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OLDER AND SOMETIMES WISER:
NEW IMAGING RESEARCH SHOWS STRENGTHS AND WEAKNESSES OF THE AGING BRAIN
Studies point to ways to improve cognition in older adults

Washington — New human research released today shows the benefits and challenges for the aging brain. The studies probe common characteristics of normal aging — including memory loss, reduced sleep quality, and decision-making problems — and suggest the benefits of exercise, hormone treatment, and social interaction. The findings were presented at Neuroscience 2011, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Neuroscientists believe the brain can remain relatively healthy as it ages. By better understanding the aging brain, researchers hope to benefit the 500 million people worldwide who are 65 or older.

Today's new findings show that:

- Physically fit older adults have fewer signs of aging in their brains, and they outperform their peers in memory tests. The findings suggest exercise may reduce age-related changes in the brain (Gene Alexander, PhD, abstract 293.05, see attached summary).
- Short-term estrogen treatment leads to growth in brain regions known to be involved with attention and memory in post-menopausal women. The findings suggest the brain's plasticity may be key to preserving cognitive function (Paul Newhouse, MD, abstract 282.11, see attached summary).
- Sleep fails to enhance the memory of older adults, unlike their younger counterparts (Rebecca Spencer, PhD, abstract 196.18, see attached summary).
- The brain's ability to process social cues is preserved as people age, despite cognitive decline and other age-related changes. The findings suggest older adults may better retain information presented in a social context (Angela Gutchess, PhD, abstract 430.07, see attached summary).
- Older adults who have a tough time making decisions choose smaller, immediate payouts rather than waiting for a larger sum in the future (Kameko Halfmann, PhD, abstract, 293.15, see attached).

"Even as the body begins to slow down as we age, the brain, when challenged by physical and mental activities, continues to grow and change," said press conference moderator Barbara Sahakian, PhD, of the University of Cambridge, who studies ways to improve cognition. "These findings offer new information about how the brain ages, and also highlights ways to educate older adults about playing a more active role in their brain health."

This research was supported by national funding agencies, such as the National Institutes of Health, as well as private and philanthropic organizations.

Related Presentation:

Nanosymposium: **Causes and Consequences of Aging**
Sunday, Nov. 13, 8–10:15 a.m., Room 140A

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Abstract 293.05 Summary

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Aerobic Fitness May Reduce Brain Aging

New findings suggest exercise may help maintain cognitive abilities of seniors

Physically fit seniors show fewer age-related changes in their brains, according to new research presented at Neuroscience 2011, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health. The findings underscore the importance of exercise for maintaining brain health throughout life.

"Our findings suggest that a high level of aerobic fitness may help diminish the changes in brain structure that occur as we get older, "said senior author Gene Alexander, PhD, of the University of Arizona.

As people age, some regions of the brain — including those responsible for attention and memory functions — begin to lose volume or shrink. To see how physical fitness affects brain aging and age-associated declines in cognition, Alexander and colleagues scanned the brains of 58 men and 65 women (ages 50 to 89 years) and evaluated their performance walking on an inclined treadmill.

The more physically fit a participant was, the less age-related brain changes they showed. In particular, exercise endurance and breathing efficiency offered the best combination of fitness measures in predicting patterns of brain aging. Individuals with higher levels of aerobic fitness also outperformed their less physically fit counterparts on tests measuring memory, executive function, and information processing.

"Identifying the fitness indices that are the best predictors of brain aging and cognitive performance may help improve exercise-based interventions — ones that could delay or prevent changes in the brain that lead to age-related cognitive decline," Alexander said.

Research was supported by the National Institute on Aging, the State of Arizona and Arizona Department of Health Services, and the Evelyn F. McKnight Brain Institute.

