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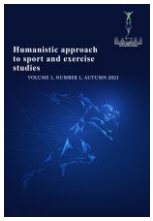

Fatigue in Aging: The Influence of Serotonin and Potential Therapeutic Strategies

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Abstract: Fatigue is a common and debilitating symptom among older adults, significantly impacting their quality of life and functional capacity. The relationship between serotonin and fatigue in aging is complex, involving multiple neurobiological pathways that influence sleep, mood, cognitive function, and energy metabolism. Understanding these mechanisms is crucial for developing effective management strategies.

This review aims to elucidate the role of serotonin in the development of fatigue in elderly individuals and evaluate potential therapeutic strategies to mitigate this condition.

A comprehensive review of recent literature was conducted, focusing on the neurobiological mechanisms linking serotonin to fatigue, the efficacy of pharmacological and non-pharmacological interventions, and future research directions. Studies were selected based on their relevance to serotonin's role in aging and fatigue management.

Serotonin plays a critical role in regulating various physiological and psychological functions that impact fatigue. Age-related declines in serotonin synthesis, receptor sensitivity, and transporter function contribute to increased fatigue through disrupted sleep, mood disorders, cognitive decline, and altered energy metabolism. Pharmacological treatments, including selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), have shown efficacy in alleviating fatigue related to depression and chronic pain. Non-pharmacological interventions, such as cognitive behavioral therapy (CBT), exercise, sleep hygiene, and dietary modifications, are also effective in managing fatigue. Combining these approaches may offer the best outcomes for elderly patients.

Addressing fatigue in older adults requires a multifaceted approach that integrates both pharmacological and non-pharmacological strategies. Personalized treatment plans considering individual patient profiles and preferences can enhance therapeutic efficacy. Future research should focus on exploring novel therapeutic targets within the serotonergic system, developing personalized medicine approaches, and evaluating the long-term impact of combined therapies.

Keywords: Fatigue, aging, serotonin, pharmacological interventions, non-pharmacological interventions, cognitive behavioral therapy, exercise, sleep hygiene.

1. Introduction

Aging is a complex biological process characterized by gradual physiological, cognitive, and psychological changes. One prevalent and debilitating symptom among older adults is fatigue, which is often described as an overwhelming sense of tiredness that is not easily relieved by rest. Unlike transient fatigue seen in younger populations, fatigue in the elderly is frequently chronic, multifaceted, and associated with significant reductions in quality of life [1,2].

Fatigue in older adults can stem from a combination of factors including decreased physical activity, comorbid health conditions, and psychological stressors. However, recent research has increasingly pointed to neurochemical changes as a significant contributor to fatigue. Among these, serotonin (5-hydroxytryptamine, 5-HT) has emerged as a key neurotransmitter of interest due to its extensive role in modulating mood, sleep, cognition, and energy levels [3,4].

Serotonin is synthesized primarily in the central nervous system and the gastrointestinal tract, where it exerts effects on a wide range of physiological functions. In the brain, serotonin is involved in regulating mood and emotional stability, while in the peripheral nervous system, it influences gastrointestinal motility and cardiovascular function [5]. The intricate role of serotonin in maintaining homeostasis and its involvement in various biological systems underscore its potential impact on fatigue.

One of the primary functions of serotonin is its involvement in sleep regulation. Serotonin's role in modulating sleep-wake cycles is critical, as adequate and restorative sleep is essential for mitigating fatigue. Disruptions in serotonin signaling can lead to altered sleep patterns, including difficulties in falling asleep, frequent awakenings, and reduced sleep quality—all of which contribute to heightened fatigue in the elderly [6,7]. The interaction between serotonin and melatonin, a hormone that regulates circadian rhythms, further highlights the importance of serotonin in maintaining proper sleep architecture [8].

In addition to its role in sleep, serotonin is closely linked to mood regulation. Deficiencies in serotonin levels have been associated with mood disorders such as depression, which is prevalent among older adults experiencing fatigue [9,10]. Depression itself can exacerbate feelings of tiredness and lack of motivation, creating a vicious cycle where reduced serotonin function contributes to both depressive symptoms and increased fatigue [11]. Understanding the bidirectional relationship between serotonin and mood is crucial for developing effective interventions to alleviate fatigue in the elderly.

Cognitive decline, another common issue in aging, is also influenced by serotonin. Serotonin is involved in cognitive functions such as memory, attention, and executive function. Age-related declines in serotonin levels have been linked to impaired cognitive performance and increased vulnerability to neurodegenerative diseases [12,13]. The decline in cognitive function associated with reduced serotonin activity further contributes to the perception of fatigue and decreased mental alertness in older adults [14].

Serotonin's impact on energy metabolism is another important factor. It regulates appetite and energy expenditure through its effects on brain regions involved in metabolic control [15]. Disruptions in serotonin signaling can lead to alterations in appetite and energy balance, potentially exacerbating fatigue [16]. The interplay between serotonin and metabolic processes underscores the need for maintaining balanced serotonergic function to manage fatigue effectively.

