Environmental Enrichment Promotes Healthy Cognitive Aging by Improving Learning & Memory and Increasing Neural Connections & Synaptic Plasticity

Giuseppe P. Cortese [1], Rikki Hullinger [2], Kenneth O'Riordan [3], Jose G. Gonzalez [4], Andrew Alexander [4], & Corinna Burger [1]

[1] Department of Neurology, University of Wisconsin-Madison, USA
[2] Neuroscience Training Program, University of Wisconsin-Madison, USA
[3] Department of Pharmacology & Therapeutics Biotechnology, Trinity College, Dublin, Ireland
[4] Department of Medical Physics & Waisman Lab for Brain Imaging and Behavior, University of Wisconsin-Madison, USA

Introduction

The aging population, individuals 65 years or older, represents 12.9% of the total US population; and it is estimated that by year 2030 this number will rise to 19%. Over 5 million individuals suffer from age-related cognitive decline, significantly increasing their risk to develop more severe forms of dementia and neurological diseases, such as Alzheimer's disease. Although these neurodegenerative diseases pose a significant challenge to the healthcare industry and remain a top priority for research investment, the projected increase in the aging population far exceeds the number of individuals that will suffer from severe dementias and/or neuro-degenerative diseases. Thus, it is of paramount importance and of high significance to study the mechanisms of age-related cognitive decline in order to develop therapeutic strategies to improve healthy cognitive aging in hopes to prevent and/or delay disease.

Age-related cognitive decline is associated with deficits of the hippocampus, a critical brain region that controls learning and memory. There has been significant progress in identifying and understanding the benefits of behavioral therapeutic strategies to suppress the negative effects of aging. To date, the most relevant findings known to suppress the cognitive decline associated with aging has been performed in human and rodent models of environmental enrichment (EE), which consist of environmental changes promoting social activity, healthy diet, frequent exercise, quality living conditions, and limited stress. Here we performed behavioral assessments, electrophysiological recordings, and magnetic resonance imaging (MRI) analyses on a rodent model of aging-associated environmental enrichment to determine the behavioral, cellular, and anatomical benefits of EE. Aged, 22-month-old F344 rats were exposed to EE for 1-month and behavioral performance was tested on the Morris Water Maze. Whole brains were fixed and MRI images were acquired to determine changes in neural connectivity of the hippocampus. For electrophysiological experiments hippocampal slices were prepared and field excitatory post-synaptic potentials were measured to determine changes in hippocampal long-term potentiation (LTP). We find that EE increases hippocampus-dependent learning and memory and synaptic plasticity, as well as hippocampal neural connectivity when compared to standard home-caged controls. This work is highly significant, as the results from this study will fill major gaps in knowledge concerning the neuro-anatomical architecture and the cellular and molecular mechanisms by which environmental enrichment slows the progression of cognitive decline in the aging brain. By understanding these mechanistic targets of enrichment we can better generate behavioral therapeutic strategies for effective preventative measures and possible treatments.

Housing Conditions for Enrichment

Aged F344 rats are exposed to SE (left panel) or EE (right panel) for 1 month before experiments are performed. SE contains 6 aged rats per box and EE contains 6 aged rats plus objects that provide environmental enrichment. SE serves as a control for social conditions (number of rats).

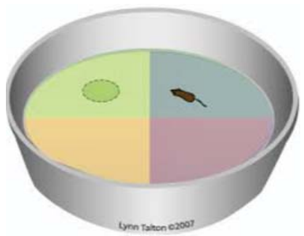
Social Enrichment (SE)

Environmental Enrichment (EE)

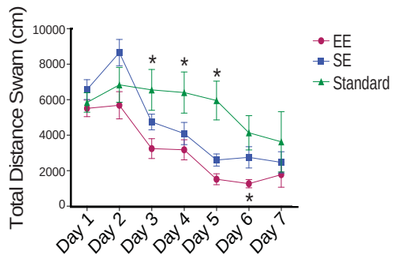
Behavioral Assessment

Hippocampus-Dependent Learning & Memory is Increased in Aged Animals Following Environmental Enrichment

Morris Water Maze (MWM)



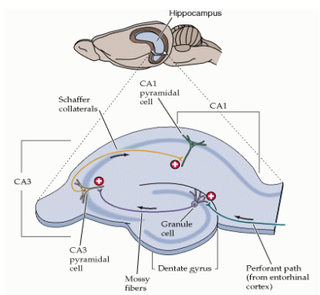
Aged: MWM Performance



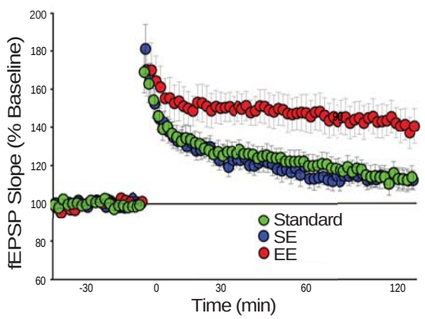
Electrophysiological Recordings

Hippocampal Long-Term Potentiation is Increased Following Environmental (EE), but not Social Enrichment (SE)

Hippocampal Slice Recordings



Aged: LTP Measurements

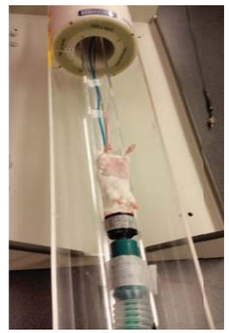


Magnetic Resonance Imaging (MRI)

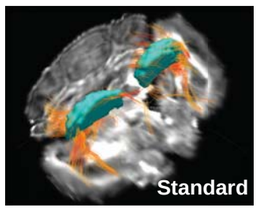
White Matter Projections from Hippocampus are Increased in Aged Animals Following Social Enrichment (SE) & Environmental Enrichment (EE)

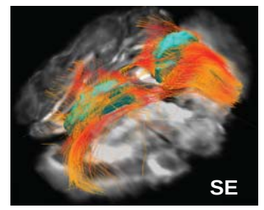
Imager

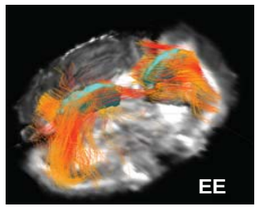
Rodent Insert



Aged: White Matter Projections







Acknowledgements

*All procedures using animals were reviewed and approved by the Animal Care and Use Committee at the University of Wisconsin-Madison.
*This work was supported by NIH/NIA R01AG048172, NIH/NIGMS T32GM007507, & NSF GRFP fellowship.
*Special thanks to S. Osting for technical assistance; and members of the Burger lab for helpful discussion and scientific input.