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## Impact of Physical Exercise on Psychological Well-being and Psychiatric Disorders

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### Review article

### Abstract

**Background:** Physical exercise is one of the major features of human health, as it is involved in several physiological processes and related to major benefits in reducing body fat, myocardial infarction, hypertension and insulin resistance risk. Physical exercise also plays a positive role in achieving psychological well-being that can be defined as a state of happiness and serenity, with low levels of distress, overall good physical and mental health and outlook and a good quality of life.

**Aim of the paper:** To review the positive effects of physical activity on psychological well-being and its possible neurobiological underpinnings, as well as its impact on several neuropsychiatric disorders, such as depression, anxiety, eating disorders, obsessive-compulsive disorder, post-traumatic stress disorder, attention-deficit/hyperactivity disorder, autism spectrum disorders, schizophrenia and some neurodegenerative disorders such as Alzheimer's and Parkinson's disease.

**Methods:** The PubMed, Scopus, Embase, PsycINFO and Google Scholar databases were searched for full text articles published in the latest thirty years on the benefits that physical activity exerts on psychological well-being.

**Results:** An impressive amount of data support the positive role of physical activity on psychological well-being and a large amount of research has focused on its beneficial effects in improving the symptoms of the main neuropsychiatric disorders, while highlighting its usefulness as an adjuvant option to psychopharmacological treatments and psychotherapy. In particular, exercise would deeply affect CNS morphology and function, through heterogeneous mechanisms including, amongst the others, the production of hormones, neurotransmitters and neurotrophins, the promotion of angiogenesis and neuroplasticity, and the regulation of gene expression.

**Conclusion:** Literature indicates that the promotion of physical activity may work like an adjunctive and/or augmentation strategy to enhance drugs or psychological treatments, or even as an alternative option in major depression.

**Key words:** Physical Exercise, Well-being, Psychological Well-being, Neuropsychiatric Disorders, Neurobiology

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## 1. Introduction

Physical exercise represents not only the basis of any kind of sport, but a fundamental aspect of human health as, besides promoting metabolic activity and cardiovascular functions, is an essential element contributing to the overall sense of well-being (Oja & Titze, 2011). Not surprisingly, a sedentary lifestyle is considered one of the most important factors of morbidity and mortality worldwide (Alves et al., 2016; Barengo et al., 2004; Bonaiuti et al., 2002; de Bruijn et al., 2013; Hirose, Hamajima, Takezaki, Miura, & Tajima, 2003; Hu et al., 2004; Huai et al., 2013; Kokkinos, Sheriff, & Kheirbek, 2011; Moore, Gierach, Schatzkin, & Matthewset, 2010; Qiu et al., 2017). High-intensity physical activity, compared to low-intensity exercise, leads to further benefits in terms of body composition and reduction of abdominal fat (Irving et al., 2008; Lee, Park, Kim, Choi, & Kim, 2012). The results of the diabetes prevention program, developed within a randomised multi-centre controlled trial with more than 3,000 participants, showed that diet and physical activity reduced the incidence of diabetes by 58%, while metformin by 31% (Knowler et al., 2002). Moreover, results related to cardiovascular disease prevention are similarly impressive and benefits have been reported amongst people who had already experienced the disease (Anderson et al., 2016; La Rovere, Bersano, Gnemmi, Specchia, & Schwartz et al., 2002). Furthermore, the implementation of recreational group sports has been considered as an additional strategy in the prevention of cardiovascular diseases, while improving different cardiac and metabolic parameters (Donnelly et al., 2013; Oda et al., 2014). Physical activity guidelines, (PAG), recommend the appropriate amount of exercise to achieve a status of physical wellness, stating the frequency, duration and intensity of exercise. Adults should practise more than 150 minutes to 300 minutes per week of moderate-intensity, or 75 minutes to 150 minutes per week of vigorous-intensity aerobic physical activity, or a combination of both (Piercy et al., 2018). It has been also demonstrated that regular exercise enhances not only physical, but also psychological well-being and quality of life (Poirel, 2017; Ussher, Owen, Cook, & Whincup 2007). A positive impact of physical exercise has been described on cognitive functions (Archer, Josefsson, & Lindwall, 2014), workplace performance (Drannan, 2016), creative thinking

(Blanchette, Ramocki, O'del, & Casey et al., 2005) and sexual well-being (Martinez, Ferreira, Castro, & Gomide, 2014). Aerobic exercise induces short and long-term effects on mood and emotional states by promoting positive effects, inhibiting negative effects and decreasing the biological response to acute psychological stress.

