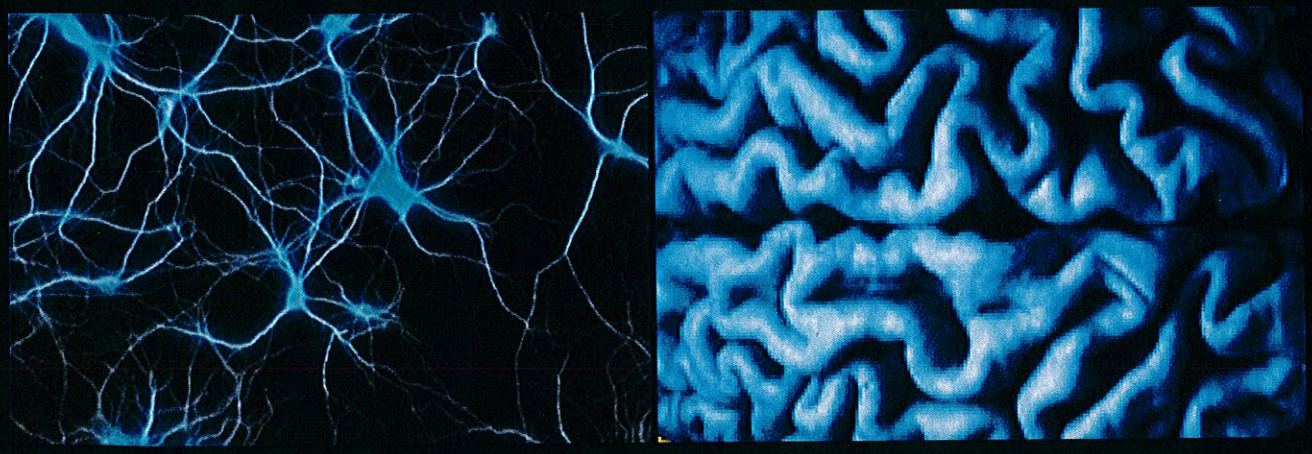

EVELYN F. McKNIGHT BRAIN INSTITUTE

RESEARCH SYMPOSIUM

OCTOBER 15, 2014

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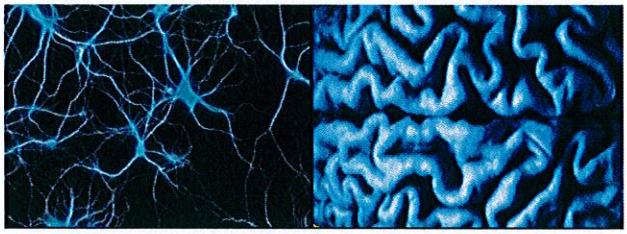

UNIVERSITY OF MIAMI MILLER SCHOOL OF MEDICINE
EVELYN F. MCKNIGHT BRAIN INSTITUTE
RESEARCH SYMPOSIUM AND CHAIR PRENSENTATION
OCTOBER 15, 2014

Attendees: Dean Pascal Goldschmidt, MD, Dr. Ralph L. Sacco, Dr. Clinton Wright, Dr. Bonnie Levin, Dr. Sara Czaja, Dr. Kunjan Dave, McKnight Brain Institute Investigators, McKnight Brain Research Foundation Trustees

9:00a.m. - 9:15a.m. Location:	Breakfast Sylvester Comprehensive Cancer Center, 1475 NW 12th Avenue, Miami, Florida 33136, Suite 1301	
9:15a.m. - 9:20a.m.	Welcome	Ralph Sacco, M.D.
9:20a.m. - 9:40a.m.	Novel determinants of cognitive function and decline in the Northern Manhattan Study	Ralph Sacco, M.D.
9:45a.m. - 10:05a.m.	When does cognitive change begin following a fall? Lessons from a life course perspective	Bonnie Levin, Ph.D.
10:10a.m. - 10:30a.m.	Cognitive function following cerebral ischemia in aged rats	Kunjan Dave, Ph.D.
10:35a.m. - 10:55a.m.	The role of health information technologies in supporting the cognition of older adults	Sara Czaja, Ph.D.

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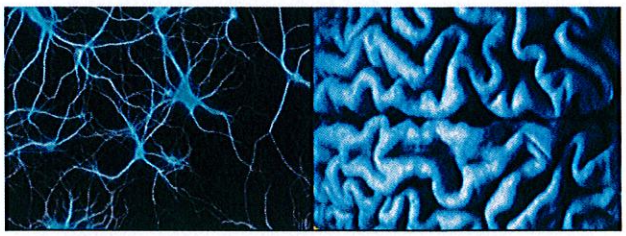
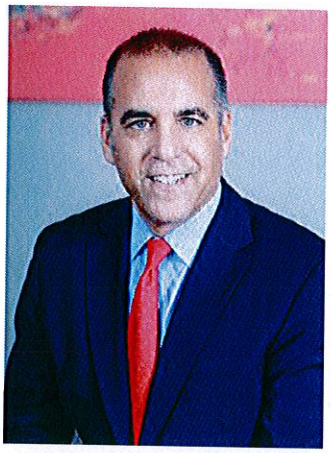


UNIVERSITY OF MIAMI MILLER SCHOOL OF MEDICINE
EVELYN F. MCKNIGHT BRAIN INSTITUTE
RESEARCH SYMPOSIUM AND CHAIR PRENSENTATION
OCTOBER 15, 2014

11:00a.m. - 12:30p.m. Location:	Lunch and Chair Presentation Clinical Research Building, 1120 NW 14th Street, Miami, Florida 33136, Suite 1381	
11:00a.m. - 11:10a.m.	Guests arrive	
11:10a.m. - 11:20a.m.	Lunch served	
11:20a.m. - 11:25a.m.	Chair program welcome	Ralph Sacco, M.D.
11:25a.m. - 11:30a.m.	Thank you	Dean Pascal J. Goldschmidt, M.D.
11:30a.m. - 11:45a.m.	Scientific Overview of the University of Miami Evelyn F. McKnight Brain Institute	Clinton B. Wright, M.D.
11:45a.m. - 11:55a.m.	Chair/Plaque Presentation	
11:55a.m. - 12:05p.m	Remarks	J. Lee Dockery, M.D.
12:05p.m. - 12:15p.m.	Photos	All
12:30p.m.	Ceremony and Lunch ends	

Ralph L. Sacco, MD, MS, FAHA, FAAN
Chairman, Department of Neurology
Olemberg Family Chair in Neurological Disorders
Miller Professor of Neurology, Public Health Sciences,
Human Genetics & Neurosurgery
Executive Director, Evelyn F. McKnight Brain Institute
Chief of Neurology Service, Jackson Memorial Hospital

University of Miami, Leonard Miller School of Medicine
1120 NW 14th Street, Suite 1352
Miami, FL 33136
Email: RSacco@med.miami.edu
Tel: 305-243-7519
Fax: 305-243-7081



Ralph L. Sacco, MD, MS, is the Chairman of Neurology, Olemberg Family Chair in Neurological Disorders, Miller Professor of Neurology, Epidemiology and Public Health Sciences, Human Genetics, and Neurosurgery, Executive Director of the Evelyn McKnight Brain Institute at the Miller School of Medicine, University of Miami, and Chief of the Neurology Service at Jackson Memorial Hospital.

A graduate of Cornell University in Bio-electrical Engineering and a cum laude graduate of Boston University School of Medicine, he also holds an MS in Epidemiology from Columbia University, Mailman School of Public Health. Dr. Sacco completed his neurology residency training and postdoctoral training in Stroke and Epidemiology at Columbia Presbyterian in New York. He was previously Professor of Neurology, Chief of Stroke and Critical Care Division and Associate Chairman at Columbia University before taking his current position as Chairman of Neurology at the University of Miami, Miller School of Medicine.

He is the Principal Investigator of the NINDS-funded Northern Manhattan Study, the Florida Puerto Rico Collaboration to Reduce Stroke Disparities, and the Family Study of Stroke Risk and Carotid Atherosclerosis, as well as co-investigator of multiple other NIH grants. He has also been the Co-Chair of international stroke treatment and prevention trials. Dr. Sacco has published extensively with over 425 peer-reviewed articles and 102 invited articles in the areas of stroke prevention, treatment, epidemiology, risk factors, vascular cognitive impairment, human genetics and stroke recurrence. His research has also addressed stroke and vascular disparities. He has been the recipient of numerous awards including, the Feinberg Award of Excellence in Clinical Stroke, the Chairman's Award from the American Heart Association, and the NINDS Javits Award in Neuroscience. He has lectured extensively at national and international meetings.

Dr. Sacco is a fellow of both the Stroke and Epidemiology Councils of the American Heart Association, the American Academy of Neurology, and the American Neurological Association, and currently serves as Vice President of the American Academy of Neurology. He is also a member of the American Association of Physicians. He was the first neurologist to serve as the President of the American Heart Association, 2010-2011, and is the current Co-Chair of the American Heart Association's International Committee.

Dr. Sacco has been a member of the World Stroke Organization since 2008. He currently chairs the Research Committee - 2012-2016, and is on the Board of Directors - 2012-2016.

