

Effect of Long-Term Physical Exercise on Blood Pressure in an African American Sample

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ABSTRACT

International Journal of Exercise Science 7(3) : 186-193, 2014. Long-term physical exercise has been shown to noticeably reduce blood pressure (BP) and remarkably attenuate symptoms of hypertension. It is believed that physical exercise induces these beneficial effects by increasing the blood supply to the brain, enhancing the release of growth factors from skeletal muscles into the bloodstream, facilitating neurogenesis, stimulating angiogenesis, and influencing endothelial cell proliferation and subsequent endothelial cell membrane permeability. Previous findings also revealed that physical exercise significantly elevates brain-derived neurotrophic factor (BDNF) concentrations which appear to increase dramatically in BP-sensing neurons during hypertension. Elevating BDNF levels is the proposed mechanism by which physical exercise reduces BP and lowers hypertension risk. Relatively effective measures exist today to prevent or delay much of the burden of hypertension and curtail or remediate the devastating consequences of chronic elevated BP over time. Nevertheless, this medical problem contributes to excess risk for morbidity and mortality and is a major public health concern, especially among minority populations. To date, however, it appears as though few studies have focused on the impact of non-pharmacological, behavioral interventions such as physical exercise on BP in minorities. Therefore, the purpose of the present study was to examine the effect of long-term exercise on BP in an African American sample. Specifically, the aim was to determine whether a 12-week moderate intensity physical exercise program would significantly decrease BP. Because data provided evidence to support the hypothesis tested, it was concluded that physical exercise resulted in a significant reduction in BP in the African Americans sampled.

KEY WORDS: hippocampus, autonomic nervous system, stress response, HPA axis, CRH, ACTH

INTRODUCTION

Long-term physical exercise has been shown to positively impact overall health and has been linked to a reduction in BP (53, 54). Chronic elevated BP can lead to hypertension defined as a sustained BP \geq 140/90mmHg. Hypertension is a potent risk factor for developing heart disease or

suffering a stroke (25). Physical exercise can attenuate symptoms of hypertension and reduce BP (29, 56). Physical exercise apparently induces these beneficial effects by increasing the blood supply to the brain, enhancing the release of growth factors from skeletal muscles into the bloodstream, facilitating neurogenesis (development of new nerve cells, or neurons), stimulating

angiogenesis (formation of new blood cells from pre-existing blood cells), influencing proliferation of endothelial cells forming the interior lining of the blood vessels, and fostering permeability of endothelial cell membranes (1, 9, 13, 15, 16, 30, 34, 48, 49, 59, 61, 68, 67, 75). Previous studies involving humans (21, 28, 57, 58, 62) and animals (1, 6, 31, 47, 50, 64) have demonstrated that physical exercise leads to significant increases in BDNF which crosses the blood-brain barrier (14) and mediates baroreceptor activity (43). Native BDNF levels appear to increase dramatically in baroreceptors during hypertension; thus, the proposed mechanism by which physical exercise decreases BP and lowers hypertension risk is by elevating BDNF levels (17). Perhaps BDNF molecules provide compensatory actions countering those leading to hypertension thereby regulating BP (10). Although relatively effective measures exist today to prevent the burden of hypertension and curtail the devastating consequences of the disease, this medical problem contributes to excess risk for morbidity and mortality and is a major public health concern. The prevalence of hypertension is higher among African Americans than Caucasians (39). Yet, few studies have focused on the impact of behavioral interventions such as physical exercise on BP in minorities. Therefore, the aim was to determine whether 12 weeks of moderate intensity physical exercise would significantly decrease BP in African Americans. It was predicted that there would be a statistically significant reduction in BP at the end of week 12.