Several studies suggest that physical activity might also be of help in a wide range of neuropsychiatric conditions, such as anxiety disorders (Aylett, Small, & Bower, 2018), depression (Rethorst, Wipfli, & Landers, 2009; Schuch et al., 2019), eating disorders (Cook et al., 2016), obsessive-compulsive disorder (OCD) (Abrantes et al., 2019), post-traumatic stress disorder (PTSD) (Rosenbaum et al., 2015; Zschucke, Gaudlitz, & Ströhle, 2013), attention-deficit/hyperactivity disorder (ADHD) (Cerrillo-Urbina et al., 2015; Chang, Labban, Gapin, & Etnier, 2012), autism spectrum disorders (ASD) (Ferreira et al., 2019; Toscano, Carvalho, & Ferreira, 2018), schizophrenia (Pajonk et al., 2010; Tréhout & Dollfus, 2018) and some neurodegenerative disorders, such as Alzheimer's (AD) (Du et al., 2018; Ebrahimi et al., 2020) and Parkinson's disease (PD) (Feng et al., 2020).

Therefore, the aim of this paper was to review and comment on the current literature exploring the benefits induced by physical exercise on psychological well-being, as well as its impact on several psychiatric disorders. The possible neurobiological basis of such positive effects will also be briefly reviewed.

## 2. Methods

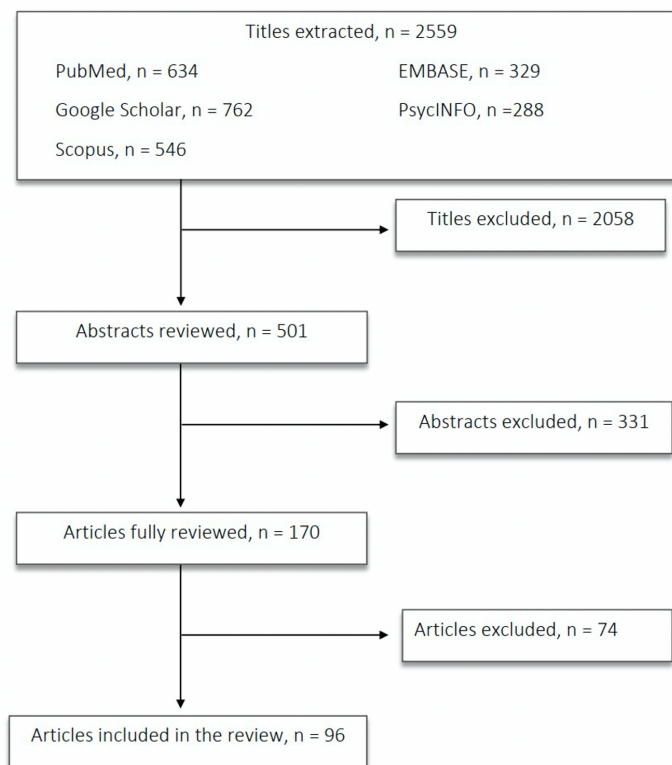
According to the PRISMA guidelines (Moher et al., 2009), PubMed, Scopus, Embase, PsycINFO and Google Scholar databases were accessed in order to research and collect English language papers published between January 1<sup>st</sup>, 1990 and May 31<sup>st</sup>, 2020. Free text terms and MeSH headings for the topics of pharmacological treatment and interaction, were combined as it follows: "(\"Psychological Well-Being\" or \"Physical Exercise\") and (\"Psychiatry\" or \"Mental Health\" or \"Mood Disorders\" or \"Bipolar Disorders\" or \"Depression\" or \"Anxiety Disorder\" or \"Schizophrenia\" or \"Obsessive-Compulsive Disorder\" or \"ADHD\" or \"Autism Spectrum Disorders\")". All the authors agreed to include in the review conference abstracts, posters and case reports if published in indexed journals.

