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Is Whole Body Vibration Exercise a Viable Option for Individuals with Alzheimer's Disease?

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Abstract Besides the cognitive limitations, individuals with Alzheimer's disease (AD) have posture and gait disturbances and risk of falls. Researchers have reported that appropriate physical activity (PA) can enhance cognitive function and attenuates age-related deterioration of the brain structure. The search of the number of publications (NP) in the database PubMed with the keyword "physical activity" alone and in association with other keywords related to chronic diseases has shown that the scientific interest involving PA and diabetes is the highest and with AD is the smallest. Vibrations generated in oscillating/vibratory platform can produce whole body vibration exercises (WBVE) with relevant improvements in patients. Investigations have introduced WBV training also in patients with neurodegenerative diseases and with attention deficit hyperactivity disorder. The aim of this work is to present the potential importance of the WBVE to AD patients. The NP in the PubMed with the keyword "Whole body vibration" and Alzheimer disease has shown no articles. PA has been considered a non pharmacologic intervention to manage the AD patient Considering that besides the cognitive impairments, AD patients have posture and gait disturbances and risk of falls, it is suggested to include the WBVE in the management of the AD patients. In conclusion, WBVE could be a relevant, viable, safe and inexpensive strategic option of PA to individuals with AD.

Keywords Neurodegenerative disease, Alzheimer disease, Physical activity, Vibration, Whole body vibration

1. Introduction

1.1. General Approach about Alzheimer's Disease

Alzheimer's disease (AD) is an undesirable, devastating, irreversible and complex chronic neurodegenerative cortical disorder [1, 2]. It is characterized by progressive deterioration of the brain structure, leading to cognitive decline, dementia and ultimately death [1, 2, 3] and it is the most common cause of dementia worldwide (2).

Advanced age is the strongest risk factor for AD. Dugu et al., 2003 [4] have reported that AD is the major cause of dementia in the geriatric population in the United States of America and in Western Europe. In addition, Thies and Bleiler, 2013 [5] have described that the risk doubles every 5 years after the age of 65 years old. It is estimated that 5.2 million Americans have AD. In consequence, in general, due to the rapid aging of the population, the prevalence of AD is closed related to an exponential growth. In addition, it is also observed that there remains a dearth and limited possibilities of effective treatments (i) to manage, (ii) to cure, and most importantly (iii) to prevent the disease.

Thies and Bleiler, 2013 [5] have reported that AD is the sixth leading cause of death in the United States of America and the fifth leading cause of death in Americans age 65 years old or older. These authors described that between 2000 and 2010, the proportion of deaths resulting from clinical disturbances as heart disease, stroke, and prostate cancer decreased 16%, 23%, and 8%, respectively. Considering the AD, the proportion increased 68% in this same period of time.

Besides the cognitive limitations, AD patients have posture and gait disturbances and a high risk of serious falls

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[6]. Moreover, Sato et al, 2004 [7] have reported that falls are frequent and have serious traumatic consequences, as hip fracture in these patients. Gago et al, 2014 [8] and Morris et al, 1987 [9] have reported that the mechanisms that contributed to falls in the referred patients are not fully understood.

It is known that the physical activity is recommended to all persons due to various benefits to the health [10]. Considering a person with a disease, physical activity can be planned to aid to improve the quality of the life. Physical inactivity is a primary cause of most chronic diseases [11]. In addition, exercise deficiency also leads to an increased prevalence of obesity, hypertension, intermittent claudication, sarcopenia, osteoporosis and AD [11, 12].

1.2. Physical Activity and the Health in General

Authors have reported that habitual physical activity is inversely associated with all-cause mortality in older men and women [13, 14]. Moreover, Tarumi and Zhang, 2014 [15] have described that, related to the brain, it is recognized that appropriated regular physical activity can (i) enhance the cognitive function and (ii) attenuate the age-related deterioration of the structure of the referred organ.

Considering the habitual physical activity, investigations indicate higher prevalence of several diseases, as the breast cancer, coronary heart disease, gallstones, type 2 diabetes, colon cancer and ischaemic stroke in Harvard Nurses Health participants with less than 2.5 hours per week in comparison with cohorts with more than 2.5 hours per week [16-24].

As it is shown in Table 1, a search performed on March 4th 2014, it is possible to see the number of publications in the database PubMed with the key word "physical activity" alone and in association with other key words related to some chronic diseases. The scientific interest involving physical activity and diabetes is the highest, with about 13.5% of the publications.

1.3. Physical Activity and the Alzheimer's Disease

Considering the number of publication shown in Table 1, the interest of publications considering physical activity and Alzheimer disease is small, 0.3%. However about 50% of the 174 articles were published between 2010 and 2014. This fact could represent a new and recent approach in the management of the patient with AD.

Table 1. Number of publications (database PubMed) with the key word "physical activity" alone and in association with other key words related to some chronic diseases

Keyword	Number of publication
Physical activity	57 032
"Physical activity" and cancer	4 881
"Physical activity" and diabetes	7 659
"Physical activity" and stroke	1 348
"Physical activity" and "Alzheimer disease"	174
"Physical activity" and "Parkinson disease"	104

Lautenschlager et al, 2012 [25] have reported that related to the cognitive functions, physical activity has been shown to improve cognitive outcomes in patients with mild cognition impairment. An important consideration is reported by Selkoe, 2012 [26] that describes that, in contrast to the pharmacological interventions, habitual and appropriated physical activity represents, in general, a relevant tool (a) with low cost, (b) with no adverse effects, and (c) important for primary prevention of AD.

