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Serotoninomics Applied to Longevity: Redefining Well-Being in Geriatric and Gerontological Practice

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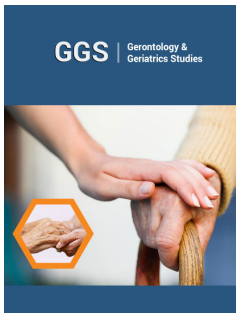

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Abstract

Ageing is a multidimensional process that transcends biological decline, encompassing emotional, symbolic and social dimensions that shape older adults' quality of life. Serotonin, a key neuromodulator of mood, sleep, cognition and resilience, undergoes significant alterations throughout the ageing process, contributing to increased vulnerability and functional deterioration. The concept of serotoninomics, proposed by Jiménez-Trejo et al. Jiménez-Trejo et al. (2015,2024,2025), expands serotonin research towards a transdisciplinary framework that integrates biosynthesis, receptor dynamics, metabolism and the symbolic impact of serotonergic function on well-being. Recent studies have highlighted serotonin's role in emotional resilience, particularly through its release in the habenula during socially and affectively charged contexts. Emerging evidence also points to the anti-aging gene Sirtuin 1 as a modulator of serotonergic biosynthesis and degradation, offering a molecular pathway to emotional and cellular longevity within the serotoninomics framework. Furthermore, age-related serotonergic decline may be addressed through integrative strategies that combine pharmacological interventions with non-pharmacological approaches such as music therapy, enriched environments, rituals, emotional validation and narrative legacy. These interventions not only enhance serotonergic activity but also strengthen autonomy and emotional clarity in geriatric care. This editorial proposal positions serotoninomics as both a clinical and symbolic model for redefining well-being in geriatric and gerontological practice, calling on professionals to curate serotonin-enhancing experiences rooted in human connection, dignity and cultural richness-reimagining longevity as a journey of emotional resonance and a sensitive legacy.

Keywords: Serotoninomics; Longevity; Habenula; Transdisciplinary neuroscience; Gerontological practice

Introduction

In all living beings, birth, growth and development also entail ageing and, eventually, passing away. Human beings are no exception; however, human ageing is a multidimensional phenomenon that transcends the biological realm. In geriatrics and gerontology, it is now recognised that emotional well-being, resilience and quality of life are not solely determined by biomarkers but are shaped by symbolic, social and affective factors [1]. Within this context, over the past 25 years, our research group has studied serotonin, a neurotransmitter that is a key modulator of mood, sleep, appetite and motivation and is emerging as a bridge between physiology and lived experience [2,3]. In older adults, it is almost a natural rule that ageing is accompanied by neuroendocrine changes, notably a progressive decline in serotonin levels, which may contribute to affective disorders, sleep disturbances and increased emotional vulnerability. Yet recent research has revealed that serotonin also plays a critical role in emotional resilience, particularly within structures such as the habenula-a small brain region

within the epithalamus involved in emotion regulation, motivation and responses to aversive stimuli. Its release may be modulated by social experiences, enriched environments, daily rituals, engaging physical and emotional activities and meaningful relationships [1].

Recent findings suggest that the anti-aging gene Sirtuin 1 may influence serotonin levels by modulating the expression of enzymes such as monoamine oxidase A (MAO_A), which is involved in serotonin degradation. This regulatory role positions Sirtuin 1 as a molecular bridge between emotional resilience and cellular longevity, reinforcing the symbolic and physiological relevance of serotoninomics in geriatric contexts [4,6]. The concept of serotoninomics, coined by our group in 2015 [2], broadens the study of the serotonergic system towards an integrative vision that includes its biosynthesis, metabolism, receptors, transporters and functions across various biological systems. This perspective allows serotonin to be explored not merely as a molecule, but as a symbol of well-being, connection and resilience, approached through diverse scientific methodologies and analytical tools [2,3,7,8]. From this standpoint, we propose that serotoninomics may serve as a geriatric care model that redefines well-being, integrating non-pharmacological strategies, symbolic practices and interdisciplinary approaches to restore serotonergic function and strengthen emotional autonomy in later life.

Serotonergic Changes in Ageing

Ageing triggers a series of neuroendocrine transformations that affect emotional and physiological homeostasis. Among these, a progressive decline in serotonergic activity stands out, affecting both the central nervous system and peripheral tissues. This reduction has been linked to changes in mood, sleep, cognition, fine motor skills and immune response [1,9]. Neuroimaging studies and neuroendocrine challenges have shown that older adults exhibit decreased availability of 5-HT1A and 5-HT2A receptors in regions such as the hippocampus, prefrontal cortex and habenula. The habenula has gained particular relevance for its role in modulating emotional resilience. It has been observed that serotonergic release in this region during emotionally contagious social interactions can promote adaptive responses to stress [10].

