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Cognitive and behavioural effects of physical exercise in psychiatric patients

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A B S T R A C T

The current review outlines the under-appreciated effects of physical exercise on the course of psychiatric disorders, focussing on recent findings from animal and human research. Several studies have shown that regular physical exercise is significantly beneficial for psychiatric patients both on a biological and a psychological level. Positive effects of controlled exercise include improved metabolic responses, neuro-protection, increased quality of life, and reduced psychopathological symptoms.

Studies investigating the effectiveness of various physical training interventions in alleviating severe mental diseases, such as Alzheimer's dementia (AD), schizophrenia (SZ) or major depressive disorder (MDD) indicate that physical exercise can relieve symptoms of depression, psychosis and dementia and more importantly can curtail further progression of these diseases. This review assesses the most effective methods of physical training for specific psychiatric symptoms.

Introducing physical exercise in therapeutic regimes would be an innovative approach that could significantly reduce the severity of psychopathological and cognitive symptoms in patients. The positive biological and molecular outcomes associated with physical exercise render it a concrete therapeutic strategy for improving the quality of live and reducing physical illness in psychiatric patients. Therefore, integrating physical activity into a patient's social life may be an effective treatment strategy. Furthermore, exercise might have the potential to be a preventative treatment within the context of multi-modal therapeutic programs.

Contents

Abbreviations: SZ, schizophrenia; AD, Alzheimer dementia; MDD, major depressive disorder; VO_2, aerobic capacity; HDL, high-density-lipoprotein; BMI, body mass index; ROS, reactive oxygen species; DNA, deoxyribonucleic acid; PET, positron-emission-tomography; BDNF, brain derived neurotrophic factor; IL-6, interleukin-6; LPS, lipopolysaccharide; SSRI, selective-serotonin-reuptake-inhibitors; MCI, mild cognitive impairment; MAPK, mitogen activated protein kinase; ERK, extracellular signal regulated kinase; ANP, atrial natriuretic peptide; CRF, cardiorespiratory fitness; apoE4, apolipoprotein E4; EEG, electroencephalography.

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1. Introduction

Physical activity refers to body movement that is produced by the contraction of skeletal muscles and that increases energy expenditure. It includes activities in the workplace (e.g., typing), around the house (e.g., household chores, such as cleaning) and during leisure time (e.g., walking, swimming, dancing, cycling). Exercise refers to planned, structured, and repetitive movement to improve or maintain one or more components of physical fitness (ACSM, 2009). There are an enormous number of studies, meta-analyses and reviews which indicates a relationship between physical and mental health and physical exercise.

Physical activity has been central to human survival. Rapoport (1990) points out that studies of the fossil record and of comparative neuroanatomy in primates demonstrate that brain size increased dramatically during hominid evolution, reaching a constant weight in modern *Homo sapiens* about 50,000–100,000 years ago. This is important as physical activity is known to enhance neuronal plasticity. Records from fossils indicate that early humans (*Homo sapiens idaltu*, hunted on foot and in groups. The success of this endeavour depended on their physical capabilities and endurance, but also on the social dynamics within the group, in order to promote goal-oriented collective behaviours. *Homo sapiens idaltu* walked great distances on a daily basis to seek adequate shelter and food. Physical effort and social interplay were so tightly related to the necessities of survival that humans evolved several neurophysiological reward systems to re-enforce these behaviours (Rapoport, 1990). Furthermore, fossil evidence suggests that endurance running is a derived capability of the genus Homo, originating about 2 million years ago, and this may have been instrumental in the evolution of the human body form (Bramble and Lieberman, 2004). Bramble and Lieberman (2004) has suggested that while running is now primarily a form of exercise and recreation, the roots of endurance running may be as ancient as the origin of the human genus. Bramble and Lieberman (2004) recommended it as a major contributing factor to the human body form.

