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EXERCISE AND SYMPTOMS OF MULTIPLE SCLEROSIS: WHAT HAS BEEN KNOWN SO FAR?

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ABSTRACT

Exercise was thought to exacerbate the symptoms of Multiple Sclerosis before now. However, an avalanche of researches reported otherwise, presently. Exercise has beneficial effects to persons with Multiple Sclerosis. These effects range from improved cognition, memory, gait and mobility, self efficacy, balance and many other improvements. The exercises known to be good for this category of patients include Strength exercise, cardiorespiratory fitness exercise and aquatic exercise. Persons with multiple sclerosis present clinically with witness, gait disturbance, cognitive decline, memory impairment, etc. These could render the persons affected incapable of observing their activities of daily living and hence would have reduced quality of life. The symptoms are due to demyelination taking place especially in the periventricular and perivenular regions of the CNS. Thankfully, exercise is now known to improve the symptoms of this condition. This is because, it is neuroregenerative, neuroprotective and it improves immune functions.

Keywords: Exercise, Multiple Sclerosis, Symptoms

INTRODUCTION

Multiple Sclerosis (MS) is a chronic remitting/ relapsing disease of unknown etiology that consists of plaques of demyelination (and axonal loss) at sites throughout the human CNS. Its pathology is characterized by areas of myelin loss in periventricular and perivenular distribution in association with conspicuous astrocytic proliferation and variable degree of neuronal and axonal damage. Only a proportion of lesions are clinically eloquent. The principal determinant of disability is neuronal degeneration and this can be extremely variable (Behan et al, 2002). Several hypotheses have been put forward to explain the pathogenesis of MS. Among these, are the autoimmune, degeneration/ metabolic and neural initiated disease hypotheses (Behan et al, 2002; Prat & Antel, 2005 & Wolfang, 2007).

Autoimmune Hypothesis

This holds that antibodies are directed against AN2, myelin components and axons (Wolfang, 2007). AN2 is a cell-surface glycoprotein expressed on oligodendrocytes progenitor cells in the developing and adults CNS (Stegmuller et al, 2002). Antibodies against AN2 have been reported in CSF from certain patients with MS with active relapse (Niehau, 2000). In invitro systems, these antibodies block migration of oligodendrocytes precursor cells, synthesis of myelin and may lead to lysis of oligodendrocytes (Zhang, 2005). Antibodies against myelin components such as myelin basic protein (MBP), proteolipid protein (PLP) and myelin

oligodendrocytes protein (MOG) interfere with remyelination. Axonal antibodies have also been found in the CSF of persons with MS with a characteristic MS axonal pathology (axonal transaction, swollen APP-staining ovoids and wallerian degeneration). However, the central epitopes that trigger the autoimmune response in MS are still unknown. The inflammatory cells in MS include primary CD8 T-lymphocytes, microglia, and macrophages. In addition, components of humoral immunity, including B-lymphocytes, plasma cells, immunoglobulin and complement have been identified in plaques.

Neurodegenerative and Metabolic Hypothesis

This holds that, MS is a neurodegenerative and metabolic disorder with a strong polygenic influence, the predominant genes being on chromosome 17 and in conjunction with environmental factors and endogenous sex hormones (Behan et al, 2002). The principal cellular abnormality appears to occur in the astrocyte and this gives rise to disruption of the blood brain barrier with secondary metabolic changes in the myelin. The process is generalized throughout the CNS, the plaques being focal areas of increased tissue damage.
Neural initiated disease Hypothesis. This implicates that, events within the CNS initiate MS disease process (Prat & Antel, 2005). A frequent speculation is that an acquired acute or persistent infection of neural cells could result in release of tissue antigens that in turn would provoke a disease relevant autoimmune response.
Physiological dysfunctions in MS

The principal physiological dysfunctions of MS are loss of muscle activation and fatigue and effects of secondary disuse (Katrina & Phu, 2004). The plaques in the CNS cause a slowed nerve conduction velocity secondary to demyelination and attempted remyelination by the body. As the disease progresses, it is believed the loss of axons and gray matter over time contribute to nerve conduction block and the presence of MS symptoms (Smith & McDonald, 1999). The nerve conduction abnormalities result in impaired central activation, reduced motor unit recruitment and discharge rates, reduced cortical drive and increased cortical activation per activity compared with people without MS (Ng, Miller & Gelinas, 2004, Rice, Vollmer & Bigland-Ritchie, 1992, Shean, Murray & Rothwell, 1997 & Rocca, Pagain & Ghezzi, 2003).