Additionally, the biosynthesis of serotonin from tryptophan is impaired by reduced activity of the enzyme tryptophan hydroxylase (Tph2), increased oxidative stress and the presence of metabolic comorbidities [3]. These changes affect not only neurotransmission but also the regulation of peripheral systems-gastrointestinal, cardiovascular and immune-where serotonin performs essential modulatory functions [11]. In this context, Sirtuin 1 emerges as a key epigenetic regulator capable of reversing cellular senescence and modulating serotonergic biosynthesis. Its activation has been associated with improved appetite regulation, reduced apoptosis and enhanced emotional stability in ageing populations [12,13]. The balance between Sirtuin 1 activators and inhibitors may determine the success of serotoninomics-based interventions aimed at promoting longevity and emotional autonomy. Understanding these changes opens doors to novel interventions that go beyond pharmacology, embracing practices that naturally stimulate serotonergic production and release. In this vein, serotoninomics provides a conceptual framework for designing geriatric care strategies that recognise serotonin's emotional and symbolic dimension as a molecule of connection, memory and well-being.

Serotoninomics as a Model of Care

Contemporary geriatric practice faces the challenge of addressing not only the physiology of ageing but also its emotional and symbolic dimensions. Within this context, serotoninomics proposes a model of care that integrates non-pharmacological interventions capable of modulating serotonergic function in an ethical, natural and culturally meaningful way [3]. Various studies have demonstrated that activities such as music therapy, moderate physical exercise, exposure to natural light, meaningful human contact and participation in everyday rituals can increase serotonin levels and improve mood in older adults [14,15]. These practices not only are accessible but also promote autonomy, social connection and a reframing of ageing as a time of legacy and fulfilment. Emotional intelligence has also been identified as an indirect modulator of serotonin and resilience. Interventions aimed at strengthening emotional skills have shown improvements in life satisfaction and adaptive capacity in older populations [16]. From the perspective of serotoninomics, geriatric care expands beyond prescriptions to the creation of enriched environments, legacy narratives and connections that stimulate endogenous well-being. This approach calls on health professionals to become serotonin curators, enabling experiences that honour the emotion, dignity and life history of each older person.

Clinical and Symbolic Applications

Serotonin has long been studied in geriatric clinical contexts, particularly in relation to depression, anxiety and cognitive decline. Selective Serotonin Reuptake Inhibitors (SSRIs) such as escitalopram, sertraline and fluoxetine are considered first-line treatments due to their safety and tolerability profiles [17,18]. These medications have shown benefits in reducing depressive symptoms and, in some cases, slowing cognitive deterioration related to conditions such as Alzheimer's disease. However, therapeutic adherence among older adults remains a challenge. Population studies have shown that only 30% to 40% of older patients maintain adequate adherence to SSRIs, negatively impacting treatment efficacy and quality of life [19]. Building upon this molecular foundation, serotoninomics may integrate Sirtuin 1 modulation as part of its therapeutic repertoire. Nutritional, environmental and symbolic interventions that activate Sirtuin 1 could enhance serotonergic resilience and contribute to a multidimensional model of care that embraces both cellular and emotional longevity [20]. In response, serotoninomics proposes an expanded clinical framework-integrating symbolic practices, meaningful relationships and legacy-building as part of treatment-which may improve adherence and strengthen therapeutic bonds. Moreover, low circulating serotonin levels have been associated with a greater risk of functional decline, cortical atrophy and the emergence of mild behavioural symptoms in older adults without dementia. This suggests serotonin's potential value as an early biomarker of emotional and cognitive vulnerability.

Conclusion

Serotonin not only regulates mood-it also balances multiple dimensions in older individuals. In geriatric contexts, its study must go beyond pharmacology and enter the terrain of connection, memory and legacy. Recent findings suggest that the anti-aging gene Sirtuin 1 may modulate serotonergic biosynthesis and degradation, offering a molecular pathway to emotional resilience and cellular longevity. Its inclusion within the serotoninomics framework reinforces the possibility of integrative care that honours both biology and biography. Serotoninomics invites health professionals to become facilitators of serotonergic care: through human contact, everyday ritualisation, emotional validation and symbolic recognition. We therefore propose that this approach be integrated into medical and gerontological training as a tool to reframe ageing and promote meaningful longevity. For to care for serotonin in life's final stage is to care for history, dignity and the possibility of fulfilment in every phase of the human journey.

Author Contributions

FJ-T: Conceptualization, Data curation, Investigation, Supervision, Validation, Writing-original draft, Writing-review and editing. JLC-E and KJ-G: Data curation, Formal analysis, Investigation, Funding acquisition, Project administration, Resources, Writing-original draft, Writing-review & editing. GC-M: Data curation, Investigation, Validation, Writing-original draft, Writing-review & editing.

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Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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