

Physical activity, brain, and cognition

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In this brief review we summarize the promising effects of physical activity and fitness on brain and cognition in children and older adults. Research in children finds that higher fit and more active preadolescent children show greater hippocampal and basal ganglia volume, greater white matter integrity, elevated and more efficient patterns of brain activity, and superior cognitive performance and scholastic achievement. Higher fit and more physically active older adults show greater hippocampal, prefrontal cortex, and basal ganglia volume, greater functional brain connectivity, greater white matter integrity, more efficient brain activity, and superior executive and memory function. Despite these promising results, more randomized trials are needed to understand heterogeneity in response to physical activity, mechanisms, and translation to public policy.

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The brain is inherently plastic; it is moldable, malleable, changes with experience and is never quiet. However, there are many factors that influence both the capability and range of brain plasticity throughout the lifespan and this is where the field of kinesiology merges with psychology and neuroscience. As will be described in this brief review, there is promising evidence that merely a modest amount of moderate intensity physical activity (PA) is necessary to take advantage of the brain's natural capacity for plasticity, resulting in improved cognitive performance, better academic achievement, and reduced risk for dementia. On the basis of the evidence described below, we argue for three overarching principles: Firstly, PA is an effective method of capitalizing on brain plasticity; secondly,

the effects of PA on brain and cognition are not uniform; some brain areas and cognitive domains are more consistently influenced by PA than others; and finally, because of the widespread effects of PA on peripheral and central physiology, there is not just one single molecular mechanism by which PA improves cognitive function, but rather a host of different pathways involved in cognitive enhancement. Yet, despite strong evidence for these general principles, we still have much to learn about PA and brain health throughout the lifespan including knowledge of dose-response, application to developmental, neurologic, and psychiatric conditions, moderators of the effects, and a better understanding of the molecular, systems, and behavioral mechanisms of PA on cognition. Answers to these, and other related, questions will be critical for transitioning PA from the laboratory environment to more widespread clinical prescription and for promoting evidence-based changes in public policy to encourage increased PA for improving cognitive function throughout the lifespan.

Childhood physical activity effects on brain and cognition

Childhood PA effects on cognition and brain is a relatively recent line of inquiry, with the seminal publication appearing 10 years ago [1]. Before that report, the body of work was predominantly directed toward the relation of PA or physical education on standardized tests of academic achievement or measures supporting academic performance [2]. However, over the past decade, considerable research efforts have focused on the benefits of PA (or aerobic fitness) on brain structure and function, cognition, and scholastic performance with the goal of understanding how these health behaviors promote effective functioning within the context of learning.

Brain structure: Research on PA and brain structure in childhood is in its infancy. Specifically, only five studies have been reported, which have used cross-sectional or relatively small sample randomized controlled designs. A few studies used diffusion tensor imaging (DTI) to investigate structural integrity of white matter tracts. Findings indicated that children who received a PA intervention had greater integrity in the uncinate fasciculus compared to the control group [3], and that attendance in the intervention related to increased integrity of the superior longitudinal fasciculus [4]. Cross-sectional studies have investigated differences in aerobic fitness on white matter integrity and subcortical structures that are critical for learning and memory. For example, Chaddock and colleagues [5] reported that higher fit children had greater white matter integrity, as indexed by fractional anisotropy, than lower fit children in several

white matter tracts including sections of the corpus callosum, corona radiata, and superior longitudinal fasciculus. Chaddock and colleagues [6,7] have also used voxel-based morphometry and observed greater gray matter volume in the hippocampus and basal ganglia (i.e., caudate nucleus, putamen, globus pallidus) in higher-fit children compared to lower-fit children. Further, higher-fit children exhibited better performance during tasks that tapped executive control and relational (i.e., associative) memory. Despite these interesting findings, the field is in need of growth to improve our understanding of PA on brain structure during development.

