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Lipid profile in Parkinson's disease: The potential role of brain-derived neurotrophic factor

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ABSTRACT

Background: Parkinson's disease is a neurodegenerative disease manifested as increased tremor, bradykinesia, rigidity, and postural instability. Brain-derived neurotrophic factor (BDNF) is essential for neurocognitive function. However, its cardiometabolic effect has recently been identified in health and disease, but not in PD. Therefore, the current study examined the relationship of BDNF with glucose and lipid profile.

Methods: This was a cross sectional comparative study where PD patients ($n = 26$) and age-matched healthy controls ($n = 27$) were recruited. Blood samples were drawn to determine BDNF, glucose, and lipid profile including total cholesterol (TC), HDL, LDL, triglyceride (TriG).

Result: The linear regression showed that BDNF predicted 11.9 % of TC ($p = 0.05$), 3.0 % of HDL ($p = 0.003$), 27.3 % of LDL ($p = 0.006$), 16.6 % of TriG ($p = 0.04$), 15.8 % of TC/HDL ($p = 0.06$), 22.1 % of TC/LDL ($p = 0.01$), and 35.1 % of TriG/HDL ($p = 0.001$) but not glucose (B = -0.006; CI = -0.19/0.18; F = 0.005; $p = 0.9$) and LDL/HDL (B = 0.06; CI = -0.17/0.3; F = 0.3; $p = 0.6$). Subsequent ANCOVA revealed differences ($p < 0.05$) in TC, HDL, LDL, TC/LDL, and TriG/HDL but not in glucose, TriG, and TC/HDL among the patients with low-BDNF versus high-BDNF.

Significance: The results demonstrate a relationship of BDNF with lipid profile suggesting the importance of BDNF for lipid metabolism in PD.

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease that affects an estimated 0.3 % (7–10 million people) of the world's population, while the prevalence can be as high as 1–2 % among the elderly [1]. The primary motor symptoms of PD are tremor`, bradykinesia`, rigidity`, and postural instability [2]. Additionally, mental and behavioral changes, sleep problems, depression, memory difficulties, and fatigue are the main non-motor symptoms of PD [3]. The disease is characterized as progressive loss of dopaminergic neurons in the substantia nigra along with the presence of Lewy bodies. The causes of the disease are unknown, however, a combination of genetic, environmental, and lifestyle risk factors have been identified [4]. About 10–20 % of all Parkinson's are attributed to genetic factors. Additionally, age, gender, head trauma, toxins, diabetes, glycemic variability, and physical activity have also been implicated in the etiology of the disease [3].

A meta-analysis study that involved 1496 participants showed an association between decreased level of circulatory brain-derived neurotrophic factor (BDNF) and PD [5]. BDNF is pivotal in the development, maintenance, and healing of the central nervous system [6]. It is found in various brain compartments; however, it is most abundant in the hippocampus and hypothalamus, areas essential for cognition [7]. BDNF is also found in the periphery including cardiovascular, muscular, and adipose tissues. The exact role of BDNF in periphery is still elusive thus deserves more examination and explanation, however it seems to regulate cardiometabolic risk factors including glucose, lipids, and lipoproteins [8–11]. Subsequently, BDNF has been implicated in the

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Table 1
Sociodemographic and clinical characteristics in the patients versus control.

	Patients ($n = 24$)	Control ($n = 27$)	P value
Gender (females, %)	38.5	40.7	–
Age (years)	56.5 ± 13.0	55.4 ± 13.1	0.70
Weight (kg)	69.9 ± 11.1	66.3 ± 9.6	0.20
Height (cm)	164.3 ± 9.5	167.4 ± 9.4	0.0001
BMI (kg/m^2)	26.0 ± 3.7	31.0 ± 5.6	0.001
Heart rate	77.8 ± 12.4	71.0 ± 13.2	0.06
Systolic blood pressure (mmHg)	122.6 ± 14.3	113.5 ± 15.8	0.033
Diastolic blood pressure (mmHg)	73.3 ± 10.3	66.4 ± 10.2	0.018
Mean arterial pressure (mmHg)	89.9 ± 10.9	82. ± 10.9	0.014
Hoehn and Yahr staging scale	1.4 ± 0.5	–	–
MDS-UPDRS (part III)	54.3 ± 29.1	–	–

Data are presented in mean ± SD. MDS-UPDRS: The Movement Disorders Society Unified Parkinson's Disease Rating Scale.

