Interrelationship between Lipid Droplets and Mitochondria in Brown Adipocytes of the Hamster

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ABSTRACT. The interrelationship between lipid droplets and mitochondria in the interscapular brown adipose tissue of the hamster was investigated by electron microscopy. The membranous structure of mitochondria began to degenerate at the site in contact with lipid droplets. From that site, mitochondrial cristae also began to collapse. After being completely surrounded by lipid droplets, these degenerating mitochondria became vacuolated within them. Finally, lipid infiltrated into these vacuoles. Mitochondrion-like structures found in the lipid droplets may be possibly residues of the degenerating mitochondrial membranes.—KEY WORDS: brown adipose tissue, electron microscopy, hamster, lipid droplet, mitochondria.

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The cytoplasm of brown adipocytes is occupied by lipid droplets and mitochondria with characteristic structures of cristae. For this reason, contact of lipid droplets with mitochondria is observed more frequently than in other tissues such as skeletal muscles and heart muscles. For this contact of lipid droplets with mitochondria, it has been suggested that mitochondria play a role as the source of energy for lipid droplets. On the other hand, Lever [3] reported that in adrenocortical cells, mitochondria were enlarged to shift to lipid droplets. Also, the limiting membrane of mitochondria is often lacking at the part in contact with lipid droplets in brown adipocytes in the rat [4]. Therefore, we used the interscapular brown adipose tissue of the hamster that holds it continuously after birth, and observed histologically the interrelationship between lipid droplets and mitochondria in adipocytes.

MATERIALS AND METHODS

Five male golden hamsters (body weight 100–120 g), 10 to 12 weeks old were used for this experiment. They were anesthetized by diethyl ether, and were fixed by perfusion with 0.1 M sodium cacodylate and then with the mixture of 2.5% glutaraldehyde and 2% paraformaldehyde in 0.1 M sodium cacodylate at pH 7.4. The interscapular brown adipose tissues were excised and immersed in the same fixative for 3 hr. The tissue blocks were postfixed in 2% osmium tetroxide buffered with 0.1 M sodium cacodylate for 3 hr, and then were dehydrated through a series of different concentrations of ethanol. The specimens were embedded in poly-bed 812 mixture. Ultrathin sections were stained with uranyl acetate and lead citrate, and observed with a transmission electron microscope at 75 KV (H-700, HITACHI).

RESULTS

Lipid droplets adhered to mitochondria with a considerable frequency in brown adipocytes. As if lipid had an affinity for mitochondria, its cactus-like projections approached the nearby mitochondria (Fig. 1). As stated above, contact of lipid droplets with mitochondria was observed more frequently than in other tissues. In mitochondria in contact with lipid droplets, remarkable changes in structure were noticed. The structural changes in mitochondria adjacent to lipid droplets in the cytoplasm were as follows: First, a lipid droplet became in contact with mitochondria. In the initial stage of this contact, membranous structures of mitochondria began to degenerate at the area of contact (Fig. 2). At this stage, the inner part of mitochondrial cristae began to collapse near the area of contact (Fig. 3). Then, the collapsed part became vacuolated. The mitochondrial cristae disappeared in the area surrounded by the lipid droplet (Fig. 4). At the stage when mitochondria were completely surrounded by the lipid droplet, most of the cristae disappeared and mitochondria existed as vacuoles in the lipid droplet (Fig. 5). After being completely embedded in the lipid droplet, mitochondria broke down to become fragments (Fig. 6). The vacuoles, themselves, appeared to comprise a part of the lipid

