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THE ANTIDEPRESSANT ROLE OF PHYSICAL EXERCISE

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ABSTRACT. Depression is considered to be the most frequent mental disorder and is encountered in medical practice in all specialties. Depression is an affective disorder characterized by a change in mood. The etiopathogeny of depression is very complex. Physical exercise plays many roles: sanogenic; anti-aging, prolongevity and active longevity; diagnostic; therapeutic; economic benefits. The antidepressant role of physical exercise has been evidenced in many researches. The current data regarding the paradoxical effect of physical exercise, as a prooxidant at high intensity and as an antioxidant at moderate intensity for a prolonged duration, pose the problem of its antidepressant effect. Through its antioxidant role, physical exercise can also be recommended in antidepressant therapy, which may be associated with drug therapy.

Key words: depression, physical exercise, etiopathogeny of depression**,** the paradoxical effect of physical exercise, oxidative stress

REZUMAT. **Rolul antidepresiv al exerciţiului fizic**. Depresia este considerat a fi cea mai frecventa afecţiune mintală, ea fiind întâlnită în taote specialităţile practicii medicale. Depresia este o afecţiunie afectivă carecterizată prin schimbări de dispoziţie. Etiopatogenia depresiei este foarte complexă. Exerciţiul fizic are multe roluri: sanogenetic, anti înbătrânire, prolongevitate şi logevitate activă; diagnostic, terapeutic, economic. Rolul antidepresiv al exerciţiului fizic a fost evidenţiat in numeroase cercetări. Studii de actualitate privind efectul paradoxal al exerciţiului fizic de prooxodant la intensităţi mari şi antioxidant la intensităţi moderate pun şi problema rolului antidepresiv al acestuia. Datorită rolului antioxidant, exerciţiul fizic poate fi recomandat în terapia antidepresivă eventual asociat cu terapie medicamentoasă.

Cuvinte cheie: depresie, exerciţiu fizic, etiopatogenia depresiei, efectul paradoxal al exerciţiului fizic, stress oxidativ

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General considerations

Depression is considered to be the most frequent mental disorder and is encountered in medical practice in all specialties. Its prevalence is 25% for women and 12% for men over the entire life duration. The onset of major depressive disorder is in 50% of the cases between the age of 20 and 50 years, with a mean of 40 years. Recent epidemiological studies even report an onset age of 20 years. After the age of 50 years, the differences in prevalence decrease, the rate of depression being equal in the two genders (Prelipceanu 2011). The disease has been associated with suicide in a proportion of 10-15% (Chapman et al. 2008).

Depression is an affective disorder characterized by a change in mood. Major depressive disorder (mono- or unipolar depression) may take various forms: major depressive disorder with psychotic factors, melancholy, atypical depression, postpartum depression, recurrent depression, treatment-resistant depression, seasonal depressive disorder, and depressive disorder with catatonic factors (Prelipceanu 2011).

Etiopathogeny

The following have been incriminated in the etiopathogeny of depression:

- neuromediators;
- neuroendocrine axes, mainly the hypothalamic-pituitary-adrenal axis;
- neurotrophic factors;
- genetic factors;
- psychosocial stressing factors;
- cognitive distortions;
- nutritional deficiency.

1. The biochemical hypothesis

The small neuromediator molecules involved in the biochemistry of depression are:

- monoamines such as acetylcholine and serotonin (Chkhartishvili et al. 2011; Mchedlidze et al. 2011; Matsukawa et al. 2010; Olivier et al. 2008; Van den Hove et al. 2006; Jang et al. 2004);
- catecholamines such as dopamine and noradrenaline (He et al. 2012; Zhang et al. 2011; Mchedlidze et al. 2011; Breuer et al. 2008);
- amino acids such as glutamate, gamma-aminobutyric acid and glycine (Prelipceanu 2011; Shirayama et al. 2011; Feeney et al. 1993);
- galanin (Ye et al. 2007);
- nitric oxide (Ferreira et al. 2012).

2. The hypothesis of stress

Depression has been associated with a number of stressors that may cause the disease.

The stressors involve:

- the quantitative aspect of the stressing situation;
- the time factor: the accelerated rate of changes, with consequences on decision and execution, as well as the duration of strain: acute or chronic, interference with the periodicity of work and rest, the extent to which an individual can anticipate this duration;
- psychosocial factors.

Mental stress increasingly replaces physical stress. The human factor is considered to be responsible for its own inadaptation. The forms of stress associated with depression are those predominantly psychic or psychosocial (Prelipceanu 2011; Riga and Riga 2008; Derevenco et al. 1992).

3. The neuroendocrine hypothesis

This hypothesis is based on the activation/inhibition of neuroendocrine axes, initiated at the level of the hypothalamus:

- hyperactivity of the hypothalamic-pituitary-adrenocortical axis (Gelfo et al. 2012; Liu and Zhou 2012);
- diminution of the activity of the hypothalamic-pituitary-gonadal axis, of the activity of the hypothalamic-pituitary-thyroid axis and STH secretion (Walf and Frye 2005; Grippo et al. 2005).

4. The cognitive hypothesis

Depression is considered to be a consequence of cognitive distortions, "automatic negative thoughts": negative self-perception, the tendency to perceive the exterior world as hostile, and expectation of future suffering and insuccess of which the patient is aware and which determine self-restrictive behavioral patterns, with a cognitive and emotional deficit (Prelipceanu 2011; Yilmaz et al. 2011; Gao et al. 2009; Henningsen et al. 2009; Teskey et al. 2007; Naudon and Jay 2005).

