

Sympathetic activity and functional masking of brown adipose tissue uncoupling protein. M Gubern, MF Chapey, MC Laury, R Portet (EPHE, Laboratoire d'Adaptation Énergétique à l'Environnement, 11 place M Berthelot, 75005 Paris, France)

Brown adipose tissue (BAT) is the major site of both non-shivering thermogenesis and diet-induced thermogenesis. BAT heat production is controlled by a mitochondrial specific uncoupling protein (UCP) which acts as a proton channel. An acute stimulation of thermogenesis does not lead to an increased UCP content, but induces a rapid unmasking of the nucleotide binding sites which regulates its activity (increase in GDP binding which is a classical test of BAT activity) (Trayhurn and Milner, 1989). The aim of this study was to examine the functional importance and the sympathetic system involvement in this masking/unmasking process.

Chemiosmotic parameters of BAT mitochondrial energization were investigated. Oxygen consumption (modulated by several additions of α -glycerophosphate) and membrane potential (main component of proton motive force, Δp) were determined simultaneously with specific electrodes. Flux/force relationships occurring in these mitochondria were established. They allowed calculation and comparison of membrane proton conductance CmH^+ (proton flux per mV proton motive force) over the entire range of Δp (Gubern *et al*, 1990).

Male Long-Evans rats (9-wk old) were exposed to cold (5 °C) (control rats C5). Bilateral

surgical denervation of interscapular BAT 4 d before killing (Sy5 rats) led to a 78% decrease in GDP-dependent CmH^+ (which is the primary functional parameter of UCP) compared to C5. Warm reexposure at 28 °C (thermal neutrality) for 4 d (WE28 rats) after 10 d at 5 °C led to a 90% decrease in CmH^+ compared to C5; BAT surgical denervation (Sy28 rats) had no additional effect. β -Agonist injection (isoproterenol, 200 μ g/kg im 1 h before killing) to Sy5 or WE28 rats greatly enhanced UCP-dependent CmH^+ up to the C5 level. In the presence of GDP which completely blocks UCP, basal CmH^+ (which was very low except for maximal values of Δp) was the same in the 4 groups. Immunological estimation of UCP content did not display any difference between the groups. This it may be concluded that the observed variations in proton conductance are the consequence of a masking/unmasking mechanism.

These results show the importance (10-fold) of these acute variations in UCP activity which was underestimated using more indirect criteria. These results agree with *in vivo* measurements of BAT heat production (Foster and Frydman, 1979).

References

- Foster DO, Frydman ML (1979) *Can J Physiol Pharmacol* 57, 257-260
- Gubern M, Yazbeck J, Chapey MF, Diotez P, Moreau F (1990) *Biochim Biophys Acta* 1015, 334-340
- Trayhurn P, Milner RE (1989) *Can J Physiol Pharmacol* 67, 811-819