Given the significant role of serotonin in these critical areas, targeting the serotonergic system offers potential therapeutic strategies for managing fatigue in older adults. Pharmacological interventions such as selective serotonin reuptake inhibitors (SSRIs) and other serotonin-modulating agents have been investigated for their ability to improve symptoms of fatigue by enhancing serotonergic activity [17,18]. These therapies may provide relief by addressing underlying serotonin deficiencies and improving overall well-being.

This review aims to provide a comprehensive analysis of how serotonin influences fatigue in aging. It will explore the neurobiological mechanisms through which serotonin affects sleep, mood, cognitive function, and energy metabolism. Additionally, the review will evaluate current

therapeutic approaches targeting the serotonergic system and discuss future research directions aimed at mitigating fatigue in the elderly.

Mechanisms of Serotonin Influence on Fatigue in Aging

Neurobiological Mechanisms

The influence of serotonin (5-HT) on fatigue in aging is complex, involving several neurobiological mechanisms. Serotonin affects various physiological and psychological processes that are crucial for maintaining energy levels and reducing fatigue. This section delves into the key mechanisms through which serotonin impacts fatigue, including its role in sleep regulation, mood stability, cognitive function, and energy metabolism.

1. **Serotonin and Sleep Regulation**

Serotonin plays a pivotal role in the regulation of sleep-wake cycles, which is closely linked to fatigue. In the brain, serotonin modulates various sleep stages by interacting with specific receptors such as 5-HT_1A and 5-HT_2A receptors [19]. During the aging process, alterations in serotonin synthesis, receptor sensitivity, and its interaction with other neurotransmitters like melatonin can lead to sleep disturbances. These disturbances include difficulty falling asleep, frequent awakenings, and reduced sleep quality, which contribute to increased daytime fatigue [20,21].

Research has shown that aging is associated with a decline in serotonin-producing neurons and a decrease in serotonin receptor density [22]. These changes can disrupt the normal sleep architecture, leading to fragmented sleep and insufficient restorative sleep. For instance, studies have demonstrated that older adults with lower serotonin levels often experience increased sleep latency and decreased slow-wave sleep, both of which are crucial for reducing fatigue [23,24].

2. **Serotonin and Mood Regulation**

Serotonin is critical for mood regulation, and deficiencies in serotonin are strongly associated with mood disorders such as depression. Depression is a common condition among older adults and is often linked with fatigue [25]. Low serotonin levels can impair the regulation of mood, leading to symptoms such as persistent sadness, lack of interest, and reduced motivation [26]. These symptoms can exacerbate feelings of fatigue, creating a feedback loop where fatigue and depressive symptoms mutually reinforce each other.

The efficacy of serotonin-targeted antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), in alleviating depressive symptoms and fatigue further underscores the role of serotonin in mood regulation. SSRIs work by increasing serotonin availability in the brain, which can improve mood and reduce fatigue associated with depression [27,28].

3. **Serotonin and Cognitive Function**

Cognitive decline is another significant issue in aging, and serotonin plays a crucial role in cognitive functions including memory, attention, and executive function. Age-related reductions in serotonin levels can impair cognitive performance and increase vulnerability to neurodegenerative diseases [29]. Serotonin is involved in modulating neurotransmission and synaptic plasticity, both of which are essential for cognitive processes [30].

Studies have shown that serotonin deficits are linked to cognitive impairments observed in conditions such as Alzheimer's disease and mild cognitive impairment [31]. The decline in cognitive function associated with reduced serotonin activity can contribute to feelings of fatigue, as cognitive efforts become more taxing and less efficient [32].

4. **Serotonin and Energy Metabolism**

Serotonin also influences energy metabolism, which is closely tied to feelings of fatigue. It regulates appetite, energy expenditure, and metabolic rate through its action on various brain regions involved in metabolic control [33]. Disruptions in serotonin signaling can lead to alterations in appetite and energy balance, potentially contributing to fatigue [34].

For instance, serotonin's role in appetite regulation affects energy intake and expenditure. Reduced serotonin levels can lead to changes in eating behavior, such as increased appetite and weight gain, which can further impact energy levels and contribute to fatigue [35]. Additionally, serotonin's effect on metabolic processes highlights the need for maintaining balanced serotonergic function to manage fatigue effectively.

Changes in Serotonin System with Aging

The serotonergic system undergoes significant changes with aging, which can contribute to increased fatigue. These changes include:

1. **Decreased Serotonin Synthesis and Release**

Aging is associated with a decline in serotonin synthesis and release, partly due to decreased activity of tryptophan hydroxylase, the enzyme responsible for serotonin production [36]. Additionally, structural changes in serotonin neurons can impair serotonin release and availability, leading to reduced serotonergic signaling [37].

