INTRODUCTION

The prevalence of cardiometabolic disease including atherosclerosis, hypertension, obesity, type 2 diabetes mellitus, and the metabolic syndrome is rising dramatically in developed and developing countries. Because clustering all known major risk factors in one individual, the metabolic syndrome contributes to increased mortality from myocardial infarction and stroke (1-3). Recently the neurotrophins nerve growth factor (NGF) (4) and brain-derived neurotrophic factor (BDNF) (5) were implicated in a positive control of various metabolic function, including glucose, lipid and energy homeostasis (6,7) as well as in the pathogenesis of cardiometabolic diseases (8-14).

Since its discovery in 1951 by Rita Levi-Montalcini, it is now well recognized that NGF is synthesized, stored, and released by submandibular salivary glands, we investigated the structure and function of these glands. Here we present our scintigraphic and echographic results of submandibular glands of patients with advanced stage of metabolic syndrome: (i) scintigraphic analysis using the radiotracer (99m)Tc-pertechnetate showed an inhibition of salivary gland excretory activity, and (ii) echographic evaluation revealed a parenchymal destruction and a prominent fibrosis of the glands. Both suggestive for the involvement of submandibular glands in decreased secretion of NGF and BDNF as implicated in the pathogenesis of metabolic syndrome.


Key words: cardiometabolic diseases, echography, NGF, BDNF, scintigraphy

SUBMANDIBULAR GLANDS IN THE METABOLIC SYNDROME

Mariana G. Hristova¹, Borislav Chaushev², Aneliya Klissarova², and Tanya Kovacheva¹
¹Private Endocrinology Consulting Office and ²Department of Nuclear Medicine, University St Marina Hospital, Varna, Bulgaria

In addition to their stimulatory action on neuronal differentiation and survival, a variety of neurotrophic factors, such as nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and ciliary neurotrophic factor, exert metabotrophic effects, including improvement of glucose, lipid and energy homeostasis. It was recently reported that plasma levels of both NGF and BDNF are reduced in patients with advanced metabolic syndrome and with acute coronary syndromes, and that NGF tissue content is decreased in human atherosclerotic coronary arteries. Since NGF and BDNF are synthesized, stored, and released by submandibular salivary glands, we investigated the structure and function of these glands. Here we present our scintigraphic and echographic results of submandibular glands of patients with advanced stage of metabolic syndrome: (i) scintigraphic analysis using the radiotracer (99m)Tc-pertechnetate showed an inhibition of salivary gland excretory activity, and (ii) echographic evaluation revealed a parenchymal destruction and a prominent fibrosis of the glands. Both suggestive for the involvement of submandibular glands in decreased secretion of NGF and BDNF as implicated in the pathogenesis of metabolic syndrome.


Key words: cardiometabolic diseases, echography, NGF, BDNF, scintigraphy

INTRODUCTION

The prevalence of cardiometabolic disease including atherosclerosis, hypertension, obesity, type 2 diabetes mellitus, and the metabolic syndrome is rising dramatically in developed and developing countries. Because clustering all known major risk factors in one individual, the metabolic syndrome contributes to increased mortality from myocardial infarction and stroke (1-3). Recently the neurotrophins nerve growth factor (NGF) (4) and brain-derived neurotrophic factor (BDNF) (5) were implicated in a positive control of various metabolic function, including glucose, lipid and energy homeostasis (6,7) as well as in the pathogenesis of cardiometabolic diseases (8-14).

Since its discovery in 1951 by Rita Levi-Montalcini, it is now well recognized that NGF is synthesized, stored and, via exo- and endocrine pathway, released by submandibular salivary glands...
(15-18). It was recently demonstrated that BDNF is also an endocrine product of these glands (19,20). Further, a new pathway of neuro-immuno-endocrine interactions has been established, namely the submandibular gland-cervical sympathetic trunk axis; it has important implications for inflammation and tissue recovery (21-24).

We therefore examine both structure and function of submandibular glands in patients with advanced metabolic syndrome. The submandibular gland has been regarded as an age-stable organ in spite of reports on its structural changes with aging (18). Twenty patients with advanced stage of metabolic syndrome were studied (mean age 45.69 +/- 2.18) and 7 controls corresponding in age and sex, without a family history of diabetes mellitus or premature coronary atherosclerosis.

Quantitative analysis of (99m)Tc-pertechnetate scintigraphy has been used in the evaluation of salivary gland function, using single head Gamma Camera System, Siemens, Diacam 1995. 2 mCi (99m)Tc-pertechnetate was injected intravenously (25). The radiopharmaceutical was accumulated in the salivary glands and emitted through their channels. Citric acid was given orally on the 20th minute to stimulate salivation and the salivary gland drainage was visualized. The time-activity curves were plotted based on the obtained scintigraphic images and the functional status of the salivary gland and its drainage capacity evaluated. From the twenty investigated patients with metabolic syndrome, 8 revealed normal fixation of the radioactive substance and preserved function. In the remaining 12 patients a low radioactive nuclide fixation was detected.

Echographic test of the submandibular gland was performed by Fukuda ultrasound diagnostic apparatus. The results showed statistically significant increase in the size of submandibular glands as well as echographic data of tissue fibrosis.

In conclusion, in patients with advanced metabolic syndrome, the decreased plasma NGF and BDNF levels may in part result from submandibular gland dysfunction. Certainly, other tissue source of these neurotrophins, such as adipose tissue (see Töre and Tunçel, and Sornelli et al in this volume of Biomedical Reviews), may also be pursuit. Likewise, the presence of mast cells in the submandibular gland be evaluated because these cells are source of and target for NGF (4,26) and possibly BDNF.

REFERENCES

5. Lebrun B, Barichert B, Moysse E, Jean A. Brain-derived neurotrophic factor (BDNF) and food intake regulation: a minireview. Auton Neurosci 2006; 126-127: 30-38.
13. Sposato V, Manni L, Chaldakov GN, Aloe L. Strepto-