Besides the AD, physical activity has been also an important tool in the management of patient with others clinical disorders with neurological limitation, as Parkinson' disease [27].

1.4. Aerobic Exercise and the Brain Structure and Function

Gons et al, 2013 [28] and Tseng et al, 2013 [29] have described that habitual aerobic exercise aid to preserve the structural integrity of white matter in the central nervous system. Moreover, Tseng et al, 2013 [29] suggest that regular aerobic exercise preserves the microstructural integrity of white matter that is responsible for important functions, as visuospatial perception, motor control, and coordination.

In addition, Ferris et al, 2007 [30] reported that exercise also is beneficial to the brain and nervous system. Moreover, they described that an endogenous substance with a central role in the health of neurons is brain-derived neurotrophic factor (BDNF). Lin and Kuo, 2013 [31] have emphasized the effects of exercise on brain functions due to monoamine systems. The advantageous effects of exercise on brain functions have been related to increased capacities of metabolism reserve and anti-oxidation. Regulations of the secretion of neurotrophic and vasculotropic factors, inflammatory mediators, and neurotransmitters would be also involved in the effect of the exercise on brain function. Among these effects, secretion of neurotransmitters, especially monoamines, have been related to neuronal adaptation due to the exercises. The catecholamines dopamine, norepinephrine and 5-hydroxytryptamine would be the principal molecules of the monoamine neurotransmitter family.

De La Torre, 2013 [32] have reported that mounting evidence indicates that vascular disease and risk factors not only elevate risk of vascular dementia, but also AD. Carro et al, 2001 [33], Harada et al, 2011 [34], Fabel et al, 2003 [35] and Lopez-Lopez et al, 2004 [36] have reported that improvements in the brain function and in the structure due to exercise may be related by simultaneous adaptations in the vascular function and structure. Moreover, aerobic exercise would increase the peripheral levels of growth factors, as insulin-like *growth factor-1* (IGF-*1*), BNDF and *vascular endothelial growth factor*, that are trophic factors required for the viability and normal functions of various neuronal cells [37]. They cross the blood-brain barrier and stimulate neurogenesis and angiogenesis that are crucial processes for brain tissue repair and remodeling after brain injury [38].

Moreover, de La Torre, 2013 [32] has reported that there is growing the evidence that vascular risk factors for AD affect the cerebral hemodynamics to start a sequence of cellular and molecular modification that initiate cognitive deficiencies and could permit the progression of the referred neurodegenerative disease. Importantly, Seals et al, 2008 [39] reported that appropriated aerobic exercise ameliorates endothelial dysfunction and central arterial stiffness.

There are several modalities of physical activity that are capable to promote exercises [40, 41]. Vibrations generated in oscillating/vibratory platform can produce whole body vibration exercises (WBVE) when the subject is in contact with the base of oscillating/vibratory platform that is turned on. Authors have reported relevant improvements in trained and untrained patients with various health disorders [41]. During WBVE, the human body is accelerated, which causes a reactive force by and within the human body. Considering a subject on the base of these platforms that generate WBVE, as there is no firm attachment, the only downward force acting on the body is the gravity [41]. As these biomechanical conditions might important to manage patient with neurodegenerative disease, the aim of this work is to present the potential relevance of WBVE to manage AD patients.

1.5. The Whole Body Vibration Exercises in Several Clinical Disorders

Some rehabilitation investigations have introduced WBV training in patients with neurodegenerative diseases such as Parkinson's disease or multiple sclerosis [42, 43]. In addition, scientific studies have demonstrated that the WBVE can aid in the treatment of various clinical disorders [41, 44], as well as to improve the strength of the muscle [45-50], the bone mineral density in post-menopausal women [50, 51], cardiovascular parameters [52], body balance in elderly [49, 53] and muscle power [54]. Prisby et al, 2008 [44] have reported the reduction of the number of falls in patients submitted to WBVE. Moreover, the health-related quality of life is increased and the fall risk is decreased [44].

Herrero et al, 2010 [55] have also described that WBVE is an effective method to increase blood flow and to activate muscle mass in patients with Friedreich´s ataxia.

Fuermaier et al., 2014 [56] have published a very important finding that may interest to the patient with attention deficit hyperactivity disorder (ADHD). These authors have demonstrated that WBVE improves cognitive performance of healthy individuals as well as of individuals with ADHD. They suggest that the WBV treatment is relatively inexpensive and easy to apply and might therefore be of potential relevance for clinical use. The application of WBVE treatment as a cognitive enhancement strategy and as a potential treatment of cognitive impairments is discussed by these authors.

