Adipose Tissue as an Endocrine Organ

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KEYWORDS

• Obesity • Adipose tissue • Endocrine • Hypoxia • Inflammation • Insulin resistance

KEY POINTS

- Obesity is a strong risk factor for developing numerous chronic diseases, primarily insulin resistance, type 2 diabetes, heart disease, and nonalcoholic fatty liver disease.
- Visceral fat is a functional endocrine organ with important influences on numerous metabolic and hormonal responses.
- Visceral adipose tissue is known to produce inflammatory adipokines, regulatory adiponectin, as well as other regulatory molecules such as leptin, cocaine and amphetamine–regulated transcript and nuclear factor κB that play important roles in the cause of these chronic diseases.
- The endocrine effects of adipose tissue during obesity and the systemic impact of this signaling need to be investigated in greater detail to understand the progression of chronic metabolic diseases.

INTRODUCTION

Obesity is one of the most important health issues in developed countries. Statistics taken between 1999 and 2004 indicate that in the United States the obesity rate for men increased from 27.5% to 31.3% and the rate for women remained steady at 33%, indicating that a significant proportion of American adults are obese as defined by a body mass index (BMI) more than 30.[1] In the past decade a growing number of children have also become obese, with 16% of girls and 18% of boys fitting the definition of obese for their age groups in 2004.[1] The root causes of obesity are diverse and can differ from simply a high-calorie diet and lack of exercise to an underlying

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medical condition such as diabetes.[2,3] Although obesity may seem simple, on a functional and metabolic level it is highly complex. Obesity has an important influence on numerous metabolic and hormonal responses including changes in sex hormones,[4] inflammation,[5,6] and insulin resistance.[2,7] Fat, visceral fat in particular, is increasingly considered to be a functional endocrine organ. Recent studies have found that, in addition to fat storage, adipose tissue is known to store lipid-based hormones[4] and to produce inflammatory adipokines,[5,6] regulatory adiponectin,[8] and other regulatory molecules such as leptin,[9] cocaine and amphetamine–regulated transcript[2] and nuclear factor κB (NFκB).[6] The organism-wide impact of this signaling cannot be underestimated, and strongly supports the theory that obesity is essentially a systemic medical condition with adipose tissue deregulation the underlying force driving the change.

Obesity is also a considerable risk factor for developing numerous other chronic diseases, such as insulin resistance, type 2 diabetes (T2D), heart disease, and nonalcoholic fatty liver disease (NAFLD). In the United States, NAFLD is currently estimated to exist in about 60% to 90% of the adult obese population,[10] compared with 15% to 30% of the general population.[11] NAFLD is not just a concern for adults but a growing number of adolescents as well.[12] Current estimates for the years 2007 to 2010 indicate that 10.7% of children in the United States are at risk for NAFLD, compared with estimates of 3.9% in 1994 to 1998.[12] Just as with adults, obesity is a major risk factor for the development of NAFLD, with estimates in obese children increasing from 20.7% in 1994 to 1998 to 38.2% in 2007 to 2010 (ie, nearly doubling).[12]

Some patients with NAFLD are at risk to progress to more severe forms of liver disease, including steatohepatosis, hepatic steatosis, nonalcoholic steatohepatosis (NASH), and ultimately cirrhosis.[11,13] About 20% of all patients with NASH are projected to develop cirrhosis of the liver within 20 years of initial diagnosis.[14]

Although the risk factors contributing to progression from NAFLD to NASH are largely unknown, adipose tissue signaling is thought to be an important driver via its promotion of both insulin resistance and proinflammatory signaling (**Fig. 1**).[15] Numerous lines of research have implicated adipose tissue via hypoxia,[6,16] inflammation[3,5,6,17] and overall endocrine disruption[18,19] in the impairment of many different organ systems, including the liver. This article discusses the endocrine effects of adipose tissue during obesity and the systemic impact of this signaling.

VISCERAL FAT COMPOSITION

In order to properly understand adipose tissue on a whole-organism level it is important to understand the components of adipose tissue and the functions of these various components. Two main types of adipose tissue are found in the human body: white adipose tissue (WAT) and brown adipose tissue (BAT).[20,21,22] Both are unique in structure, function, and when and where they occur in the body.[20] Both types of adipocytes store lipids to some extent in the form of triglycerides, but other functions of these cells are unique.[3] BAT in humans is typically associated with fetuses and infants and is defined by its main characteristic of being able to use fat to create heat in a unique process known as nonshivering thermogenesis via the expression of uncoupling protein 1 (UCP1) in the mitochondria.[20] It was widely thought that BAT represented at most 1% of adipose tissue in adult humans[23] until recent studies found areas of tissue resembling the metabolic profile of BAT in adult humans,[24] localized to areas such as the upper thoracic cavity and neck.[24,25]

In contrast, WAT is the more common type of adipose tissue in human adults and is designed for quick storage and release of lipids in response to metabolic conditions,