Review

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Cognitive Benefits of Exercise Intervention

T. Archer[1,3], S. Ricci[2], F. Massoni[2], L. Ricci[2], Max Rapp-Ricciardi[1,3]

[1]University of Gothenburg, Department of Psychology, Box 500, SE 40530 Gothenburg, Sweden; [2]Department of Anatomical, Histological, Medical Legal and Locomotive System Sciences, La Sapienza University of Rome, Italy; [3] Network for Empowerment and Well Being, Sweden

Abstract

Exercise, as a potent epigenetic regulator, implies the potential to counteract pathophysiological processes and alterations in most cardiovascular/respiratory cells and tissues not withstanding a paucity of understanding the underlying molecular mechanisms and dose-response relationships. In the present account, the assets accruing from physical exercise and its influence upon executive functioning are examined. Under conditions of neuropsychiatric and neurologic ill-health, age-related deterioration of functional and biomarker indicators during healthy and disordered trajectories, neuroimmune and affective unbalance, and epigenetic pressures, exercise offers a large harvest of augmentations in health and well-being. Both animal models and human studies support the premise of manifest gains from regular exercise within several domains, besides cognitive function and mood, notably as the agency of a noninvasive, readily available therapeutic intervention. ***Clin Ter 2016; 167(6):e180-185. doi: 10.7417/CT.2016.1965***

Key words: *Exercise, cognition, executive function, biomarkers, ageing, performance*

Introduction

In the present account the exercise as a potent epigenetic regulator and the assets accruing from physical exercise and its influence upon executive functioning are examined by a literature review.

In addition to provide therapeutic benefits by increasing the muscle thickness and function (1), the cognitive benefits accruing from activity and exercise by the aged have been demonstrated repeatedly (2). In general, physical exercise intervention studies present significant and large improvements in physical capacity, in some cognitive and cognitive-affective domains, and in quality of life. These benefits seem to be more-or-less equivalent between frail and non-frail participants (3). The cognitive domains most sensitive to aging include executive functions such as planning, inhibition, task switching, maintenance and manipulation of information (4,5), processing speed and episodic memory, i.e., memory of previous events (6,7). The aging-related decline in cognitive function may be exacerbated by cardiovascular disease and cardiovascular risk factors, such as hypertension, diabetes, obesity, elevated total cholesterol, chronic inflammatory condition (8,9).

Moderate aerobic effort has positive effects on fibrinolysis, blood viscosity and vascular tone (10). Aerobic exercise programs appear to hold promise for decelerating the progression of age-related neural changes and thereby reducing the risk for mild cognitive impairment as well as dementia. These programs combined with elevations of cortico-releasing factor are associated with increased cerebral blood volume and hippocampal neurogenesis (11), cerebral perfusion (12), altered white matter (13,14), and enhanced functional connectivity within neural networks that determine executive function and episodic memory (15-17). In a study controlling for demographics, chronic health problems, and acculturation in elderly Latinos assigned to both light and moderate/vigorous-intensity physical activity (PA), Wilbur et al. (18) observed that the cognitive benefits, including episodic memory and executive function (inference control, inattention, and word fluency, were evident for both light-intensity and moderate/vigorous physical activity, although these effects appear to be domain-specific. Importantly, as indicated by Hayes et al. (19), aerobic-based activities that require coordination, e.g. ballroom dancing or 'water aerobics' or skiing/ice-skating, in combination with strength training would be expected to produce further cognitive and brain-health benefits. Taken together, these diverse studies serve to emphasize the influence of physical exercise in the augmentation of the cognitive involved spatial learning and memory together with the cellular and molecular mechanisms involved in neuroplasticity (20).

