מכון ויצמן למדע
WEIZMANN INSTITUTE OF SCIENCE
Science Tips

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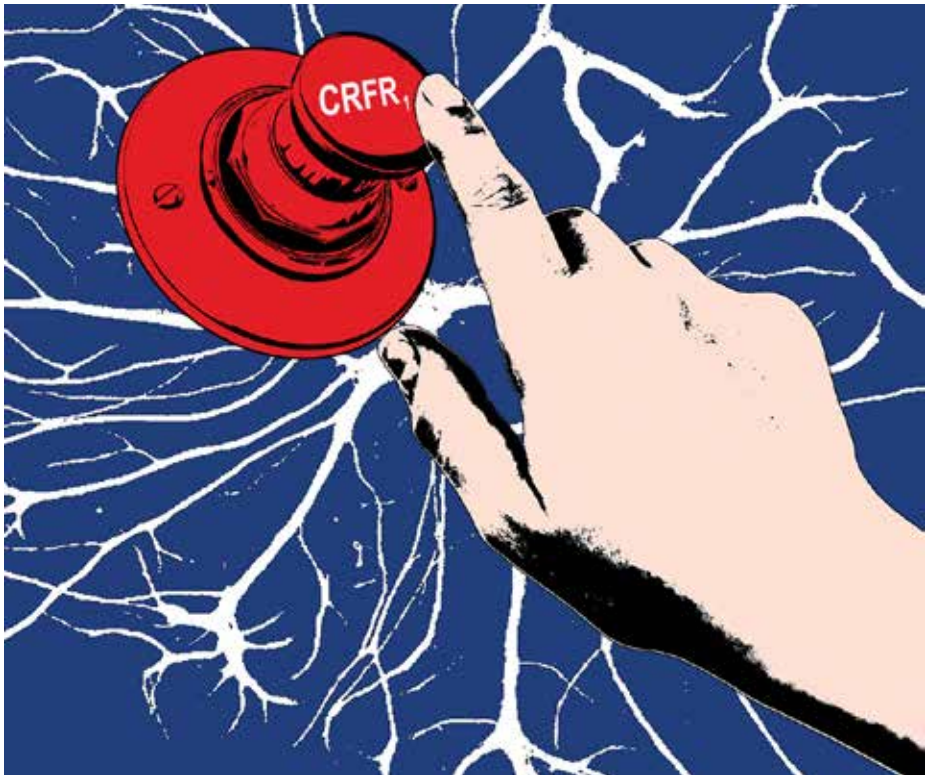
Receptive to Stress

A stress receptor in the brain is found to regulate metabolic responses to stressful situations differently in male and female mice

In the face of stress, our body diverts metabolic resources to its emergency response. It has been thought that the sympathetic nervous system – the body's instinctive system for reacting to stress – directs this activity, but Weizmann Institute of Science research now shows that neurons in the brain have a surprising role to play. The findings, which recently appeared in *Cell Metabolism*, may, in the future aid in developing better drugs for such stress-related pathologies as eating disorders.



"We would instinctively expect the receptor to be expressed on the cells that suppress hunger"

Dr. Yael Kuperman began this study as part of her doctoral research in the lab of Prof. Alon Chen of the Neurobiology Department. Kuperman, presently a staff scientist in the Veterinary Resources Department, Chen and research student Meira Weiss focused on an area of the brain called the hypothalamus, which has a number of functions, among them helping the body adjust to stressful situations, controlling hunger and satiety, and regulating blood glucose and energy expenditure.

When stress hits, cells in the hypothalamus step up the activation of a receptor on their outer walls called $CRFR_1$. It was known that this receptor contributes to the rapid activation of the sympathetic nerve network – increasing heart rate, for example. But since this area of the brain also regulates the body's energy balance, the team thought that the $CRFR_1$ receptor might play a role in this, as well.

Chen and his group characterized the cells in a certain area of the hypothalamus, finding that the receptor is expressed in around half of those that arouse appetite and suppress energy expenditure. These cells comprise one of two main populations in the hypothalamus – the second promotes satiety and burning energy. "This was a bit of a surprise," says Kuperman, "as we would instinctively expect the receptor to be expressed on the cells that suppress hunger."

To continue investigating, the researchers removed the $CRFR_1$ >>>

<<< receptor just from the cells that arouse appetite in the hypothalamus, in lab mice, and then observed how this affected their bodily functions. At first, they did not see any significant changes, confirming that this receptor is saved for stressful situations. When they exposed the mice to stress – cold or hunger – they got another surprise.

When exposed to cold, the sympathetic nervous system activates a unique type of fat called brown fat, which produces heat to maintain the body's internal temperature. When the receptor in the brain was removed, body temperature dropped dramatically – but only in the female mice. Even afterward their temperatures failed to stabilize, while male mice showed hardly any change.

Fasting produced a similarly drastic response in the female mice. Normally when food is scarce, the brain sends a message to the liver to produce glucose, conserving a minimum level in the blood. But when food was withheld from female mice missing the $CRFR_1$ receptor, the amount of glucose their livers produced dropped significantly. In hungry male $CRFR_1$-deficient mice, like those exposed to cold, the metabolism was barely affected.

"We discovered that the receptor has an inhibitory effect on the nerve cells, and this is what activates the sympathetic nervous system," says Kuperman.

Among other things – revealing exactly how this receptor works and how it contributes to the stress response – the findings show that male and female bodies may exhibit significant differences in their metabolic response to stressful challenges. Indeed, the fact that the receptor is known to suppress eating may help explain why women are much more prone to eating disorders than men.