Brain function: Over the past decade, several correlational studies have demonstrated a relationship between PA or aerobic fitness and brain function using event-related brain potentials (ERPs) and functional magnetic resonance imaging (fMRI) techniques (e.g., [8[•],9,10[•]]). However, more recently, randomized controlled trials have demonstrated the beneficial effects of extended participation in PA programs on brain function using fMRI [11,12[•]] or ERP [13[•],14] measures. Importantly, these improvements in brain function have been accompanied by improvements in cognition, with executive control functions appearing especially susceptible to PA intervention [13[•]] — see Figure 1. Such findings

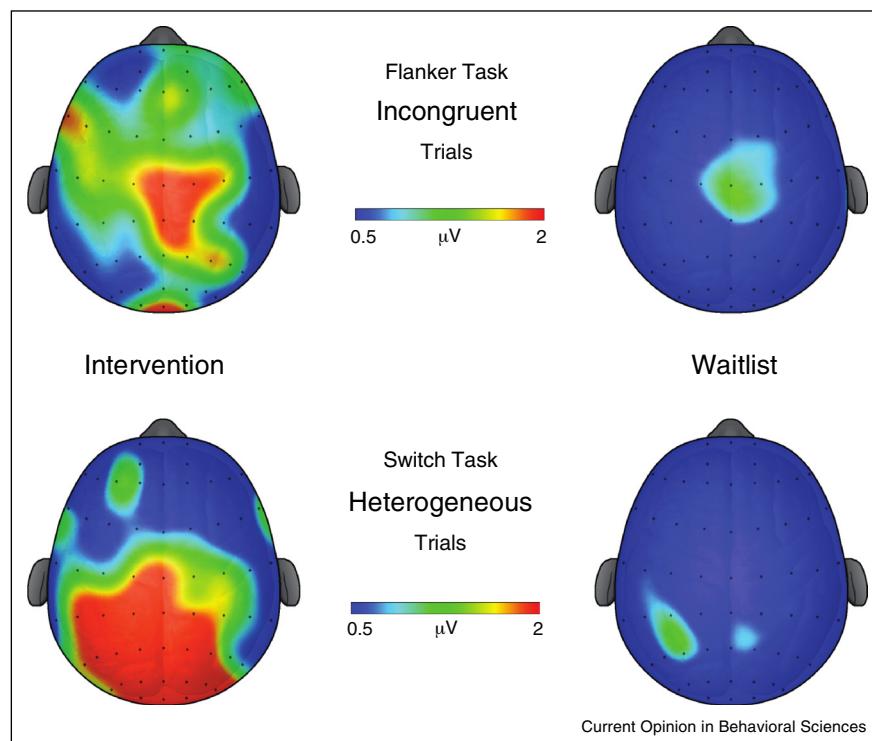
are promising and indicate that prolonged PA participation relates to improved cognition and beneficial changes to underlying brain function.

Scholastic performance: One benefit to studying the relation of PA to childhood cognition is the applicability to real-world scholastic performance. Unlike adults, who lead idiosyncratic lives, virtually all children in western culture receive some form of formal education, which provides the opportunity to assess how PA (or other health behaviors) influences performance on scholastic assessments, including standardized academic achievement tests. Although there is a general lack of consensus, the vast majority of findings point to a beneficial relation of PA and aerobic fitness to scholastic performance, with higher marks observed for academic achievement tests and classroom-based assessments [15–17].

Effects of physical activity on brain and cognition in late adulthood

The examination of the effects of PA on brain and cognition in older adulthood is more established than that of younger age groups, with many of the seminal studies published between 1975 and 2000. Although results from several of these earlier studies were equivocal about the effects of PA on cognition, more recent

Figure 1



Topographic scalp distribution of the change in P3-ERP amplitude during a flanker task (top) and a switch task (bottom) for the intervention group (left) and waitlist group (right). P3 amplitude increased in the intervention group at post-test only for conditions requiring greater amount of executive control across both tasks. Adapted from Hillman et al. [13[•]].