Executive functioning associated with the prefrontal cortex is often an earlier marker of age decline in cognition (21), e.g. disruption of white matter tracts, especially within the PFC, may be a mechanism for age-related changes in memory functioning (22). Within this context of age-linked vulnerability, neurotrophic and inflammatory processes appear to induce opposite effects on neuroplasticity and neuroreparation, but also produce opposite effects on mitochondrial functions, oxidative phosphorylation and glycolytic

Correspondence: E-mail:serafino.ricci@uniroma1.it

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processes, as modulated by stress and glucocorticoid action (23, 24); these oxidative metabolism disorders, implicated in neurologic and psychiatric conditions may have an onset far pre-dating symptom debut. Brain-derived neurotrophic factor (BDNF) conjoins physical activity to changes in respiratory efficiency and these effects may be opposed by inflammatory cytokines, implicated in neurodegenerative conditions (25). A period of supervised regular exercise improves the pulmonary function (26). Leckie et al. (27) examined BDNF serum levels, as a mediator of the effects of a 1-year walking intervention on executive function, in 90 older adults with a mean age of around 66 years. They observed that age moderated the effect of intervention group on changes in BDNF levels, with those in the highest age quartile showing the greatest increase in BDNF after 1-year of moderate intensity walking exercise, and concluded that both age and BDNF serum levels are essential factors that ought to be taken into account in considerations of the mechanisms through which chosen exercise interventions influence cognitive outcomes, particularly in elderly populations. In a 16-week multimodal physical exercise program on peripheral BDNF levels and on Tumor Necrosis-α (TNF-α) and Interleukin- 6 (IL-6) as pro-inflammatory markers in cognitive healthy elderly individuals and in elderly with mild cognitive impairment (MCI), Nascimento et al. (28) assessed cognitive functions (Montreal Cognitive Assessment), prior to and after the exercise intervention. They assigned thirty cognitively healthy participants and thirty-seven MCI participants control and exercise-trained groups. The exercise-trained participated in a multimodal physical training program over a 16-week period. The results showed a significant difference in between-subjects interaction, which indicates the beneficial contribution of training on the reduction of TNF-α and IL-6 and on the improvement of BDNF peripheral concentrations. Cognitive functions also presented significant improvements for MCI trained group. In conclusion, physical exercise was effective to reduce pro-inflammatory cytokines and to improve BDNF peripheral levels, with positive reflexes on cognition. It is likely that this study provides the first evidence of the longitudinal effects of a multimodal physical exercises protocol on peripheral concentrations of pro-inflammatory cytokines and related cognition performance in elderly MCI individuals (29).

In a cross-sectional sample of 382 women over 50-years-of-age, Valdes et al. (30) observed a strong correlation between leukocyte telomere length and a subset of cognitive performance measures, implying that telomere length may offer a biomarker for cognitive aging in women prior to the onset of dementia (see also Cherkas et al. and telomere connection, below) (31). In groups of elderly participants, exercised versus sedentary, regular physical exercise promoted behavioral and electrophysiological performance pertaining to executive control and contributed evidence for the beneficial effects of open-skill exercise on the task-switching paradigm (32).In a comparison of cognitive training versus cognitive training plus exercise training in a sample of healthy elderly individuals, considerable gains were obtained by the exercise group with regard to cognitive state, letter verbal fluency, and immediate and delayed verbal memory (33). Executive functioning offers a cornerstone of an individual's cognitive sufficiency, capacity and functional integrity: improvements in executive functioning were shown to be related to adherence to exercise post- intervention (34) whereas Anderson-Hanley et al. (35) found that for older adults aerobic "exergaming", video games that are also a form of exercise relying on technology that tracks body movement or reactions, yielded greater cognitive benefit than traditional exercise alone. In a follow-up study that examined the relationship between executive function, self-regulation, and exercise behavior in the post-intervention (naturalistic) period, Anderson-Hanley et al. (35) obtained an important relationship between executive functioning, self-regulation, and exercise behaviors during the employment of ever-gaming with individuals presenting poorer executive functioning are likely to ever-game more frequently.