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Research Symposium
University of Miami
Miller School of Medicine
October 15, 2014

University of Miami Miller School of Medicine

UHealth
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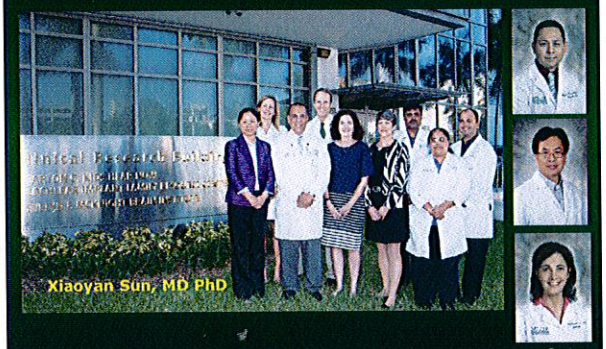

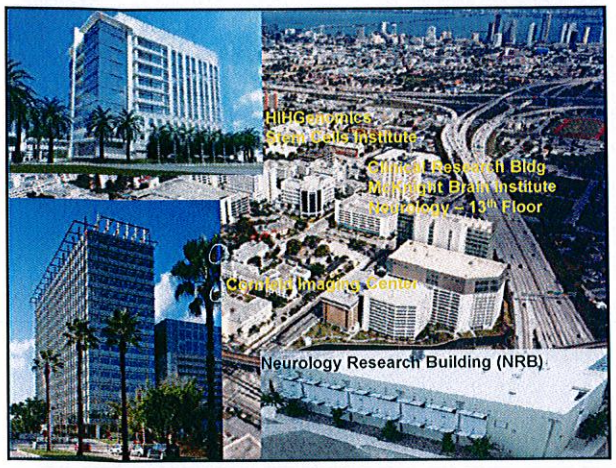

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Radiology
- Noam Alperin, PhD
- Ahmet Bagci, PhD

Human Genetics
- Susan Blanton, PhD
- Juan Young, PhD

Psychiatry
- Elizabeth Crocco, MD

Evelyn F. McKnight Chair
in Learning and Memory in Aging

For the
Scientific Director of our
McKnight Brain Research Institute

Novel Determinants of Cognitive Function and Decline in the Northern Manhattan Study

Ralph L. Sacco, MS MD FAAN FAHA
Olemberg Family Chair in Neurological Disorders
Miller Professor of Neurology, Public Health Sciences, Human Genetics, & Neurosurgery
Executive Director, Evelyn McKnight Brain Institute
Miller School of Medicine, University of Miami
Jackson Memorial Hospital

Supported by grants R37 NS 29993, U54 NS 081763, R01 NS 240807, R01 42912, 047655, DE 13094, Evelyn McKnight Brain Institute
Consultant: Boehringer Ingelheim (RESPECT), UCSF (SOCRATES DSMB), DCRI (EUCLID DSMB)

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM
Evelyn F. McKnight Brain Institute

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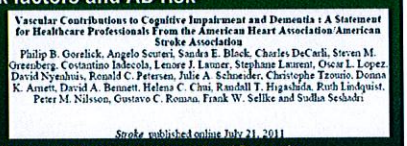
Novel Determinants of Cognitive Function and Decline

- Vascular Disease and Cognition
- Northern Manhattan Study Design
- AHA Ideal CV Health and Cognition
- Infectious Burden and Cognition
- Future NOMAS Plans

Relationships between Vascular and Neurodegenerative Processes in Cognitive Impairment and Dementia

- It is accepted that many traditional risk factors for stroke are also risk markers for AD and VCI
- There may be a convergence of pathogenic mechanisms in vascular and neurodegenerative processes which cause cognitive impairment
- Epidemiologic studies also point to linkages between traditional CV risk factors and AD risk



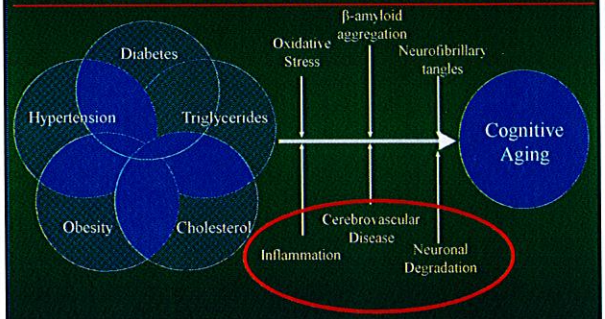
Vascular Contributions to Cognitive Impairment and Dementia : A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Philip B. Gorelick, Angelo Scuteri, Sandra E. Black, Charles DeCarli, Steven M. Greenberg, Costantino Iadecola, Lenore J. Launer, Stephane Laurent, Oscar L. Lopez, David Nyenhuis, Ronald C. Petersen, Julie A. Schneider, Christophe Tzourio, Donna K. Arnett, David A. Bennett, Helena C. Chui, Randall T. Higashida, Ruth Lindquist, Peter M. Nilsson, Gustavo C. Roman, Frank W. Sellke and Sudha Seshadri

Stroke, published online July 21, 2011

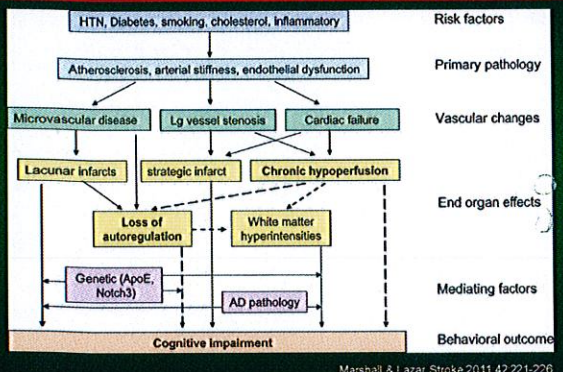
Gorelick et al. Vascular Contributions to Cognitive Impairment and Dementia. AHA/ASA Scientific Statement. Stroke; 2011

Possible Mechanisms For Vascular Risk Factors and Dementia



Middleton, L. E. et al. Arch Neurol 2009;66:1210-1215.

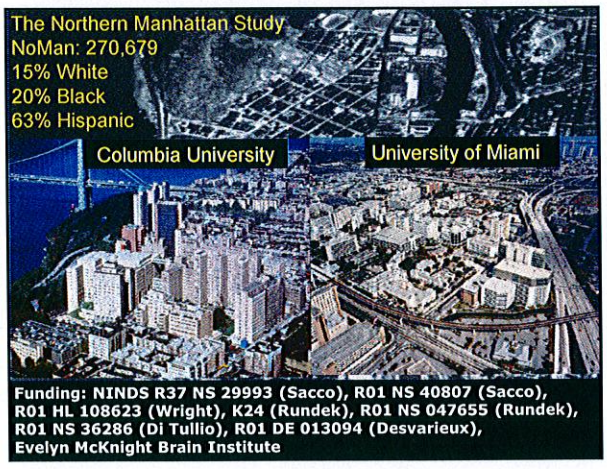
Model for the Pathophysiology of VCI



Marshall & Lazar Stroke 2011;42 221-226

The Northern Manhattan Study

NoMan: 270,679
15% White
20% Black
63% Hispanic



Funding: NINDS R37 NS 29993 (Sacco), R01 NS 40807 (Sacco), R01 HL 108623 (Wright), K24 (Rundek), R01 NS 047655 (Rundek), R01 NS 36286 (Di Tullio), R01 DE 013094 (Desvarieux), Evelyn McKnight Brain Institute

NORTHERN MANHATTAN STUDY
Prospective Cohort

1993 — 1998 — 2003 — 2008 — 2015

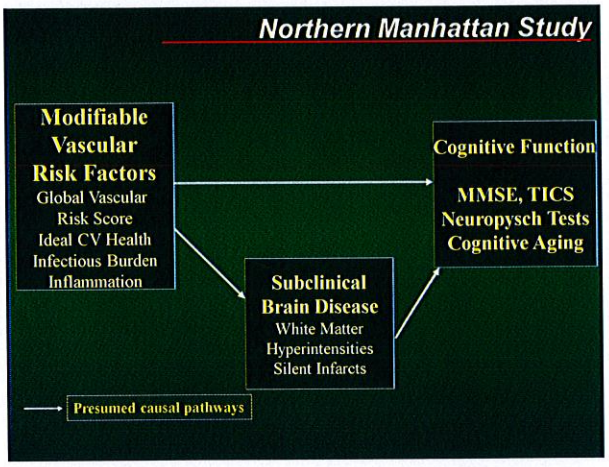
BASELINE ASSESSMENT
- Sociodemographics
- Vascular Risk Profile
- BP Measures
- Anthropometrics
- Fasting bloods
- Neurogical Exam
- N = 3,298

CIMT sub-study
- Candidate gene substudy
- Brain-MRI substudy
- Cognitive decline substudy
- GWAS

Annual Follow-up
Phone Screen, In-person Validation, Hospital Surveillance
Stroke MI Death

Funding: NINDS R37 NS 29993 (Sacco), R01 NS 40807 (Sacco), R01 HL 108623 (Wright), K24 (Rundek), R01 NS 047655 (Rundek), R01 NS 36286 (Di Tullio), R01 DE 013094 (Desvarieux), Evelyn McKnight Brain Institute

Northern Manhattan Study



Risk Factors
Northern Manhattan Study

Alcohol, Physical Activity, Obesity, Homocysteine

Diet: Mediterranean Pattern, Salt, Fat, Diet Soda

HDL, LDL, Lp(a), Metabolic Syndrome, HOMA Index, GFR

Social Factors: Isolation, SES, Depression

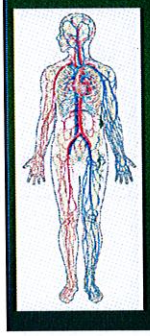
Cardiac
- Patent Foramen Ovale
- Aortic Arch Atheroma
- LVH, LV Mass
- Left Atrial Size
- Subclinical AF

Inflammation & Infection
- Chlamydia Pneumoniae
- Periodontal Disease
- White Blood Cell Count
- TNF alpha Receptor levels
- CRP, Cytokines

Cardiovascular Risk

Improving Global Vascular Risk Prediction With Behavioral and Anthropometric Factors

The Multiethnic NOMAS (Northern Manhattan Cohort Study)



NOMAS Global Vascular Risk Model

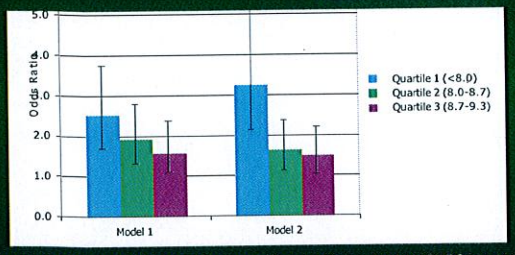
New Risk Factor Variables
Waist (inches)
Moderate alcohol consumption
Moderate-to-heavy physical activity
Moderate-to-heavy physical activity * male gender
Peripheral vascular disease
Sociodemographic Variables
Age (years)
Black race
Hispanic ethnicity
Male gender
Traditional Risk Factor Variables
Systolic blood pressure (mm Hg)
Diastolic blood pressure (mm Hg)
Diastolic blood pressure * anti-hypertensive medication
Fasting blood sugar (mg/dL)
Former smoking
Current smoking
Total cholesterol:HDL (mg/dL)

Sacco RL et al. J Am Coll Cardiol 2009;54:2303-11

Association Between Northern Manhattan Study Global Vascular Risk Score and Successful Aging

Jessica R. L. Warsch, MD, PhD, Tatjana Rundek, MD, PhD,* Myunghee C. Paik, PhD,† Mitchell S. V. Elkind, MD, MS,‡§ Ralph L. Sacco, MD, MS,*‖ and Clinton B. Wright, MD, MS*‖*

J Am Geriatr Soc 61:519–524, 2013

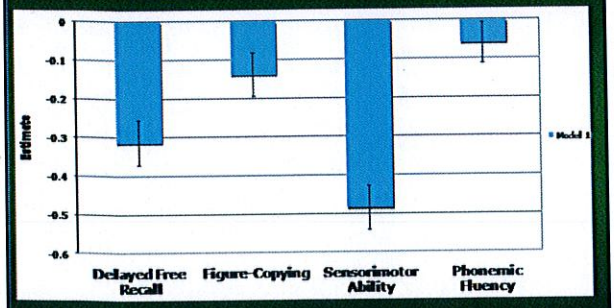


Odds ratio for Successful Aging without cognitive decline and better GVRS scores
Model 1 adjusted for length of time between baseline and follow-up cognitive testing only
Model 2 adjusted for years of education, health insurance status, and follow-up time.

