"Thinking, Moving and Feeling: Common Underlying Mechanisms?"
4th Annual AGS/NIA/Hartford Bedside-to-Bench Conference
September 5-7, 2007

CONFERENCE PROGRAM

TABLE OF CONTENTS

CONFERENCE AGENDA

SEPTEMBER 5, 2007 - EVENING SESSION			
Overview and epidemiological evidence for co-occurrence of disorders of cognition, movement and mood in the older adult (Studenski moderator)			
TIME	**SPEAKER**	**TOPIC/AGENDA ITEM**	**Program Pages**
6:00-6:15 PM	Studenski, Nayfield, Wagster	Welcome, rationale and goals of the conference	
6:30-6:45 PM	Newman	Epidemiologic evidence for the co-occurrence of mood, cognition, and movement disorders	7, 43
6:45-7:15 PM	Raji	Cognition, mood and movement disorders in older Mexican Americans	9, 53
7:15-7:45 PM	Wagster	Transdisciplinary and Integrative Approaches to Brain & Behavioral Changes with Age	11, 59
7:45-8:15 PM	Hadley	Research Approaches to Multidimensional Aging Problems: "Its" and "Thems"	12, 60
8:15-9:00 PM		*Discussion*	
SEPTEMBER 6, 2007 - DAY 1			
Potential common causal pathways from multiple basic and clinical perspectives			
TIME	**SPEAKER**	**TOPIC/AGENDA ITEM**	**Program Pages**
Continental Breakfast will be served.			
Initiation Factors (Lipsitz moderator)			
7:30-8:00 AM	Schon	Mitochondrial function, oxidative stress and potential effects on movement, cognition and mood	13, 67
8:00-8:30 AM	Convit	Nutritional/metabolic influences on mood, cognition and movement	14, 71
8:30-9:00 AM	Ferrucci	Inflammation "Why can't I think clearly, walk straight and be happy?"	15, 72
9:00-9:30 AM		*Discussion*	
9:30-9:45 AM		*Break*	
CNS Changes (Zigmond moderator)			
9:45-10:15 AM	Cotman	Trophic factors	16, 73
10:15-10:45 AM	Granholm	The Common Vulnerability of cholinergic and dopaminergic neurons with aging: the role of transmitters and growth factors	17, 74
10:45-11:15 AM	Emborg	Current Challenges in animal models of disease	18, 75
11:15-11:45 AM	Troncoso	*Discussion*	
11:45-12:30 PM		*LUNCH*	
Methodological issues and techniques (Wagster moderator)			
12:30-1:00 PM	Holtzer	Cognitive and genetic predictors of motor outcomes in aging	20, 78
1:00-1:30 PM	Milberg	Exploring relationships between risk factors, neuropsychological measures, and structural changes in the brain	22, 85
1:30-2:00 PM	Hausdorff	Movement and mobility testing and the effects of cognition and mood	23, 88
2:00-2:30 PM	Camicoli	Current and emerging imaging techniques	25, 93
2:30-3:00 PM		*Discussion*	
3:00-3:15 PM		*Break*	

3:15-3:45 PM	Aizenstein	Affect: Biology and Measurement	29, 99
3:45-4:15 PM	Bennett	Pathological evidence for the common causation of cognitive, movement and mood disorders	30, 106
4:15-4:45 PM	Lipton	Genetic approaches to common causation	32, 119
4:45-5:15 PM	Niederehe	*Discussion*	
5:15-6:00 PM		*BREAK*	
6:00-8:00 PM		Working dinner in small groups. **See next page for details.**	
8:00-9:00 PM		*Group Reports, Feedback, & Discussion* Studenski moderator	
SEPTEMBER 7, 2007 - DAY 2			
TIME	**SPEAKER**	**TOPIC/AGENDA ITEM**	**Program Pages**
Continental Breakfast will be served. Program committee's draft summary of day 1 is posted for comments. E-mail comments, too.			
Implications for clinical practice speakers and discussion (Verghese moderator)			
7:30-8:00 AM	Verghese	Exercise as an intervention across mood and cognition	33, 120
8:00-8:30 AM	Bohnen	Pharmacological and DBS effects on Parkinsons disease-effects on movement, cognition and mood	34, 125
8:30-9:00 AM	Monjan	Effect of sleep disorders on cognition, mood and movement? What do we know?	37, 133
9:00–9:30 AM	Lipsitz	Cardiovascular Risk, Cerebral Microvascular Disease, and their Consequences	38, 138
9:30-10:00 AM		*Discussion*	
10:00-10:30 AM	Nayfield	CHF and anemia: effects on cognition, mood and movement	40, 145
10:30-11:00 AM	Bhasin	Sex hormones: Movement, mood, and other health related outcomes	41, 146
11:00-11:30 AM	Duncan	Stroke effects on cognition, mood and movement: implications for practice	42, 147
11:30-12:00 PM		*Discussion*	
12:00-1:30 PM		Lunch and small group sessions. **See next page for details.**	
1:30-2:30 PM		*Group Reports, Feedback, & Discussion.* Summary discussion of priorities. Studenski moderator	
2:30 PM		**OPEN SESSION ENDS**	

SMALL GROUP SESSION INFORMATION

Please sign up for your preferred small group sessions at the registration table. Small Group Sessions are as follows:

DAY 1 (WORKING DINNER)

GROUP #1 – Initiation Factors *(Independence Ballroom)*
Moderator: Lipsitz
Recorder: Verghese

GROUP #2 – CNS Changes *(Patriot Room I)*
Moderator: Zigmond
Recorder: Studenski

GROUP #3 - Methodological issues and techniques *(Patriot Room II)*
Moderator: Wagster
Recorder: Nayfield

DAY 2 (WORKING LUNCH)

GROUP #1 – Neural Systems *(Independence Ballroom – Front)*
Moderator: Verghese
Recorder: Zigmond

GROUP #2 – Circulatory Systems *(Independence Ballroom – Back)*
Moderator: Lipsitz
Recorder: Nayfield