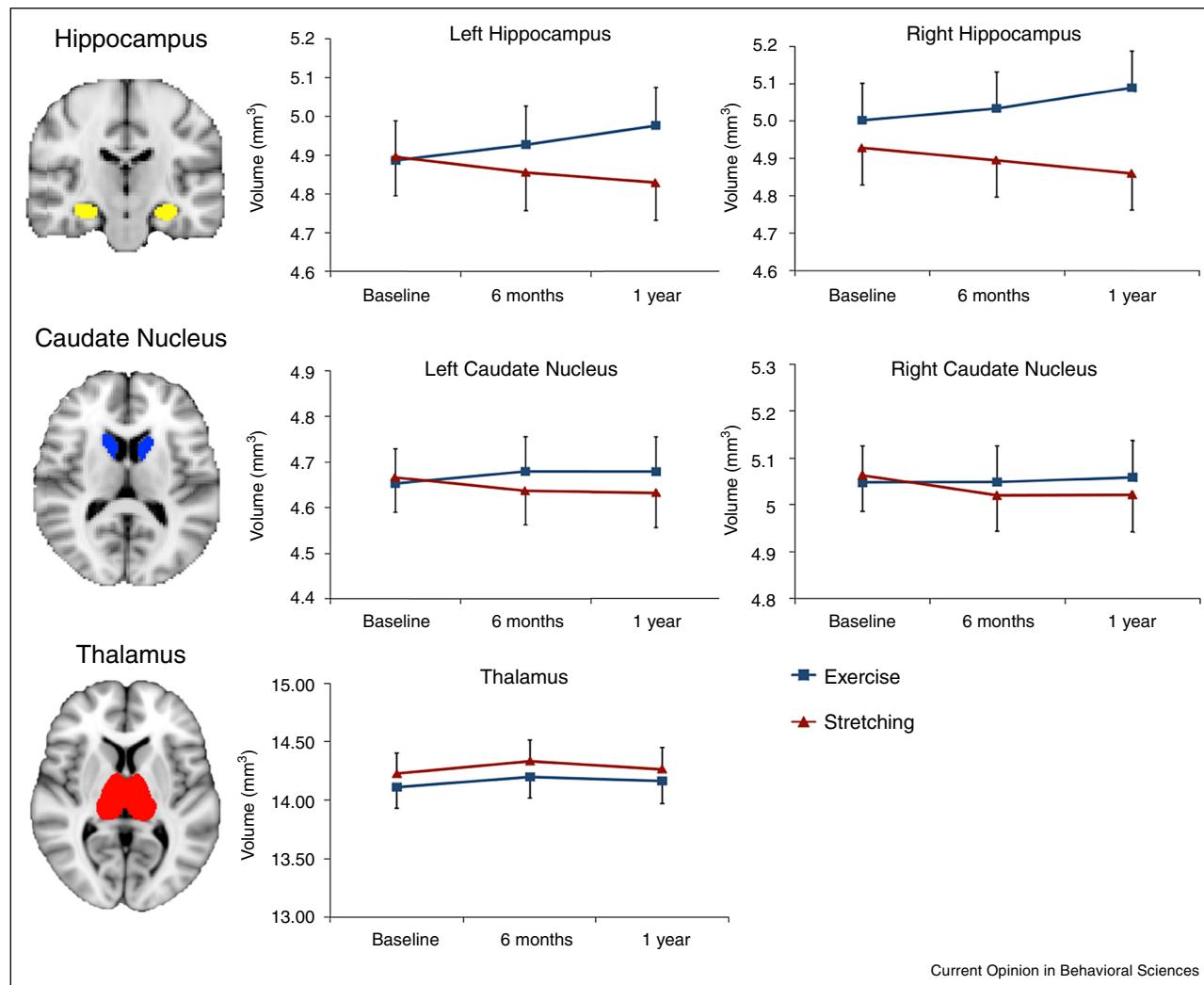
meta-analyses and neuroimaging studies have shown convincing patterns that PA is an effective method for enhancing brain and cognition in late life.