Ideal Cardiovascular Health

- AHA defined "ideal cardiovascular health" and we have documented the strong relationship with stroke, MI, and vascular death in NOMAS
- Ideal CV Health factors may also impact cognitive or brain health.
- We examined the relationship between the number of ideal CV health metrics with
  - Mini-Mental State Exam
  - Domains of cognitive performance (language, memory, executive function, processing speed)
  - Cognitive Decline

Global Vascular Risk Score and Cognitive Functions: Northern Manhattan Study



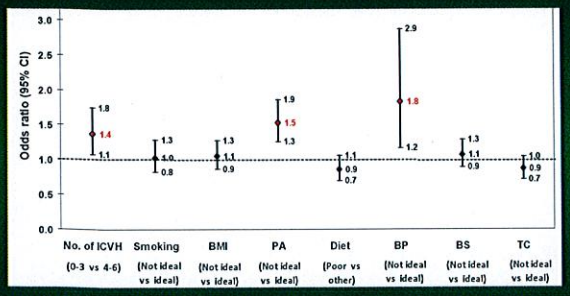
*Model 1 is adjusted for education

Loring and Wright

AHA Ideal Cardiovascular Health Life's Simple 7

	Ideal	Intermediate	Poor
Smoking	Never or quit > 1 year	Quit < 1 year	Current
BMI	< 25 kg/m²	25 - <30 kg/m²	≥ 30 kg/m²
Physical activity	≥ 75 min/wk vigorous or ≥ 150 min/wk moderate or equivalent combination	1-74 min/wk vigorous or 1-149 min/wk moderate or equivalent combination	No moderate or vigorous activity
Diet	4-5 healthy components	2-3 healthy components	0-1 healthy components
Blood pressure	Untreated & SBP < 120 & DBP < 80 mmHg	Treated to <120/<80 or 120-139/80-89 mmHg	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg
Fasting glucose	Untreated & < 100 mg/dL	Treated to <100 mg/dL or 100-125 mg/dL	>126mg/dL
Total cholesterol	Untreated & < 200 mg/dL	Treated to < 200 mg/dL or 200-239 mg/dL	≥ 240 mg/dL

Ideal CV Health and MMSE in NOMAS



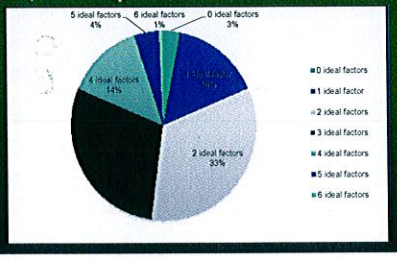
Standardized residual of MMSE < -0.84 after regressed on age, sex, education, race-ethnicity, sex*education and race-ethnicity*education
Adjusted for health insurance, marriage and number of friends

Cognitive Assessment

- Cognitive domain Z scores derived from factor analysis of neuropsychological battery
  - Memory
  - Language
  - Executive function
  - Psychomotor speed
- Z scores for change in performance incorporate age, education, time between assessments

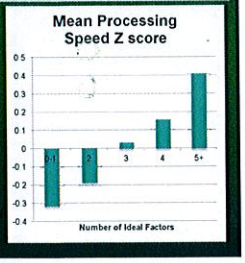
NOMAS Study Sample

- 1078 with baseline cognitive data with 756 with follow-up cognitive data
  - Mean age at baseline = 64 ± 8
  - Mean age at first cognitive assessment = 72 ± 8
  - 39% Male; 65% Hispanic, 16% NH-White, 19% NH-Black



ICVH and Baseline Cognition

	Executive Function Effect (P)	Language Effect (P)	Memory Effect (P)	Processing Speed Effect (P)
Number of ideal CV factors	0.010 (0.66)	0.004 (0.86)	0.034 (0.14)	0.110 (<0.0001)



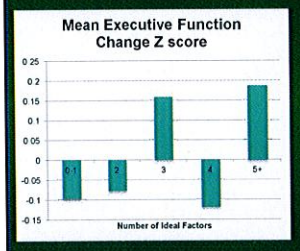
Controlling for age, sex, race/ethnicity, years of education, insurance status, time from baseline to neuropsych assessment

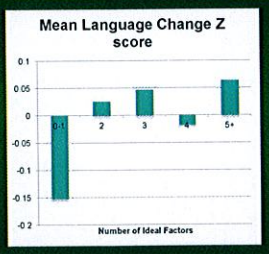
ICVH and *Change* in Cognitive Performance Over Time

	Executive Function Effect (P)	Language Effect (P)	Memory Effect (P)	Processing Speed Effect (P)
Number of ideal CV factors	0.058 (0.08)	0.035 (0.28)	0.059 (0.07)	0.124 (0.0002)

Change Z score adjusts for age, education, and time between 2 assessments
Model adjusted for sex, race/ethnicity, insurance status, time from baseline to neuropsych assessment.

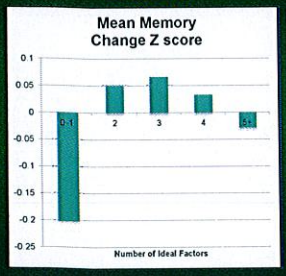
Less Effects for Change in Executive Function and Language





ICVH and *Change* in Cognition

Memory



Processing Speed

Change Z score adjusts for age, education, and time between 2 assessments

ICVH Components and Processing Speed

Ideal vs. not ideal	Initial assessment processing speed Effect (P)	Change in performance processing speed Effect (P)
Blood pressure#	-0.03 (0.81)	0.24 (0.12)
BMI	0.18 (0.004)	0.15 (0.09)
Total Cholesterol	0.03 (0.53)	-0.02 (0.81)
Smoking	0.18 (0.005)	0.20 (0.03)
Physical activity	0.09 (0.11)	0.11 (0.18)
Diabetes	0.18 (0.001)	0.18 (0.03)
Diet	0.52 (0.25)	-0.46 (0.51)

#Systolic BP was asscciated with change in processing speed
Controlling for age, sex, race/ethnicity, years of education, insurance status, time from baseline to neuropsych assessment. All ICVH components are mutually adjusted.

Infection, Inflammation & Cognition

- Chronic infections and immune system responses to them are potentially damaging to brain structure and function
- In NOMAS a composite index of serologic measures of exposure to *Helicobacter pylori*, *Chlamydia pneumoniae*, herpes simplex virus I and II, and cytomegalovirus has previously been associated with:
  - Incident stroke
  - Carotid plaque thickness

Infectious burden and cognitive function

The Northern Manhattan Study

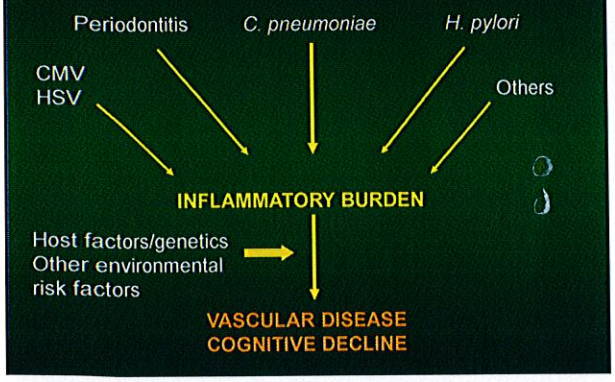
Table 2 Association of the infectious burden index with cognitive function*

	Unadjusted	Adjusted for demographics†	Adjusted for demographics, general, and vascular risk factors‡
MMSE			
Difference in baseline MMSE per SD in IBI	−0.77 (−0.95 to −0.58) <0.0001	−0.16 (−0.34 to −0.002) 0.05	−0.17 (−.34 to 0.01) 0.06
MMSE ≤24	1.58 (1.36 to 1.82) <0.0001	1.23 (1.04 to 1.45) 0.019	1.26 (1.06 to 1.51) <0.01
TICS-m			
Difference in baseline TICS-m per SD in IBI	−1.92 (−2.24 to −1.61) <0.0001	−0.66 (−0.93 to −0.37) <0.0001	−0.68 (−0.97 to −0.39) <0.0001
Annual change in TICS-m per SD in IBI	0.03 (−0.01 to 0.07) 0.18	0.03 (−0.01 to 0.07) 0.13	0.03 (−0.01 to 0.07) 0.13

Mira Katan, MD
Yeseon Park Moon, MS
Myunghee Cho Paik, PhD
Ralph L. Sacco, MD, MS
Clinton B. Wright, MD
Mitchell S.V. Elkind,

Neurology® 2013;80:1209-1215

"Burden" of Infectious Disease?



