ASSOCIATION OF BRAIN-DERIVED NEUROTROPHIC FACTOR WITH PSYCHOSOMATIC DISORDERS IN HYPERTENESIVE PATIENTS

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Introduction and Objectives

• BDNF plays an important role in the pathomechanism of depression and cardiovascular (CV) diseases:

➢ BDNF gene polymorphism increases susceptibility to bipolar depression *(Post. 2007; Chen. 2006)*

➢ serum BDNF levels decrease in major depression. but increase when symptoms are relieved by antidepressant treatment *(Hashimoto. 2004)*

➢ plasma BDNF correlates with the risk factors of CV *(Golden. 2010)*

➢ plasma BDNF decreases in acute coronary syndrome *(Manni. 2005)*

• Mood disorders are independent risk factors of CV *(Pratt. 1996; Musselman. 1998)*

• Affective temperaments have pathophysiological roles *(Előry. 2011)*

Objectives: We investigated in hypertensive patients the change of serum BDNF level and its correlation with the arterial stiffness parameters and psychosomatic disordes including depression, anxiety and affective temperaments.

Methods

• **Patients:** three separate primary care, Budapest

• **Cross-sectional study**:

•101 patients with chronic hypertension (> 12 months antihypertensive medication, 23 had type-2 diabetes mellitus, 16 anxiolytic medication)

•16 age-matched healthy controls

• **Questionnaires:**

• **Affective temperaments:**Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A).

• **Depression**: Beck Depression Inventory (BDI)

• **Anxiety**: Hamilton Anxiety Scale (HAM-A)

• **Measurement of serum BDNF :** ELISA kit

• **Evaluation of laboratory parameters**

• **Arterial stiffness recordings:** PulsePen

Results

Baseline demographic, clinical data, laboratory parameters and medication

	Control N=16	HT N=62	HT+DM N=23	HT+BZD N=16
N (male:female)	16 (6:10)	62 (24:38)	23 (6:17)	16 (4:12)
Age (year)	66.1 ± 1.36	62.6 ± 1.57	64.1 ± 1.98	67.3 ± 2.63
Body height [cm]	168 ± 2.04	167.8 ± 1	163.5 ± 1.94	165 ± 2.11
Body weight [kg]	74.1 ± 2.45	79.9 ± 1.86	**83.7 ± 2.1***	76.6 ± 4.27
AC [cm]	99.1 ± 2.78	102.8 ± 1.72	**106 ± 2.02***	99.9 ± 3.33
BMI [kg/m2]	26.2 ± 0.66	28.3 ± 0.59	**31.4 ± 0.89***	28 ± 1.33
Glucose [mmol/L]	5.26 (4.89-5.84)	5.36 (5.03-5.98)	**7.13 (6.3-7.77)***	5.11 (4.83-6.38)
CKD-EPI GFR [mmol/L]	78 ± 3.03	78.13 ± 2.15	75.3 ± 3.16	76.42 ± 4.02
Uric acid [µmol/L]	317.3 ± 13.5	314.2 ± 12	323.2 ± 12.12	318.4 ± 13.5
Cholesterol [mmol/L]	5.55 (4.78-6.6)	5.31 ± 0.13	**4.3 (3.7-4.7)***	5.5 ± 0.24
Triglyceride [mmol/L]	1.26 ± 0.13	1.69 ± 0.15	1.62 (1.12-1.97)	**1.98 ± 0.21***
ACE-inhibitors [n (%)]	-	41 (66.13%)	15 (65.22%)	8 (50%)
ARBs	-	14 (22.58%)	17 (73.91%)	4 (25%)
Calcium-channel blockers	-	28 (45.16%)	9 (39.13)	8 (50%)
Beta-blockers	-	29 (46.77%)	14 (60.87%)	**14 (87.5%)#**
Diuretics	-	34 (54.84%)	**15 (65.22%)#**	5 (31.25)
Antiplatelet medication	-	15 (24.19%)	**13 (56.52%)#**	7 (43.75%)