Cognitive performance: Cross-sectional, observational, and randomized clinical trials of PA in late adulthood have demonstrated that engaging in PA may preserve and/or enhance cognitive function even in cognitively impaired individuals (e.g., [18]). Summaries of these studies can now be found in several meta-analyses, most of which confirm that PA positively influences cognitive function in late adulthood with small to moderate sized effects [19]. In a meta-analysis of 18 randomized PA trials, engaging in moderate intensity PA resulted in enhanced cognitive function across all cognitive domains examined, but with the largest effect sizes for indices of executive

function [20]. Meta-analyses of longitudinal observational studies have also confirmed that self-reported engagement in PA is associated with nearly a 40% reduced risk of experiencing cognitive decline over several years [21]. These, and other studies, make a convincing argument that both continuing to engage in, and starting to engage in, PA in late adulthood may have a profound effect on maintaining cognitive health, improving function, and reducing the risk of developing cognitive impairment.

Brain structure: There have been now more than 30 published studies of PA or fitness on brain structure in older adults (>60 years) with the majority showing positive associations (see [22]). Such effects are important since increasing age is associated with brain atrophy and loss of volume, which precedes and predicts conversion to

Figure 2



A randomized physical activity intervention in 120 older adults demonstrated that moderate intensity walking exercise for one year increased the size of the hippocampus while the size of the hippocampus for the stretching and toning control group showed a slight reduction. There were no significant changes for the size of either the caudate nucleus or thalamus. Adapted from Erickson *et al.* [31*].

dementia. Higher aerobic fitness levels have been associated with larger gray matter volumes in older adults in several areas including the frontal cortex [23,24], hippocampus [25,26], and caudate nucleus [27]. Longitudinal observational studies have also shown that greater amounts of PA are associated with larger gray matter volumes in these regions, and greater volume is, in turn, associated with a reduced risk of cognitive impairment [28]. These cross-sectional and observational results in older adults are further supported by clinical trials that have shown that six-months to one-year of regular PA is associated with an increase in both frontal cortex [29^{••},30] and hippocampal volume [31^{••},32,33] — see Figure 2. These effects on gray matter volume are accompanied by differences found in white matter integrity. For example, several studies have reported that higher cardiorespiratory fitness levels and PA are associated with greater white matter integrity along several tracts linking frontal and subcortical areas [34–36] and that greater changes in fitness after an intervention was associated with an increase in white matter integrity [37]. In sum, there is now convincing evidence that PA and fitness influence brain structure, characterized by both gray matter volume and white matter integrity, in late adulthood.

Brain function: Both task-evoked fMRI and resting state studies of intrinsic brain connectivity have also been conducted in relation to participation in PA or fitness in late adulthood. These studies have found that higher fitness levels [38], greater amounts of PA [39], and randomized trials [40^{••},41] are associated with increased neural efficiency during cognitively challenging tasks. In addition, higher fitness levels and randomized interventions are associated with increased connectivity between hippocampal, prefrontal and cingulate regions [42,43[•]]. Importantly the changes that are observed in both task-evoked fMRI paradigms and in resting state paradigms are associated with improvements in cognitive performance, indicating that these changes are not meaningless by-products of engaging in exercise, but have behavioral relevance.

Conclusions and future directions

In sum, there is now substantial evidence that greater PA and higher fitness levels are associated with better brain and cognitive health for children and older adults. However, there are clearly a number of important gaps in the literature. For example, there is growing evidence that the benefits of PA may vary as a function of genetic factors [44,45[•]] and dietary factors [46], which may help explain heterogeneity in effect sizes in the literature. With regard to genetics several studies have reported that PA can reduce the potential detrimental effects of the APOE e4 allele on cognition and biomarkers for brain pathology [47[•]] but see [48]. However, most of these studies tend to have relatively small samples and focus on a single gene. Another important issue for future studies is how best to

combine different cognitive training protocols or intellectual engagement activities with PA or exercise in an effort to enhance cognitive and brain health [49–51]. Additional animal research is needed to further elucidate the molecular and cellular mechanisms that underlie the beneficial effects of exercise on cognition and performance [52]. Finally, although a number of scientific and governmental organizations have made specific recommendations for PA and exercise for different populations, we generally do a poor job of meeting even the minimal amount of activity on a weekly basis [53,54]. Therefore, it will be important to continue to examine the factors that motivate and those that detract from maintaining recommended levels of PA [55].

Conflict of interest statement

None declared.

