Authors: Jamie R. Kleiner [1], Brian M. Schilder [1], Chet C. Sherwood [1], Kimberley A. Phillips [2]

Affiliations:

[1] The George Washington University, Department of Anthropology, Center for the Advanced Study of Human Paleobiology, Washington, DC

[2] Department of Psychology, Trinity University, San Antonio, TX 78212, United States; Southwest National Primate Research Center, Texas Biomedical Research Institute, San Antonio, TX

Title: Animal Model Indicating an Interaction between MS and Exercise's Impact on Adult Hippocampal Neurogenesis

While multiple sclerosis (MS) is typically understood as an autoimmune disease that degrades motor functioning, it can also have significant impacts on cognition. Previous studies suggest that MS affects the hippocampus, damaging patients' cognitive spatial and memory abilities. Dysregulation of adult hippocampal neurogenesis (AHN), the birth of new granule cells (neuroblasts) which are necessary for proper memory formation, may be a mechanism by which MS disrupts hippocampal functioning. Some research suggests that exercise may lessen some neuropathological effects of MS. The present study utilized marmoset monkeys (*Callithrix jacchus*) to model the neurobiological impacts of MS and exercise therapy on AHN. Eight adult male marmosets were sensitized to myelin oligodendrocyte (MOG) glycoprotein (MOG 34-56) in incomplete Freund adjuvant. This was injected into eight adult male marmosets, inducing autoimmune encephalomyelitis (EAE) which models the neurobiological effects of MS in humans with relapse-remitting MS. An additional four control subjects were injected with incomplete Freund adjuvant alonesaline. Half of the EAE and control subjects engaged in aerobic exercised for 30 minutes, three days/week for 10 weeks. Sections across the antero-posterior length of the hippocampus were immunohistochemically stained for doublecortin (DCX) as a marker for neuroblasts. Stereologic counts of the absolute number, proportion (relative to granule cells) and density of DCX cells were quantified in the dentate gyrus of the hippocampus, divided into the Granule Cell Layer (GCL) and the Subgranular Zone (SGZ), where neuroblasts proliferate. Our findings showed that although neither EAE nor exercise statuses had a significant main effect on any of the DCX cell measures alone ($p><0.05$), there was a significant interaction between these two variables (ANOVA, $F_{df}=7.103$, $p=0.029$). Exercise increased absolute DCX cell numbers in the EAE group but decreased it in the control group. Similarly, non-significant trends were observed for %DCX cells and DCX cell density. These results suggest a relationship between exercise and EAE's impact on AHN. This supports the hypothesis that exercise mitigates the impacts of MS on AHN. Thus, this interaction may be a physiological explanation of the benefit human patients see with exercise therapy, regarding spatial and memory cognition.