GROUP #3 – Metabolic, Inflammatory & Humeral Systems *(Patriot Room I)*
Moderator: Studenski
Recorder: Newman

SMALL GROUP SESSION ASSIGNMENT

All Small Group Sessions will be asked to identify and report back on:

1. Key Gaps
2. Barriers & Opportunities
3. Methodological Work
4. Research Priorities

CONFERENCE GRANT OVERVIEW

In 2003, the AGS was awarded NIA support for a three-year conference series "Bedside to Bench". The goal of this conference series is to heighten research attention on clinical geriatric issues that are of pressing concern clinically, or have the potential to greatly improve clinical care or prevention for older adults if scientific knowledge is advanced. The short-term outcome of each of the proposed conferences is to identify the recommended research agenda for pressing clinical geriatrics issues. The ultimate outcome of the recommended research will be to obtain research results that can be translated into improved clinical care and health outcomes of older adults.

In 2006, the NIA renewed the grant for an additional three years. "Thinking, Moving and Feeling: Common Underlying Mechanisms?" is the fourth Bedside-to-Bench research conference, sponsored by the American Geriatrics Society, the National Institute on Aging (NIH), and the John A Hartford foundation. "Thinking, Moving and Feeling," provides opportunities to learn about cutting edge research developments; participate in drafting recommendations for future research; and network with colleagues and leaders in the field. Three earlier Bedside-To-Bench conferences were held in 2004, 2005 and 2006. Future conferences include a 2008 conference on idiopathic fatigue of aging and a 2009 conference concerning inflammation and nutrient metabolism.

CONFERENCE ORGANIZERS

U13 OVERSIGHT BOARD

Marie Bernard, MD
Marie-Bernard@ouhsc.edu

Rafael Lentigua, MD
ral4@columbia.edu

Susan Nayfield, MD
nayfiels@mail.nih.gov

Joseph Ouslander, MD
jouslan@emory.edu

Stephanie Studenski, MD MPH
StudenskiS@dom.pitt.edu

PLANNING COMMITTEE

LewLipsitz, MD
lipsitz@hrca.harvard.edu

Susan Nayfield, MD, MSc*
nayfiels@mail.nih.gov

Stephanie Studenski, MD, MPH
StudenskiS@dom.pitt.edu

Joe Verghese, MD
jverghes@aecom.yu.edu

Michael Zigmond, PhD
zigmondm@upmc.edu

QUESTIONS AND COMMENTS

Please feel free to email Christine Campanelli at ccampanelli@americangeriatrics.org with any questions or comments you may have about this conference. Your feedback is highly appreciated!

FUNDING ORGANIZATIONS

The 4th Annual Bedside to Bench Conference, *Thinking, Moving and Feeling: Common Underlying Mechanisms?,* is sponsored by grants from The National Institute on Aging, the American Geriatrics Society, and the John A. Hartford Foundation.

AMERICAN GERIATRICS SOCIETY

Founded in 1942, the American Geriatrics Society (www.americangeriatrics.org) is a nationwide, not-for-profit association of geriatrics health care professionals dedicated to improving the health, independence, and quality of life of all older people. The Society supports this mission through activities in clinical practice, professional and public education, research, and public policy. With an active membership of over 6,700 health care professionals, the Society has become a pivotal force in shaping attitudes, policies, and practices in geriatric medicine.

JOHN A. HARTFORD FOUNDATION

Founded in 1929, the John A. Hartford Foundation is a committed champion of training, research and service system innovations that promote the health and independence of American's older adults. Through its grantmaking, the Foundation seeks to strengthen the nation's capacity to provide effective, affordable care to this rapidly increasing older population by educating "aging-prepared" health professionals (physicians, nurses, social workers), and developing innovations that improve and better integrate health and supportive services. The Foundation was established by John A. Hartford. Mr. Hartford and his brother, George L. Hartford, both former chief executives of the Great Atlantic & Pacific Tea Company, left the bulk of their estates to the Foundation upon their deaths in the 1950s. Additional information about the Foundation and its programs is available at www.jhartfound.org.

NATIONAL INSTITUTE ON AGING

The NIA is the leading federal agency supporting and conducting biomedical, social and behavioral research and training related to aging and the diseases and special needs of older people. It is part of the National Institutes of Health—The Nation's Medical Research Agency. NIH includes 27 institutes and centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

PARTICIPANT DIRECTORY

PLANNING COMMITTEE

LewLipsitz, MD
lipsitz@hrca.harvard.edu

Susan Nayfield, MD, MSc*
nayfiels@mail.nih.gov

Stephanie Studenski, MD, MPH
StudenskiS@dom.pitt.edu

Joe Verghese, MD
jverghes@aecom.yu.edu

Michael Zigmond, PhD
zigmondm@upmc.edu

SPEAKERS

Howard Aizenstein, MD
aizensteinhj@upmc.edu

David Bennett, MD
dbennett@rush.edu

Shalender Bhasin, MD
Shalender.Bhasin@bmc.org

Nicolaas I. Bohnen, MD, PhD
nbohnen@umich.edu

Richard Camicoli, MD
rcamicio@ualberta.ca

Antonio Convit, MD
antonio.convit@med.nyu.edu

Carl W. Cotman, MD
cwcotman@uci.edu

Pamela Duncan, PhD, PT, FAPTA, FAHA
pamela.duncan@duke.edu

Marina E. Emborg, MD, PhD
emborg@primate.wisc.edu

Luigi Ferrucci, MD*
ferruccilu@grc.nia.nih.gov

Lotta Granholm-Bentley, MD
granholm@musc.edu

Evan Hadley, MD*
HadleyE@nia.nih.gov

Jeffrey M. Hausdorff, PhD
jhausdor@bidmc.harvard.edu

Roee Holtzer, MD
rholtzer@aecom.yu.edu

Richard B. Lipton, MD
rlipton@aecom.yu.edu

William Milberg, MD
William_Milberg@hms.harvard.edu

Andrew A. Monjan, PhD, MPH*
monjana@gw.nia.nih.gov

Anne Newman, MD, MPH
newmana@edc.pitt.edu

Mukaila Raji, MD, MSc
muraji@utmb.edu

Eric Schon, PhD
eas3@columbia.edu

Molly Wagster, MD*
wagsterm@nia.nih.gov

**denotes NIH Representative*

PARTICIPANT DIRECTORY (CONT'D)