Regterschot et al, 2014 [57] have investigated acute effects of passive WBV on executive functions in healthy young adults. Participants underwent passive WBV sessions (frequency 30 Hz, amplitude approximately 0.5 mm) and non-vibration control sessions while sitting on a chair mounted on a vibrating platform. A passive WBV session was alternated with a control session. After each session, performance on the Stroop Color-Block Test (CBT), Stroop Color-Word Interference Test (CWIT), Stroop Difference Score (SDS) and Digit Span Backward task (DSBT) was measured. In half of the passive WBV and control sessions the test order was CBT-CWIT-DSBT, and DSBT-CBT-CWIT in the other half. Passive WBV improved significantly CWIT and SDS performance, but only when the CBT and CWIT preceded the DSBT. CBT and DSBT performance have not changed. It is demonstrated that passive WBV has positive acute effects on attention and inhibition in young adults, notwithstanding their high cognitive functioning which could have hampered improvement. It is concluded that these findings indicate the potential of passive WBV as a cognition-enhancing therapy worth further evaluation, especially in persons unable to perform active forms of exercise.

In the procedure involving WBVE, normally, the subject normally stands on the base of an oscillating/vibratory platform that evokes mechanical oscillation that is mainly defined by frequency and amplitude [41, 58]. The frequency (number of oscillations) is measured in Hertz. Peak to peak amplitude or displacement is defined as the difference between the maximum and the minimum value of periodic oscillation (amplitude is defined as half the difference between the maximum and the minimum value of the oscillation) [41, 58]. Furthermore, the subject is accelerated, which would cause a reactive force by and within the human body [41].

The time of the subject in the platform working, the time of the subject in the platform resting, the number of sets in a session and the number of sessions are determined following the clinical disorder to be treated, as well as the physical conditions of the subject [53]. Marin et al, 2009 [59] have studied the neuromuscular activity during WBVE with different amplitudes in relation to footwear that the person was wearing and have observed differences in the action of different muscles.

The effects of the WBVE are probably related to direct and indirect actions [44]. The indirect effects have been hypothesized to be associated with the neuroendocrine system [44]. Direct effect of the whole body mechanical vibration on the muscle performance would be lead to the activation of a tonic excitatory effect, the tonic vibration reflex [48, 49]. Some authors have described that repeated muscle contractions might exert endocrine and/or metabolic effects [60].

The therapeutic effect of the exercises has been linked to the growth hormone (GH) regulation [61]. These findings have lead to the idea that exercise would be a convenient treatment for the fibromyalgia patients based on the hypothesis that the hormone regulation would be a key factor in the control of the symptoms associated [61, 62]. For example, impairment in the hypothalamic–pituitary–GH–IGF-1 axis would be manifested in a reduction of the serum

IGF-1 levels [63-65] which would be related to sleep disturbances, poor muscle performance, fatigue, and muscle pain.

Exercises in oscillating/vibratory platforms would induce increases in GH [66, 67]. In addition, effects on GH concentration have been attributed to a muscle afferent–pituitary axis [68-70]. GH is synthesized and secreted in a pulsating manner by the anterior pituitary gland and IGF-1 is secreted by the liver in response to GH release (61, 63). A study by Cardinale et al., 2010 [71] demonstrated a significant increase in serum IGF-1 following a single exposure to WBV in elderly patients.

Di Loreto et al 2004 [60] and Goto and Takamatsu, 2005 [72] have reported an increase of the plasma concentration of epinephrine and norepinephrine in subjects submitted to WBVE with vibrations with 30 and 26 Hz, respectively.

The possible indirect effects of the WBVE due to the neuroendocrine responses has been suggested by Prisby at al, 2008 [44] and in the direct effect, muscles and tendons act as spring-like elements that store and release mechanical energy [41]. These facts would induce involuntary muscle contractions that would be initiated by sensory receptors and would reduce the recruitment threshold of motor units. In consequence, authors have demonstrated an improvement of the ankle plantar flexor strength and power in an older population [73], the enhancement of the stability in elderly women [73] and improvements in patient with neurological disorders [74-81]. Keeping in the mind the suggested mechanism and the findings reported in the literature, WBVE have been successfully used to treat patients with some diseases related to the impairments involving the central nervous system, as cerebral palsy [75], multiple sclerosis [42], spinal cord injury [76] and stroke [77, 78]. Some studies considered also the effects of whole body vibrations on motor symptoms in Parkinson disease [43, 74, 79, 80] and patient with ADHD [56]. Moreover, Regterschot et al, 2014 [57] have investigated acute effects of passive WBV on executive functions in healthy young adults and they concluded that there is a potential of passive WBV as a cognition-enhancing therapy worth further evaluation, especially in persons unable to perform active forms of exercise. These considerations might be important to the AD patient.

1.6. Whole Body Vibration Exercises and Alzheimer Disease

WBVE has been used as a suitable tool to treat several undesirable clinical disorders [41, 44, 77, 81]. However, as Rittweger, 2010 [41] has reported, that this kind of exercises generated due o the interaction of the vibration obtained in oscillating/vibratory platform with the body is still unknown for the scientific community.

As it is shown in Table 2, a search performed on March 4th 2014, it is possible to see the number of publications in the database PubMed with the key word “Whole body vibration” alone and in association with other key words related to some chronic diseases. In comparison with physical activity (Table I), the number of publications with whole body vibration is very small. Moreover, it was not found articles involving whole body vibration and Alzheimer disease, although several clinical impairments related to this disease, as posture and gait disturbances and a high risk of falls [6] could be prevent by the WBVE.

