BRIEF COMMUNICATION

Chronotype, Myokines, and Muscle Mass: A New Dimension in Metabolic Disorders

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Chronotype refers to an individual's innate preference for the timing of sleep-wake cycles and daily activities, which is governed by their circadian rhythm. People show distinct variations in their chronotype, primarily categorized by their inclination towards either morningness or eveningness, which affects sleep onset, wake time, and the timing of cognitive and physical activities (Table 1). Based on these preferences, individuals can be classified as morning types, evening types, or intermediate types. Notably, this preference for morning or evening activity is a relatively stable characteristic influenced by intrinsic factors.

At the population level, an evening chronotype is independently linked to an increased risk of metabolic syndrome and diabetes. Evening chronotype has been associated with metabolic irregularities and changes in body composition in middle-aged adults, even when controlling for factors like sleep duration and lifestyle. People with an evening chronotype tend to have higher fat mass and lower lean mass compared to those with a morning chronotype. These effects on body fat and lean mass are found to be independent of obesity. Studies show that individuals with an evening chronotype have a significantly higher mean percentage of body fat, while those with a morning chronotype tend to have a higher percentage of lean mass[1].

Several factors may be responsible for this association between chronotype and body composition. Melatonin, a pineal hormone entrained in the 24-hour environmental light-dark cycle, is a reliable circadian system marker and its levels peak at night. Melatonin is suppressed by light; thus, individuals with evening chronotype who have greater exposure to light at night, are likely to have lower melatonin levels. Low melatonin levels have been shown to contribute to muscle loss, primarily by affecting oxidative stress and muscle regeneration processes, leading to an increased risk of muscle degradation and atrophy, leading to a lower muscle mass[2,3]. Patients with evening chronotype are more likely to take afternoon naps. Habitual daytime napping is associated with adverse health outcomes such as metabolic disorders and sarcopenia[4].

Individuals with an evening chronotype tend to exhibit a higher body mass index (BMI) and increased plasma C-reactive protein (CRP) levels. They also demonstrate a stronger cortisol response when subjected to stress. Glucocorticoids play a role in regulating lipid metabolism in both adipose tissue and the liver, while also promoting hepatic gluconeogenesis and peripheral insulin resistance. Prolonged activation of the hypothalamic-pituitary-adrenal axis and an elevated cortisol secretion can lead to the accumulation of visceral fat and an increase in body weight. The combination of higher CRP levels and an intensified cortisol response may contribute to the elevated risk of metabolic disorders in individuals with an evening chronotype.

Testosterone levels, are expected to be highest in the morning but they may peak later in the day for individuals with evening chronotype. Testosterone has a role in maintaining muscle mass by promoting muscle protein synthesis. This delayed testosterone peak in evening chronotypes can affect the timing of muscle repair and growth, potentially leading to reduced anabolic effects on skeletal muscle, lower muscle mass, and reduced skeletal strength[5].

Shift work, particularly among individuals with an evening chronotype are at higher risk of adverse changes in body composition and metabolic health. Shift workers with evening chronotypes exhibit a higher propensity for increased adiposity and unfavorable body composition, including elevated fat mass and reduced lean muscle mass[6]. This might be mediated by poor sleep quality, irregular eating patterns, and elevated cortisol levels, which further exacerbate metabolic disturbances. It has been observed that evening chronotypes tend to engage

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Table 1. Chronotype, Body Composition and Risk of Metabolic Disorders

Characteristic	Morning chronotype	Intermediate chronotype	Evening chronotype
Sleep-Wake pattern	Wake up early in the morning and go to sleep early at night Higher energy levels in the morning	Follow a moderate schedule	Wake up late in morning and go to sleep late at night Higher energy levels in the evening
Body composition	Lower fat mass, higher lean mass	Balanced body composition	Higher fat mass, lower lean mass
Risk of metabolic disorders	Lower risk	Moderate risk	Higher risk
Metabolic signature	Lower TG, higher HDL-C, lower HOMA-IR	Intermediate TG, intermediate HDL-C, intermediate HOMA-IR	Higher TG, lower HDL-C, higher HOMA-IR
Hormonal signature	Normal cortisol response to stress, normal testosterone peak, higher melatonin	Strong cortisol response to stress, normal testosterone peak, intermediate melatonin	Stronger cortisol response to stress, delayed testosterone morning peak, lower melatonin

TG = Triglycerides; HDL-C = High-density lipoprotein cholesterol; HOMA-IR = Homeostasis model assessment of insulin resistance.

in behaviors such as higher alcohol consumption and erratic meal timing, contributing to unhealthy body composition[7].

Skeletal muscle secretes signaling molecules known as myokines, which interact with other organs and play a crucial role in regulating muscle mass and function. Myokines mediate the positive effects of muscle mass and physical activity on overall health[8]. For instance, myostatin, a specific myokine, is secreted in greater amounts from the muscles of obese individuals. Myostatin mRNA levels are lower in those without sarcopenia than in those with the condition. Increased myostatin expression in both muscle tissue and plasma correlates with greater insulin resistance and is linked to higher levels of intramuscular fat in the mid-thigh region. Elevated myostatin in muscle acts as a negative regulator of muscle growth, resulting in decreased lean body mass[9,10]. Conversely, irisin, another myokine, is released by contracting skeletal muscles and is associated with beneficial effects. Low circulating irisin levels are a marker of muscle weakness and atrophy, while higher levels promote muscle growth and the browning of white adipose tissue, leading to better body composition with reduced fat and increased muscle mass. Levels of myokines have shown association with insulin resistance and risk of metabolic disorders such as type 2 diabetes and metabolic syndrome[11,12].

While the greater lean mass in morning chronotype, has been attributed to higher levels of physical activity, it is possible that myokines may mediate the muscle accumulation in individuals. The skeletal muscles have their own intrinsic clock and this clock may have an impact on secretion of myokines.

Unravelling these aspects of chronotype, skeletal muscle clocks, and myokines may open up newer diagnostic and therapeutic modalities for metabolic disorders. In future, the diagnosis of sarcopenia may be objectively confirmed from myokine profiles. Resetting of muscle clock or exogenous administration of myokines may be potential therapeutic options for increasing lean mass and reducing fat mass. In face of the onslaught of metabolic disorders, myokines and chronotype may prove to invaluable management options in the near future.

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