TRAVEL GRANT RECIPIENTS

Patricia Boyle, PhD
Patricia_Boyle@rush.edu

Ihab M. Hajjar
ihabhajjar@hrca.harvard.edu

Marco Inzitari, MD
InzitariM@edc.pitt.edu

Elizabeth Kvale
EKvale@aging.uab.edu

Cheryl Sterling Lynch
lynchcp@upmc.edu

Aanand Dinkar Naik
anaik@bcm.tmc.edu

Kalpana Padala, MD
kpadala@unmc.edu

Prasad Padala, MD
ppadala@unmc.edu

Caterina Rosano, MD, MPH
RosanoC@edc.pitt.edu

Jane Saczynski
saczynsj@mail.nih.gov

Lan Yao
lyao@med.umich.edu

ATTENDEES & DISCUSSANTS

Dallas Anderson, PhD*
andersda@mail.nih.gov

Eddie Billingslea, PhD*
billingsleae@mail.nih.gov

Neil Buckholtz, PhD*
buckholn@mail.nih.gov

Michelle Carlson
mcarlson@jhsph.edu

Wen Chen, PhD*
chenw@mail.nih.gov

Basil Eldadah, MD*
eldadahb@nia.nih.gov

Jovier Evans, PhD*
jevans1@mail.nih.gov

Andrew Monjan, PhD*
monjana@mail.nih.gov

Marcelle Morrison-Bogorad, PhD*
morrisom@mail.nih.gov

George Niederehe, PhD*
gniedere@mail.nih.gov

Suzana Petanceska, PhD*
petanceskas@mail.nih.gov

Juan C. Troncoso, MD
troncoso@jhmi.edu

Jessie M. Van Swearingen, MD
jessievs@pitt.edu

Bradley Wise, PhD*
wiseb@mail.nih.gov

Angela Wisniewski, PharmD
amw25@buffalo.edu

Sara L. Wright, PhD
sarawrig@med.umich.edu

Rosemary Yancik, MD*
yancikr@nia.nih.gov

**denotes NIH Representative*

Epidemiologic evidence for the co-occurrence of mood, cognition, and movement disorders

Newman
September 5, 2007
6:30-6:45 PM

Speaker Information

Anne B. Newman, MD, MPH is a Professor of Epidemiology and Medicine at the University of Pittsburgh in Pittsburgh, PA.

Key Presentation Slides attached – See page 43.

Talk Summary

In older adults, impairments in mood, cognition and mobility are common. The epidemiology of these impairments differs somewhat from the epidemiology of the specific conditions of major depression, dementia and mobility disorders. A review of the literature shows that each of these impairments is a risk factor for the others, which demonstrates that co-occurrence is greater than would be expected by chance alone. Interest is growing in further evaluating linkages between impairments, though few studies have examined all three simultaneously. Several factors are associated with each impairment and may partly explain the associations between them. These factors include age itself, being a woman, having cardiovascular disease, stroke and other common chronic conditions. Higher levels of inflammatory markers and low levels of hemoglobin are also associated with each of these impairments. A higher white matter grade on brain MRI seen in all three impairments suggests a role for the central nervous system. Approaches that target common, shared risk factors should increase the likelihood of achieving old age with preserved function in all domains.

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Cognition, mood and movement disorders in older Mexican Americans

Raji

September 5, 2007

6:45-7:15 PM

Speaker Information

Mukaila A. Raji, MD, MSc is an Associate Professor of Internal Medicine-Geriatrics and Director of Memory Loss Clinics at the University of Texas Medical Branch in Galveston, Texas.

Key Presentation Slides attached – See page 53.

Talk Summary

Obesity, diabetes, metabolic syndrome, low physical activity, and low serum vitamin D are common conditions in older Mexican Americans. Data from National Health and Nutrition Examination Survey show that Mexican Americans have the highest age-adjusted prevalence of metabolic syndrome (32%) and lowest levels of leisure-time physical activity among the three major ethnic groups in US. Epidemiological studies show that these vascular risk factors are associated with co-occurrence of cognitive, mood and movement disorders. In particular, diabetes and metabolic syndrome are independent predictors of incident cognitive, depressive and mobility disorders in Mexican American elders. Because of the shared risk factors (e.g. diabetes-related fronto-cortical ischemia), any of the disorders (e.g., depression) could be initial presentation in a patient. Over time and with persistence of risk factors, other disorders (e.g., cognitive decline) may emerge. Understanding the underlying mechanisms is key to developing culturally appropriate tests to prevent mental and mobility disorders in Mexican American elders, a rapidly growing segment of US population.

Key References

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Transdisciplinary and Integrative Approaches to Brain & Behavioral Changes with Age

Wagster
September 6, 2007
7:15-7:45 AM

Speaker Information

Molly V. Wagster, PhD is head of the Neuroscience & Neuropsychology of Aging Program at the National Institute on Aging/National Institute of Health in Bethesda, MD.

Talk Summary

Emotional valence may impact the ability to accurately recall information at any age, but particularly in the older adult. Prioritization of resources while having to perform dual tasks such as walking and memorizing, or walking and performing a mathematical calculation, also change as we age. During this talk, I will present some of the interesting behavioral findings related to the interplay of the domains of cognition, emotion, and movement and how information about these interactions may guide us in developing strategies or aids for maintenance of successful performance. An overview of some of the neurochemical and anatomical correlates for these domains as well as possible common causal mechanisms in the decline of these systems will be presented. Finally, opportunities within the NIH to encourage basic research, translational research, and research tool development to further the investigations of these domains will be discussed.

