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Aerobic exercise effects on cognitive and neural plasticity in older adults

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Older adults frequently experience cognitive deficits accompanied by deterioration of brain tissue and function in a number of cortical and sub-cortical regions. Because of this common finding and the increasing ageing population in many countries throughout the world, there is an increasing interest in assessing the possibility that partaking in or changing certain lifestyles could prevent or reverse cognitive and neural decay in older adults. In this review we critically evaluate and summarise the cross-sectional and longitudinal studies that assess the impact of aerobic exercise and fitness on cognitive performance, brain volume, and brain function in older adults with and without dementia. We argue that 6 months of moderate levels of aerobic activity are sufficient to produce significant improvements in cognitive function with the most dramatic effects occurring on measures of executive control. These improvements are accompanied by altered brain activity measures and increases in prefrontal and temporal grey matter volume that translate into a more efficient and effective neural system.

Brain deterioration and cognitive decline are considered common characteristics of ageing. However, it is clear that not everyone experiences senescence at the same rate or to the same degree. Individual differences in the quality of cognitive and brain function in old age suggest that deterioration and decay are neither ubiquitous nor inevitable characteristics of ageing. This begs the following question: what are the factors that explain some of the individual differences in old age, allowing some people to retain cognitive and brain function, while pushing others into a trajectory of decline and decay?

In addition to determining individual difference factors, recent interventions demonstrate that cognitive and brain deterioration is not unalterable and that the older adult brain retains some plasticity that can be taken advantage of in order to reverse deterioration and decay that may already be manifest. In this review we summarise research on the effect of aerobic exercise on preventing and reversing cognitive and brain decay in old age and provide practical recommendations for utilising exercise to take advantage of the brain's natural capacity for plasticity.

COGNITIVE AND BEHAVIOURAL RESEARCH

Ageing is often characterised by deterioration of both white matter and grey matter tissue in the prefrontal, temporal, and parietal cortices with relative sparing of tissue in other regions such as primary motor and visual cortex.¹ Tissue deterioration is often accompanied by decline in cognitive

function, with the greatest deficits occurring on measures of executive control such as task coordination, planning, goal maintenance, working memory, and task switching.² However, it is these executive control processes that appear to be the most amenable to an aerobic exercise intervention. For example, Kramer *et al*³ randomly assigned participants to either an aerobic exercise intervention group (moderate walking) or a control group (stretching and toning). Both groups attended the same number of intervention sessions and received the same amount of health instruction, so the main difference between the two groups was the aerobic aspect of the intervention for the walking group. Cognitive testing on a comprehensive neuropsychological battery was conducted both before and after spending 6 months in the exercise programme. Over the 6 month period Kramer and colleagues found that the walking group not only became more aerobically fit, but also showed enhanced executive function, as indexed by task switching, stopping, and selective attention tasks, compared with the stretching and toning control group. In contrast, cognitive tasks that tapped non-executive processes such as processing speed were minimally affected by the aerobic intervention.⁴ These results suggested three main points: (a) that 6 months of moderate aerobic exercise could reliably reverse age-related cognitive decline, (b) that the benefits of aerobic exercise on cognitive function were disproportionately greater for tasks of executive control, suggesting some specificity for aerobic exercise on cognitive and brain function, and (c) that older adults retain their capacity for plasticity and that even executive processes, or those processes that show the greatest rate of decline, remain highly tractable.

Other longitudinal and randomised clinical trials have reported similar results to those described above, e.g.⁵, yet the results from some studies have been more equivocal regarding the influence of aerobic exercise on offsetting or reversing cognitive deficits in old age.⁶ One potential explanation for this ambiguity is in the type of cognitive processes assessed in the intervention. As just described, Kramer and colleagues^{3,4} reported that executive control processes were more affected by the exercise intervention than other cognitive processes (i.e. processing speed). In a meta-analysis of 18 randomised trials assessing the effects of exercise on cognitive function, Colcombe and Kramer⁷ reported that exercise broadly improves cognitive function across a number of domains including spatial functioning and executive control. However, they also revealed several significant moderators of exercise on cognitive function. For

example, executive functioning improved more than other cognitive functions. This highlights the specificity that aerobic exercise has on cognitive function and suggests that studies that do not assess executive functioning may not show large improvements in cognitive performance as a function of an exercise intervention.