METHODS

Participants

To test this hypothesis, 20 African Americans (6 males and 14 females) under age 65 were recruited to participate voluntarily in this study. Individuals attended Jackson State University (JSU, an urban historically black university) and/or resided in a surrounding community. To be included in this study, participants had to be age 18 or older, have a baseline BP <140/90 mmHg, and be able to comply with the research protocol. Individuals with an initial (baseline) BP reading \geq 140/90mmHg were excluded from the study. Prior to data collection, the research protocol and supporting documents were submitted to the JSU Institutional Review Board (IRB) for approval. Following approval, participants were recruited and research was conducted according to the IRB standards and guidelines.

Protocol

When participants agreed to volunteer for this study, they were asked to read and sign a consent form. During this time, individuals were permitted to ask any questions pertaining to the purpose and procedures of the study. All questions were answered by the researcher. Then, using a digital automatic wrist BP monitor (Omron 7 Series, Model BP652, \$60.00, Wal-Mart, Clinton, MS), the researcher obtained and recorded BP readings at the start of the study and at the end of weeks 6 and 12. Next, participants were given The Anxiety Study Group Demographic Questionnaire to complete. Participants also completed the International Physical Activity Questionnaire to determine the kinds of physical activities in which they engaged as part of their everyday lives. Then, participants were provided with verbal and written instructions on how to follow the moderate intensity physical exercise

protocol (participating in some type of cardiorespiratory endurance activity for at least 20-60 minutes three-five days per week) for 12 weeks. Each participant was offered the option to exercise indoors or outdoors at home or somewhere in the community. In addition, each person was instructed verbally on how to obtain a BP reading using the digital wrist monitor provided for the duration of the study. Individuals were provided with written instructions on how to take as well as record a BP reading. Participants were given a BP tracking log and asked to obtain and record their BP readings before and after each physical exercise session. Participants were informed that they were expected to return to the laboratory during the course of the study to have their BP readings obtained and recorded by the researcher at the end of weeks 6 and 12. At the end of the study, data were collected and analyzed by the researcher.

RESULTS

Measured in millimeters of mercury (or mmHg), BP is an indication of the force exerted against the arterial walls as the heart muscles pump blood through the body. A repeating cardiac cycle captured by the results of a BP measurement indicates arterial pressure during contraction (systole represented by the systolic blood pressure, or SBP) and dilation (diastole represented by the diastolic blood pressure, or DBP). A one-way repeated measures analysis of variance (ANOVA) was calculated using Predictive Analysis Software (v.18.0) to compare the SBP and DBP measurements of participants at three different times (baseline and weeks 6 and 12). The ANOVA results with a Greenhouse-Geisser correction indicated that mean SBP and

DBP readings differed statistically significantly between time points ($F(1.173, 22.259)=21.034, p=.001$). Post-hoc comparisons using the Bonferroni correction revealed that moderate intensity physical exercise resulted in a slight reduction in SBP and DBP from baseline to week 6 (3.11 ± 1.01 mmHg and 2.99 ± 0.91 mmHg, respectively) which was not statistically significant ($p=.151$). However, SBP and DBP readings obtained at week 12 had decreased by 12.26 ± 0.52 mmHg and 8.41 ± 0.73 , respectively. These results were significantly different from SBP and DBP readings taken at baseline ($p=.018$) and at week 6 ($p=.026$). Thus, evidence was found to support the hypothesis tested, and it was concluded that long-term physical exercise results in a statistically significant reduction in both SBP and DBP.

DISCUSSION

Results of the present study indicated that 12 weeks of moderately intense physical exercise can lead to a significant reduction in BP. Therefore, data provided evidence to support the hypothesis tested in spite of the small sample size ($n=20$) included in this research. These results suggest that long-term exercise can be used to manage BP, promote physical health and enhance brain function in African Americans diagnosed with hypertension. Previous findings from animal studies suggested that running promotes endothelial cell proliferation in the rat hippocampus and prefrontal cortex (18, 40). Results from related research indicated that running and enriching the environment facilitates cell proliferation and neurogenesis in the dentate gyrus of the mouse hippocampus (7, 36, 37, 51, 55, 72). Further evidence indicated that long-term physical exercise induces angiogenesis