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References

1. Hillman CH, Castelli DM, Buck SM: **Aerobic fitness and neurocognitive function in healthy preadolescent children.** *Med Sci Sports Exerc* 2005, **37**:1967–1974.
2. Sibley BA, Etner JL: **The relationship between physical activity and cognition in children: a meta-analysis.** *Pediatr Exerc Sci* 2003, **15**:243–256.
3. Schaeffer DJ, Krafft CE, Schwarz NF, Chi L, Rodrigue AL, Pierce JE, Allison JD, Yanasak NE, Liu T, Davis CL et al.: **An 8-month exercise intervention alters frontotemporal white matter integrity in overweight children.** *Psychophysiology* 2014, **51**:728–733.
4. Krafft CE, Schwarz NF, Chi L, Weinberger AL, Schaeffer DJ, Pierce JE, Rodrigue AL, Yanasak NE, Miller PH, Tomporowski PD et al.: **An 8-month randomized controlled exercise trial alters brain activation during cognitive tasks in overweight children.** *Obesity (Silver Spring)* 2014, **22**:232–242.
5. Chaddock L, Erickson KI, Holtrop JL, Voss MW, Pontifex MB, Raine LB, Hillman CH, Kramer AF: **Aerobic fitness is associated with greater white matter integrity in children.** *Front Hum Neurosci* 2014, **8**:584.
6. Chaddock L, Erickson KI, Prakash RS, Kim JS, Voss MW, VanPatter M, Pontifex MB, Raine LB, Konkel A, Hillman CH et al.: **A neuroimaging investigation of the association between aerobic fitness, hippocampal volume, and memory performance in preadolescent children.** *Brain Res* 2010, **1358**:172–183.
7. Chaddock L, Erickson KI, Prakash RS, VanPatter M, Voss MW, Pontifex MB, Raine LB, Hillman CH, Kramer AF: **Basal ganglia volume is associated with aerobic fitness in preadolescent children.** *Dev Neurosci* 2010, **32**:249–256.
8. Chaddock L, Erickson KI, Prakash RS, Voss MW, VanPatter M, Pontifex MB, Hillman CH, Kramer AF: **A functional MRI investigation of the association between childhood aerobic fitness and neurocognitive control.** *Biol Psychol* 2012, **89**:260–268.
- This study showed that higher fit children had greater hippocampal volume and performed better on a hippocampal-dependent memory task compared to lower fit children.
9. Pontifex MB, Raine LB, Johnson CR, Chaddock L, Voss MW, Cohen NJ, Kramer AF, Hillman CH: **Cardiorespiratory**