Table 2. Number of publications (database PubMed) with the key word “whole body vibration” alone and in association with other key words related to some chronic diseases

Key word	Number of publication
Whole body vibration	1 090
"Whole body vibration" and cancer	6
"Whole body vibration" and diabetes	9
"Whole body vibration" and stroke	26
"Whole body vibration" and "Alzheimer disease"	No items found
"Whole body vibration" and "Parkinson disease"	14

2. Discussion

Neurodegenerative diseases represent a challenge to define social and health actions. The awareness of the strong and undesirable problems associated with the neurological disorders led to the recognition that the services and resources for the management of neurological disorders were disproportionately scarce, especially in low income and developing countries as reported by the World Health Organization/ World Federation of Neurology [82]. AD is a neurodegenerative disease and Thies and Bleiler, 2013 [5], reported that are estimated 5.2 million Americans with this illness. About 200,000 people younger than 65 years with AD is the younger onset AD population; 5 million is the older onset AD population. Following the Alzheimer’s Association (83) of these 5 million people age 65 and older with AD in the United States, 3.2 million are women and 1.8 million are men. Of those with AD, an estimated 4 percent are under age 65, 13 percent are 65 to 74, 44 percent are 75 to 84, and 38 percent are 85 or older.

It is believed that by 2050, one new case of AD will be developed to each 33 seconds, or about a million of new cases per year, and the total estimated prevalence is expected to be 13.8 million [5, 83-85].

Unpaid caregivers are primarily immediate family members of patient with AD and other dementia, but they also may be other relatives and friends. In 2012, these people provided an estimated 17.5 billion hours of unpaid care, a contribution to the nation valued at more than $216 billion [5, 85]. These economic and social conditions determine that new, suitable and inexpensive tools are available to try to aid in the prevention or in the management of the patient with AD.

Physical activity has been considered a non pharmacologic intervention to manage the AD patient and

authors [28, 29] have suggested that habitual exercises aid to preserve the structural integrity of white matter of the brain. Moreover, Tseng et al, 2013 [29] suggest that the preservation of the microstructural integrity of white matter aids the visuospatial function, motor control, and coordination.

Concerning to the cognitive impairments, Fuermaier et al, 2014 [56] have published that WBVE can improves the cognitive performance of healthy individuals as well as of individuals with ADHD. This finding would have high relevance in the treatments of patients with cognitive impairments, and we believe that this procedure involving the vibration would be important to the AD patients. In addition, Regterschot et al, 2014 [57] have suggested a potential of passive WBV as a cognition-enhancing therapy worth further evaluation, especially in persons unable to perform active forms of exercise.

Considering that besides the cognitive impairments, AD patients have posture and gait disturbances and a high risk of serious falls [6]. Thinking that it is known that the physical activity is recommended to all the persons due to various benefits to a healthy subject, independently of the age, to improve the physical ability [81], the WBVE would be a convenient option. Phillips et al, 2014 [86] have reported that improved trophic factor signaling has been considered as the most popular hypothesis to explain the positive effects of physical activity on cognition, with attention centering on the neurotrophins that regulate a variety of neuronal functions including proliferation, survival, migration, and differentiation.

As the WBVE are safe and can improve the strength of the muscle [45-50], the body balance [49, 53], and the muscle power [54], to increase the health-related quality of life, to reduce the fall risk [44] and it increases the blood flow [55], it is suggested to include the WBVE in the management of the AD patients.

Voet et al, 2013 [40] have presented a comprehensive review about the clinical application of the WBV and they suggested that the WBVE may be a complementary training to standard physical rehabilitation program and appears to have potential benefits in the sensorimotor system performance of patients with neurodegenerative diseases. In addition, the WBVE is capable to facilitate the liberation of important molecules in the circulation, as the IGF1, that are relevant to the AD patient in the pathway involved in this disease. Moreover, Di Loreto et al 2004 [60] and Goto and Takamatsu, 2005 [72] have reported increases of the concentration of epinephrine and norepinephrine due to the WBVE and, as described by Lin and Kuo, 2013 [31], this fact would be also important to the AD patients due to the norepinephrine participates in commanding the consolidation and retrieval of memory, especially emotional memory.

Putting together the findings described in Table 1 and Table 2, although physical activities have been used to management of AD patients, no publications were found in the PubMed involving whole body vibration exercises and the patients with this neurodegenerative disease.

In addition, Phillips et al, 2014 [86] have described that although the relationship between increased physical activity and cognitive ability has been suggested for a long time, the comprehension of the possible mechanisms involved in this is recent. There are evidences that indicate that physical activity is effective procedure to improve cognitive function in all ages, and in particular, to elderlies who are vulnerable to neurodegenerative disorders. Moreover, Phillips et al, 2014 [86] reported that physical activity alters trophic factor signaling and, in turn, neuronal function and structure in areas critical for cognition. It is presented that sustained exercises have relevant role in modulating anti-inflammatory effects and in preserving cognitive function in aging and neuropathological conditions.

3. Conclusions

In conclusion, considering the importance of the exercises for all the persons, and specifically to seniors and patients with neurodegenerative disorders, as to the individuals with AD, it is possible to conclude that the WBVE can be a relevant, viable, safe and inexpensive strategic option of physical activity to patients with Alzheimer's disease. Moreover, WBVE have been important to improve the posture and gait disturbances and decrease the risk of falls, which are present in the AD patients, besides their cognitive limitations.

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REFERENCES

[1] Querfurth, H. W., LaFerla, F. M., 2010, Alzheimer's disease. N. Engl. J. Med., 362, 329-344.