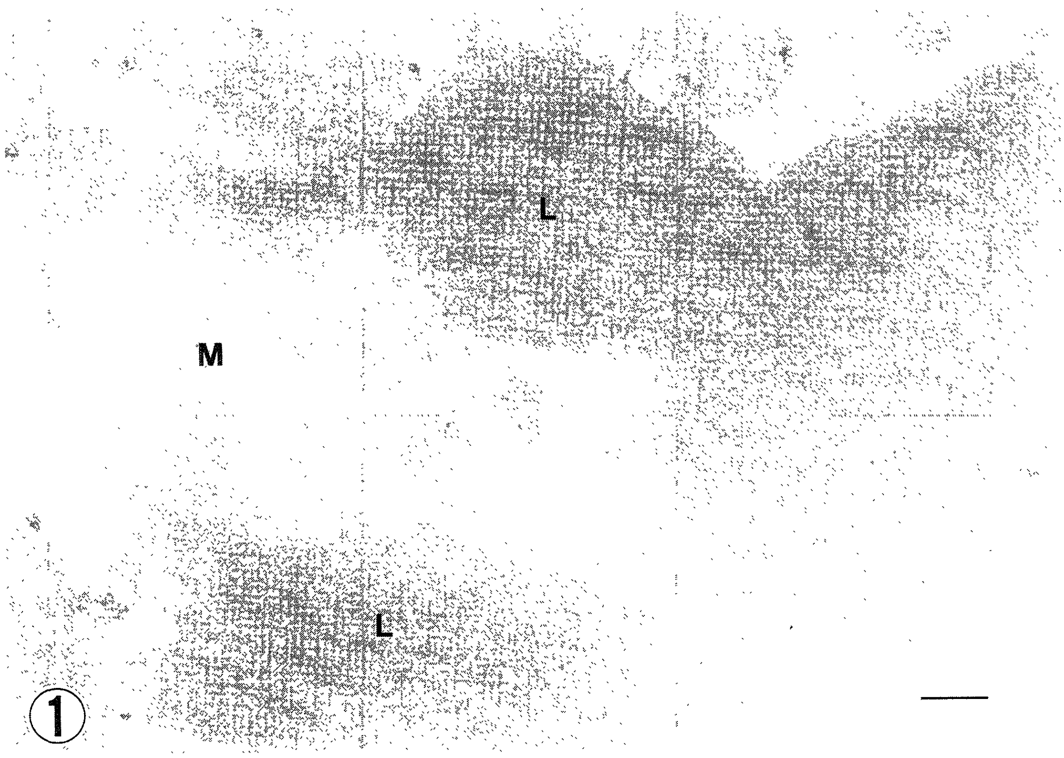

Fig. 1. A brown adipocyte of the hamster. Projections of lipid droplets are in contact with mitochondria. L: lipid droplet, M: mitochondrion, Bar=0.5 μm, × 17,600.

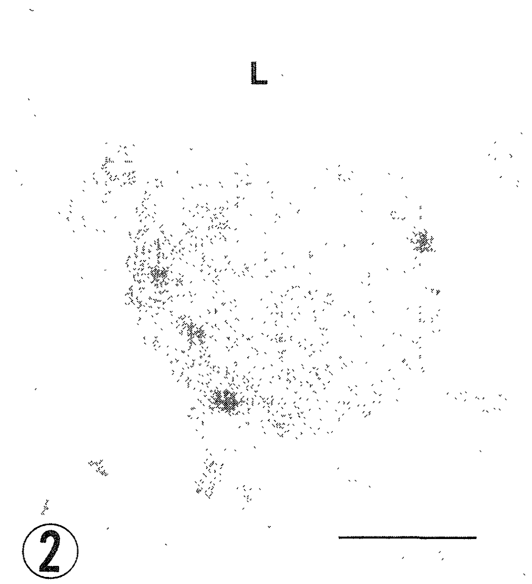

Fig. 2. Collapse of membranous structures at the area of contact between lipid droplets and mitochondria. L: lipid droplet, Bar=0.5 μm, × 37,200.

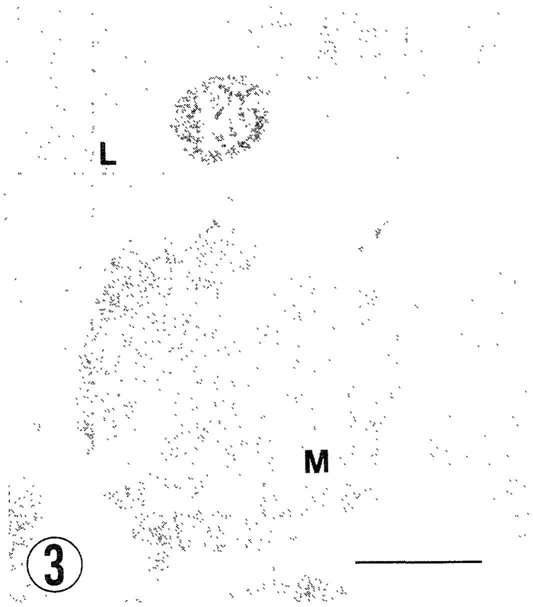

Fig. 3. Collapse of mitochondrial cristae near the area of contact. L: lipid droplet, M: mitochondrion, Bar=0.5 μm, × 33,600.

Fig. 4. The degenerating mitochondria are gradually surrounded by lipid droplets. Mitochondrial cristae disappear in the area embedded in lipid droplets. L: lipid droplet, M: mitochondrion, Bar=0.5 μm, × 36,900.

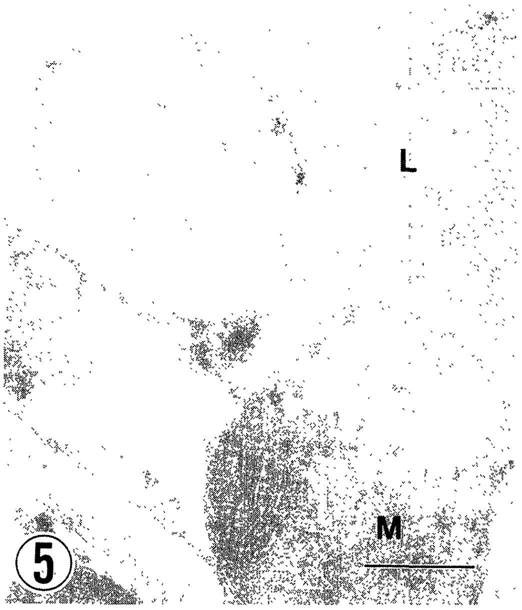

Fig. 5. When a mitochondrion is completely surrounded by a lipid droplet, its cristae disappear and it becomes a vacuole. L: lipid droplet, M: mitochondrion, Bar=0.5 μm, × 29,000.

