Review / Revisão

Post-Traumatic Stress Disorder and Psychophysiological Interactions of Brain Patterns, Exercise, and Non-Drug Treatment: An Integrative Review

Transtorno de estresse pós-traumático e interações psicofisiológicas de padrões cerebrais, exercício e tratamento não medicamentoso: uma revisão integrativa

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Review Article

Artigo de Revisão

Post-Traumatic Stress Disorder, Exercise, Cortical Patterns, Psychophysiological Interactions, and Non-Drug Treatment: An Integrative Review

Transtorno de estresse pós-traumático, exercício, padrões corticais, interações psicofisiológicas e tratamento não-medicamentoso: uma revisão integrativa

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Abstract

Introduction: Post-traumatic stress disorder (PTSD) is a prominent mental health problem in military veterans and in the general population. It can last from few months to several years, causing various disabilities to individuals suffering from the disorder. There are non-drug options that may not only contribute and may be even necessary for the full recovery of patients with PTSD.

Objective: To examine the interactions between physiological-psychophysiological and electrophysiological aspects (cortical patterns) with physical exercise, seeking possible non-pharmacological alternatives for the treatment of patients with post-traumatic stress disorder (PTSD).

Results and Discussion: Hippocampal dysfunction causes PTSD and problems in brain functioning (anxiety, depression, and cognitive impairment), as well as impairments in mitochondrial function and neuroplasticity. Physical exercise and self-regulatory neuromodulation can contribute, and even be indispensable, to the recovery of these patients.

Conclusion: Physical exercises, through induced improvement of the level of brain-derived neurotrophic factor, enhancement of mitochondrial function and induction of neuroplasticity and the rate of apoptosis in the hippocampus. Physical exercise contributes to the full recovery of patients with PTSD, and autoregulatory neuromodulation is indicated for adjuvant indication.

Key Points
- Hippocampal dysfunction caused by trauma (psychological/physical) causes PTSD and other mental health problems.
- Hippocampal dysfunction causes impairments in mitochondrial function and neuroplasticity.
- Physical exercise and self-regulatory neuromodulation can contribute to the recovery of these patients.

Keywords: exercise, brain, autonomic nervous system, Polyvagal Theory, integrative medicine.

Resumo

Introdução: O transtorno de estresse pós-traumático (TEPT) é um problema de saúde mental proemi-

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nente em militares veteranos e, também, na população em geral. Pode durar desde apenas alguns meses a vários anos, causando diversas incapacidades aos indivíduos que sofrem com o transtorno. Existem opções não-medicamentosas que podem, não apenas contribuir, como até mesmo serem necessárias para a recuperação integral de pacientes com TEPT.

Objetivo: Examinar as interações entre aspectos fisiológicos-psicofisiológicos e eletrofisiológicos (padrões corticais) com exercício físico, buscando possíveis alternativas não-medicamentosas para o tratamento de pacientes com transtorno de estresse pós-traumático (TEPT).

Resultados e Discussão: A disfunção do hipocampo e causa o TEPT e problemas no funcionamento cerebral (ansiedade, depressão e comprometimento cognitivo), além de prejuízos na função mitocondrial e na neuroplasticidade. O exercício físico e a neuromodulação autorregulatória podem contribuir, e até serem indispensáveis, para a recuperação desses pacientes.

Conclusão: Exercícios físicos, por meio da melhora induzida do nível do fator neurotrófico derivado do cérebro, do aprimoramento da função mitocondrial e da indução à neuroplasticidade e a taxa de apoptose no hipocampo. O exercício físico contribui para a recuperação integral de pacientes com TEPT, bem como, a neuromodulação autorregulatória está indicada para indicação coadjuvante.

Pontos Chave
- *A disfunção do hipocampo causada pelo trauma (psicológico/físico) causa o TEPT e outros problemas em saúde mental.*
- *A disfunção do hipocampo causa prejuízos na função mitocondrial e na neuroplasticidade.*
- *O exercício físico e a neuromodulação autorregulatória podem contribuir para a recuperação desses pacientes.*

Palavras-chave: exercício físico, sistema nervosa autônomo, Teoria Polivagal, medicina integrativa.

Post-Traumatic Stress Disorder, Exercise, Cortical Patterns, Psychophysiological Interactions, and Non-Drug Treatment: An Integrative Review

Introduction

Post-traumatic stress disorder (PTSD) is a prominent mental health problem in military veterans and the general population(1). Before considering PTSD, it is important to understand the definition of stress, which is: "the *set of reactions that an organism develops when subjected to a situation that requires an effort to adapt*"(2), which involve physiological reactions associated with mental decisions and, consequently, behavioral actions. Stress is marked by a state of hyperexcitability to trigger the necessary response of the individual to cope with stressful stimuli(3). The presence of chronic stress triggers psychological and physiological responses (hormonal and neuronal) that occur due to the body's search for the maintenance of the state of homeostasis. These alterations result in behavioral responses that can manifest themselves as: anxiety disorders and depression; decreased food intake and gastrointestinal dysfunctions; decline in sexual behavior(3). According to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5)(1), the difference between acute stress disorder and PTSD is that the former resolves within one month, while to become PTSD, symptoms extend beyond one month. It can last from few months to many years(1).