The following inclusion criteria were adopted: studies carried out in clinical sample of adults and children/adolescents; reliable diagnosis of psychiatric disorders according to structured interviews and standardised criteria; reliable assessment of outcome measures. All the authors equally contributed in identifying potential information specific to this topic amongst the titles and abstracts of the publications.

### 3. Results

The first selection excluded 2058 titles because: a) duplicates; b) not concerning the scope of the paper;

c) not informative enough. The second selection excluded 331 abstracts after being read and reviewed, as the information reported did not fulfill the scope of our paper and/or the presented information did not seem relevant to the discussed topic. Subsequently, 74 articles were excluded after being completely read and evaluated, as they did not provide enough information and/or resulted sufficiently in line with our review. Finally, 96 papers were included in the present review (figure 1).



**Figure 1 : Article selection flow chart**

#### 3.1 Physical activity and psychological well-being

Nowadays, the concept of psychological well-being has gained increasing importance. According to psychological dictionaries, it is a state of happiness and contentment, with low levels of distress, overall good physical and mental health and outlook, or good quality of life. Although different definitions have been proposed (Dodge, Daly, Huyton, & Sanders 2012), psychological well-being has been considered as a multifactorial subjective sense of satisfaction in several aspects of life (Eger & Maridal, 2015). It can be described as a positive mental state whose baseline is set by life background and

personality, meaningfully influenced by daily events and experiences (Eger & Maridal, 2015). The concept of psychological well-being encompasses two important facets. The first is related to the extent to which people experience positive emotions and feelings of happiness. Sometimes this aspect of psychological well-being is referred to as subjective well-being (Diener, 2000). Subjective well-being is a necessary part of psychological well-being, but on its own it is not enough as, besides positive emotions, the experience purpose and meaning is equally important.

Two types of psychological well-being can be identified: the hedonic and the eudaimonic (Steptoe,

Deaton, & Stone, 2015). The first refers to the subjective feelings of happiness and includes two components, an affective (high positive affect and low negative affect) and a cognitive one (satisfaction with life). Happiness would result from both high affect and satisfaction (Carruthers & Hood, 2004). According to the psychologist Carol Ryff (Ryff & Keyes, 1995), the eudaimonic psychological well-being refers to the purposeful aspects of psychological well-being that includes the following six factors: self-acceptance, personal growth, purposes in life, environment mastery, autonomy, and positive relations with others.

Theories about psychological well-being generally focus on understanding its structure or the dynamics with the conceptualisation of Ryff being the most widely accepted. It should be emphasised that psychological well-being is relatively stable and is influenced by previous experiences, daily events and underlying personality. However, exposure to moderately stressful traumatic events can help to build resilience and actually protect psychological well-being (Khoshaba & Maddi, 1999). Although, short periods of adversity may be helpful in building resilience, long-term stress may well lead to serious illness, including cardiovascular disease, diabetes and immune system alterations (Chandola et al, 2008).

**Table 1.**

*Psychological domains improved by physical exercise*

Mood	Achievement of calm and peaceful sensation Reduced anger and internal tension
Anxiety	Decreased anxiety levels and better managing skills
Self-esteem	Better body image Improved social interaction
Cognitive functions	Attention Inhibitory control Cognitive flexibility Declarative, spatial memory and working memory Improved information processing, problem solving and decision making
Other benefits	Increased workplace performances Increased sexual well-being

Physical activity has been demonstrated to have a positive impact on psychological well-being (Ussher et al., 2007) (Table 1). The activation state that typically follows physical exercise leads to a calm and peaceful sensation, and it may reduce anger and internal tension (Ekkkekakis & Backhouse, 2014). Single sessions of moderate exercise can reduce short-term physiological reactivity and help manage psychosocial stressors (Biddle, Fox, & Boutcher, 2003). The implementation of physical activity also plays a role in reinforcing self-concept and self-esteem in children and adolescents, possibly improving social interactions (Archer et al., 2014). Moreover, in younger age groups, physical fitness might stimulate academic achievement, mainly through an improvement in cognitive skills (Donnelly et al., 2016; Dwyer, Sallis, Blizzard, Lazarus, & Dean, 2001; Tomporowski, Lambourne, & Okumura, 2011).

