 (78.6)	CDR >0.5	100–107 (101.1 $\pm$ 1.7)	61.9	67.4	41.5	24.3 <sup>†</sup> (19.2 female; 43.1 male)
Heidelberg Centenarian Study <sup>32</sup>	90 (90)	MMSE <sup>§</sup> <11 or GDS >3	100 (100.20 $\pm$ 0.41)	52 or 59 <sup>  </sup>	NA	NA	25
Danish Centenarian Study <sup>33</sup>	207 (78)	ICD-10	100	51	NA	NA	25
New England Centenarian Study <sup>34</sup>	74 (86)	CDR >0.5	100–110	76	NA	NA	16.2
Korean Centenarian Study <sup>35</sup>	89 (87.6)	CDR >0.5	100–115 (102.4 $\pm$ 2.6)	61.8	NA	NA	6.7
Finnish Centenarian Study <sup>36</sup>	179 (84.4)	DSM-III-R	100–NA	56	NA	NA	44
Sydney Centenarian Study <sup>37</sup>	200 (70.5)	MMSE <24	95–106 (97.40 $\pm$ 2.29)	54	51.4	44.1	NA

\*Number in parentheses is the prevalence of dementia after inclusion of individuals with dementia who were withdrawn from the study. <sup>†</sup>Prevalence in total cohort. <sup>§</sup>Short version with full score at 21. <sup>||</sup>Prevalence based on MMSE and GDS cut-offs. Abbreviations: CDR, clinical dementia rating; DSM, Diagnostic and Statistical Manual of Mental Disorders; DSM-III-R, DSM-III, revised; GDS, global deterioration scale; ICD, International Statistical Classification of Diseases and Related Health Problems; MMSE, Mini-Mental State Examination; NA, not available.

# **IOM Report on Cognitive Aging**

## **Recommendations to research funders and researchers:**

- Explore cognitive aging as separate from dementia and other neurodegenerative diseases in basic, applied, and clinical research**
- Expand research on the trajectories of cognitive aging and improve assessments of cognitive changes and impacts on daily function**
- Focus research on risk and protective factors for cognitive aging and ... implementation of interventions aimed at ... maintaining cognitive health**

## Case Illustration

### At 93

- Retired middle school teacher
- Living alone
- Able to carry out all iADLs despite chronic polio affecting gait
- No known memory problem, can identify children and grandchildren

### At 104

- Advanced dementia
- Dependent in basic ADLs
- Amnesia with other domains involved
- Does not recognize family members

# McKnight Neuroimaging Core & Brain Aging Registry

MBRF provided funds to establish:

- MRI and Cognitive Cores to support a Brain Aging Registry
- N=200 (50 per MBI)
- MRI will be harmonized across sites

Inclusion criteria

- Age 85+
- Successfully aging physically (no major physical disability, independent in basic activities of daily living)
- Successfully aging cognitively (<1SD age/edu, normal iADLs; subjective complaints allowed)

Exclusions

- Medical condition expected to seriously limit life expectancy
- Vision, hearing deficits, <6<sup>th</sup> grade reading level, unable to follow protocol

# Brain Aging Registry

## Pre-screening

- Global cognitive screen to exclude frank dementia
- Sociodemographic and medical histories
- Screen for neuropsychiatric symptoms

## Screening Visit

- QOL, sleep quality, physical activity, subjective memory symptoms
- Clinician assessment (vision, hearing) and neurological examination
- Neuropsychological screening battery (NACC and NIH-TB)