According to the U.S. Department of Health and Human Services(4), the literature is well established regarding the benefits of physical activity for all aspects of human health(4), including mental health(5–9). The definition of physical activity is "*any bodily movement produced by skeletal muscles that results in energy expenditure*", and physical exercise is "*a subset of planned,* *structured and repetitive physical activity, which has as its final or intermediate objective the improvement or maintenance of physical fitness'*(10). The literature shows that both the relationship between physical activity and stress and mental health are bidirectional. This means that both the level of stress can decrease the level of physical activity, and the level of physical activity can decrease the level of stress(11–13). Similarly, in relation to mental health, the level of physical activity can improve mental health, and mental health problems can also lead to a decrease in the level of physical activity(14,15). In addition to exercise, there are other non-drug options that may be necessary for the full recovery of PTSD patients.

The aim of the present study was, from an integrative medicine perspective, to examine the interactions between physiological-psychophysiological and electrophysiological aspects (cortical patterns) with physical exercise, seeking possible non-pharmacological alternatives for the treatment of patients with post-traumatic stress disorder (PTSD).

Methods

This is an integrative review study(16), with searches conducted in the PubMed and Google Scholar databases, in English or Portuguese, which included the terms: "*PTSD*", "*Post-traumatic stress disorder*", "exercise", "physical activity", "*mental health*", "*neurofeedback*", e "*brain*"; using Boolean operators "*AND*" e "*OR*". Original studies as well as review studies were included.

Results and Discussion

Post-traumatic stress disorder (PTSD)

In the physiology of stress, all organ systems participate in physiological-psychophysiological reactions related to stress and mental health and depending on the strength of the traumatic stressor stimulus and the duration of the symptoms, the greater the consequences on the individual's health and quality of life can be. Chronic stress affects the immune system, the brain and, consequently, human behavior due to the interactions between them(17). According to Bower & Kuhlman(17), in the occurrence of a disease, there is an overlap between symptoms and neural correlates and symptoms of depression and other psychiatric disorders. In this context, repeated immune activation or chronic inflammation can influence the development of mental health symptoms and problems, or even lead to milder changes in emotion, cognition and behavior(17), and affective states influence the state of inflammation and oxidative stress, which have detrimental effects on health(18–22).

The difference between acute stress disorder and PTSD is that the former resolves within a month, while to become PTSD, the symptoms extend beyond a month, and can last from just few months to many years(1). There is evidence that the amygdala-hippocampal region is functionally and morphologically involved in the etiology of PTSD(23). Some symptoms of PTSD are: distressing, recurrent, and involuntary intrusive memories of the traumatic event; hypervigilance state; avoidance behaviors of places and/or situations that recall the traumatic episode; emotional detachment from your feelings or other people's; negative thoughts about themselves; negative changes in cognition and mood; hyperexcitability; recurring nightmares with related content related to the traumatic event; intense (or prolonged) psychological distress and/or intense physiological reactions to exposure to internal or external signs that symbolize or resemble some aspect of the traumatic event(1). In addition, the presence of mental health comorbidities such as: depressive disorders, personality disorders, functional neurological symptoms disorder, somatic symptom disorder, eating disorders, substance-related disorders, sleep disorders, among others, is frequent. These symptoms may appear immediately after the event, but they may also appear years later and are associated with high levels of social, professional and physical disabilities(1).

Among the most frequent situations that trigger PTSD include military combat, accidents, aggressions, natural or man-made disasters(24). It is noteworthy that the military and/or emergency rescue professions are the categories with the highest prevalence in comparison with the others(1). Given these characteristics, the lifetime incidence of PTSD is expected to be high. In the United States, where there are records of population data, the relative risk of incidence of PTET up to 75 years of age is 8.7% and the estimated prevalence at 12 months is 3.5%(1). In Brazil, only one study on the prevalence of PTSD was identified in a population sample (n=5,037), in the city of São Paulo, which was 3.7% in 12 months(25), similar to that found in the American population.

The impact of PTSD on the lives of these patients encompasses several aspects of the individual, since, in addition to the characteristic symptoms, there are changes in brain structure and function, and cognitive performance is decreased. In addition, the chances of people with PTSD developing diabetes, obesity, and metabolic syndrome are higher compared to apparently healthy people. This can be explained by the fact that the level of physical activity of these patients is reduced in comparison with their practice before PTSD(24).

Neuropsychophysiological Effects of Trauma: The Polyvagal Theory

Porges(26–28), seeking a better understanding of the neuropsychophysiology of trauma, developed the Polyvagal Theory, identifying alterations in the functioning of the *vagus* nerve in the presence of psychological symptoms resulting from a traumatic event. Porges(26–28) explains that, in humans, the subsystems of the autonomic nervous system (ANS) have a phylogenetic order linked to social communication – aspects that involve: facial expression, vocalization, listening, among others; mobilization – fight-or-flight behaviors; and immobilization – behavior of playing dead, vasovagal syncope and annulment behavior.

It is through Porges' Polyvagal Theory(28,29) that the link between the body, mind and nervous system in coping with trauma-related symptoms can be better understood. Porges(28,29). The ANS, in mammals, provides neurophysiological substrates for adaptive behavioral strategies and, therefore, the physiological state of the individual has a limiting role on the amplitude of behavior and psychological experience(28,29). The ANS connects effective psychological experience, emotional expression, facial expressions, vocal communication, and the contingent of social behavior. Thus, there is a covariation between atypical autonomic regulation and psychiatric and behavioral disorders that involve difficulties in the appropriate regulation of the individual in their social, emotional, and communication behaviors. An imbalance in the regulation of the ANS may occur with a reduction in the activation of the myelinated (ventral) bundle of the *vagus* nerve, with an increase in the influence of the sympathetic system on the heart(28). Porges(29) also explains that traumatic experiences readjust the ANS to be trapped in defense states, which leads to changes in the respiratory rhythm, according to the author, a more sensitive marker for vulnerability to stress than heart rate(26,28), symptoms present in individuals with PTSD(1).

