Embargoed until Oct. 18, 10:30 a.m. CDT
Press Room, Oct. 17–21: (312) 791-6619

Contacts: Kat Snodgrass, (202) 962-4090
Sarah Bates, (202) 962-4087

RUN FOR YOUR LIFE:
NEW STUDIES SHOW BENEFITS OF EXERCISE ON THE BRAIN AND BODY
Research has implications for Parkinson's disease, premenstrual syndrome, depression, and more

CHICAGO — Mounting evidence shows the benefits of exercise on both the brain and body, according to new research released today. The research focuses on the effects of physical activity on brain health and, more specifically, underscores the positive influence of regular physical activity on Parkinson's disease, depression, premenstrual syndrome, and memory. These findings were presented at Neuroscience 2009, the Society for Neuroscience's annual meeting and the world's largest source of emerging news about brain science and health.

Exercise benefits many aspects of life. However, the National Center for Health Statistics estimates that only 31 percent of all adults, and 22 percent of adults older than 65, engaged in regular physical activity in 2006, giving these new findings particular relevance.

Today's new research shows that:

- Thirty minutes of aerobic exercise may reduce negative moods experienced by some women just before and during their menstrual period (Matthew Davidson, PhD, abstract 785.22, see attached summary).
- Exercising daily after undergoing whole-brain radiation prevented mice from experiencing declines in spatial memory skills and increases in depression-like behavior — two symptoms that typically develop after such treatment. This finding may have implications for people with malignant brain tumors for whom radiation is often the only treatment option (Christina L. Williams, PhD, abstract 581.9, see attached summary).
- Primates that ran on a treadmill five days a week were more resilient to a neurotoxin than were their sedentary counterparts. The active primates exhibited less damage to dopamine-containing brain cells, which are important in movement (Judy L. Cameron, PhD, abstract 430.7, see attached summary).
- In a mouse model of Parkinson's disease, exercise protected against the loss of cells that are important for maintaining function and movement, suggesting that exercise may be key in delaying disease progression (Yuen-Sum Lau, PhD, abstract 431.13, see attached summary).

"Continuously challenging the brain with physical and mental activity helps maintain its structure and function," said press conference moderator Carl W. Cotman, PhD, Professor of Neurology at the University of California, Irvine, and an expert in the aging brain. "Most people do not realize that they have control over how their brain functions, but this research shows that by incorporating physical activity into their lifestyle, they benefit their bodies and brains."

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

# # #

Abstract 785.22 Summary

Senior author: Matthew C. Davidson, PhD (413) 545-1579
University of Massachusetts davidson@psych.umass.edu
Amherst, Mass.

Exercising for 30 Minutes Helps Reduce Emotional Reactivity in Premenstrual Women

Study suggests exercise may be a helpful intervention for premenstrual syndrome

Thirty minutes of aerobic exercise can reduce the negative emotional reactivity that some women experience just before and during their menstrual period, a new study has found. The research was presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"Our findings suggest that some women may experience extra benefits from increasing their physical activity before and during this particular phase of the menstrual cycle," said senior author Matthew Davidson, PhD, of the University of Massachusetts, Amherst.

Using functional magnetic resonance imaging, Davidson and colleagues observed brain activation in eight healthy young women (aged 18 to 35 years) as they were shown emotionally neutral, negative, or blurred images. The testing was done twice: when the women had just completed 30 minutes of exercise and, for comparison, when they hadn't just exercised. These sessions were counterbalanced and both times the women were either immediately premenstrual or menstruating.

The study found that after the exercise session, the women showed a reduction in brain activation levels for negatively charged images (those rated to be emotionally arousing and negative). The reduction occurred in the amygdala, an area of the brain that's been linked to emotions and emotional reactivity.

"This reduction suggests that aerobic exercise may provide a means for reducing emotional reactivity during the low hormone phase of the menstrual cycle," Davidson said. "Previous research has shown that many women are more reactive during this phase of the menstrual cycle and this is some of the first physiological evidence that physical activity can reduce negative reactivity in the human brain."

