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Dance Round

WE DANCE ROUND IN A RING AND SUPPOSE,
BUT THE SECRET SITS IN THE MIDDLE AND KNOWS.
ROBERT FROST

NEUROBIOLOGY OF ADIPOSE TISSUE

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Adipose tissue's secretory phenotype paradigm shift has been upregulating since December 1, 1994, the birthday of leptin, an endocrine signaling protein (adipokine), which triggered the development of adipoendocrinology. Today, more than hundred adipokines are identified. Here an update of adipose-derived neurotrophic factors and neuropeptides and their receptors is presented, raising a hypothesis of neuroendocrine potential of this dynamic tissue. ***Biomed Rev 2008; 19: 45-48.***

Key words: adipose tissue, neurotrophins, neuropeptides

INTRODUCTION

Today, adipose tissue (mainly its white phenotype) is increasingly recognized as a dynamic tissue which may, by sending and receiving different types of protein and non-protein signals, communicate with many organs in the human's body. Indeed, an extensive body of work has revealed that adipose tissue expresses not only metabolic, but also endo-, auto-, intra- and paracrine phenotypes. This new biology is achieved predominantly through synthesis, storage, and release (that is, secretion) of adipokines, which include more than hundred highly active signaling proteins abundantly secreted by adipose tissue, particularly when hypertrophied, inflamed or other related conditions (1-12). These factors may contribute to brain, immune, vascular and metabolic functions, including feeding behavior, memory, learning, circadial rhytm, inflammation, immunity, vascular tone, and insulin resistance.

There is at present evidence that the sharing of ligands (growth factors, cytokines, and adipokines) and their receptors constitute a "global" molecular language of the human's body, including neural, immune and adipose cells. For instance, leptin and adiponectin exert effects on hypothalamus, sympathetic nerves and immune cells (reviewed in 5-7, 13, also see 14-16). Noteworthy, though the brain has been recognized as

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a prominent site of neuropeptide synthesis for more than 30 years, it was recently be discovered that adipose-specific genes (e.g. for leptin, resistin and adiponectin) are also expressed in the brain (17,18), and that leptin exerts neuroprotective effect (19,20). Moreover, substance P, neuropeptide tyrosine (NPY), calcitonin gene-related protein, kisspeptin and other neuropeptides (21-26) as well as amino acid neurotransmitters (27) are also produced by adipose tissue. In the same vein, most hypothalamic and pituitary neuropeptides, hormones and releasing factors, termed "adipotrophins" (28), express their receptors in adipose tissue, creating hypothalamic-pituitary-adipose axis (29), and possibly, pineal-adipose axis. Further, adipose stem cells appear to be a promising therapeutic tool in brain injury (30,31). Noteworthy, various neurotrophic factors including nerve growth factor (NGF), brain-derived neurotrophic factor (24,32-36), also vascular endothelial growth factor and angiopoietin (37-39), are produced and released from adipose tissue.

While NGF was first discovered by Rita Levi-Montalcini in 1951 as nerve growth stimulating factor produced in largest amount by submandibular glands (40, also 41 for extraneuronal actions of NGF, and 42,43 for BDNF), it appears today that the adipose tissue might be a major biological source of NGF and other neurotrophic factors as well as neuropeptides and neurotransmitters, selected examples being indicated in Table 1. Altogether, this complex secretory capacity raises a hypothesis of neuroendocrine potential of adipose tissue.

***Table 1**. Adipose tissue-produced factors affecting nerve cells**

Neuropeptides
Neuropeptide tyrosine (NPY)
Substance P
Calcitonin gene-related peptide
Adrenomedullin
Somatostatin
Agouti protein
Kisspeptin

Neurotrophic factors
Nerve growth factor
Brain-derived neurotrophic factor
Ciliary neurotrophic factor
Metallothioneins
Glial cell line-derived neurotrophic factor
Angiopoietin-1
Vascular endothelial growth factor

Neurotransmitters
Glutamate
Gamma-aminobutyric acid (GABA)

Others
Leptin
Adiponectin
Insulin-like growth factor
Free fatty acids

** References included 14-16, 21-29, 32-38, 44.*

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