Press Release

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Little friends in the gut control social behavior through stress hormone pathway

Gut feeling, an idiom widely used in western culture, describes an instinctive feeling but not knowing the exact reason. Now a team of National Cheng Kung University (NCKU) and California Institute of Technology (Caltech) scientists has explored how gut bacteria influence mouse social behavior through a distinct stress response pathway in the brain. The novel finding, discussed in an article published in the journal Nature on July 15, 2021, has solved a missing piece of the connection between the gut and the brain, the authors say.

Social interactions among animals mediate essential behaviors, including mating, nurturing, and defense. Social behavior provides benefits such as increases survival, offers security, reduces energy expenditure. The deficit in social interaction is often observed in people with psychiatric disorders, such as autism, schizophrenia, depression, social anxiety, etc. While the intestinal bacteria contribute to social behavior in mice, gut-brain connections that regulate this complex behavior and its underlying neural basis remain poorly understood. The NCKU-Caltech team reveals that the microbiota modulates neuronal activity in specific brain regions in male mice to regulate stress responses and social behavior. Social deficit in mice without gut bacteria is associated with elevated levels of the stress hormone corticosterone, which is primarily produced by activating the hypothalamus-pituitary-adrenal (HPA) axis, a well-known system for stress response. Accordingly, removal of the adrenal gland, blockade of the glucocorticoid receptor, and pharmacological inhibition of corticosterone synthesis effectively correct social deficits modulated by gut bacteria. Genetic deletion of the glucocorticoid receptor in specific brain regions and chemogenetic inactivation of corticotrophin-releasing hormone (CRH)-expressing neurons in the paraventricular nucleus of the hypothalamus (PVN) rescue social impairments caused by microbiome depletion. Conversely, specific activation of CRH-expressing neurons in the PVN of mice is sufficient to induce social deficits. Finally, the team identifies a specific bacterial species, *Enterococcus faecalis*, that promotes social activity and reduces stress hormone in mice following social stress. These discoveries demonstrate that the gut microbiome can modulate social interactions via specific neuronal circuits that control stress responses in the brain.

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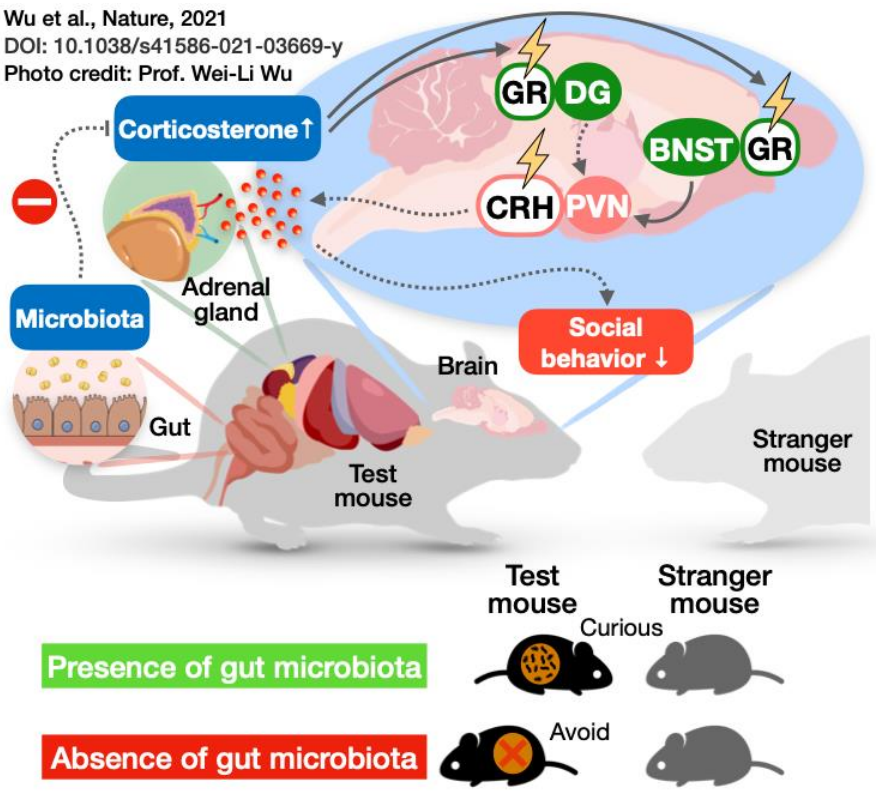
research was conducted by Prof. Wei-Li Wu and his team in the Department of Physiology at NCKU in collaboration with the team led by Prof. Sarkis Mazmanian of the Division of Biology and Biological Engineering at Caltech.



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