

**Carl Cotman and The Effects of Voluntary Exercise on Increased BDNF  
Expression:**  
Implications for Resisting Detrimental Effects of Age-Related Cognitive Decline

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Brain-Derived Neurotrophic Factor (BDNF) is a member of the neurotrophic family responsible for the viability and function of a variety of neuronal subtypes within the brain. Carl W. Cotman has been investigating the effects of voluntary exercise on the up-regulation of BDNF and the practical applications of this line of research to resisting age-related cognitive decline and neurodegeneration. Cotman's early research examined the increase in BDNF mRNA across a variety of regions within the brain in response to exercise. It was surprising that physical activity was linked to BDNF up-regulation in caudal areas of the brain, including the hippocampus, as Cotman initially suspected a link between exercise and BDNF expression only in motor regions. From this, Cotman refined his focus to such correlations with respect to the caudal regions of the brain, and applied his findings to the possibility that both learning and memory might be enhanced by regular exercise. Current research in this area has been targeted at elucidating the molecular underpinnings of the relationship between exercise and BDNF expression via identification of the relevant pathways.

Due to BDNF's role in enhancing synaptic efficacy, neuronal connectivity, and use-dependent plasticity, Cotman's line of investigation may prove to be crucially important to many areas of neuroscience. Further, his research has implications for slowing the detrimental effects of aging on synaptic welfare, a focus that is of paramount importance to the adult population. Cotman has also investigated the possibility that a decline in BDNF may be associated with loss of cognitive function and his findings have led to the hypothesis that increasing BDNF expression may prevent such loss of function.

Logically, further research is being carried out in this area for application to clinical and preventative measures.

Other researchers have also sought to examine possible mechanisms underlying age-related neurodegeneration. Specifically, studies by Croll et al. examined the expression of both TrkB (the high affinity BDNF receptor) and BDNF with respect to age and cognitive condition. Their results showed that, while levels of TrkB mRNA declined with both age and cognitive capacity, age-related decline in BDNF mRNA was not significantly predictive of hindered cognitive performance. This finding illuminates the possibility that the observed age-related cognitive decline might be a direct result of a reduction in TrkB expression, and not a function of compromised BDNF expression. Thus, Cotman's findings may be interpreted as providing a means for increasing signal intensity for a weakened detection system, though they specify little about addressing the shortcomings of the detection system. This presents the prospect that therapy may be more efficiently targeted at regulating trkB receptor expression rather than focusing on increasing levels of circulating BDNF.

Cotman's research scope has been refined over the past decade and has yielded many exciting findings with respect to retarding the adverse effects of aging on cognitive processes. However, his work has been perhaps overly emphatic of correlational analysis while underemphasizing mechanistic investigation, until only recently. Specifically, there has been limited clarification of the neurobiology linking exercise, BDNF expression, and cognitive performance. Thus, future research in this area should aim to expose such mechanisms so that a more complete understanding of the positive effects of exercise on neural maintenance may be understood.

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