Table 2
Anti-Parkinsonian medications.

Drug name	Number of patients taking the drug
Sinemet	28
Amantadine hydrochloride	14
Sifrol	3
Stalevo	3
Parlodel	2
Gabatnex	2

cardiometabolic disorders including obesity [12], diabetes [13,14], and coronary heart disease [15,16]. In facts, attempts are in progress to develop BDNF mimetics for metabolic disorder therapy [17,18].

While the relationship between BDNF and PD is well established, the lipid and lipoprotein relationship with PD is still equivocal. Studies have shown that lipids are lowered and may accelerate the development of PD while others have shown increased or unchanged lipid profile [19]. For example, low levels of LDL and total cholesterol (TC) are associated with a greater incidence of PD [20], while higher circulatory level and intake [21] reduces the risk of developing [22] and progressing [23] of PD, and improved executive and fine motor function in patients [24]. In contrast, higher levels [25] and consumption [26] of cholesterol might adversely affect the risk and manifestations of PD while HDL reduces the risk of PD [27]. However, a meta-analysis for 246,112 subjects, of which 5488 PD cases, found no relationship between cholesterol level and risk of PD [28]. With respect to glucose homeostasis, long-term glycemic variability with or without diabetes has been shown to be associated with PD development [29]. Therefore, the current study aims at comparing glucose and lipoprotein profile in PD patients versus healthy controls. Additionally, the relationship of circulatory glucose and lipoprotein with BDNF in PD patients was elucidated. According to the previous results [20–24,26–29], the changes in glucose and lipoprotein among the PD patients cannot be predicted while BDNF is expected to be related to glucose and lipoprotein profile in the PD patients. The results of the current study would help in understanding the changes in glucose and lipoprotein profile due to PD and the importance of BDNF for glucose and lipoprotein metabolism in PD patients. Subsequently, examine the therapeutic potential of BDNF in neurodegenerative diseases, particularly PD.

2. Methods

2.1. Patients and recruitment

The study is cross-sectional comparative observational designed to examine BDNF and glucose and lipid profile among PD patients and healthy controls. Sequential PD patients attending routine neurology clinic appointments at King Abdulla University Hospital (KAUH) or Princess Basma Hospitals, Irbid, Jordan were screened for eligibility by a neurology consultant; the clinician who is responsible for their care. Eligible subjects were invited to participate in the study. Age and gender-matched healthy individuals were recruited from the local community to serve as the controls for this study.

Idiopathic PD patients confirmed by neurologist examination ages 30–80 years with sufficient capacity to give informed consent and stage 1–4 in the modified Hoehn and Yahr were recruited to participate. Patients with unstable medical conditions (i.e. uncontrolled diabetes mellitus) or injuries (i.e. hip faction) were excluded from the study. Each participant signed an informed consent after accepting to participate and receiving oral and written information about the study. The study was approved by the Institutional Research Board of Jordan University of Science and Technology, Irbid, Jordan (approval ID: MA20200481).

2.2. Blood sampling

Venous blood (6 mL) was collected from each subject after overnight fasting into EDTA tubes. Tubes were immediately centrifuged, and plasm was transferred into new tubes and stored at −80 °C until used.

2.3. Circulatory blood lipids and glucose

Fasting blood glucose, TC, LDL, HDL, and triglyceride (TriG) were determined in all participants at diagnostic laboratories of King Abdullah University Hospital using the Roche Analyzer and Roche reagents (Roche Diagnostics, Basel, Switzerland). The results are expressed as mmol/L. TC/HDL, LDL/HDL, TriG/HDL, and TC/LDL ratios were subsequently calculated.

2.4. Circulatory BDNF

Plasma BDNF levels were measured by the ELISA method, using commercially available kits (Quantikine kit, R&D system, Minneapolis, USA) according to the manufacturer's instructions [30,31]. Standards were measured in triplicates whereas samples were measured in duplicate. Samples of patients and controls were analyzed together in the same ELISA plates [31]. Plates were read using tat Fax 2100 plate reader (Awareness Technology, Palm City, FL, USA) at 450 nm.

2.5. Statistical analysis

Statistical Package for the Social Sciences (Version 21) was used for all data analysis. Data were presented as mean ± SD and percentages. The Student's t-test was used to compare sociodemographic and clinical characteristics between the patients and the controls. Pearson's product-moment correlation were used to examine the relationship of plasma BDNF with glucose and blood lipid profile including glucose, TC, HDL,

Table 3
ANCOVA comparison for plasma glucose, lipid, and BDNF profile in the patients versus the control.

