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Automated system promises precise control of medically induced coma

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Putting patients with severe head injuries or persistent seizures into a medically induced coma currently requires that a nurse or other health professional constantly monitor the patient's brain activity and manually adjust drug infusion to maintain a deep state of anesthesia. Now a computer-controlled system developed by Massachusetts General Hospital (MGH) investigators promises to automate the process, making it more precise and efficient and opening the door to more advanced control of anesthesia. The team, including colleagues from Massachusetts Institute of Technology (MIT), reports successfully testing their approach in animals in the open access journal *PLOS Computational Biology*.

"People have been interested for years in finding a way to control anesthesia automatically," says Emery Brown, MD, PhD, of the MGH Department of Anesthesia, Critical Care and Pain Medicine, senior author of the report. "To use an analogy that compares giving anesthesia to flying a plane, the way it's been done is like flying a direct course for hours or even days without using an autopilot. This is really something that we should have a computer doing."

As part of a long-term project investigating the physiological basis of general anesthesia, Brown's team at MGH and MIT has identified and studied patterns of brain activity reflecting various states of anesthesia. One of the deepest states called burst suppression is characterized by an electroencephalogram (EEG) pattern in which brief periods of brain activity – the bursts – are interrupted by stretches of greatly reduced

activity that can last for seconds or longer. When patients with serious head injuries that cause a buildup of pressure within the skull or those with persistent seizures are put into a medically induced coma to protect against additional damage, the goal is to maintain brain activity in a state of burst suppression.

Although anesthesiologists have had computer-assisted technologies for many years, no FDA-approved system exists that completely controls anesthesia administration based on continuous monitoring of a patient's brain activity. Until the current study, Brown notes, no one had demonstrated the level of control required for a completely automated system. Keeping patients at a precise level of brain activity for several days, as required for medically induced coma, appeared to be both a feasible goal and one that cried out for the sort of computer-controlled system called a brain-machine interface.

Adapting programs they had previously developed to analyze the activity of neurons, Brown's team developed algorithms to read and analyze an EEG pattern in real time and determine a target level of brain activity – in this case the stage of burst suppression. Based on that target, an automated control device adjusts the flow of an anesthetic drug to achieve the desired brain state, and real-time analysis of the continuous EEG readings is fed back to the system to insure maintenance of the target. When the researchers tested their system in a rodent model, the actual EEG-based measure of burst suppression tracked the target trajectory almost exactly.

"As far as we know, these are the best results for automated control of anesthesia that have ever been published," says Brown, who is the Warren M. Zapol Professor of Anesthesia at Harvard Medical School and the Edward Hood Taplin Professor of Medical Engineering and Computational Neuroscience at MIT. "We're now in discussions with the FDA for approval to start testing this in patients." The MGH has also

applied for a patent for the technology.

Among the benefits of such a system, Brown explains, would be the ability to maintain medical coma at a more precise, consistent level than can be done manually and using lower doses of anesthetic drugs, a reduction that is possible with any computer-assisted technology. Eliminating the need to devote one intensive-care nurse on each shift to continuous monitoring of one patient would significantly change ICU staffing needs. Further development of the system to control and maintain the full range of anesthesia states should introduce a powerful new tool to the entire field.

Provided by Massachusetts General Hospital

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