Physical exercise exerts a positive impact on physical health through various different avenues, for example, exercise has been shown to affect positively cognitive performance based upon a relocation of cortical activity which seems to contribute the development of brain connectivity. Wollseiffen et al. (36) studied the effects of different types of breaks (work-pauses) upon the cognitive performance and related cortical activity among office-based employees. The working-day was organized such that breaks were filled with exercise, resting or a usual break compared with a control condition wherein employees continued working without any break. Cognitive performance was assessed using the d2-R test, a test of attention, and two commercially available cognitive tasks. Brain cortical activity was recorded using electroencephalography before and after the breaks. Each individual's mood was analysed using a profile of mood state. Their results indicated a positive effect of a 3-min 'boxing intervention' on cognitive performance, mirrored by a decrease in prefrontal cortex activity. Although perceived psychological state was increased after the usual break, this is reflected in neither cortical activity nor cognitive performance. Since bike activity resulted also in an increase in brain prefrontal region α-2 activity, a positive effect of exercise on neuro-cognitive performance was concluded. Similarly, high-intensity interval training, as opposed to moderate-intensity continuous training, performed in a real-world gym setting improves cardio-metabolic risk factors and psychological health in physically inactive adults, as well as ensuring greater adherence and compliance (37). Following a six-week exercise program, Wagner et al. (38) obtained an improvement of physical fitness in most subjects, healthy young adults with regard to cytokine and BDNF integrity, and a positive correlation between the degree of fitness improvement and increased brain-derived neurotrophic factor (BDNF) levels. Increased levels of biomarkers for BDNF, e.g. BDNF-positive cells and serum BDNF, are associated with improved cognitive performance and psychological health (39-41).

Physical exercise assets

Physical exercise offers both ontogenetic and epigenetic propensities that attest to benefits within several health domains affecting neurobehavioral, brain regional, cellular and physiological mechanisms. Psychological well-being, cognitive, emotional, motor, behavioral, clinical, recuperative,

epigenetic and health domains all make considerable impact upon individuals' propensity for and compliance with regular exercise and physical activity and *visa versa* throughout the lifespan development (42-48, 50-58). Generally, four types of well-being are considered: (i) Hedonic well-being which consists of deriving pleasure and happiness from different aspects of life ("feeling good"), (ii) Eudaimonia which consists of a mature and actively virtuous life-style ("doing good"), (iii) Wellness which consists of the absence of disease or infirmity ("good physical health"), and (iv) Prosperity which consists of consisting of success in endeavors and good fortune ("prosperity"). In contrast, ill-being has been defined as the absence of health, happiness and prosperity due to infirmity or physical disability, unhappy or dissatisfied, socially isolated or alienated, unsuccessful or unfulfilled. Health has been described variously to conform with a state of physical, mental and social well-being through which individuals apply their own abilities, cope with the normal stresses of life, live and work productively, fruitfully and constructively, with adequate community contribution (48, 49). Parkinson's disease is associated with a variety of non-motor symptoms, such as problems of remembering and mood, that significantly reduce quality of life, even in the early stages of the disease (59-61). Reynolds et al. (62) have outlined the means through which, across the stages of the disease, physical exercise exercise-interventions contribute a treatment strategy with the unique ability to ameliorate a range of non-motor symptoms while also alleviating the classic motor symptoms of the disease. Neuroinflammation imparts a markedpathological feature of neurogenerative disorders by advancing the neurotoxic back-drop to the observed cognitive deterioration (63-65). Accumulated dysregulation of hippocampal neurogenesis provides a critical mechanism underlying the cognitive impairment associated both with normal aging and the neurocognitive deficits presented in preclinical models of Alzheimer's disease and other forms of neuropathology (66). Ryan and Nolan (67) have examined notions concerning exercise-induced effects on hippocampal neurogenesis, cognitive functioning and neuroinflammation; the postulate the physical exercise presents greater potential as a pro-neurogenic and anti-inflammatory (as in cardiac disease) (68), non-invasive, non-pharmacological intervention for cognitively-based neurological disorder accumulated much preponderance.