Objective & Methods

- To examine the association between infectious burden index (IBI) and domain-specific cognitive performance
  - –At baseline cognitive assessment
  - –At second assessment 6 years later

Baseline Cognitive Associations

Effect of IBI (N=588)

Model	Exec. function	Language
1: age, sex, bl-npsych	-0.31, <0.0001*	-0.30, <0.0001
2: 1 + edu, race/eth, ins	-0.12, 0.002	-0.07, 0.04
3: 2 + WMH, SBI, BV	-0.12, 0.002	-0.07, 0.04
4: 2 + modfiable VRFs	-0.11, 0.003	-0.07, 0.05

Model	Memory	Processing speed
1: age, sex, bl-npsych	-0.22, <0.0001	-0.23, <0.0001
2: 1 + edu, race/eth, ins	-0.06, 0.11	-0.07, 0.06
3: 2 + WMH, SBI, BV	-0.06, 0.11	-0.07, 0.06
4: 2 + modfiable VRFs	-0.06, 0.11	-0.07, 0.07

*parameter estimate, p-value

Interleukin 6 Plasma Concentration Associates with Cognitive Decline: The Northern Manhattan Study

Alexis Economos[a,b] Clinton B. Wright[a-c] Yeseon Park Moon[d] Tatjana Rundek[a-c] LeRoy Rabbani[e] Myunghee C. Paik[f] Ralph L. Sacco[a-c] Mitchell S.V. Elkind[c,g]

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Neuroepidemiology 2013;40:253–259

Follow-up Cognitive Assessment

Effect of IBI, p-value
N=419, mean f/u 6 ± 2 years

Model	Exec. function	Language
1: sex, race/eth, ins	-0.09, 0.11*	-0.09, 0.10
3: 1 + WMH, SBI, BV	-0.09, 0.11	-0.08, 0.11
4: 1 + modfiable VRFs	-0.08, 0.14	-0.09, 0.10

Model	Memory	Processing speed
1: sex, race/eth, ins		-0.10, 0.08
3: 2 + WMH, SBI, BV		-0.09, 0.09
4: 2 + modfiable VRFs	-0.14, 0.01	-0.10, 0.08

parameter estimate, p-value

NOMAS Future Plans Year 23 and Beyond (2015-19)

OUTCOMES	PRIMARY EXPOSURES	AIM
Cognitive Trajectories	Immune Network MRI Markers	1 2
Dementia	Immune network MRI Markers	3
Functional Outcomes	Vascular RFs; Global Vascular Risk Score	4
Ischemic Stroke Subtypes	Race-Ethnicity and Vascular RFs	5

Inflammatory & Immune Biomarkers

Immune molecules to be measured (61-plex)	
Type of immune molecule	**Immune molecule**
IL1 superfamily	IL1α, IL1β, IL1ra, IL18
IL12 cytokine family	IL12p40, IL12p70, IL23
IL17 family	IL17A, IL17F
Type I interleukin, γ chain family	IL2, IL4, IL7, IL9, IL13, IL15, IL21
Type I interleukin, β chain family	GMCSF/CSF2, IL5
IL10 cytokine family	IL10, IL22
IL6 (gp130) cytokine family	IL6, IL27, IL31, LIF
Type I IFN	IFNα2, IFNβ
Type II IFN	IFNγ
TNF superfamily	TNFα/TNFSF2, TNFβ/TNFSF1, sFasLigand/TNFSF6, TRAIL/TNFSF10
CC Chemokines	MCP1/CCL2, MIP1α/CCL3,MIP1β/CCL4, RANTES/CCL5, MCP3/CCL7, eotaxin/CCL11
CXC Chemokines	GROα/CXCL1, IL8/CXCL8,MIG/CXCL9, IP10/CXCL10, SDF1/CXCL12
PDGF family & VEGF subfamily	PDGFBB, PlGF1, VEGFA, VEGFD
Cell adhesion molecules	sICAM1/CD54, VCAM1/CD106
Serine protease inhibitors	PAI1
Adipose-derived hormones	Leptin, resistin

Infectious Burden & Cognition

- Greater IB index was associated with worse cognitive performance on MMSE, TICS, and Neuropsychological testing.
- Cognitive impairment may be driven by effects on executive function and language ability
- Greater IB index was also associated with decline in memory performance over time
- Research on inflammatory and immune networks and cognitive function may lead to interventions with anti-inflammatory agents for preserving cognitive health

ICVH and Cognition

- ICVH score is associated with processing speed performance at baseline and over time.
- The ICVH components driving the associations are BMI, smoking, diabetes, and SBP.
- Non-significant trends were also seen with change in executive function and memory performance over time.
- The particular association with processing speed suggests a process partly mediated by subclinical cerebrovascular disease affecting intra- and inter-hemispheric connections.

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Dr. Bonnie Levin is the Alexandria and Bernard Schoninger Professor of Neurology and Director of the Division of Neuropsychology in the Department of Neurology at the University of Miami, Miller School of Medicine. She received her BS from Georgetown University and her Ph.D. from Temple University. She completed an internship at the Boston Children's Hospital where she was a clinical fellow in Psychiatry at Harvard Medical School and an externship at the Boston VA Hospital.

Dr. Levin is a neuropsychologist whose research examines neurocognitive and affective changes associated with neurodegenerative disease and the normative aging process. Her work examines the role of cardiometabolic risk factors in cognitive decline. Another focus has been the inter-relationship between behavioral and motor symptoms in Parkinson's disease and the neural circuitry underlying memory and age related cognitive change. Her current work is aimed to advance our understanding of frontal striatal circuit function in cognition and to generate data that will improve our knowledge of key clinical parameters associated with differential rates of cognitive decline. Current projects include: examining which components of the metabolic syndrome predict cognition, identifying imaging and clinical correlates of white matter changes associated with the aging process and linking structural and metabolic markers underlying different symptom profiles in neurodegenerative disease.

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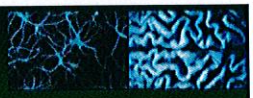


Evelyn F. McKnight Brain Institute

Research Symposium
University of Miami
Miller School of Medicine
October 15, 2014

CDC report:

- One in three older adults (aged 65 or older) fall each year
- Less than half report it to their health care provider
- Leading cause of fatal and non-fatal injuries
- In 2012, 2.4 million nonfatal falls; 722,000 were hospitalized

When does cognitive change begin following a fall? Lessons from a life course perspective

Bonnie E. Levin, Ph.D.
October 15, 2014

CDC report:

- In 2012, direct medical costs= $30 billion
- Men are more likely to die from a fall compared to women
- Women more than 2x more likely to fracture their hip
- Older non-Hispanics have higher fall rates than Hispanics

What is a TBI?

A TBI occurs when there is a sudden physical insult to the brain. The TBI may result from a closed head injury, a penetrating head injury or repetitive concussions.

What causes falling?

- 31% accident/environment
- 17% gait/balance disorder
- 15% other specified
- 13% dizziness/vertigo
- 10% drop attack
- 5% unknown
- 4% confusion
- 3% visual problems
- 3% postural hypotension

Outcomes linked to falling:

- 20-30% who fall suffer moderate to severe injuries.
- Cognitive impairments may be acute or delayed, often involve higher order skills, especially attention and new learning.
- Sensory losses (blurred vision, double vision, light insensitivity), smell, taste, hearing.
- Emotional problems: mood swings, depression, apathy, irritability

Fear of falling directly related to reduced mobility, physical

Unresolved questions:

- Who will exhibit a negative health outcome following a TBI?
- Who will show evidence of memory loss?
- Who will deteriorate over time and progress to dementia?
- How do we track the multifactorial array of cognitive, affective, neurologic, and behavioral clinical endpoints?

Traditional approach to understanding the relationship between falls and cognitive decline in the context of the aging process has been to focus on specific risk factors and to quantify the relative contribution for a specific outcome such as memory loss.

What is Life Course Epidemiology?

Life course epidemiology is the study of antecedent events, exposures, and biological predispositions and their impact on later health outcomes.

Revisiting TBI and Cognitive Change:

- TBI risk factors have not been shown to be readily modifiable or lead to successful intervention. "Too little, too late?"
- Therefore, we need to think about a fall as an adverse event on a trajectory that is viewed in the context of the life span

Advantages of Using a Life Course Framework (LCF):

- Focuses on key life events and their interrelationships
- Based on the premise that early life exposures, *including those seemingly unrelated to the TBI*, may put an individual on a higher risk trajectory compared to others not exposed
- Differential early life exposures, combined with trauma, can produce a cascading effect, resulting in an accumulation of risk, or *chaining of risk*, that increases the probability of a negative outcome

Demographic risk factors:

- Age
- Gender
- Socioeconomic position
- Ethnicity

Lifestyle Risk Factors:

- Alcohol and substance abuse
- Smoking
- Prior TBI
- Fitness/Exercise
- Sleep

Developmental risk factors:

- Lifetime chronic stress
- Psychological resilience
- Psychopathology
- Learning disabilities

Educational and Vocational History/Social Drift:

- Occupation and occupational changes
- Health literacy

Medical Risk Factors:

- Childhood acquired viruses
- CAD
- Hypertension
- Diabetes and metabolic syndrome components
- Kidney function

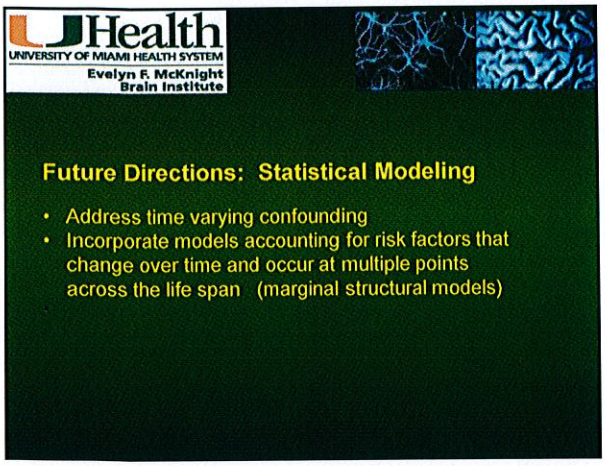
Future Directions: Methods and Statistical Modeling Using a Life Course Perspective

Statistical caveat:

While traditional generalized linear models (linear regression, survival analyses), have been useful at looking at the relationship between risk factors and outcome, this statistical approach is not ideal for examining how exposures and antecedent events co-occur and impact an individual trajectory across the life course over time.

Future Directions: Methods

- Contextualize risk factors : stop thinking of individual risk factors as isolated events
- Broaden our risk assessment: think holistic
- Incorporate a developmental perspective and measure risk factors earlier in life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Future Directions: Statistical Modeling
• Address time varying confounding
• Incorporate models accounting for risk factors that change over time and occur at multiple points across the life span (marginal structural models)

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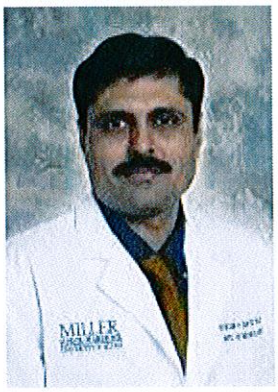

Presently, Dr. Kunjan R. Dave is a Research Associate Professor and Associate Director of Cerebral Vascular Disease Research Laboratory, Department of Neurology, University of Miami Miller School of Medicine. Dr. Dave received his Ph.D in Biochemistry in 2000 from the M. S. University of Baroda, India. During his PhD training he worked on several research projects including secondary complications of diabetes, Alzheimer's disease and drug toxicity among others. From 1999 to 2000 Dr. Dave served at the Zandu Pharmaceutical Works, Mumbai, India, as a Biochemist, where he participated in a drug development program. Dr. Dave then joined the Department of Neurology, University of Miami as a post-doctoral fellow with Dr. Miguel A. Perez-Pinzon. Dr. Dave has performed research essential for the understanding cerebral ischemia pathophysiology and Amyotrophic Lateral Sclerosis. The goal of Dr. Dave's research is to study potential signaling pathways responsible for neuronal death in neurodegenerative diseases, especially cerebral ischemia. Investigation of intracellular signaling pathways may lead to the development of novel therapies for patients with neurodegenerative diseases and stroke. He is also working on a project determining the effect of cerebral ischemia on cognitive function in old rats.