Scientific Presentation: Sunday, Nov. 13, 1–2 p.m., Halls A–C

293.05, Relationship of aerobic fitness to brain aging and cognition in older adults
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TECHNICAL ABSTRACT: Level of physical fitness may be an important factor influencing the effects of brain aging and age-related cognitive decline. We used multiple measures of aerobic fitness in a cohort of healthy older adults 50-89 years of age to identify how individual differences in physical fitness relate to brain aging and age-associated cognitive decline. Healthy adults (n=123; 65F/58M; mean ±sd age = 67.9 ± 10.0; mean ± sd Mini-Mental State Exam = 29.1 ± 1.2) were screened to exclude neurological, psychiatric, and medical illnesses that could affect cognitive function, including hypertension. Multivariate network analyses with voxel-based morphometry (VBM; SPM8 Dartel) and the Scaled Subprofile Model (SSM) were performed with T1 weighted 3T volumetric magnetic resonance imaging (MRI) scans to identify a gray matter pattern associated with brain aging. Performance on aerobic fitness measures, assessed during a graded exercise treadmill test, was subsequently tested in relation to the age-associated MRI network pattern and indices of neuropsychological function. Multivariate SSM VBM network analysis identified a linear combination of patterns that predicted age ($R2 = 0.48$, $p = 8.71e\text{-}19$). This combined pattern was characterized by reductions in bilateral lateral and medial frontal, parietal, lateral temporal, and cerebellar regions with relative preservations in thalamic, occipital, and medial temporal regions including the hippocampus. Higher expression of the age-related network pattern was associated with poorer performance on multiple fitness indices. The best combination of fitness measures in predicting brain aging included overall treadmill exercise time, ventilatory efficiency, and the difference between basal and maximal respiratory rate ($p = 6.67e\text{-}7$). A higher combined fitness index score related to brain aging was predictive of better performance on measures of memory, executive function, and processing speed in this cohort ($6.08e\text{-}9 < p < 0.04$). Individual differences in levels of aerobic fitness are associated with an age-related pattern of MRI gray matter and associated cognitive performance. Identifying those fitness indices that are the best predictors of brain aging and cognitive performance may aid efforts in developing and evaluating exercise based interventions for age-related cognitive decline.

Abstract 282.11 Summary

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Short-term Estrogen Therapy Changes Brains of Postmenopausal Women

Hormone-induced growth may help preserve cognitive function

Short-term estrogen treatment increases the volume of cortical gray matter — brain cells and their uninsulated connections — in postmenopausal women, a new study shows. The research, which reveals potential brain benefit for short-term hormone replacement therapy, was presented at Neuroscience 2011, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Researchers, led by Paul Newhouse, MD, of Vanderbilt University, imaged the brains of 24 healthy postmenopausal women who took either estrogen or a placebo for three months. After treatment, the women who took estrogen had more gray matter in parietal, temporal, and prefrontal areas of the brain. These regions are known to be involved in attention, decision-making, and memory.

"Our findings suggest the brain remains responsive to estrogen treatment even after menopause, and that this responsiveness or plasticity is important for preserving cognitive functioning, especially in the early postmenopausal period," said Newhouse.

The findings suggest that long-term hormone treatment, shown to have adverse effects on health in postmenopausal women, may be unnecessary for cognitive benefit. "Short-term estrogen treatment in normal postmenopausal women is sufficient to increase gray matter in the brain," Newhouse concluded. "We believe this change in gray matter density may be related to potentially beneficial effects of estrogen on brain function after menopause," he said.

Research was supported by the National Institute on Aging.

Scientific Presentation: Sunday, Nov. 13, 3–4 p.m., Halls A–C

282.11, Estradiol increases cortical gray matter in healthy postmenopausal women
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TECHNICAL ABSTRACT: One of the major problems regarding research on the cognitive effects of postmenopausal estrogen therapy is that relatively little is known about the relationship between the effects of postmenopausal estrogen therapy (ET) on brain morphology. Hormone therapy (HT) users have been shown to have greater gray matter volumes in prefrontal, temporal, and parietal cortices, anterior hippocampus, and cerebellum compared to nonusers which correlates with improved cognitive performance and duration of treatment. However, there are no prospective experimental studies of ET effects on cortical gray matter in postmenopausal women (PMW). We studied 24 healthy PMW (51-71; mean age 59.1± 5.6) who received either oral 17-beta estradiol (E2) 1 mg or placebo for three months. Each subject received a baseline MRI structural scan prior to treatment and at the end of the three month treatment period. The scans were performed on a Philips 3T Magnet using a sagittal T1-weighted SPGR sequence. To study longitudinal changes in gray matter density, the subject's second scan was registered to their baseline image and these images segmented into gray, white, and CSF compartments using voxel-based morphometry (VBM) as implemented in SPM8. The resulting gray and white probability images were then normalized to the SPM T1 template and smoothed using a 10mm FHMW kernel. Statistical comparisons were then performed using GLM statistics as implemented in SPM8. There were no baseline differences between treatment groups. The E2-treated group showed multiple areas of increased gray matter density concentrated in the parietal, temporal, and prefrontal cortices bilaterally compared to placebo-treated subjects. The structures involved including the middle and inferior frontal gyri (BA 6, 47) and post central and inferior temporal gyri (BA 3, 20). These areas are consistent with those involved in attentional processes, and episodic and working memory, cognitive domains that we have shown previously to be experimentally modified by E2 treatment interacting with cholinergic system activity (e.g., Dumas, et al, Hormones and Behavior 53: 159-169, 2008). We conclude that short-term E2 treatment increases cortical gray matter density in healthy PMW, consistent with findings from the primate literature and clinical samples, suggesting that E2-induced neuroplasticity remains after menopause. Such plasticity may be important in preserving cognitive function, especially in the early postmenopausal period.

