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Brain-Derived Neurotrophic Factor (BDNF) Levels In Relation To Depression in Egyptian Diabetic Women: A Pilot Study

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Abstract

Background: Brain-derived neurotrophic factor (BDNF) is a crucial moderator of neuronal plasticity in adults, a potential association between BDNF and depression has been reported. Besides BDNF plays a role in glucose and energy metabolism. **Methods:** This work included 180 women (25-55 years old). Ninety diabetic patients with the clinical diagnosis of depression and 90 were normal controls. Plasma BDNF was evaluated using ELISA. The Zung Self‐ Rating Depression Scale (SDS) consisting of 20 objects with a Likert‐ type scale after each was used. HbA1c were measured in each patient using a clinical auto-analyzer. **Results:** BDNF levels in serum decreased significantly in diabetic depressed women compared to controls. Moreover, BDNF levels were inversely proportional to age, BMI, HbAc1 and LDL.**Conclusion**: The study suggests that age, BMI, HbAc1 have a definite impact on the circulating levels of BDNF in peripheral blood. The outcomes delineate that BDNF could participate in glucose impairment and lipid metabolism in diabetic patients.

*Keywords***:** Brain-Derived Neurotrophic Factor (BDNF); BMI; Depression; HbAc1; lipid profile; type 2 diabetes mellitus

Introduction

Pharmacological, genetic, and behavioral studies have associated the BDNF dysregulation to neurological and chief psychiatric disorders, comprising anxiety and mood disorders [1][2]. Several reports have presented a potential link between BDNF and depression [3][4]. Platelets is the master source of the peripheral BDNF, that store, bind, and release BDNF upon activation [5]. Some researches proposed that BDNF plays an imperative role in regulating body weight and energy homeostasis [6][7]. Furthermore, a previous meta-analysis proven a mutual linkage between obesity & depression in humans [8]. Nevertheless, the association between body weight and BDNF in depression is not well-defined. BDNF appears to be involved in the favorable action of exercise, that plays an imperative part in the management and prevention of DM type 2, obesity, and other features of metabolic syndrome [9]. Besides, BDNF regulates energy metabolism and glucose and prevents β cells exhaustion. Consequently, BDNF could be useful in the management and prevention of numerous diseases comprising diabetes mellitus[8][10].

Significant relationship among BDNF gene variant rs6265 and the seriousness of depression was noted in patients [11][12]. Patients with depression and type 2 diabetes exhibited increased serum cortisol and circulatory levels of miR-128 whereas diminished BDNF concentrations and shortened telomeres were described. These neuroendocrine signs were more significantly changed in individuals with combined depression and diabetes [13].

Accordingly, the objective of the present work was to estimate BDNF concentrations in serum of depressed diabetic patients and explore the probable relations

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between BDNF levels and other factors such as body mass index (BMI), age and serum lipids.

1. Patients and Methods

This work included 180 women (25-55 years old). Ninety diabetic patients with the clinical diagnosis of depression and 90 were normal controls.

Assessment of Lipid Profile

Blood samples were obtained after overnight fasting. Serum cholesterol, triglyceride, and high-density lipoprotein cholesterol (HDL-C) were measured by enzymatic colorimetric methods with commercially available kits (COBAS 311, Roche Diagnostics GmbH, Mannheim, Germany), and low-density lipoprotein cholesterol (LDL-C) was calculated according to the Friedewald formula.

Assessment of Blood glucose

Blood glucose measures were determined enzymatically using the hexokinase method (Roche Diagnostics GmbH, Mannheim, Germany).

Assessment of HbA1c

Blood HbA1c was determined with a COBAS 311 analyzer using the particle-enhanced immunoturbidimetric method (Roche Diagnostics, Mannheim, Germany.

Quantification of BDNF

BDNF levels in serum were measured using commercial enzyme-linked immunosorbent assays (ELISA) following the manufacturer's instructions (DuoSet BDNF ELISA, R&D).

Written informed consent was taken from all the patients. Patients with history of epilepsy, autoimmune disease or malignant disease were excluded. The Zung Self‑Rating Depression Scale (SDS) consists of 20 items with a Likert‑type scale after each item. The scores for each item ranged from 1 to 4, and the SDS ranges from a raw score of 20 to a raw score of 80. Some items were reverse scored (i.e., they go from 4 down to 1). SDS scores were classified as normal (<50), mild depression (50–59), moderate to marked major depression (60–69), and severe to extreme major depression (>70) [14].

Statistical analysis

The data obtained from this study was analyzed using SPSS (Chicago, IL, USA). Nearly all parameters examined were asymmetrically distributed. Thus, correlations were calculated using Spearman's correlation coefficient. For the comparison of cohorts, the non-parametric Mann–Whitney U-test for two independent samples was used. P-values <0.05 were regarded as statistically significant. Boxplot graphs were created using SPSS, displaying the median (line within the box), interquartil range (edges of the box) and extremes (vertical lines). Outliers (all cases more distant than 1.5 interquartil ranges from the upper or lower quartil) were omitted in the graphs. The relationships between BDNF, and obesity indices were examined with Pearson's correlations.

2. Results

The characteristics of the participants are illustrated in Table (1). All of 180 adults accepted to participate in the work. Significant alterations in age, BMI and HbAc1were found between the depressed diabetic women versus the controls. While no differences were observed between them regarding the serum lipids.

Table (2) shows the correlations between plasma BDNF, age, BMI, HbAc1 and serum lipids in patients and controls. A negative correlation between plasma BDNF levels, age, BMI, HbAc1 and LDL was observed in patients but not in controls. There was no significant correlation of BDNF with lipid parameters among patients and controls.

