Circadian/Sleep Disturbance and Systemic Inflammation in the Development of Delirium

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Delirium continues to be a leading cause of preventable morbidity and mortality after critical illness or surgery in hospitalized elderly patients. A fundamental aspect of many physiological functions including sleep is the adherence to ~24 hour cycles, known as circadian rhythms. There is emerging evidence for the potential role of circadian/sleep disturbances in the risk for delirium. For instance, disturbances in circadian rhythm and sleep are significantly more common in advanced age, becoming more pronounced after critical illness, and in neurodegenerative diseases such as Alzheimer’s disease. A potential mechanism linking delirium and circadian/sleep dysfunction is the neuroinflammatory changes after circadian/sleep disturbance as observed in both animal and human models. In this project, we will test the hypothesis that earlier-life circadian/sleep disturbance plays a critical role prior to the development of delirium, and that it does so by inducing a chronically high inflammatory state, particularly in those with genetic predisposition to delirium in the setting of known variants for circadian/sleep disturbances and inflammation.