Aerobic exercise and resistance training can exert positive effects in healthy adults, by enhancing mood and positive self-opinion, especially in terms of change of self-perception, self-body image and satisfaction through weight loss or improving muscle tone, thus leading to a greater sense of autonomy and personal control over the body appearance and functioning (Biddle et al., 2003). Aerobic exercise has been demonstrated to induce transient effects on cognition after a single exercise session and persistent effects on cognition following regular exercise over the course of several months. People who regularly perform aerobic exercise (e.g. running, jogging, brisk walking, swimming and cycling) show greater scores on neuropsychological function and performance tests measuring some cognitive functions, such as attentional control, inhibitory control, cognitive flexibility, working memory updating and capacity, declarative memory, spatial memory

and information processing speed (Archer et al., 2014; Chang et al., 2012). The transient effects of exercise on cognition include improvements in most executive functions (e.g. attention, working memory, cognitive flexibility, inhibitory control, problem solving and decision making) and information processing speed for a period of up to 2 hours after exercising (Dietrich, 2006). Physical activity can also enhance workplace performances, mainly based on the improvement in mood and subjective health, thus encouraging companies to give incentives in order to

promote physical activity in employees (Blanchette et al., 2005; Coulson, McKenna, & Field, 2008; Drannan, 2016; Gondola, 1986; Steinberg et al., 1997). The effects of exercise on cognition have important implications for stimulating adult productivity, preserving cognitive function in old age, preventing or treating certain neurological disorders, and improving the overall quality of life.

Furthermore, physical exercise improves sexual activity and secondarily the overall sense of psychological well-being (Martinez et al., 2014).

**Table 2.**

*Beneficial effects of physical exercise on psychiatric disorders*

Anxiety disorders	Overall reduced anxiety symptoms
PTSD	Reduction of hyperarousal, irritable behaviour or outbursts of rage, hypervigilance and poor concentration
Depression	Improvement of mood
Eating disorders	Increased subjective well-being
OCD	Reduction of comorbid depressive symptoms
Schizophrenia	Improvement of both positive and negative symptoms
ADHD	Improvement of hyperactivity and inactivity
ASD	Reduction of aggressive and stereotyped behaviours

*Note.* PTSD: post-traumatic stress disorder, OCD: obsessive-compulsive disorder, ADHD: attention-deficit hyperactivity disorder  
ASD: Autism spectrum disorder

### 3.1.1 Anxiety disorders

Available studies indicate that regular aerobic exercise elicits benefits for individuals with anxiety disorders (Asmundson et al., 2013; Schuch et al., 2019), including panic disorder (Ekkekakis & Backhouse, 2014), agoraphobia (Wedekind et al., 2010), generalised anxiety disorder (GAD) (Herring, Monroe, Gordon, Hallgren, & Campbell 2019), and social anxiety disorder (Merom et al., 2008). Physical activity has been demonstrated to be useful to treat anxiety, given the findings of an inverse association between the former and the latter (Stubbs et al., 2018). Moreover, it has been demonstrated that both aerobic and anaerobic physical activity reduce anxiety symptoms and improve mood in patients with panic disorder and social phobia. A recent systematic review and meta-analysis reported an inverse association between physical exercise and anxiety symptoms, any anxiety disorders and GAD (McDowell, Dishman, Gordon, & Herring, 2019).

### 3.1.2 Depression

Physical exercise seems to have a superior effect in decreasing depressive symptoms and improving quality life, and comparable to psychological and antidepressant treatments (Cooney et al., 2013), especially in mild-moderate depression as an add-on strategy (Mura, Moro, Patten, & Carta, 2014). These findings are strongly supported by clinical trials assessing the effectiveness of two-four months of physical activity (Josefsson, Lindwall, & Archer, 2014). Subtypes of depressive disorder and specific types of exercise have been shown to be of positive benefit: for instance, yoga might be useful in reducing prenatal depression symptoms (Gong, Ni, Shen, Wu, & Jiang, 2015). According to a recent meta-review (Stubbs et al., 2018), a combination of aerobic and moderate intensity endurance exercises (about 150 minutes) twice or three times a week, professionally supervised, is associated with an improvement of outcomes and quality life in major depression, potentially preventing relapses after