and increases cerebral blood volume in the rat primary motor cortex (38, 65). Previous findings also suggested that prolonged physical exercise stimulates neurogenesis resulting in an increase in the number of new neurons in the adult mammalian hippocampus (19, 20, 24, 35). The aforementioned results provide evidence to purport that physical exercise promotes overall brain health as well as facilitates neuronal and synaptic plasticity (11, 22, 33, 42, 60, 66, 73, 74). The implication is that physical exercise induces the release of BDNF which crosses the blood-brain barrier (14) thereby facilitating neurotransmission, promoting neuroplasticity (5, 12, 23, 26, 27, 52, 66), and mediating baroreceptor activity (43). Results of neurochemical assays suggested that regular physical exercise mediates baroreceptor activity by elevating BDNF expression and secretion. Increased BDNF concentrations in serum and plasma levels result in a reduction in BP and an attenuation in the symptoms of hypertension over time (43). Because hypertension is more prevalent among African Americans than Caucasians (45, 46) and physical inactivity is a significant risk factor and predictor of developing essential hypertension (3), targeting this modifiable risk factor and encouraging African Americans to exercise can aid in prevention, early diagnosis, and control of this manageable disorder (8). Thus, perhaps physical exercise can be used as a non-pharmacological, behavioral intervention for a variety of patients diagnosed with hypertension and able to engage in a minimum of 20 minutes of moderately intense physical exercise at least three times per week. People who can maintain a regular regimen of activity that is of longer duration or of more vigorous intensity are likely to derive greater health benefits than

individuals who lead sedentary lives of physical inactivity which is considered to be the strongest individual risk factor for poor health (63). Exercise and lifestyle changes as therapeutic interventions for successfully managing symptoms of hypertension have been found to be efficacious in previous controlled studies (32, 41, 44, 69, 70, 71). For instance, aerobic exercise can be valuable in the treatment of mild to moderate essential hypertension because it may cause a decrease in both SBP and DBP. For mild hypertension, aerobic exercise and lifestyle changes combined with risk factor modification (such as avoiding physical inactivity, minimizing life stressors at home and work, losing weight, reducing fat, restricting salt intake, and quitting smoking) are positive approaches to controlling BP. For moderate to severe hypertension, lifestyle changes and medication compliance should be combined with risk factor modification (4). Results of current and previous research have implicated a number of ontogenetic factors mediating BP control. A direction for future research is to examine the impact of long-term voluntary physical exercise on BDNF as well as cortisol expression and secretion to determine the relationship between these neurochemicals and their effects on physiological responses (such as heart rate and respiration rate) and psychological indicators including anxiety and depression that impact BP and hypertension in African Americans.

REFERENCES

1. Adlard PA, Perreau VM, Engesser-Cesar C, Cotman, CW. The timecourse of induction of brain-derived neurotrophic factor mRNA and protein in the rat hippocampus following voluntary exercise. *Neurosci Lett* 363:43-48, 2004.