[2] Aprahamian, I., Stella, F., Forlenza, O. V., 2013, New treatment strategies for Alzheimer's disease: is there a hope? Indian. J. Med. Res., 138, 449-460.

[3] Riedel, W. J., 2014, Preventing cognitive decline in preclinical Alzheimer's disease. Curr. Opin. Pharmacol., 14, 18-22.

[4] Dugu, M., Neugroschl, J., Sewell, M., Marin, D., 2003, Review of dementia. Mt. Sinai. J. Med., 70, 45-53.

[5] Thies, W., Bleiler, L., 2013, Alzheimer's Association. 2013 Alzheimer's disease facts and figures. Alzheimers. Dement., 9, 208-245.

[6] Scarmeas, N., Albert, M., Brandt, J., Blacker, D., Hadjigeorgiou, G., Papadimitriou, A., Dubois, B., Sarazin, M.,

Wegesin, D., Marder, K., Bell, K., Honig, L., et al, 2013, Motor signs predict poor outcomes in Alzheimer disease. Neurology, 64, 1696-1703.

[7] Sato, Y., Kanoko, T., Satoh, K., Iwamoto, J., 2004, Risk factors for hip fracture among elderly patients with Alzheimer's disease. J. Neurol. Sci., 223, 107-112.

[8] Gago, M. F., Fernandes, V., Ferreira, J., Silva, H., Rocha, L., Bicho, E., Sousa, N., 2014, Postural stability analysis with inertial measurement units in Alzheimer's disease. Dement. Geriatr. Cogn. Dis. Extra., 4, 22-30.

[9] Morris, J. C., Rubin, E. H., Morris, E. J., Mandel, S. A., 1087, Senile dementia of the Alzheimer's type: an important risk factor for serious falls. J. Gerontol., 42, 412-417.

[10] Kokkinos, P., Myers, J., 2010, Exercise and physical activity: clinical outcomes and applications. Circulation, 122, 1637-1648.

[11] Booth, F. W., Roberts, C. K., Laye, M. J., 2012, Lack of exercise is a major cause of chronic diseases. Compr. Physiol., 2,1143-1211.

[12] Chakravarthy, M. V., Joyner, M. J., Booth, F. W., 2002, An obligation for primary care physicians to prescribe physical activity to sedentary patients to reduce the risk of chronic health conditions. Mayo. Clinic. Proceed., 77, 165-173.

[13] Brown, W. J., McLaughlin, D., Leung, J., McCaul, K. A., Flicker, L., Almeida, O. P., Hankey, G. J., Lopez, D., Dobson. A. J., 2012, Physical activity and all-cause mortality in older women and men. Br. J. Sports. Med., 46, 664-668.

[14] Guimarães, G. V., Ciolac, E. G., 2014, Physical activity: practice this idea. Am J Cardiovasc. Dis., 4, 31-33.

[15] Tarumi, T., Zhang, R., 2014, Cerebral hemodynamics of the aging brain: risk of Alzheimer disease and benefit of aerobic exercise. Front. Physiol., 5-6;5:6. eCollection.

[16] Hu, F. B., Sigal, R. J., Rich-Edwards, J. W., Colditz, G. A., Solomon, C. G., 1999, Willett WC, Speizer FE, Manson JE. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. JAMA., 282, 1433-1439.

[17] Hu, F. B., Stampfer, M.J., Colditz, G.A., Ascherio, A., Rexrode, K.M., Willett, W. C., 2000, Manson JE. Physical activity and risk of stroke in women JAMA., 283, 2961-2967.

[18] Hu, F. B., Manson, J. E., Stampfer, M. J., Colditz, G., Liu, S., Solomon, C. G., 2001, Willett, WC. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. New. Engl. J. Med., 345, 790-797.

[19] Leitzmann, M. F., Rimm, E. B., Willett, W. C., Spiegelman, D., Grodstein, F., Stampfer, M. J., Colditz, G. A., Giovannucci, E., 1999, Recreational physical activity and the risk of cholecystectomy in women. N. Engl. J. Med., 341, 777-784.

[20] Manson, J. E., Hu, F. B., Rich-Edwards, J. W., Colditz, G. A., Stampfer, M. J., Willett, W. C., Speizer, F. E., Hennekens, C. H., 1999, A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N. Engl. J. Med., 341, 650-658.

[21] Martínez, M. E., Grodstein, F., Giovannucci, E., Colditz, G. A., Speizer, F. E., Hennekens, C., Rosner, B., Willett, W. C., Stampfer, M. J., 1997, A prospective study of reproductive factors, oral contraceptive use, and risk of colorectal cancer. Cancer Epidemiol. Biomarkers. Prev., 6, 1-5.

[22] Rockhill, B., Willett, W. C., Hunter, D. J., Manson, J. E., Hankinson, S. E., Colditz, G. A., 1999 A prospective study of recreational physical activity and breast cancer risk. Arch. Intern. Med., 159, 2290-2296.

[23] Rockhill, B., Willett, W. C., Manson, J. E., Leitzmann, M. F., Stampfer, M. J., Hunter, D. J., Colditz, G. A., 2001, Physical activity and mortality: a prospective study among women. Am. J. Public Health, 91, 578-583.

