

Neurobiology

The biological reality of psychosomatic disease

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ABSTRACT

The latest neurobiological research is revealing important and influential neural pathways between the brain to organ systems, indicating the potential power of mind-body medicine.



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The idea that our brains influence our physical and mental health is both commonplace and somewhat taboo. We've heard that exercise can cheer us up, and stress can make us queasy, but the placebo effect "fools" us into getting well. Such mind-body connections, essential for healthy organ function, are often viewed with skepticism partly there hasn't been a firm biological basis for them. That is now changing. By identifying the neuronal highway between the brain and the adrenal medulla (which secretes hormones that characterize the fight-or-flight response), our team has shown psychosomatic illnesses can be very real.

We mapped these pathways using rabies virus as a transneuronal tracer. This approach can reveal neural circuitry because the virus infects only nerve cells and spreads by infecting neurons that interact with each other. Injecting rabies virus into limb muscles can reveal the networks involved in voluntary movement; injections into laryngeal muscles can reveal the central circuits responsible for vocalization. In addition to establishing the hardwiring of brain pathways, this technique can reveal similarities and differences in the neural circuitry between rodents and monkeys, for instance, which has important implications for research into the causes and treatments of human neurological disorders.

In our nonhuman primate experiments, we injected rabies virus tracer into the adrenal medulla, a gland at the top of the kidney that produces stress hormones such as adrenaline and cortisol. The virus replicates, first spreading to motor neurons in the thoracic spinal cord and continuing up to the cerebral cortex. By tracking its journey, we identified neurons that typically interact with each other, uncovering the neuronal network from the adrenal medulla to the brain.

We found that in monkeys, the cortical influence over the adrenal medulla originates from three distinct cortical networks known to be involved in movement, cognition, and mood. That potential link between the cortical control of "core" muscles and the regulation of sympathetic output might explain why core exercises, such as yoga and Pilates, are said to ameliorate stress. Also, several lines of evidence suggest that poor control of core muscles – a slumped posture – is associated with altered stress responses, sadness, and muddled thinking.

A second, small focus of output to the adrenal medulla hints at a link between the activation of facial muscles that create a "real" smile and a reduction in response to stress. A third, larger region of output from the motor network corresponds to the sensory representation of the trunk and organs. It may provide a neural reason for the reduction of anxiety and stress that follows the passive stimulation of back muscles during a massage.

Our experiments also suggest there is neural circuitry that links negative feelings, such as sadness and cognitive control processes, to immediate responses in stressful situations. It may be useful to consider all

three cortical networks that influence the adrenal medulla as key nodes of a "stress and depression connectome." That could offer new targets for the treatment of depression and other mood disorders.

The adrenal medulla is considered to be our "first responder" in situations requiring fight or flight. So, one might expect the input to it to be common across species. But there are key differences between the rat and the monkey. The primary motor cortex, primary somatosensory cortex, and a single secondary motor area account for ~93% of the cortical input to the adrenal medulla in the rat. In contrast, the monkey adrenal medulla receives input not only from cortical motor areas (~53%) but also from cortical areas involved in cognition and mood (~35%).

Also, the monkey adrenal medulla receives substantial input from motor areas of the cerebral cortex that don't exist in the rat. Each network found in the monkey has a human equivalent. These observations suggest that nonhuman primate models are essential for understanding key aspects of human neurological diseases and how they could be treated.

Our findings indicate the concept of psychosomatic illness should not be disdained but embraced by modern medicine. We suggest adopting the view reflected at the end of "Harry Potter and the Deathly Hallows" where Harry says, "Tell me one last thing, is this real? Or has this been happening inside my head?" Professor Dumbledore replies: "Of course it is happening inside your head, Harry, but why on earth should that mean that it is not real?"