Strategy might prevent infections in patients with spinal cord injuries

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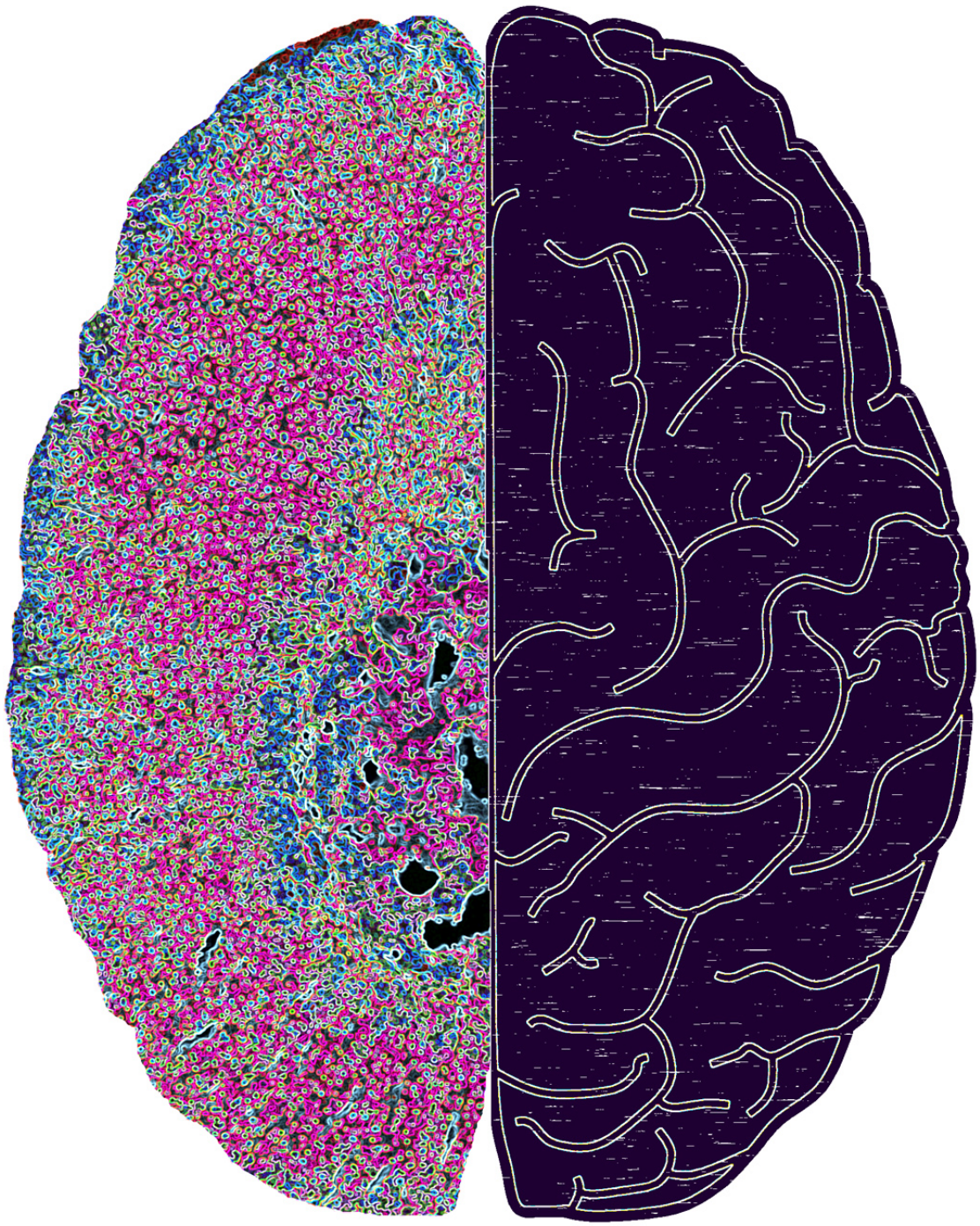

Stylized representation of a newly-discovered signaling pathway active after spinal cord injury, which sees the injured central nervous system use adrenal

hormone production to potentially disrupt the immune system in a way that lead to severe infections. (Courtesy H Prüss, A Thiriot). Credit: The Ohio State University Wexner Medical Center

New research led by The Ohio State University Wexner Medical Center found a potential therapeutic strategy to prevent infections in patients with spinal cord injuries.

This research using mice with spinal cord injuries breaks new ground in the development of treatments to prevent and reduce the incidence of infections without the use of antibiotics, and its results have been published online in the journal *Nature Neuroscience*.

The study builds on previous Ohio State-led research that found spinal cord injury causes the immune system to become "paralyzed," and thus less able to fight off infections such as pneumonia. Pneumonia is the main cause of death in patients both after acute and chronic spinal cord injury. Decreasing disability infections has a strong impact on the lives of people with spinal cord injury.

"Despite its clinical relevance, the underlying mechanisms of how spinal cord injury causes a systemic immune shut down are far from being understood. After eight years of work, we were able to identify an entirely new mechanism for how spinal cord injury weakens the immune system," said principal investigator Dr. Jan M. Schwab, neurologist and physician at Ohio State's Neurological Institute, who collaborated with researchers from several institutes in Germany, along with the University of Alabama in Birmingham, Harvard Medical School and Boston's Children's Hospital.

Researchers demonstrated that susceptibility to spontaneous pneumonia

and severe lymphopenia after spinal cord injury resulted from a maladaptive sympathetic-neuroendocrine reflex involving the adrenal glands. Lymphopenia is an abnormally low level of lymphocytes or white blood cells that manage microbial host defense.

The identification of this two-stage pathological reflex arc - consisting of nerve pathways between the spinal cord and the adrenal glands, as well as a hormone-mediated link with the immune system - helps to deepen our understanding of the interconnections between the nervous and immune system.

The discovery of this 'immune system paralysis' and its underlying mechanisms represents an important step on the path to improving the treatment of spinal cord injury patients. Rather than merely experiencing the more obvious symptom of motor-sensory paralysis, paraplegic patients also experience a paralysis of the immune system.

"Based on our findings, we hypothesize that therapeutic normalization of the glucocorticoid and catecholamine imbalance in spinal cord injury patients could be a promising treatment strategy," Schwab said. "This could lead to new treatments to prevent or reduce infections in patients suffering with these injuries without antibiotics, thereby reducing disability and mortality."

Disrupting nerve fibers to the adrenal glands by high-level but not low-level thoracic spinal cord transection resulted in almost complete suppression of circulating norepinephrine levels and profound stimulation of systemic corticosterone levels. Identical findings were seen in human patients with traumatic complete spinal cord injury, researchers wrote. Given that infections are highly prevalent in spinal cord injured patients, orthodox antibiotic treatments start to lose their effectiveness with time due to the development of resistances.

More information: Harald Prüss et al, Spinal cord injury-induced immunodeficiency is mediated by a sympathetic-neuroendocrine adrenal reflex, *Nature Neuroscience* (2017). DOI: 10.1038/nn.4643