Cognitive function following cerebral ischemia in aged rats

Kunjan R. Dave

Charles Cohan, Jake Neumann, Clinton Wright, Miguel Perez-Pinzon

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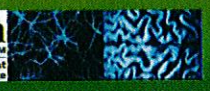
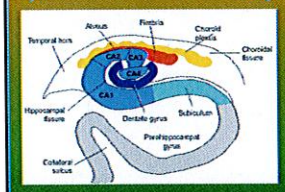


Evelyn F. McKnight Brain Institute Research Symposium
October 15, 2014

Cardiac arrest and hippocampal damage

Delayed hippocampal damage in humans following cardiorespiratory arrest

Carol K. Petito, MD; Edward Feldmann, MD; William A. Pulsinelli, MD, PhD; and Fred Plum, MD



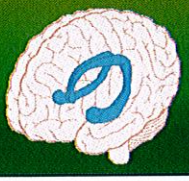
	Cardiac arrest			
	Present			Not present
	L	R	L&R	L&R
Number examined	29	29	–	–
Number involved (irrespective of region)	27	28	35 (100%)	0
Distribution				
CA4	21	21	27	8
CA3	20	23	28	7
CA2	16	17	21	14
CA1	27	26	33	2
Prosubiculum	20	22	27	8
Subiculum	17	21	24	11
Dentate fascia*	12	11	16	19

Cardiac arrest and cerebral ischemia

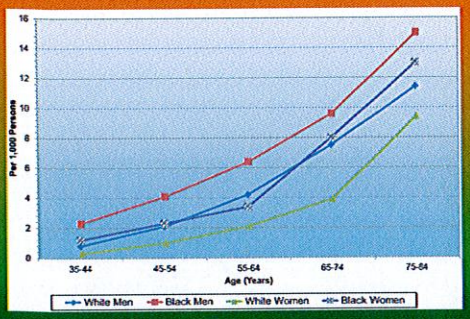
- 633,000 people experience CA every year in USA
- 60% die from extensive brain injury
- Successfully resuscitated cardiac arrest survivors have a 9-15% chance of surviving to hospital discharge

Cognitive Dysfunction & the Hippocampus

- Hippocampus
  - Important for:
    - Learning
    - Spatial memory
- Cognitive dysfunction following cerebral ischemia
  - Memory
  - Attention
  - Executive Function
  - Motor Function



Incidence of heart attacks age, sex, and race



Heart disease and stroke statistics--2014 update: a report from the AHA. Circulation. 2014; 129: e28-e292.

Goal

- To study the interaction of aging and cerebral ischemia on cognitive decline.

Summary

- Prevalence of cardiac arrest is higher in middle age and older population.
- Majority of all survivors have cognitive deficits.
- Prevalence, severity and course of cognitive problems in cardiac arrest survivor are not well characterized.

Models of global cerebral ischemia in aged rats

- Few laboratories use this model
- Study short-term survival
- High post-ischemia mortality

Hegde et al. PLoS One. 2012; 7: e35015.
Morton et al. Neuropathol Appl Neurobiol. 2012; 38: 710-22.
Morton et al. Brain Res. 2010; 1354: 11-9.
Xu et al. Brain Res. 2010; 1358: 181-9.
Ritter et al. Microcirculation. 2008; 15: 397-376.
Ito et al. Curr Neurovasc Res. 2008; 5: 249-74.
Candelario et al. NAGRA. 2004; 17: 109-18.

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Research report

Mild cardiopulmonary arrest promotes synaptic dysfunction in rat hippocampus

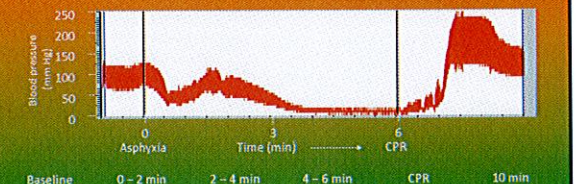
Kunjan R. Dave[a,1], Ami P. Raval[c,1], Ricardo Prado[a], Laurence M. Katz[b], Thomas J. Sick[a], Myron D. Ginsberg[a], Raul Busto[a], Miguel A. Pérez-Pinzón[a,*]

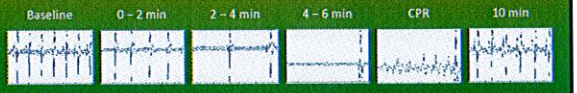
16 Induction of Asphyxia Cardiac Arrest in a Rat as a Model of Global Cerebral Ischemia

Kunjan R. Dave, Ricardo Prado, and Miguel A. Perez-Pinzon

Manual of stroke models in rat. 2009; Editor: Y. Wang-Fisher; Publisher: CRC Press

Representative blood pressure tracing and ECG

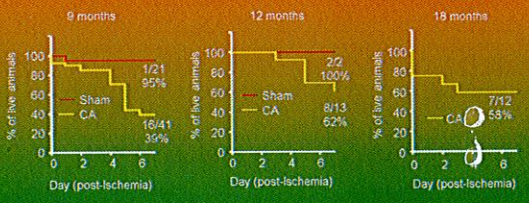


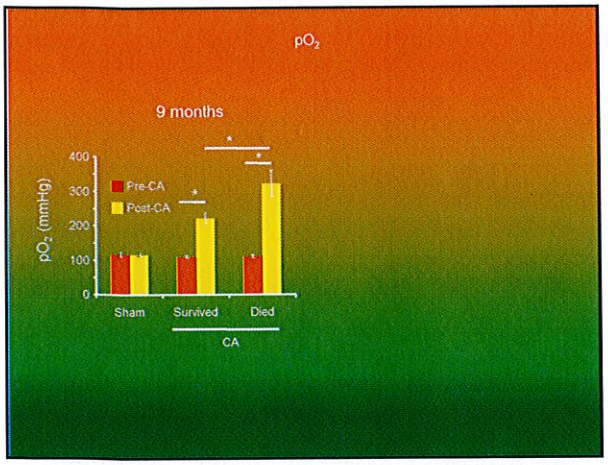


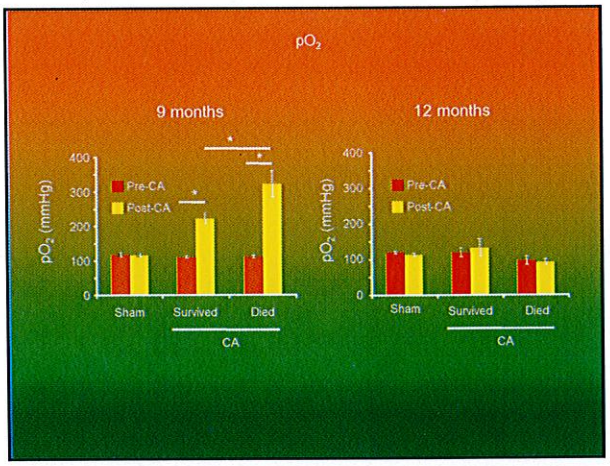
Overview of the procedure

- Anesthetized with 5% isoflurane (30:70/oxygen:nitrous oxide)
- Cannulate femoral vein and artery
- Intubate the animal, paralyze, connect to mechanical ventilation
- Maintain animal's temperature, and blood gas in normal range
- Induce asphyxial cardiac arrest by disconnecting the ventilator
- After CA, connect ventilator to the endotracheal tube (100 % Oxygen)
- Administer a bolus injection of epinephrine and sodium bicarbonate
- Manual chest compressions until MAP reaches 50 mm Hg

Survival





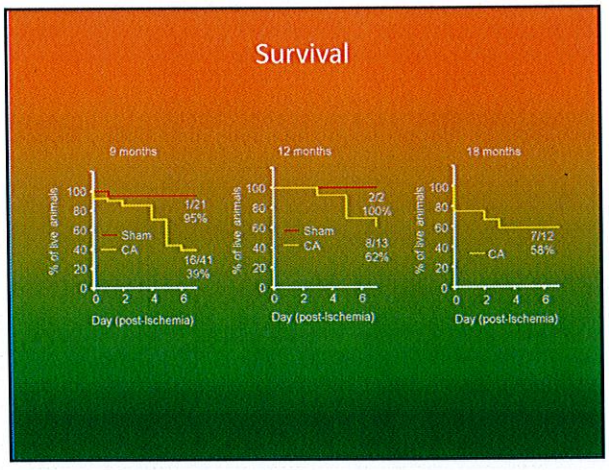


Part 9: Post–Cardiac Arrest Care
2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

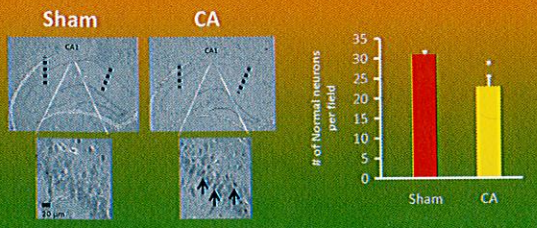
Mary Ann Peberdy, Co-Chair*; Clifton W. Callaway, Co-Chair*; Robert W. Neumar; Romergryko G. Geocadin; Janice L. Zimmerman; Michael Donnino; Andrea Gabrielli; Scott M. Silvers; Arno L. Zaritsky; Raina Merchant; Terry L. Vanden Hoek; Steven L. Kronick

- Although 100% oxygen may have been used during initial resuscitation, providers should titrate inspired oxygen to the lowest level required to achieve an arterial oxygen saturation of ≥94%, so as to avoid potential oxygen toxicity.
- Oxygenation of the patient should be monitored continuously with pulse oximetry.

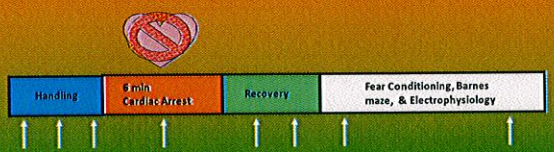
Peberdy et al. Circulation. 2010; 122: S768-86.