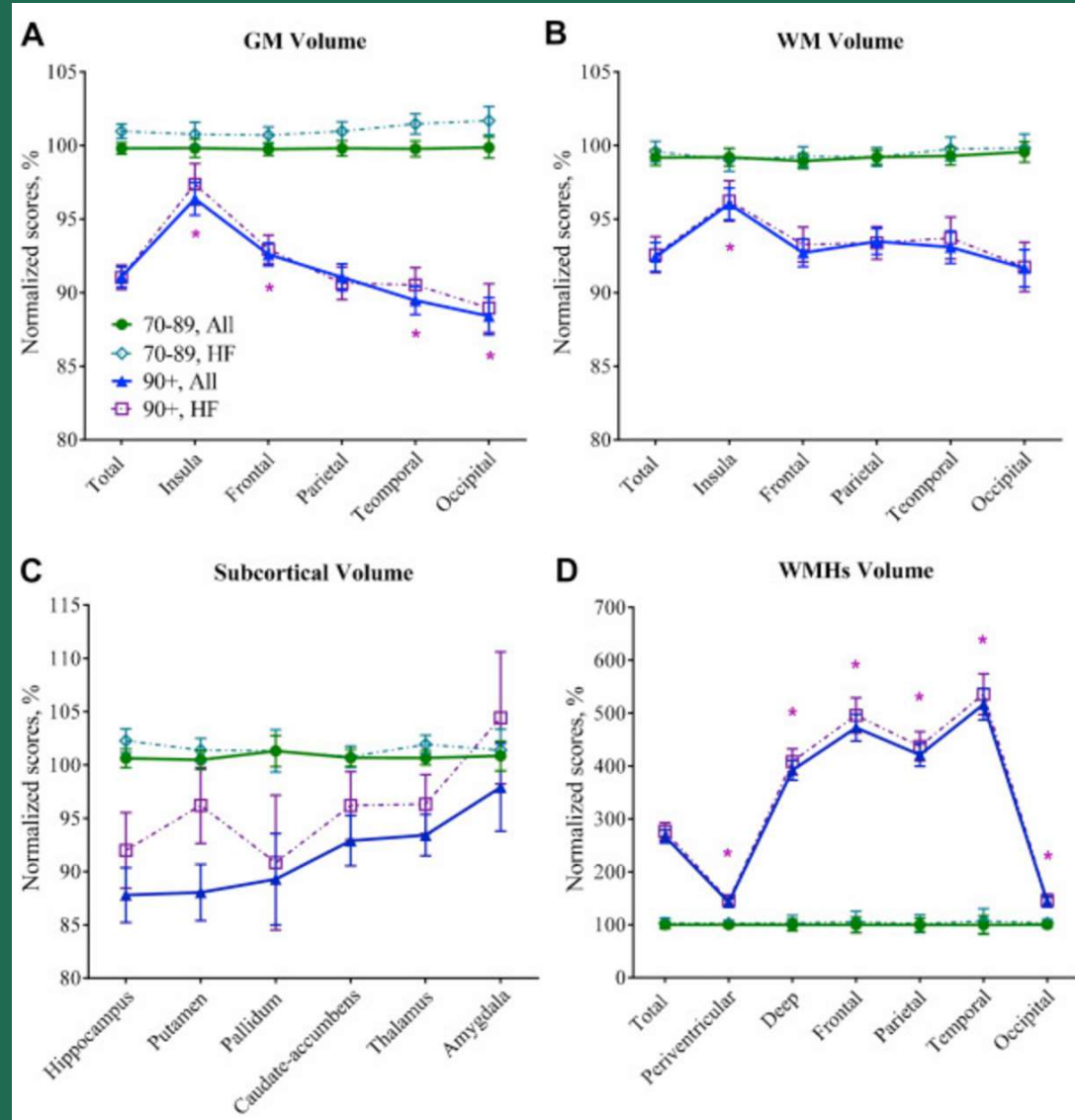
## Enrollment Visit

- Neuropsychological assessment (focused)
- Actigraphy
- Computerized functional assessments
- Blood samples
- Saliva
- Brain MRI