hospitalisation (Gerber et al., 2019). Several studies suggested that the effects of physical exercise might be similar to antidepressants and psychotherapy, mainly in untreated patients (Mikkelsen, Stojanovska, Polenakovic, Bosevski, & Apostolopoulos 2017; Peluso & Guerra de Andrade, 2005), so that it has been proposed as an alternative intervention in patients who cannot undergo a pharmacological treatment (Craft & Perna, 2004; Kvam, Kleppe, Nordhus, & Hovland, 2016).

### *3.1.3 Eating disorders*

The impact of physical activity on eating disorders is still a controversial matter. On one hand, in patients affected by anorexia nervosa, hyperactivity is pursued with the purpose of burning-off more calories, representing one of the psychopathological mechanisms of this disorder. On the other hand, regular and multidisciplinary monitored physical activity could be useful to limit the harmful consequences of hyperactivity (Achamrah, Coëffier, & Déchelotte, 2016), especially in bulimic and binge-eating patients (Blanchet et al., 2018; Mathisen et al., 2020). In any case, physical activity seems to enhance subjective well-being and psychosocial impairment, representing an important alternative for those patients who refuse or cannot undergo cognitive-behavioural therapy (CBT).

### *3.1.4 Obsessive-compulsive disorder*

Although, the evidence is weaker when compared that of other disorders, aerobic activity has been demonstrated to be helpful in OCD (Abrantes et al., 2019). Physical exercise, as adjunct treatment, seems to be helpful in reducing some depressive symptoms frequently comorbid in OCD, or to enhance self-efficacy through the “mastery hypothesis”. The acquisition of exercise skills may increase self-efficacy for managing OCD symptoms and a better compliance to treatment. Again, exercise may be a distraction from focusing on obsessive thoughts or engaging in compulsive behaviours, and it may decrease the negative impact of life stress. Encouraging results suggested further benefits through the association of a structured physical exercise program with CBT (Brown et al., 2007).

### *3.1.5 Post-traumatic stress disorder*

Findings on the impact of physical activity on PTSD are still limited, but intriguing (Fetzner & Asmundson, 2015; Manger & Motta, 2005). A

recent study highlighted that several types of physical activity, especially outdoor recreation have a good impact on military veterans PTSD patients, being able to reduce the core symptoms of the disorder, in particular hyperarousal, irritable behaviour or explosions of rage, hypervigilance, and poor concentration (Walker, Smith, Limbert, & Colclough et al., 2020). Physical activity also seems to exert an important, positive impact on the quality of sleep (Kredlow, Capozzoli, Hearon, Calkins, & Otto, 2015; Saidi, Davenne, Lehorgne, & Duché, 2020). A recent meta-analysis showed that physical activity might be a promising augmentation strategy to improve PTSD and depressive symptoms (Rosenbaum et al., 2015).

### *3.1.6 Schizophrenia*

In schizophrenic patients, moderate physical activity seems to enhance positive symptoms, helping restrain auditory hallucinations and redirecting attention away from their clinical condition, and negative ones, giving a better sense of community, and also cognitive functions (Bowie, Grossman, Gupta, Oyewumi, & Harvey, 2014; Firth et al., 2018).

### *3.1.7 Neurodevelopmental disorders*

Benefits of physical exercise have also been reported in neurodevelopmental disorders. ADHD patients seem to undergo an improvement in hyperactivity, inactivity and impulsion after physical activity (Cerrillo-Urbina et al., 2015). In ASD children, benefits have been shown related to the reduction of aggressive and stereotyped behaviour (Oriel, George, Peckus, & Semon, 2011), or improvements in several psychosocial domains (Celiberti, Bobo, Kelly, Harris, & Handleman, 1997), in intellectual functioning and self-concept (Gabler-Halle, Halle, & Chung, 1993). Further benefits are overall obtained through high-intensity exercises (Prupas & Reid, 2001).

