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*Circadian Multiscale Activity Regulation and the Risk for Delirium in Elderly Hospitalized Patients*

**Abstract**

Developing effective interventions for delirium in the elderly urgently requires a better understanding of modifiable risk factors and underlying mechanisms in earlier life. There is evidence that alterations in the ~24-hour sleep/wake cycle, known as circadian rhythms, coincide with the development of delirium. Disturbances in circadian rhythm and sleep are more common in the elderly, in neurodegenerative diseases such as Alzheimer's dementia, and become more pronounced after critical illness. Inflammatory changes have been shown after circadian/sleep disruption, while conditions associated with delirium often involve high inflammatory states. This project hypothesizes that earlier life circadian/sleep regulation predicts incident delirium after hospitalization, and that systemic inflammatory burden underlies this link. We propose the analysis of rest/activity data collected from wearable technology (actigraphy watches), repeated serum high-sensitivity (hs-CRP) and insulin-like growth factor-1 (IGF-1) measurements and genetic data in middle/elderly age subjects from ~100,000 subjects aged between 40-69 years who were recruited between 2006 and 2010, and agreed to have their health followed. Taken together, the proposed aims may provide modifiable, objective measures of delirium risk, expand on our knowledge of delirium pathophysiology, and lead to novel genetic insights into how circadian/sleep regulation and inflammation influence future delirium vulnerability.