# MRI Metrics Differ in the Oldest Old

N=70 age 90+

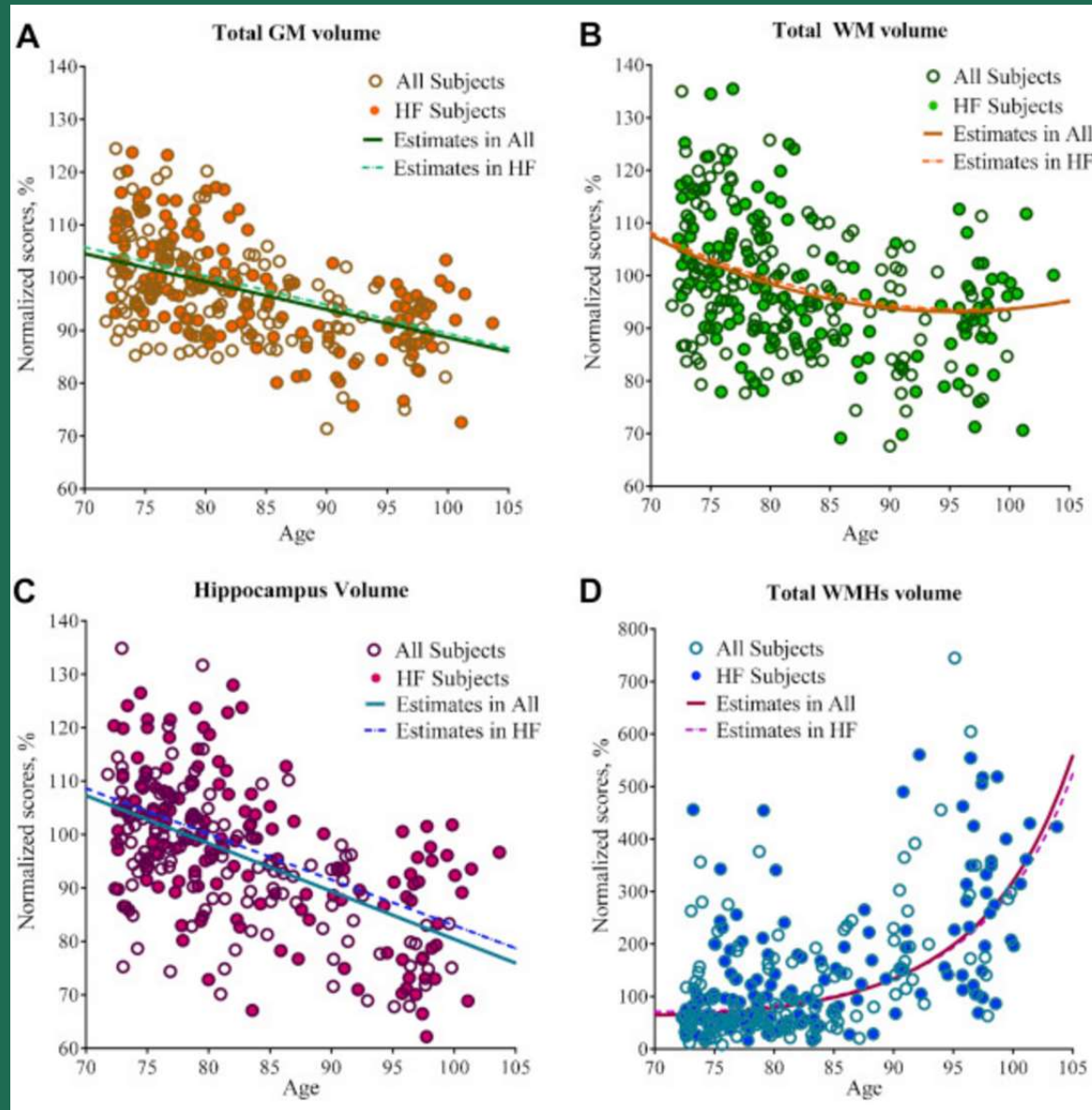
43 High  
Functioning



# Variability of Brain MRI Measures in the Oldest Old

N=70 age 90+

43 High  
Functioning



# McKnight Neuroimaging Core MRI Sequences

## Anatomical measurements

- MPRAGE: structural anatomy
- 3D T2: Freesurfer anatomical parcellations
- Diffusion: HARDI sequence, structural connectivity

## Functional measurements

- Resting state fMRI: functional connectivity
- Task-based BOLD: function
- MRS MEGAPRESS: GABA concentration in ROI
- ASL 2D and Cine PC/Blood Flow: cerebral perfusion, vessel elasticity, total volumetric blood flow, brain strain

## Measurements of pathology

- T2 Flair: white matter hyperintensities and subclinical vascular lesions
- Hippocampal subfield measurements (TBD)
- Neurite orientation dispersion density imaging (NODDI)

# McKnight Neuroimaging Core MRI Tolerability

Magn Reson Imaging. 2004 Nov;22(9):1299-304.

## **Tolerance of MRI procedures by the oldest old.**

Wollman DE<sup>1</sup>, Beeri MS, Weinberger M, Cheng H, Silverman JM, Prohovnik I.

### **⊕ Author information**

#### **Abstract**

**OBJECTIVES:** The study aimed to evaluate the feasibility and discomfort of magnetic resonance imaging (MRI) procedures in the oldest-old subjects (age > 90 years) using a survey design in a university-affiliated neuroimaging research center.

**PARTICIPANTS:** Forty-one community-dwelling, elderly subjects were considered for participation. Twenty-nine of them underwent voluntary, extensive MRI scanning (up to 1 h) as part of a project on brain function in the oldest old. Thirteen oldest old (OO, range 90-93 years, mean 92 years) were compared to 16 young old (YO, range 72-80 years, mean 76 years).

**MEASUREMENTS:** Likert-style questionnaire on satisfaction following extensive MRI scanning session (up to 1 h) was administered. Data were analyzed by an analysis of variance (gender by age group).