	Patients (n = 26)	Control (n = 27)	P value
Glucose (mmol/L)	7.1 ± 3.0	6.0 ± 1.7	0.25
Total cholesterol (mmol/L)	4.7 ± 0.7	5.3 ± 1.0	0.18
High density lipoprotein (mmol/L)	1.0 ± 0.2	1.0 ± 0.2	0.60
Low density lipoprotein (mmol/L)	3.2 ± 0.7	3.6 ± 1.0	0.10
Triglyceride (mmol/L)	2.1 ± 1.2	2.9 ± 4.0	0.81
TC/HDL (mmol/L)	4.9 ± 1.2	5.3 ± 1.6	0.70
TC/LDL (mmol/L)	1.5 ± 0.2	1.5 ± 0.4	0.52
Tri/HDL (mmol/L)	2.4 ± 1.9	3.4 ± 5.7	0.90
BDNF (mg/dl)	1.3 ± 1.4	2.6 ± 1.6	[a]0.04

Data are presented in mean ± SD.
[a] Indicate significant.

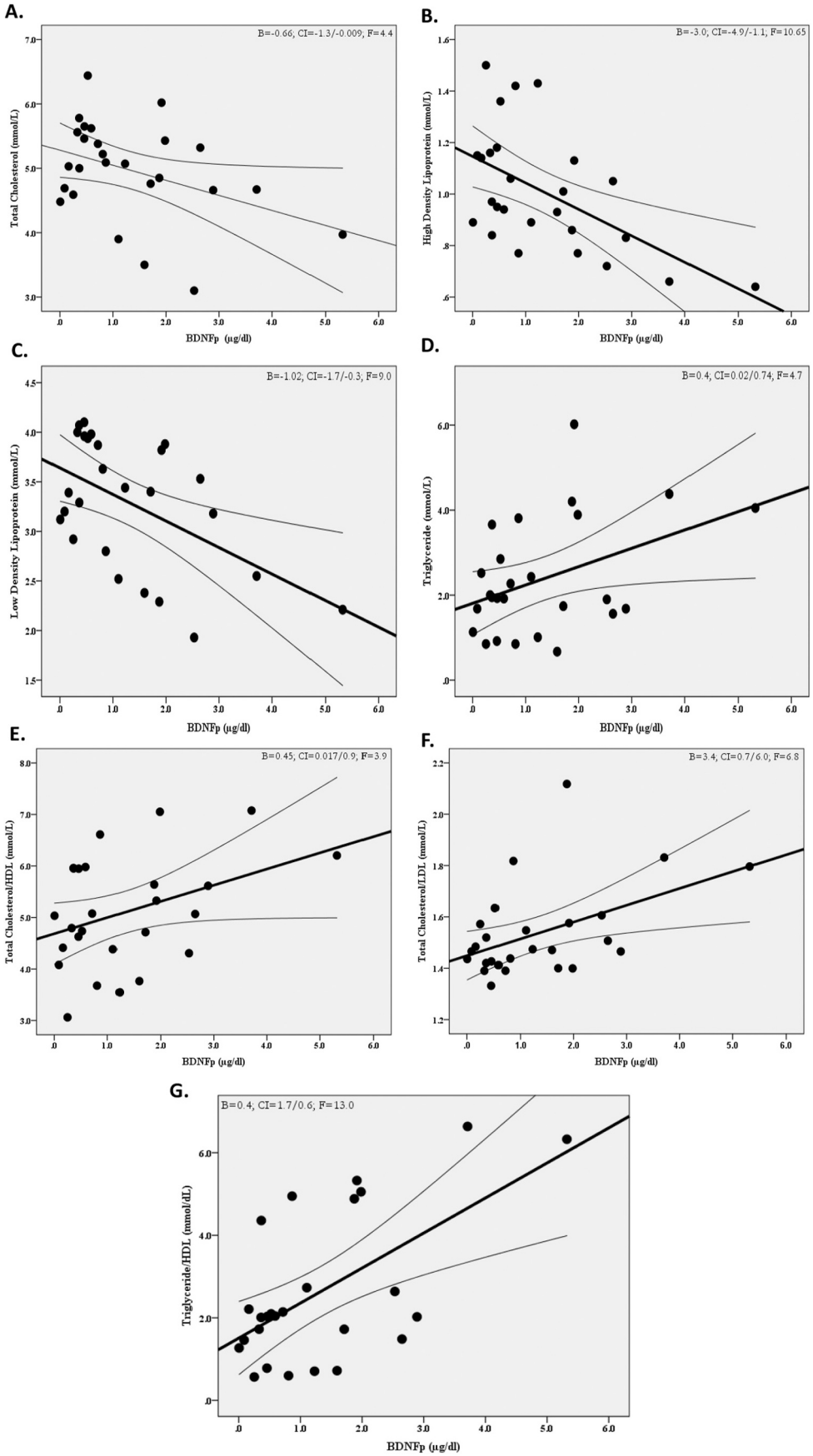

Fig. 1. The linear regression in the PD patients showing BDNF predicted (A) 11.9 % of TC ($p = 0.05$), (B) 3.0 % of HDL ($p = 0.003$), (C) 27.3 % of LDL ($p = 0.006$), (D) 16.6 % of TriG ($p = 0.04$), (E) 15.8 % of TC/HDL ($p = 0.06$), (F) 22.1 % of TC/LDL ($p = 0.01$), and (G) 35.1 % of TriG/HDL ($p = 0.001$).

Table 4
ANCOVA comparison for plasma glucose and lipid profile in the patients with low versus High BDNF.

	Low BDNF (n = 12)	High BDNF (n = 12)	P value
Glucose (mmol/L)	7.2 ± 2.9	7.0 ± 3.5	0.57
Total cholesterol (mmol/L)	5.1 ± 0.5	4.4 ± 0.8	[a]0.007
High density lipoprotein (mmol/L)	1.1 ± 0.2	0.9 ± 0.2	0.06
Low density lipoprotein (mmol/L)	3.6 ± 0.4	2.7 ± 0.7	[a]0.001
Triglyceride (mmol/L)	1.6 ± 0.6	2.7 ± 1.5	0.086
TC/HDL (mmol/L)	4.8 ± 1.0	5.1 ± 1.4	0.70
TC/LDL (mmol/L)	1.4 ± 0.6	1.6 ± 0.2	[a]0.01
Tri/HDL (mmol/L)	1.5 ± 0.7	3.5 ± 2.3	[a]0.04

Data are presented in mean ± SD.
[a] Indicate significant.

