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Celebrating the legacy of Russel J. Reiter: a pioneer in melatonin research

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In neuroscience, few contributions have been as transformative as the work of Russel J. Reiter in the field of melatonin research. As we approach the 60th anniversary of his landmark publications in *Science* and *Nature* in 1965, co-authored with Roger A. Hoffman [1, 2], it is only fitting to reflect on the profound impact that these studies have had on the understanding of circadian rhythms, sleep, and the neurobiology of aging. Reiter's work has been instrumental in establishing melatonin as a critical biomolecule, not only for its role in regulating sleep cycles but also for its broader physiological significance. This editorial celebrates the lasting influence of his research and examines how it continues to shape the trajectory of neuroscience today.

A groundbreaking discovery

In the early 1960s, the field of neurochemistry was on the cusp of major developments, but there were still many gaps in understanding how hormones influenced the brain and body's circadian rhythms. Reiter and Hoffman's 1965 publications marked a pivotal moment in neuroscience. Their research unveiled melatonin as a hormone produced by the pineal gland in response to light-dark cycles. This discovery challenged previous conceptions and laid the groundwork for subsequent studies that would connect melatonin's secretion to sleep-wake regulation and broader physiological processes [3].

At the time, the idea that the pineal gland played such an essential role in regulating sleep and biological rhythms was controversial. The notion of an endogenous molecule coordinating biological rhythms was a novel concept that was not immediately accepted. However, as the decades passed, the validity of their work was proven, and melatonin's central role in sleep, seasonal adaptation, and even aging came to be recognized as foundational to circadian biology [4]. Their contribution can now be seen as a key

chapter in the larger story of how molecular biology and neurochemistry converge to regulate behavior and physiology.

Melatonin beyond sleep: a multifaceted hormone

While much of the early research into melatonin focused on its role in sleep-wake cycles, Reiter's work expanded the scope of inquiry into other vital functions of the hormone. In the years following his initial publications, Reiter continued to explore melatonin's broader impact on human health, including its influence on immune function, neuroprotection, and even cancer prevention [5–7]. By the 1990s, he was a key figure in advocating for the hormone's role as an antioxidant [8], suggesting that melatonin could be a potent defense against oxidative stress, which has been implicated in aging and neurodegenerative diseases.

Reiter's research on melatonin also extended to its use as a therapeutic agent. His insights into the hormone's ability to regulate circadian rhythms have had direct therapeutic applications, especially in the treatment of sleep disorders, jet lag, and seasonal affective disorder [3, 9, 10]. As clinical use of melatonin as a supplement became widespread, Reiter became an advocator of the endorsement of melatonin-based therapies. His work continues to inform therapeutic strategies aimed at optimizing sleep health and managing circadian disruptions in modern society, which are becoming increasingly prevalent with the rise of artificial light and global travel.

A visionary and a mentor

Beyond his research, Reiter's commitment to advancing science extended to his role as a mentor and educator. Over his long and productive career, he nurtured the next generation of researchers, many of whom have gone on to make significant contributions to neuroscience, pharmacology, and sleep medicine. His ability to inspire and collaborate with a diverse range of scientists has left an indelible mark on the field of melatonin research and beyond. Reiter's vision for an integrated understanding of how the brain regulates behavior through hormones and neurochemicals has set the stage for interdisciplinary research that bridges molecular biology, neuroscience, endocrinology, and even fields like psychology and aging. The authors of this paper had the privilege to work with him in the context of melatonin's neuroprotective and neurorestorative actions in the context of ischemic stroke [5, 11].

Reiter's role as a thought leader in melatonin research is complemented by his commitment to public engagement. In fact, Reiter is not only a researcher but also a passionate advocate for the importance of sleep and circadian health. He still works tirelessly to communicate the significance of these processes, both to the scientific community and the public at large. This commitment has contributed to the increasing awareness of the importance of sleep in maintaining overall health, a message that resonates with growing concerns about sleep deprivation in modern society.

The legacy lives on

As we commemorate the 60th anniversary of Russel J. Reiter's pioneering research on melatonin, it is important to recognize that the field he helped shape is as vibrant and active as ever. Today, research on melatonin continues to explore new frontiers in neuroscience and medicine. Recent studies have expanded our understanding of how melatonin influences neurodegenerative diseases like Alzheimer's disease, how it interacts with signaling pathways associated with neuroprotection, and how its levels change across the lifespan [12–14]. Moreover, the rise of light-based therapies for sleep disorders and the increasing popularity of melatonin as a supplement in the wellness industry highlight the enduring relevance of Reiter's work.

Russel J. Reiter's pioneering work on melatonin has very recently extended into understanding its potential therapeutic role in COVID-19 infection due to its anti-inflammatory, antioxidant, and immune-regulating properties [15]. Reiter has long emphasized melatonin's ability to modulate the immune system and its antioxidant capacity, which may help mitigate the cytokine storm—a hyperinflammatory response

often seen in severe COVID-19 cases. Given that COVID-19 is associated with increased oxidative stress and inflammation, melatonin's capacity to scavenge free radicals and reduce inflammation could be of significant benefit [16]. Additionally, Reiter's research on melatonin's neuroprotective effects may offer insights into its potential role in mitigating long-term neurological complications in COVID-19 patients that include fatigue, concentration, and memory disturbances. A very central role of this action is attributed to the melatonin's ability to stabilize mitochondrial function and slow wave sleep, which controls β-amyloid removal from the aged brain, as the review by Doris Loh and Russel J. Reiter in *Exploration of Neuroscience* emphasizes [17].

Russel J. Reiter's contributions to neuroscience extend far beyond the discovery of melatonin. His work opened the door to new research on circadian rhythms and their role in regulating not only sleep but also mood, metabolism, and aging. As the scientific community celebrates the 60th anniversary of these groundbreaking papers, it is time to acknowledge the profound impact that Reiter's research has had on our understanding of neuroscience. His legacy not only answered some of the most intriguing questions of his time but also inspired future generations to continue seeking answers. In a world in which the rhythm of life is increasingly disrupted, the significance of his work remains as pertinent today as it was six decades ago.

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Author contributions

DMH: Writing—original draft, Writing—review & editing. EK: Writing—review & editing.

Conflicts of interest

Ertugrul Kilic who is the Associate Editor and the Guest Editor of *Exploration of Neuroscience* had no involvement in the decision-making or the review process of this manuscript. Dirk M. Hermann is the Editor-in-Chief and the Guest Editor of *Exploration of Neuroscience*.

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