During the last century, industries have automated many processes in developed countries and survival no longer depends on heavy physical activity. Since the 1990s, the American Heart Association, the World Health Organization (WHO) and the International Sport Physician Association (FIMS), have acknowledged that the lack of physical activity is a risk-factor for physical diseases, whereas life expectancy has increased for people with an active lifestyle. Medicinal treatment together with controlled physical activity is often administered to attenuate various disorders, such as hypertension, diabetes mellitus, osteoporosis and depression (Hellmich, 2010). From the above mentioned evolutionary point of view, a targeted approach is needed to compensate for the lack of physical activity that currently prevails in the developed world.

The biological effects of exercise within the human body are numerous and include cardiovascular, pulmonary, metabolic, muscular, molecular, and immunological changes, as well as changes in brain functioning and anatomy. Cardiovascular parameters include aerobic capacity (VO_2), lactate and ventilatory thresholds, and work efficiency. Oxygen consumption and carbon dioxide production are also of interest, as well as the metabolic parameters of glucose, cholesterol, cortisol, high-density-lipoprotein (HDL), insulin and factors such as body mass index (BMI) and body weight. Clinical studies also indicate an increase in endorphin production, an increase in neurotransmitter (serotonin, norepinephine, dopamine) and endocannabinoids (anandamide) production, an increase in functional plasticity, an increase in neuronal messenger cells, an increased release of neurotrophic factors and an increase in brain structures, e.g., the hippocampus (Pajonk et al., 2010; Rovio et al., 2010). More recently, there has been a debate about the role of reactive oxygen species (ROS), which are generated by regular exercise and are associated with the production of antioxidants, DNA (deoxyribonucleic acid) repair and protein degrading enzymes (Deslandes et al., 2009).

The question is whether these effects, particularly on the brain, are purely physical, or if they might have potential for improving psychiatric disorders. Evidences from clinical studies (Blumenthal et al., 2007; Hirsch et al., 2003; Rolland et al., 2007) indicate that physical exercise might have positive effects on the outcome of different mental diseases, e.g., major depressive disorders (MDD), Alzheimer's dementia and schizophrenia (SZ). Schizophrenia, major depressive disorders and Alzheimer's dementia are three severe and chronic forms of mental illnesses that rank among the ten most frequent causes of mental disability (Rossler et al., 2005). The pathogenesis of these disorders is thought to be a complex interplay between genetic and environmental factors (van Os et al., 2008). Although SZ and MDD differ in several important aspects from typical primary neurodegenerative disorders, such as AD, there is increasing evidence that they may share some core pathophysiological and molecular mechanisms. For example, the clinical manifestation of SZ includes negative symptoms such as anhedonia, avolition and social withdrawal, and decreased energy levels, as well as positive symptoms like hallucinations, delusions and thought disorders (Oertel-Knöchel et al., 2011). These negative symptoms of SZ mirror those observed for MDD, such as loss of energy, social withdrawal, and melancholia. There are only a few studies concerning physical exercise in MDD, but these indicate that it is an effective treatment for depression (e.g., Stathopoulou et al., 2006) and for the prevention of depression (Lampinen and Heikkinen, 2003).

Overall, similarities of symptoms of SZ, MDD and AD are depressive symptoms and cognitive deficits. In elderly people, there is a large overlap between MDD and neurodegenerative disorders. Some studies suggest that more than 50% of patients with AD suffer from co-morbid minor or major depression (Usman et al., 2010). Cognitive deficits that typically occur in MDD can be difficult to distinguish from those in early dementia (Robbins et al., 1996). Here, current studies indicate that physical exercise has comparable effects on depressive symptoms and cognitive deficits in all aforementioned psychiatric diseases, namely AD, MDD and SZ. Accordingly, several studies suggest that psychiatric patients suffer from a higher degree of physical illness (Smith et al., 2010). For example, when compared with controls, SZ patients are known to have a higher body weight (Wetterling et al., 2004), changes in pain perception and a higher prevalence of HIV, hepatitis, diabetes, cardiovascular illnesses, sexual dysfunction and osteoporosis (Prottengeier and Leucht, 2008). Further empirical studies have shown that patients with SZ have an increased somatic morbidity, consisting of a high consumption of nicotine, unbalanced nutrition, cardio-pulmonary deficits and a lower life expectancy (Laursen, 2011).

The question arises whether controlled physical training could reduce pathophysiological mechanisms in psychiatric patients. We