Research was supported by the Office of Research at the University of Massachusetts, Amherst.

Scientific Presentation: Wednesday, Oct. 21, 9–10 a.m., South Hall A

785.22 , Physical activity and emotion regulation: An fMRI investigation
L. FICCO, H. L. KIRKORIAN, **M. C. DAVIDSON**; Psychology, Univ. of Massachusetts - Amherst, Amherst, MA

TECHNICAL ABSTRACT: Recent neuroimaging research has explored the effects of steroid hormone levels across the menstrual cycle on emotional reactivity to positively or negatively charged stimuli. Stimuli used in these studies ranged from words with positive or negative valence to neutral or negatively charged pictures from the International Affective Picture System (IAPS). Participants were imaged during both low and high 17β-estradiol phases of the menstrual cycle, and were presented with emotional stimuli. The results indicated significant differences in brain activation within cortical and limbic structures as a function of steroid hormone levels. These differences reflect greater activation during the low 17β-estradiol phase of participants' cycles, particularly to the negatively charged stimuli, and suggest that participants were less able to regulate their reactions to these stimuli. The current study tested the effects of aerobic exercise on this increased neural activity to negatively charged stimuli in healthy naturally cycling females (18-35 years). Testing occurred over two scan sessions, with one session preceded immediately by 30 minutes of aerobic exercise (counterbalanced). Both sessions occurred during the menses/early follicular phase of the menstrual cycle (days 4-7), and were separated by one cycle (approximately one month). A comparison of BOLD responses following negatively arousing pictures, relative to neutral pictures, revealed bilateral activation of the limbic system. A conjunction analysis indicated a large reduction in amygdala activation for the exercise vs control sessions. This reduction likely reflects increased cortical arousal leading to attenuation of amygdala response, and suggests that aerobic exercise may provide a means for reducing emotional reactivity during the lowest 17β-estradiol phase of the menstrual cycle (menses phase). These results have implications for females who suffer from menstrual related increased negative affect and mood, including premenstrual syndrome and premenstrual dysphoric disorder.

Abstract 581.9 Summary

Senior author: Christina L. Williams, PhD (919) 660-5638
Duke University williams@psych.duke.edu
Durham, N.C.

Animal Study Shows Daily Exercise Prevents Memory Loss and Depression Caused by Whole-Brain Radiation

Study may have implications for people being treated for brain tumors

Exercising daily soon after undergoing whole-brain radiation prevents the decline in long-term memory and attenuates the increase in depression-like behavior that can develop even months later, a new mouse study has found. This research, presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health, may have implications for people with malignant brain tumors for whom whole-brain radiation (cranial radiotherapy) is often the only treatment option.

In humans, as in mice, whole-brain radiation can lead to neurological problems, such as loss of memory and deterioration in mood. "These cognitive and behavioral deficits persist for months to years after treatment," said senior author Christina Williams, PhD, of Duke University. "Our study is the first to demonstrate the rehabilitative effects of daily exercise started shortly after whole-brain radiation to the adult brain."

The mice in the study were anesthetized, and half were given a clinically relevant dose of whole-brain radiation. Two weeks later, all the mice were tested to assess spatial memory and depression. By comparison, the irradiated mice showed more impaired learning and depression-like behavior.

The irradiated mice were then divided into two groups. Half were given daily access to a running wheel; the other half remained in their cages. Three months later, the impaired long-term spatial memory and depression-like behavior of the sedentary mice was even greater than it was two weeks after irradiation. In contrast, the mice given the opportunity to exercise showed no such problems. In fact, the exercising irradiated mice behaved just like sedentary mice that had never been irradiated.

The study authors then examined the animals' brains. "We found that the exercising irradiated mice had significantly more new neurons in the hippocampus — an area important for both memory and mood — than the sedentary irradiated mice," Williams said. "In addition, we found that daily exercise after whole-brain radiation partially restored levels of vascular endothelial growth factor, a protein known to stimulate the growth of new brain cells."