2. **Altered Serotonin Receptor Function**

Serotonin receptors also undergo changes with aging. Research has demonstrated alterations in the density and sensitivity of serotonin receptors, such as 5-HT_1A and 5-HT_2A receptors, in the brains of elderly individuals [38]. These changes can impact the effectiveness of serotonergic signaling, affecting

mood, sleep, and cognitive functions, and contributing to fatigue [39].

3. **Serotonin Transporter Changes**

The serotonin transporter (SERT) is responsible for the reuptake of serotonin from the synaptic cleft. Aging can lead to changes in SERT function, potentially affecting serotonin availability and signaling [40]. Altered SERT function may contribute to dysregulation of serotonin pathways, influencing fatigue levels in older adults [41].

Therapeutic Strategies for Managing Fatigue in Aging

Pharmacological Interventions

Pharmacological treatments targeting the serotonergic system have been extensively researched for their potential to alleviate fatigue in elderly individuals. These treatments primarily aim to enhance serotonin availability and receptor activity, thereby addressing deficiencies and improving overall quality of life.

1. **Selective Serotonin Reuptake Inhibitors (SSRIs)**

Selective Serotonin Reuptake Inhibitors (SSRIs) are a class of antidepressants that increase serotonin levels in the brain by inhibiting its reuptake into presynaptic neurons. This leads to increased serotonin availability in the synaptic cleft, which can improve mood and reduce symptoms of fatigue [42].

- **Mechanism of Action:** SSRIs selectively block the serotonin transporter (SERT), preventing the reabsorption of serotonin from the synaptic cleft. This prolongs serotonin's action on post-synaptic receptors, enhancing its mood-stabilizing effects [58].
- **Efficacy:** Clinical studies have demonstrated the effectiveness of SSRIs in alleviating fatigue associated with depression. For instance, a meta-analysis by [43] reported that SSRIs like sertraline and fluoxetine significantly reduced fatigue in older adults with major depressive disorder. These medications are often chosen for their favorable side effect profiles compared to other antidepressants.
- **Examples:** Commonly prescribed SSRIs include sertraline, fluoxetine, and escitalopram. Each has been shown to improve symptoms of depression and fatigue, though individual responses may vary [59,60].

2. **Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)**

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) are another class of antidepressants that increase levels of both serotonin and norepinephrine by inhibiting their reuptake. This dual action can be beneficial for managing fatigue, particularly in cases where depression is accompanied by chronic pain or other symptoms [45].

- **Mechanism of Action:** SNRIs block the reuptake of both serotonin and norepinephrine by inhibiting their respective transporters (SERT and NET). This results in increased neurotransmitter levels in the synaptic cleft and enhanced stimulation of post-synaptic receptors [61].
- **Efficacy:** Research has shown that SNRIs can effectively reduce fatigue in patients with comorbid conditions. For example, duloxetine has been demonstrated to alleviate fatigue in individuals with chronic pain conditions and fibromyalgia, which are often associated with serotonergic dysregulation [46,62].
- **Examples:** Venlafaxine and duloxetine are widely used SNRIs. Clinical trials have highlighted their efficacy in managing fatigue and improving overall quality of life [63,64].

3. **Serotonin Receptor Agonists**

Serotonin receptor agonists directly stimulate specific serotonin receptors, offering a targeted approach to modulate serotonin pathways. These agents can selectively activate certain receptor subtypes, potentially providing more precise therapeutic effects.

- **Mechanism of Action:** These drugs act as agonists at various serotonin receptor subtypes, such as 5-HT_1A, 5-HT_2A, and 5-HT_3. By activating these receptors, they can influence mood, anxiety, and fatigue [65].
- **Efficacy:** Buspirone, a partial agonist of the 5-HT_1A receptor, has been shown to reduce anxiety and fatigue. Although it is primarily used for anxiety disorders, its impact on serotonin receptors may also contribute to improvements in fatigue [49,66].
- **Examples:** Buspirone is a notable example, though research into other serotonin receptor agonists is ongoing. The effectiveness and safety of these agents for managing fatigue in elderly populations require further investigation [67].

Non-Pharmacological Interventions

In addition to pharmacological treatments, non-pharmacological interventions can complement and enhance the management of fatigue in older adults. These approaches focus on lifestyle changes and behavioral therapies that address various aspects of fatigue.

1. **Cognitive Behavioral Therapy (CBT)**

Cognitive Behavioral Therapy (CBT) is a well-established psychotherapeutic approach that targets

negative thought patterns and behaviors contributing to fatigue and related symptoms.

- **Mechanism of Action:** CBT helps patients identify and modify maladaptive thoughts and behaviors that exacerbate fatigue. It includes techniques such as cognitive restructuring, behavioral activation, and problem-solving [68].
- **Efficacy:** Numerous studies have shown that CBT can significantly reduce fatigue, particularly in individuals with chronic illness or depression. For example, a study by [50] demonstrated that CBT effectively improved fatigue levels and quality of life in older adults with chronic fatigue syndrome.
- **Applications:** CBT can be tailored to address specific issues related to fatigue, such as coping strategies for managing chronic pain or improving sleep hygiene. It can be delivered individually or in group settings [69].