Key References

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Verghese, J., R. B. Lipton, C. B. Hall, G. Kuslansky, M. J. Katz, and H. Buschke, Abnormality of gait as a predictor of non-Alzheimer's dementia. New England Journal of Medicine, vol. 347, pp. 1761-8, 2002.

Research Approaches to Multidimensional Aging Problems: Its and Thems

Hadley

September 5, 2007

7:45-8:15 PM

Speaker Information

Evan Hadley, M.D. is head of the Geriatrics and Clinical Gerontology Program at the National Institute on Aging in Bethesda, MD.

Key Presentation Slides attached – See page 60.

Talk Summary

An important consideration regarding multiple aging conditions is the extent to which they share common contributing factors. Identifying a common contributor to multiple conditions has benefits for developing effective therapies, lessening polypharmacy and design of clinical trials. Strategies to identify contributors to multiple outcomes include ascertaining clustering among a set of outcomes, and identifying multiple effects of "candidate" risk factors. The presence of multiple comorbidities, common in the older population, poses special challenges for these strategies, for which appropriate statistical techniques are needed. Many contributory factors to multiple conditions in old age also have protective effects against other conditions, implying a need for to develop analogs of these factors having with selective effects. Aging mechanisms acting over the life span may contribute to multiple conditions in old age, but their role may be masked in old age by the confounding effects of late-stage diseases and their complications. "Life-course" research approaches in humans and laboratory animals would be useful in identifying such effects and testing intervention strategies.

Mitochondrial function, oxidative stress and potential effects on movement, cognition and mood

Schon
September 6, 2007
7:30-8:00 AM

Speaker Information

Eric A. Schon, PhD is a Lewis P. Rowland Professor of Neurology at Columbia University in New York, NY.

Key Presentation Slides attached – See page 67.

Talk Summary

Mutations in the mitochondrial respiratory chain (comprised of polypeptides encoded by both mitochondrial DNA [mtDNA] and nuclear DNA [nDNA]) cause a wide variety of neuromuscular disorders, but they are all fundamentally characterized by a severe decline or even failure in oxidative energy metabolism. Importantly, the degree of impairment is not a linear function of the number of mutated mtDNAs co-existing with normal genomes (i.e. heteroplasmy), but rather can be viewed as the integration of a number of interacting factors that determine a threshold for dysfunction (e.g. the specific mutation involved; the specific cell types most involved; the kinetics of segregation of the mutation; inter- vs intra-organellar heteroplasmy; inter- vs intra-cellular heteroplasmy). In addition, while most mutations are maternally inherited, they can also arise spontaneously, either in the germline (i.e. in oogenesis) or in somatic cells (i.e. in early embryogenesis and during normal aging). The roles of heteroplasmy, mutation type, and mtDNA plasticity will be discussed in relation to the pathogenesis of "classical" mitochondrial diseases, with ramifications for potential effects on cognition and mood in disorders not typically deemed to be mitochondrial in origin.

Key References

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Metabolic influences on cognition and brain in aging

Convit

September 6, 2007

8:00-8:30 AM

Speaker Information

Antonio Convit, MD is an Associate Professor of Psychiatry and Child and Adolescent Psychiatry and the Associate Director and Medical Director at the Center for Brain Health at NYU School of Medicine in New York, NY.

Talk Summary

With the elderly living longer and getting heavier as they age, the rates of Type 2 Diabetes Mellitus (T2DM) and insulin resistance (pre-diabetes) are rising. There is a developing literature demonstrating that elderly individuals with alterations in peripheral glucose regulation, ranging from insulin resistance to T2DM have associated cognitive dysfunction. Here I present some preliminary data demonstrating that among middle aged and elderly individuals with well-controlled T2DM of relatively short duration, there are specific problems in recent memory, namely the ability to learn and recall new information. In addition, impaired glucose regulation is also associated with volume reductions of the hippocampus, one of the brain structures responsible for recent memory. These findings also pertain to non-diabetic insulin resistant individuals. In addition, I will present novel data linking insulin resistance with retinal vascular abnormalities as well as some specific gender effects on the modulating effect of BDNF on the associations between insulin resistance and cognition.

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Inflammation "Why can't I think clearly, walk straight and be happy?"

Ferrucci

September 6, 2007

8:30-9:00 AM

Speaker Information

Luigi Ferrucci, MD is the Director of Longitudinal Studies in Clinical Research at the National Institute on Aging in Baltimore, MD.

Talk Summary

I will be speaking about the interaction between physical function, cognitive function and mood, and why they tend to deteriorate harmonically in certain older individuals.

I hypothesize that the link between them is two-fold. First, all of them may be influenced by the progressive derangement of the homeostatic equilibrium that occurs in a substantial percentage of older persons. In particular, I explore the possible role of inflammation and the NF-kappaB system. The second connection is related to specific biological mechanisms that implement physiologically the "use or lose principle". These mechanisms potentially may cause an amplification the homeostatic dysregulation that leads to accelerated health and functional deterioration. Further understanding of these mechanisms requires a focused research agenda and a strong interaction between clinicians and researchers.

Trophic factors

Cotman

September 6, 2007

9:45-10:15 AM

Speaker Information

Carl W. Cotman is a Professor and the Director of the Institute for Brain Aging and Dementia at the University of California, Irvine in Irvine, CA.

Talk Summary

Human and other animal studies demonstrate that exercise targets many aspects of brain function and has broad effects on overall brain health. The benefits of exercise have been best defined for learning and memory, protection from neurodegeneration and alleviation of depression, particularly in elderly populations. Exercise increases synaptic plasticity by directly affecting synaptic structure and potentiating synaptic strength, and by strengthening the underlying systems that support plasticity including neurogenesis, metabolism and vascular function. Such exercise-induced structural and functional change has been documented in various brain regions but has been best-studied in the hippocampus --- the focus of this review. A key mechanism mediating these broad benefits of exercise on the brain is induction of central and peripheral growth factors and growth factor cascades, which instruct downstream structural and functional change. In addition, exercise reduces peripheral risk factors such as diabetes, hypertension and cardiovascular disease, which converge to cause brain dysfunction and neurodegeneration. A common mechanism underlying the central and peripheral effects of exercise might be related to inflammation, which can impair growth factor signaling both systemically and in the brain. Thus, through regulation of growth factors and reduction of peripheral and central risk factors, exercise ensures successful brain function.

