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Centrally acting nesfatin-1 induces non-shivering thermogenesis in Brown Adipose Tissue (BAT) via the melanocortin pathway

Luka Levata, Riccardo Dore, Olaf Jöhren, Hendrik Lehnert and **Carla Schulz**
Center of Brain, Behavior and Metabolism (CBBM), Germany

Nesfatin-1 is an anorexigenic peptide expressed both in adipose depots and hypothalamic nuclei that regulate food consumption. Recently, our group has reported that centrally administered nesfatin-1 also increases overall energy expenditure. We thus performed a study, using Wistar rats and C57BL/6 mice to examine if centrally acting nesfatin-1 employs the melanocortin system toward energy homeostasis, and elicits sympathetic outflow to interscapular brown adipose tissue (iBAT) to initiate thermogenesis. Healthy male animals of both species were stereotaxically implanted with intracerebroventricular cannula to receive central injections. First, with the application of direct calorimetry, we demonstrated that in rats nesfatin-1 [25 pmol] elicits a substantial increase in dry heat loss that lasts for 7 hours ($p<0.01$). This effect was fully precluded ($p<0.01$) by the co-administration with an equimolar dose of SHU9119, a potent MC3/4 receptor antagonist. The RT-PCR analysis showed that centrally administered nesfatin-1 [100 pmol] promoted POMC and MC3 receptor mRNA expression ($p<0.01$) in the hypothalamus and, as a trend, also of MC4 receptor mRNA. This was accompanied by increased DIO2 mRNA expression ($p<0.01$) and trend of increase in UCP1 and PGC-1α mRNA in iBAT. Moreover, the assessment with infrared thermography revealed that centrally delivered nesfatin-1 [300 pmol] in mice enhances ($p<0.01$) iBAT, as well as ocular surface temperature ($p<0.05$). We also demonstrated that this effect is completely abolished ($p<0.01$) when administered in pair with SR59230A [5 mg/kg], a potent and highly selective β3-adrenoceptor blocker. Finally, the increase in heat production instigated by nesfatin-1 promotes a reduction in body weight ($p<0.05$), which exhibits a prolonged duration even after overnight ad libitum access to food. Altogether, we herein provide evidence that the increase in energy expenditure instigated by nesfatin-1 is a process mediated via the central melanocortin system that in turn sets off iBAT thermogenesis, ultimately leading to a reduction in body mass. Centrally acting nesfatin-1 instigates catabolic effects.

Biography

Luka Levata is currently a Doctoral Researcher at Center for Brain, Behavior and Metabolism (University of Lübeck). With his academic background in neuroscience, he is interested in deciphering neural circuits in the brain that regulate feeding behavior and metabolic activities. The brain incessantly communicates with other body organs to control all homeostatic processes, including energy expenditure. He is using animal models to investigate mechanisms of energy expenditure under physiologically relevant conditions.

Luka.Levata@uksh.de

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