People with MS who suffer from loss of muscle activation and control often experience difficulty in participating in both activities of daily living and leisure activities (Motl, Snook & McAuley, 2006 & Stuifbergen, Bloiz & Harrison, 2006). This can lead to a gradual decrease in physical activity. It has been shown that in persons with MS, physical limitations are positively correlated with physiological changes (Katrina & Phu, 2004). However, these limitations have been shown to be similar to those that occur in healthy people who have experienced prolonged physical inactivity. Secondary disuse results in reduced muscle force as a consequence of changes in metabolic levels, failure of excitation-contraction coupling mechanism and reduced muscle fiber size and number (Kent-Brawn, Sharma & Miker, 1994; Sharma, Kent-Brawn & Mynhier, 1995; de Haan, de Ruiter & Van Der Wande, 2000 & Kent-

Brawn& Ng, 1997) and through reduced cardiorespiratory fitness as a consequence of lower V02 maximum, higher overall oxygen consumption per activity and earlier achievement of the anaerobic threshold (Kent-Brawn et al, 1997 & Ponichtera, 1993).

Clinical Presentation

Clinically, the core features are relapses, presumed to result from acute inflammatory demyelination and progression of neurological disability as a result of inflammatory demyelination, gliosis and axonal loss (Pawate & Sriram, 2010). The clinical presentations of MS are divided into four broad types. In 80% of patients, MS presents as relapsing remitting disease (RRMS) that usually lasts for 15 years, characterized by exacerbations and remissions and partial response to immunomodulatory therapy. The disease then takes in a more insiduos course with a monotonous progressive loss of motor functions and is referred to as secondary progressive disease (SPMS). In 15% of patients, MS is progressive from onset (Primary progressive MS); nonetheless, this disease subtype is similar to secondary progressive MS. In a smaller subset of patients who begin with primary progressive symptoms, show clinical relapses are called progressive relapsing type. According to Longmore et al (2004), the clinical features of MS are fatigue, weakness, spasticity, numbness, pins and needles, trigeminal neuralgia, dysaesthesia, urge incontinence, swallowing disorders, constipation, sexual dysfunction, diplopia, nystagmus, optic neuritis, ataxia, intention tremor, cognitive decline, memory impairment, dementia, depression or rarely euphoria and vertigo. Epilepsy and aphasia are rare.

Exercise and Multiple Sclerosis

There is considerable debate over the safety and appropriateness of prescribing strenuous physical activity for persons with MS (Katrina & Phu, 2009). Before now, exercise was thought to worsen the signs and symptoms of MS or even increase the disease activity. However, exercise is now accepted as an important aspect of symptomatic treatment for persons with MS (Rietberg et al, 2005). According to Mezzapessa et al (2008), it is important to encourage people with MS to start a regular exercise program early in the disease course. Targeting identified deficits can maximize their physical abilities through neuroplastic adaptations and prevention of the secondary effects of inactivity. This can in turn improve quality of life by reducing levels of physical disability, improving employment sustainability, and reducing the utilization of welfare benefits and health services.

It has been shown that, people with a recent diagnosis of MS, who have no observable physical disability (Expanded Disability Status Scale score of between 0-2) already have kinematic, kinetic, balance and muscle activities changes (Benedetti et al, 1999 & Martin et al 2006). This sub-group of people is the most likely to experience brain adaptations as neuroplasticity and decreased central activation is more effective in people with fewer lesions (Mezzapesa et al, 2008). Filipi et al (2010) concluded in their study that, as in the case for the general population, exercise significantly improves the overall condition of people with MS. Participation in structured resistance training program has positive effects on gait,

balance, and level of fatigue, as well as cognition. Researches investigating the use of aquatic exercise and general exercise support that, they provide improved muscle strength, improved fitness, improved gait and mobility, reduced fatigue, increased quality of life or sense of wellbeing, pain relief, improved balance and improved joint range of motion (Coxhead, 2009). Katrina and Phu (2009) wrote that, lower levels of evidence show the benefits of strength training in MS patients as: improved walking speed and endurance, improved self efficacy, improved gait kinematics, improved immune system function, improved respiratory muscle strength, reduced fatigue, reduced physical and social disability and reduced symptoms of coronary artery disease.