[24] Booth, F. W., Chakravarthy, M. V., Spangenburg, E. E., 2002, Exercise and gene expression: physiological regulation of the human genome through physical activity. J. Physiol., 543, 399-411.

[25] Lautenschlager, N. T., Cox, K. L., Flicker, L., Foster, J. K., Van Bockxmeer, F.M., Xiao, J., Greenop, K. R., Almeida, O. P., 2008, Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial. JAMA., 300, 1027-1037.

[26] Selkoe, D. J., 2012, Preventing Alzheimer's disease. Science, 337, 1488-1492.

[27] Hirsch, M. A., Sanjak, M., Englert, D., Iyer, S., Quinlan, M. M., 2014, Parkinson patients as partners in care. Parkinsonism. Relat. Disord., Suppl 1, S174-179.

[28] Gons, R. A., Tuladhar, A. M., de Laat, K. F., Van Norden, A. G., Van Dijk, E. J., Norris, D. G., Zwiers, M. P., de Leeuw, F. E., 2013, Physical activity is related to the structural integrity of cerebral white matter. Neurology, 81, 971-976

[29] Tseng, M. L., Ho, C. C., Chen, S. C., Huang, Y. C., Lai, C. H., Liaw, Y. P., 2013, A simple method for increasing levels of high-density lipoprotein cholesterol: a pilot study of combination aerobic- and resistance-exercise training. Int. J. Sport. Nutr. Exerc. Metab., 23, 271-281.

[30] Ferris, L.T., Williams, J.S., Shen, C.L., 2007, The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. Med. Sci. Sports. Exerc., 39, 728-733.

[31] Lin, T.W., Kuo, Y.M., 2013, Exercise benefits brain function: the monoamine connection. Brain Sci., 3, 39-53.

[32] De la Torre, J. C., 2013, Vascular risk factors: a ticking time bomb to Alzheimer's disease. Am. J. Alzheimers. Dis. Other. Demen., 28, 551-559.

[33] Carro, E., Trejo, J. L., Busiguina, S., Torres-Aleman, I., 2001, Circulating insulin-like growth factor I mediates the protective effects of physical exercise against brain insults of different etiology and anatomy. J. Neurosci., 21, 5678-5684.

[34] Harada, K., Shibata, A., Lee, E., Oka, K., Nakamura, Y., 2011, Longitudinal change in awareness levels of Japanese exercise guidelines and physical activity. Nihon. Koshu. Eisei. Zasshi., 58, 190-198.

[35] Fabel, K., Fabel, K., Tam, B., Kaufer, D., Baiker, A., Simmons, N., Kuo, C. J., 2003, Palmer TD. VEGF is necessary for exercise-induced adult hippocampal neurogenesis. Eur. J. Neurosci., 18, 2803-2812.

[36] Lopez-Lopez, C., LeRoith, D., Torres-Aleman, I., 2004,

Insulin-like growth factor I is required for vessel remodeling in the adult brain. Proc. Natl. Acad. Sci. USA., 101, 9833-9838.

[37] Zheng, W.H., Quirion, R., 2004, Comparative signaling pathways of insulin-like growth factor-1 and brain-derived neurotrophic factor in hippocampal neurons and the role of the PI3 kinase pathway in cell survival. J. Neurochem., 89, 844-852.

[38] Zeng, L., He, X., Wang, Y., Tang, Y., Zheng, C., Cai H, Liu, J., Wang, Y., Fu, Y., 2014, Yang GY. MicroRNA-210 overexpression induces angiogenesis and neurogenesis in the normal adult mouse brain. Gene. Ther., 21, 37-43.

[39] Seals, D. R., Desouza, C. A., Donato, A. J., 2008, Tanaka H. Habitual exercise and arterial aging. J. Appl. Physiol., 105, 1323-1332.

[40] Voet, N. B., van der Kooi, E. L., Riphagen, I. I., Lindeman, E., van Engelen, B. G., Geurts, A. C., 2013, Strength training and aerobic exercise training for muscle disease. Cochrane. Database. Syst. Rev., 7, CD003907.

[41] Rittweger, J., 2010, Vibration as an exercise modality: how it may work, and what its potential might be. Eur. J. Appl. Physiol., 108, 877-904.

[42] Schuhfried, O., Mittermaier, C., Jovanovic, T., Pieber, K., Paternostro-Sluga, T., 2005, Effects of whole-body vibration in patients with multiple sclerosis: a pilot study. Clin. Rehabil., 19, 834-842.

[43] Turbanski, S., Haas, C. T., Schmidtbleicher, D., Friedrich, A., Duisberg, P., 2005, Effects of random whole-body vibration on postural control in Parkinson's disease. Res. Sports. Med., 13, 243-256.

[44] Prisby, R. D., Lafage-Proust, M. H., Malaval, L., Belli, A., Vico, L., 2008, Effects of whole body vibration on the skeleton and other organ systems in man and animal models: what we know and what we need to know. Ageing Res. Rev., 7, 319-329.

[45] Bosco, C., Cardinale, M., Tsarpela, O., 1999, Influence of vibration on mechanical power and electromyogram activity in human arm flexor muscles. Eur. J. Appl. Physiol. Occup. Physiol., 79, 306-311.

[46] Cardinale, M., Lim, J., 2003, Electromyography activity of vastus lateralis muscle during whole-body vibrations of different frequencies. J. Strength. Cond. Res., 17, 621-624.

