The orchestration of autonomous and behavioral thermoregulation

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Within the thermoneutral zone it is a balancing act to adjust skin blood flow such that there is neither net heat gain nor heat loss and body deep tissue temperatures are maintained close to 37°C (1). From an economical point of view this mechanism for thermoregulation can be considered as cheap, as there are little nutrient or water resources used that wouldn’t already be expended to sustain life (11). A healthy body can resort to more expensive mechanisms in case the thermal challenge goes beyond what can be compensated for by vasoconstriction or vasodilation, such as (non)-shivering thermogenesis at the cost of chemical energy contained in nutrients or sweating at the cost of body water. Thus, there seems to be an efficient order in the recruitment of thermo-effectors, which allows for body temperature regulation at minimal cost of nutrients and water.

But how does thermal behavior fit in this order? With the wide variety of behavioral outcomes (e.g., the clothing we wear, shelters we build and air conditioning we operate) behavioral thermoregulation is widely recognized as the strongest mechanism through which humans have been able to cope with even the harshest climates on earth (1, 9, 15). Moreover, while there is a physiological cost for behavioral thermoregulation; in case of humans the largest energy cost is often placed outside of the body and comes for instance from transferring chemical energy in fossil fuels to electricity. Interestingly, even these energy requirements associated with thermal behavior for air conditioning systems and heaters show a remarkable resemblance to the classic physiological thermoneutral zone (4). In animal studies the behavioral aspect of thermoregulation has been embraced as a part of their physiological integrative regulatory system, but for humans this is not yet supported broadly by experiments (6, 12). Schlader et al. recognized this lacuna and have begun to decipher how thermal behavior is a product of human physiology to respond to a thermal challenge or even to avoid it.

In this edition Schlader et al. hypothesized that thermal behavior fits in the orderly recruitment of thermo-effectors as follows: 1) vasomotor responses, 2) behavioral responses, and 3) sweating or metabolic responses (13). Their results support this hypothesis by showing consistently for heating and cooling that non-glabrous skin blood flow changes immediately with changes in skin temperature, followed by the initiation of a behavioral response. The behavioral response preceded changes in core body temperature both for heating and cooling, which confirms their earlier findings that thermoregulatory behavior can be in time to prevent significant internal thermal perturbations (14). Interestingly, during heating, while there was a steady incline in skin blood flow *before* the behavioral response, there was also a marked increase in skin blood flow *after* the behavioral response. This observation thus leaves room for discussion whether during heating skin blood flow regulation acts as the first line of defense alone or actually in concert with thermal behavior. Perhaps we should even consider to split the skin blood flow response in the sympathetic adrenergic and sympathetic cholinergic responses for the orderly recruitment of thermo-effectors.

Another interesting aspect about the hypothesis tested by Schlader et al. is that the order of recruitment is a function of the relative physiological cost; which implies that it is influenced by how the costs are assessed – and these may be expected to change with factors such as initial hydration level, nutritional state, acclimation, age and pathology (13). Indeed, there is evidence that the skin temperature threshold for initiation of thermal behavior is significantly higher after passive acclimation, but it is not known whether the order of thermo-effector recruitment is influenced (8). Furthermore, age or pathology related impairment to both afferent and efferent thermoregulatory pathways may disturb the thermo-effector recruitment and thereby the efficiency of the thermoregulatory response (16).

The study by Schlader et al. focused on responsive thermoregulation, i.e. thermoregulation in response to a thermal challenge. Nevertheless, one aspect of behavioral thermoregulation is that it can also occur in anticipation of a thermal challenge (e.g., put on a coat before you go out when it freezes). As this behavior is not in response to a change in thermal state the question raises how the human brain reward system learns to minimize or avoid thermoregulatory costs, or how it forgets irrelevant anticipations (5).

Moreover, how does the body get to the order of responses that is most cost effective and how does that fit in current views of the functional architecture of the thermoregulatory system? Individual thermo-effectors are controlled via *"...independent integrators arranged in parallel at every level of the nervous system, each level facilitated or inhibited by the levels above and below…" (7, 10, 11).* On the lowest level neural thermal receptors *code* the local thermal state of body tissues; in turn the information is integrated at the level of the spinal cord, brain stem and hypothalamus for autonomous thermoregulation, however, for thermal sensation the integration pathway is different and projects from the brainstem to the cortex (3). These distinctive pathways may in part explain why the relative contribution of the thermal information from skin and core tissues is not uniformly distributed between autonomous thermo-effectors and thermal sensation (ratio core:skin temperature 3.1:1 for vasomotor responses, 3.6:1 for metabolic responses and 1:1 for thermal sensation) (2, 15). However, they do not directly explain the order of thermo-effector recruitment.

In summary, Schlader et al. elegantly show that human behavioral thermoregulation fits in the orderly recruitment of thermo-effectors according to the relative physiological costs. Thereby paving the way to explore and understand the underlying regulatory and integrative human physiology explaining how this order is orchestrated.

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