The vagus nerve

To understand the relationship between the functioning of the nervous system and the symptoms of PTSD, according to the Polyvagal Theory, it is important to consider its physiology. The ANS has parts in the central nervous system and the peripheral nervous system, controlling (involuntarily) the glands and smooth muscle of all internal organs (viscera). Together with the endocrine glands, the ANS participates in the regulation of important body functions without a clear involvement of the cerebral cortex. Its branches are divided into central and peripheral. The ANS innervates smooth muscle (blood vessel and organ walls), heart muscle, and glandular cells. Functionally, the

ANS is divided into the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS)(30). The functions of the PNS include decreased heart rate, relaxation of the sphincters of the gastrointestinal and urinary tracts and increased glandular and intestinal activity. The result of these processes is the storage of energy and the regulation of body functions (such as digestion and urination). On the other hand, there is the NHS, whose function is described as the "fight or flight" response, which occurs in stressful situations. Therefore, the SNS has opposite functions to the SNP. The main neurotransmitter of the SNS is acetylcholine, which acts on muscarinic receptors (located in the heart and viscera) and nicotinic receptors (located in the adrenal medulla and muscles)(30,31).

The *vagus* nerve (from the Latin *nervus vagus* = wandering nerve) is part of the PNS, being the longest and most complex cranial nerve (X) among the cranial nerves. It is a mixed nerve (with afferent and efferent fibers) with the following functions (Frame 1)(32).

The *vagus* nerve is also involved in the inflammation process, and its stimulation activates its anti-inflammatory cholinergic pathway, which, at the molecular level, is characterized by the signals communicated through the *vagus* nerve (probably with the participation of the splenic nerves), through the release of acetylcholine to negatively regulate the inflammatory actions of macrophages, which play a fundamental role in inflammation(35).

The vagus nerve is responsible for reducing heart rate, regulating breathing and the activity of the organs of the digestive system (resting and digesting)(33). Porges(26–28) related psychological sequelae of trauma with the respiratory rhythm and highlighted that there is a need to recover the notion of safety in the patient's environment so that the balance of the vagus nerve is reestablished(29). Figure 1 shows the anatomy of the vagus nerve and its passage in the vicinity of the hippocampal tonsil(34).

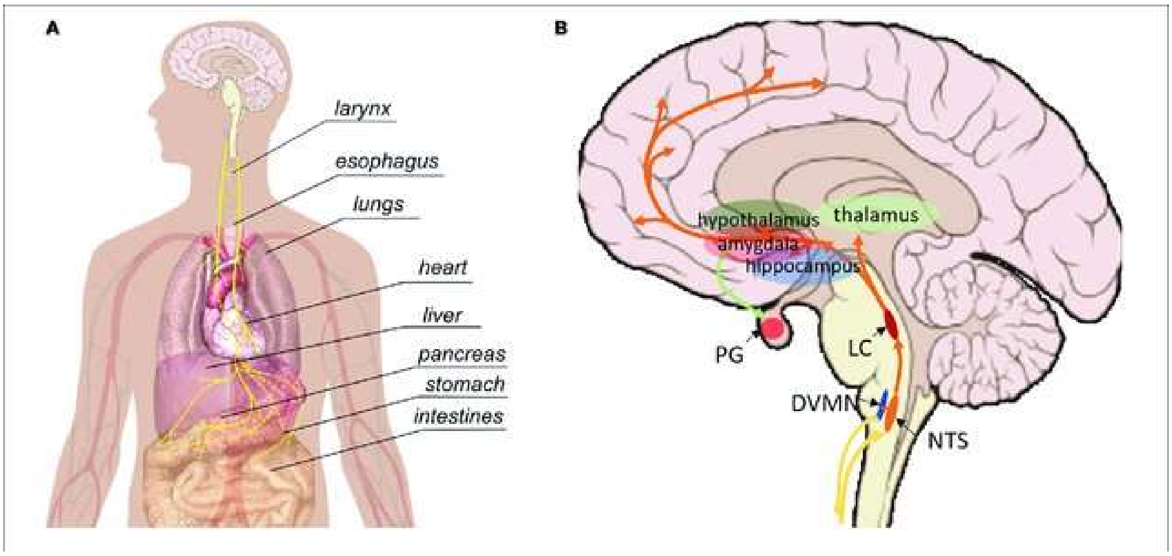
The ANS participates in brain activity and pathophysiology in the presence of PTSD through the orexin neural system(36). Orexinergic neurons originate in the lateral hypothalamus and project widely to the main neurotransmitter systems, autonomic neurons, the hypothalamic-pituitary-adrenal (HPA) axis and the neural circuits related to fear(36). Orexinergic neurons release two neuropeptides (or hypocretins): orexin-A and orexin-B(37). Orexins can modulate the actions of major neurotransmitter systems, including the monoaminergic neurotransmitters serotonin, dopamine, noradrenaline and other important neurotransmitters, including histamine and acetylcholine, which affect PTSD-related behaviors(36).

Orexin is part of a complex circuit that integrates aspects involved with energy metabolism, cardiovascular function, hormonal homeostasis and sleep-wake behaviors(37), in addition to being related to physical activity behavior. Mavanji *et al.*(38), based on an animal model, observed that the orexin-serotonin axis detects metabolic signals, including energy expenditure, and activates structures such as the motor cortex to modify behavioral outputs, such as voluntary (or spontaneous) physical activity.