Physical exercise and executive function

Non-pharmacological therapies, such as physical exercise interventions, present an appealing alternative or add-on to current pharmacological treatment of cognitive symptoms in patients with dementia. Executive functioning involves several of the highest levels of behavioral functions peculiar to homo sapiens, including complex planning, working memory, reasoning, task flexibility, abstract thinking, problem-solving and developing empathy and attachment (69-72). Moderate-intensity continuous exercise has been found to promote acutely the facilitation of executive functioning likely through the selective activation of neurophysiological and psychological processes (73, 74). A primary phase of an overall meta-analysis revealed a positive overall effect of physical exercise interventions on cognitive function. The secondary phase analyses yielded evidence that physical activity interventions were equally beneficial in patients with Alzheimer's disease and in patients with AD or a non-AD related dementia diagnosis (75). The combined (i.e. aerobic and non-aerobic) exercise interventions and aerobic-only exercise interventions exerted a positive effect on cognitive performance whereas this association was absent for non-aerobic exercise interventions. In conclusion, the authors found that interventions offered at both high frequency and at low frequency exerted positive effects on cognitive function. The findings of meta-analysis imply that physical activity interventions influence positively cognitive function in patients presenting dementia. Barcelos et al. (76) assessed the influence of exercise on executive functioning under conditions of low- and high-demand cognitive tasks, using the ever-gaming technique, in older adults. Individuals in the high cognitive demand group performed at a higher level compared to those individuals in the low cognitive dose condition. Everyday functioning improved across both exercise conditions (mental and physical). Their preliminary results indicated that for older adults, cognitive benefit while exer-gaming increased concomitantly with higher doses of interactive mental challenges.

Exercise "stress tests" are applied widely to assess cardiovascular function and to detect abnormalities in the study of cognitive processes, in particular executive functioning. Tsukamoto et al. (77) studied the extent to which high-intensity interval exercise impacted upon post-exercise executive functioning immediately after and during post-exercise recovery in twelve healthy male subjects using cycle ergometer with executive functioning assessed by Stroop test, pre-exercise and post-exercise. Although the functional improvement was equivalent for both high-intensity interval exercise and moderate-intensity continuous exercise, the former improvement, concurrent with both physiological and psychological changes, was sustained during the 30-min post-exercise recovery in the former case whereas in the latter case functioning returned to pre-exercise levels. Higher levels of objectively measured moderate to vigorous physical activity, rather than light physical activity extent or sedentary time extent, were associated with lower prevalence of cognitive impairment and better performance in memory and executive function in aging individuals (78). The effects of different types of martial arts physical training was studied in middle-aged adults with executive functioning, cognitive performance assessed by the Stroop Color and Word test. Although all three exercise conditions, two types of martial art training and aerobic exercise (walking), improved attention and processing speed, only the two martial art conditions improved the highest order of cognitive performance, executive function. The effect of the 2 martial art conditions on executive function was not different. The improvement in executive function was due possibly to the increased cortical demand required by the more complex, coordinated motor tasks of martial art exercise compared to the more repetitive actions of walking (79). Scott et al. (80) administered a comprehensive neuropsychological battery and underwent a Six Minute Walk Test, with blood pressure measures, from which pulse pressure was derived as an indicator of vascular auto-regulation, obtained immediately before and after the walk to normal older adults. The worse levels of

executive function scores exhibited a stronger relationship with post-exercise pulse pressure than pre-exercise pulse pressure implying that this measure, following system stress in the form of walking, may be more reflective of the state of vascular integrity and associated executive dysfunction in older adults than baseline physiological measures.

The promotion of physical activity programs in order to improve inmates QoL and allow a better social integration (81) and in many diseases the interventions aimed at improving rehabilitation programs, regular psychosocial support, and follow-up may give persons a more satisfying lifestyle (82).

