

Lung injury

Lung injury is a result of a blast wave passing through lung tissue, causing tissue disruption at the capillary-alveolar interface.

Mechanical ventilation is a well-known precipitant of acute lung injury and is strongly associated with the development of acute delirium and anxiety phenotypes. In prior studies, we demonstrated that IL-6 mediates neuropathological changes in the frontal cortex and hippocampus of animals with mechanical ventilation-induced brain injury; however, the effect of systemic IL-6 inhibition on structural and functional acute neuropsychiatric phenotypes is not known. We hypothesized that a murine model of mechanical ventilation-induced acute lung injury (VILI) would induce neural injury to the amygdala and hippocampus, brain regions that are implicated in diverse neuropsychiatric conditions, and corresponding delirium- and anxiety-like functional impairments. Furthermore, we hypothesized that these structural and functional changes would reverse with systemic IL-6 inhibition. VILI was induced using high tidal volume (35 cc/kg) mechanical ventilation. Cleaved caspase-3 (CC3) expression was quantified as a neural injury marker and found to be significantly increased in the VILI group compared to spontaneously breathing or anesthetized and mechanically ventilated mice with 10 cc/kg tidal volume. VILI mice treated with systemic IL-6 inhibition had significantly reduced amygdalar and hippocampal CC3 expression compared to saline-treated animals and demonstrated amelioration in acute neuropsychiatric behaviors in open field, elevated plus maze, and Y-maze tests. Overall, these data provide evidence of a pathogenic role of systemic IL-6 in mediating structural and functional acute neuropsychiatric symptoms in VILI and provide preclinical justification to assess IL-6 inhibition as a potential intervention to ameliorate acute neuropsychiatric phenotypes following VILI ¹⁾

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Anwar F, Sparrow NA, Rashid MH, Guidry G, Gezalian MM, Ley EJ, Koronyo-Hamaoui M, Danovitch I, Ely EW, Karumanchi SA, Lahiri S. Systemic interleukin-6 inhibition ameliorates acute neuropsychiatric phenotypes in a murine model of acute lung injury. Crit Care. 2022 Sep 13;26(1):274. doi: 10.1186/s13054-022-04159-x. PMID: 36100846.

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