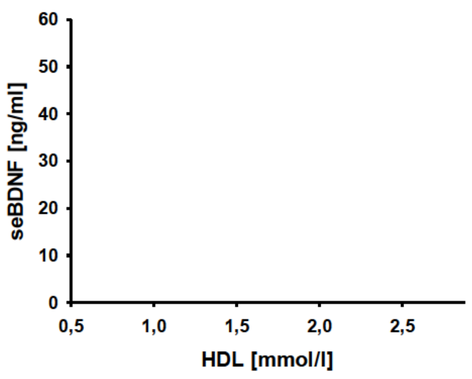
Haemodynamic data and arterial stiffness parameters

	Control N=16	HT N=62	HT+DM N=23	HT+BZD N=16
HR [1/min]	71.9 ± 2.06	70.4 ± 1.2	71.1 ± 2.22	76.2 ± 3.97
SBPB [Hgmm]	118.6 ± 2.22	126.2 ± 1.87	**128.6 ± 3.02***	125 ± 3.41
DBPB [Hgmm]	68.4 ± 1.5	69.8 ± 1	67.4 ± 1.7	69.5 ± 2.29
MBPB [Hgmm]	88.2 ± 1.53	90.8 ± 1.16	89.7 ± 1.92	88.6 ± 2.44
PPB [Hgmm]	50.2 ± 1.86	56.4 ± 1.5	**61.2 ± 2.31***	55.5 ± 2.78
Central SBP [Hgmm]	115.9 ± 2.25	122.8 ± 1.97	**127 ± 3.1***	122 ± 3.02
Central DBP [Hgmm]	68.4 ± 1.5	66.8 ± 1	67.4 ± 1.7	69.5 ± 2.29
Central MBP [Hgmm]	88.2 ± 1.53	91.7 ± 1.2	91.5 ± 2	90.8 ± 2.31
Central PP [Hgmm]	47.5 ± 2.05	53.1 ± 1.6	**59.6 ± 2.59***	52.5 ± 2.51
Amplification pressure [Hgmm]	14.4 (12.2-17.2)	15.1 (11.8-17.6)	13.8 (11-16.3)	15 (11.5-18.4)
Pulse pressure amplification	1.12 ± 0.03	1.08 ± 0.01	**1.04 ± 0.02***	1.09 ± 0.05
PWV [m/sec]	8.6 (7.41-9.61)	8.52 (7.4-9.83)	9.2 (8.42-9.91)	9.4 (8.41-11.81)
A.I. (%)	12 (7.9-17.8)	17.48 ± 1.54	**20 (13.5-27.5)***	18.19 ± 3.85

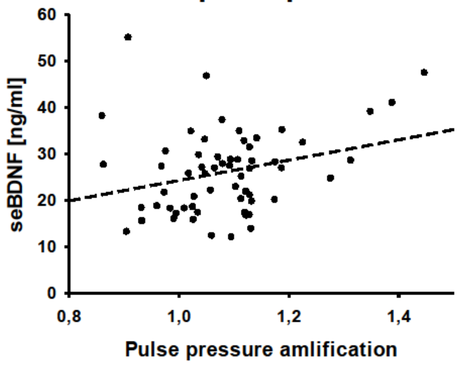
Data represent Mean SEM. *p < 0.05 *vs.* Control, #p < 0.05 *vs.*HT. *AC: abdominal circumference; BMI: body mass index; CKD-EPI GFR: glomerular filtration rate assessed by the chronic kidney disease epidemiology collaboration glomerular filtration rate equation; ARBs: angiotensin II receptor blockers , HT: hypertensive, DM: diabetes mellitus, BZD:* benzodiazepine *, HR: heart rate; SBPB: systolic brachial pressure; DBPB: diastolic brachial pressure; MBPB: mean brachial pressure; PPB: brachial pulse pressure; Central SBP: central systolic blood pressure; Central DBP: central diastolic blood pressure; Central MBP: central mean blood pressure; Central PP: central pulse pressure; PWV: pulse wave velocity; AI: augmentation index.*