Conclusion

Several manifestations of physical exercise providing health benefits for aging individuals are evident in healthy and functional muscles and bones, increased strength and endurance, angiogenesis and neurogenesis, the reduced risk for chronic disease such as overweight and diabetes, improved self-esteem and psychological well-being, and higher levels of subjective and psychological well-being as well as reduced stress, anxiety and depression. Since a sedentary lifestyle impacts adversely on happiness, psychological well-being and several important positive personal attributes, most physical activity interventions, if properly designed and maintained appear to promise a satisfying degree of improvement. Physical exercise influences cognitive, emotional, learning, daily activities and neurophysiological domains, both directly and indirect (83), thereby rendering it essential that this noninvasive, nonpharmacological intervention ought to form a part of children's and adolescents' long-term health programs.

References

1. Leonard JH, Paungmali A, Sitilertpisan P, et al. Changes in Transversus Abdominis Muscle Thickness after Lumbo-Pelvic Core Stabilization Training among Chronic Low Back Pain Individuals. Clin Ter 2015; 166(5):e312-6.
2. Zheng Z. et al. Combined cognitive-psychological-physical intervention induces reorganization of intrinsic functional brain architecture in older adults. Neural Plast 2015; 713104
3. Bherer L. Cognitive plasticity in older adults: effects of cognitive training and physical exercise. Ann N Y Acad Sci 2015; 1337(1):1-6
4. Goh JO, An Y, Resnick SM. Differential trajectories of age-related changes in components of executive and memory processes. Psychol Aging 2012; 27:707–19
5. Head D, Kennedy KM, Rodrigue KM, et al. Age differences in perseveration: cognitive and neuroanatomical mediators of performance on the Wisconsin Card Sorting Test. Neuropsychologia 2009; 47:1200–3
6. Anderson ND. et al. Recollection- and familiarity-based memory in healthy aging and amnestic mild cognitive impairment. Neuropsychology 2008; 22:177–87
7. Bender AR, Naveh-Benjamin M, Raz N. Associative deficit in recognition memory in a lifespan sample of healthy adults. Psychol Aging 2010; 25:940–8
8. Cohen RA. et al. Vascular and cognitive functions associated with cardiovascular disease in the elderly. J Clin Exp Neuropsychol 2009; 31:96–110.
9. O'Brien PD, Hur J, Hayes JM, Backus C, Sakowski SA, Feldman EL. BTBR ob/ob mice as a novel diabetic neuropathy model: Neurological characterization and gene expression analyses. Neurobiol Dis 2015; 73:348-55
10. Conti AA, Macchi C. Protective effects of regular physical activity on human vascular system. Clin Ter 2013; 164(4):293-4
11. Pereira AC. et al. An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. Proc Natl Acad Sci 2007; 104:5638–43
12. Chapman SB. et al. Shorter term aerobic exercise improves brain, cognition, and cardiovascular fitness in aging. Front Aging Neurosci 2013; 5:75
13. Johnson NF, Kim C, Clasey JL, et al. Cardiorespiratory fitness is positively correlated with cerebral white matter integrity in healthy seniors. Neuroimage 2012; 59:1514–23
14. Tseng BY. et al. White matter integrity in physically fit older adults. Neuroimage 2013; 82:510–6
15. Nouchi R. et al. Beneficial effects of short-term combination exercise training on diverse cognitive functions in healthy older people: study protocol for a randomized controlled trial. Trials 2012; 13:200
16. Ruscheweyh R. et al. Physical activity and memory functions: an interventional study. Neurobiol Aging 2011; 32(7):1304-19
17. van de Rest O. et al. Effect of resistance-type exercise training with or without protein supplementation on cognitive functioning in frail and pre-frail elderly: secondary analysis of a randomized, double-blind, placebo-controlled trial. Mech Ageing Dev 2014; 136-137:85-93
18. Wilbur J. et al. The relationship between physical activity and cognition in older Latinos. J Gerontol B Psychol Sci Soc Sc 2012; 67(5):525-34
19. Hayes SM, Alosco ML, Forman DE. The Effects of Aerobic Exercise on Cognitive and Neural Decline in Aging and Cardiovascular Disease. Curr Geriatr Rep 2014; 3(4):282-90
20. Cassilhas RC, Tufik S, de Mello MT. Physical exercise, neuroplasticity, spatial learning and memory. Cell Mol Life Sci. 2015 Dec 8. PMID: 26646070
21. Hakun JG, Zhu Z, Johnson NF, Gold BT. Evidence for reduced efficiency and successful compensation in older adults during task switching. Cortex 2015; 64:352-62
22. Nordahl CW. et al. White matter changes compromise prefrontal cortex function in healthy elderly individuals. J Cogn Neurosci 2006; 18(3):418-29
23. Gibson GE, Starkvo A, Blass JP, et al. Cause and consequence: mitochondrial dysfunction initiates and propagates neuronal dysfunction, neuronal death and behavioral abnormalities in age-associated neurodegenerative diseases. Biochim Biophys Acta 2010; 1802(1):122-34
24. Zhao W. et al. Impaired mitochondrial energy metabolism as a novel risk factor for selective onset and progression of dementia in oldest-old subjects. Neuropsychiatr Dis Treat 2015; 11:565-74
25. Markham A, Bains R, Franklin P, et al. Changes in mitochondrial function are pivotal in neurodegenerative and psychiatric disorders: how important is BDNF? Br J Pharmacol 2014; 171(8):2206-29

