DIFFERENCES IN HEAT PRODUCTION BETWEEN ADIPOCYTES FROM OBESE AND NORMAL WEIGHT INDIVIDUALS

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1. Introduction

It has been established since early this century [1,2] that normal individuals can keep their weight fairly constant for long periods of time in spite of marked changes in caloric intake [1,2], indicating variations in the metabolic efficiency of the normal cell. Recently, these concepts have been extended into the area of obesity research, and a number of groups have presented data implicating that differences in metabolic efficiency may indeed contribute to the development or perpetuation of obesity [3–7]. Here we have employed microcalorimetry as a tool for measurements of heat production in isolated fat cells, providing a new approach to the assessment of metabolic efficiency by direct registration of energy waste. Adipocytes from obese and normal weight individuals have been studied.

2. Materials and methods

One group of 14 obese patients and one group of 12 matched controls, subjectively healthy, were studied. The sex, age and weight distributions are shown in table 1. No patients with primary hormonal disturbances were included in the study.

Open biopsies from the gluteal region were taken in the morning after 10 h fasting. Local anaesthesia with 1% Carbocain was given intradermally. The obese patients had been on a standardized weight-maintaining diet for 5 days and the controls had been on their own regular diet.

Adipocytes were isolated from the biopsy material by collagenase treatment as in [8]. With the short collagenase treatment time used (20–30 min) no floating fat was observed in the adipocyte preparations from patients or controls. The fat cell suspension was washed by repeated centrifugation, and 0.9 ml samples, corresponding to 0.45 ml packed cells, were taken for microcalorimetric measurements. Aliquots of the cell suspension were extracted by isopropanol to allow exact measurements of the lipid weight. The microcalorimetric measurements were performed with the cells suspended in 0.05 M Krebs-Ringer bicarbonate buffer (pH 7.4) containing 0.1 U/ml insulin and 11 mmol/l glucose. Microcalorimeters of the thermopile heat conduction type were used. Samples were enclosed in a stainless steel ampoule. Suspensions containing $1-2 \times 10^6$ cells in 1 ml buffer produce a heat effect that can be estimated with a precision of ~2%. Heat production in adipocytes from obese patients as well as normal subjects was stable for $\geqslant 4$ h. The instrument and its operation have been described in [9].

Adipocyte size was measured in frozen sections and in adipocyte suspensions, with no significant difference between the two techniques in patients or controls. Cells (100) were measured under the light microscope, and from the mean cellular diameter, mean cell volume and triglyceride content were calculated. The number of cells could then be estimated from these data and the lipid weight of the isopropanol extract.

Table 1
Clinical data and heat production data from obese patients and control subjects

Number	Age	Sex	Body weight (kg)	Fat cell size (μg lipid/cell)	Broca's index	Heat production (μW/g fat tissue)	Heat production (pW/cell)
Patients							
1	34	F	115		2.0	21	
2	41	F	119		2.1	20	
3	37	M	116	0.82	1.4	5	4.1
4	37	M	200	0.63	2.9	46	29.0
5	31	F	123	0.42	1.9	56	23.5
6	36	F	101	0.24	1.3	103	24.7
7	38	F	143	0.68	2.4	52	35.4
8	32	F	128	1.02	1.8	41	41.8
9	34	M	155	0.57	1.9	39	22.2
10	25	F	92	0.26	1.8	14	3.6
11	34	M	155	1.04	1.8	26	27.0
12	45	M	124	0.80	1.6	48	38.4
13	41	F	129	0.63	1.8	50	31.3
14	48	M	150	0.73	1.7	35	25.7
Mean ± S D	36.6 ± 5.8	8F/6M	132.0 ± 27.2	0.65 ± 0.3	1.9 ± 0.4	39.7 ± 23.9	25.6 ± 11.8
Control subjects							
1	34	M	79	0.38	1.0	89	33.8
2	40	M	79	0.35	1.0	94	32.9
3	34	F	58	0.40	1.0	63	25.2
4	36	F	65	0.46	0.8	85	39.1
5	34	M	75	0.34	0.9	170	57.8
6	30	F	58	0.42	0.9	150	63.5
7	38	M	82	0.39	1.0	180	70.2
8	44	F	65	0.33	0.9	180	59.4
9	24	F	62	0.52	0.9	120	62.4
10	34	M	75	0.32	0.9	180	57.6
11	34	M	67	0.36	0.9	90	32.4
12	24	M	67	0.28	0.8	200	56.4
Mean ± S D	33.8 ± 5.8	7M/5F	69.3 ± 8.4	0.38 ± 0.07	0.9 ± 0.1	133.4 ± 48.1	49.2 ± 15.3