- fitness and the flexible modulation of cognitive control in preadolescent children.** *J Cogn Neurosci* 2011, **23**:1332-1345.
10. Voss MW, Chaddock L, Kim JS, Vanpatter M, Pontifex MB, Raine LB, Cohen NJ, Hillman CH, Kramer AF: **Aerobic fitness is associated with greater efficiency of the network underlying cognitive control in preadolescent children.** *Neuroscience* 2011, **199**:166-176.
- This study showed that higher fit children had greater efficiency of brain activation in neural networks supporting executive function compared to lower fit children.
11. Chaddock L, Erickson KI, Voss MW, Knecht AM, Pontifex MB, Castelli DM, Hillman CH, Kramer AF: **The effects of physical activity on functional MRI activation associated with cognitive control in children: a randomized controlled intervention.** *Front Hum Neurosci* 2013, **7**:72.
12. Davis CL, Tomporowski PD, McDowell JE, Austin BP, Miller PH, Yanasak NE, Allison JD, Naglieri JA: **Exercise improves executive function and achievement and alters brain activation in overweight children: a randomized, controlled trial.** *Health Psychol* 2011, **30**:91-98.
- This study used a randomized controlled trial with overweight children to show that physical activity selectively improved executive function in a dose-response fashion.
13. Hillman CH, Pontifex MB, Castelli DM, Khan NA, Raine LB, Scudder MR, Drollette ES, Moore RD, Wu CT, Kamijo K: **Effects of the FITKids randomized controlled trial on executive control and brain function.** *Pediatrics* 2014, **134**:e1063-e1071.
- This study used a randomized controlled trial to show that physical activity intervention increased brain activation and improved executive function in preadolescent children.
14. Kamijo K, Pontifex MB, O'Leary KC, Scudder MR, Wu CT, Castelli DM, Hillman CH: **The effects of an afterschool physical activity program on working memory in preadolescent children.** *Dev Sci* 2011, **14**:1046-1058.
15. Castelli DM, Centeio EE, Hwang J, Barcelona JM, Glowacki EM, Calvert HG, Nicksic HM: **The history of physical activity and academic performance research: informing the future.** *Monogr Soc Res Child Dev* 2015. (in press).
16. Donnelly JE, Greene JL, Gibson CA, Smith BK, Washburn RA, Sullivan DK, DuBose K, Mayo MS, Schmelzle KH, Ryan JJ et al.: **Physical activity across the curriculum (PAAC): a randomized controlled trial to promote physical activity and diminish overweight and obesity in elementary school children.** *Prev Med* 2009, **49**:336-341.
17. Hillman CH, Erickson KI, Kramer AF: **Be smart, exercise your heart: exercise effects on brain and cognition.** *Nat Rev Neurosci* 2008, **9**:58-65.
18. Lautenschlager NT, Cox KL, Flicker L, Foster JK, van Boekxmeer FM, Xiao J, Greenop KR, Almeida OP: **Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial.** *JAMA* 2008, **300**:1027-1037.
19. Smith PJ, Blumenthal JA, Hoffman BM, Cooper H, Strauman TA, Welsh-Bohmer K, Browndyke JN, Sherwood A: **Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials.** *Psychosom Med* 2010, **72**:239-252.
20. Colcombe S, Kramer AF: **Fitness effects on the cognitive function of older adults: a meta-analytic study.** *Psychol Sci* 2003, **14**:125-130.
21. Sofi F, Valecchi D, Bacci D, Abbate R, Gensini GF, Casini A, Macchi C: **Physical activity and risk of cognitive decline: a meta-analysis of prospective studies.** *J Intern Med* 2011, **269**:107-117.
22. Erickson KI, Leckie RL, Weinstein AM: **Physical activity, fitness, and gray matter volume.** *Neurobiol Aging* 2014, **35**(Suppl. 2): S20-S28.
23. Colcombe SJ, Erickson KI, Raz N, Webb AG, Cohen NJ, McAuley E, Kramer AF: **Aerobic fitness reduces brain tissue loss in aging humans.** *J Gerontol A Biol Sci Med Sci* 2003, **58**:176-180.
24. Weinstein AM, Voss MW, Prakash RS, Chaddock L, Szabo A, White SM, Wojcicki TR, Mailey E, McAuley E, Kramer AF et al.: **The association between aerobic fitness and executive function is mediated by prefrontal cortex volume.** *Brain Behav Immun* 2012, **26**:811-819.
