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Exercise benefits for the aging brain depend on the accompanying cognitive load: insights from sleep electroencephalogram

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ABSTRACT

Although exercise clearly offsets aging effects on the body, its benefits for the aging brain are likely to depend on the extent that physical activity (especially locomotion) facilitates multisensory encounters, curiosity, and interactions with novel environments; this is especially true for exploratory activity, which occupies much of wakefulness for most mammals in the wild. Cognition is inseparable from physical activity, with both interlinked to promote neuroplasticity and more successful brain aging. In these respects and for humans, exercising in a static, featureless, artificially lit indoor setting contrasts with exploratory outdoor walking within a novel environment during daylight. However, little is known about the comparative benefits for the aging brain of longer-term daily regimens of this latter nature including the role of sleep, to the extent that sleep enhances neuroplasticity as shown in short-term laboratory studies.

More discerning analyses of sleep electroencephalogram (EEG) slow-wave activity especially 0.5–2-Hz activity would provide greater insights into use-dependent recovery processes during longer-term tracking of these regimens and complement slower changing waking neuropsychologic and resting functional magnetic resonance imaging (fMRI) measures, including those of the brain's default mode network. Although the limited research only points to ephemeral small sleep EEG effects of pure exercise, more enduring effects seem apparent when physical activity incorporates cognitive challenges. In terms of "use it or lose it," curiosity-driven "getting out and about," encountering, interacting with, and enjoying novel situations may well provide the brain with its real exercise, further reflected in changes to the dynamics of sleep.

"Few people know how to take a walk. The qualifications are endurance, plain clothes, old shoes, an eye for nature, good humor, vast curiosity, good speech, good silence and nothing too much."

Ralph Waldo Emerson (1803–1882)

1. More than just physical exercise alone?

Unquestionably exercise has marked benefits for physical health, and ostensibly it promotes cortical plasticity and delays natural aging processes within the brain [1]. Although this latter topic has been the focus of several findings and reviews outside the field of sleep, it seems that the level of multisensory stimulation, curiosity, and cognitive load accompanying the exercise may well play a more crucial role in placing demands on the brain for "use it or lose it," which will be described in detail shortly. By utilizing the sleep electroencephalogram (EEG) and over the longer term, we argue that much more can be gleaned about the extent to which this cognitive stimulation during physical activity is to the betterment of "use it or lose it" for the aging brain.

Although a review by Angevaren et al. [2] was circumspect over why some cognitive functions improved with aerobic exercise while others were insensitive, a subsequent [3] extensive meta-analysis found a significant effect of exercise in preventing cognitive decline. Despite these authors noting that the underlying biologic mechanisms remained unclear, they pointed to exercise-related enhancement of the brain vascular system (angiogenesis), further implicating brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1, and IL-6. To varying extents, these mechanisms promote neurogenesis, neuroplasticity, neuroprotection, growth, and differentiation, both during development and in the adult brain. However, it is still unclear the extent to which such changes are specific to the exercise itself.

Indeed increased brain vascularization would seem to be an effective strategy to minimize or delay the cognitive decline associated with aging; however, exercise can be counterproductive when taken to excess, as it leads to reduced cerebral oxygenation possibly causing reduced recruitment of the brain's motor areas and glycogen depletion in astrocytes [4]. In these respects, the

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release of IL-6 within the brain during prolonged exercise may be more of a neuroprotective countermeasure, rather than having a positive effect on neuroplasticity. Another caveat relating to potential exercise benefits for the brain is that these effects can disappear when the regimen is ended. For example [5] monkeys trained to run on a treadmill over 5 months showed cognitive improvements together with increased vascularity in the motor cortex that disappeared after a 3-month sedentary period. However, monkeys are normally physically active and [5] comparisons were made with a sedentary control group sitting on immobile treadmills in this study. Thus it could be argued that the physically active monkeys exhibited the cognitively normal state, whereas this inactivity led to suboptimal cognition that also may have occurred in the experimental group of whom were subsequently returned to the inactivity. Thus these findings can be interpreted in the opposite way to that proposed by the authors. The loss of beneficial effects of exercise on cognitively related brain mechanisms following exercise cessation also have been shown with mice [6], in which elevated hippocampal BDNF levels receded within a few weeks of exercise cessation.

Such BDNF levels cannot be determined in humans, and although BDNF can be measured in serum the actual sources of BDNF within and outside the brain are varied [7], especially as BDNF is affected by other nonexercise influences such as energy balance [7]. While acute exercise does temporarily increase human serum BDNF [cf. 8], the relevance for potential neuroprotective effects or longer-term cognitive enhancement remains unclear in cause and effect, even though serum BDNF levels are related both to magnetic resonance imaging (MRI) determined shrinkage of the hippocampus and memory deficits for older humans [9].