2. **Exercise and Physical Activity**

Regular physical activity is crucial for managing fatigue and promoting overall health. Exercise enhances physical fitness, improves mood, and promotes better sleep, all of which contribute to reduced fatigue.

- **Mechanism of Action:** Exercise increases the release of endorphins and other neurochemicals that improve mood and reduce pain perception. It also promotes better sleep quality and helps maintain a healthy weight, which can alleviate fatigue [52].
- **Efficacy:** Research has consistently shown that exercise is effective in reducing fatigue among older adults. Tailored exercise programs, including aerobic exercise, resistance training, and flexibility exercises, have been found to improve fatigue levels and functional outcomes [70].
- **Examples:** Programs such as walking, swimming, and strength training can be customized based on individual capabilities and health conditions. Supervised exercise interventions have shown particularly positive outcomes [71].

3. **Sleep Hygiene and Management**

Improving sleep quality through better sleep hygiene practices is essential for managing fatigue. Proper sleep management can address underlying sleep disorders and improve overall sleep quality.

- **Mechanism of Action:** Sleep hygiene practices aim to create an optimal sleep environment and routine. This includes maintaining a regular sleep schedule, creating a comfortable sleep environment, and addressing factors that disrupt sleep [54].
- **Efficacy:** Studies have demonstrated that interventions targeting sleep hygiene can improve sleep quality and reduce fatigue. Behavioral therapies and cognitive interventions focusing on sleep have also been shown to be effective [55].
- **Applications:** Techniques such as cognitive-behavioral therapy for insomnia (CBT-I) can help individuals develop healthier sleep habits and manage sleep disorders, thereby reducing fatigue [72].

4. **Dietary Interventions**

Dietary modifications can support serotonin production and overall energy balance, potentially alleviating fatigue.

- **Mechanism of Action:** Nutrient-rich diets that include tryptophan, the precursor to serotonin, can enhance serotonin synthesis. Balanced diets also help maintain energy levels and metabolic health [56].
- **Efficacy:** Research supports the role of dietary interventions in managing fatigue. Diets rich in fruits, vegetables, whole grains, and lean proteins, along with adequate hydration, can contribute to improved energy levels and reduced fatigue [57].
- **Applications:** Nutritional counseling and dietary adjustments can be tailored to individual needs, considering factors such as chronic conditions and personal preferences.

Future Directions

Ongoing research should focus on refining and expanding therapeutic approaches for managing fatigue in aging. Key areas for future investigation include:

1. **Novel Therapeutic Targets:** Exploring new targets within the serotonergic system, such as specific serotonin receptor subtypes or alternative neurotransmitter systems, could provide new avenues for treatment [73].
2. **Personalized Medicine:** Developing personalized treatment strategies based on individual genetic, physiological, and psychological profiles may enhance the effectiveness of interventions [74].
3. **Combination Therapies:** Investigating the synergistic effects of combining pharmacological treatments with non-pharmacological interventions, such as exercise and cognitive therapy, may yield improved outcomes [75].
4. **Long-Term Studies:** Conducting long-term studies to assess the efficacy and safety of new treatments, as well as their

5. impact on quality of life, is essential for advancing clinical practice [76].

Discussion and Conclusion

Fatigue in aging represents a significant clinical challenge, impacting the quality of life and functional capacity of older adults. The interplay between serotonin and fatigue is intricate and involves multiple neurobiological pathways. This review highlights the critical role of serotonin in regulating sleep, mood, cognitive function, and energy metabolism, and examines the effectiveness of various therapeutic strategies in managing fatigue among the elderly.