26. Christopher LK, Kosai NR, Reynu R, et al. Effect of Exercise on Pulmonary Function Tests in Obese Malaysian Patients. Clin Ter 2015; 166(3):105-9
27. Leckie RL. et al. BDNF mediates improvements in executive function following a 1-year exercise intervention. Front Hum Neurosci 2014; 8:985
28. Nascimento CM, et al. Physical exercise in MCI elderly promotes reduction of pro-inflammatory cytokines and improvements on cognition and BDNF peripheral levels. Curr Alzheimer Res 2014; 11(8):799-805
29. Nascimento CM. et al. Physical exercise improves peripheral BDNF levels and cognitive functions in mild cognitive impairment elderly with different bdnf Val66Met genotypes. J Alzheimers Dis 2015; 43(1):81-91
30. Valdes AM. et al. Leukocyte telomere length is associated with cognitive performance in healthy women. Neurobiol Aging 2010; 31(6):986-92
31. Cherkas LF. et al. The effects of social status on biological aging as measured by white-blood-cell telomere length. Aging Cell 2006; 5(5):361-5
32. Tsai CL, Wang WL. Exercise-mode-related changes in task-switching performance in the elderly. Front Behav Neurosci 2015; 9:56
33. Rahe J. et al. Effects of cognitive training with additional physical activity compared to pure cognitive training in healthy older adults. Clin Interv Aging 2015; 10:297-310
34. Best JR, Nagamatsu LS, Liu-Ambrose T. Improvements to executive function during exercise training predict maintenance of physical activity over the following year. Front Hum Neurosci 2014; 8:353
35. Anderson-Hanley C. et al. Executive function and self-regulated exergaming adherence among older adults. Front Hum Neurosci 2014; 8:989
36. Wollseiffen P. et al. Short Bouts of Intensive Exercise During the Workday Have a Positive Effect on Neuro-cognitive Performance. Stress Health. 2015 Oct 9. doi: 10.1002/smi.2654
37. Shepherd SO. et al. Low-Volume High-Intensity Interval Training in a Gym Setting Improves Cardio-Metabolic and Psychological Health. PLoS One 2015; 10(9):e0139056
38. Wagner G. et al. Hippocampal structure, metabolism, and inflammatory response after a 6-week intense aerobic exercise in healthy young adults: a controlled trial. J Cereb Blood Flow Metab 2015; 35(10):1570-8
39. Kim K. et al. Effects of treadmill exercise-intensity on short-term memory in the rats born of the lipopolysaccharide-exposed maternal rats. J Exerc Rehabil 2015; 11(6):296-302
40. Takamatsu Y, Tamakoshi K, Waseda Y, et al. Running exercise enhances motor functional recovery with inhibition of dendritic regression in the motor cortex after collagenase-induced intracerebral hemorrhage in rats. Behav Brain Res 2015; 300:56-64
41. Xiong JY. et al. Long-term treadmill exercise improves spatial memory of male APPswe/PS1dE9 mice by regulation of BDNF expression and microglia activation. Biol Sport 2015; 32(4):295-300
42. Archer T. Physical exercise alleviates debilities of normal aging and Alzheimer's disease. Acta Neurol Scand 2011; 123:221-38
43. Archer T. Influence of physical exercise on traumatic brain injury deficits: scaffolding effect. Neurotox Res 2012; 21:418-34
44. Archer T. Influence of physical exercise on traumatic brain injury deficits: scaffolding effect. Neurotox Res. 2012; 21(4):418-34