Figure 1 shows significant decrease of BDNF levels in patients compared to controls.

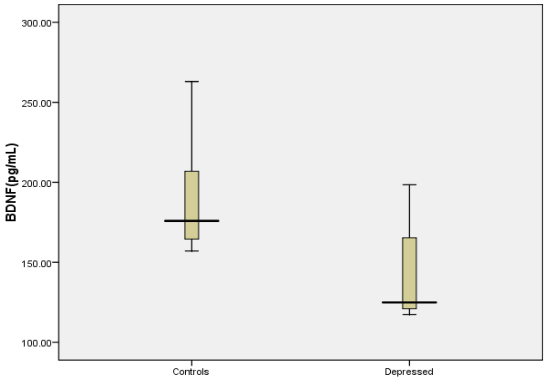

Figure 1: Plasma BDNF in cases and controls

Table (1): The laboratory findings, clinical features and characteristics of the studied groups

Variables	Depressed Mean± SD	Controls Mean± SD
Age	56.30*±1.33	35.62±1.40
BMI	34.25*± 1.745	17.48±1.42
FBS	186.20*±53.43	92.37±+35.03
HbA1c	7.4600*±1.03	4.37±1.32
TG	121.08±33.80	92.48±35.85
HDL	35.34±14.04	40.92±7.44
LDL	118.37±33.53	79.31±19.63
Total cholesterol	143.45±38.67	145.45±23.06

*P < 0.05 (Significant difference between patient and control group

Table (2): Correlation of plasma BDNF, age, BMI, HBA1C and serum lipids in cases and controls

	Depressed		Controls	
Parameters	r	p	r	p
BDNF- BMI	-0.562	0.002	-0.062	0.62
BDNF- Age	-0.433	0.052	-0.032	0.52
BDNF- HbA1c	-0.544	0.002	-0.244	0.42
BDNF- cholesterol	0.047	0.800	0.147	0.450
BDNF- HDL	0.183	0.323	0.123	0.123
BDNF- TG	-0.122	0.515	-0.022	0.615
BDNF- LDL	-0.62	0.039	-0.062	0.568

3. Discussion

The current study inspected alterations in the serum level of BDNF and its correlations with the clinical and biochemical parameters in diabetic women with depression. We found that levels of BDNF were significantly lower in patients in comparison with control individuals [15]. BDNF concentrations were diminished in DM T2 and were independent of obesity as Krabbe et al. found [16]. However, some researchers found an association of serum levels of BDNF with stress and anxiety. A previous work found decreased serum levels of BDNF in post-traumatic stress disorder. The administration of exogenous BDNF could prevent the detrimental impact of the metabolic syndrome. We observed a significant reduction of BDNF levels in serum with increasing the age. This is supported by the observation of Golden et al., [17] that delineated the significant decrease in BDNF serum levels in females interrelated with body weight and advancing age.

Some evidence indicated declining expression of the high-affinity BDNF receptor trkB in certain regions of brain and peripheral ganglia throughout the normal aging process [18][19].
In this study, a negative correlation between serum BDNF levels, age, BMI, HbAc1 and LDL was observed in patients but not in controls.

Tsuchida et al., [20] reported a positive association among serum concentrations of BDNF and diastolic blood pressure, triglyceride, low-density lipoprotein (LDL) cholesterol, total cholesterol, adipose tissue mass and body mass index. Furthermore, the preceding studies revealed that serum levels of BDNF are diminished in DM type 2 independently of obesity [10][21].

Some studies have postulated an association between glucose levels or lipid and BDNF in animal models as BDNF decreases the free fatty acids levels, cholesterol and glucose in blood [19][20]. Moreover, BDNF levels are lessened in obese persons. In obesity the role of BDNF appears to be mainly centrally mediated but peripheral contribution could not be disregarded. Some researches proposed that BDNF-knockout rats were more disposed to obesity when compared to control [20][22]. Nevertheless, once tropomyosin receptor kinase B (TrkB) is genetically deleted, a primary BDNF receptor, caused hyperphagia and obesity [23]. These results proposed a crucial role of BDNF in reducing appetite, thus reinforce a negative energy balance. CNS TrkB triggers a cascade of reactions, once activated with BDNF which consequently reduces eating desire and weight gain. Previous studies proposed that different environmental, genetic, psychological, biological, and social factors are encompassed in the prognosis and pathophysiology of depression [24][25].

In fact, it has been proposed that the relating connection between DMT2 and depression possibly will be BDNF [26]. However, it is identified that depression is a risk factor for diabetes mellitus type 2 development, whereas greatest patients with diabetes mellitus type 2 also have depression. This led to the elucidated that BDNF could has a significant role associating type 2 diabetes mellitus and depression [22].

Neurotrophic elements like brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and glial cell line-derived neurotrophic factor (GDNF) are the essential signaling molecules in the development and maintenance of the peripheral and central nervous systems [27]. The function and concentration of BDNF in diabetes seems to be connected with and disturbed by the occurrence of insulin resistance [28][29]. Explicitly, diabetes mellitus augmented the risk of depressive symptoms, and the transition to death was greater in individuals with depressive symptoms and diabetes mellitus [29][15]. It was evidenced that a low BDNF concentrations in serum was a risk factor for diabetic retinopathy. Additionally, in people with diabetic peripheral neuropathy, BDNF serum concentrations were lower when compared with a group with diabetes without complications [30][31] [32] [33]. The BDNF could be a novel therapeutic process in controlling of metabolic syndrome, DMT2 and obesity in both their avoidance and treatment [26] [27][34].

4. Conflicts of interest

None

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5. References

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