Non-selective Beta-Adrenergic Agonist Infusion Acutely Stimulates the Temperature of Brown Adipose Tissue in Adult Males

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Background

Over the past decade, brown adipose tissue (BAT) has emerged as a potential therapeutic target to combat childhood and adult obesity, due to its potential to dissipate energy through mitochondrial uncoupling.

There is convincing evidence to suggest that BAT is under sympathetic control and can be activated through β-adrenoceptor (AR) stimulation. Hypercortisolism, when pharmacologically induced in rodents, leads to an inhibitory effect on BAT activity and suppression of norepinephrine-induced mitochondrial uncoupling. Little is known about the role of glucocorticoids in human BAT function, and whether they affect adrenergic activation of thermogenesis.

Aims

1. To examine whether nonselective ß-AR stimulation with Isoprenaline (ISO) activates BAT in humans, measured by Infrared Thermography (IT).

2. To investigate the effects of acute hypercortisolaemia on human BAT function by infusing hydrocortisone (HC).

Methods

Eight healthy males (Table 1) were studied following HC infusion (0.2 mg.kg^{-1}.min^{-1} for 16 hrs) or saline. Infusions were given in a double-blind, randomized fashion. BAT thermogenesis was measured by IT before, during, and after a 60 min ISO infusion (25 ng.kg fat free mass^{-1}.min^{-1}). Thermal images were taken at a rate of 4/min 15 min prior to and throughout the ISO infusion, and 2/min for 15 min post infusion. The temperature of the supraclavicular fossa was analysed using Matlab software (Figure 1). iButtons recorded skin temperature every minute and were taped within the supraclavicular fossa (main site of BAT) and lateral of the umbilicus. HR and BP were recorded every 5 minutes using continuous ECG monitoring. ANOVA' statistics were used with P<0.05. Ethical approval was given.

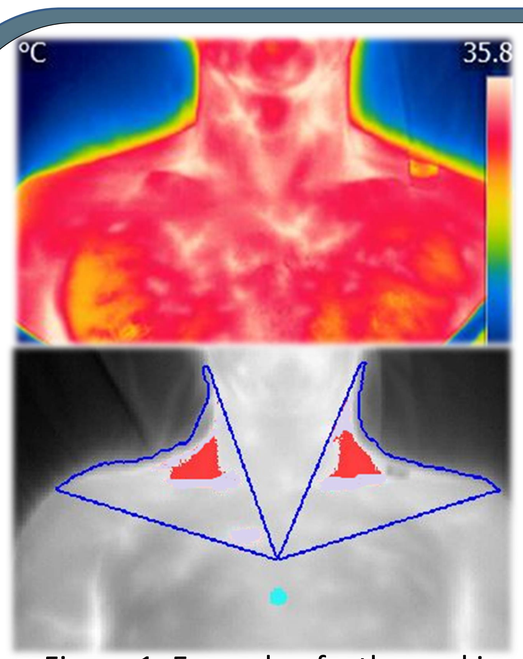

Figure 1. Example of a thermal image taken during ISO infusion and the same image analysed in Matlab software.

Table 1. Participant characteristics

N	**8 males**
Age (years)	23.13 ± 4.53
Weight (kg)	74.13 ± 6.92
BMI (kg·m^2)	22.78 ± 1.12
WHR	0.84 ± 0.05
Trunk Fat (g)	7538 ± 1412
Leg Fat (g)	5580 ± 961
Visceral Fat (g)	202 ± 96

Mean ± Standard deviation shown; NEFA, non-esterified fatty acids Fat mass measurements obtained by DXA

Results

ISO infusion resulted in significant ß-adrenergic mediated increases in heart rate (47 ±4 bpm) peaking at 45 min (Figure 2a).

ISO infusion resulted in a highly localized increase in local temperature within the supraclavicular region compared to baseline (Δ 0.54 ±0.08° C, *P*=0.001 [Figure 2c,d])

HC resulted in a lesser increase in BAT temperature during ISO infusion (Δ 0.51 ± 0.09° C, *P*=0.01 [Figure 2c,d]). Further, basal BAT temperature is increased in HC compared to saline (Figure 2b).