The effect of aerobic exercise training on cognitive function also seems to extend to older adults with dementia. For example, Heyn and colleagues⁹ conducted a meta-analysis to examine whether exercise training is beneficial for people with dementia and related cognitive impairments. They found that, across 12 randomised trials, aerobic exercise interventions reliably reversed cognitive impairments in demented individuals with an effect size of 0.57. This finding suggests that the benefits of exercise training on cognition are not limited to those without pathology and that even individuals with some brain deterioration can demonstrate cognitive improvements with the appropriate interventions.

NEUROIMAGING RESEARCH

The results from Colcombe and Kramer⁷ suggest that the brain regions most related to executive control, including prefrontal and parietal circuits, might be more pliable and the most affected by aerobic exercise training. In support of this hypothesis, Colcombe *et al*⁹ demonstrated, in a cross-sectional sample of fitter and less fit older adults, that fitter individuals had greater grey matter volume in the prefrontal, parietal, and temporal regions and greater white matter volume in the genu of the corpus callosum than their less fit counterparts. This finding remained significant even after controlling for potentially confounding factors and suggested that at least some of the individual variability in brain volume decline with advancing age could be attributed to variation in fitness levels (see also ¹⁰). Further supporting the claim that aerobic fitness moderates age-related deterioration of brain tissue, Marks *et al*¹¹ reported in a cross-sectional study that fitter older adults had higher fractional anisotropy obtained from diffusion tensor imaging in several white matter regions, suggesting that aerobic fitness maintains the integrity of the white matter tracts leading towards and away from the prefrontal regions. In sum, cross-sectional results argue that higher levels of aerobic fitness can reliably preserve brain volume and white matter integrity in older adults.

Colcombe and Kramer⁷ reported in their meta-analysis that studies with more women showed greater effects of aerobic exercise training on cognition than studies with fewer women. It was speculated that the loss of oestrogen and the presence of hormone replacement therapy (HRT) in postmenopausal women contributed to this gender effect. In support of this idea, a study using young female rodents reported that the effect of exercise on increasing levels of brain-derived neurotrophic factor, a critical molecule in the development of new neurons and learning and memory processes, is dependent on the presence of oestrogen, and that the combined effects of aerobic exercise and oestrogen replacement are greater than those of either exercise or oestrogen replacement alone.¹² Erickson *et al*¹⁵ examined the relationship between HRT and fitness levels on brain volume and executive control in a cross-sectional sample of postmenopausal women. They reported that fitter women, regardless of HRT status, showed enhanced cognitive and brain volume measures compared with their less fit peers. In addition, it was found that women with fewer than 10 years of HRT use had a greater volume of grey matter in the prefrontal and temporal cortices and performed better on a task

measuring executive control than women who had taken HRT for longer than 16 years. However, Erickson *et al* also reported that higher aerobic fitness levels reliably offset the negative effects of long-term HRT use and augmented the short-term benefits of HRT use. This finding indicated that multiple lifestyle factors can have interactive effects on brain and cognition in old age, and may also explain the finding that studies with more women participants show larger effects of exercise training on cognitive function.

Recent evidence also suggests that aerobic fitness may moderate brain volume changes in dementia patients. Consistent with the meta-analysis described earlier,⁹ Burns and colleagues¹⁴ reported that patients in the early stages of Alzheimer's disease who were more aerobically fit had less whole-brain atrophy and white matter atrophy than those patients less aerobically fit. This relationship remained significant even after controlling for potentially confounding variables. These results suggest that aerobic exercise may be one preventive measure against the development of Alzheimer's dementia, and are consistent with rodent models of Alzheimer's demonstrating that voluntary exercise can reduce and even reverse some of the symptoms¹⁵⁻¹⁷ (however, see ¹⁸).