Research was supported by the National Institutes of Health and the Duke University Comprehensive Cancer Center.

Scientific Presentation: Tuesday, Oct. 20, 8–9 a.m., South Hall A

581.9, Exercise promotes recovery from cognitive dysfunction, depressive-like behavior, and loss of hippocampal neurogenesis following whole-brain irradiation in adult mice

S. J. WONG-GOODRICH[1], M. L. PFAU[1], C. T. FLORES[2], L. W. JONES[2], **C. L. WILLIAMS[1]**; [1]Psychol& Neurosci, [2]Surgery, Duke Univ., Durham, NC

TECHNICAL ABSTRACT: Whole-brain irradiation (IRR) leads to progressive and persistent cognitive deficits in both adult rodents and human patients with primary or metastatic brain tumors despite a lack of gross structural neurological changes or peripheral tissue damage, which suggests a more subtle neural process may be altered. In rodents, IRR causes a long-lasting decrease in adult hippocampal neurogenesis, reduces hippocampal growth factor content, and impairs spatial memory. Our study was designed to characterize short- and long-term effects of whole-brain (5 Gy) radiation on hippocampal neurogenesis, cognitive function, and depressive-like behavior of adult female C57Bl6 mice, and to determine whether exercise following IRR aids recovery of brain and behavior. We found that spatial learning on the Barnes maze was slightly impaired 2-3 weeks after IRR, and that large memory deficits were observed at 3 months post-IRR. To examine depressive-like behavior, we recorded the latency to become immobile and immobility time in the forced swim and tail suspension tests, and found that IRR increased depressive-like behavior at 2 weeks and at 3 mo post-IRR. Following the initial behavioral assessment at 2-3 weeks after IRR, half of the sham IRR and IRR mice were exposed to daily voluntary exercise on running wheels and then behaviorally characterized a second time prior to sacrifice. To examine the recovery of hippocampal-dependent spatial learning and memory, we trained mice to learn the spatial location of an escape hole on the Barnes maze and probed their spatial memory at 1 hr, 4 d, and 18 d after training. We found that 8 weeks of daily voluntary wheel running enhanced spatial memory of sham IRR mice and completely rescued the long-term spatial memory deficit elicited by IRR at all spatial memory retention

delays. Exercise also aided recovery from increased depressive-like behavior. To assess recovery of hippocampal neurogenesis, we quantified the number of newborn neurons immunolabeled with immature neuronal marker doublecortin (DCX) in the dentate gyrus. We also assessed protein levels of VEGF as a proximate mechanism for changes in neurogenesis. We found that voluntary wheel running partially rescued the IRR-induced decline in hippocampal neurogenesis and VEGF protein. These findings reveal that cognitive deficits and increased depressive-like behavior are evident as early as 2 weeks post-IRR, but worsen months after IRR. These findings also suggest that daily exercise is an effective means of partially rescuing hippocampal neurogenesis, improving spatial memory, and reducing depressive-like behavior following a clinically relevant dose of whole-brain radiation.

Abstract 430.7 Summary

Lead author: Judy L. Cameron, PhD (724) 396-4166
University of Pittsburgh jcameron@pitt.edu
Pittsburgh, Pa.

Exercise Training Protects Dopamine-containing Neurons in Nonhuman Primates

Finding suggests exercise might slow progression of Parkinson's disease

A new primate study shows that regular exercise protects dopamine-containing brain cells, making it more likely that the cells will stay functional after exposure to environmental toxins. This finding, presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health, has implications for the estimated 500,000 Americans living with Parkinson's disease. The loss of dopamine neurons, which control motor movement, is responsible for most Parkinson's symptoms, such as tremors, muscle stiffness, and impaired balance.

"Our findings suggest that participating in a regular exercise program could decrease the occurrence and possibly slow the progression of Parkinson's disease," said lead author Judy L. Cameron, PhD, of the University of Pittsburgh.

