



Evaluation of Brain Derived Neurotrophic Factor (BDNF) hormone levels associated with obesity in some adult men

Ghadeer hamid AL-Ardhi^{1*} and Noran jameel Ibraheem²

¹Department of biology, Faculty of Science of Physical Education, University of Babylon, Al Hilla, Iraq

²Department of biology, Faculty of Science for women, University of Babylon, Al- Hila, Iraq

Abstract : Evaluated of BDNF hormone level in some adult's men according to measures of obesity categories.

Methods: The study was conducted in the College of Science for women, University of babylon, Al- Hila, Iraq. Study population involving (98) adult's men at age (20-50 years), the blood samples were taken from subjects at the morning during 8:30-10:30 o'clock for the period at the beginning of November 2015 till April 2016, and used ELIZA kit to assay the serum BDNF hormone level. The population of our study was classified depending on their anthropometric (physical) characteristics which included the body mass index(BMI), body fat percentage, and waist circumference (WC) measurements.

Results: The results showed a significant increase in BDNF level ($p < 0.05$) in obese groups according to their anthropometric (physical) characteristics as compared with leaner groups.

Conclusion: The state of anthropometric (physical) measurements which included (BMI, body fat percentage, and WC) which have worked to influence on the level of serum circulating BDNF hormone in population of this study.

Key words: Brain Derived Neurotrophic Factor (BDNF) hormone, obesity, adult men.

Introduction:

Obesity is a worldwide medical condition in which excess accumulation of fat that may impair health¹.

The major causes for obesity including the lack of physical activity, excessive eating, and endocrine and genetic predisposition^{2,3} and the obesity is associated with multiple alteration in the endocrine system including abnormal circulating blood hormone concentrations, which can be due to changes in the pattern of their secretion and/or metabolism, altered hormone transport and /or action at the level of target tissue⁴, thus, obesity and its associated disorder are growing epidemic across the world⁵.

BDNF is known to play an important role in such factors as neuronal outgrowth, differentiation, synaptic connection, and neuronal repair⁶.

A higher level in BDNF would be related to better brain health, in that manner, general significant decreased level in BDNF relates to many mental disorders such as depression, Schizophrenia, Huntington disease and Parkinson disease⁷. There was finding that certain types of physical exercise have been increased

(three fold) in BDNF level synthesis in the human brain, which is partly responsible for exercise induced improvements in cognitive function⁸.

BDNF has high- affinity binding to its receptor, tropomyosin- related kinase B: (TrkB) as showed by Kubota *et al*⁹, to express in various brain regions, including energy homeostasis within the hypothalamus and the hindbrain in adult animals¹⁰.

Based on these data from animal's experiments, it is possible that impairment of BDNF production in the experimental animals causes increased food intake, and weight gain, this is one of hypothesized pathogenesis role for this neurotrophin in human obesity. This suggests that changes in circulating BDNF in obese are likely secondary to the altered energy balance occurring in obese¹¹.

For that reason, our study has been debated whether the obesity influence on BDNF hormone level among our population study.

Materials and Methods:

Subjects and Blood collection

The study population included (98) volunteer apparently healthy of ages between (20-50) years. Those subjects were non- smokers, not suffering from any other serious systemic illnesses like diabetes, mellitus, cardiac diseases, renal diseases and hepatic diseases to ensure non-interference with outcome of this study.

Those selected healthy adult men were divided into subgroups according to their body mass index (fat mass) and body fat percentage (fat distribution) and waist circumference (fat abdominal).

Non-fasting blood samples were taken from the subjects enrolled in this study at the morning during 8:30-10:30 o'clock for the period at the beginning of November 2015 till April 2016.

Anthropometric measurements:

Calculation of BMI by dividing weight (in kilograms) by square height (in meters)¹², and the Body fat percentage was calculated by the specific formula¹³:

Lean body weight =94.42+1.082(weight in pound)-4.15(waist in inches)

Body fat %= (body weight –lean body weight *100)/body weight.