The Common Vulnerability of cholinergic and dopaminergic neurons with aging: the role of transmitters and growth factors

Granholm
September 6, 2007
10:15-10:45 AM

Speaker Information

Ann-Charlotte ("Lotta") Granholm-Bentley, MD is a Professor at the Department of Neurosciences and Director for the Center on Aging at the Medical University of South Carolina in Charleston, SC.

Talk Summary

The aged brain undergoes subtle but progressive changes in many systems, leading to functional alterations. Primarily, it has been shown that both motor dysfunction and memory loss appear with normal aging and that these get progressively worse with increasing age. The risk to develop dementia is thought to double every 5 years over 50 years of age, to reach up to 50% of the population >80 years, and prevalence of extrapyramidal symptoms will also reach >50% in individuals over 85. Interestingly, transmitter systems involved in dementia (cholinergic forebrain neurons and locus coeruelus neurons) and motor coordination (dopaminergic substantia nigra neurons) undergo similar alterations with age, and the rate of deterioration in these transmitter systems varies greatly between individuals. Possible mechanisms for age-related degeneration of both dopaminergic and cholinergic neurons include neuroinflammation caused by over-active microglia, oxidative stress, reduced growth factor support, and altered hormone balance. The potential role of these different cascades as well as appropriate animal models for them will be discussed in this presentation.

Current Challenges in animal models of disease

Emborg

September 6, 2007

10:45-11:15 AM

Speaker Information

Marina E. Emborg, M.D. Ph.D. is a Senior Scientist at the Wisconsin National Primate Research Center and Department of Anatomy at University of Wisconsin in Madison, WI.

Key Presentation Slides attached – See page 75.

Talk Summary

Animal models are extensively used to understand causes and mechanisms of disease as well as to test new therapies. There are numerous examples of animal experimentation that led to effective treatments. Yet, there are as many cases in which the results of clinical trials did not agree with the ones obtained in animal studies. These failed clinical translations bring questions about the animal models and research methods, as well as how the tests were translated into the clinic. Interactions between basic and clinical researchers as well as patients are providing clues to better understand neurological disease and prioritize experiments. A key element of the experimental design is the animal model to be utilized. An ideal model of disease is the one generated by the same agent that causes the disease and presents the same features of the disease, including its timeline of development. Yet modeling is challenging, as several neurological disorders seem to have a multi-etiology. Furthermore, patients diagnosed with the same disease present variations in signs, intensity and changes overtime suggesting the presence of disease subtypes and multi-systemic degeneration. Can these challenges be overcome? A first step is to realize that there are not perfect models of disease. To provide relevant data, the models have to match the scientific question to be answered. The different models of a given disease can be used to represent different aspects and, possibly, subtypes of the disease, each one of them with its own timeline of development. To minimize the limitations of the models and increase their predictive clinical validity, it is essential the use of an adequate experimental design, with multiple outcome measures of clinical relevance, appropriate number of animals, randomization of treatment group assignment and blind acquisition of data. This conceptualization facilitates the model application, the clinical translation of findings and provides clues for the development of new models.

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Neuropsychological testing and the effects of mood and movement

Holtzer

September 6, 2007

12:30-1:00 PM

Speaker Information

Roee Holtzer, MD is an Assistant Professor in Psychology and Neurology at Ferkauf and the Department of Neurology at the Albert Einstein College of Medicine/Yeshiva University in New York, NY.

Key Presentation Slides attached – See page 78.

Talk Summary

This presentation will provide a brief overview concerning the association between cognitive and motor function in aging. A main question/challenge is how to advance current knowledge in this area to identify mechanisms of motor decline in aging that can be detected early and be modified in treatment. Methodological challenges that are inherent in cognitive assessment and in relating cognitive performance to motor function will be discussed. Then, a three-level approach to the study of cognitive and motor function in aging will be described. 1) Use clinical Neuropsychology to a) demonstrate associations between separate cognitive functions and motor outcomes such as gait and falls b) generate hypotheses concerning the relations of specific cognitive processes and motor function that will have to be assessed with more refined paradigms. 2) Incorporate a cognitive neuroscience approach, in concert with clinical neuropsychological tests, to examine whether and how more refined and specific cognitive processes may explain motor decline in aging. 3) Initiate a theory-based approach that is anchored in our cognitive motor studies to identify specific genotypes that may underlie the current behavioral findings.

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Exploring relationships between risk factors, neuropsychological measures, and structural changes in the brain

Milberg
September 6, 2007
1:00-1:30 PM

Speaker Information

William Milberg, PhD is the Associate Director for Research at the GRECC VA Boston Healthcare System and Department of Psychiatry Harvard Medical School in Boston, MA.

Key Presentation Slides attached - See page 85.

Talk Summary

An examination of the case of the rise and fall of the status of the diagnostic category of "Vascular Dementia" reveals the importance of considering the specific neurobiological impact of different conditions that presage the onset of cognitive decline in older adults.

Recent data suggests that syndromes of cognitive impairment in older adults have distinct neuropsychological signatures, and very deep roots within what has been usually considered to be normal aging. Data from our lab suggests that variations in the structure of grey and white matter may be related to variations in cognitive ability in healthy middle aged and older adults, and that these changes set the stage for cognitive disorders in late life.

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Gait and dual tasking: the effects of cognition and mood

Hausdorff

September 6, 2007

1:30-2:00 PM

Speaker Information

Jeffrey M. Hausdorff, PhD is the Director of the Laboratory for Gait and Neurodynamics at the Tel-Aviv Sourasky Medical Center.