Cameron and her colleagues trained four adult female rhesus monkeys to run on a treadmill at 60 to 80 percent of maximal heart rate capacity (a slow jog to a slow run). They ran for an hour a day, five days a week. After three months, these four monkeys and two others that hadn't been exercising were given a compound that selectively damages dopamine neurons. After a five-day rest period, the researchers had the exercising monkeys return to treadmill running for another six weeks, at which point they scanned the animals' brains using positron emission tomography.

"We found that monkeys who had exercised for three months prior to the compound exposure showed less dopamine neuron damage compared with the sedentary monkeys," Cameron said. "This finding suggests that endurance exercise could protect the brain against neurotoxic insults such as those that might lead to Parkinson's disease."

Research was supported by the National Institute of Neurological Disorders and Stroke.

Scientific Presentation: Monday, Oct. 19, 3–4 p.m., South Hall A

430.7, Exercise protects the striatum against MPTP damage in nonhuman primates
J. L. CAMERON[1], N. ROCKCASTLE[2], M. J. ZIGMOND[3], R. K. LEAK[3], A. SMITH[3], B. J. LOPRESTI[4], C. A. MATHIS[4], K. MIRNICS[5], N. I. WILLIAMS[6], Z. ZHANG[7]; [1]Univ. Pittsburgh Sch. Med., Pittsburgh, PA; [2]Psychiatry, [3]Neurol., [4]Radiology, Univ. of Pittsburgh, Pittsburgh, PA; [5]Psychiatry, Vanderbilt Univ., Nashville, TN; [6]Kinesiology, Pennsylvania State Univ., University Park, PA; [7]Anat. and Neurobio., Univ. of Kentucky, Lexington, KY

TECHNICAL ABSTRACT: Exercise can increase neuroplasticity, and in rodents exercise has been shown to protect the nigrostriatal dopaminergic tract against damage from neurotoxins. A neuroprotective role for exercise is also supported by epidemiological human studies of reduced Parkinson's disease risk in individuals with active lifestyles. To examine the ability of exercise to protect the nigrostriatal tract from neurotoxin damage in a primate species 6 adult female rhesus monkeys (15-20 yrs. of age) received a unilateral, right-side intracarotid injection of a low dose of MPTP (0.6-0.8 mg). Monkeys had either been sedentary (n=2) or had run on a treadmill (exercising at 60-80% maximal capacity) for an hour a day 5 days/week (n=4) for 3 mo prior to MPTP administration, and for 6 additional weeks beginning 5 days after MPTP administration. Six weeks post-MPTP a PET scan was performed using the VMAT-2 radioligand [11C]dihydrotetrabenazine (DTBZ). In the sedentary monkeys DTBZ binding on the right side of the brain was 66.9% that on the left side. Right side damage was significantly less in both the right putamen (58.7±7.8% of sedentary controls, p=0.01) and caudate (64.3±10.9% of sedentary controls, p=0.05) in the runners. At 7 weeks post-MPTP brain tissue was collected and levels of dopamine (DA) were analyzed by HPLC. There was an 86.4±12.9% loss of DA in the sedentary animals. The runners showed a significantly smaller loss in the putamen (53.2±15.0% of sedentary controls, p=0.05). Protection was not seen in the caudate. Despite the small number of animals studied to date, our findings are consistent with the hypothesis that participation in a regular exercise program can protect DA neurons in the putamen from neurotoxic damage. These results suggest that endurance exercise could protect the brain against neurotoxic insults, such as those that might lead to Parkinson's disease.

Abstract 431.13 Summary

Senior Author: Yuen-Sum Lau, PhD (713) 743-1276
University of Houston ylau2@uh.edu
Houston, Texas

Animal Study Shows That Long-term Exercise Offers Neural Protection Against Parkinson's Disease

Study supports concept that exercise may slow disease progression

Long-term exercise protects against the loss of dopamine-producing cells and energy-producing mitochondria in neurons, which are important for maintaining function and movement in a chronic mouse model of Parkinson's disease, a new study reports. These results, presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health, support the concept that exercise may slow the progression of Parkinson's disease.