45. Archer T. Health benefits of physical exercise for children and adolescents. J Novel Psychother 2014; 4:203
46. Archer T. Physical exercise as an epigenetic factor determining behavioral outcomes. Clin Exp Psych 2015; 1:1. DOI: 10.4172/cep.1000e101
47. Archer T. Exercise alleviates aurism spectrum disorders. Autism Open Access 2015;5:2. DOI:10.4172/2165-7890.1000150
48. Archer T. Exercise as therapy: health and well-being. J Intellect Disabil – Diagnos Treatm 2015; 3:76-81
49. Ricci S, Massoni F, Di Meo M,et al. Correlation among measures of stress, indicators of biohumoral nature and medico-legal considerations. Riv Psich 2013; 48(2):113-20
50. Archer T. Exercise influences in depressive disorders: symptoms, biomarkers and telomeres. Clin Depress 2015;1:1. DOI. 10.4172/cdp.1000e101.
51) Archer T, Garcia D. Physical exercise influences academic performance and well-being in children and adolescents. Int J School Cogn Psychol 2014;1:e102. DOI: 10.4172/1234-3425.1000e102
52. Archer T, Garcia D. Exercise and dietary restrictions for promotion of neurohealth benefits. Health 2015; 7:136-52
53. Archer T, Garcia D. Exercise intervention in traumatic brain injury. Trauma & Acute Care 2015; 1:1-3
54. Archer T, Kostrzewa RM. Physical exercise alleviates ADHD symptoms: regional deficits and development trajectory. Neurotox Res 2012; 21(2):195-209
55. Archer T, Kostrzewa RM. Physical Exercise Alleviates Health Defects, Symptoms, and Biomarkers in Schizophrenia Spectrum Disorder. Neurotox Res 2015; 28(3):268-80
56. Archer T, Josefsson T, Lindwall M. Effects of physical exercise on depressive symptoms and biomarkers in depression. CNS Neurol Disord Drug Targets 2014; 13(10):1640-53
57. Garcia D, Archer T. Positive affect and age as predictors of exercise compliance. PeerJ 2014;2:e694. DOI: 10.7717/peerj.694
58. Massoni F, Simeone C, Ricci P, et al. Papillary thyroid carcinoma and medico-legal considerations. Min Med 2013;104(4):493-4
59. Fauser M. et al. Intraindividual Variability of Nonmotor Fluctuations in Advanced Parkinson's Disease. J Parkinsons Dis 2015; 5(4):737-41
60. Klingelhoefer L, Reichmann H. Pathogenesis of Parkinson disease-the gut-brain axis and environmental factors. Nat Rev Neurol 2015; 11(11):625-36
61. Liu WM et al. The impact of nonmotor symptoms on quality of life in patients withParkinson's disease in Taiwan. Neuropsychiatr Dis Treat 2015; 11:2865-73
62. Reynolds GO, Otto MW, Ellis TD, et al. The Therapeutic Potential of Exercise to Improve Mood, Cognition, and Sleep in Parkinson's Disease. Mov Disord. 2015 Dec 30. doi: 10.1002/mds.26484
63. Levy Nogueira M, Epelbaum S, Steyaert JM, et al. Mechanical stress models of Alzheimer's disease pathology. Alzheimers Dement. 2015 Dec 21. doi: 10.1016/j.jalz.2015.10.005
64. Lian H. et al. Astrocyte-Microglia Cross Talk through Complement Activation Modulates Amyloid Pathology in Mouse Models of Alzheimer's Disease. J Neurosci 2016; 36(2):577-89
65. Rosenberger AF. et al. Increased occurrence of protein kinase CK2 in astrocytes in Alzheimer'sdisease pathology. J Neuroinflammation 2016; 13(1):4
66. Ortiz-Matamoros A, Salcedo-Tello P, Avila-Muñoz E, et al.