These findings could aid in developing psycho-pharmaceutical treatments, especially since drugs can enter the hypothalamus with relative ease. Indeed, several pharmaceutical companies have already begun developing drugs to block the $CRFR_1$ receptor for the possible treatment of anxiety disorders or depression. The scientists caution, however, that because the cells are involved in energy balance, blocking the receptor could turn out to have such side effects as weight gain.

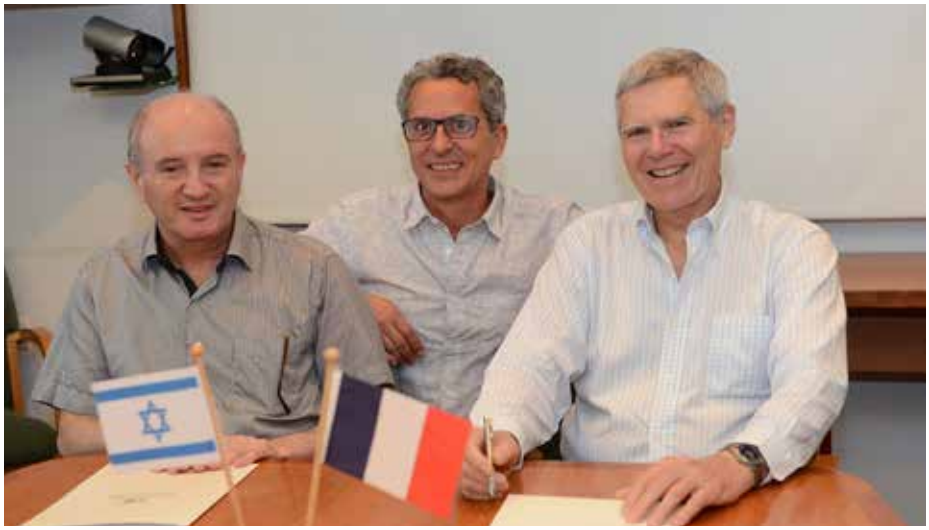
Prof. Alon Chen's research is supported by the Henry Chanoch Krenter Institute for Biomedical Imaging and Genomics; the Perlman Family Foundation, Founded by Louis L. and Anita M. Perlman; the Adelis Foundation; the Irving I Moskowitz Foundation; European Research Council; the estate of Toby Bieber; and the Ruhman Family Laboratory for Research in the Neurobiology of Stress.

http://www.cell.com/cell-metabolism/fulltext/S1550-4131(16)30169-3

École Polytechnique and the Weizmann Institute of Science Sign Cooperation Agreement

Jacques Biot, President of École Polytechnique (Palaiseau, France), and Prof. Daniel Zajfman, President of the Weizmann Institute of Science (Rehovot, Israel), signed a cooperation agreement to develop and promote collaboration in higher education and research between the two institutions.

"Both presidents – of Polytechnique and the Weizmann Institute of Science – have fully endorsed this initiative, enabling its quick success"



(l-r) Weizmann Institute of Science President Prof. Daniel Zajfman, Prof. Victor Malka and École Polytechnique President Jacques Biot

With this agreement, École Polytechnique and the Weizmann Institute of Science, both renowned for their high standards of quality in academics and research, seek to promote the exchange of students and faculty members, as well as to foster scientific and academic cooperation in topics of common interest.

A laboratory-initiated collaboration

Prof. Victor Malka, Research Director at the Laboratory of Applied Optics, a joint laboratory of École Polytechnique, ENSTA ParisTech and CNRS, joined the Physics of Complex Systems Department of the Weizmann Institute of Science in October 2015. Malka is committed to bring École Polytechnique and WIS closer: "It felt natural to >>>

>>> me to initiate this collaboration, to create scientific cooperation. Both presidents – of Polytechnique and the Weizmann Institute of Science – have fully endorsed this initiative, enabling its quick success."

Malka's research deals with laser-plasma accelerators. This accelerator concept, invented 30 years ago, has enabled researchers to obtain particle beams with unique properties. Very energetic, extremely bright and tunable in energy, these beams open new opportunities in such diverse fields such as medicine, chemistry, biology and materials science.

Recent improvements at the Laboratory of Applied Optics have opened the path to treating cancerous tumors. Research projects in this lab have yielded new perspectives, for example, on the detection of breast cancerous tumors at a very early stage. This new laser-plasma technology can also be used for industrial applications as it produces high-resolution, three-dimensional images of dense materials, for example those used in airplane parts.

Malka is currently working towards an association between the Laboratory of Applied Optics and the Weizmann Institute of Science Faculty of Physics to develop applications for laser-plasma accelerators. Under his initiative, two students from the Weizmann Institute of Science have already started PhD research at LOA.

About the Weizmann Institute of Science

The Weizmann Institute of Science in Rehovot, Israel, is one of the world's top-ranking multidisciplinary research institutions. Noted for its wide-ranging exploration of the natural and exact sciences, the Institute is home to 2,700 scientists, students, technicians and supporting staff. Institute research efforts include the search for new ways of fighting disease and hunger, examining leading questions in mathematics and computer science, probing the physics of matter and the universe, creating novel materials and developing new strategies for protecting the environment.

Weizmann Institute news releases are posted on the World Wide Web at

http://wis-wander.weizmann.ac.il/

http://www.eurekalert.org

About the École Polytechnique

École Polytechnique is the leading French institute which combines top-level research, academics, and innovation at the cutting-edge of science and technology. Its various graduate-level programs – Ingénieur Polytechnicien, Master's, Graduate Degree, PhD track and PhD – are highly selective and promote a culture of excellence with a strong emphasis on science, anchored in humanist traditions. As a widely internationalized university, École Polytechnique offers a variety of international programs and attracts a growing number of foreign students and researchers from around the globe (currently 30% of students and 39% of faculty members).