In addition to being a key modulator in neurotransmitter systems, orexin plays an important role in the acquisition, expression, and extinction of fear, as well as modulating fear avoidance behaviors, and is also involved in sleep disturbances, hypervigilance, and increased startle responses and stress responses (marked physiological responses to fear/stress)(36). The authors explain that after trauma or acute stress, the basolateral amygdala transmits sensory information to the central nucleus of the amygdala and, in turn, to the hypothalamus and other subcortical and brainstem regions to promote fear and threat behaviors. Orexin plays an important role in the activation of the activity of the sympathetic nervous system and in the stress responses of the HPA axis, so that the activation of orexin prevents the extinction of fear and promotes avoidance behaviors, factors also observed by Porges(26–28) in the study of the post-trauma symptoms and *vagus* nerve dysregulation.

Afferents	**Efferent**
1. General somatic afferent (sensitive) of the laryngopharynx, larynx, and tongue root 2. Special visceral afferent (gustatory) from tongue root and epiglottic lingual papillae • general visceral afferent (sensitive) of the thoracic and abdominal organs	1. General visceral efferent (parasympathetic) of the thoraco-abdominal organs • Special visceral efferent of the palatoglossus muscle of the tongue and various muscles of the soft palate, pharynx, and larynx

Frame 1 – Functions of the *vagus* nerve (cranial nerve X)(32).



Fonte: *Selective Neuromodulation of the vagus Nerve*, Fitchett *et al.*(34)

Figure 1 – *Vagus* nerve and hippocampal amygdala.

Studies investigating changes in brain physiology resulting from laboratory interventions are carried out in animal models; regarding the relationship between orexin and the *vagus* nerve, studies of this type have indicated that the expression of orexin coincides with the cerebral innervation of the *vagus* nerve, influencing respiratory activity(39) and that its presence in the prefrontal cortex may be involved in the wakefulness-promoting effects of *vagus* nerve stimulation(40).

Recent literature indicates that orexin is involved, along with the *vagus* nerve, in cardiac rhythms(41) with a modulating effect on the immune system(42). Couvineau *et al.* Stuart *et al.*(42) discussed in their review that there is a synergistic and dynamic relationship between the nervous and immune systems, thus, orexins also have neuroprotective and immuno-regulatory, i.e., anti-inflammatory, properties. The authors concluded that orexins have therapeutic potential for use in other pathologies that have an immunological component, including multiple sclerosis, Alzheimer's disease, obesity, intestinal diseases, narcolepsy, septic shock and cancers(42). In addition, for Kaplan *et al.*(36) The study of the orexinergic neural system provides a better understanding of the important mechanisms involved in multiple behaviors related to PTSD.

Physical exercise: an integrative intervention

Physical exercise and mental health

According to the literature, physical exercise consistently contributes to reduce/prevent mental health symptoms such as anxiety and depression(5–9). The lack of consensus regarding the type of physical activity to be applied for greater mental health benefits (7–9) can be explained by the fact that the individual chooses the practice that better suits him/her. However, there is a wealth of literature regarding the benefits to mental health, which was extensively investigated by Hamer *et al.*(8,12).

In an epidemiological study conducted in Scotland, in a population sample (n=19,842), Hamer *et al.*(8) identified the dose-response effect of physical exercise on mental health: at least 20 min/week of any physical activity to obtain mental health benefits. These findings are extremely important, considering that the prevalence of adults around the world was 28% of people who did not reach the minimum standard of regular physical activity(43), a term that refers to a weekly practice of at least 150 minutes of moderate-intensity physical activity plus two days of muscle-strengthening activity, according to the current edition of the *Physical Activity Guidelines for Americans*(4). Additionally, the study by Hamer *et al.*(8) demonstrated that, in addition to the mental health benefits, with the practice of only 20 minutes/week of any physical activity, there was a greater reduction in the risk of psychological distress for greater volume and/or intensity. That is, the higher the level of physical activity, the greater the benefits for mental health. In addition, daily physical activity was associated with a lower risk of psychological distress after adjusting for age, gender, socioeconomic group, marital status, body mass index, chronic disease and smoking(8). Corroborating these findings, a recent systematic review study concluded that physical activity is highly beneficial for improving symptoms of depression, anxiety, and distress in a wide range of adult populations, including the general population, people with diagnosed mental health disorders, and people with chronic illnesses. The recommendation was that physical activity should be a fundamental approach in the treatment of depression, anxiety and psychological distress(44).

A recent observational study conducted with 739 young adults in China observed a moderating effect of exercise intensity on the direct and indirect influence of self-concept on negative emotions(45). Self-concept affects social behaviors and physical activity modulates adrenal and cardiovascular reactivity to psychosocial stress(46).