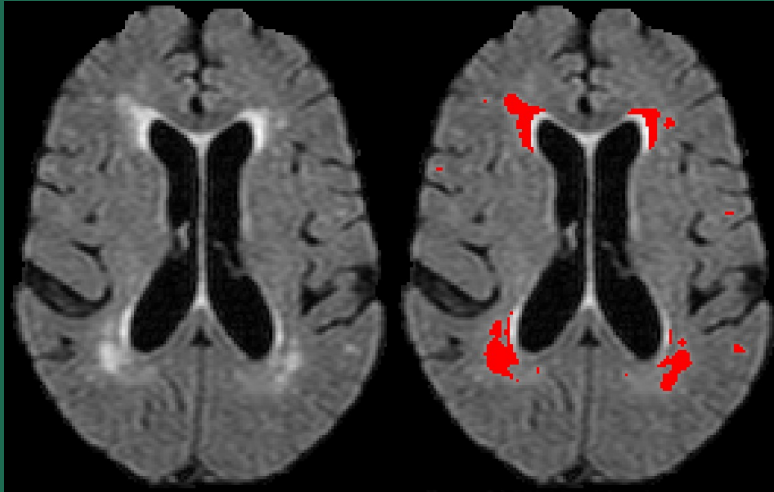
**RESULTS:** All subjects reported positive experiences with no significant difficulties or concerns. There were minor differences in some rated items, with the OO and males slightly less comfortable than YO and females, respectively. Overall, the OO tolerated the procedures as well as the YO.

**CONCLUSION:** Very long MRI sessions are feasible, even in the oldest-old subjects, and are not associated with any significant discomfort. Prior screening and thorough education of the subjects probably help to minimize anxiety and dropout.

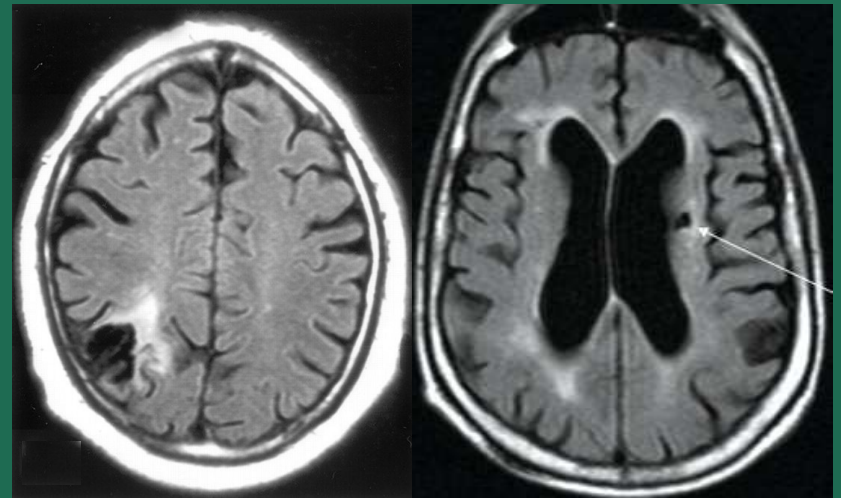
PMID: 15607102 [PubMed - indexed for MEDLINE]

# Subclinical Vascular Brain Damage

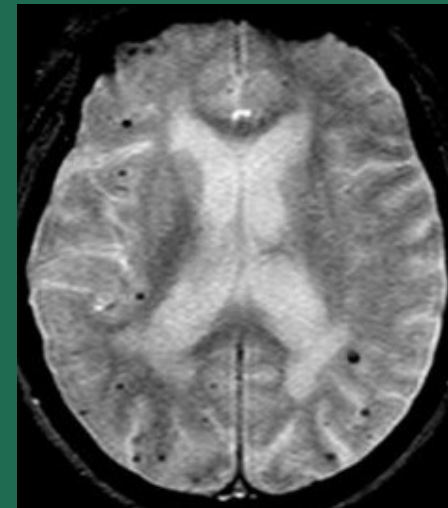
**white matter  
hyperintensities**



**subclinical Infarcts**



**brain atrophy**



**microbleeds**

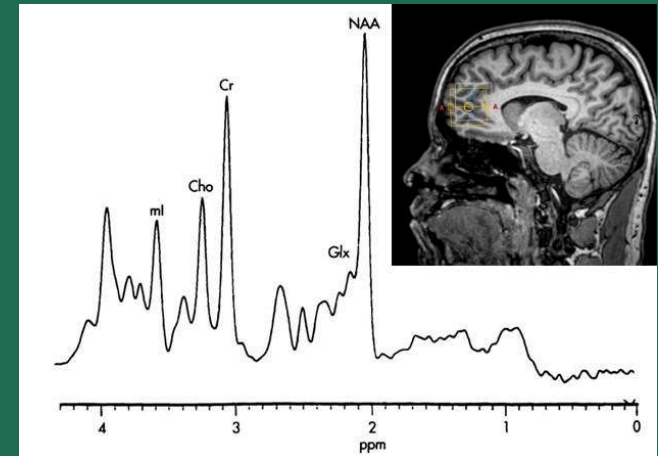
# Population Prevalence of Subclinical Infarction (3 mm+)