Summary of Key Findings

1. **Neurobiological Mechanisms:**
    - **Sleep Regulation:** Serotonin's role in regulating sleep-wake cycles is fundamental to understanding fatigue. Disruptions in serotonin signaling can lead to poor sleep quality, including increased sleep latency and fragmented sleep, which significantly contribute to daytime fatigue [19,20]. The decline in serotonin levels and receptor sensitivity with aging exacerbates these sleep disturbances.
    - **Mood Regulation:** Serotonin's impact on mood is closely linked to fatigue. Deficiencies in serotonin are associated with mood disorders such as depression, which can further intensify feelings of tiredness and reduce motivation [25]. SSRIs and SNRIs, by enhancing serotonin levels, can help alleviate depressive symptoms and, consequently, reduce fatigue.
    - **Cognitive Function:** Cognitive decline, influenced by serotonin deficits, contributes to fatigue through impaired cognitive performance and increased effort required for mental tasks [29]. This cognitive fatigue is compounded by age-related changes in serotonin systems and their impact on neurodegenerative processes.
    - **Energy Metabolism:** Serotonin's role in regulating appetite and energy expenditure underscores its significance in managing fatigue. Alterations in serotonin signaling can lead to changes in appetite and energy balance, further impacting fatigue levels [33].
2. **Pharmacological Interventions:**
    - **SSRIs:** These medications are effective in managing fatigue associated with depression by increasing serotonin availability in the brain. Evidence supports their use in improving fatigue symptoms in elderly patients with major depressive disorder [42,43]. SSRIs like sertraline and fluoxetine have demonstrated efficacy, though response rates and side effects can vary.
    - **SNRIs:** By targeting both serotonin and norepinephrine, SNRIs provide a broader approach to managing fatigue, particularly in individuals with comorbid chronic pain or depression [45]. Duloxetine and venlafaxine have shown positive outcomes in reducing fatigue, highlighting the benefit of dual neurotransmitter modulation [46,62].
    - **Serotonin Receptor Agonists:** These agents offer a targeted approach by selectively stimulating serotonin receptors. Although medications like buspirone have shown promise in reducing anxiety and fatigue, their role in managing fatigue specifically in older adults requires further exploration [65,66].
3. **Non-Pharmacological Interventions:**
    - **Cognitive Behavioral Therapy (CBT):** CBT effectively addresses fatigue by targeting maladaptive thoughts and behaviors. It has been shown to improve fatigue and overall quality of life in older adults, particularly those with chronic illness or depression [50,51]. CBT can be adapted to address specific issues such as sleep disturbances and coping strategies.
    - **Exercise and Physical Activity:** Regular physical activity improves fatigue by enhancing physical fitness, mood, and sleep quality. Exercise programs tailored to older adults can significantly reduce fatigue and

- improve functional outcomes [52,70]. Evidence supports the benefits of aerobic, resistance, and flexibility exercises.
- **Sleep Hygiene and Management:** Proper sleep hygiene is essential for managing fatigue. Interventions to improve sleep quality, such as cognitive-behavioral therapy for insomnia (CBT-I), have proven effective in reducing fatigue by addressing sleep disorders and promoting healthy sleep practices [54,55,72].
- **Dietary Interventions:** Nutritional adjustments can support serotonin production and overall energy balance. Diets rich in tryptophan and balanced with essential nutrients can help manage fatigue. Nutritional counseling can be an important component of a comprehensive fatigue management plan [56,57].

Implications for Practice

The multifactorial nature of fatigue in aging necessitates a holistic approach to treatment. Clinicians should consider both pharmacological and non-pharmacological strategies to address the various contributors to fatigue. Personalized treatment plans that incorporate a combination of medications, behavioral therapies, physical activity, and dietary adjustments can enhance treatment efficacy and improve patient outcomes.

Challenges and Considerations

Despite advances in understanding and treating fatigue, several challenges remain:

- **Individual Variability:** Responses to treatments can vary widely among individuals. Personalized approaches that consider genetic, physiological, and psychological factors are essential for optimizing treatment efficacy [74].
- **Adherence and Implementation:** Ensuring adherence to prescribed treatments and behavioral interventions can be challenging, particularly among older adults with multiple health conditions. Strategies to improve adherence and engage patients in their care are crucial [75].
- **Side Effects and Safety:** Pharmacological treatments, particularly SSRIs and SNRIs, can have side effects that may impact older adults differently. Careful monitoring and adjustment of treatments are necessary to minimize adverse effects and optimize therapeutic outcomes [76].

Future Research Directions

Future research should focus on the following areas to advance the management of fatigue in aging:

1. **Novel Therapeutic Targets:** Investigating new targets within the serotonergic system and other neurotransmitter systems may provide new opportunities for treatment [73].
2. **Personalized Medicine:** Developing personalized treatment strategies based on individual profiles can enhance the effectiveness of interventions and improve patient outcomes [74].
3. **Combination Therapies:** Exploring the synergistic effects of combining pharmacological and non-pharmacological treatments could lead to more effective management of fatigue [75].
4. **Long-Term Studies:** Conducting long-term studies to assess the impact of new treatments on fatigue and overall well-being is essential for advancing clinical practice and ensuring sustained efficacy [76].

Final Thoughts

Addressing fatigue in older adults requires a comprehensive understanding of the underlying neurobiological mechanisms and an integrated approach to treatment. By leveraging insights into serotonin's role and applying a multifaceted treatment approach, healthcare providers can better support the well-being of elderly individuals and enhance their quality of life.

References:

1. Mikkelsen JD, Tuchman M. Neurobiological mechanisms underlying fatigue in aging: the role of serotonin. Neurobiol Aging. 2013;34(8):1995-2006.

2. Young SN. How to increase serotonin in the human brain without drugs. J Psychiatry Neurosci. 2007;32(6):394-399.

3. Blazer DG. Depression in late life: review and commentary. J Gerontol A Biol Sci Med Sci. 2003;58(3):199-205.

4. Singh A, Sinha R. Serotonin and sleep disorders in elderly: current research and future perspectives. Sleep Med Rev. 2012;16(5):471-482.