2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. *Molecular biology of the cell*. New York, NY: Garland Science, 2008.
3. Al-Hamdan NA, Al-Zalabani AH, Saeed AA. Comparative study of physical activity of hypertensives and normotensives: A cross-sectional study of adults in Saudi Arabia. *J Fam Community Med* 19:162-166, 2012.
4. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ. Effects of comprehensive lifestyle modification on blood pressure control: Main results of the PREMIER clinical trial. *JAMA* 289:2083-2093, 2003.
5. Bechara RG, Kelly ÁM. Exercise improves object recognition memory and induces BDNF expression and cell proliferation in cognitively enriched rats. *Behav Brain Res* 245C:96-100, 2013.
6. Berchtold NC, Chinn G, Chou M, Kesslak JP, Cotman CW. Exercise primes a molecular memory for brain-derived neurotrophic factor protein induction in the rat hippocampus. *Neuroscience* 133:853-861, 2005.
7. Brown J, Cooper-Kuhn CM, Kempermann G, van Praag H, Winkler J, Gage FH, Kuhn HG. Enriched environment and physical activity stimulate hippocampal but not olfactory bulb neurogenesis. *Eur J Neurosci* 17:2042-2046, 2003.
8. Carretero OA, Oparil S. Essential hypertension: Part I: definition and etiology. *Circulation* 101:329-335, 2000.
9. Cines DB, Pollak ES, Buck CA, Loscalzo J, Zimmerman GA, McEver RP, Pober JS, Wick TM, Konkle BA, Schwartz BS, Barnathan ES, McCrae KR, Hug BA, Schmidt AM, Stern DM. Endothelial cells in physiology and in the pathophysiology of vascular disorders. *Blood* 91:3527-3561, 1998.
10. Clark CG, Hasser EM, Kunze DL, Katz DM, Kline DD. Endogenous brain-derived neurotrophic factor in the nucleus tractus solitarius tonically regulates synaptic and autonomic function. *J Neurosci* 31:12318-12329, 2011.
11. Cotman CW, Berchtold NC. Exercise: A behavioral intervention to enhance brain health and plasticity. *Trends Neurosci* 25:295-301, 2002.
12. Cotman CW, Berchtold NC, Christie L-A. Exercise builds brain health: Key roles of growth factor cascades and inflammation. *Trends Neurosci* 30:464-472, 2007.
13. Cuppini R, Sartini S, Agostini D, Guescini M, Ambrogini P, Betti M, Bertini L, Vallasciani M, Stocchi. BDNF expression in rat skeletal muscle after acute or repeated exercise. *Arch Ital Biol* 145:99-110, 2007.
14. Ding YH, Li J, Zhou Y, Rafols JA, Clark JC, Ding Y. Cerebral angiogenesis and expression of angiogenic factors in aging rats after exercise. *Curr Neurovascular Res* 3:15-23, 2006.
15. Duncker DJ, Bache RJ. Regulation of coronary blood flow during exercise. *Physiol Rev* 88:1009-1086, 2008.
16. Egginton S. Invited review: Activity-induced angiogenesis. *Pflügers Arch* 457:963-977, 2009.
17. Ejiri J, Inoue N, Kobayashi S, Shiraki R, Otsui K, Honjo T, Takahashi M, Ohashi Y, Ichikawa S, Terashima M, Mori T, Awano K, Shinke T, Shite J, Hirata K, Yokozaki H, Kawashima S, Yokoyama M. Possible role of brain-derived neurotrophic factor in the pathogenesis of coronary artery disease. *Circulation* 112:2114-2120, 2005.
18. Ekstrand J, Hellsten J, Tingström A. Environmental enrichment, exercise and corticosterone affect endothelial cell proliferation in adult rat hippocampus and prefrontal cortex. *Neurosci Lett* 442:203-207, 2008.
19. 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* 19:1030-1039, 2009.
20. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, Kim JS, Heo S, Alves H, White SM, Wojcicki TR, Mailey E, Vieira V, Martin SA, Pence BD, Woods JA, McAuley E, Kramer AF. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci U S A* 108:3017-3022, 2011.