### *3.1.8 Neurodegenerative disorders*

Several researchers, including random clinical trials (RCTs), highlighted a positive role of physical exercise in AD, such as improvements on cognitive functions and daily performance, likely decreasing the amount of the amyloid plaques (Du et al., 2018). Different kinds of physical activity may lead to different effects, and the specificity of training can be

a key factor in designing a successful exercise schedule.

Aerobic exercise improves the executive control functions, running through frontal and prefrontal brain regions, which are deeply compromised in patients with PD. Performing a regimen of 20 minutes-aerobic exercise three times per week for eight weeks on a stationary activity cycle has proved effective in enhancing several cognitive functions in early-mild stages PD patients. However, the latter benefits induced by physical activity might be compromised due to the peculiar neurochemical alterations of the frontal lobe in PD patients. Moreover, a positive effect induced by physical exercise in terms of improving balance, gait, functional capacity and strength in these patients has been described (Deslandes et al., 2009; Goodwin, Richards, Taylor, Taylor, & Campbell, 2008; Mehrholz et al., 2015). Benefits regarding pain, a symptom experienced by about 85% PD patients and which is commonly associated with a worsened quality of life, have been highlighted, as well (Allen, Moloney, van Vliet, & Canning, 2015).

### 3.2 Neurobiological basis of psychological well-being

Several findings indicate that physical activity may influence different structures and processes in the central nervous system (CNS), such as the activity of different neurotransmitters, neuroplasticity and gene expression (Lin & Kuo, 2013; Lista & Sorrentino, 2010).

Physical activity may indeed promote angiogenesis, neurogenesis through increasing the levels of brain-derived neurotrophic factor (BDNF), synaptogenesis and glycogenesis in different brain areas, mainly in hippocampus and neocortex (Ehninger & Kempermann 2003; Ekstrand, Hellsten, & Tingströmet, 2008; Hirase & Shinohara, 2014; Steiner et al., 2004). Neurogenesis in the dentate gyrus is considered the key cellular modification related to physical exercise (Andersen, Morris, Amaral, Bliss, & O'Keefe, 2007; Van Praag, 2008), in association with a buildup of the grey matter volume in the hippocampus and in the frontal regions (Colcombe et al., 2006; Kleemeyer et al., 2015; Thomas et al., 2016). In addition, when physical exercise is performed at low or moderate intensity, blood flow and oxygenation increase, thus

determining a greater distribution of nutrients in the brain (Bhambhani, Malik, & Mookerjee, 2007).

Furthermore, oxytocin, a nonapeptide hormone acting as neurotransmitter in the brain and peripheral tissues, seems to be one of the mediators of physical exercise's benefits, as it may decrease the activation of stress processes and, as such, promote relaxation and well-being (De Dreu et al., 2008).

Other studies highlighted the relationship between physical activity and  $\beta$ -amyloid peptides ( $A\beta$ ), the main constituents of extracellular senile plaques in AD patients:  $A\beta$  peptides are derived by proteolytic cleavages of the amyloid precursor protein (APP), a transmembrane protein physiologically present in many tissues (Andreasen et al., 2001). Research showed that treadmill exercises might reduce circulating  $A\beta$  peptides levels and might improve cognitive deficits and decrease neurotoxicity (Koo, Kang, Ho, Yang, & Cho, 2016).

The increased levels of BDNF induced by physical exercise might lead to cognitive improvement, or they could be protective against brain damage and contribute to maintain concentration, especially in combat sports (Griffin et al., 2011; Schor, Silva, Almeida, Pereira, & Arida, 2019)

Further data indicates controversial results with the relationship between physical exercise and other neurotrophins, such as nerve growth factor (NGF) (Bansi, Bloch, Gamper, & Kesselring, 2013; Gold et al., 2003; Roh, Cho, Yoon, & So, 2017).

Physical activity seems to positively influence an individual's ability to cope with psychological stress (Gustafsson, Sagar, & Stenling, 2017), that is the result of the sympathetic-vagal balance (Zou et al., 2018). It is well known that stress activates the sympathetic nervous system and hypothalamic-pituitary-adrenal (HPA) axis, through releasing stress hormones that in turn induce specific cytokine cascades (Archer et al., 2014). Therefore, daily physical activity seems to reduce stress symptoms, in particular by decreasing circulating cortisol levels and heart rate, and improving the overall function of the immune system (Mucci et al., 2020).

