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commentary

The first *Highlighted Topics* article selected for this issue of the *Journal of Applied Physiology*, "Role of IL-6 in LPS-induced nuclear STAT3 translocation in sensory circumventricular organs during fever in rats," by Harré and colleagues (p. 2657–2666), applies a new molecular neuroanatomic approach to look at the location of cytokine-induced genomic activation in the brain. Cytokines released into the systemic circulation are thought to act on the brain at the circumventricular organs (CVOs), sites that lack a blood-brain barrier. For nearly 20 years, investigators have believed that sensory CVOs [e.g., the vascular organ of the lamina terminalis (OVLT) and the subfornical organ (SFO)] are involved in fever induction pathways (Blatteis et al., *Brain Res Bull* 11: 519–526, 1983); however, no molecular evidence has clearly supported this hypothesis. The cytokine interleukin-6 (IL-6) is regarded as an endogenous mediator of lipopolysaccharide (LPS)-induced fever. Cells that are activated by IL-6 respond with nuclear translocation of the transcription factor STAT3. Harré and colleagues used STAT3 immunohistochemistry to analyze the exact location of this cytokine action on the brain. After systemic LPS and IL-6 treatment, in doses proven to induce fever responses, the only brain structures that responded with a marked nuclear STAT3 translocation were the OVLT and the SFO. This nuclear STAT3 translocation was observed 2 h after LPS treatment, whereas it occurred only 1 h after IL-6 application, reflecting the time delay for LPS induction of the cytokine IL-6. These authors present the first molecular evidence for an IL-6-induced STAT3-mediated genomic activation of OVLT and SFO cells and support the proposed role of these brain areas as sensory structures for humoral signals created by the activated immune system. In addition, STAT immunohistochemistry may reveal the locations of cytokine-specific genomic activation in the brain with distinct STAT molecules as neuroanatomic markers.

The second *Highlighted Topics* article featured in this issue, "Ambient temperature for experiments in rats: a new method for determining the zone of thermal neutrality," by Romanovsky and colleagues (p. 2667–2679), is an *Innovative Techniques* article, which examines current methods and proposes a new one for finding the thermoneutral zone (TNZ) in the rat. A common misperception is that an animal has the same TNZ in different experimental setups. In reality, the TNZ strongly depends on the physical environment and varies widely across experimental conditions. However, current methods for determining the TNZ are applicable only to a limited set of experimental conditions and require elaborate equipment. Romanovsky and colleagues developed a novel, broadly applicable approach that rapidly determines whether given conditions are neutral, subneutral, or supraneutral for a given animal. On the basis of the current definition of TNZ (the range of ambient temperature at which body core temperature regulation is achieved only by control of sensible heat loss), the authors proposed three criteria of thermoneutrality: *1*) the presence of high-magnitude fluctuations in skin temperature of body parts serving as specialized heat exchangers with the environment (e.g., rat tail), *2*) the closeness of skin temperature to the median of its operational range, and *3*) a strong negative correlation between body core and skin temperatures. The authors used thermocouple thermometry and liquid crystal thermography to find the TNZ in five rat strains. Under the conditions tested (no bedding or filter tops, no group thermoregulation), the temperature range of 29.5–30.5°C satisfied all three TNZ criteria in Wistar, BDIX, Long-Evans, and Zucker lean rats. Fat Zucker rats had a slightly lower TNZ (28.0–29.0°C). Skin thermometry or thermography is a definition-based, simple, and inexpensive technique, handy for determining whether given conditions are neutral, subneutral, or supraneutral for a given animal. Although tested only in the rat, the same approach is likely to be applicable to all endothermic animals that possess specialized heat-exchange organs. It may be used to solve a variety of problems, ranging from standardization of biomedical experiments to optimization of housing for agricultural animals to development of automatic climate control systems for human patients.

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