3. Results

The principal clinical data are enlisted in table 1. The mean heat production (table 1) was about 3-times lower in adipocytes from obese than lean subjects when compared on a weight basis (fig.1); due to the difference in adipocyte size (table 1), the difference was less striking when expressed as pW/cell, but still statistically significant ($p < 0.001$) (fig.2).

4. Discussion

There is increasing evidence that obesity is associated with an increased metabolic efficiency. This view is based mainly on clinical observations demonstrating that spontaneously obese can maintain their body weight on a significantly lower caloric intake than experimentally obese [3]. The further examination of this hypothesis has been based mainly on indirect measurements of caloric consumption. Recently, microcalorimetry has been introduced as a tool for direct measurements of heat production in various biological systems [10]. Here this technique has been applied to isolated fat cells, allowing a direct estimation of the metabolic efficiency of the cell. Comparison of heat production of adipocytes from obese and lean subjects demonstrated significantly lower heat production in obese than in lean controls. As indicated above, there is no evidence that a preferential breakage of larger cells during the procedures would have contributed to the lower values measured in cell preparations from the obese patients.

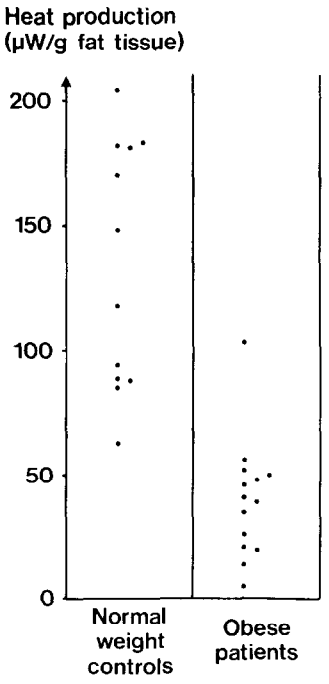

Fig.1. Adipocyte heat production in obese patients and lean control subjects, expressed as μW/g tissue.

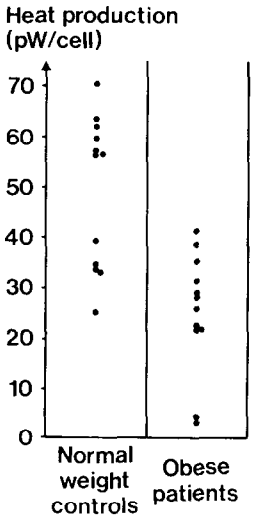

Fig.2. Adipocyte heat production in obese patients and lean control subjects, expressed per cell.

The biochemical background for the altered heat production is unknown. In fact most metabolic functions studied (e.g., lipid uptake and mobilization, glucose utilization) seem to be increased in adipocytes from the obese [11]. However, the relative contribution of various metabolic pathways to the total heat production of the adipocyte is unknown. The reasons for the low heat production in adipocytes from obese thus remain speculative. It is possible that the observed difference in heat production could be related to a restricted activity of metabolic pathways leading to energy consumption without net transport, so-called futile cycles.

A loss of thyroid-induced Na^+- and K^+-dependent ATPase activity in genetically obese mice has been shown [7]. Thus, it is also possible that the observed

differences in heat production in adipocytes from obese and normal individuals may be related to an alteration in the activity of this enzyme system, which has been claimed to regulate many metabolic functions including energy balance and thermogenesis [12,13]. The difference may also reflect alterations at the level of oxidative phosphorylation.

Thus our data strongly support the hypothesis that differences in metabolic efficiency may be an important pathogenetic factor in obesity. Several questions arise from this study:

Is the difference in heat production restricted to adipose tissue, or can it be demonstrated in other organs such as blood cells and muscle?

Is the decrease in heat production a cause or a consequence of obesity?

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