LDL, TriG, TC/HDL, LDL /HDL, TriG/HDL, and TC/LDL in the patients. The correlation coefficient (r-value) was used to determine the strength of the relationship of BNDF with glucose and blood lipid profile. ANCOVA was used to compare glucose, TC, HDL, LDL, TriG, TC/HDL, LDL /HDL, TriG/HDL, and TC/LDL among the patients versus the controls and among the patients with low versus high BDNF, after adjusting for age, gender, BMI, and mean arterial pressure. The participants were divided above and below the 50th percentile.

3. Results

3.1. The participants

The participants' sociodemographic and clinical characteristics are presented in Table 1, age, weight, height, BMI, and cardiovascular indices. A total of 24 patients and 27 age-matched healthy controls, with age range 31–76 years, were recruited to the study. As in Table 1, the ranges for the Hoehn and Yahr Staging Scale score and the MDS-UPDRS (Part III) for the patients' sample were 1–4 and 19–93, respectively. Additionally, the patients' prescribed medications are presented in Table 2.

3.2. Relationship of Parkinson's disease with circulatory lipid profile and BDNF

The ANCOVA, shown in Table 3, revealed no differences ($p > 0.05$) in lipid profile measures, whereas plasma BDNF was lower in the patients versus the controls.

3.3. Relationship of BDNF with Lipid Profile

As in Figs. 1, the Pearson's product-moment correlation in the patients only, showed that BDNF was related to TC ($r = -0.40$; $p = 0.05$), ($r = -0.60$; $p = 0.003$), LDL ($r = 0.50$; $p = 0.006$), TriG ($r = 0.40$; $p = 0.04$), TC/HDL (r = 0.40; $p = 0.06$), TC/LDL (r = 0.5; $p = 0.01$), and of TriG/HDL ($r = 0.60$; $p = 0.001$), however, was not related to glucose ($r = -014$; $p = 0.9$). As in Table 4, subsequent ANCOVA revealed differences in TC ($p = 0.007$), HDL ($p = 0.06$), LDL ($p = 0.001$), TC/LDL ($p = 0.01$), and TriG/HDL ($p = 0.05$) but not in glucose ($p = 0.70$), TriG ($p = 0.10$), and TC/HDL ($p = 0.70$) among low-BDNF versus high-BDNF groups.