Romberg et al (2004) in a randomized study found that, long term exercise led to significant and clinically meaningful changes in the walking speed of patients with mild to moderate MS. This was accompanied by significant improvements in upper extremity endurance. The intervention showed no effect between the groups on lower extremity strength, VO2 peak, static balance or manual dexterity. The clinical relapses of MS were evenly distributed between the groups showing that exercise has no detrimental effect on MS activity. In another study by Castellano et al (2008), MS and controlled subjects showed similar cytokine response to exercise. Cytokines play an important role in the pathogenesis of MS and a major target for treatment interventions. Regular exercise reduces functional loss associated with Multiple Sclerosis (MS). However, the impact of exercise on inflammatory mediators associated with disease activity remains inadequately explored.

Carl et al (2007) proposed that, reduction of inflammation by exercise is a common means by which exercise reduces peripheral risk factors for cognitive decline and neurodegeneration. In human, robust effects of exercise have been most clearly demonstrated in aging population, where sustained exercise participation enhances learning and memory, improves executive function, counteracts age related and disease related mental decline and protects against age related atrophy in brain areas crucial for higher cognitive processes (Colcombe & Kramer, 2003). Exercise has also neuroprotective effects and therapeutic and protective effects (Carl et al, 2007). The neuroprotective effects have been best defined with respect to reducing brain injury, and delaying onset of decline in several neurodegenerative diseases. For example, engaging individuals affected by stroke in post stroke therapeutic exercise programs accelerates functional rehabilitation. Clinical trials assessing the efficacy of post-stroke exercise typically combine cardiovascular training (treadmill or exercise bike) with weight training or targeted movement therapy and the improvements are probably due to the combination of interventions. Randomized and crossover clinical trials demonstrate the efficacy of aerobic or resistance training exercise (2-4 months) as a treatment for depression in both young and older individuals. The benefits are similar to those achieved with antidepressants (Carl et al, 2007).

Mechanisms of Exercise Effects on Neuronal health

Exercise modulates a range of supporting systems for brain maintenance and plasticity including neurogenesis, enhanced CNS metabolism and angiogenesis (Carl et al, 2007). In both young and old animal, exercise stimulates proliferation of the neuronal progenitor population, increases the number of new neurons and promotes survival of these new cells. At present, Brain derived neurotrophic factor (BDNF), Insulin like Growth factor (IGF-I), and vascular derived Endothelial Growth factor (VEGF) are the principal growth factors known to mediate the effects of exercise on the brain. These growth factors work in concert to produce complementary functional effects, modulating both overlapping and unique aspects of exercise-related benefits in brain plasticity, function and health. Whereas IGF-I and BDNF mediate behavioural improvements with exercise, the interactive effects of IGF-I with VEGF seem to orchestrate exercise-induced neurogenesis and angiogenesis.

CONCLUSION

Exercise was thought to have a detrimental effect on MS (Romberg et al). However, bodies of evidences now accept exercise as an integral part of management of MS symptoms (Rietberg et al, 2005). Exercise improves cognition, memory, fitness, mobility and gait, Range of motion, walking speed and endurance, self efficacy, immune function, inflammation, respiratory muscle strength, reduced physical disability and symptoms of coronary artery disease (Carl et al, 2007, Colomber & Kramer, 2003, Coxhead, 2009, Katrina & Phu, 2009 & Romberg et al, 2004). The exercises for this patient's category include strength exercise, aquatic exercise and cardiorespiratory fitness exercise. Nonetheless more rigorous clinical trials need to be carried out preferably in multidisplinary approach to effectively evaluate the yet unexplored benefits of exercise for these patients.

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