<u>Study</u>	<u>Age</u>	<u>% Prevalence for SCI</u>		<u>Estimated US population 1998</u>	<u>Estimated US SBI Population Prevalence (N)</u>
		<u>Prevalence (%)</u>			
ARIC	55-64	11%		22,989,000	2,528,790
CHS	65-69	22%		9,515,000	2,093,300
	70-74	28%		8,780,000	2,458,400
	75-79	32%		7,238,000	2,316,150
	80-85	40%		4,748,000	1,899,200
	85+	43%		4,054,000	1,743,220
<b>TOTAL</b>					<b>13,039,070</b>

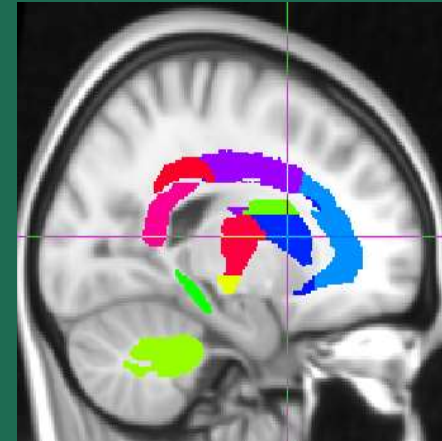
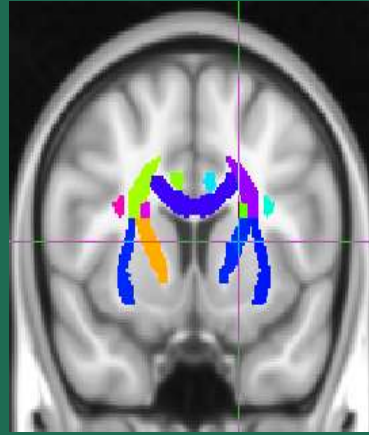
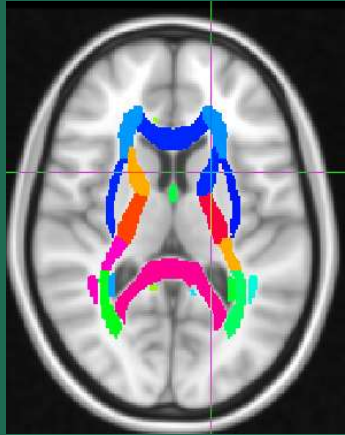
Courtesy of George Howard

# Cerebral Metabolites from 1H-MRS

- **N-Acetyl aspartic acid (NAA):**
  - Neuron integrity
- **Choline (Cho):**
  - Cell membrane integrity/demyelination/inflammation
- **Creatine (Cr):**
  - Brain energy metabolism
- **Myo-Inositol (ml):**
  - Glial cell integrity
- **Glutamate/Glutamine (GLX):**
  - Neurotransmitter concentration