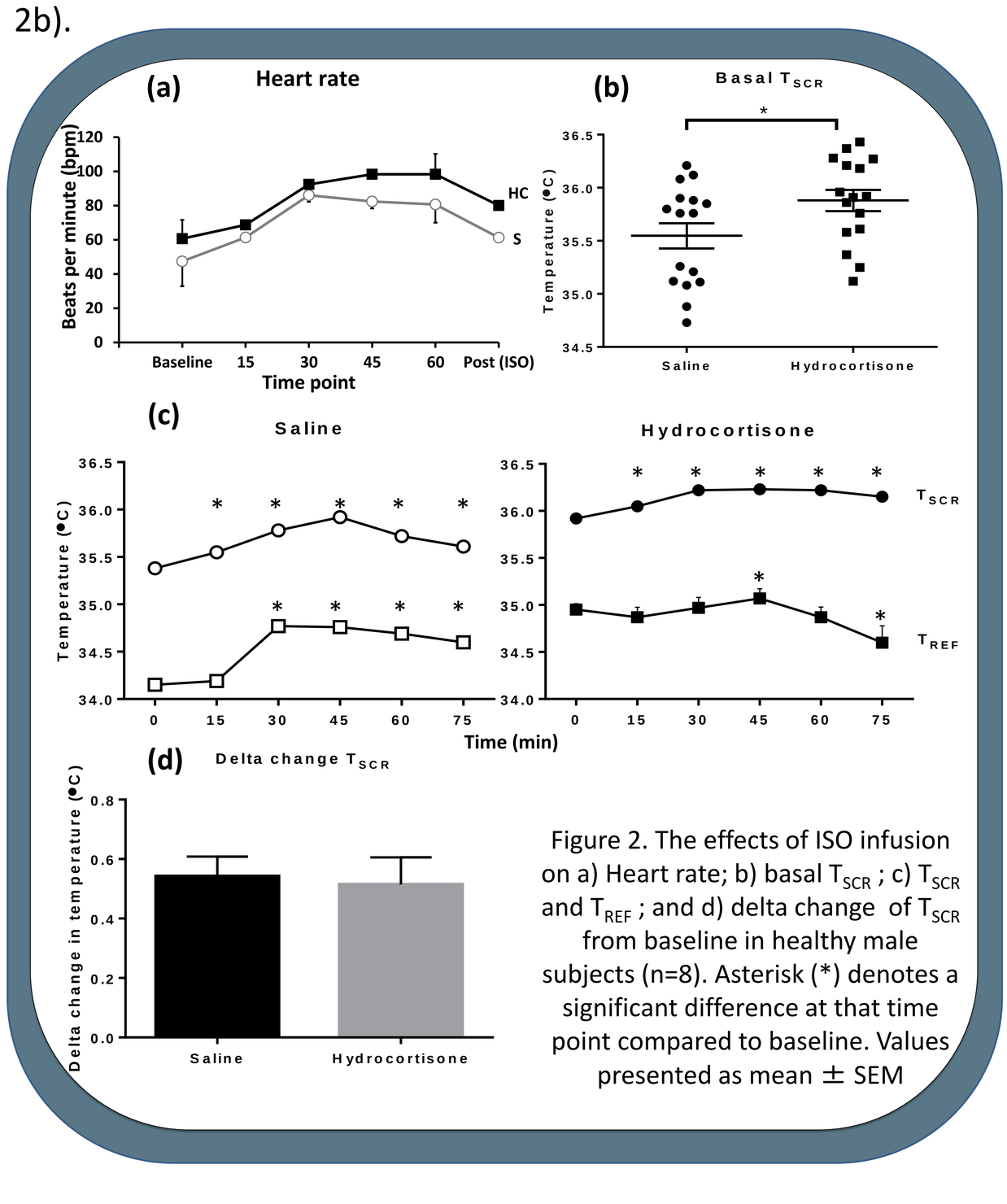

Figure 2. The effects of ISO infusion on a) Heart rate; b) basal T_{SCR} ; c) T_{SCR} and T_{REF} ; and d) delta change of T_{SCR} from baseline in healthy male subjects (n=8). Asterisk (*) denotes a significant difference at that time point compared to baseline. Values presented as mean ± SEM

Conclusions

ß-adrenergic stimulation induced dynamic changes in BAT activity that was measurable by IT. This confirms IT as a simple, non-invasive method for assessment of real-time BAT function. Acute hypercortisolaemia resulted in blunting of the adrenergic-mediated increase in BAT activity, possibly due to glucocorticoid-dependent BAT pre-activation. Future studies should focus on the effects of chronic glucocorticoid excess on human BAT function, and whether tissue-specific inhibition of glucocorticoid activity/generation can contribute to increased BAT thermogenesis.