Decrease in number of normal neurons 1 week after CA (9 months old)



Experimental Design

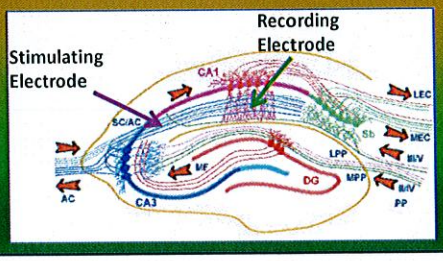


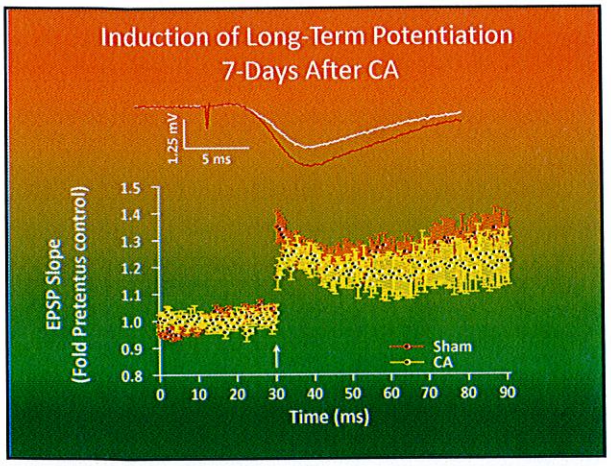
Learning, Memory, and Electrophysiology

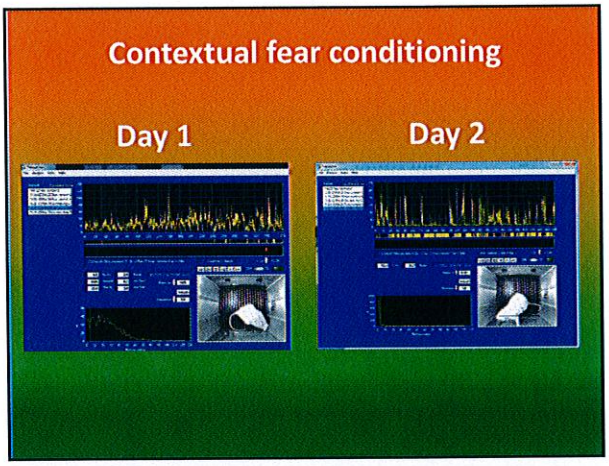
- The hippocampus is critical for memory formation (encoding)
- Synaptic plasticity
  - Ability for a synapse between two neurons to change the strength of their electrical conductance due to stimulation or disuse.

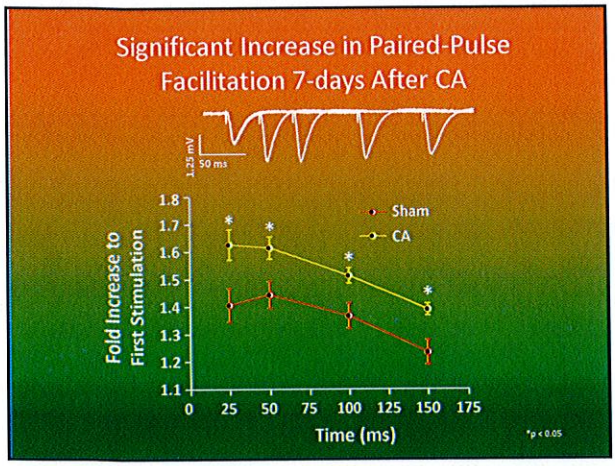
Synaptic Plasticity in Acute Brain Slice 7-Days After CA

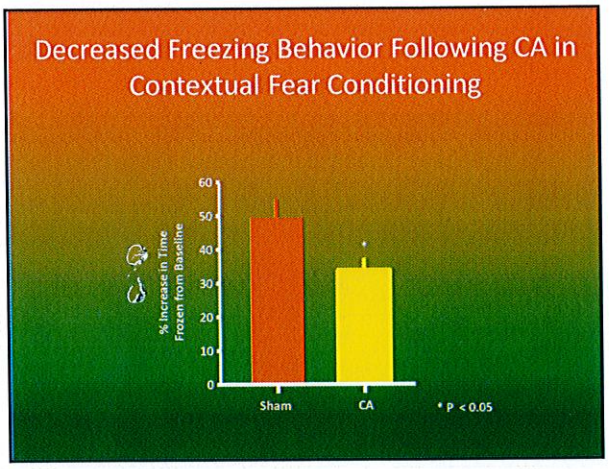
- Hippocampal CA1 neuron synaptic plasticity
  - Long-term potentiation
  - Paired-pulse facilitation



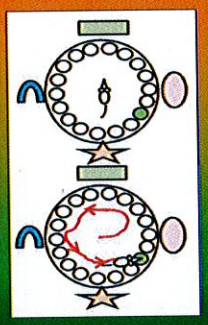

Induction of Long-Term Potentiation
7-Days After CA
1.25 mV
5 ms
EPSP Slope
(Fold Pretentus control)
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0 10 20 30 40 50 60 70 80 90
Time (ms)
Sham
CA


Contextual fear conditioning
Day 1
Day 2

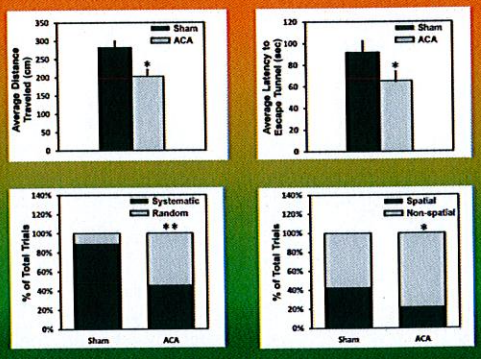

Significant Increase in Paired-Pulse
Facilitation 7-days After CA
1.25 mV
50 ms
Fold Increase to
First Stimulation
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
0 25 50 75 100 125 150 175
Time (ms)
Sham
CA
*p < 0.05


Decreased Freezing Behavior Following CA in
Contextual Fear Conditioning
% Increase in Time
Frozen from Baseline
60
50
40
30
20
10
0
Sham
CA
* P < 0.05

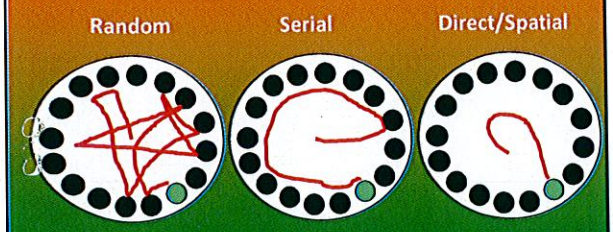
Barnes circular platform maze



Spatial memory is impaired following CA



Random, serial, direct/spatial search strategies



Summary

- Cerebral ischemia:
  - Results in a decreased number of normal hippocampal CA1 neurons
  - Induces synaptic dysfunction
  - Promotes spatial memory deficits

Future studies

- Characterize histological and behavioral outcomes following CA in aged rats.
- Improve sensitivity of tests used to determine cognitive outcomes.
- Determine effects of enriched environment and physical exercise on cognitive functions following cerebral ischemia.

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  - NS054147
  - NS34773
  - NS073779

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Sara J. Czaja is a Leonard M. Miller Professor in the Departments of Psychiatry and Behavioral Sciences, and Industrial Engineering at the University of Miami. She is also the Scientific Director of the Center on Aging at the University of Miami and the Director of the Center on Research and Education for Aging and Technology Enhancement (CREATE). CREATE is funded by the National Institute on Aging involves collaboration with the Georgia Institute of Technology and Florida State University. The focus of CREATE is on the interface between older adults and technology systems in work, healthcare and living settings.

Dr. Czaja has extensive experience in aging research and a long commitment to developing strategies to improve the quality of life for older adults. Her research interests include: aging and cognition, aging and healthcare access and service delivery, family caregiving, aging and technology, human-computer interaction, training, and functional assessment. She has received funding from the National Institutes of Health, Administration on Aging, National Science Foundation, the Markle and Langeloth Foundations, AT&T, and IBM to support her research. Dr. Czaja is very well published in the field of aging and has written numerous books, book chapters and scientific articles and servers on the editorial board of several top tier journals. She is a fellow of the American Psychological Association, the Human Factors and Ergonomics Society and the Gerontological Society of America. She is also President Elect of Division 20 (Adult Development and Aging) of the American Psychological Association.

She is also a member of the National Research Council/National Academy of Sciences Board on Human Systems Integration and the Institute of Medicine Committee on the Public Health Dimensions of Cognitive Aging.

The Role of Information Technology in Supporting Cognition for Older Adults

Sara J. Czaja, PhD
Department of Psychiatry and Behavioral Sciences
Center on Aging
University of Miami Miller School of Medicine

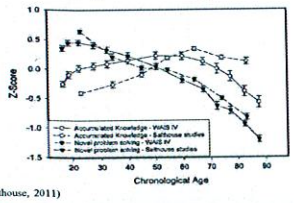
Prepared for the University of Miami Miller School of Medicine
Evelyn F. McKnight Brain Institute
Research Symposium
October 15, 2014

Background

- Cognitive abilities are linked to performance on a wide variety of tasks that are important to everyday living and independence:
  - Medication and financial management
  - ADLs
  - Driving
  - Work-related activities
  - Learning of new skills
- Older adults often experience challenges in everyday activities such as medication and financial management, driving, and learning new skills.