Abstract 196.18 Summary

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A Good Night's Sleep Fails To Boost Memory in Older Adults

Findings suggest the benefit of sleep to cognition is reduced during aging

Sleep fails to improve older adults' performance on a memory test, a new study found. The research was presented at Neuroscience 2011, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Prior research suggests that sleep enhances memory; changes in memory and sleep quality are common during the aging process. The new study suggests these changes may be related.

Researchers, led by Rebecca Spencer, PhD, of the University of Massachusetts, taught 24 older and 25 younger adults to navigate through a series of 10 rooms presented on a computer screen. Each room had three different colored doors, one of which led the participant to the next virtual room. Participants had to accurately navigate all 10 rooms four times to demonstrate they had learned the task.

After a 12-hour interval spent either awake or asleep, participants were tested on how well they remembered navigating the virtual rooms. While younger adults who got a good nights' sleep made fewer errors than those awake for 12 hours, older adults who slept performed no better than those who had not.

"Our research suggests that *changes* in the aging brain, rather than the restorative effects of sleep itself, may underlie some of the memory problems that older adults experience," said Spencer. "If so, sleep could be considered a target for future memory-enhancing therapeutics," Spencer said.

Research was supported by the National Institute on Aging.

Scientific Presentation: Sunday, Nov. 13, 9–10 a.m., Halls A–C

196.18, Loss of the cognitive benefit of sleep in older adults
L. B. KURDZIEL, **R. M. C. SPENCER**; Univ. of Massachusetts, Amherst, MA

TECHNICAL ABSTRACT: Sleep has been shown to benefit memory in healthy young adults; however, the relationship between sleep and memory is less clear in older adults. Motor sequence learning does not improve with sleep in older adults (Spencer, Gouw, & Ivry, 2007) whereas episodic memory does (Aly & Moscovitch, 2010). This distinction could represent an effect of age on sleep-dependent consolidation of either sequential learning or motor learning. We therefore investigated the role of sleep on a non-motor sequence learning task. Participants learned a sequence of 10 uniquely colored "doors" in order to navigate through 10 virtual rooms. Within each room, individuals used trial-and-error to determine which one of three doors was the correct door. In the first session, one room was added with every trial, gradually building up to the entire 10-door sequence. Participants continued to navigate through this sequence until they chose only the correct doors in four consecutive trials. Memory for the sequence was probed 12 hours later following either an interval of wake (e.g., 8am-8pm) or an interval containing sleep (e.g., 8pm-8am). An additional probe phase assessed whether learning was of individual correct doors or the sequence of correct doors. Importantly, performance of young adults benefited from sleep on this task: they made significantly fewer errors on the probe task following a 12 hour period with sleep than following a 12 hour period awake ($t(23) = -2.07$, $p < 0.05$). In addition, young adults made fewer distracter errors, demonstrating that the actual *sequence of the doors was better remembered following sleep. Performance of older adults, however, did not benefit from the sleep interval ($t(22) = 0.34$, $p =$* 0.74). Results support a general decrement in sleep-dependent consolidation of sequence learning in older adults. This is consistent with work demonstrating that neural replay in older animals loses the sequential order observed during waking behavior (Gerrard et al., 2008).

Abstract 430.07 Summary

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Brain's Ability To Process Social Cues is Preserved as People Age

By engaging social information processing system, older adults may better retain information

New research suggests the brain's ability to process social cues is preserved as people age, despite cognitive decline and other age-related changes. These findings were presented at Neuroscience 2011, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

As people age, their ability to process non-social information slows, and their ability to remember details declines. Brittany Cassidy and Angela Gutchess, PhD, of Brandeis University asked whether the same was true for social information. They found the brain system for evaluating social information was intact in older adults, and that it may better distinguish between emotionally relevant and irrelevant information.

Using functional magnetic resonance imaging (fMRI), the researchers observed brain activation in 15 younger and 15 older adults as they formed opinions about people pictured and described in a related sentence. Participants were asked to make personal ("Do I want this person to play a role in my life?") and non-personal ("Does this person have a pet?") social judgments regarding the person pictured or to answer an unrelated non-social question ("Does this sentence have any three-syllable words?").

In response to the social questions about the person in the picture, both younger and older adults showed activation in the dorsal and ventral medial frontal cortex and temporoparietal junction — regions known to be involved when thinking about others. Younger, but not older, adults also had greater activity in the posterior cingulate gyrus — a brain region involved in assigning value to incoming social information — when responding to social but non-personal questions. In contrast, older adults had greater activity in the right temporal pole (believed to store information about social behavior) when responding to social but not non-social questions.

"Our findings suggest older adults have more reliance on experience-based social concepts when evaluating and forming impressions of others. By presenting information in a way that engages this preserved social information processing system, older adults may better process and retain information for later use," Gutchess said.

Research was supported by the National Institute on Aging.