Key Presentation Slides attached – See page 88.

Talk Summary

While long thought to be an "automatic" process, a growing body of research has demonstrated that gait utilizes cognitive input and, more generally, that it is influenced by mood and affect. This talk briefly reviews some of this recent evidence while also describing methodological issues that need to be considered when investigating these relationships. A focus is placed on gait variability, a measure of the stride-to-stride fluctuations in walking. Gait variability is of interest because of its association with fall risk and disability and because it can be used as a reflection of the automaticity of walking, in addition to more traditional measures such as gait speed. One method for investigating the automaticity of gait and its relationship to cognitive function is to investigate the effects of dual tasking and the deployment of the "posture first" strategy. It is not surprising that when gait becomes less automatic, for example, among patients with neurodegenerative disease, the magnitude of the stride-to-stride fluctuations of gait increases. In such patients, cognitive loading (i.e., dual tasking) further increases the stride-to-stride variability of gait. Patients with Parkinson's disease and healthy adults of similar age slow down when they walk and perform a concurrent task, while a large increase in variability is seen only in the patients. Preliminary intervention studies, in the form of motor training and pharmacologic therapy, also support the idea that gait relies upon cognitive function and that interventions which enhance mental health may be a target for improving gait and mobility as well as mental function. The implications of these findings for understanding the factors that regulate walking and mobility and the potential clinical ramifications will also be discussed briefly.

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Current and emerging imaging techniques

Camicoli
September 6, 2007
2:00-2:30 PM

Speaker Information

Richard Camicioli, MD is an Associate Professor of Medicine at the University of Alberta in Edmonton, Alberta, Canada.

Key Presentation Slides attached – See page 93.

Talk Summary

We will focus on imaging approaches that can be applied to understanding the neural basis for age-related gait changes. We will highlight where these methods have also been applied to understanding cognitive and mood changes with aging. The discussion will focus on magnetic resonance imaging methods, but positron emission tomography and single photon computed tomography imaging approaches will also be mentioned. Future research directions will be suggested.

Overview

Common imaging approaches have been used to identify the neural basis for gait, cognitive and mood changes in aging. While the neural substrates may be overlapping, few studies have examined these together in the same populations. Studies examining gait and depression have been mostly cross sectional, though longitudinal studies are being undertaken. More longitudinal studies have examined cognition. Some recent large studies such as the LADIS study, which is examining the implications of white matter disease in multiple domains may offer answers to the question of a common basis for such problems.

Cross-sectionals studies include case reports, case-series, correlative studies and case-controlled studies. Some studies have done on a randomly selected population. Longitudinal studies have been done in the general older population and those with identified impairment. Studies examining people for cerebro-vascular events have included gait or mood changes as an outcome measure, but have generally emphasized general health, vascular endpoints and cognitive outcomes.

Imaging modalities that have been used have included computerized tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and single photon emission ct (SPECT). MRI has been especially useful because of its sensitivity and non-invasive nature. MRI technology has mainly been used to examine age-related white matter change (ARWMC) and lesions in relation to gait, cognition and mood. Developments in examining white matter with MRI such as magnetization transfer imaging, diffusion tensor imaging and magnetic resonance spectroscopy offer complementary information regarding white matter integrity. Functional MRI can look at changes in blood flow with task performance, but give the interference of movement with obtaining MRI signal, gait has not be examined directly. Indirect approaches include “imagining” walking while examining changes in blood flow or metabolism, an approach that can also be used with PET. SPECT offers the potential to examine gait indirectly and have occasionally been used. Such methods have also been useful in cognitive paradigms and in the study of patients with depression.

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Affect: Biology and Measurement

Aizenstein

September 6, 2007

3:15-3:45 PM

Speaker Information

Howard J Aizenstein is an Assistant Professor of Psychiatry at the Western Psychiatric Institute and Clinic at the University of Pittsburgh Medical School in Pittsburgh, PA.

Key Presentation Slides attached – See page 99.

Talk Summary

In this presentation I will briefly review what is known about the biology of the primary mood disorders and discuss some of the more common depression measurement scales. Particular emphasis will be given to geriatric depression. The primary mood disorders include major depressive disorder, bipolar disorder, and the milder variants of dysthymia and cyclothymia. The classic formulation of the mood disorder uses a biopsychosocial framework, where it is understood that all three components play important roles in the etiology and treatment of the mood disorder. For geriatric psychiatry the primary biological model has been the vascular depression hypothesis of late-life depression, which suggests that subclinical cerebrovascular disease can predispose to depression. Many neuroimaging studies have supported the vascular depression hypothesis, by finding increased cerebrovascular changes (specifically small vessel ischemic disease in the white matter) relative to non-depressed elderly controls. The gold standard for a research diagnosis of depression is the structured clinical interview (SCID), which utilizes the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria. A variety of self-administered and clinician administered rating scales have been used to assess the severity of depression symptoms and will be discussed during this presentation. These include the Hamilton Rating Scale for Depression (HRSD/HAM-D), the Beck Depression Inventory (BDI), and the Geriatric Depression Scale (GDS).

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Pathological evidence for the common causation of cognitive, movement and mood disorders

Bennett
September 6, 2007
3:45-4:15 PM

Speaker Information

David A. Bennett, MD is the Director at the Rush Alzheimer's Disease Center in Chicago, IL.

Key Presentation Slides attached – See page 106.

Talk Summary

The talk will review the design of two large, longitudinal epidemiologic studies of aging that include data on cognitive and motor function, mood, and organ donation at death: the Religious Orders Study and the Rush Memory and Aging Project. Using data from these two cohorts, three sets of evidence of a shared etiopathogensis between cognitive and motor impairment with aging will be presented including: a) evidence that change in cognitive function is related to change in motor function; b) evidence that some shared risk factors predict change in cognitive function and motor function; and c) evidence that some common neuropathologic indices are related to both cognitive and motor function. Data will also be presented on the association of depressed mood with cognitive function, motor function, and neuropathologic indices.