Waist in inches = waist in cm /2.54

Weight in pound = weight in kg *2.2

Considerable attention that recommended thresholds of waist circumference in men (102 cm) that correlated with BMI 30 as noted by National Institutes of health in1998(14), owing to that individuals with a waist circumference greater than proposed thresholds generally have worse metabolic profile(15)however the cut- off point values of waist circumference for men (90 cm) associated with BMI of (25kg/m²) which was applied on our subjects by reason that action level of WC are more opportune with demographic factors with our study population and provided more significant data.

Accordingly, our population were divided into two subgroups according to their waist circumference measurements, one of which includes individuals with a large (WC)≥ 90 cm, the other group included the subjects with a small (WC) < 90 cm.

Determination of serum BDNF concentration

Human BDNF concentration was measured by Enzyme Linked Immune Sorbent Assay as mentioned in procedure of Elabscience Biotechnology company kit.

The standard curve of BDNF determination was plotted in figure1 as below:

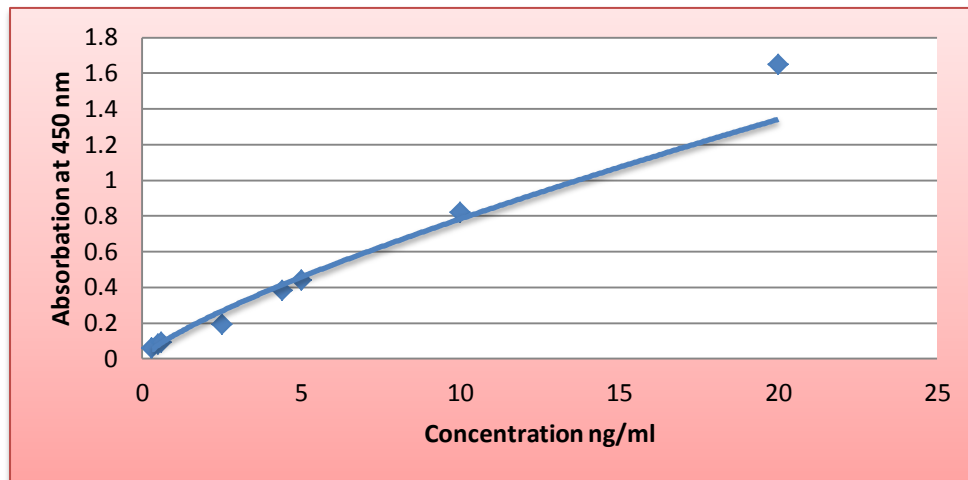


Figure 1: The standard curve of BDNF concentration

Statistical Analysis:

Data analysis were performed on SPSS (version 18.0) software, data are being expressed as mean \pm SD, a nova and student's t-test were used to determine any statistical difference among investigated parameters among subjects. The p value <0.05 were considered statistically significant.

Result:

Figure 2 showed that overweight group had higher significant ($p < 0.05$) level in serum BDNF hormone (19.6 ± 8.6 ng/ml) than those in obese and normal weight group (16.6 ± 4.9 ng/ml), (15.2 ± 6.8 ng/ml) respectively.

