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Could PCSO-524® be a potential adjuvant treatment to sleep therapy in the management of depression?

Felipe H. Arakaki [a], Ellen M.S. Xerfan [b], José Carlos F. Galduróz [a], Sergio Tufik [a], Monica L. Andersen [a,*]

[a] Departamento de Psicobiologia - Universidade Federal de Sao Paulo (UNIFESP), Brazil
[b] Programa de Pós-Graduação em Medicina Translacional – Universidade Federal de Sao Paulo (UNIFESP), Brazil

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ABSTRACT

Sleep is essential in neural system homeostasis due to its regulation of the immunological system and inflammatory cytokines. Poor sleep quality can induce a pro-inflammatory state and aggravate depressive symptoms. Depression has been linked with high levels of peripheral and central pro-inflammatory markers. In this context, we highlight a possible role for PCSO-524®, a nutritional supplement extracted from the New Zealand green lipped mussel that has already been shown to have anti-inflammatory effects, as an adjuvant treatment for depression alongside sleep therapy. Although there are not as yet any studies on its use in treating depression, it has been demonstrated to be a promising treatment in another condition that has been linked with inflammation, attention deficit/hyperactivity disorder, and in some other neurodegenerative disorders. Therefore, PCSO-524®, associated with good sleep quality, could be an option to reinforce depression management.

To the Editor,

Sleep is vital to the regulation of the organism as a whole, including neural system homeostasis. Some of the mechanisms responsible for neuronal balance and protection from the development of neurological and psychiatric disorders are related to the immunological system and the production and modulation of inflammatory cytokines (Irwin, 2019).

Impaired sleep can elevate pro-inflammatory cytokines, and is associated with several disorders including cognitive impairment, neurodegenerative diseases, attention-deficit/hyperactivity disorder (ADHD) and depressive disorders (Irwin, 2019; Dunn et al., 2019). In this context, we call attention to depression, and in particular, the role of neuroinflammation in this disease. According to the World Health Organization (WHO, 2017), 4.4% of the global population suffer from this disorder (Depression and Other Common Mental Disorders, 2017). Köhler et al. (2016) indicated that an inflammatory state, with elevated levels of peripheral and central pro-inflammatory markers, has a potential role in the aetiological pathways of depression, and was related with active depressive episodes (Kohler et al., 2016). One of the markers that participates in triggering this inflammatory state is cyclooxygenase 2 (COX-2). This enzyme is identified in depression, and is expressed in resident cells of the brain, such as neuronal, glial, endothelial and infiltrating blood cells (Minghetti, 2004; Song et al., 2018).

Given the role of inflammatory mediators in depression, that could also be affected by poor sleep quality, we highlight the possible use of a product that seems to show important anti-inflammatory effects – PCSO-524®.

PCSO-524® (Lyprinol®/Omega XL®) is a patented nutritional supplement comprehending marine lipids from *Perna canaliculus*, the New Zealand green lipped mussel, associated with olive oil and vitamin E (Doggrell, 2011; Mickleborough et al., 2015; Gibson et al., 1981). This extract has been shown to have an anti-inflammatory effect, especially in the muscles, through the inhibition of the COX-2 and 5-lipoxyeganse (LOX) pathways (which normally metabolize arachidonic acid), leading to a reduction in pro-inflammatory leukotriene, prostaglandin, and cytokine production (Doggrell, 2011; Mickleborough et al., 2015). Here, we discuss whether this product could play a role in the inflammatory mechanisms of the brain, and, enhanced by sleep regulation, be used in the treatment of depression.

Depression can be triggered by a higher inflammatory state that is enhanced by sleep quality impairment, which contributes to the maintenance of these neuroinflammatory conditions in a vicious circle

* Corresponding author at: Universidade Federal de São Paulo, Rua Napoleão de Barros, 925, Vila Clementino - 04024-002 - Sao Paulo/SP – Brazil.
E-mail address: ml.andersen12@gmail.com (M.L. Andersen).

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(Kiecolt-Glaser et al., 2015). The inflammation associated with depression and other psychiatric disorders is characterized by an increase in C-reactive protein and pro-inflammatory cytokines, especially interleukin (IL)-1, IL-6 and TNF-α (Kohler et al., 2016; Kiecolt-Glaser et al., 2015; Berk et al., 2013). These cytokines are known to have a depressogenic effect, and can be found at higher levels secondary to stressful conditions, including poor sleep quality (Kiecolt-Glaser et al., 2015; Berk et al., 2013). Previous data have shown that even short periods of sleep deprivation can lead to higher levels of IL-6 and TNF-α (Vgontzas et al., 2003), and they seem to be able to pass through the blood-brain barrier (Kohler et al., 2016). A number of studies have suggested that they could impair neurotransmission, which is related to mood stability, thereby inducing depressive manifestations (Kohler et al., 2016; Kiecolt-Glaser et al., 2015; Berk et al., 2013). Although there is no direct evidence as yet on the effect of PCSO-524® on depression, it is reasonable to hypothesize that it could play a role in reducing cytokine imbalance and sleep impairment - given its effect on neuroinflammation - and have a potential impact on depression. As decreased sleep quality is connected with depression, this supplement may improve both conditions. These hypotheses could guide new research regarding further development of inflammatory biomarkers to help the clinical control and depression management, and its relationship with impaired sleep (Berk et al., 2013).

Although there are no studies on the use of PCSO 524® in the treatment of depression, in a neurological context, (Zhu et al., 2019) observed a possible neuroprotective effect of this supplement in experimental models *in vitro*, in respect of Alzheimer's disease, with neuronal cell cycle assays. In one of the stages of this study, there was a reduction in neuronal apoptosis, neurotoxicity and inflammation. It has been suggested that this supplement could be have the potential to delay or even prevent neurodegenerative cell cycle events (Zhu et al., 2019).

PCSO-524® has been demonstrated to be associated with the inhibition of the release of prostaglandins, such as COX-1 and COX-2, (Doggrell, 2011) which have previously been shown to play a role in neurodegeneration (Calsolaro and Edison, 2016). PCSO-524® may, therefore, not only have an effect on the depression associated with Alzheimer's disease, but it could also have potential in other neurodegenerative conditions, and on the brain as a whole.

In another neurological context Kean et al. (2017), found PCSO-524® to be a promising treatment for ADHD symptoms, such as attention deficit, impulsivity and hyperactivity manifested in children and adolescents with this disorder. Given the possible role of inflammation in both ADHD and depression, we hypothesize that this supplement might bring benefits in relation to the treatment of depression, especially when considering the possible regulation of COX-2 and some pro-inflammatory cytokines that participate in this mood disorder.

Our hypothesis is, therefore, supported by clinical studies that show evidence of the effectiveness of PCSO-524® in inflammatory and neurodegenerative conditions (Doggrell, 2011; Mickleborough et al., 2015; Zhu et al., 2019). Given the possible neuroinflammatory aetiology of the disease, it would be worthwhile exploring its use, combined with sleep therapy (because of sleep's important role in the regulation of inflammatory processes) (Irwin, 2019), as an adjuvant treatment for depression. This could provide a new and effective option to improve the treatment and control of this mood disorder.

Declaration of Competing Interest

The authors declare no conflict of interest.

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