



## Low level of 900 MHz radiofrequency stimulates cold responses in rodents

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In the world, there is a near ubiquitous presence of a low-intensity radiofrequency electromagnetic field (RF) radiation, due to telecommunications as mobile phones and their base stations. However, their rapid expansion raises concerns about possible interaction with biological mechanisms. Recently, at intensity levels below the threshold to produce thermal effects, 900 MHz-RF exposure has also recently been elicited biological effects, resembling reactions to cold in rats and mice.

First study [1] showed that rats repeatedly exposed (5 weeks, 23h/24) to RF at continuous waves (CW) 900 MHz with an intensity of 0.3mW/kg at warm ambient temperature, had a subcutaneous tail temperature 1.2°C lower than controls, due to maintained vasoconstriction. Moreover, exposed rats ate more than controls. A second study [2] demonstrated that exposed rats in similar condition felt cold since they chose an ambient temperature of 31°C compared to control rats that chose 28°C, only during the day-sleep period. Similarly, Arendash et al. [3] showed that repeated RF exposure (twice 1h/day for 1 week) at 918 MHz with an intensity between 17 and 35 V.m-1 induced a body temperature increase of 1°C in mice after one week of RF exposure, but not in the first days. We found similar results in a replicated study [4]. All of these results have revealed significant effects of low-intensity RF (below the thermal threshold) on the thermoregulatory system in rodents, paradoxically reflecting a reaction to cold instead of the usual known reactions to warm at higher levels.

The possible mechanism of RF is an activation of thermogenesis. In fact, quick and short temperature increases could involve a specific tissue dedicated to heat metabolism in rodents, the brown adipose tissue. One main enzyme of heat production is the uncoupling protein 1 (UCP1) in brown tissue mitochondria. Heat production implicate lipolysis with production of metabolites like non-esterified fatty acids (NEFA) and fatty acids (FGF21). The pathway involves the sympathetic nervous system with the noradrenaline, a neurotransmitter responsible for vasoconstriction and thermogenesis. To investigate the possible effectors of the observed temperature modifications in rodents and the involved pathways, mice have been exposed to RF for 7 consecutive days, (twice 1h/day for 1 week) at CW 900 MHz signal with an intensity of 0.16 W/kg. Moreover, Wistar rats have been exposed to CW 900 MHz RF during 7 days, 23 hours per day in reverberation chambers at a SAR of 0.35 W/kg. We quantified Ucp1 expression by qPCR and UCP1 protein concentration by immunohistochemistry, in the brown adipose tissue, but also for comparison in the inguinal white adipose tissue. Noradrenaline, NEFA and FGF21 have been measured in the plasma.

The UCP1 protein was not increased in the brown adipose tissue of mice, but in the white inguinal adipose tissue (10,2% vs 3.6%,  $p < 0.001$ ). mRNA Ucp1 was not significantly increased in both tissues. In responses to cold stimuli, both rats and mice exposed to RF showed changes in the morphology of white and brown adipocytes: size of lipid droplets was reduced:  $1440 \pm 81 \mu\text{m}^2$  in the mice exposed group vs  $2357 \pm 157 \mu\text{m}^2$  in the sham one. The NA concentration of the exposed rats was 3.5-fold higher compared to the sham rats ( $p = 0.03$ ). The NEFA concentration in exposed rats was 2-fold higher than in sham rats ( $p = 0.03$ ). Concerning plasma FGF21, the concentration in exposed rats tended to be higher compared to sham rats ( $247 \pm 45 \text{ pg/ml}$  vs  $379 \pm 65 \text{ pg/ml}$ ,  $p = 0.1$ ). These findings indicate that 900 MHz RF exposure at non-thermal levels produces a browning of the inguinal white adipose tissue in both studied species, mice and rats, thus mimicking reactions to cold, as was previously seen for other parameters and behaviors.

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