Role of wnt signaling in the control of adult hippocampal functioning in health and disease: therapeutic implications. Curr Neuropharmacol 2013; 11(5):465-76
67. Ryan SM, Nolan YM. Neuroinflammation negatively affects adult hippocampal neurogenesis andcognition: can exercise compensate? Neurosci Biobehav Rev 2015; 61:121-31
68. Massoni F, Ricci P, Simeone C, et al. Cardiac death in aortic valve sclerosis and coronary artery disease. An autopsy report. Acta Med Med 2014; 30:77-80
69. Monsell S. Task switching. Trends Cogn Sci 2003; 7:134-40
70. Rhodes SM et al. Executive functions predict conceptual learning of science. Br J Dev Psychol 2016 Jan 11. doi: 10.1111/bjdp.12129
71. Vernon-Feagans L, Willoughby M, Garrett-Peters P. Family Life Project Key Investigators. Predictors of Behavioral Regulation in Kindergarten: Household Chaos, Parenting, and Early Executive Functions. Dev Psychol. 2016 Jan 11
72. Ware AL. et al. Gray Matter Integrity Within Regions of the Dorsolateral Prefrontal Cortical-Subcortical Network Predicts Executive Function and Fine Motor Dexterity in Spina Bifida. Neuropsychology. 2016 Jan 11. PMID: 26752120
73. Ando S. et al. The effects of exercise under hypoxia on cognitive function. PLoS One 2014;8(5):e63630
74. Uc EY. et al. Phase I/II randomized trial of aerobic exercise in Parkinson disease in a community setting. Neurology 2014; 83(5):413-25
75. Groot C. The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized control trials. Ageing Res Rev 2016; 25:13-23
76. Barcelos N. et al. Aerobic and Cognitive Exercise (ACE) Pilot Study for Older Adults: Executive Function Improves with Cognitive Challenge While Exergaming. J Int Neuropsychol Soc. 2015;21(10):768-79.
77) Tsukamoto H. et al. Greater impact of acute high-intensity interval exercise on post-exerciseexecutive function compared to moderate-intensity continuous exercise. Physiol Behav. 2016; 155:224-30
78. Zhu W. et al. Association Between Objectively Measured Physical Activity and CognitiveFunction in Older Adults-The Reasons for Geographic and Racial Differences in Stroke Study. J Am Geriatr Soc 2015; 63(12):2447-54
79. Douris P. et al. Martial Art Training and Cognitive Performance in Middle-Aged Adults. J Hum Kinet 2015; 47:277-83
80. Scott BM. et al. Post-exercise pulse pressure is a better predictor of executive function than pre-exercise pulse pressure in cognitively normal older adults. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 2015; 1-13
81. Mannocci A, Masala D, Mipatrini D, et al. The relationship between physical activity and quality of life in prisoners: a pilot study. J Prev Med Hyg 2015; 56(4):E172-5
82. Masala D, Mannocci A, Unim B, et al Quality of life and physical activity in liver transplantation patients: results of a case-control study in Italy. Transplant Proc 2012; 44(5):1346-50
83. Archer T, Ricci S, Garcia D, Ricciardi MR. Neurodegenerative aspects in vulnerability to schizophrenia spectrum disorders. Neurotox Res 2014;26(4):400-13