4. Discussion

The study examined the changes in glucose, TC, HDL, LDL, TriG, TC/HDL, TC/LDL, and TriG/HDL in PD patients versus health controls. Additionally, the relationship of BDNF with glucose and lipoprotein profile indices was determined. The results showed no differences in glucose and lipid profile while BDNF was lower among the patients versus controls. Uniquely, BDNF was related to TC, HDL, LDL, TriG, TC/HDL, TC/LDL, and TriG/HDL in the patients. Additionally, TC and LDL were greater while TC/LDL and TriG/HDL were less in the patients with low versus high BDNF. These results are useful, as they show no difference in glucose and lipid profile in PD versus healthy individuals. Importantly, they demonstrated, for the first time, the relationship of BDNF with lipid profile in PD patients.

The relationship of PD with lipid profile is controversial and complex. For example, lowered circulatory lipids [32,33] has been attributed to reduced biosynthesis [34] and linked to the PD diagnosis [20], progression [23], incidence [35], and severity [36]. Similarly, the importance of dietary [21] and circulating [27] lipids for reducing the risk, development, progression, and delaying the symptoms of the disease has been suggested. However, a meta-analysis showed that levels of lipids were not related to the risk, development, progression, symptoms, and incidence of the disease [28] and was not altered in the patients versus the control [37]. Similarly, the current results revealed no differences in lipid profile in the patients versus the control suggesting no changes in lipid profile due to PD.

In the current study, BDNF levels were lower in the PD group than in the control group. This is in agreement with recent studies that have demonstrated reduced BDNF levels among PD patients [38–40] and was linked to disease duration, severity, symptoms, and levodopa treatment [40], and cognitive [38] and cardiovascular [39] functions. In fact, the therapeutic potential of BDNF for PD is being examined [41].

In the current study, BDNF was related to lipid profile indices in the patients. Additionally, the results revealed lower TC and LDL levels and greater TC/LDL and TriG/HDL in the patients with high versus low BDNF implying a role of BDNF in cardiometabolic risk factors. These findings are unprecedented in PD and suggest the involvement of circulatory BDNF in lipid metabolism [42]. Studies in animals suggest the involvement of BDNF in regulating synaptic [43] and neuronal [44] cholesterol metabolism, a mechanism important for the central nervous system repair, regenerative, and resilience capacity, especially after injury. However, no studies examined the role of circulatory BDNF in lipid metabolism in PD and few in other populations [42,45–48]. Opposite to the current findings, BDNF was positively related to TC and LDL among the elderly [42] and Korean adults [47] to TriG in adolescents [46], Korean adults [47], and schizophrenics [45]. Similar to the current results, however, BDNF was inversely associated with TC/HDL and LDL in the elderly [48]. Apparently, the relationship of BDNF with lipids is conflicting and considerably affected by genetic, environmental, and disease factors [47–50]. Subsequently, future studies are needed to examine this relationship under a variety of genetic and environmental factors including diet, exercise, smoking, and diseases, particularly in PD.

4.1. Implications

Ample evidence has shown the importance of brain BDNF for metabolism. However, few studies have examined the relationship of circulatory BDNF with lipid profile and none in PD. According to the results, circulatory BDNF is related to lipid profile in the patients. These findings suggest the importance of BDNF for modifying lipid profile in PD. Given the role of lipids in the risk, development, and progression of PD, BDNF can be considered while designing and implementing therapeutic planes for the patients.

5. Conclusions

The current study examined the changes in lipids and the relationship of BDNF with lipids among PD patients. The results showed no alterations in lipids in the patients versus the controls. Additionally, lipids were favorably different in the patients with high versus low circulatory BDNF, suggesting the importance of BDNF for lipid metabolism among PD patients.

CRediT authorship contribution statement

Mahmoud Alomari: conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; writing - original draft and review & editing. Hanan Khalil: conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Project administration; Resources; Supervision; writing - original draft and review & editing. Omar Khabour: conceptualization; Data curation; Investigation; Methodology; Project administration; Resources; Software; writing - original draft and review & editing. Karem Alzoubi: conceptualization; Data curation; Investigation; Project administration; Resources; writing - original draft and review & editing.

Declaration of competing interest

None.

Data availability

Data will be made available on request.

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