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UNRAVELING STRESS:
Understanding the Mechanisms for Coping

Stress is one of life's universal experiences—everyone is familiar with it, regardless of who they are, where they live, or what they do. But while stress is common, it is hardly simple. Dr. Alon Chen of the Weizmann Institute of Science's Department of Neurobiology is working to clarify the biological underpinnings of stress and elucidate the brain's mechanisms for coping with the condition.

Dr. Alon Chen

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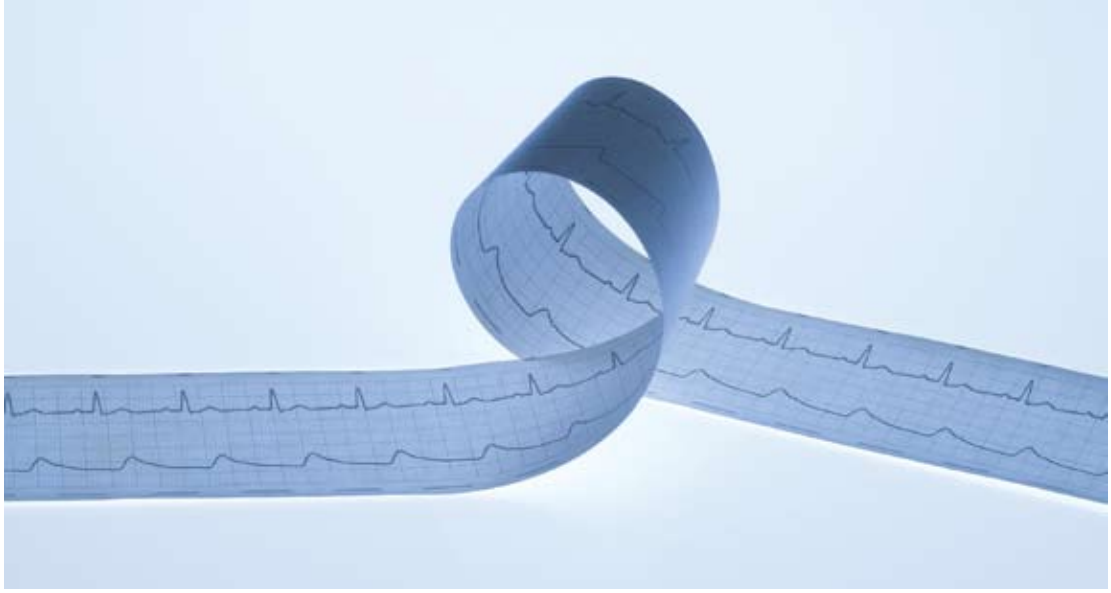
Dr. Chen defines stress as the result of any demand or challenge to homeostasis—our internal balance system—and says it is important to remember that stress can be real or perceived, current or anticipated, physiological or psychological, or a mixture of these. In addition, the perception of and response to stress are very individual, and both genetic and environmental factors play a role in how a person copes. Many scientists believe that stress is left over from early human existence, when challenging situations required an instinctive "fight or flight" response. Today, people have more choices; however, when confronted with stress, the body still automatically activates a series of coordinated responses organized to protect homeostatic equilibrium and, thus, enhance the probability of survival.

Two biological systems—the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis—play an important part in this stress response. The response mounted by the HPA axis involves the corticotropin releasing factor (CRF), which belongs to the urocortin family of peptides and receptors. Dr. Chen's research focuses on the role of this family of small proteins in mediating both the central (overseen by the brain) and peripheral (involving the heart, muscles, and pancreas) response to stress.

By developing genetically modified mice, Dr. Chen creates models that he can use to study the roles of the CRF/urocortin family in the stress response. Each member of the CRF/urocortin family is encoded by a different gene, so he creates modified versions of the genes and uses viruses as "delivery boys" to transport these altered genes to diverse brain regions. This is truly science at the cutting edge; thanks to the recent genetic mapping of the brain, Dr. Chen is able to deliver the modified genes to parts of the brain known to correspond to feeding, anxiety, memory, and so on. "And then," he explains, "we can ask a great variety of questions. If we manipulated a region which is associated with anxiety, we're going to check the anxiety of this mouse. If we manipulated its metabolism region, we're going to check its metabolism."

Through this methodology, Dr. Chen can



couple what he knows about the genome, as well as the peptides and receptors involved in the stress response, with his manipulations of the genetic makeup (genotype), to learn how they affect the actual observed properties (phenotype) of the mice. "We are trying to bridge the gap between the genotype and the phenotype. A lot of people are trying to do this in different fields, and I am trying to do it in the stress field."

The stress response can be associated with Type 2 diabetes, heart disease, and other illnesses, as well as psychological conditions and mood disorders, because "when it's not properly regulated, it affects different organs and different systems."

But why is bridging the gap between the genotype and phenotype so important? Because understanding the neurobiology of stress could provide important insights into how, exactly, stress affects—or even causes—psychological and physiological disorders. "Just by learning the mechanism, understanding the basic players and components of the stress response and how they interact, we can hopefully develop tools to manage different stress-related diseases," says Dr. Chen. Such disorders include psychological diseases and mood disorders, but also Type 2 diabetes, heart disease, and other illnesses. As Dr. Chen explains, the stress response can be associated with many diseases because "when it's not properly regulated, it affects different organs and different systems."

Furthermore, Dr. Chen is asking questions about environmental enrichment—providing the mice with running wheels, games, interactions with other mice, and so on—and anxiety. He is also exploring eating and feeding as they relate to stress, and collaborating with other Weizmann scientists to investigate the impact of stress on reproduction. The myriad ways in which stress impacts the body and mind are just beginning to be unraveled. Dr. Chen's research could result not only in a better understanding of this common problem, but also in vastly improved ways of treating it, leading to a healthier and happier world.

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