Background

- Aging is generally associated with changes in cognitive abilities including changes in:
  - Memory (working memory, prospective memory, episodic memory)
  - Attention, Processing Speed
  - Executive Functioning
  - Reasoning, Problem Solving, Decision Making



(Salthouse, 2011)

Background

- Information technologies can be used to support cognitive abilities of older adults and the performance of everyday living tasks:
  - Assessment
  - Cognitive training
  - Coaching
  - Cognitive Engagement and Social Connectivity
  - Performance of tasks
  - Caregiver Support/Monitoring

UM Technology-Based Functional Assessment and Training Battery

- Encompasses a wide range of real world activities:
  - Medication Management
  - ATM/banking
  - Prescription refill via voice menu
  - Kiosk Ticket Purchase and Wayfinding
  - Online Forms Completion
  - Shopping
- High ecological validity – simulations are based on real world tasks
- Computer-based/multimedia format
- Real time performance data
- Flexible format – easily adapted for varying difficulty, language

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Task Performance

	Sample	Mean	Std. Deviation
ATM Task: Total Incorrects**	Non-impaired	2.85	2.21
	Patients	5.37	5.08
Prescription Task: Incorrect and Invalid	Non-impaired	2.32	2.74
	Patients	3.47	3.46
Form Task: Time in secs***	Non-impaired	159.75	138.47
	Patients	300.58	200.32
Doctors Task: Percent Correct***	Non-impaired	67.39	17.94
	Patients	45.58	21.21

*** p < .001; ** p < .01

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Correlations

	TMT	BACS	HVLT	LNST	Fluency	ATM (time)	ATM - Efficiency	Form (time)	Prescription (time)	Prescription (# of correct)	Doctor (time)	Doctor (# of correct and valid)
UPSA	.404**	.645**	.480**	.616**	.331**	-.411**	.344**	-.584**	-.434**	.446**	-.383**	.645**
TMT		.539**	.405**	.521**	.231*	-.154	.178	-.192	-.301*	.157	-.210	.236
BACS			.460**	.483**	.282*	-.454**	.383**	-.523**	-.419**	.362**	-.254	.300*
HVLT				.533**	.352*	-.281*	.409**	-.406**	-.338**	.278*	.005	.321*
LNS					.258*	-.068	.230	-.164	-.015	.378**	-.110	.331*
Fluency						.015	.077	-.131	-.072	.205	.142	.141
ATM (time)							-.362**	.718**	.560**	-.079	.513**	-.272
ATM - Efficiency								-.279*	-.251	.416**	-.021	.407*
Form (time)									.630**	-.230	.503**	-.398**
Prescription (time)										.106	.295*	-.249
Prescription Performance											-.188	.411**
Doctor (time)												-.128

** p < .01; * p <

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Cognitive Training

- Training of component cognitive abilities:
  - Posit Science: The Brain Fitness Program; Brain HQ
    - Attention
    - Memory
    - Speed of Processing
    - Navigation
  - Lumosity
  - UM Brain Fitness Pavillion

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What can an Aware Home do?

- Recognize crisis
  - Accident, fire, stove left on
- Support everyday cognition
  - Medical monitoring & rehabilitation
  - Memory support
- Provide awareness of daily and long-term trends
- Improve connections with friends & family

Cognitive Supports

- Technology Coaches
  - Reminders of procedures
  - Corrective feedback
- Prospective Memory Aids
  - Reminders of when to do something
- Robotic Aids
  - Assistance with task performance

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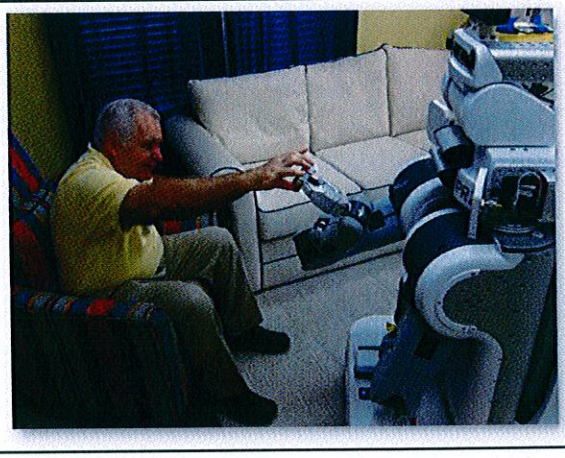

Cognitive Engagement and Social Connectivity

- Learn new skills
  - Online learning programs
  - Languages
  - Work activities
- Games
- Social network applications
  - e.g., email, forums
- Information seeking

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Preliminary Findings

- Able to successfully train all participants on PRISM
- Benefits of using PRISM:
  - Communicate with family members (grandchildren, children)
  - Reconnect with past (e.g., happenings in hometown)
  - Renewed friendships
  - New friends through "buddy system"
  - Opportunities for new learning
  - Find information related to health, other interests
  - Learn about resources
  - Fun, entertainment - games

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Church Newsletter

St. Benedict's Episcopal Church
A Part of the Anglican Community

People Are Important

Congratulations to who completed the Senior program run by the University of Miami. She had to take a 3hr oral test every month and a 5 hr written test on the computer for a year to complete the course. She completed the course on June 11th and is now eligible to keep the computer and printer that was given to her to do the course.

"My name XYZ. I feel very very fortunately of being part of the PRISM program with the University of Miami. I' m lonely and alone and I appreciate the computer so much. It has brought me a lot of the email, a lot of information from the internet. As pass time, I play the games. And I thank everybody involved with the PRISM program for this opportunity. ... I love the email, I can' t get out, so I love the email. And when I want some information, I go on Google or Yahoo. And when I am able to seat longer, I like to play the games so keep my mind going.. I think its very helpful to me... when I was without it for few days, I really really miss it. really did."

Support for Family Caregivers

- Permits access to a wider array of information and services
- Presents opportunities for social interaction
  - Other caregivers
    - Support groups
    - Forums
  - Family members and friends
- Monitoring of loved ones
- Connections to healthcare professionals

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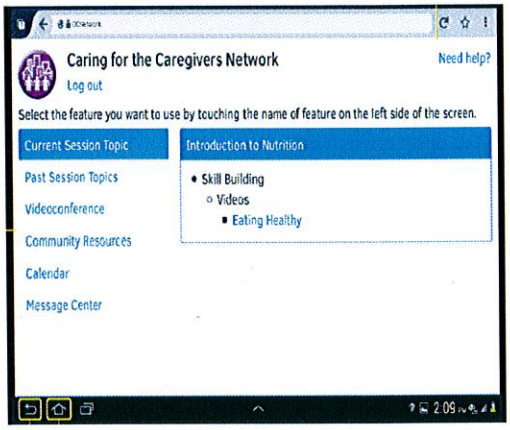

Conclusions

Technology can play an important role in supporting cognition of older adults and their caregivers but there is a need for:

- Greater understanding of the types of challenges older adults encounter when performing everyday activities.
- Greater attention to usability issues in interface design.
- Identification of the optimal balance between technology support, augmentation, replacement.
- A focus on issues of motivation, self-efficacy, integration, engagement, safety, privacy, social connectedness.
- Develop strategies to match technology support with active engagement.

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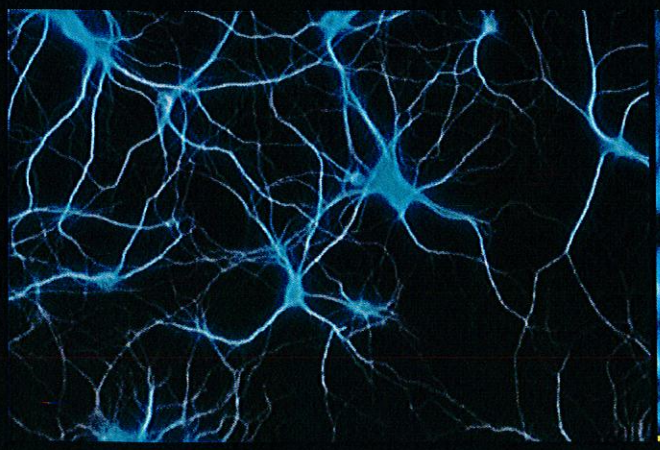

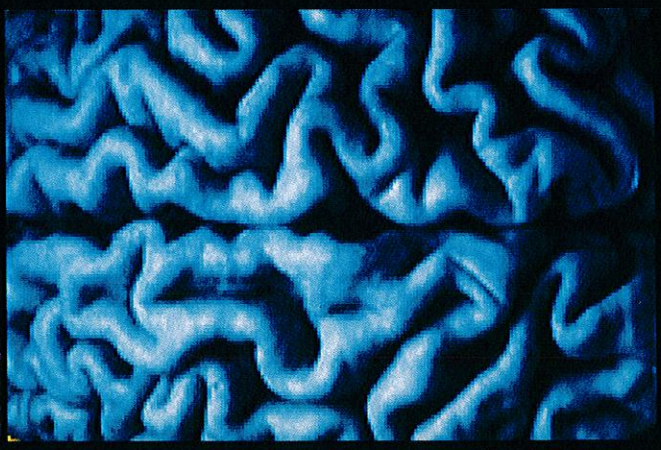

EVELYN F. McKNIGHT BRAIN INSTITUTE

CHAIR PRESENTATION

OCTOBER 15, 2014

PRESENTED TO THE
EVELYN F. McKNIGHT BRAIN INSTITUTE
BOARD OF TRUSTEES

THE LEONARD M. MILLER SCHOOL OF MEDICINE

THE UNIVERSITY OF MIAMI

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UNIVERSITY OF MIAMI HEALTH SYSTEM

UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE

Pascal J. Goldschmidt, M.D.
Senior Vice President for Medical Affairs and Dean
University of Miami Miller School of Medicine
CHIEF EXECUTIVE OFFICER, UNIVERSITY OF MIAMI HEALTH SYSTEM

AND

RALPH L. SACCO, M.D., M.S., FAHA, FAAN
Chairman, Department of Neurology
Olemberg Family Chair in Neurological Disorders
Miller Professor of Neurology, Public Health Sciences,
Human Genetics and Neurosurgery

Cordially invite you to a lunch
and ceremonial presentation of

Evelyn F. McKnight Chair for
Learning and Memory in Aging
to
Clinton B. Wright, M.D., M.S.
Scientific Director, Evelyn F. McKnight Brain Institute

Wednesday, October 15, 2014
11:00 a.m. – Reception
11:20 a.m. – Lunch and Ceremony

University of Miami Miller School of Medicine
Clinical Research Building
1120 NW 14th Street, Thirteenth Floor
Miami, Florida 33136

Business Attire

RSVP to (305) 243-1388 or
bdagosti@med.miami.edu

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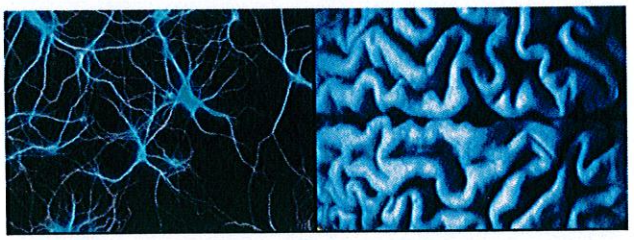
Evelyn F. McKnight
Brain Institute



The Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging

The occupant of the Evelyn F. McKnight Chair for Learning and Memory in Aging will serve as the Scientific Director of the Evelyn F. McKnight Brain Institute at the University of Miami, and will be responsible for administering the Institute and establishing the research programs that further its purpose.