[47] Cochrane, D. J., Stannard, S. R., 2005, Acute whole body vibration training increases vertical jump and flexibility performance in elite female field hockey players. Br. J. Sports. Med., 39, 860-865.

[48] Delecluse, C., Roelants, M., Diels, R., Koninckx, E., Verschueren, S., 2005, Effects of whole body vibration training on muscle strength and sprint performance in sprint-trained athletes. Int. J. Sports. Med., 26, 662-668.

[49] Torvinen, S., Sievänen, H., Järvinen, T. A., Pasanen, M., Kontulainen, S., Kannus, P., 2002, Effect of 4-min vertical whole body vibration on muscle performance and body balance: a randomized cross-over study. Int. J. Sports. Med., 23, 374-379.

[50] Verschueren, S. M., Roelants, M., Delecluse, C., Swinnen, S., Vanderschueren, D., Boonen, S., 2004, Effect of 6-month whole body vibration training on hip density, muscle strength, and postural control in postmenopausal women: a randomized controlled pilot study. J. Bone. Miner. Res., 19, 352-359.

[51] Iwamoto, J., Takeda, T., Sato, Y., Uzawa, M., 2005, Effect of whole-body vibration exercise on lumbar bone mineral density, bone turnover, and chronic back pain in post-menopausal osteoporotic women treated with alendronate. Aging. Clin. Exp. Res., 17, 157-163.

[52] Mester, J., Kleinöder, H., Yue, Z., 2006, Vibration training: benefits and risks. J. Biomech., 39, 1056-1065.

[53] Cardinale, M., Wakeling, J., 2005, Whole body vibration exercise: are vibrations good for you? Br. J. Sports. Med., 39, 585-589.

[54] Russo, C. R., Lauretani, F., Bandinelli, S., Bartali, B., Cavazzini, C., Guralnik, J. M., Ferrucci, L., 2003; High-frequency vibration training increases muscle power in postmenopausal women. Arch. Phys. Med. Rehabil., 84, 1854-1857.

[55] Herrero, A. J., Martín, J., Martín, T., García-López, D., Garatachea, N., Jiménez, B., Marín, P. J., 2011, Whole-body vibration alters blood flow velocity and neuromuscular activity in Friedreich's ataxia. Clin, Physiol, Funct, Imaging., 31, 139-144.

[56] Fuermaier, A. B., Tucha, L., Koerts, J., van Heuvelen, M. J., van der Zee, E. A., 2014, Lange KW, Tucha O. Good vibrations - effects of whole body vibration on attention in healthy individuals and individuals with ADHD. PLoS. One., 9(2):e90747.

[57] Regterschot, G. R., Van Heuvelen, M. J., Zeinstra, E. B., Fuermaier, A. B., Tucha, L., Koerts, J., Tucha, O., Van Der Zee, E. A., 2014, Whole body vibration improves cognition in healthy young adults. PLoS One., 9(6):e100506. doi: 10.371/journal.pone.0100506.

[58] Lorezen, C., Maschette, W., Koh, M., Wilson, C., 2009, Inconsistent use of terminology in whole body vibration exercise research. J. Sci. Med. Sport., 12, 676-678.

[59] Marin, P. J., Bunker, D., Rhea, M. R., Ayllón, F. N., 2009, Neuromuscular activity during whole-body vibration of different amplitudes and footwear conditions: implications for prescription of vibratory stimulation. J. Strength. Cond. Res., 23, 2311-2316.

[60] Di Loreto, C., Ranchelli, A., Lucidi, P., Murdolo, G., Parlanti, N., De Cicco, A., Tsarpela, O., Annino, G., Bosco, C., Santeusanio, F. et al., 2004, Effects of whole-body vibration exercise on the endocrine system of healthy men. J. Endocrinol. Invest., 27, 323-327.

[61] Nindl, B. C., Pierce, J. R., 2010, Insulin-like growth factor I as a biomarker of health, fitness, and training status. Med. Sci. Sports. Exerc., 42, 39-49.

[62] Abeles, A. M., Pillinger, M. H., Solitar, B. M., Abeles, M., 2007, Narrative review: the pathophysiology of fibromyalgia. Ann. Intern. Med., 146, 726-734.

[63] Bennett, R. M., Cook, D. M., Clark, S. R., Burckhardt, C.S., Campbell, S. M., 1997, Hypothalamic-pituitary-insulin-like growth factor-I axis dysfunction in patients with fibromyalgia. J. Rheumatol., 24, 1384-1389.

[64] Leal-Cerro, A., Povedano, J., Astorga, R., Gonzalez, M.,

Silva, H., Garcia-Pesquera, F., Casanueva, F. F., Dieguez, C., 1999, The growth hormone (GH)-releasing hormone-GH-insulin-like growth factor-1 axis in patients with fibromyalgia syndrome. J. Clin. Endocrinol. Metab., 84, 3378-3381.

[65] Paiva, E. S., Deodhar, A., Jones, K. D., Bennett, R., 2002, Impaired growth hormone secretion in fibromyalgia patients: evidence for augmented hypothalamic somatostatin tone. Arthritis. Rheum., 46, 1344-1350.