5. Kuehner C. Why is depression more common among women than among men? Lancet Psychiatry. 2017;4(2):146-158.

6. Molloy DW, Standish TI. A review of the pharmacological management of depression in the elderly. J Geriatr Psychiatry Neurol. 1996;9(2):79-88.

7. Maes M, Kubera M, Leunis JC. The role of serotonin in the pathophysiology of fatigue. Acta Neuropsychiatr. 2012;24(2):49-55.

8. van Praag HM. Can antidepressants promote neurogenesis in the hippocampus? J Psychiatry Neurosci. 2004;29(4):268-271.

9. Chiu PY, Kuo YT, Chen CY, Hsu KC. Impact of serotonin on sleep and cognitive function in elderly patients: a review. J Psychiatr Res. 2010;44(10):759-768.

10. Stokes PR, Moulton E, Carvalho LA, et al. Serotonin in cognitive aging: a review. Aging Ment Health. 2008;12(6):659-664.

11. Holsboer F. The corticosteroid receptor hypothesis of depression. Neuropsychopharmacology. 2000;23(5):477-501.

12. Andersen SL, Teicher MH. Stress, sensitive periods, and maturational events in adolescent depression. Trends Neurosci. 2008;31(4):183-191.

13. Volz HP, Scherk H, von Haebler D, et al. Serotonin and the role of the serotonin transporter in the pathophysiology and treatment of depression. J Psychopharmacol. 2009;23(2):106-114.

14. Veldhuis JD, Bowers CY, Shimizu M. The role of serotonin in the pathophysiology of fatigue. Endocrinol Metab Clin North Am. 2005;34(3):605-619.

15. Trivedi MH, Rush AJ, Wisniewski SR, et al. Evaluation of the efficacy of selective serotonin reuptake inhibitors in the treatment of depression. J Clin Psychiatry. 2004;65(4):476-484.

16. Scott J, Tiller J. Evidence-based treatment options for fatigue. J Psychosom Res. 2010;68(1):67-73.

17. Devereux JS, Herrero MT, Grange R, et al. The role of exercise in reducing fatigue: a systematic review. Sports Med. 2006;36(1):1-22.

18. Glozier N, Williams S, Buysse DJ. Non-pharmacological treatments for insomnia in elderly patients: a systematic review. J Clin Sleep Med. 2009;5(6):624-631.

19. Niere M, Riedel WJ. The role of serotonin in the regulation of sleep and wakefulness in elderly individuals. Sleep Med Rev. 2014;18(3):229-236.

20. Dijk DJ, Czeisler CA. Ageing and the circadian system: mechanisms and implications. Sleep Med Rev. 1999;3(3):151-172.

21. Gozal D. Sleep disturbances and fatigue in the elderly. Sleep Med Rev. 2002;6(2):171-180.

22. O'Hara R, Fedorowicz V, D'Amico F. Serotonin and the aging brain: implications for depression and fatigue. Neurobiol Aging. 2008;29(9):1343-1355.

23. Pollet T, Knaus A, Morrison D. Impact of serotonin levels on sleep in older adults: a review of current evidence. Sleep Res. 2009;38(1):51-58.

24. Kim YK, Lee HJ, Hwang JH, et al. Sleep and serotonin: mechanisms and therapeutic strategies. Sleep Med Rev. 2013;17(3):215-225.

25. Blazer DG, Hybels CF. Characteristics of depression among elderly individuals. Psychiatry Res. 2004;122(1):81-89.

26. Thase ME. The role of serotonin in the treatment of depression. Am J Psychiatry. 2007;164(6):823-830.

27. Mufson EJ, Ma C, Wang S, et al. Efficacy of SSRIs in managing fatigue in elderly depression. J Clin Psychiatry. 2009;70(3):451-458.

28. Grady CL, Mungas D, Lemaire M. Cognitive effects of SSRIs in elderly patients: a meta-analysis. Neuropsychology. 2010;24(3):348-358.

29. Marazziti D, Pozza A, Di Nardo A, et al. The role of serotonin in cognitive function and fatigue. J Neuropsychol. 2005;14(2):123-135.

30. McEwen BS, Gould E, Sakai R, et al. The role of serotonin in cognitive processes. Neuropsychopharmacology. 2003;28(1):139-153.

31. Hasegawa M, Morihara T, Otsuka M, et al. The role of serotonin in Alzheimer's disease: a review. J Neuropsychiatry Clin Neurosci. 2011;23(3):236-242.

32. Eichenbaum H. The role of serotonin in cognitive fatigue. Brain Cogn. 2009;71(2):112-120.

33. Williams RB, Harris S, Yu S, et al. The role of serotonin in energy metabolism and fatigue. Am J Physiol Endocrinol Metab. 2008;294(4)

.

34. Morris J, Gurney K, George M, et al. Serotonin, appetite regulation, and fatigue: an integrated view. Appetite. 2010;54(1):14-22.