Physical exercise, stress and *vagus* nerve regulation

Stress (psychological suffering) is among the causes of the development of other diseases, both physical and mental, especially when the effort to adapt is persistent (chronic stress)(2). Stress-related psychological disorders are associated with an excessive increase in inflammation and oxidative stress, which are the main causes of endothelial and metabolic dysfunction, related to cardiovascular and metabolic diseases(47) and affect the functioning of the autonomic nervous system(36,41,42). For Hamer *et al.*(8,12), such responses contribute to stimulating the immune system and explain the association of physical activity with well-being and mental health, because physical exercise improves endothelial function and arterial stiffness, reducing the signaling of inflammatory and oxidative damage in vascular tissue, in addition to promoting the increase of antioxidant enzymes and increasing the availability of nitric oxide, effects that comprehensively promote functional performance, as well as healthy aging(48). The antioxidant and anti-inflammatory responses of physical exercise, which mainly occur in adipose tissue, skeletal muscles, the immune system, and the cardiovascular system, have a modulating effect on anti-inflammatory/proinflammatory cytokines(11,21). Thus, physical exercise favors the health of the endothelium, which is no longer considered only as the inner lining of blood vessels but is a complex organ that performs important functions in metabolic homeostasis(49), helping to prevent the excessive accumulation of cholesterol inside the arteries and even promoting the reduction of the thickness of the accumulated cholesterol layer. This benefit is due to the effect of the tangential frictional force of the blood inside the arteries (*shear stress*)(50). Thus, physical exercise is presented as a modulator of the physiological effects of stress(3) on the body, through the extra production of nitric oxide(11,21,51). An experimental study (n=111) found that regular physical exercise is associated with emotional resilience to acute stress in healthy adults(52).

It should also be considered that the relationship between physical exercise and stress is bidirectional. On the one hand, exercise can contribute to reducing stress by presenting, in addition to the previously mentioned benefits related to cardiovascular, metabolic and immunological health(11,12,21,47,53), which, in turn, are related to brain health, especially in the long term(54), since physical exercise at moderate and high intensities has long-lasting effects on cortical activity and mood(55), promoting stress reduction and favoring mental health(8,12).

On the other hand, high levels of stress are associated with lower levels of physical activity(11–13), probably due to decreased orexin levels(38). Therefore, stress can have a differential impact on the initiation, adherence and abandonment of exercise(13). According to Stults-Kolehmainen and Sinha(13), there is evidence that the combination of stress management programs with exercise interventions can contribute to reducing the lack of adherence to physical activity.

The importance of physical exercise in the regulation of the ANS is fundamental, as it activates it by regulating the immune system due to its anti-inflammatory (parasympathetic and sympathetic bundles) and inflammatory (sympathetic bundle) effects(11,51). In addition, exercise training increases cardiac vagal activity, and the possible mechanisms involved include mediation via angiotensin II or nitric oxide(56).

Physical exercise combined with complementary interventions, such as dietary modification, is a necessary strategy to increase the efficacy of physical exercise in cardiovascular diseases(47) in addition to promoting the health of all other organ systems. An adequate diet reduces PNS activity, improves mitochondrial redox function, and minimizes oxidative stress, as well as chronic inflammation(47). While physical exercise promotes neuropsycho-biological responses (integrated response) that promote adaptations in the immune system, in the HPA axis, which regulates the release of cortisol in the bloodstream and in the ANS(12,53). Thus, physical exercise modulates adrenal and cardiovascular reactivity to psychosocial stress(46,52).

An experimental study examined the effects of 15 minutes of exercise on the stationary bike on the plasma concentration of orexin-A and there was a significant increase in plasma orexin-A ($p<0.01$), peaking at 30 min after the exercise session. It was the only study with such a focus found to date. It is suggested that further studies should continue this investigation.

In short, physical exercise is related to several *vagus* nerve bundles, which, therefore, may explain its influence on the health of the following systems: cardiorespiratory-vascular(11,21,56,57,57–59); immunological (3,11,12,21,60); mental health (8,11,12,21,22,59,61) – modulating the production of nitric oxide, which reduces inflammation(11,21) favoring brain and gastroenterological function (51,62). Preclinical studies on the relationship between microbiota and psychiatric illness have consistently pointed to the positive relationship between a healthy microbiota and mental health(63,64), and clinical trials have shown that physical exercise modulated the profile of the gut microbiota(65).

Physical exercise and post-traumatic stress disorder (PTSD)

A narrative review, based on 19 participating studies (nine observational and ten interventional), discussed the effects of aerobic exercise on PTSD recovery(24). The authors considered that there are barriers to the initiation of traditional treatment – psychological and/or pharmacological, which include: feeling of stigma, motivation, costs and access to treatments. The results showed that both observational and interventional studies support the notion that aerobic exercise, alone or in combination with standard treatments, promotes positive mental health benefits in individuals with PTSD, both military and civilian, of both sexes. The potential mechanisms by which aerobic exercise has the potential to attenuate PTSD symptoms are neuropsychophysiological, which include exposure and desensitization to internal arousal cues[1] , enhancement of cognitive function, exercise-induced neuroplasticity[2] , normalization of HPA axis function, and reductions in inflammatory markers(24).

A randomized clinical trial in which patients with PTSD were randomly assigned to one of two intervention groups: the traditional treatment group (psychotherapy, drug intervention, and group therapy) and the experimental group that received the traditional treatment and additionally participated in a 12-week exercise intervention that involved three resistance training sessions with 30 min/week and a pedometer-based walking program. The patients who, in addition to receiving conventional care, participated in the exercise program showed significant differences in terms of improvement in depressive symptoms, sleep quality and waist circumference(70).

A recent systematic review study gathered evidence that physical activity recovers PTSD symptoms, decreases the frequency of intrusive thoughts related to trauma by sternum stimuli, decreases anxiety symptoms, improves social functioning, relieves the mind of worries, improves social interactions, promotes healthy coping strategies for challenging situations, decreases muscle tension. Moreover, it improves attention, harmony in life, balance, energy level, mindfulness, control of physical reactions, and reduces cognitive decline and insomnia. Through all these effects, the benefits for the individual include the physical, psychological, cognitive and social aspects, resulting in improved health and quality of life(71).

