Diurnal Modulation of Persistent Inward Currents in Human Spinal Motor Neurons

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Résumé

Alpha motor neurons constitute the final common pathway for movement control (Sherrington, 1906). They integrate ionotropic excitatory and inhibitory inputs *via* non-linear processes shaped by intrinsic membrane properties, notably persistent inward currents (PICs) (Heckmann et al., 2005). These voltage-dependent depolarizing currents amplify synaptic inputs (PICs amplification) and sustain motor neuron firing even when net inputs decline (PICs prolongation) (Binder et al., 2020). PICs activation is modulated by serotoninergic-noradrenergic projections from the brainstem. While circadian fluctuations in these neuromodulators have been reported in brain tissue (e.g., Matheson et al., 2015), whether similar variations occur at the spinal level, affecting PICs activation, remains unclear. Importantly, inhibitory inputs can significantly reduce/suppress PICs activation. Using H-reflex assessments, human studies have suggested that spinal inhibition is reduced in the evening compared to the morning (Lagerquist et al., 2006). These time-of-day differences in inhibitory mechanisms may contribute to diurnal variations in PICs activation. Despite evidence of diurnal fluctuations in spinal inhibitory inputs and brainstem neuromodulators, the potential impact of time-of-day on PICs activation - a key determinant of motor output - remains unexplored.

The present study aimed to determine whether the effects of PICs amplification and prolongation on motor unit behavior differs between the early morning and late afternoon, time points typically corresponding to the bathyphase and acrophase of neuromuscular performance, respectively. We hypothesized that PICs activation would be greater in the late afternoon, reflecting reduced inhibitory drive and/or increased neuromodulatory input, without expecting direct associations with maximal strength.

Seventeen healthy participants (4; 27.5±5.6 years) completed two (randomized) sessions on separate days: early morning (7:00–8:30 a.m.) and late afternoon (5:00–6:30 p.m.). Participants performed isometric dorsiflexion tasks with triangular force profiles. Tasks were performed (1) at 40% of the session's maximal voluntary force (*relative condition*), and (2) 40% of the initial visit's maximal voluntary force (*absolute condition*). Using decomposition of electromyographic signals, we identified the discharge patterns of a large sample of motor units. We used complementary approaches to distinguish the respective contribution

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of neuromodulatory-inhibitory inputs to PICs activation. PICs prolongation was estimated through paired motor unit analysis (ΔF metric), and the contribution of neuromodulatory-inhibitory inputs on PICs activation were assessed via complementary geometric analysis (Beauchamp et al., 2023).

We observed significantly greater PICs prolongation (ΔF) and synaptic input amplification (acceleration phase of motor unit discharge) in the late afternoon compared to the early morning, regardless of contraction intensity (relative or absolute). These changes were not correlated with maximal force, which increased significantly in the late afternoon. Complementary metrics revealed no significant time-of-day differences in brace height, a proxy for neuromodulatory input. In contrast, attenuation - indicative of patterns of local inhibition - was significantly lower in the late afternoon under the relative force condition.

These findings suggest that alpha motor neurons exhibit diurnal fluctuations in intrinsic excitability, marked by increased PICs activation in the evening. Notably, these variations appear primarily driven by reduced inhibitory inputs to spinal motor neurons (rather than neuromodulatory drive), enhancing their responsiveness to excitatory inputs in the late afternoon relative to the early morning.

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