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Genetic approaches to common causation

Lipton

September 6, 2007

4:15-4:45 PM

Speaker Information

Richard B. Lipton, MD is a Professor of Neurology, Psychiatry, Epidemiology and Population Health and Vice-Chairman of the Department of Neurology at Albert Einstein College of Medicine in Bronx, NY.

Talk Summary

From a genetic perspective, cognitive and motor aging comprise a heterogeneous set of complex traits most likely influenced by a multiplicity of genes as well as environmental risk factors. Traditional genetic approaches in this area have focused on specific diseases which influence cognitive and motor function. While some for these diseases are Mendelian (eg, Huntington's disease) most are complex and genetically heterogeneous (Alzheimer's disease, Parkinson's disease). Specific diseases have often been approached using high density families to probe the genetics of rare Mendelian forms of illness. This approach sometimes identifies pathways involved in the more common forms of illness. Family aggregation and twin studies are used to estimate heritability. Case control studies are often used to assess candidate gene or to support whole genome association studies. These disease-focused approaches can also be applied to non-disease phenotypes (longevity, frailty, global and domain specific cognitive or motor status and change). Once potential genes are identified they can be expressed in non-mammalian (drosophilia or nematodes) or mammalian models to probe the biological mechanisms of potentially pathogenic genotypes, sometimes leading to insights into disease mechanisms and to targets for treatment. Identification of genetic risk factors can also facilitate assessment of environmental risk factors. In this brief talk, I will use Alzheimer's and Parkinson's disease, longevity and cognitive phenotypes to illustrate the promise and the pitfalls of genetic approaches to cognitive and motor aging.

Exercise as an intervention across mood and cognition

Verghese

September 7, 2007

7:30-8:00 AM

Speaker Information

Joe Verghese, MBBS, MS is an Associate Professor of Neurology at the Albert Einstein College of Medicine in Bronx, NY.

Key Presentation Slides attached – See page 120.

Talk Summary

There is increasing evidence from observational studies that engagement in mental and physical exercises is associated with improved cognitive and physical health in older adults. A number of cohort studies have reported that increased level of participation in cognitively stimulating activities is associated with reduced risk of dementia in older adults. On the other hand, the evidence for the role of physical exercises in reducing risk of dementia is less clear. Randomized trials that have examined the role of mental and physical exercises in preserving cognitive health are lacking. On the other hand, the role of physical exercise has been better explored in the context of treating depression. Clinical trials of physical activities in depression, especially in older adults, will be briefly reviewed; implications, limitations, and future directions will be discussed.

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Pharmacological and DBS effects on Parkinsons disease- effects on movement, cognition and mood

Bohnen
September 7, 2007
8:00-8:30 AM

Speaker Information

Nicolaas I. Bohnen, MD, PhD is an Associate Professor of Radiology & Neurology at the University of Michigan, and the Director of the Parkinson Clinic at the Ann Arbor VA in Ann Arbor, MI.

Key Presentation Slides attached – See page 125.

Talk Summary

The pathobiological model of Parkinson disease (PD) based on dopaminergic nigrostriatal denervation has been a successful research paradigm for decades and has led to effective pharmacotherapy for the motor manifestations of this condition. Non-motor comorbidity of PD is common and includes cognitive changes, dementia, psychosis, mood (depression, anxiety), behavioral changes, autonomic, olfactory and visual changes. Recent quality of life studies have emphasized the importance of such non-motor manifestations. Dopamine replacement pharmacotherapy is generally ineffective to alleviate non-motor comorbidity. It is increasingly becoming clear that the nigrostriatal model of PD is insufficient to explain the full clinical spectrum of this disorder. Braak et al. have proposed a new pathological classification schema of PD based on the sequential deposition of Lewy bodies and Lewy neurites in the brainstem and brain. This model provides a new paradigm for a better understanding of not only non-motor but also extrastriatal aspects of this disorder. This new paradigm represents a shift from a nigrostriatal dopaminocentric view of PD to that of a multisystems neurodegeneration syndrome involving but not limited to monoaminergic (DA, NE, 5HT) and cholinergic transmitter systems. Cholinergic denervation in PD dementia may be more extensive and severe than Alzheimer disease. Cholinergic denervation also in part accounts for the dysexecutive syndrome in PD. Although serotonergic denervation is prominent in PD, it may not fully explain the depressive syndrome found in this disorder.

Pharmacotherapies of motor and non-motor symptoms represent unique challenges because of trade-offs between relative effects of motor versus non-motor benefits. For example, increasing dopaminergic drugs may alleviate motor problems but may lead to psychosis. Cholinergic drug treatment may help cognitive impairment but may lead to worsening parkinsonism. Similarly, recent evaluations of DBS (deep brain stimulation) surgery in PD, in particular of the subthalamic nucleus (STN), have shown negative effects on cognition, mood, and behavior that may reflect selective involvement of basal ganglia-thalamocortical associative, limbic and motor circuits that become disrupted at the level of the surgical target.

The recognition of PD as a multisystems neurodegeneration syndrome affecting multiple neurotransmitter systems and the anatomic close proximity of striato-thalamo-cortical circuits that affect motor, cognitive and behavioral functions is important for proper management of this disorder.

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Effect of sleep disorders on cognition, mood and movement? What do we know?

Monjan

September 7, 2007

8:30-9:00AM

Speaker Information

Andrew A. Monjan, PhD, MPH is Chief of the Neurobiology of Aging Branch of the Neuroscience and Neuropsychology of Aging Program within the National Institute on Aging.

Key Presentation Slides attached - See page 133.