Cortical patterns

In the last decade, there has been an increase in the publication of studies on computational methods applied to medicine. The use of artificial intelligence (or *machine learning*) has promoted great advances in the field of understanding the integrated systems that involve body-mind-brain through the identification of cortical patterns and their distribution of normality. Thus, the body of evidence of the integrative relationship of brain health, mental health, and body health has been increasing. The activity patterns of cortical networks are specifically associated with the processes of attention, cognitive control, social cognition, affectivity, emotion regulation and motivation(72–74). Electro-encephalography (EEG) allows us to examine cortical activity by capturing electrical signals in the scalp. The brain basically works on four frequencies: δ (delta: <4z); θ (theta: 4-8Hz); α (alpha: 8-13Hz); and β (beta: 14-22Hz)(75). Cortical patterns have been studied since 1945(76). Knowledge in neuroscience has advanced in such a way that it is known that problems in integration and communication between brain areas and structures represent an inadequate functioning of neurological

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Editor's Note:

[1] *Internal arousal cues*: When high arousal cues are present, as in the case of fear arousal, the dedication to presently activated thoughts, inclinations and processing strategies can be intensified, and may even affect visual acuity(66,67).

[2] *Neuroplasticity*: It is a continuous process that modifies existing neural networks, mediating structural and functional adaptations of synapses in response to changes in behavior, i.e., the brain's ability to create new and reorganize existing synaptic connections(68,69).

activities, resulting in a decrease in brain and psychomotor performance(73,74).

Cortical patterns in people with depression are different in comparison with apparently healthy people(77,78). Thus, cortical activity in individuals with PTSD is altered in comparison with people without the disorder(79,80). A meta-analysis study (n=69) showed that exposure to trauma is associated with an increase in the automatic amplitude of *event-related potential* (ERP[3]), concluding that exposure to trauma is associated with increased early processing of received stimuli and that PTSD accentuates the processing of affective stimuli and decreases the processing of non-affective stimuli(81). Such findings would indicate an impairment of cognitive function, which was corroborated in the experimental studies by Veltmeyer *et al.*(82.83).

An integrative review study on the neuropsychophysiology of PTSD brought together considerations regarding the biological aspects of endocrine rhythms and sleep disorders observing the effects on cortical activity related to this complex syndrome(79). The authors explained that the most typical endocrinological changes were decreased daytime cortisol secretion[4] and hyperactivation of the SNS. Such alterations are related to impairment in the consolidation of emotional memories, attention, learning, vigilance and increased arousal, which explains the decrease in cognitive performance. In this context, the data collected regarding the synchrony and functional connectivity of temporal cortical activity demonstrated abnormalities in the alpha, beta and gamma frequency bands that can affect attentional and memory processes(79).

Specifically in the treatment of PTSD, training with NFBK for autoregulatory neuromodulation has been effective in improving symptoms(85).

Neuromodulation

Currently, there are different types of neuromodulations applied in recovery and rehabilitation of patients with distinct health problems/symptoms, and the techniques are divided into two categories: invasive and non-invasive(86). Among the non-invasive techniques is *neurofeedback* (NFBK), which is self-regulatory neuromodulation(72–74), also known as training with the use of BCI (*brain-computer interface*)(87).

The strategy of training by capturing physiological signals (respiratory rate, heart rate, body temperature, degree of muscle contraction), known as *biofeedback*(88,89), emerged in the 70s, with the search by scientists for training methods aimed at the self-control of emotions by athletes and the consequent focus necessary for a cognitive-psychomotor performance that favored the maximum performance of high-performance athletes. A recent systematic review examined the literature between 2012-2022 and the results showed that the use of training using the NFBK technique in athletes had a significant impact on physical fitness and sports performance(90). The authors concluded that training using the NFBK, properly planned and conducted, promoted a reduction in stress levels, increased self-control capacity for physiological factors, increased behavioral efficiency, and improved reaction speed to a stimulus(90).

Other experimental studies, also quite recent, published in 2023 and 2024, continued to corroborate the evidence of the effectiveness of self-regulatory neuromodulation among athletes. In the javelin throw (n=20), an Olympic modality, it was demonstrated that the NFBK promoted a significant improvement in the performance of the executive control network and in the ability to throw darts (psychomotor performance), related to the improvement in the cortical processes involved with attentional performance(91).

Editor's Note:

[3] *Event related potential* (ERP): Event-related potential (ERP) is a measurement technique performed via electroencephalography that measures direct neural responses to a specific sensory, cognitive or motor stimulus(80).

[4] Which is associated with depression and the incidence of type 2 diabetes(84).

In judo athletes (n=24)(92), the KFBK improved reaction times to visual stimuli, both in simple and complex tasks, which did not occur in the control group. In addition, the most marked improvement occurred in the reaction times of complex tasks, which, according to the authors, indicated the high effectiveness of NFBK training in improving this skill.

In professional golf athletes (n=44), a single session of NFBK *sensory-motor rhythm (*SMR) training was shown to increase SMR power and improve golf performance compared to the control group. In addition, the athletes reported less attention engagement, less conscious control of motor details and were more relaxed in the task of performing their shot, suggesting that there was less effort in performing the task with improvement in calm, stable and calm and effortless mental states during the preparation of the shot(93).

