

Editorial

The Circadian Rhythms: Frailty in the Elderly Revisited

Garbarino S¹, Lanteri P², Guglielmi O¹ and Sannita WG^{1*}¹Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal/Child Sciences (DINO GMI), University of Genova, Italy²Department of Medical and Surgery Neuroscience, Neurology Center, Rehabilitation – Continuity of Care, Institute G. Gaslini, Italy***Corresponding author:** Walter G Sannita, Department of Neuroscience, Ophthalmology, Genetics, Mother and Child Health, University of Genova, Genova, Italy**Received:** April 30, 2019; **Accepted:** June 19, 2019;**Published:** June 26, 2019

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Frailty is a concept label for a subgroup of elderly subjects (~7-12% in Western countries) with a severe combination of impaired motility and cognition, multimorbidity, sarcopenia and reduced autonomy that results usually in impoverished quality of life and greater marginalization, very often in adverse health outcome. It is conceived as a consequence of reduced homeostatic reserves and cumulative decline in several (brain, endocrine, immune, metabolic, muscle) physiological systems during a lifetime [1]. The possible contributions of (aging-related) functional changes in the circadian system deserve some attention but have been overlooked thus far.

The circadian rhythm is essential to the homeostatic mechanisms and functional balance that guarantee survival, adaptation and efficient action and determines the sleep structure. It also sets time windows, particularly in the alternation of sleep and wakefulness [2-4]. Disordered circadian rhythms are typically associated with insomnia or daytime sleepiness, impaired adaptation or efficiency during the day, and impoverished quality of life. There is full evidence that misalignment with the physiological circadian rhythms due to sleep disorders or inadequate sleeping increases health risks and often starts pathophysiological processes ending up in metabolic, cardiovascular and/or psychiatric disorders and multimorbidity; working at night or in shifts is in this respect a reference model [5,7]. The alignment between sleep timing and the circadian phase is also progressively lost with aging; the circadian phase advances and sleep, the body core temperature, motor activity, and melatonin phase advance as well;

the circadian rhythm amplitude is reduced and its period shortened. There is a general consensus based on animal studies that the activity of suprachiasmatic nuclei governing the circadian system is reduced with aging and the clock gene expression is altered [8].

The time disarrangement over the 24 hrs. between circadian rhythms (particularly the sleep-wakefulness cycle) and the daily activities can impair physiological adaptation, often to unfitting levels [5-7]. Paradigmatic in this regard are shift-working and the peak incidence of severe adverse cardiovascular events (such as myocardial infarction, sudden cardiac death, stroke) in the morning hours, when subjects re-assume their daily activities. Pathophysiological causes are, among others, the circadian increase in platelet aggregation, arterial blood pressure, vasoconstriction, and plasma cortisol (in turn increasing the coronary sensitivity to catecholamines), and the reduction in fibrinolysis and heart rate [9].

Humans are usually protected by sleep in these and other time windows of physiologically reduced physical efficiency [10]. The protection is nevertheless weakened when subjects are active in circadian phases otherwise best suited for sleep; this vulnerability is compensated for during adulthood and with adequate availability of physical reserves, but may become crucial in the elderly, when it often adds to the effects of sleep disorders common among the aged. The impact of changes in the circadian rhythms (either due to sleep/wakefulness misalignment or aging) should be taken into proper consideration when defining the frailty phenotype and when planning work in shifts [7]. Counterbalancing behaviors should be identified and reinforced to prevent adverse effects; systematic research is warranted.

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