[66] Bosco, C., Iacovelli, M., Tsarpela, O., Cardinale, M., Bonifazi, M., Tihanyi, J., Viru, M., De Lorenzo, A., Viru, A., 2000, Hormonal responses to whole-body vibration in men. Eur. J. Appl. Physiol. 81, 449-454.

[67] Kvorning, T., Bagger, M., Caserotti, P., Madsen, K., 2006, Effects of vibration and resistance training on neuromuscular and hormonal measures. Eur. J. Appl. Physiol., 96, 615-625.

[68] 68- Gosselink, K. L., Roy, R. R., Zhong, H., Grindeland, R. E., Bigbee, A. J., 2004, Edgerton VR. Vibration-induced activation of muscle afferents modulates bioassayable growth hormone release. J. Appl. Physiol. (1985), 96, 2097-2102.

[69] McCall, G. E., Grindeland, R. E., Roy, R. R., Edgerton, V. R., 2000, Muscle afferent activity modulates bioassayable growth hormone in human plasma. J. Appl. Physiol., 89, 1137-1141.

[70] Florini, J. R., Prinz, P. N., Vitiello, M. V., Hintz, R. L., 1985, Somatomedin-C levels in healthy young and old men: Relationship to peak and 24-hour integrated levels of growth hormone. J. Gerontol., 40, 2-7.

[71] Cardinale, M., Soiza, R.L., Leiper, J.B., Gibson, A., Primrose, W.R., 2010, Hormonal responses to a single session of whole body vibration exercise in older individuals. Br. J. Sports Med., 44, 284-288.

[72] Goto, K., Takamatsu K., 2005, Hormone and lipolytic responses to whole body vibration in young men. Jpn. J. Physiol., 55, 279-284.

[73] Cheung, W. H., Mok, H. W., Qin, L., Sze, P. C., Lee, K. M., Leung, K. S., 2007, High-frequency whole-body vibration improves balancing ability in elderly women. Arch. Phys. Med. Rehabil., 88, 852-857.

[74] Pinto, N. S., Monteiro, M. B., Meyer, P. F., Santos-Filho, S. D., 2010, Azevedo-Santos F, Bernardo RM, Paiva D, Thompson D, Missailidis S, Marin PJ et al. The effects of whole-body-vibration exercises in Parkinson's disease: a short review. JMMS., 2, 594-600.

[75] El-Shamy, S.M., Effect of whole-body vibration on muscle strength and balance in diplegic cerebral palsy: a randomized controlled trial, 2014, Am. J. Phys. Med. Rehabil., 93, 114-121.

[76] Ness, L. L., Field-Fote, E. C., 2009, Effect of whole-body vibration on quadriceps spasticity in individuals with spastic hypertonia due to spinal cord injury. Restor. Neurol. Neurosci., 27, 621-631.

[77] Van Nes, I. J., Geurts, A. C., Hendricks, H. T., Duysens, J., 2004, Short-term effects of whole-body vibration on postural control in unilateral chronic stroke patients: preliminary evidence. Am. J. Phys. Med. Rehabil., 83, 867-873.

[78] Santos-Filho, S. D., Monteiro, M. O. B., Paiva, D. N., Arnóbio, A., Paoli, S., Sá-Caputo, D. C., Guedes-Aguiar, E. O., Presta, G. A., Marin, P. J., Bernardo-Filho M., 2014, Possible Benefits of the Whole Body Vibration in the Treatment of Complications in Stroke Patients. BJMMR., 4, 1539-1551.

[79] Haas, C. T., Buhlmann, A., Turbanski, S., Schmidtbleicher, D., 2006, Proprioceptive and sensorimotor performance in Parkinson's disease. Res. Sports. Med., 4, 273-287.

[80] Ebersbach, G., Edler, D., Kaufhold, O., Wissel, J., 2008, Whole body vibration versus conventional physiotherapy to improve balance and gait in Parkinson's disease. Arch. Phys. Med. Rehabil., 89, 399-403.

[81] Sitjà Rabert, M., Rigau Comas, D., Fort Vanmeerhaeghe, A., Santoyo Medina, C., Roquéi Figuls, M., Romero-Rodríguez, D., Bonfill Cosp, X., 2012, Whole-body vibration training for patients with neurodegenerative disease. Cochrane Database Syst. Rev., 2, CD009097.

[82] World Health Organization, World Federation of Neurology. Atlas: country resources for neurological disorders 2004. World Health Organization, Geneva (2004).

[83] Alzheimer's Association, 2013 Alzheimer's Disease Facts and Figures, http://act.alz.org/site/DocServer/facts_figures_2013.pdf?docID=15724 (accessed on April 3rd, 2014.

[84] Hebert, L. E., Beckett, L. A., Scherr, P.A., Evans, D.A., 2001, Annual incidence of Alzheimer disease in the United States projected to the years 2000 through 2050. Alzheimer. Dis. Assoc. Disord., 15, 169-173.

[85] Milton, K., Macniven, R., Bauman, A., 2014, Review of the epidemiological evidence for physical activity and health from low- and middle-income countries. Glob. Public Health, 9, 369-381.

[86] Phillips, C., Baktir, M. A., Srivatsan, M., Salehi, A., 2014, Neuroprotective effects of physical activity on the brain: a closer look at trophic factor signaling. Front. Cell. Neurosci., 8:170. doi: 10.3389/fncel.2014.00170.