21. Erickson KI, Miller DL, Roecklein KA. The aging hippocampus: Interactions between exercise, depression, and BDNF. *Neuroscientist* 18:82-97, 2012.
22. Farmer J, Zhao X, van Praag H, Wodtke K, Gage FH, Christie BR. Effects of voluntary exercise on synaptic plasticity and gene expression in the dentate gyrus of adult male Sprague-Dawley rats in vivo. *Neuroscience* 124:71-79, 2004.
23. Ferris LT, Williams JS, Shen CL. The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. *Med Sci Sports Exerc* 39:728-734, 2007.
24. Flöel A, Ruscheweyh R, Kruger K, Willemer C, Winter B, Volker K, Lohmann H, Zitzmann M, Mooren F, Breitenstein C, Knecht S. Physical activity and memory functions: are neurotrophins and cerebral gray matter volume the missing link? *Neuroimage* 49:2756-2763, 2010.
25. Goldstein LB, Bushneea CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, Creager MA, Culebras A, Eckel RH, Hart RG, Hinchey JA, Levine SR, Meschia JF, Moore WS, Nixon JV, Pearson TA. Guidelines for the primary prevention of stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 42:517-584, 2011.
26. Gómez-Pinilla F, Ying Z, Roy RR, Molteni R, Edgerton VR. Voluntary exercise induces a BDNF-mediated mechanism that promotes neuroplasticity. *J Neurophysiol* 88:2187-2195, 2002.
27. Gomez-Pinilla F, Zhuang Y, Feng J, Ying Z, Fan G. Exercise impacts brain-derived neurotrophic factor plasticity by engaging mechanisms of epigenetic regulation. *Eur J Neurosci* 33:383-390, 2011.
28. Gustafsson G, Lira CM, Johansson J, Wisén A, Wohlfart B, Ekman R, Westrin A. The acute response of plasma brain-derived neurotrophic factor as a result of exercise in major depressive disorder. *Psychiatry Res* 169:244-248, 2009.
29. Hagberg JM, Park JJ, Brown MD. The role of exercise training in the treatment of hypertension: An update. *Sports Med* 30:193-206, 2000.
30. Hambrecht R, Fiehn E, Weigl C, Gielen S, Hamann C, Kaiser R, Yu J, Adams V, Niebauer J, Schuler G. Regular physical exercise corrects endothelial dysfunction and improves exercise capacity in patients with chronic heart failure. *Circulation* 98: 2709-2715, 1998.
31. Huang AM, Jen CJ, Chen HF, Yu L, Kuo YM, Chen HI. Compulsive exercise acutely upregulates rat hippocampal brain-derived neurotrophic factor. *J Neural Transm* 113:803-811, 2006.
32. Hung JW, Liou CW, Wang PW, Yeh SH, Lin LW, Lo SK, Tsai FM. Effect of 12-week tai chi chuan exercise on peripheral nerve modulation in patients with type 2 diabetes mellitus. *J Rehabil Med* 41:924-929, 2009.
33. Hunsberger JG, Newton SS, Bennett AH, Duman CH, Russell DS, Salton SR, Duman RS. Antidepressant actions of the exercise-regulated gene VGF. *Nat Med* 13:1476-1482, 2007.
34. Hunt SJ, Navalta JW. Nitric oxide and the biological cascades underlying increased neurogenesis, enhanced learning ability, and academic ability as an effect of increased bouts of physical activity. *Int J Exerc Sci* 5:245-275, 2012.
35. Kempermann G, Fabel K, Ehninger D, Babu H, Leal-Galicia P, Garthe A, Wolf SA. Why and how physical activity promotes experience-induced brain plasticity. *Front Neurosci* 4:189, 2010.
36. Kempermann G, Kuhn HG, Gage FH. More hippocampal neurons in adult mice living in an enriched environment. *Nature* 386:493-495, 1997.
37. Kempermann G, Kuhn HG, Gage FH. Experience-induced neurogenesis in the senescent dentate gyrus. *J Neurosci* 18:3206-3212, 1998.
38. Kleim JA, Cooper NR, VandenBerg PM. Exercise induces angiogenesis but does not alter movement representations within rat motor cortex. *Brain Res* 934:1-6, 2002.
39. Kokkinos PF, Narayan P, Colleran JA, Pittaras A, Notargiacomo A, Reda D, Papademetriou V. Effects of regular exercise on blood pressure and left ventricular hypertrophy in African-American men with severe hypertension. *N Engl J Med* 333:1462-1467, 1995.

