Study suggests remembering surgery might be real in rare cases

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In pre-clinical studies, researchers at Sunnybrook have uncovered a receptor that may underlie resistance to the memory-suppressing component of the anesthetic state in some rare cases.

Traditionally, general anesthesia was thought to depress brain function in a non-specific way but this research is at the forefront of a complete change in our understanding as to how anesthetics work. Modern research shows that anesthetics interact with multiple varieties of specific proteins known as receptors. A receptor is a molecule on the surface of a cell that serves as a recognition or binding site for a drug, neurotransmitter or other cellular or immunological components. The receptors and brain regions are individually affected and have different outcomes. With this new knowledge, researchers can look at new ways of using anesthetic compounds, designing them to target specific proteins in order to selectively produce the desirable effects in various parts of the central nervous system.

"We have found in a pre-clinical mouse model that a receptor exists that may mediate some of the memory-suppressing components of anesthesia," says Dr. Beverley Orser, principal investigator of the study and anesthesiologist at Sunnybrook Health Sciences Centre. "We studied a mouse that lacked this receptor and were able to show resistance to amnesia with no change in sedation or the immobilizing properties of the drug. Thus we could dissect the individual components of the anesthetic state. Our next step is to explore altered expression of this protein in humans." An implication of the study is that altered function or expression of the protein in humans possibly altered sensitivity during anesthesia.

Patients often worry about awareness or recall of surgical events during anesthesia (also known as intra-operative awareness); and while such events are rare and brief, they do require more research. "We and others have found that individual components of anesthesia - sedation, hypnosis, analgesia, and immobility - affect nerve cells differently to block their transmissions and provide powerful neuro-depressive effects," says Dr. Orser, who is also a professor of anesthesiology and physiology at the University of Toronto. "By finding correct target receptors for the amnesia-inducing effects of anesthesia, we were able to identify a population of mice that showed a genetic resistance to memory impairment during anesthesia, and it may become possible to identify patients at risk for intra-operative awareness in the future, because they lack those receptors."

Researchers are now trying to identify which cell receptors are the targets of current drugs, to understand how they interact together to change the cell's function to produce both desired and unwanted 'symptoms' of anesthesia, so they can optimize their use, limit side effects, and further efforts towards the development of new anesthetics. "It is important for us to look at each component of anesthesia separately and to begin teasing them apart, so we can optimize the effects we want while limiting those we do not," says Dr. Orser.

While general anesthetics provide the desired effects of suppressing consciousness and memory and relieving pain associated with surgery, they also involve unwanted effects, such as the repression of cardiorespiratory function, which must be carefully monitored throughout an operation.

There are two categories of anesthesia: the kind delivered by inhalation, and that which is delivered intravenously through a needle. Anesthesia is a behavioural state involving a lack of feeling that serves to offset surgical insult and painful stimuli. General anesthetics have the power to suppress neuronal activity throughout the central nervous system, which encompasses the brain and spinal cord and controls heart rate and breathing. The following stages of anesthesia occur concurrently but are separate entities:

- Sedation: reduced arousability, longer response times, decreased movement, brain activity drops;
- Unconsciousness: hypnosis, impaired perception of/response to stimuli, deeper brain depression;
- Immobility: temporary paralysis in response to stimuli, suppression of neuronal activity;
- Analgesia: absence of pain, muscle relaxation, attributed to depression of spinal cord activity; and
- Amnesia: absence of memory/recall for the anesthetized period, many brain structures involved.

"Anesthesiologists in Canada are highly skilled and generally techniques are very safe, but there is always interest in improving," says Dr. Orser. "Based on our new knowledge, we want to learn how to use currently available drugs in a better way and be able to tailor anesthesia to each individual patient." In addition, anesthetics can be used as probes or tools to investigate related areas such as memory, consciousness and perception of pain, including drugs such as sedatives, sleep aids and memory drugs.

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