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This Week's Citation Classic

Anand B K & Brobeck J R. Hypothalamic control of food intake in rats and cats. *Yale J. Biol. Med.* **24**:123-40, 1951. [Lab. Physiol., Yale Univ., New Haven, CT]

Bilateral destructions of a well localised area in lateral hypothalamus led to complete cessation of eating, while lesions involving ventromedial nuclei or the region between these and lateral area produced hyperphagia and obesity. The lateral region (hunger mechanism) was designated 'feeding center' and the medial (inhibitory control) 'satiety center.' [The *SCI*® indicates that this paper has been cited over 400 times since 1961.]

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"Development of obesity in animals following bilaterally placed destructive lesions in or ventrolateral to the ventromedial nuclei of the hypothalamus had been established through studies of Hetherington, Brobeck, and others,[1,2] primarily from a marked increase in food intake.

"In 1950, while working at Yale University and trying to stereotaxically place such hypothalamic lesions in the albino rats to make them hyperphagic, I was much disconcerted to find that my rats immediately after such lesions completely stopped eating and would die of starvation. Little did I realise at the moment that this may lead to the discovery of an important hypothalamic area controlling our hunger mechanism, which discovery would change our concepts about the nervous mechanisms concerned with our feeding behaviour and regulation of energy balance.

"To better understand the hypothalamic mechanisms we carried out investigations to discover the effects on food intake of small electrolytic lesions placed in the different areas of the hypothalamus which resulted in the discovery of a well localised area in the lateral hypothalamus, the bilateral destruction of which by very small lesions resulted in a complete loss of feeding behaviour to the point where the rat would die of starvation. If, however, this area was destroyed on one side only normal feeding persisted. This small hypothalamic area is so precisely located that even lesions as much as 0.5 mm away from it do not disturb feeding.

"We confirmed that bilateral lesions involving ventromedial nuclei produce hyperphagia and obesity. We also showed that destructive lesions between these nuclei and the lateral area also result in overeating, thus demonstrating laterally projecting inhibitory effects of the medial hypothalamic mechanism over the lateral area. As the hyperphagia resulting from medial lesions was converted into aphagia by subsequent lateral lesions, it was considered that the lateral area is the primary mechanism for hunger resulting in the urge to eat and hence constitutes the 'feeding center.' As the medial area provides an inhibitor mechanism for the lateral, this constitutes the 'satiety center.'

"Further studies carried out after my return to New Delhi not only confirmed the presence of these 'centers' in other animals; these also elucidated the nervous mechanisms for controlling and regulating our entire feeding behaviour which regulates the body's energy balance. They also established that the hypothalamic centers provide the basic urge of hunger and satiation, operating through the *level of utilisation of glucose* within the nerve cells of these regions. Sensory afferents from the stomach and other intestinal regions also activate the satiety center.

"The publication of this paper in 1951 resulted in the initiation of many similar experimental studies almost all over the world. The interest generated by such studies has also resulted in a number of special international symposia and seminars, etc., and the establishment of an international society for the study of feeding and drinking mechanisms.

"As the paper cited above was the first one to describe the presence of the hypothalamic control mechanisms for the feeding behaviour, it explains its high citation frequency."

1. **Hotheriogtoa A W & Ranson S W**. Hypothalamic lesions and adiposity in the rat. *Anat. Rec.* **78**:149-72, 1940.
2. **Broback J R, Tepperman J & Long C N H**. Experimental hypothalamic hyperphagia in the albino rat. *Yale J. Biol. Med* **15**:831-53. 1943.