In the area of rehabilitation, a case study reported the application of NFBK in the recovery of an Olympic athlete who presented loss of self-confidence after injury, impairing his performance(94). The results showed:

> *"Dramatic and statistically significant changes that could not be explained by measurement error were observed in the patient"* (94).

Neurofeedback training in the case examined increased the amplitude of the attention component in the anterior cingulate cortex and of beta activity on the medial prefrontal cortex. Therefore, the conclusion of the study pointed out that even few sessions of NFBK:

> "*in a high-performance brain can significantly activate the prefrontal cortical areas associated with increased confidence in sports performance*"(94).

In addition, still in relation to injury recovery in high-performance athletes, a study examined the application of NFBK in addition to neuromuscular training in the recovery of athletes with chronic ankle instability (n=62). The results showed that neuromuscular training combined with NFBK was significantly more effective than the isolated application of neuromuscular training. The benefits of adding NFBK to traditional treatment were that there was improvement in postural control, ankle proprioception, anxiety, and depression. The authors concluded by recommending NFBK training as an adjuvant therapy in the rehabilitation of athletes with chronic ankle instability(95).

Also in the general population, NFBK is beginning to be explored as a recovery and health promotion strategy. The technique has been used to improve cognition, treat patients with mental health symptoms (anxiety, depression, attention deficit hyperactivity disorder: ADHD, among others) and even recover from brain injuries and fibromyalgia(73,74,96–98).

An experimental study (n=80) examined the effect of NFBK on reducing the level of stress reaction by comparing various stressors in the biochemical, muscular, and psychomotor sphere in a randomized controlled trial. Training with NFBK promoted a reduction in the negative effects of exposure to stress in humans, and there were differences in the level of influence according to the stressor applied(99).

Self-regulatory neuromodulation performed through training with NFBK can promote the activation or inhibition of cortical activity in specific areas of the brain related to memory, cognition, affective states and mental health symptoms, which can, due to the bidirectional association between mental health and physical activity(14,15), lead the individual to adopt behaviors that favor their health, which involve: food intake, physical activity, sleep quality, among others. Such behaviors, in turn, will promote the health of all organ systems and favor brain health(54).

Although there is controversy regarding the efficacy of NFBK in relation to laboratory situations(100,101), there is a growing literature regarding the benefits perceived in the context of individuals' lives(87,102–104), including people in the context of high-performance sports performance(88–90,92,94,95).

Physical exercise and cortical patterns

There is ample evidence of the benefits of physical exercise for brain health and performance, such as: cognitive performance(105–107), promotion of healthy functioning of the satiety center(108) and gastrointestinal tract(109), with anti-inflammatory properties(108). The study by Schneider *et al.* (55) demonstrated that there are long-lasting effects of physical exercise on cerebral cortical activity, which may have influences on general well-being, in addition, the authors found an association between cortical activity and mood, reflecting the basic principle regarding brain patterns(77). This can be explained by the fact that physical exercise reduces inflammation in the body and favors the microbiota, which is also related to the reduction of mental health symptoms(63,64) and favorable changes in cortical activity patterns(63).

There is evidence of neuroplasticity promoted by physical exercise(68), and the literature is consistent with both observational and intervention studies that indicate that aerobic exercise, alone or in combination with standard treatments, exerts positive benefits for mental health among individuals with PTSD(24).

Exercise-induced neuroplasticity is related both to vascular circulation factors (increased tissue oxygenation) and to the marked increase in the expression of the *brain-derived neurotrophic factor (BDNF)* gene, one of the main contributors to learning processes and memory formation(110,111).

One study examined the acute effect of incremental exercise on cortical activity in patients with mental health problems and apparently healthy people. The results showed no significant differences in cortical activity responses in the alpha band between the groups, and there were differences in gamma responses in the prefrontal cortex that were significantly greater on the left side of individuals with mental health symptoms compared to healthy individuals (p<0.05)(78)(78).

According to Hortobágyi *et al.*(68) Both aerobic training and resistance training can promote neuroplasticity, but further studies investigating the dose-response pattern regarding exercise intensity are still needed for this to occur. The authors explain that this question is highly relevant because exercise-induced neuroplasticity presumably underlies improvements in motor and cognitive functions in healthy people and people with various types of neurological disorders. For Hegberg *et al.*(24) The potential mechanisms that may explain the positive impact of aerobic exercise on PTSD are psychological and neurophysiological, which favorably modify the patterns of cortical activity, improving cognition, attention, and memory.

The literature review of the study by Moriarty *et al.*(112) gathered evidence of the effects of physical exercise on cortical activity, which were:

- *A single session of aerobic exercise influenced neurophysiological pathways that promote increased post-exercise cognitive functioning (processing speed, working memory, and executive function);*
- *High-intensity exercise sessions in conjunction with low-moderate intensity exercise can contribute to performance in several cognitive constructs;*
- *A single session mind-body therapy, such as yoga, enhanced memory and processing speed;*
- *The acute effect of moderate exercise on the brain was increased dorsolateral prefrontal activation, and improved cognitive performance;*
- *The dorsolateral prefrontal cortex is responsible for cognitive control and goal-directed behavior, as well as being highly active during memory retrieval and in response to mentally strenuous tasks;*
- *The left dorsolateral prefrontal cortex has been associated with processing speed and executive function, and appears to be influenced by acute exercise;*

- *Low-moderate intensity physical exercise promotes an increase in cerebral blood flow and oxygenation, which can promote the distribution of nutrients throughout the brain and induce arousal during subsequent cognitive tests; and*
- *Both high-intensity and low-intensity aerobic exercise (including yoga) induced activation of the prefrontal cortex and improved cognitive functioning post-exercise.*