25. Erickson KI, Prakash RS, Voss MW, Chaddock L, Hu L, Morris KS, White SM, Wojcicki TR, McAuley E, Kramer AF: **Aerobic fitness is associated with hippocampal volume in elderly humans.** *Hippocampus* 2009, **19**:1030-1039.
26. Makizako H, Liu-Ambrose T, Shimada H, Doi T, Park H, Tsutsumimoto K, Uemura K, Suzuki T: **Moderate-intensity physical activity, hippocampal volume, and memory in older adults with mild cognitive impairment.** *J Gerontol A Biol Sci Med Sci* 2014.
27. Verstynen TD, Lynch B, Miller DL, Voss MW, Prakash RS, Chaddock L, Basak C, Szabo A, Olson EA, Wojcicki TR et al.: **Caudate nucleus volume mediates the link between cardiorespiratory fitness and cognitive flexibility in older adults.** *J Aging Res* 2012, **2012**:939285.
28. Erickson KI, Raji CA, Lopez OL, Becker JT, Rosano C, Newman AB, Gach HM, Thompson PM, Ho AJ, Kuller LH: **Physical activity predicts gray matter volume in late adulthood: the Cardiovascular Health Study.** *Neurology* 2010, **75**:1415-1422.
29. Colcombe SJ, Erickson KI, Scalf PE, Kim JS, Prakash R, McAuley E, Elavsky S, Marquez DX, Hu L, Kramer AF: **Aerobic exercise training increases brain volume in aging humans.** *J Gerontol A Biol Sci Med Sci* 2006, **61**:1166-1170.
- This study demonstrated that a randomized exercise intervention increased gray matter volume in older adults.
30. Ruscheweyh R, Willemer C, Kruger K, Duning T, Warnecke T, Sommer J, Volker K, Ho HV, Mooren F, Knecht S et al.: **Physical activity and memory functions: an interventional study.** *Neurobiol Aging* 2011, **32**:1304-1319.
31. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, Kim JS, Heo S, Alves H, White SM et al.: **Exercise training increases size of hippocampus and improves memory.** *Proc Natl Acad Sci U S A* 2011, **108**:3017-3022.
- This study demonstrated that a one-year exercise intervention increased the size of the hippocampus in older adults.
32. Niemann C, Godde B, Voelcker-Rehage C: **Not only cardiovascular, but also coordinative exercise increases hippocampal volume in older adults.** *Front Aging Neurosci* 2014, **6**:170.
33. Ten Brinke LF, Bolandzadeh N, Nagamatsu LS, Hsu CL, Davis JC, Miran-Khan K, Liu-Ambrose T: **Aerobic exercise increases hippocampal volume in older women with probable mild cognitive impairment: a 6-month randomised controlled trial.** *Br J Sports Med* 2014.
34. Burzynska AZ, Chaddock L, Voss MW, Wong CN, Gothe NP, Olson EA, Knecht A, Lewis A, Monti JM, Cooke GE et al.: **Physical activity and cardiorespiratory fitness are beneficial for white matter in low-fit older adults.** *PLOS ONE* 2014, **9**:e107413.
35. Johnson NF, Kim C, Clasey JL, Bailey A, Gold BT: **Cardiorespiratory fitness is positively correlated with cerebral white matter integrity in healthy seniors.** *Neuroimage* 2012, **59**:1514-1523.
36. Tian Q, Erickson KI, Simonsick EM, Aizenstein HJ, Glynn NW, Boudreau RM, Newman AB, Kritchevsky SB, Yaffe K, Harris TB: **Physical activity predicts microstructural integrity in memory-related networks in very old adults.** *J Gerontol A Biol Sci Med Sci* 2014, **69**:1284-1290.
37. Voss MW, Heo S, Prakash RS, Erickson KI, Alves H, Chaddock L, Szabo AN, Mailey EL, Wojcicki TR, White SM et al.: **The influence of aerobic fitness on cerebral white matter integrity and cognitive function in older adults: results of a one-year exercise intervention.** *Hum Brain Mapp* 2013, **34**:2972-2985.
38. Prakash RS, Voss MW, Erickson KI, Lewis JM, Chaddock L, Malkowski E, Alves H, Kim J, Szabo A, White SM et al.: **Cardiorespiratory fitness and attentional control in the aging brain.** *Front Hum Neurosci* 2011, **4**:229.
39. Smith JC, Nielson KA, Woodard JL, Seidenberg M, Verber MD, Durgerian S, Antuono P, Butts AM, Hantke NC, Lancaster MA et al.: **Does physical activity influence semantic memory**