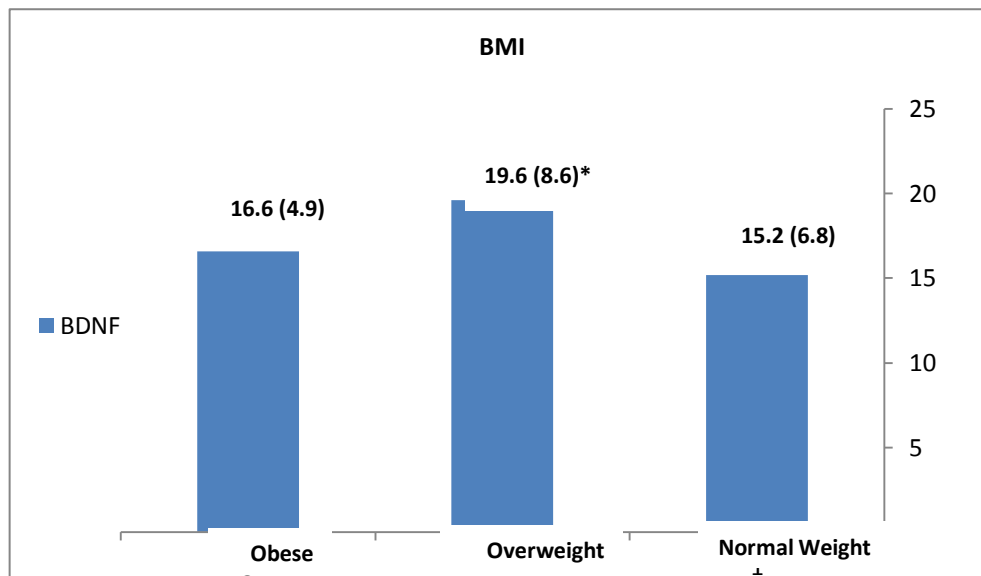


Figure 2: Values of BDNF hormone according to body mass index categories.

* $p < 0.05$ vs. normal weight group.

Our results exhibited that serum BDNF concentration hormone were non-significant difference between subjects in obese and fitness group (17.8 ± 6.0 ng/ml), (18.0 ± 6.0 ng/ml) respectively, but there was a significant decline ($p < 0.05$) of BDNF level in acceptable group (13.4 ± 5.5) versus with fitness individuals as showed in figure 3.

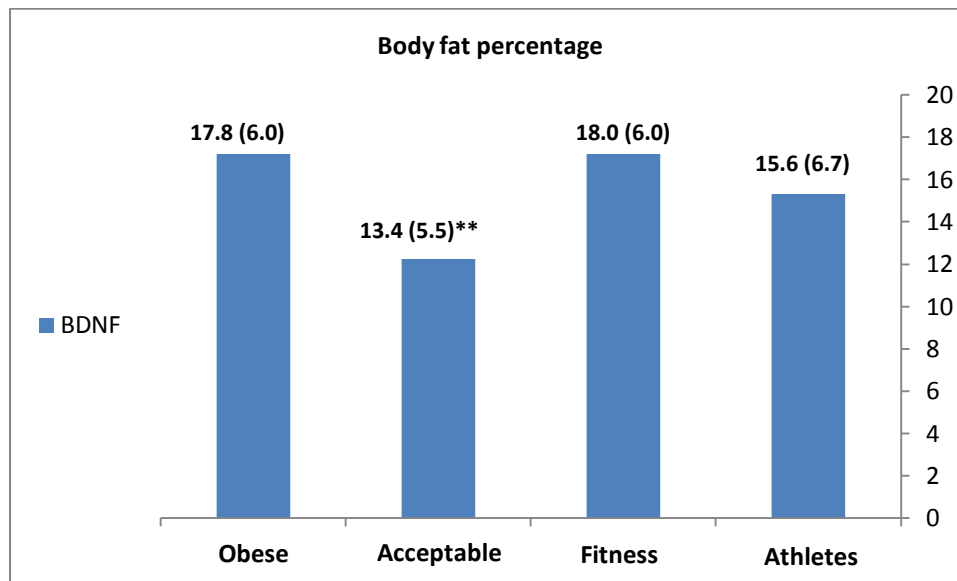


Figure 3: Values of BDNF hormone according to body fat percentage categories.
**** p< 0.05 vs. fitness group.**

There were non-significant differences were seen in the serum BDNF concentration hormone between large (WC) and small (WC) groups as showed in figure 4.