Scientific Presentation: Monday, Nov. 14, 2:30–2:45 p.m., Room 201

430.07, Age-related changes to the neural correlates of social evaluation
B. S. CASSIDY, **A. H. GUTCHESS**; Dept. of Psychology, Brandeis Univ., Waltham, MA

TECHNICAL ABSTRACT: Previous aging-related neuroimaging research has largely concentrated on items lacking socio-emotional context, and has demonstrated pervasive age-related cognitive decline. However, more recent work suggests that there exists a specialized neural system underlying social information and memory that functionally, may be relatively spared with age. Older adults may selectively engage these regions depending on the orientation of the task at hand, consistent with findings that older adults adapt to cognitive decline by deploying resources when orienting to personally meaningful stimuli. We investigated how presentation context affects the neural substrates of social cognition, and how these activations change with age using fMRI. Fifteen young and 15 older adults viewed faces paired with trait-inferring sentences, and were instructed to form impressions of the people on the screen. They also responded to a prompt that was either personally meaningful ("Do I want this person to play a role in my life?"), social but personally irrelevant ("Does this person have a pet?") or non-social ("Does the sentence have any three-syllable words?"). Conjunction analyses revealed that both young and older adults engaged regions widely implicated in mentalizing and social cognition when making social relative to non-social evaluations, including dorsal and ventral medial prefrontal cortex, precuneus, temporoparietal junction, and temporal pole. Additionally, older adults had enhanced activation relative to young in the right temporal pole when making social relative to non-social evaluations, suggesting more reliance on experience based social concepts when evaluating and forming impressions of others. Interestingly, young, but not older, adults had greater activation in bilateral posterior cingulate gyrus when deciding if individuals had pets relative to whether they would want the individual in their lives, potentially reflecting a focus on evaluating ambiguous social stimuli for later use. Overall, the findings demonstrate the preservation of the neural correlates underlying social evaluation and impression formation with age, and suggest that the functioning of these regions might be mediated by age-related changes in socio-emotional goals.

Abstract 293.15 Summary

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Older Adults with Weak Decision-Making Skills Choose Immediate Monetary Gains Over Larger Delayed Payouts

Findings suggest tool to help identify people with decision-making problems

Older adults who have problems with decision-making choose smaller, immediate payouts over larger gains, new research found. The study was presented at Neuroscience 2011, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

While previous research has shown that younger people tend to be more willing to reap an immediate gain over a long-term reward — a concept known as future discounting — older, unimpaired adults are often more willing to wait.

To see if older adults who do poorly on decision-making tasks differed from others of the same age, researchers led by Kameko Halfmann and Natalie Denburg, PhD, of the University of Iowa posed 36 "sooner" versus "later" reward scenarios to older and middle-aged adults. Participants were asked to answer questions such as, "Would you prefer $20 today or $25 in two weeks?" Compared with unimpaired older adults — who consistently chose larger future rewards — those with decision-making problems acted more like the younger individuals in the study, who chose immediate gain.

"Future discounting behavior is becoming increasingly relevant in older adulthood, which involves an array of time-value trade-off decisions regarding both finance and health. Our research may allow us to one day develop targeted interventions to alleviate problematic decision-making in old age," Halfmann said.

Research was supported by the Dana Foundation Grant in Brain and Immuno-Imaging Grant.

Scientific Presentation: Sunday, Nov. 13, 3–4 p.m., Halls A–C

293.15, Age-related differences in discounting the future
K. HALFMANN, A. WHITLATCH, W. HEDGCOCK, D. TRANEL, N. DENBURG; Univ. of Iowa, Iowa City, IA

TECHNICAL ABSTRACT: When asked to choose between sooner and later monetary rewards and losses, individuals tend to delay costs and fast-track benefits. However, previous research studying this temporal discounting phenomenon in older adults has led to conflicting results. Whereas one study found that older adults discounted the future less than their younger counterparts, another study indicated that older adults discounted the future at a greater rate than younger adults. These equivocal results are likely due, at least in part, to differing methodologies involving subject sampling and discounting delay intervals (e.g., delay intervals of up to 30 years). Here, we conducted a study that eliminated some of these confounding factors to elucidate whether there are indeed age-related differences in temporal discounting. Thus, four groups of participants were examined: young, middle-aged, older-unimpaired (cognitively-intact older adults with strong decision-making abilities), and older-impaired (cognitively-intact older adults with weak decision-making abilities). Across 72 trials, participants were asked to choose between sooner-smaller and later-larger monetary rewards and losses, where delays varied between two and six weeks, and monetary rewards and losses varied between $13 and $48. Results indicated that there were significant age-related differences in temporal discounting, such that older-impaired adults and young adults discounted the future at a greater rate than older-unimpaired adults and middle-aged adults. This suggests that the temporal component of decision-making may be specifically susceptible to age-related differences, which will be discussed in the context of several cognitive neuroscience theories of aging.