# JHU DTI-based WM atlas description

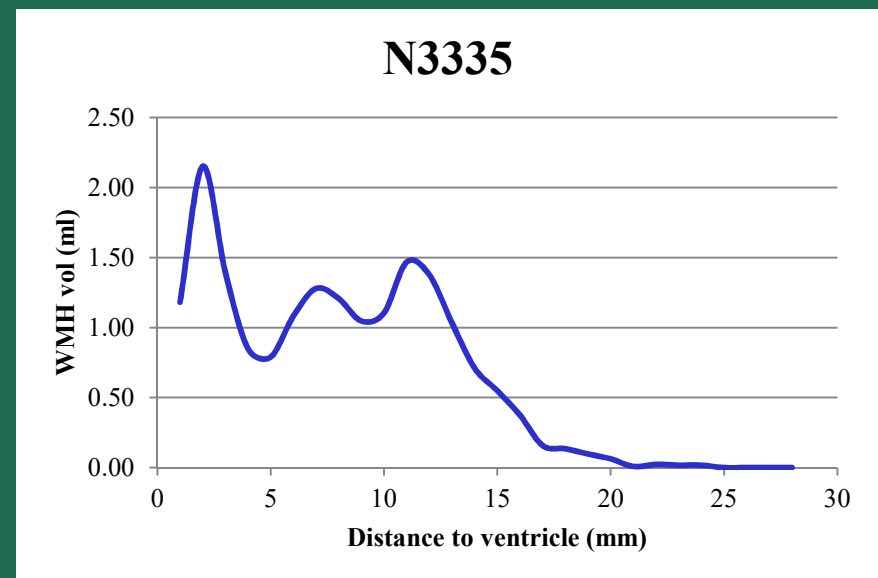


ICBM-DTI-81 white-matter labels atlas

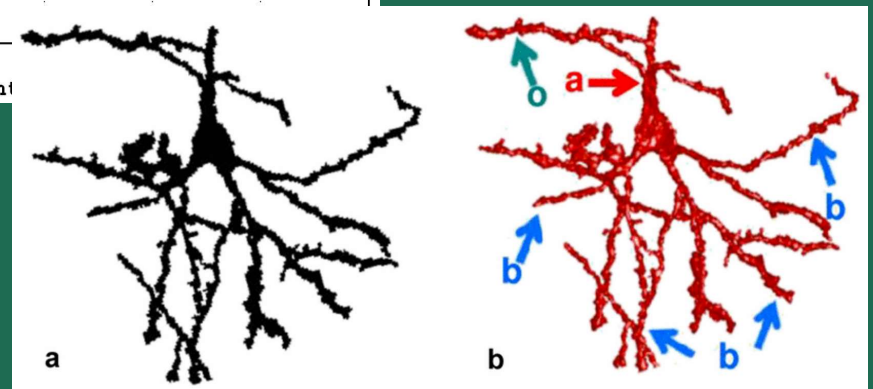
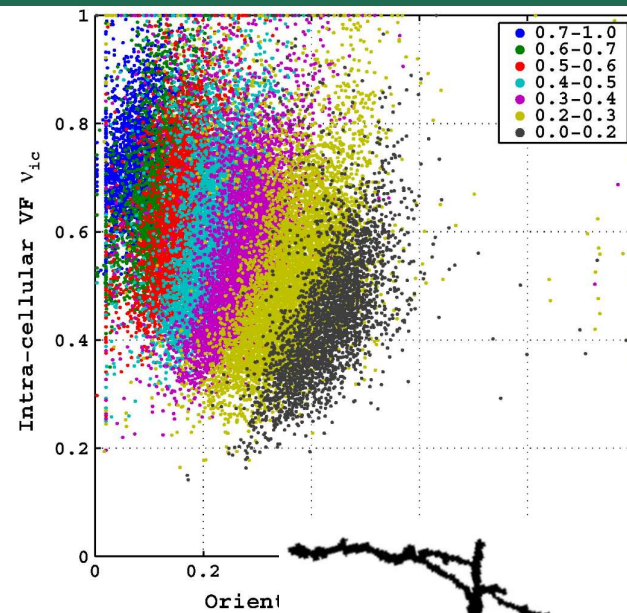
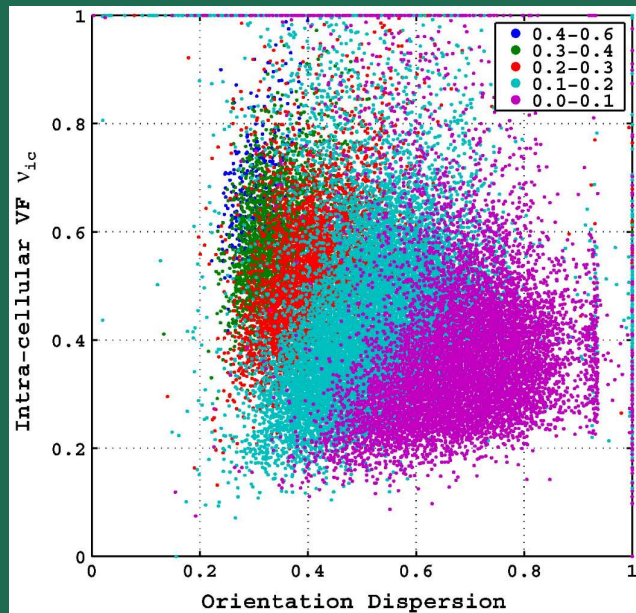
WMH overlaid on 48 white matter tract labels

