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Paediatric patients with type 1 diabetes exhibit reduced brown adipose tissue heat signature following cold stimulation

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Introduction

Brown adipose tissue (BAT) is a key component of the body's defence against cold challenge and possesses the ability to convert large amounts of chemical energy to heat, conferred by a unique protein, uncoupling protein-1, diverting mitochondrial respiration from the production of adenosine triphosphate.[1] In humans, the largest BAT depot is in the supraclavicular region. Sympathetic nervous system stimulation induces glucose uptake into brown adipose tissue, as does insulin.[2] Despite significant improvements in recent years, people with type 1 diabetes mellitus maintain blood glucose levels higher than healthy controls, in order to avoid recurrent hypoglycaemia. In addition, insulin is administered into the peripheral circulation, rather than the portal circulation, altering the balance of peripheral and portal levels. Although hyperglycaemia leads to peripheral insulin resistance in muscle and white adipose tissue,[3] it is not known if the same applies to BAT.

BAT is most abundant in children and adolescents and declines with age. The high ionising radiation required for PET-CT, the previous gold standard imaging method, excluded children from prospective studies. We have developed a technique to measure the heat signature of supraclavicular BAT using infrared thermography.[4]

Methods

Sequential thermal images were obtained of the supraclavicular region of 20 children and young people with type 1 diabetes (D) and 20 healthy controls (C), before and during stimulation, administered using a cooling blanket around the right forearm, set to 15°C (Fig1). Images were analysed using our semi-automated analysis method[4] to calculate the 95th percentile and compared to a sternal reference region (Fig2).

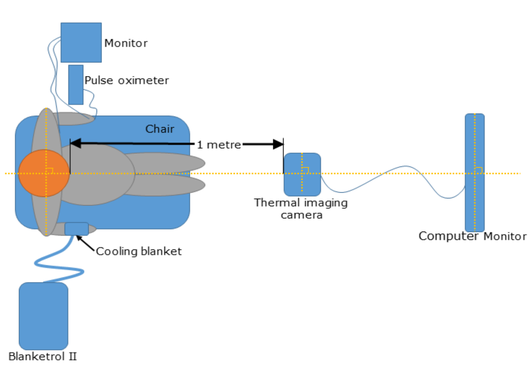

Figure 1 Study session set up

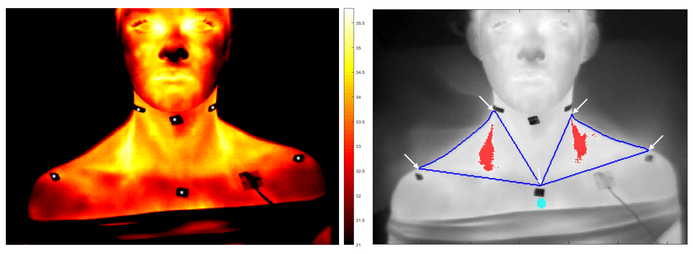

Figure 2 A Thermal image with apices (*) identified to allow automated analysis **B** Image post-analysis, showing contour of region of interest (blue), upper decile hotspot (red) and reference region (cyan)

References: [1]Cannon B et al. Physiol Rev 2004;84:277-359; [2]Orava J et al. Cell Metab 2011;14:272-279; [3]Yki-Järvinen H et al. New Engl J Med 1986;315:224-230; [4]Law J et al. J Nucl Med 2018;59:516-522

Results

Characteristics (age, gender, height, weight and BMI) were similar between the groups. Following cold stimulation, the diabetes group had a lower absolute supraclavicular temperature (D: 35.0±0.6°C; C: 35.4±0.6°C; $p<0.05$) which remained significantly lower when compared to a sternal reference point (D: 1.8±0.4°C; C: 2.1±0.5°C; $p<0.05$) (Table1, Fig3). There was no difference no difference in the supraclavicular temperature response to cold stimulation (-0.1°C, $p>0.1$) but a trend towards a smaller change in the relative temperature (-0.1°C, $p<0.1$).

Patients with diabetes were on intensive insulin therapy (CSII, n=7; MDI, n=13) and 11 were within 2 years of diagnosis (range 0.1-15.5 years). HbA1C was 55 (IQR 44-62) mmol/mol and post-imaging blood glucose was 8.9 (IQR 5.6-12.2) mmol/L. Supraclavicular temperatures were not associated with either HbA1C or blood glucose level.

	Diabetes group	Control group	p
Resting T_{SCV}	35.0±0.6	35.3±0.6	0.09
Resting T_{Rel}	1.7±0.4	1.9±0.5	0.16
Stimulated T_{SCV}	35.0±0.6	35.4±0.6	0.04
Stimulated T_{Rel}	1.8±0.4	2.1±0.5	0.03
ΔT_{SCV}	0.1±0.1	0.1±0.1	0.10
ΔT_{Rel}	0.1±0.1	0.2±0.2	0.06

Table 1 Results of infrared thermographic analysis by group. P values are results of unpaired T-tests. T_{Rel}: Relative temperature; T_{SCV}: Supraclavicular temperature; ΔT: Change in temperature from baseline

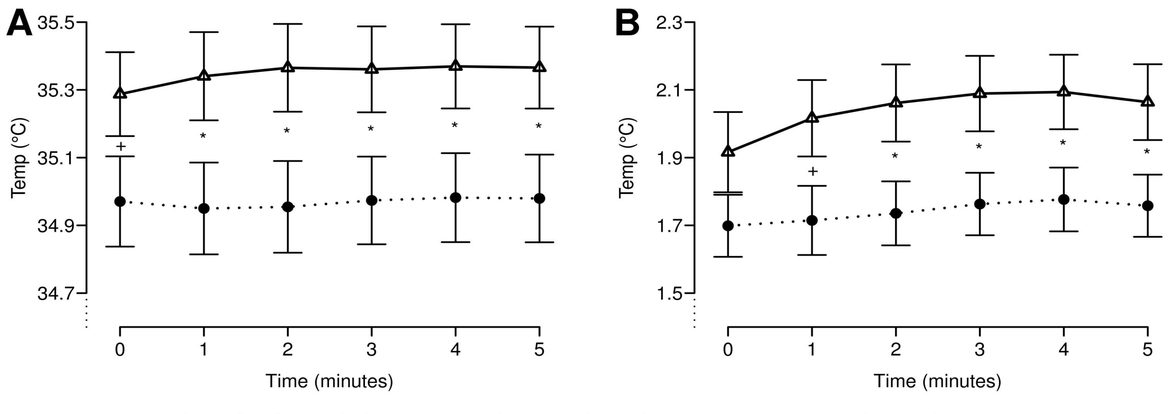

Figure 3 Results of infrared thermographic analysis by group **A** Supraclavicular temperature and **B** Relative temperature. $^{+}0.05<p<0.1$; $^{*}p<0.05$. Open triangles: control group; closed circles: diabetes group.

Conclusions

The relationship between BAT and insulin is complex. In the physiological state, insulin is strongly suppressed by sympathetic nervous system control. Since exogenous insulin is not responsive to the sympathetic nervous system, it is unable to be suppressed following a cold challenge which could be an explanation for the lower stimulated supraclavicular temperature.

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