- activation in amnestic mild cognitive impairment? Psychiatry Res** 2011, **193**:60-62.
40. Colcombe SJ, Kramer AF, Erickson Kl, Scalf P, McAuley E, Cohen NJ, Webb A, Jerome GJ, Marquez DX, Elavsky S: **Cardiovascular fitness, cortical plasticity, and aging.** *Proc Natl Acad Sci U S A* 2004, **101**:3316-3321.
This study was the first to demonstrate the positive effects of a randomized exercise intervention on functional MRI activation.
41. Smith JC, Nielson KA, Woodard JL, Seidenberg M, Rao SM: **Physical activity and brain function in older adults at increased risk for Alzheimer's disease.** *Brain Sci* 2013, **3**:54-83.
42. Burdette JH, Laurienti PJ, Espeland MA, Morgan A, Telesford Q, Vechlekar CD, Hayasaka S, Jennings JM, Katula JA, Kraft RA: **Using network science to evaluate exercise-associated brain changes in older adults.** *Front Aging Neurosci* 2010, **2**.
43. Voss MW, Prakash RS, Erickson Kl, Basak C, Chaddock L, Kim JS, Alves H, Heo S, Szabo AN, White SM et al.: **Plasticity of brain networks in a randomized intervention trial of exercise training in older adults.** *Front Aging Neurosci* 2010, **2**.
This study demonstrated that participating in one year of exercise could alter the brains intrinsic connectivity between frontal, hippocampal, and parietal regions.
44. Erickson Kl, Banducci SE, Weinstein AM, Macdonald AW 3rd, Ferrell RE, Halder I, Flory JD, Manuck SB: **The brain-derived neurotrophic factor Val66Met polymorphism moderates an effect of physical activity on working memory performance.** *Psychol Sci* 2013, **24**:1770-1779.
45. Smith JC, Nielson KA, Woodard JL, Seidenberg M, Durgerian S, Hazlett KE, Figueiro CM, Kandah CC, Kay CD, Matthews MA et al.: **Physical activity reduces hippocampal atrophy in elders at genetic risk for Alzheimer's disease.** *Front Aging Neurosci* 2014, **6**:61.
This study found that participating in greater amounts of physical activity reduced the consequences of the APOE e4 gene polymorphism on loss in hippocampal volume.
46. Leckie RL, Manuck SB, Bhattacharjee N, Muldoon MF, Flory JM, Erickson Kl: **Omega-3 fatty acids moderate effects of physical activity on cognitive function.** *Neuropsychologia* 2014, **59**: 103-111.
47. Head D, Bugg JM, Goate AM, Fagan AM, Mintun MA, Benzinger T, Holtzman DM, Morris JC: **Exercise engagement as a moderator of the effects of APOE genotype on amyloid deposition.** *Arch Neurol* 2012, **69**:636-643.
This study showed that physical activity may mitigate the effects of the APOE e4 gene polymorphism on amyloid plaque pathology.
48. Lindsay J, Laurin D, Verreault R, Hebert R, Helliwell B, Hill GB, McDowell I: **Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health and Aging.** *Am J Epidemiol* 2002, **156**:445-453.
49. Anderson-Hanley C, Arciero PJ, Brickman AM, Nimon JP, Okuma N, Westen SC, Merz ME, Pence BD, Woods JA, Kramer AF et al.: **Ergaming and older adult cognition: a cluster randomized clinical trial.** *Am J Prev Med* 2012, **42**:109-119.
50. Fabre C, Chamari K, Mucci P, Masse-Biron J, Prefaut C: **Improvement of cognitive function by mental and/or individualized aerobic training in healthy elderly subjects.** *Int J Sports Med* 2002, **23**:415-421.
51. Theill N, Schumacher V, Adelsberger R, Martin M, Jancke L: **Effects of simultaneously performed cognitive and physical training in older adults.** *BMC Neurosci* 2013, **14**:103.
52. Voss MW, Erickson Kl, Prakash RS, Chaddock L, Kim JS, Alves H, Szabo A, Phillips SM, Wojcicki TR, Mailey EL et al.: **Neurobiological markers of exercise-related brain plasticity in older adults.** *Brain Behav Immun* 2013, **28**:90-99.
53. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD, Bauman A: **Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association.** *Med Sci Sports Exerc* 2007, **39**:1423-1434.
54. Tucker JM, Welk GJ, Beyler NK: **Physical activity in U.S.: adults compliance with the Physical Activity Guidelines for Americans.** *Am J Prev Med* 2011, **40**:454-461.
55. McAuley E, Mullen SP, Szabo AN, White SM, Wojcicki TR, Mailey EL, Gothe NP, Olson EA, Voss M, Erickson K et al.: **Self-regulatory processes and exercise adherence in older adults: executive function and self-efficacy effects.** *Am J Prev Med* 2011, **41**:284-290.