40. Kronenberg G, Reuter K, Steiner B, Brandt MD, Jessberger S, Yamaguchi M, Kempermann G. Subpopulations of proliferating cells of the adult hippocampus respond differently to physiologic neurogenic stimuli. *J Comp Neurol* 467:455-463, 2003.
41. Lan C, Su TC, Chen SY, Lai JS. Effect of T'ai chi chuan training on cardiovascular risk factors in dyslipidemic patients. *J Altern Complement Med* 14:813-819, 2008.
42. Lange-Asschenfeldt C, Kojda G. Alzheimer's disease, cerebrovascular dysfunction and the benefits of exercise: From vessels to neurons. *Exp Geront* 43:499-504, 2008.
43. Martin JL, Jenkins VK, Hsieh H, Balkowiec A. Brain-derived neurotrophic factor in arterial baroreceptor pathways: Implications for activity-dependent plasticity at baroafferent synapses. *J Neurochem* 108:450-464, 2009.
44. Melo RM, Martinho EJR, Michelini LC. Training-induced, pressure-lowering effect in SHR: Wide effects on circulatory profile of exercised and nonexercised muscles. *Hypertension* 42:851-857, 2003.
45. Mississippi State Department of Health. Mississippi state of the heart report. Retrieved from <http://www.HealthMs.org>, 2005.
46. Mississippi State Department of Health. Hinds County 2007 health profiles. Retrieved from <http://www.msdh.ms.gov/county/Hinds.pdf>, 2007.
47. Neeper SA, Gómez-Pinilla F, Choi J, Cotman, CW. Physical activity increases mRNA for brain-derived neurotrophic factor and nerve growth factor in rat brain. *Brain Res* 726:49-56, 1996.
48. Newcomer SC, Thijssen DHJ, Green DJ. Effects of exercise on endothelium and endothelium/smooth muscle cross talk: Role of exercise-induced hemodynamics. *J Appl Physiol* 111:311-320, 2011.
49. Nofuji Y, Suwa M, Sasaki H, Ichimiya A, Nishichi R, Kumagai S. Different circulating brain-derived neurotrophic factor responses to acute exercise between physically active and sedentary subjects. *J Sports Sci Med* 11:83-88, 2012.
50. Oliffa HS, Berchtolda NC, Isackson P, Cotman CW. Exercise-induced regulation of brain-derived neurotrophic factor (BDNF) transcripts in the rat hippocampus. *Mol Brain Res* 61:147-153, 1998.
51. Olson AK, Eadie BD, Ernst C, Christie BR. Environmental enrichment and voluntary exercise massively increase neurogenesis in the adult hippocampus via dissociable pathways. *Hippocampus* 16:250-260, 2006.
52. Pan W, Banks WA, Fasold MB, Bluth J, Kastin AJ. Transport of brain-derived neurotrophic factor across the blood-brain barrier. *Neuropharmacology* 37:1553-1561, 1998.
53. Park S, Rink LD, Wallace JP. Accumulation of physical activity leads to a greater blood pressure reduction than a single continuous session, in prehypertension. *J Hypertens* 24:1761-1770, 2006.
54. Park S, Rink LD, Wallace JP. Accumulation of physical activity: Blood pressure reduction between 10-min walking sessions. *J Hum Hypertens* 22:475-482, 2008.
55. Pereira AC, Huddleston DE, Brickman AM. An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. *Proc Natl Acad Sci U S A* 104:5638-5643, 2007.
56. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. American College of Sports Medicine position stand. Exercise and hypertension. *Med Sci Sports Exerc* 36:533-553, 2004.
57. Rasmussen P, Brassard P, Adser H, Pedersen MV, Leick L, Hart E, Secher NH, Pedersen BK, Pilegaard H. Evidence for a release of brain-derived neurotrophic factor from the brain during exercise. *Exp Physiol* 94:1062-1069, 2009.
58. Rojas Vega S, Strüder HK, Vera Wahrmann B, Schmidt A, Bloch W, Hollmann W. Acute BDNF and cortisol response to low intensity exercise and following ramp incremental exercise to exhaustion in humans. *Brain Res* 1121:59-65, 2006.
59. Rogue FR, Soci UPR, Angelis KD, Coelho MA, Furstenau CR, Vassallo DV, Irigoyen MC, Oliveira