Along with the greater oxygenation of the brain promoted by physical exercise, a probable cause for the acute increase in cognitive performance is the positive regulation of BNDF(112). So, Moriarty *et al.*(112) in their experimental study conducted on physically active people, they proposed to compare the acute effects of moderate- to high-intensity exercise and low-intensity yoga exercise on prefrontal cortex oxygenation during cognitive tasks performed immediately after each exercise session, and additionally examined BDNF expression. Cortical activation in the prefrontal region was higher after moderate-intensity exercise, compared to high- and low-intensity exercise, and there was no linear correlation between cortical activation and cognitive performance. The findings of the study also pointed out that higher intensity exercise was associated with lower scores in processing speed and cognition, indicating that fatiguing exercise can be detrimental to performance in subsequent cognitive processes(112). As for serum BDNF, there was no change after an acute exercise session(112). However, there was an association between basal BDNF and processing speed. The authors argued that these results suggest that a higher resting BDNF value is possibly linked to cognitive functioning. They also explained that there is an association between the increase in the exercise metabolite lactate (an indicator of greater metabolic stress) and an increase in plasma BDNF.

Knowledge advances every day towards a better understanding of how exercise physiology results in mental health and brain benefits. According to Seo *et al.*(113), explain that hippocampal dysfunction causes PTSD and problems in brain functioning (anxiety, depression, and cognitive impairment), in addition to impairments in mitochondrial function and neuroplasticity. Physical exercise can contribute to the recovery of these patients through induced improvement in the level of brain-derived neurotrophic factor, improvement of mitochondrial function, and induction of neuroplasticity and the rate of apoptosis in the[5] hippocampus. Therefore, the authors concluded that exercise can be an important non-pharmacological intervention for the prevention and treatment of the pathobiology of PTSD.

Based on the theoretical model of bidirectionality of the relationship between physical activity, physical health, mental health and stress, it is plausible that the relationship between physical activity and brain activity, in an analogous way, is also bidirectional. In this sense, the physiological effects of exercise related to the *vagus* nerve may contribute to regaining its regulation. According to Porges(26–29), the functioning of the *vagus* nerve is altered in the presence of psychological trauma, leading to changes in cortical patterns and impairing the individual's psychosocial functioning. According to Porges(26–29), one of the main indicators of vulnerability to stress is the respiratory rhythm. In this sense, for recovery, activities that involve breathing exercises can be combined with relaxation exercises. The benefits of physical exercise to the endothelium are multiple for the individual, both for their physical and mental health. Physical exercise decreases inflammation and regulates energy systems, as well as promotes exposure and desensitization to

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Editor's Note:

[5] *Apoptosis: A type of cell death, in which a series of molecular steps in a cell lead to its death. It is a method that the body uses to get rid of unnecessary or abnormal cells. The process of apoptosis can be blocked in cancer cells. Also called programmed cell death*(114).

internal arousal cues and neuroplasticity, improves cognitive function, and can help regulate *vagus* nerve systems, normalizing the function of the HPA axis(24). In this context, aiming at an integrative approach, physical training, together with NBFK training, can provide physical-psychophysiological and electrophysiological benefits, which influence each other, contributing to the comprehensive recovery of patients with PTSD.

Other therapeutic approaches, in addition to physical exercise and NFBK, which may favor the recovery of patients with PTSD found during the development of this study, were the contribution of nutritional factors that, in addition to physical exercise, promote *vagus* nerve regulation, decrease inflammation and improved mood (62,115) and acupuncture(116).

Strong points and limitations of the study

The strength of the present study was to examine complex phenomena that make up the recovery of patients with PTSD, which emerges as result of psychological/physical trauma, triggering psychophysiological responses that lead to impairment in the healthy functioning of the individual.

A limitation of the study is that a systematic review methodology was not adopted with a view to developing a meta-analysis, because the theme, in addition to being new, presents high complexity in the psychophysiological interactions addressed. Thus, due to the comprehensiveness of the individual aspects involved in the processes, this is a topic that requires further clinical investigation, also indicating the relevance of the present study.

Conclusion

The present study aimed to examine the interactions between physiological-psychophysiological and electrophysiological aspects (cortical patterns) with physical exercise, from an integrative medicine perspective, seeking possible non-pharmacological alternatives for the treatment of patients with post-traumatic stress disorder (PTSD).

The literature is consistent regarding the benefits of physical activity for patients with PTSD, improving cardiorespiratory, endocrine, vascular and electrophysiological (cortical activity) physiology. Evidence suggests that for the greatest mental and brain health benefits, the recommended intensity for physical exercise is moderate.

The set of physiological benefits induced by physical exercise indicates that it can contribute to regulating the *vagus* nerve in the recovery from trauma, acting in sectors such as heart rate regulation, the functioning of the gastrointestinal system, promoting the balance of appetite and satiety. Thus, it benefits brain health and activity, and the concomitant use of the NFBK self-regulatory neuromodulation technique can enhance the recovery speed of PTSD patients through the normalization of healthy patterns of cortical functioning.

Intervention studies that focus on self-regulatory neuromodulation along with the practice of physical exercise should be conducted, preferably in population samples, to identify the adjuvant therapies necessary to promote recovery from various types of psychological trauma, with a view to shortening the recovery time of patients with PTSD.

Conflict of interests

There is no conflict of interest in this study.

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