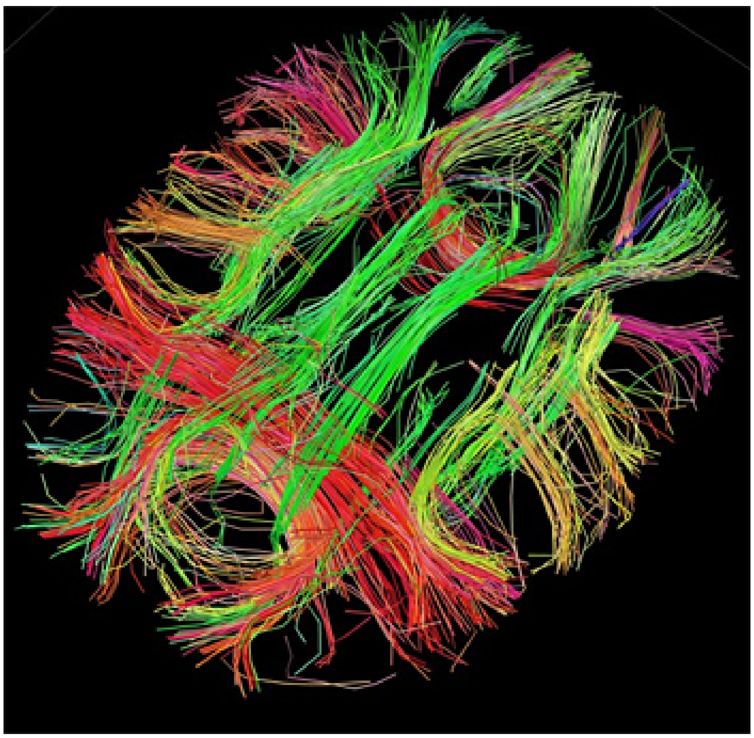
Studies reveal how anesthesia's brain effects differ in older adults and in children

August 14 2015



White matter fiber architecture of the brain. Credit: Human Connectome Project.

Recent Massachusetts General Hospital (MGH) investigations into the neurobiology underlying the effects of general anesthesia have begun to reveal the ways different anesthetic agents alter specific aspects of the brain's electrical signals, reflected by EEG (electroencephalogram) signatures. While those studies have provided information that may lead to improved techniques for monitoring the consciousness of patients receiving general anesthesia, until now they have been conducted in relatively young adult patients. Now a series of papers from MGH researchers is detailing the differences in the way common anesthetics affect the brains of older patients and children, findings that could lead to ways of improving monitoring technology and the safety of general anesthesia for such patients.

"Anesthesiologists know well that the management of patients age 60 or older requires different approaches than for younger patients," says Emery Brown, MD, PhD, of the MGH Department of Anesthesia, Critical Care and Pain Medicine. "The doses required to achieve the same anesthetic state in older patients can be as little as half what is needed for younger patients. Explanations for that difference have focused on age-related declines in cardiovascular, respiratory, liver and kidney function, but the primary sites of anesthetic effects are the brain and central nervous system."

Patrick Purdon, PhD, also of the MGH Department of Anesthesia, Critical Care and Pain Medicine, adds, "We know even less about how anesthetic drugs influence brain activity in children, and the current standard of care for assessing the brain state of children under anesthesia calls only for monitoring vital signs like heart rate and blood pressure. This lack of knowledge is especially troubling, given recent studies suggesting an association between early childhood surgery requiring general anesthesia and later cognitive problems."

Brown and Purdon lead an MGH research team investigating the neural mechanisms of general anesthesia that in recent years has identified EEG signatures indicating when patients lose and regain consciousness and the EEG patterns - called oscillations - produced by specific drugs while patients are unconscious. In young adults, anesthesia-induced unconsciousness is associated with medium frequency (around 10 Hz)

EEG oscillations called frontal alpha waves that are highly synchronized between the cerebral cortex and thalamus, a pattern that is believed to block communication between those brain structures.

Two papers from the MGH team recently published in the *British Journal of Anaesthesia* are the first to take a detailed look at anesthesia-induced brain changes in older patients. Purdon and Brown are co-corresponding authors of one study that analyzed detailed EEG recordings of 155 patients aged 18 to 90 receiving either propofol or sevoflurane. That study found that the EEG oscillations of older patients were two to three times smaller than those of younger adults with reduced occurrence of frontal alpha waves. The synchronization between the cortex and thalamus occurred at slightly lower frequencies in older patients, who were more likely than younger patients to experience a state called burst suppression that reflects profoundly deep anesthesia at lower doses. The other BJA study, led by MGH anesthesiologist Ken Solt, MD, found that older animals took two to five times longer than younger animals to recover from equal anesthetic doses and observed similar age-related differences in EEG patterns as seen in the patients.

Another study appearing in the same issue of BJA - co-corresponding authors Purdon and Oluwaseun Akeju, MD, MGH Anesthesia, Critical Care and Pain Medicine - analyzed EEG patterns of 54 patients ranging from infancy through age 28 during anesthesia with sevoflurane. They found that anesthesia-induced EEG signals tripled in power from infancy until around age 6 and then dropped off to the typical young adult level at around age 20. Frontal alpha waves were not observed in children under the age of 1, suggesting that the brain circuits required for cortical/thalamic synchronization had not yet developed. Purdon and Brown were also co-authors of an eLife study led by Boston Children's Hospital investigators Laura Cornelissen, PhD, and Charles Berde, MD, PhD, that detailed the EEG activity of infants 6 months and younger, showing how their patterns evolved toward those more typical of adults over just a few months.

"It appears as though the structure of anesthesia-induced brain dynamics mirrors brain development in children, with different brain wave patterns 'turning on' at ages that coincide with known developmental milestones," says Purdon. "In older patients we see a similar effect but in reverse, with certain brain waves decaying in a manner consistent with brain aging. It's been known that commercially available EEG-based anesthesia monitors were developed for young adults, and while they are limited for that population - reducing brain activity to a single number - they are even more inaccurate for children and the elderly. These studies illustrate why this is the case and suggest a new, age-specific monitoring paradigm that - along with monitors that track a broader range of EEG signals - could help avoid both anesthesia-induced neurotoxicity in children and post-operative delirium and cognitive dysfunction in elderly patients."

Brown adds, "Understanding how the brain's responses to anesthesia change with age allows us to provide personalized, patient-specific strategies for monitoring the brain and dosing the anesthetics, thereby moving us closer to side-effect free anesthesia care."

Provided by Massachusetts General Hospital