## Distance Maps

Volume of WMH as a function of distance from the ventricle wall

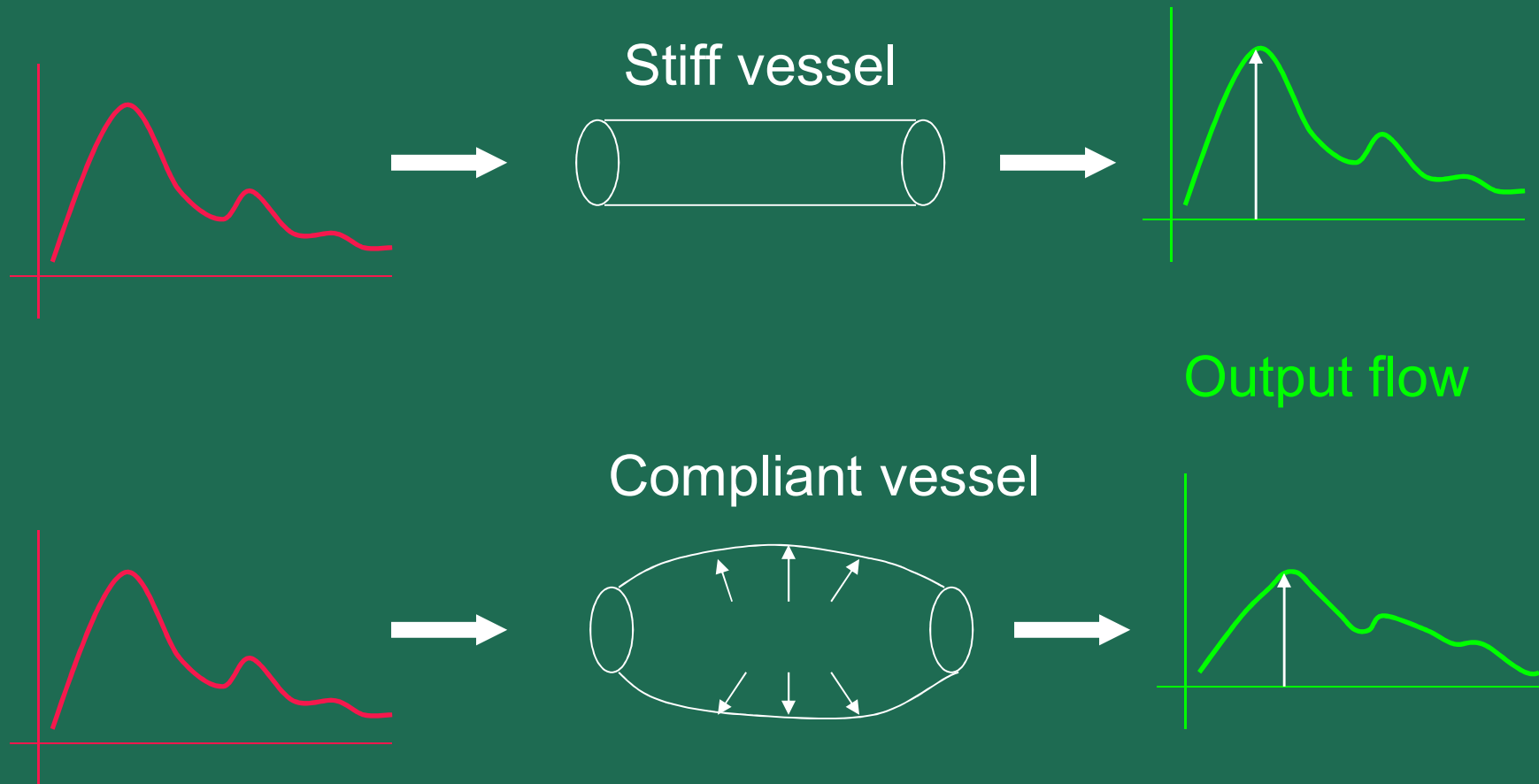


# Neurite Orientation Dispersion Density Imaging (NODDI)



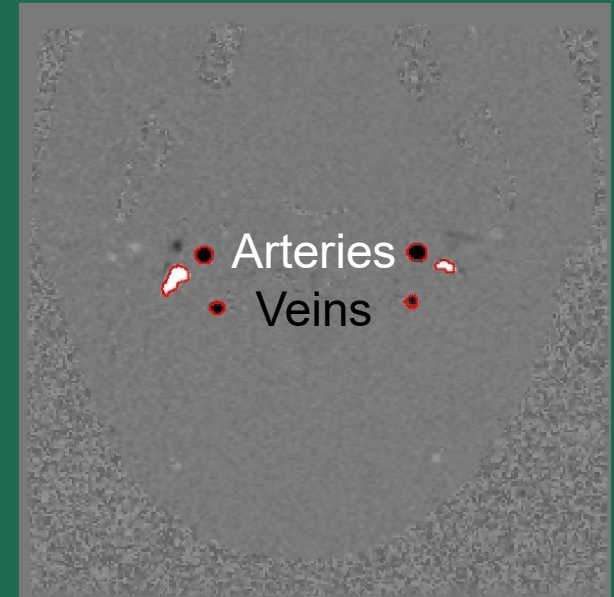
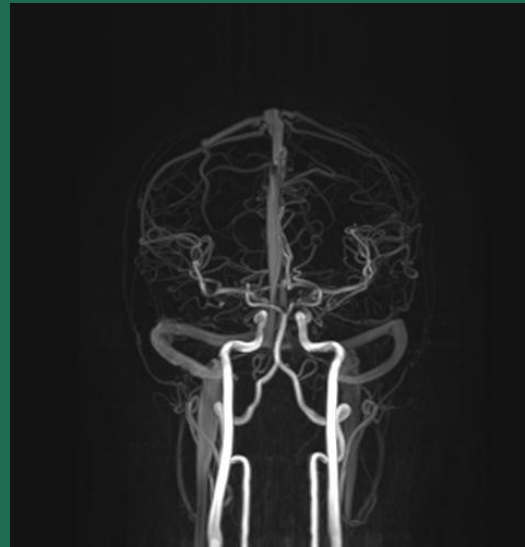
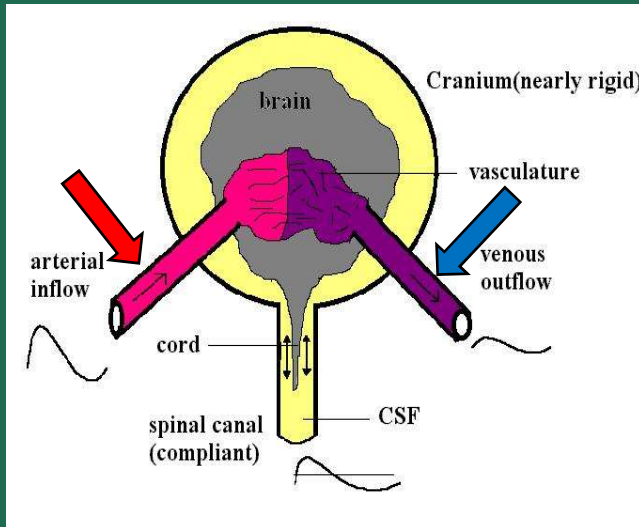
Quantification of neurite density in humans with correlation to animal models