5. The neurotrophic hypothesis

It is based on neurodegenerescence through the reduced effect of neurotrophic factors (NGF – nerve growth factor, neurotrophins; BDNF – brain-derived neurotrophic factor), which decrease in depression and cause hippocampal atrophy, decreased synaptic plasticity, decreased neurogenesis and gliogenesis (Yang et al. 2012; Kaae et al. 2012; Hemanth Kumar et al. 2012; Ye et al. 2011; Nowak et al. 2010; Fortunato et al. 2009; Song et al. 2009; Huston et al. 2009; Allaman et al. 2008; Jayatissa et al. 2006).

6. The hypothesis of nutritional deficiencies

Depression has been correlated with vitamin nutritional deficiencies (vitamin B_2, vitamin B_6, vitamin B_{12} and folic acid), omega-3 fatty acids and a tryptophan deficient diet (Yang et al. 2012).

7. The hypothesis of the disturbance of mineral homeostasis

Depression has been associated with the excess of Zn and heavy metals: Al, Pb, Hg (Cope et al. 2011; Brocardo et al. 2007; Null and Feldman 1995).

8. The hypothesis of seasonal variations

The absence of sun exposure and the winter season have been related to depressive syndromes (Friedman et al. 2011; Goldman et al. 2009).

9. The genetic hypothesis

Molecular genetic studies provide arguments regarding the implication of the short arm of chromosome 11 and possibly, chromosome X in depression.

The hypothesis is based on the 2-3-fold increased frequency of depression in the first degree relatives of patients and on the 50% concordance of the disease in monozygotic twins (Prelipceanu 2011).

Roles of physical exercise

Physical exercise plays many roles: sanogenic; anti-aging, prolongevity and active longevity; diagnostic; therapeutic; economic benefits (Bruja et al. 2013).

The beneficial effects of moderate exercise on immunity have been evidenced in young people compared to elderly; in patients infected with HIV; in patients with certain types of cancer; in chronic fatigue syndrome; in space flights (Tache and Boboş 2011).

Physical exercise has beneficial effects of normalizing glycemia in type 2 diabetic patients; beneficial effects of stimulating antioxidant mechanisms in case of moderate intensity and duration exercise; it plays a role in functional recovery after sports and other traumas (injuries); in locomotor disorders (kinesiotherapy); treatment of mental diseases, neuroses (depresssion, schizophrenia, anxiety), diabetes, coagulation disorders and fibrinolysis, dyslipidemia, cardiovascular disorders (coronary disease, hypertension) (Sbenghe 1999).

The antidepressant role of physical exercise has been evidenced in researches on:

- human subjects, patients with various forms of depression (Matthews et al. 2011; Franco et al. 2010; Weber and Edwards 2010; O'Connor 2007; Liu 2009; Krogh et al. 2009; McKercher et al. 2009; Blumenthal et al. 2007; Leppämäki et al. 2004; Conn 2010);
- rodents with induced depression (Dimatelis et al. 2012; He et al. 2012; Hendriksen et al. 2012; Sigwalt et al. 2011; Marais et al. 2009; Garza et al. 2004; Russo-Neustadt et al. 2000).

The antidepressant action mechanisms of physical exercise can be explained by:

- the increase of post-training brain serotonin levels (Dey et al. 1992);
- the increase of the level of brain tryptophan, a serotonin precursor (Soares et al. 2003);
- prevention of the decrease in serotonin and noradrenaline levels and restoration of dopamine levels (He et al. 2012);
- the mediator role of the macrophage migration inhibitory factor in the alteration of serotonin neurotransmission and in the induction of brain neurogenesis through the neurotrophic factor (Moon et al. 2012);
- the role of lactate for the alteration of fatty acid metabolism, partly mediated through the activation of the transforming growth factor in moderate intensity exercise (Yamada et al. 2012);
- the role in the hyporegulation of the functional level of proteins in the hippocampus, which is hyperregulated in animal depression models, through the early separation of the offspring from their mothers (Dimatelis et al. 2012);
- the increase in the level of neurotrophic factors (brain derived neurotrophic factor – BDNF) in the striated bodies and the hippocampus and the increase of neuronal plasticity (Marais et al. 2009; Garza et al. 2004);
- the implication of the pathways of phosphatidylinositol 3' kinase (PI-3K), mitogen-activated protein kinase (MAPK), and cyclic adenosine monophosphate (cAMP) in neuroprotection at hypothalamic level (Yang et al. 2012).

Conclusions

The current data regarding the paradoxical effect of physical exercise (Tache and Ciocoi-Pop 2013), as a prooxidant at high intensity and as an antioxidant at moderate intensity for a prolonged duration, pose the problem of its antidepressant effect. Oxidative stress has been involved in the pathogenesis of more than 100 diseases, including depression (Tache 2000).

The antidepressant role of physical exercise in depression could be explained through its antioxidant effect: by the stimulation of antioxidant defense mechanisms at muscular level, through the nuclear factor kappa B (NF-kappaB) and mitogen-activated protein kinase (MAPK), and by the stimulation of the secretion of serotonin and its precursors, having in their turn an antioxidant role, and through the MAPK pathway with a neuroprotective effect.

Through its antioxidant role, physical exercise can also be recommended in antidepressant therapy, which may be associated with drug therapy.

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