Correlations

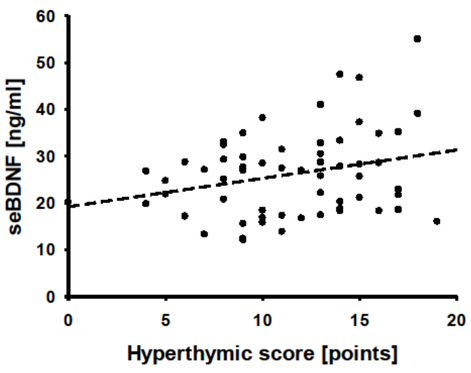
Serum BDNF and serum HDL



Serum BDNF and pulse pressure amplification



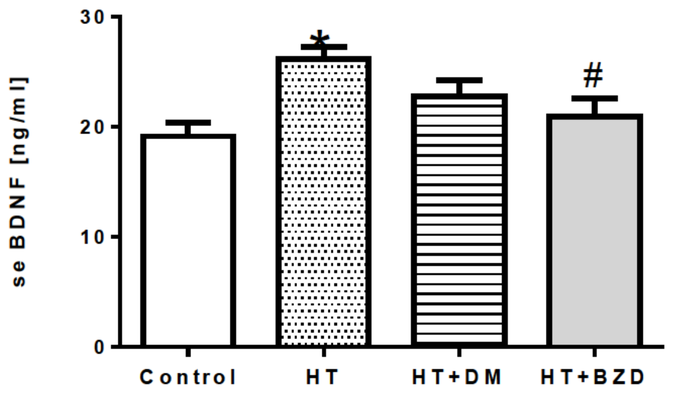
Serum BDNF and TEMPS-A hyperthymic score



TEMPS-A, BDI and HAM-A scores of the subjects

	Control N=16	HT N=62	HT+DM N=23	HT+BZD N=16
Depressive	5.5 (4-6)	7 (5-9)	7 (4-10)	**8.5 (6-12)*#**
Cyclothymic	2 (0.25-3.75)	2.5 (1-5)	3 (1-7)	**6 (4.25-9.5)*#**
Hyperthymic	12.63 ± 0.98	11.4 ± 0.51	11.17 ± 0.82	**8.75 ± 1.26*#**
Irritable	2.5 (2-4)	3 (2-6)	3 (2-5)	**6 (3-9.75)***
Anxious	3 (1-5.75)	5 (2-9)	7 (1-8)	**13 (8.25-18.75)*#**
BDI	2 (1-5.5)	**5 (3-9)***	**6 (4-11)***	**13 (7.5-15.75)*#**
HAM-A	2.5 (0-5.5)	**5 (2-9)***	**5 (2-12)***	**18 (7-25)*#**

Serum BDNF levels



*p < 0.05 *vs.*Control, #p < 0.05 *vs.*HT. , *HT: hypertensive, DM: diabetes mellitus, BZD:* benzodiazepine

Summary

• BDNF level was higher in hypertensive patients compared to controls. However in those patients who took regularly anxiolytic treatment the level of BDNF was similar to controls.

• Positive correlations were found between BDNF and HDL levels, pulse pressure amplification and hyperthymic temperament score.

Conclusions

Our results suggest a complex psychosomatic involvement of BDNF in the pathophysiology of hypertension. The positive correlation of increased serum BDNF in treated chronic hypertensive patients with the hyperthymic temperament score and HDL level suggest a vasculo-protective effect of the protein. Therefore BDNF could serve as therapeutic target in the future in cardiovascular diseases.

Fundings: LP008/2015. Hungarian Society of Hypertension. OTKA.- K100909. - K 108688. KMR 12-1-2012-0074

DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.