The studies described thus far have been cross-sectional in nature, and are, therefore, inherently limited in the breadth of the conclusions that can be drawn regarding the capability of aerobic exercise to reverse brain decay. In a longitudinal and randomised trial over 6 months, Colcombe *et al*¹⁹ reported that, indeed, the brain is capable of retaining its plastic nature well into older adulthood, and that 6 months of aerobic exercise is enough to reverse some of the age-related cortical decay. They found that the 6 months of aerobic training increased grey matter volume in the frontal and superior temporal lobe, and increased white matter volume in the genu of the corpus callosum, while the control group underwent a slight decline in cortical volume. These results suggest that even relatively short exercise interventions can begin to restore some of the losses in brain volume associated with normal ageing.

In addition to structural changes that occur in the brain as a function of aerobic fitness or an exercise intervention, functional changes also occur in the neural networks that underlie specific cognitive processes. For example, in another longitudinal and randomised trial over 6 months, Colcombe *et al*,²⁰ using functional magnetic resonance imaging, found that, during a focused attention task, aerobically trained older adults, but not controls, showed increased neural activity in the frontal and parietal regions of the brain that are thought to be involved in efficient attentional control, and a reduction in the dorsal region of the anterior cingulate cortex, which is thought to be sensitive to behavioural conflict. Similar neurophysiological changes have been observed as a function of fitness levels in studies using event-related potentials.²¹⁻²³ Finally, in a small sample of middle-aged adults, a 3 month exercise intervention increased cerebral blood volume in the dentate gyrus of the hippocampus, which was in turn associated with improvements in verbal learning and memory scores.²⁴ This finding is potentially important given an association between cerebral blood volume in the dentate gyrus and neurogenesis in mice and the neurogenic properties of exercise in the dentate gyrus.²⁵

PRACTICAL RECOMMENDATIONS AND LIMITATIONS

Given the extant literature summarised in this review on the effect of aerobic exercise on brain and cognition, it can be safely recommended that moderate levels of exercise can serve as both a preventive measure against age-related cognitive and brain

deterioration and a treatment to reverse decay and cognitive deficits already present in older adults. This result is also consistent with a large epidemiological literature that generally suggests that higher levels of physical fitness and physical activity can reduce the likelihood of developing cognitive impairments.²⁶ Most of the interventions have been 3 to 6 months and few have yet gone beyond 6 months. Therefore, it remains unknown whether longer durations of exercise produce longer-lasting and stronger effects than a 6 month intervention. In addition, according to one meta-analysis,⁷ the combination of aerobic and non-aerobic regimens produces greater benefits to cognitive function than either type of exercise by itself. Indeed, an understanding of the interactions and the effects of multiple types of exercise regimens and factors such as the use of HRT, cognitive, social or nutritional interventions is in its infancy.^{27–28} In fact, some researchers have postulated that the neural and cognitive benefits of exercise must occur within the context of cognitive engagement in order for the effects of exercise to be effective.²⁹ Yet other factors such as genetic predispositions and the frequency, magnitude, and type of exercise, as well as the presence of certain diseases, are likely to moderate the beneficial effects of exercise reviewed here. Although recent studies have argued that aerobic exercise and physical activity can also serve to protect against the development of dementia, the extent to which pathological decline can be reversed or treated with an exercise regimen remains unknown. However, there is mounting evidence that exercise has beneficial cognitive and neural effects on a number of populations besides those with dementia, including children,³⁰ multiple sclerosis patients,³¹ and Parkinson's patients.³² In sum, although many questions remain unanswered regarding the effect of exercise on brain and cognition,³³ we can safely argue that an active lifestyle with moderate amounts of aerobic activity will likely improve cognitive and brain function and reverse the neural decay frequently observed in older adults.

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