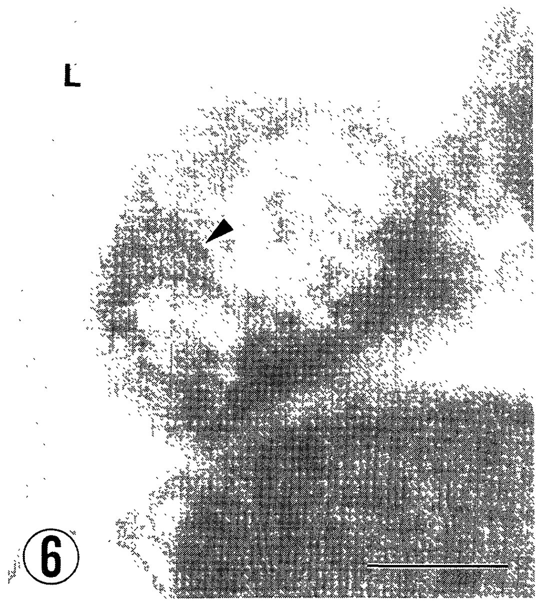

Fig. 6. A degenerating mitochondrion in a lipid droplet. The outer membrane of mitochondrion has disappeared. L: lipid droplet, ◀: crista, Bar=0.5 μm, × 38,000.

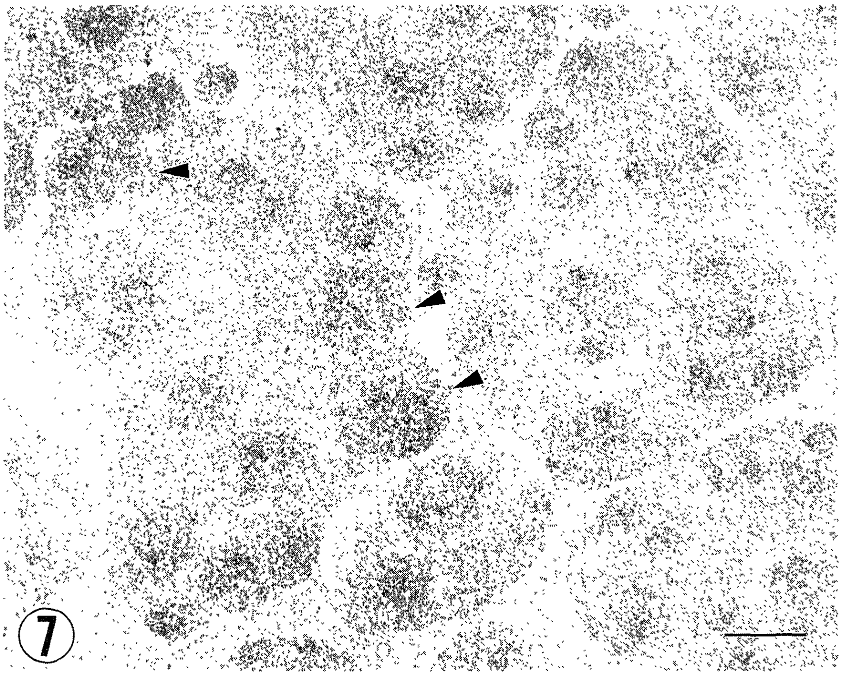

Fig. 7. Mitochondrion residue-like structures (arrows) are seen in lipid droplets. Bar=0.5 μm, × 22,400

droplet. During this process, mitochondrial residue-like structures were found in lipid droplets (Fig. 7). The foregoing process was observed to progress in a cell at a time.

DISCUSSION

The interrelationship between lipid droplets and mitochondria in brown adipocytes is an important subject in the context of lipogenesis and lipolysis. This interrelationship has been observed in various ways. For example, the ratio of lipid droplets to mitochondria is increased with age [1]. The amount of lipid droplets is decreased under lower temperatures [2, 5]. When the volume of lipid is decreased, each lipid droplet is lessened in size, and the quantity of mitochondria and the number of cristae are increased [8]. Loncar and Afzerius [6] reported that in the brown adipose tissue of the cat, lipid droplets were enlarged by fusion of small-sized lipid droplets and also by autolysis of mitochondria. Thus, in spite of the presence of an intimate interrelationship between lipid droplets and mitochondria, it has not been so far discussed that the former may directly influence the structural changes in the latter.

Our foregoing observations show that the enlargement of lipid droplets is following by disappearance of mitochondria. Thus lipid droplets give a direct influence on mitochondria. In addition, brown adipocytes themselves are not degenerated even when mitochondria in them have been degenerated. The structural changes in mitochondria begin to occur from the site where lipid droplets attached them. It is interesting to note that in hypotrophic muscles such as muscle dystrophy, the quantity of lipid droplets is increased, while carnitine acetyltransferase activity in the mitochondria adjacent to lipid droplets is abolished, as evidence of lipid metabolism [7]. The trigger of the structural changes in mitochondria in contact with lipid droplets may be due to changes in metabolic activity.

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