# Effect of Stiffness on Flow Dynamics



Measurements of vascular expansion require both the input and output flow rates

# MRI measurement of Cerebral Blood Flow

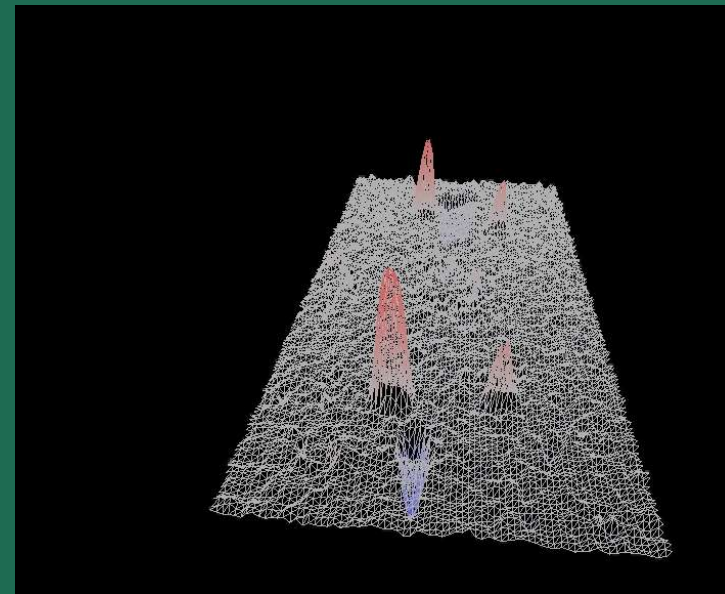


## Pulsatility Measures:

- Arterial Pulsatility index
- Arterial expansion
- Venous pulsatility index
- Venous expansion
- A-V (vascular) expansion

## Volumetric Measures (partial list)

- Frontal, parietal, temporal, occipital
- Hippocampus
- Cerebral WM
- Ventricular volume



# Frontiers In Aging Neuroscience Special Issue

## Neuroimaging Approaches to the Study of Cognitive Aging

Edited by: Gene Alexander, Ron Cohen, Kristina Visscher, Adam Woods, Clinton Wright

### Topics to date

- Overview
- Structural neuroimaging
- Functional neuroimaging
- Neuroimaging of white matter lesions and subclinical vascular lesions
- Magnetic Resonance Spectroscopy for assessing age-associated cerebral metabolite alterations
- Diffusion weighted Imaging
- Brain Stimulation in the characterization of brain physiology and as a therapeutic tool in Cognitive Aging
- Statistical approaches for the study of cognitive and brain aging
- Functional Near Infrared Spectroscopy (fNIRS)
- Cognitively Engaging Activity is Associated with Cortical and Subcortical Volumes (published)

# Future Directions

- Focused enrollment of participants 85+ years of age
- Begin to characterize the sample using multi-modal imaging of structure and function
- Correlate imaging with rich data across cognitive and health dimensions
- Develop collaborative programs that include other MBI resources and strengths of each Institute

# Miami McKnight Brain Institute

## Faculty

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