Talk Summary

Contrary to common beliefs, healthy older adults do not sleep less than their younger counterparts. Older Americans average seven hours of sleep a night. Many of the sleep problems in older adults are associated with medical illness, rather than aging per se. Individuals with multiple medical problems have a particularly high risk of sleep problems. Sleep problems in older adults are associated with medical illness, rather than aging per se, particularly: heart disease, lung disease, depression, and stroke. Multiple medical problems increase the probability of : sleeping < 6 hours/night, insomnia symptoms, daytime sleepiness, unpleasant feelings in legs, diagnosis of any sleep disorder. Bodily pain, exercise frequency, ambulatory limitation, and obesity are related to sleep problems in older adults. Sleep deprivation also is associated with attention and memory problems, and metabolic disorders such as insulin resistance. Sleep, a state that occupies a third of our lives, is a vital component of health and healthy aging.

Cardiovascular Risk, Cerebral Microvascular Disease, and their Consequences

Lipsitz
September 7, 2007
9:00–9:30 AM

Speaker Information

Lewis A. Lipsitz, MD is the Chief of Gerontology at Beth Israel Deaconess Medical Center and a Professor of Medicine at Harvard Medical School in Boston, MA.

Key Presentation Slides attached - See page 138.

Talk Summary

Several cardiovascular (CV) risk factors, particularly hypertension and diabetes, have been found to be associated with abnormal executive cognitive function, slow gait, and depressive symptoms. Central nervous system control of these functions resides, in part, in frontal regions of the brain. Recent brain MRI studies have demonstrated significant relationships between CV risk factors and frontal subcortical hyperintensities in white matter tracks traveling from the frontal cortex through watershed areas where hypoperfusion may cause ischemic damage. The volume of white matter abnormalities on MRI is inversely correlated with cerebral blood flow in these regions and is thought to represent small vessel ischemic damage (microangiopathy) in the brain. Hypertension, diabetes, and episodes of transient hypotension associated with both, may reduce cerebral blood flow and result in ischemic damage. Antihypertensive treatment with angiotensin converting enzyme inhibitors can improve cerebral blood flow and may prevent cognitive and functional decline. It is important to recognize the effects of CV risk factors on executive functions, because the executive cognitive abilities necessary to optimally reduce risk may be impaired. Effective CV risk reduction may ultimately prevent age-related abnormalities in cognition, mobility, and mood that derive from frontal subcortical microvascular disease.

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CHF and anemia: effects on cognition, mood and movement

Nayfield

September 7, 2007

10:00-10:30 AM

Speaker Information

Susan G. Nayfield, MD, MSc is the Chief of the Geriatrics Branch of the Geriatrics and Clinical Gerontology Program within the National Institute on Aging in Bethesda, MD.

Talk Summary

Anemia and heart failure are common problems in geriatrics practice that have important implications for cognition, affect, and functional status. In general, anemia and heart failure in older adults are associated with limitations in physical performance, including ADLs and IADLs; increased risk of frailty; and increased mortality. Impaired cognition and depression have been associated with anemia and heart failure both as independent diagnoses and as common comorbidities.

While specific problems with impaired cognition and affect may depend on the etiology of the anemia, the clinical principle of identifying and treating underlying deficiency states to improve hemoglobin and replete other physiologic compartments remains the first line in management. Improvement in hemoglobin is usually associated with increase in physical performance but may not improve cognitive function.

The co-occurrence of anemia and heart failure present specific clinical challenges. Iron deficiency is common among heart failure patients and should be evaluated in all patients with both conditions. The use of erythropoietin (with or without iron supplements) to treat anemia occurring with heart failure is currently in large clinical trials but appears promising in improving hemoglobin as well as cardiac function and physical performance.

Sex hormones: Movement, mood, and other health related outcomes

Bhasin

September 7, 2007

10:30-11:00 AM

Speaker Information

Shalender Bhasin, MD is a Professor of Medicine at Boston University School of Medicine and Chief of the Section of Endocrinology, Diabetes and Nutrition at Boston Medical Center in Boston, MA.

Talk Summary

Over fifty cross-sectional and several longitudinal studies are in agreement that total and free testosterone, and DHEA concentrations decline with advancing age. Sex hormone binding globulin concentrations increase with aging; therefore, the free and bioavailable testosterone concentrations decline to a greater extent than total and free testosterone concentrations. Epidemiologic studies have demonstrated that total and free testosterone levels are associated with appendicular skeletal muscle mass, grip strength, bone mineral density, physical function, libido, co-morbid conditions, visuo-spatial cognition, verbal memory and verbal fluency, and overall mortality. Testosterone supplementation increases muscle mass, maximal voluntary muscle strength, and leg power in men. These anabolic effects of testosterone are related to the administered dose and to prevailing testosterone concentrations. Compared to younger men, older men are equally responsive to the anabolic effects of graded doses of testosterone, but experience a higher frequency of adverse effects. Testosterone administration improves self-reported physical function, but it is not known whether testosterone improves performance-based measures of physical function and health-related outcomes in older men with functional limitations are not known.

Testosterone administration to young and older men is associated with hypertrophy of both type I and II muscle fibers. The latter hypertrophy is attended by increased numbers of muscle satellite cells. The mechanisms by which testosterone induces skeletal muscle hypertrophy are poorly understood. Emerging data suggest that testosterone promotes the commitment and differentiation of mesenchymal, multipotent cells into the myogenic lineage and inhibits their differentiation into the adipogenic lineage by activation of Wnt signaling through a noncanonical pathway that involves association of androgen receptor with beta-catenin and TCF-4.

Testosterone administration improves sexual function in young, hypogonadal men. However, the effects of testosterone on erectile function and response to phosphodiesterase inhibitors have not been rigorously studied. The effects of testosterone on cognition have not been rigorously examined in adequately-powered RCTs.

Short term administration of testosterone in replacement doses is safe; long term risks of testosterone therapy on prostate and cardiovascular event rates are unknown. Erythrocytosis remains the most frequent, dose-limiting adverse effect of testosterone therapy in older men in clinical trials.

Rehabilitation effects on all three

Duncan

September 7, 2007

11:00-11:30 AM

Speaker Information

Pamela W Duncan Ph.D., P.T, FAPTA, FAHA is a Professor in the Division of Physical Therapy & Department of Community and Family Medicine at Duke University in Durham, NC.

Key Presentation Slides attached – See page 147.