With regard to how physical activity affects mood symptoms, recent studies highlighted that the feeling of well-being that follows physical activity could be linked to an overexpression of cannabinoid receptors and to their increased serum levels, together with those of endorphins (Mikkelsen et al., 2017). The effects on stress, mood and anxiety seem to be also

related to an activation of the protein kinase mTor in those areas of the brain involved in cognition, mood and ageing (Mikkelsen et al., 2017). Aerobic exercise is related to an activation of mitochondriogenesis that is involved in neuroplasticity, in synaptic strength and cellular resilience of neuronal circuits. Moreover, physical exercise seems to be also associated with the expression of c-fos, a gene playing a key role in several processes such as cell proliferation and differentiation following a wide range of different stimuli (Silvestre, Gil, Tomasini, Bussolino, & Caputto, 2010). Although, further research is necessary to substantiate these preliminary observations, it has been suggested that this mechanism might underpin the effects of physical exercise in the prevention of drug addiction (Lynch, Peterson, Sanchez, Abel, & Smith, 2013).

#### 4. Discussion and Conclusions

This paper analytically reviewed the available literature on the possible impact of physical exercise on the overall psychological well-being, as well as, more specifically, on some psychiatric disorders.

The positive effects of regular physical activity on health are well known and supported by an increasing amount of data showing its involvement in promoting metabolic activity, cardiovascular functions and immune system, as well as in improving general and psychological well-being. Well-being is a positive outcome indicating that people perceive that their lives are good, and psychological well-being can be defined as a state of happiness and contentment, with low levels of distress, overall good physical and mental health and outlook.

Not surprisingly, the effects of physical activity have been investigated in a broad range of neuropsychiatric conditions. Different data would indicate that regular aerobic exercise might improve symptoms associated with a variety of CNS disorders and may be used as an adjunct therapeutic strategy in these disorders (Brown et al., 2007; Cooney et al., 2013; Craft & Perna, 2004; Kvam et al., 2016; Mikkelsen et al., 2017; Peluso & Guerra de Andrade, 2005; Rosenbaum et al., 2015). There is clear evidence of exercise treatment efficacy for major depressive disorders, anxiety disorders and ADHD patients, and there are indications of certain effectiveness in several other psychiatric conditions, such as OCD, schizophrenia and ASD (Abrantes et al., 2019; Asmundson

et al., 2013; Cerrillo-Urbina et al., 2015; Mikkelsen et al., 2017; Oriol et al., 2011; Schuch et al., 2019). The American Academy of Neurology's clinical practice guideline for mild cognitive impairment indicates that clinicians should recommend regular exercise (two times per week) to individuals who have been diagnosed with this condition (Gerber et al., 2019). Reviews of clinical evidence also support the use of exercise as an adjunct therapy for some neurodegenerative diseases, particularly AD and PD (Koo et al., 2016; Deslandes et al., 2009; Goodwin et al., 2008; Mehrholz et al., 2015). Some pre-clinical and scattered clinical data support the use of exercise as an adjunct therapy for the treatment and prevention of drug addiction. Data is also available to suggest the possible neurobiological underpinnings of the beneficial effects of physical exercise including changes in neurotransmitter functions, neuroplasticity and gene expression (Lin & Kuo, 2013; Lista & Sorrentino, 2010).

In spite of the amount of the empirical data on this topic supporting positive effects, nevertheless the "real findings" derived from controlled studies are still meager. Similarly, the possible neurobiological explanations of these effects still need to be fully elucidated.

In any case, the literature would suggest that the promotion of physical activity may constitute a tool to be widely used, given its easy and cheap implementation in neuropsychiatry as an adjunctive and/or augmentation strategy to enhance drug or psychological treatments, or even as an alternative option in major depression (Mikkelsen et al., 2017). In any case, further controlled studies are necessary to clearly explore and assess the impact of regular physical activity on CNS functions and disorders.

#### Conflict of Interests

The authors declare no conflict of interests.



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