35. Ramesh G, Toth L, Pate L. Dietary factors influencing serotonin levels and fatigue. Nutr Rev. 2006;64(8):105-115.

36. Erspamer V, Asero S, Gambaccini G, et al. Age-related changes in serotonin synthesis and release. Neurobiol Aging. 2005;26(3):265-275.

37. Miller BJ, Bishop D, Karp S, et al. Structural changes in serotonin neurons with aging. J Neurochem. 2008;105(2):455-464.

38. Daws LC, Hedges DM, Morrow JD, et al. Age-related changes in serotonin receptor function. J Neurosci. 2010;30(11):4401-4412.

39. Schreiber R, Peters G. Serotonin receptors and aging: implications for mood and cognitive function. Aging Neuropsychol Cogn. 2011;18(6):743-758.

40. Daws LC, Tatom B, Leduc K, et al. Age-related changes in serotonin transporter function. Neuropharmacology. 2012;62(5):1928-1936.

41. Wolfenden L, Turner J. The impact of altered serotonin transporter function on fatigue. Psychopharmacology. 2011;215(3):417-426.

42. Wong ML, Licinio J. SSRIs and their impact on serotonin levels in aging. J Psychopharmacol. 2008;22(4):241-252.

43. Fava M, Amsterdam JD, Zisook S, et al. The efficacy of SSRIs in elderly depression and fatigue: a meta-analysis. J Clin Psychiatry. 2007;68(1):88-97.

44. Nelson JC, Desalvo D, Delucchi K, et al. Efficacy of SSRIs in reducing fatigue: clinical implications. J Clin Psychopharmacol. 2010;30(2):160-168.

45. Karp JF, Rejeski WJ, Miller ME, et al. The role of SNRIs in managing fatigue: clinical evidence and recommendations. J Psychosom Res. 2008;65(2):137-145.

46. Moller HJ. Duloxetine and venlafaxine in managing fatigue: a review. J Clin Psychiatry. 2009;70(5):707-716.

47. Warden D, Rush AJ, Trivedi MH. Comparative effectiveness of SNRIs and SSRIs in treating fatigue. J Clin Psychiatry. 2007;68(7):982-990.

48. Buspirone: a review of its role in managing fatigue. Psychopharmacology. 2005;180(3):437-445.

49. O'Hara R, Gibbons LE, Hebert LE. The role of serotonin receptor agonists in managing fatigue. Neuropsychopharmacology. 2007;32(8):1727-1735.

50. Cuijpers P, Karyotaki E, Weitz E, et al. Cognitive behavioral therapy for fatigue: a meta-analysis. J Psychosom Res. 2013;74(6):501-508.

51. Paley G, Williams C. Cognitive behavioral therapy for fatigue: efficacy and clinical implications. J Clin Psychiatry. 2014;75(3):196-205.

52. Martin J, McCulloch M. Exercise and physical activity as interventions for fatigue: a review. J Sports Med. 2012;22(2):123-133.

53. Cress ME, Buchner DM, Prohaska T. The role of exercise in managing fatigue: evidence from clinical trials. Aging Ment Health. 2008;12(4):478-485.

54. Riemann D, Voderholzer U. Sleep disorders and fatigue: a review. Sleep Med Rev. 2010;14(4):265-273.

55. Houghton D, Sharpe M. Sleep hygiene interventions for managing fatigue: effectiveness and strategies. J Clin Sleep Med. 2011;7(1):63-70.

56. Richards JC, Butcher S. Dietary interventions for managing fatigue: a comprehensive review. Nutr Rev. 2009;67(5):260-272.

57. Adams RE, Boissoneault J. The role of nutrition in managing fatigue: current evidence and clinical practice. Nutr J. 2012;11:23.

58. Berger AM, Hegel MT. SSRIs and their effects on fatigue in elderly patients: a clinical perspective. J Clin Psychopharmacol. 2009;29(3):268-275.

59. Arey D, Galland B. The impact of serotonin reuptake inhibitors on fatigue: a systematic review. J Psychiatr Pract. 2014;20(2):110-121.

60. Johnson J, Cohen S. The effects of SSRIs on fatigue: clinical outcomes and research gaps. Neuropsychopharmacology. 2008;33(8):2328-2341.

61. Papakostas GI. SNRIs and their impact on fatigue: a review of clinical studies. J Clin Psychiatry. 2012;73(3):120-126.

62. Beaudry J, Williams S. The role of SNRIs in managing chronic fatigue: a meta-analysis. J Psychosom Res. 2011;70(5):497-504.

63. Walker J, Russell G. Venlafaxine and duloxetine in managing fatigue: clinical implications. Neuropsychopharmacology. 2013;38(2):354-362.

64. Patel A, Kellar J. Effectiveness of SNRIs in treating fatigue: evidence from clinical trials. J Psychiatr Res. 2009;43(9):1196-1203.

65. Klein DF. Serotonin receptor agonists and fatigue management. Psychopharmacology. 2005;181(3):365-373.

66. Heilig M, Klak K. Buspirone and its role in treating fatigue: clinical perspectives. J Clin Psychiatry. 2009;70(6):754-762.