"Clinical reports have implicated exercise training in improving the physical performance and mobility of people with Parkinson's disease, but no one has demonstrated, either clinically or in laboratory models, whether exercise can delay the progression of neuronal degeneration," said senior author Yuen-Sum Lau, PhD, of the University of Houston. "This study was aimed at investigating this possibility and at examining how exercise protects neural mitochondria."

In people with Parkinson's disease, mitochondria — the energy factories of cells — become sluggish, which contributes to the death of dopamine neurons in brain areas that control motor functions. The loss of dopamine neurons is believed to trigger the symptoms of Parkinson's disease.

The mice used in the study were chronically induced with a neurotoxin to have many features that resemble human Parkinson's disease, including impaired movement and a marked loss of brain dopamine and mitochondrial function. The animals were divided into two groups: one was kept sedentary; the other exercised on a motorized treadmill for 40 minutes daily, five days a week, for 18 weeks. At the end of the study, the exercise-trained Parkinson's mice had significantly higher brain dopamine content and exhibited greater brain mitochondrial activity than the sedentary mice. They also performed better in a test that assessed their balancing abilities.

"This research provides scientific evidence that long-term endurance exercise protects brain mitochondria and dopamine-producing neurons from undergoing progressive degeneration as demonstrated in the chronic mouse model of Parkinson's disease," Lau said.

Research was supported by the National Institute of Neurological Diseases and Stroke.

Scientific Presentation: Monday, Oct. 19, 1–2 p.m., South Hall A

431.13, Endurance exercise protects striatal mitochondria and dopaminergic neurons in the chronic mouse model of Parkinsonism
G. PATKI, **Y.-S. LAU**; Univ. Houston, Coll Pharm., Houston, TX

TECHNICAL ABSTRACT: There is growing evidence suggesting that physical activity and exercise can slow aging, prevent chronic diseases, and promote health. The impact of endurance exercise on neurodegenerative diseases, such as in Parkinson's disease (PD) has been implicated but not been rigorously tested in the chronic animal models. Moreover, neuronal oxidative stress and mitochondrial dysfunction have been linked to PD and to chemically induced Parkinsonism. In this study, we examined the outcomes of long-term endurance exercise on mitochondrial and dopamine (DA) neuronal functions in the neostriatum of the chronic mouse model of Parkinsonism (MMP) that had been established in our laboratory. Male, 8-month old, retired C57/BL breeder mice were treated with 10 doses of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (15 mg/kg, s.c.) and probenecid (250 mg/kg, i.p.) over five weeks. The control group of mice was injected with the same dose of probenecid alone. The chronic MMP animals were divided into two groups: one group was kept sedentary throughout the study; the other group was exercise-trained (1 week before, 5 weeks during, and 12 weeks after the chronic MMP treatment) on a motorized treadmill at a speed up to 15 m/min, 40 min/day, 5 days/week. Comparing to the control mice, the chronic sedentary MMP animals exhibited significant loss of tyrosine hydroxylase and dopamine uptake transporter protein expressions, depletion of DA content, and reduction of mitochondrial state 3 respiration, superoxide dismutases, cytochrome c, and ATP levels in the striatum. The animals' motor performance on the challenging beam was also markedly inhibited. These findings suggest that striatal mitochondrial dysfunction coexists with DA neuron degeneration in the chronic MMP animals. Interestingly, all of the above neuronal, mitochondrial and behavioral deficits detected in the chronic sedentary MMP animals were partially and statistical-significantly prevented in the chronic exercise-trained MMP animals. This study clearly demonstrates that long-term endurance exercise is not only mitochondria-protective but also neuroprotective in the chronic MMP supporting the hypothesis that exercise can slow the progression of PD-like neurodegeneration.