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BRAIN-DERIVED NEUROTROPHIC FACTOR: A NEW ADIPOKINE

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Since leptin discovery in 1994, an extensive body of work has been demonstrating that adipose tissue (mainly its white phenotype) expresses not only metabolic, but also endocrine and paracrine phenotypes, particularly in adipobiology of disease. This new biology is achieved predominantly through secretion of adipokines, which include more than hundred highly active signaling proteins. However, studies on adipobiology of neurotrophins have recently emerged, nerve growth factor being one example of adipose-derived neurotrophins. Here we present data showing that brain-derived neurotrophic factor is also expressed in both white and brown adipose tissue. ***Biomed Rev 2007; 18: 85-88.***

Key words: adipose tissue, neurotrophins, diabetes, stress

INTRODUCTION

Today, there is a growing awareness that the adipose tissue is an active endocrine and paracrine organ producing multiple signaling proteins designated adipokines (1-6). There is evidence indicating that the neurotrophin nerve growth factor (NGF) is also produced by adipose tissue (2,7,8), whereas to the best of our knowledge, there is only one paper (9) revealing adipose-derived brain-derived neurotrophic factor (BDNF), another important member of the protein family of neurotrophins. Neurotrophins exert their action not only on nerve cells, but also act on a number of other cell types including immune cells (10) and pancreatic beta cells (11). Recent studies also demonstrate that NGF and BDNF exert metabotrophic effects on glucose and lipid metabolism (5,11,12) and that the plasma concentration of NGF and/or BDNF of subjects with coronary atherosclerosis (7), acute coronary syndrome (13), metabolic syndrome (7,14,15) and obesity/diabetes (15,16) is significantly altered (also see 17,18). Hence the question was asked whether the presence of BDNF might also be altered in both white and brown adipose tissues (WAT and BAT, respectively).

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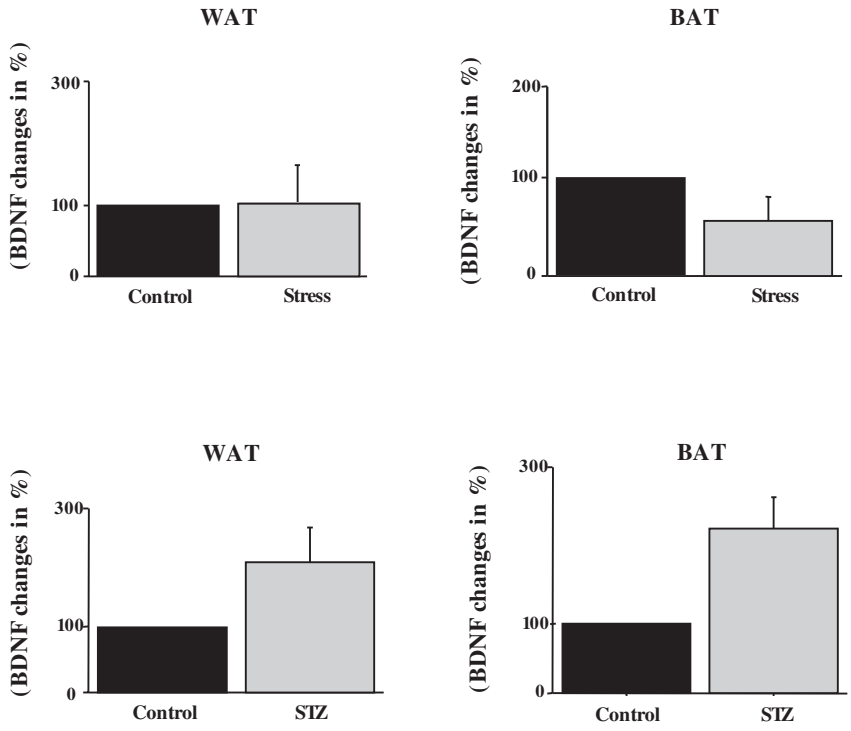

Figure. *The concentration of BDNF in epicardial white adipose tissue (WAT) and brown adipose tissue (BAT) of controls compared to the concentration of BDNF in stressed mice (Stress) and diabetic rats (STZ). The BDNF concentration is expressed as pg/g of tissue and all assays were performed in duplicate. Data are represented as pg/g wet tissue and all assays were performed in duplicate.*

Stress was produced in adult male mice of Swiss CD-1 strain first by social isolation for 8 weeks followed by housing with a fellow male mice of the same strain and age for 60 min, isolated for the same time period. This profile leads to aggressive behavior and fighting. Intact male subjects of the same strain and age were used as control group.

Diabetes was induced in Sprague Dawley male rats by a single intravenous injection of streptozotocin (STZ) at a dose of 60 mg/kg dissolved in PBS (17,18). Rats were considered diabetic and included in the study if they had a fasting plasma glucose level >350 mg/dl. An equal number of male rats received a physiological solution and served as controls.

Stressed and diabetic animals and their respective controls were sacrificed with an overdose of Nembutal, and WAT of the epicardial region and BAT of the interscapular region were taken and used for BDNF immunoenzymatic assay, and for paraformaldehyde fixation for histological analysis (data not shown).

Brain-derived neurotrophic factor was measured by an ELISA kit, "BDNF Emax Immunoassay System number G7611" by Promega, (Madison, WI, USA), following the manufacturer's instructions.

For housing, care and experimental procedures, we followed the guidelines indicated by Intramural Committee and Institutional Guidelines in accordance with National and International law (EEC council directive 86/609, OJ L 358, 1, 12 December1987) and the NIH principles of laboratory animal care (NIH publication no. 85-23, revised 1985).

WAT AND BAT SYNTHESIZE AND STORE BDNF

Diabetic rats displayed enhanced levels of BDNF in the adipose tissues analyzed ($p<0.05$). Specifically, ANOVA revealed a mild increase in both WAT and BAT ($p=0.08$ in post-hocs). However, BDNF presence was not altered in stressed mice (Figure).

The cellular source of BDNF in WAT and BAT is not known. Since the adipose tissue contains mast cells (19), and these cells are known to be both source of and target for NGF (10,20), we investigated the number of mast cells in WAT and BAT (data not shown).

BDNF IS A NEW ADIPOKINE

A novel aspect of our study is the observation that BDNF is found in both BAT and WAT of mice and rats, suggesting that BDNF might be a new member of the adipokine family of proteins. Whether NGF and BDNF play similar, overlapping or different roles in adipose tissue is at present not clear. Nevertheless, BDNF is known to be a potent metabokine, that is, exerts various metabotrophic effects, including anorexigenic and anti-diabetic effects (5,11,12,21-26). Note that in addition to NGF (2,7,8), BDNF (9 and present data) and other neurotrophic factors (5,26), various neuropeptides such as *agouti* protein, somatostatin, adrenomedullin, calcitonin gene-related peptide, substance P and neuropeptide tyrosine (NPY) (27-33) as well as receptors for neuropeptides and hypothalamic and pituitary hormones are expressed in adipose tissue (34-36), raising a hypothesis of neuroendocrine potential of adipose tissue.

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