The Chair occupant will ensure that the highest quality research projects are supported, aimed at an understanding of normal brain aging and its impact on cognition and memory. In addition, the Chair occupant will facilitate interactions among those scientists who can interact synergistically to develop novel approaches to understanding the neural mechanisms of memory loss in aging and potential therapeutic interventional strategies.

The initial person appointed to the Chair will be Clinton Wright, M.D., M.S.

Clinton B. Wright, MD, MS
Scientific Director
Evelyn F. McKnight Brain Institute
Associate Professor
Department of Neurology
University of Miami, Miller School of Medicine

Clinical Research Building
1120 NW 14th Street, Suite 1349
Miami, FL 33136
Email: c.wright21@med.miami.edu
Tel: 305-243-1664
Fax: 305-243-7081

Dr. Wright is Associate Professor of Neurology, Public Health Sciences, and Neuroscience, and Scientific Director of the McKnight Brain Institute. He is Chief of the Division of Cognitive Disorders in the Department of Neurology and Co-Director of the State of Florida Alzheimer's Disease Initiative (ADI) Memory Disorder Center at UM.

Dr. Wright's research focus is on the effects of vascular risk factors on brain structure and function, with an emphasis on subclinical damage such as covert infarcts, white matter lesions, and brain atrophy. His research also focuses on vascular cognitive impairment with an emphasis on early cognitive changes and the interaction between aging, vascular damage, and Alzheimer disease. He has an R01 from the National Heart, Lung, and Blood Institute to study mineral metabolism in relation to vascular disease and cognition. He also leads a pilot clinical trial as part of a Bugher Foundation/American Heart Association Center of Excellence to study the effects of exercise and cognitive training in mild stroke patients. In the past, a National Scientist Development Grant from the American Heart Association, as well as an Independent Scientist Award from the National Institute of Neurological Disorders and Stroke have funded Dr. Wright's work. Dr. Wright is a member of the Alzheimer's Disease Research Grant Advisory Board of the Florida Department of Health. He is also a member of the American Heart Association, the American Academy of Neurology and the Alzheimer Association.

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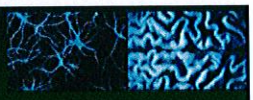
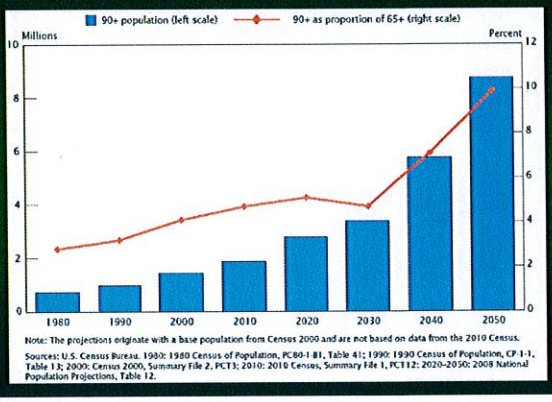


Evelyn F. McKnight Brain Institute

Chair Presentation

University of Miami Miller School of Medicine
October 15, 2014

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.

Overview of UM MBI

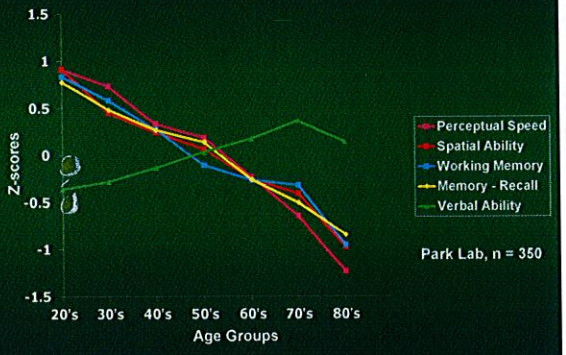
Mission

Discover the causes of age-related cognitive decline and develop prevention and treatment strategies

Vision

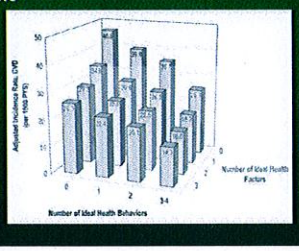
To be a world class center of excellence for clinical translational research and education to ameliorate cognitive aging

Age-Related Cognitive Changes



Is super-healthy-aging the best phenotype?

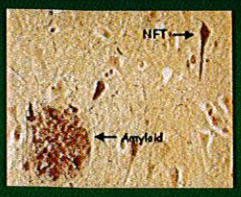
- More than ¼ of American adults have multiple risk factors for heart disease and stroke
- The percentage of adults with no risk factors and the proportion that engage in healthy lifestyles is low
- In NOMAS, no person had all 7 ideal CVH factors, only 4.4% of the cohort had 5 or 6 CVH factors, and the majority of the cohort (62.4%) had only 2 or 3 ideal factors



Burning questions about healthy vs. pathological cognitive aging

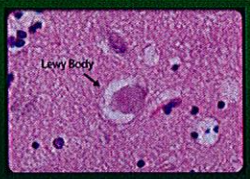
- What is "normal" cognitive aging and how does it differ from pathological cognitive decline?
- Do all cognitive functions eventually decline, and why are some functions seemingly spared?
- Do certain cognitive functions improve as people age?
- What occurs as people reach very advanced age (i.e. if we live long enough are we destined to decline)?
- What factors (genetic, vascular, etc.) determine the trajectories of cognitive changes in the very old?
- What are the brain changes that predict stability?

Important "age related" pathologies



amyloid plaques
Neurofibrillary tangles

alpha synuclein

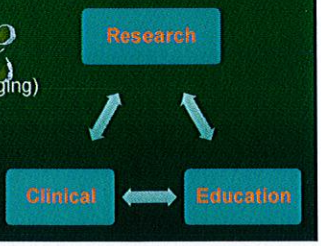


UM McKnight Brain Institute

Reaches across the University, involving departments both at Coral Gables and the Miller School

Current research involves the following departments and disciplines:

- Electrical Engineering
- Genomics
- Neurology
- Psychiatry (Center On Aging)
- Psychology
- Public Health Sciences
- Radiology



UM MBI Education

Professional
- Physicians in training (residents and fellows)
- General practitioners, allied health professionals

Caregivers
- Collaboration with Center on Aging
- UM Memory Center, Florida Department of Elder Affairs programs

Community
- CoA Brain Fitness Pavillion
- Brain Fair

UM MBI Research Approaches

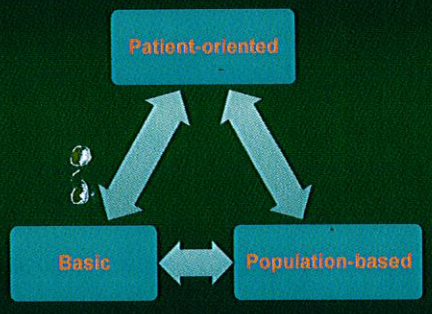
Community Samples

Single-center
- Northern Manhattan Study

Multi-center
- McKnight Brain Aging Registry of the Oldest Old
- Center for Research and Education on Technology Enhancement (CREATE)
- Hispanic Communities Health Study/Study of Latinos

Consortia
- Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE)

Diverse Research Strategies



Focus on Early Detection

Assessment
- Cognitive (highly sensitive neuropsychological tests)
- Functional (computerized "ecologically valid" real-world tasks)
- Brain imaging
  - Nuclear medicine (PET): amyloid and tau
  - MR: volumes and cortical thickness, WM integrity, brain blood flow and perfusion, functional activity and connectivity, cerebral metabolism and pathology
- Transcranial magnetic stimulation (TMS)

Evelyn F. McKnight
Brain Aging Registry of the Oldest Old

Participants
Age 85 and over
Successfully aging physically and cognitively

Assessments
Multi-modal MR imaging data
Cognitive data
Motor and sensory data (activity monitoring)
Sociodemographic, behavioral rating scales, and vascular risk factor data
Blood

UM MBI Research Approaches

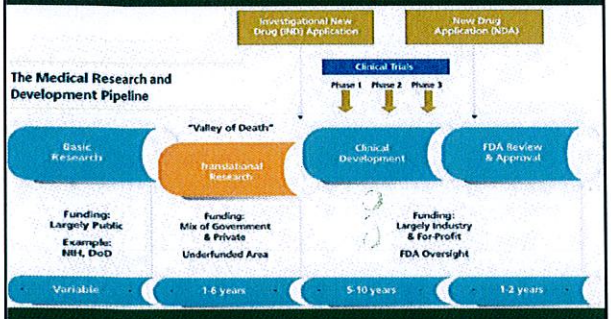
Basic Science & Translational
- McKnight Animal Behavior Core

Patient-Oriented

Clinical Registry
- Evelyn F. McKnight Memory Clinic Aging Registry

Clinical trials
- Bugher Exercise & Cognitive Training in CVD
- Systolic Pressure Intervention Trial (SPRINT)
- Augmenting Cognitive Training (ACT) Study (collaboration with UF MBI)
- Stem cells in mild cognitive impairment (planning)

Medical R&D Pipeline



"For every 10,000 compounds…only one is approved."
90% of drug development projects fail before testing in humans

http://www.fastercures.org/assets/TranslationalScience.pdf

Focus on Early Action

Interventions

Basic science, translational
- Resveratrol, PKC-epsilon

Lifestyle interventions
- Exercise
- Cognitive training
- Mindfulness meditation

Other approaches
- Transcranial DC or magnetic stimulation
- Stem cells (planning)
- Resveratrol (if translation succeeds)

Summary

- Research and education interact with clinical components to achieve our mission
- Education is a core component at all levels
- UM MBI spans basic, translational, patient-oriented, and community-based approaches to understanding age-related cognitive decline
- Focus on early detection through novel assessments
- Interventions include cognitive training, lifestyle modifications, biologics, and novel drug therapies

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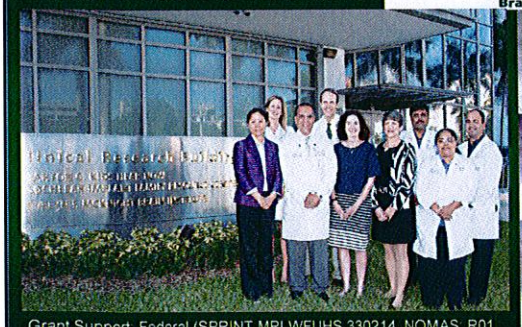

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