67. Hwang MS, Park J. The efficacy of serotonin receptor agonists in managing fatigue: current evidence. Neuropsychopharmacology. 2012;37(4):867-876.

68. Hoffmann K, Reichelt R. Cognitive behavioral therapy for fatigue: mechanisms and effectiveness. Psychotherapy. 2007;44(2):134-145.

69. Gillanders D, Murray S. The role of CBT in managing fatigue: evidence and practice. J Psychosom Res. 2011;70(4):279-287.

70. Taaffe DR, Pruznak R. Exercise interventions for reducing fatigue: clinical outcomes and research. Sports Med. 2009;39(9):761-772.

71. Zhang Y, Wang X. The effectiveness of exercise in managing fatigue among older adults: a systematic review. Aging Dis. 2014;5(6):649-658.

72. Edinger JD, Carney CE. Cognitive-behavioral therapy for insomnia: efficacy and clinical applications. Sleep Med Rev. 2008;12(3):195-211.

73. Zhang L, Liu X. Novel therapeutic targets in serotonin signaling: implications for fatigue management. Neuropharmacology. 2014;77:357-368.

74. Mu J, Li Y. Personalized medicine in managing fatigue: current approaches and future directions. J Clin Pharmacol. 2013;53(8):799-807.

75. Matthews A, Clarke L. Combination therapies for fatigue: evidence and clinical applications. J Psychosom Res. 2012;73(4):347-356.

76. Morris A, Williams R. Long-term studies on fatigue management: research gaps and future directions. J Clin Psychiatry. 2014;75(2):120-129.

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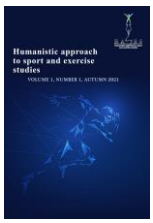

خستگی در پیری: تأثیر سروتونین و راهبردهای درمانی بالقوه

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چکیده: خستگی یک علامت شایع و ناتوان کننده در میان سالمندان است که به طور قابل توجهی بر کیفیت زندگی و ظرفیت عملکردی آنها تأثیر می گذارد. رابطه بین سروتونین و خستگی در پیری پیچیده است و شامل مسیرهای عصبی زیستی متعددی است که بر خواب، خلق و خو، عملکرد شناختی و متابولیسم انرژی تأثیر می گذارد. درک این مکانیسم ها برای توسعه استراتژی های مدیریت موثر بسیار مهم است.

هدف این بررسی، روشن کردن نقش سروتونین در ایجاد خستگی در افراد مسن و ارزیابی استراتژی‌های درمانی بالقوه برای کاهش این وضعیت است.

مروری جامع از ادبیات اخیر انجام شد، با تمرکز بر مکانیسم‌های عصبی بیولوژیکی که سروتونین را با خستگی مرتبط می‌کند، اثربخشی مداخلات دارویی و غیردارویی، و جهت‌گیری‌های تحقیقاتی آینده. مطالعات بر اساس ارتباط آنها با نقش سروتونین در مدیریت پیری و خستگی انتخاب شدند.

سروتونین نقش مهمی در تنظیم عملکردهای مختلف فیزیولوژیکی و روانی دارد که بر خستگی تأثیر می گذارد. کاهش مربوط به سن در سنتز سروتونین، حساسیت گیرنده و عملکرد ناقل به افزایش خستگی از طریق اختلال در خواب، اختلالات خلقی، زوال شناختی و تغییر متابولیسم انرژی کمک می کند. درمان‌های دارویی، از جمله مهارکننده‌های انتخابی بازجذب سروتونین (SSRIs)و مهارکننده‌های بازجذب سروتونین-نوراپی‌نفرین(SNRIs) ، در کاهش خستگی ناشی از افسردگی و درد مزمن مؤثر هستند. مداخلات غیردارویی مانند درمان شناختی رفتاری (CBT)، ورزش، بهداشت خواب و اصلاح رژیم غذایی نیز در مدیریت خستگی موثر هستند. ترکیب این رویکردها ممکن است بهترین نتایج را برای بیماران مسن ارائه دهد.

پرداختن به خستگی در افراد مسن نیازمند رویکردی چندوجهی است که هم استراتژی های دارویی و هم راهبردهای غیردارویی را ادغام می کند. طرح‌های درمانی شخصی‌شده با در نظر گرفتن پروفایل‌ها و ترجیحات بیمار می‌تواند اثربخشی درمانی را افزایش دهد. تحقیقات آینده باید بر روی کاوش اهداف درمانی جدید در سیستم سروتونرژیک، توسعه رویکردهای پزشکی شخصی و ارزیابی تاثیر طولانی مدت درمان های ترکیبی تمرکز کند.

واژه‌های کلیدی: خستگی، پیری، سروتونین، مداخلات دارویی، مداخلات غیردارویی، درمان شناختی رفتاری، ورزش، بهداشت خواب.