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Introduction:
A long-term cognitive impairment that resembles Alzheimer’s disease (AD) is a known complication of acute critical illnesses that affects up to 2 million individuals annually in the US. Mechanical ventilation (MV) is a hallmark critical care intervention that is strongly associated with cognitive decline.

Methods:
We subjected double transgenic Alzheimer’s disease (Adtg) (APP/PSEN1) and wild-type (WT) mice to MV for 4 hours and compared to spontaneously breathing (SB) controls. Cerebral soluble/insoluble amyloid-β (Aβ) and neurological and systemic markers of inflammation were quantified. Hippocampal blood-brain barrier permeability was quantified using a novel methodology that enabled assessment of small and large molecule permeability across the blood-brain barrier. Immunohistochemistry was used to assess the regional relationship between amyloid-β1–40 and acute vascular disruption and neuronal injury.

Results:
See image

Conclusion:
Short-term MV resulted in increased cerebral soluble Aβ1-40 and increased cerebral TNF-α and IL-6 concentrations. BBB permeability and neuronal injury were decreased in mechanically ventilated ADtg mice, whereas BBB permeability and neuronal injury were increased in mechanically ventilated WT mice compared to their respective SB controls. There was increased distribution of Aβ1-40 in regions of acute vascular disruption, resulting in lower BBB permeability. Overall, these results support a possible physiological role for Aβ1-40 to decrease BBB permeability and neuronal injury during the acute stress of MV, however it is expected that long-term sustained of this putative protective pathway will contribute to neurodegeneration and cognitive impairment.