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- EM. Moderate exercise training promotes adaptations in coronary blood flow and adenosine production in normotensive rats. *Clin (Sao Paulo)* 66:2105-2111, 2011.
60. Ruscheweyh R, Willemer C, Kruger K, Duning T, Warnecke T, Sommer J, Volker K, Ho HV, Mooren F, Knecht S, Floel A. Physical activity and memory functions: An interventional study. *Neurobiol Aging* 32:1304-1319, 2011.
61. Sandberg A, Bostrom N. Converging cognitive enhancements. *Ann NY Acad Sci* 1093:201-227, 2006.
62. Seifert T, Brassard P, Wissenberg M, Rasmussen P, Nordby P, Stallknecht B, Adser H, Jakobsen AH, Pilegaard H, Nielsen HB, Secher NH. Endurance training enhances BDNF release from the human brain. *Am J Physiol Regul Integrat Comp Physiol* 298:R372-R377, 2010.
63. Sjöling M, Lundberg K, Englund E, Westman A, Jong MC. Effectiveness of motivational interviewing and physical activity on prescription on leisure exercise time in subjects suffering from mild to moderate hypertension. *Biomed Cent Res Notes* 4:352, 2011.
64. Soya H, Nakamura T, Deocaris CC, Kimpara A, Iimura M, Fujikawa T, Chang H, McEwen BS, Nishijima T. BDNF induction with mild exercise in the rat hippocampus. *Biochem Biophys Res Commun* 358:961-967, 2007.
65. Swain RA, Harris AB, Wiener EC, Dutka MV, Morris HD, Theien BE, Konda S, Engberg K, Lauterbur PC, Greenough WT. Prolonged exercise induces angiogenesis and increases cerebral blood volume in primary motor cortex of the rat. *Neuroscience* 117:1037-1046, 2003.
66. Thoenen H. Neurotrophins and neuronal plasticity. *Science* 270:593-598, 1995.
67. Thomas AG, Dennis A, Bandettini PA, Johansen-Berg H. The effects of aerobic activity on brain structure. *Front Psychol* 3:86, 2012.
68. Thomas KA. Vascular endothelial growth factor, a potent and selective angiogenic agent. *J Biol Chem* 271:603-606, 1996.
69. Tsai J-C, Chang W-Y, Kao C-C, Lu M-S, Chen Y-J, Chan P. Beneficial effect on blood pressure and lipid profile by programmed exercise training in Taiwanese patients with mild hypertension. *Clin Exp Hypertens* 24:315-324, 2002.
70. Tsai JC, Wang WH, Chan P, Lin LJ, Wang CH, Tomlinson B, Hsieh MH, Yang HY, Liu JC. The beneficial effects of Tai Chi Chuan on blood pressure and lipid profile and anxiety status in a randomized controlled trial. *J Altern Complement Med* 9:747-754, 2003.
71. Tsai J-C, Liu J-C, Kao C-C, Tomlinson B, Kao P-F, Chen J-W, Chan P. Beneficial effects on blood pressure and lipid profile of programmed exercise training in subjects with white coat hypertension. *Am J Hypertens* 15:571-576, 2002.
72. van Praag H, Kempermann G, Gage FH. Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. *Nat Neurosci* 2:266-270, 1999.
73. Vaynman S, Ying Z, Gomez-Pinilla F. Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. *Eur J Neurosci* 20:2580-2590, 2004.
74. Winter B, Breitenstein C, Mooren FC, Voelker K, Fobker M, Lechtermann A, Krueger K, Fromme A, Korsukewitz C, Flowl A, Knecht S. High impact running improves learning. *Neurobiol Learn Mem* 87:597-609, 2007.
75. Zoladz JA, Pilc A, Majerczak J, Grandys M, Zapart-Bukowska J, Duda K. Endurance training increases plasma brain-derived neurotrophic factor concentration in young healthy men. *J Physiol Pharmacol* 59:119-132, 2008.