Although a regimen of physical exercise can reverse potential hippocampal atrophy with increases in hippocampal blood flow and volume [10], the same effect also is apparent with a variety of nonexercise cognitive stimulations [10,11] in healthy individuals, particularly with activities involving novel experiences over a few weeks (i.e., meditation [12], driving taxis [13], revising for examinations [14]) in which hippocampal volume continued to increase well beyond the examination period in the latter case. Interestingly Lövdén et al. [15] reported that healthy younger and older men performing a cognitively demanding spatial navigation task every other day over 4 months displayed navigation-related gains in performance and more stable hippocampal volumes, compared with control participants; these improvements were maintained for several months posttraining.

For the cortex and in healthy older individuals, there are significant associations between the level of physical fitness gray matter volumes in the prefrontal cortex (PFC) and performance at those executive skills including working memory focusing on this region, comprising approximately 30% of the cortex. The PFC is particularly active in wakefulness [16] and also is the cortical region most affected by age-related cognitive decline. Two exercise studies are of particular interest here, as they indicate that there may be more to the effects of exercise on the PFC than expected. Kramer et al. [17] reported that healthy sedentary older adults showed greater improvements with PFC tasks following the walking after 6 months of either static muscle toning (indoors) vs outdoor walking exercise. However, maximal oxygen consumption only improved by a fairly small 5% following the walking (−3% for the toning) compared to what seemed to be greater improvements to executive function. Weinstein et al. [18] utilized MRI scans of PFC gray matter volume, particularly of the dorsolateral PFC in their cross-sectional study of 142 adults (mean age, 67 y) and found a positive correlation between executive task performance and physical fitness. Although it seemed that physical fitness was the mechanism promoting better PFC function, it is just as likely that both are common effects of a mentally and physically active outgoing lifestyle.

Nevertheless, Erickson and Kramer [19] concluded in their review that 6 months of moderate levels of aerobic activity for humans is sufficient to produce significant improvements with PFC executive functions and for temporal lobe gray matter volumes. However, the effects of subsequent exercise cessation were not determined. Related findings [20,21] from a year-long indoor walking program in healthy older adults also pointed to improvements in white matter integrity in these same cortical areas accompanied by a better working memory with increased aerobic fitness, but there were no improvements with other measures of executive function. Walking was on an indoor circular track without much visual novelty, and interestingly these authors noted elsewhere [22] that these improvements may have been greater with more environmental stimulation.

2. Cognitively demanding locomotion

Physical activity, especially locomotion, indicates a potential cognitive challenge to the brain to the extent that cognition is inseparable from physical activity [23,24], with locomotion serving as an intrinsic feedback mechanism to the brain. Within the context of human aging, both are involved with reciprocal stimulation of neuroplasticity [24]. Moreover, an enriched environment combined with physical activity and challenging cognitive tasks has been seen as the basis for potential interventions promoting successful aging [24].

For mammals in the wild, there is no separation of physical and cognitive activity with many mostly spending wakefulness in purposeful locomotion; the mammals are preoccupied by exploratory behaviors largely associated with foraging for food often necessitating curiosity vs the inherent risks, especially the exposure to predation and the "payoff" in the cost of the energy expended to obtain the food vs its nutritional value [cf. 25].

Beneficial effects of environmental enrichment originally focused on the developing rodent brain, and the pioneering work of Rozenzweig and Bennett [26] led to more sophisticated supportive studies [27]. In contrast, Mustroph et al. [28] recently argued that increased hippocampal neurogenesis depended more on aerobic exercise than any associated environmental enrichment, at least for rodents. Their latest study [28] comprised four groups of mice exposed to running-only, enrichment-only, running plus enrichment, and standard cage groups for 32 days. The running-only group ran equivalent distances to those in the running plus enrichment. Enrichment comprised "rotating novel tactile, visual, dietary, auditory, and vestibular stimuli into the cages." Combination of enrichment and running did not significantly increase hippocampal neurogenesis beyond that of running alone, and hence the authors' conclusions. However, one might question the realism of such studies, as these stimuli might be seen more as "playthings" within the restricted and safe confines of a cage containing ad lib forage-free food, all of which contrast with the challenges accompanying foraging in the wild. For this animal, more challenging stimulation with its smell-dominated brain might have been found in a multiodorous refuse tip with competition for foraging and inherent dangers of predation.

The impact of this cognitively demanding locomotion (CDL) in the most efficient method of improvement for brain and behavior remains poorly studied in humans, as are any consequences due to the cessation of such exercise programs and what would be required to maintain or reinstate any such benefits [11]. For older adults, physical activity in isolation may not be the key to improved cognitive abilities, but they should instead include the cognitive challenges encountered through walking within and

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