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1

The rediscovery of BAT in adult humans using imaging

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Human brown adipose tissue has been acknowledged in newborns and children but in adults the first printed publications are from the beginning of 20th century. Further evidence of the existence of adult brown fat was published throughout the century but only very recently the functionality of active brown adipose tissue *in vivo* in adulthood was confirmed. This was contributed mainly by advanced imaging technology, namely hybrid positron emission tomography (PET) and computed tomography (CT), being able to combine functional and anatomical imaging data. Functionality is most commonly measured with glucose analog, 18F-fluoro-2-deoxy-D-glucose (FDG) but other tracers for other functions than glucose uptake have been introduced as well. Growing body of evidence has increased the knowledge of the role of brown adipose tissue in human metabolism and energy expenditure, providing a promising option for the management of body weight balance and disturbed glucose and lipid metabolism.

Early findings

The existence of brown adipose tissue (BAT) has been recognized in mammals since 16th century. Swiss scientist, Conrad Gesner described this tissue being “neither fat, nor flesh, but something in between” [1]. High amount of small intracellular lipid droplets indicated adipose tissue while high amount of mitochondria was consistent with muscle tissue. Mitochondria indeed, along with dense vasculature and large lipid droplet surface area are mainly responsible for the high metabolic capacity

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of BAT. Currently it is recognized that both high number of mitochondria and configuration of mitochondria (densely packed cristae) have central role in oxidative capacity of brown adipocytes [2].

In the beginning of 20th century BAT was appreciated as an endocrine gland and was described to locate in the supraclaviluar region [3]. Mr Edward Bonnot described this gland in 1908 as "a paired organ, irregular in shape, but definite in outline, situated on the shoulder and side of neck, between the superior border of the scapula and clavicle, with a large process extending upward to the mastoid process of the temporal bone" in adult cadavers. This corresponds considerably well with the current findings with *in vivo* imaging (Fig. 1.). Along the anterior border of the gland there is chain of deep lymphatic glands [3]. Mr Bonnot gives also detailed description of the vasculature of the gland in the same report, and the lower part of the gland is supplied through the transverse cervical artery [3]. Later in 1920 William Cramer published the results "on glandular adipose tissue" in man and several animal species [4], where he described this tissue as a "second gland-like type of tissue, the cells of which are filled with globules giving all the typical histo-chemical reactions for fat". In this report three typical sites for the tissue (subscapular, perivertebral and perirenal) are given, and interscapular region is regarded as a separate anatomical organ. Interestingly, Cramer describes the tissue being functionally distinct from the typical adipose tissue but being functionally related to thyroid and adrenal glands, as well as suggesting this tissue having functional importance for great vessels, such as aorta, due to anatomical adherence [4].

Post-mortem studies on brown adipose tissue

In the mid-20th century and thereafter BAT was classified as an adipose tissue which has an exceptional capacity for higher oxygen consumption than traditional white adipose tissue and thereby energy expenditure.

A detailed description of the distribution of brown adipose tissue in humans from infancy to late adult life was given by Juliet Heaton in 1972 [5]. These autopsy studies revealed that while the appearance of brown fat cells decline with age in more peripheral sites, such as anterior abdominal wall and subscapular region, they remain in more central sites. Of these central sites, Heaton highlighted renal and suprarenal, para-aortic, neck and mediastinum deposits. Despite this report and description, majority of the reports during following years concentrated on infant brown adipose tissue and its importance for thermogenesis during early infancy. Also Japanese researchers showed that perirenal fat contains brown adipocytes being detectable in 72% of the subjects [6]. In infants, the perirenal samples contained always a high amount of brown adipocytes while later in adulthood individual variation was high. Interestingly though they found brown adipocytes in perirenal fat from a 86-year old man [6].

First *in vivo* studies

Further suggestions on the existence of functional brown adipose tissue in man was given by Rothwell and Stock in 1979, when they, in the ground-breaking article on diet-induced thermogenesis

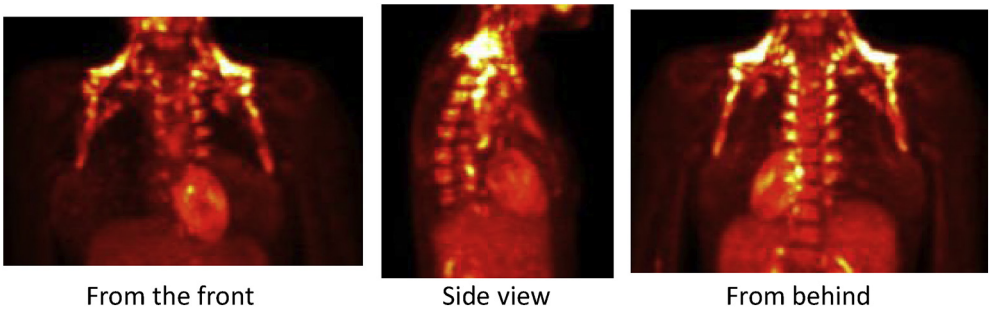

Fig. 1. Metabolic activationof supraclavicular adipose depot with ^{18}FDG PET/CT. Bright colour indicates high uptake of glucose tracer observed from various projections.