**////Title: Does Mechanical Ventilation Cause Further Brain Trauma?**

**////Stand-first**:

Mechanical ventilation is a medical treatment that artificially enables the body to breathe. Despite being a potentially life-saving intervention, there are concerns it can cause damage to vital organs, such as the brain and lungs. Dr Thiago Bassi from Simon Fraser University in Canada, has undertaken a review of published studies in this field. His findings indicate a potential link between ventilator usage and cognitive impairment whilst highlighting the need for further research.

**////Body text:**

When our bodies struggle to move air in and out of the lungs, medical professionals turn to mechanical ventilation to maintain the vital function of delivering oxygen and removing carbon dioxide. Mechanical ventilation is typically undertaken in medical intensive care units, using a piece of equipment called a ventilator, which assists with or facilitates the act of breathing. This treatment has featured heavily in the world’s media during the COVID-19 pandemic, and we have seen unprecedented volumes of patients requiring the use of mechanical ventilation.

Ventilators are a modern advancement on what was colloquially known as the iron lung, originally used in the 1900s during the polio epidemic. These early machines enabled the first widespread use of negative pressure ventilation, where sub-atmospheric pressure is placed on the body to draw air into the lungs. There is an alternative method that relies on positive pressure, air is pushed into the lungs through a face mask or more invasively via a tube in the trachea.

Despite mechanical ventilation being a potentially life-saving intervention, there are concerns that it can cause further damage to the diaphragm, lungs and brain. In neonatal care, a wealth of research has demonstrated that ventilator-induced brain damage is a significant concern, whereas amongst adult populations this is yet to be evidenced.

Dr Thiago Bassi from Simon Fraser University in Canada, and his research partners Dr Elizabeth Rohrs and Dr Steven Reynolds, have undertaken a systematic review of published research studies on ventilator-induced brain injury. They were particularly focused on investigating the link between medical ventilation and the development of delirium, cognitive impairment (such as memory and attention deficits) and neuro-inflammation that was not caused by a pre-existing condition.

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Looking at the published preclinical studies, Dr Bassi found evidence to suggest that mechanical ventilation is a contributing factor to brain trauma. Preclinical studies often use animal subjects to medically model the impact of adverse effects before any testing is undertaken on humans. These studies concluded that this further brain damage was caused either by inflammation or altered nerve signals in the brain.

One study demonstrated that subjects who had been mechanically ventilated for longer than 6 hours had signs of greater inflammation, compared to those who received a similar treatment but only for one hour. As many of the patients who receive ventilation treatment are critically ill, it can be difficult to determine whether the original injury or illness is also a contributing factor to further brain injury.

One study reviewed by Dr Bassi tried to counteract this issue by administering mechanical ventilation to pigs and comparing the results between subjects who had a lung injury and those who did not. The findings suggested that as both groups showed signs of inflammation, despite one having no previous injury, mechanical ventilation must be a contributing factor.

Studies also showed evidence of mechanical ventilation leading to an alteration in neural signals, particularly in the vagus nerve, which helps to regulate the function of our internal organs. Changes to the signals within this nerve can lead to inflammation and ultimately the death of cells within the brain.

Dr Bassi encountered a study in which the vagus nerve was inactivated before mechanical ventilation took place, to demonstrate how without disturbed signals, subjects were much less likely to experience any further damage to their brains. These findings strengthen the theory that the vagus nerve is responsible for triggering brain injury during ventilation.

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Dr Bassi also noted that there appears to be a relationship between the volume of airflow during mechanical ventilation and the level of damage. More specifically, some studies have shown a connection between activity in the brain and the amount of air that was breathed in and out.

One such study used magnetic resonance imaging to analyse activity in a part of the brain called the hippocampus whilst ventilation was taking place. This area of the brain plays a major role in learning and memory. The imaging revealed that a higher rate of air volume during ventilation led to greater activity in the hippocampus. This greater rate of activity was directly associated with an increase in brain injury during mechanical ventilation. A similar pattern was demonstrated across other important brain regions.

There is also some evidence to suggest that the duration of mechanical ventilation may impact the severity of the injury and further research is needed to examine the effect of ventilation power and pressure.

The clinical studies reviewed by Dr Bassi provide strong evidence that mechanical ventilation can lead to cognitive impairment. Research using experimental mice demonstrated that after 6 hours of mechanical ventilation, cognitive functioning scores were much lower in mice that did not receive ventilation or only for a short duration.

A few clinical studies have also shown that patients who exhibit delirium related to mechanical ventilation are more likely to experience longer-term cognitive impairment. Delirium is a form of psychological disturbance, and includes confusion and reduced awareness of surroundings. Those who did not experience these symptoms following treatment were much less likely to have lasting cognitive effects. However, Dr Bassi has highlighted that these studies are not able to demonstrate a causal link between mechanical ventilation and delirium, meaning there may be other factors involved.

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Despite the wealth of evidence linking mechanical ventilation with adverse effects, it is very difficult to isolate this from other factors experienced by those undergoing this treatment. Most patients are sedated at the time of treatment which renders them physically immobile. They are also likely to be receiving a high volume of medication which could negatively impact cognitive functioning.

Dr Bassi notes that due to the widespread medical usage of mechanical ventilation, clinical testing in human patients is difficult to undertake. He concludes that more preclinical testing is required to further investigate this area of concern, emphasising that scientists must try to control as many potentially confounding factors as possible.

This SciPod is a summary of the paper ‘Systematic review of cognitive impairment and brain insult after mechanical ventilation’ published in Critical Care. DOI: https://doi.org/10.1186/s13054-021-03521-9

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