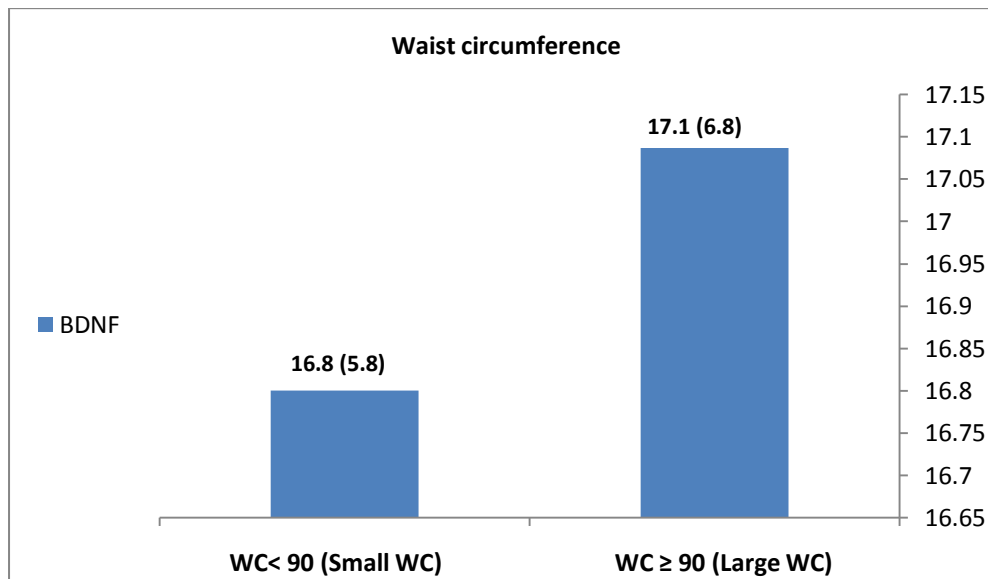


Figure 4: Values of BDNF hormone according to waist circumference categories.

Discussion:

Recent publications become apparent that BDNF is present outside of the CNS and circulates systemically^{16,17} and according to studies which depending on animal models have shown that conditions linked to metabolic dysfunction, e.g. obesity can be modified by manipulation of BDNF in the brain and in the peripheral circulation¹⁸.

In view of the above presented, the data of serum BDNF concentration in our study pointed that there was an increase of serum BDNF level in obese subjects compared with leaner group subjects. This is consistent with observation who suggested that BDNF level increase in obesity to compensate for its association pathophysiologic conditions because of its potential role in improving energy metabolism¹⁹. Other hypothesis

which reported that increase in BDNF level in obesity may represent an adaptive mechanism to counteract the condition of positive energy imbalance by stimulating energy expenditure and decreasing food ingestion¹¹, so this may explain that BDNF concentration has been influenced by BMI and body fat percentage of subjects in our study. Our observation are agreement with some authors²⁰⁻²² whom confirmed that elevated levels of plasma /serum BDNF concentrations may be an early marker of pathological metabolic changes in the body. As regarded with our results about the serum of BDNF concentration which is revealed the non- significant between subjects who have large WC and small WC as showed in figure 4 this may have attributed to that BMI value has been proved to closely related with body fat, while fails to measure abdominal fat as suggested by Camhi *et al*²³. Other study showed not related between measure of BMI with the WC measure owing to that BMI affected by physical activity but not lead to reduction in waist circumference measurements²⁴.

As the relationship between BDNF and weight homeostasis in human, has been more difficult²⁵ so that studies were examined concentration of BDNF don't have reached to conclusive results²⁶. Depending on the data from animal experimental which showed that adipose tissue BDNF/TrkB axis has a substantial influence on the feeding behavior and obesity in female mice²⁷ and found that BDNF and its receptor TrkB expression in adipose tissue changed by diet with high- calorie, and the role of TrkB from adipocytes led to decreased food intake and reduce accumulation of fat in female mice fed a high-calorie diet, thus, inhibition of adipose tissue BDNF/TrkB axis may be decrease obesity.

In humans, other reports on genetic variant have shown an association between the BDNF and TrkB axis and obesity in both adults and children²⁸. Moreover, as noted by Kernie *et al*²⁹ who reported that BDNF and its receptor TrkB observed in various hypothalamus nuclei associated with early behavior and obesity, suggested that serum BDNF level reflects the eating behavior and obese condition of human.

Other literatures pointed that the sedentary behavior that causes high levels of fat mass may inhibit release of BDNF in morbid obese, but our subjects in the present study are not have the same response, owing to they were not affected by morbid obesity.

Conclusion:

Despite the concentration of BDNF was significantly increase in obese groups but these level of BDNF hormone was not reveal dramatically shift in obese groups as compared with leaner group this likely that our population were not affected with morbid obesity.

References:

1. Wang C, Chan JS, Ren L, and Yan JH. Obesity Reduces Cognitive and Motor Functions across the Lifespan Volume 2016 (2016), Article ID 2473081, 13 pages
2. James WP. The fundamental drivers of the obesity epidemic. *Obes Rev.* 2008 Mar;9 Suppl 1:6-13
3. Bleich S, Cutler D, Murray C, and Adams A. Why is the developed world obese? *Annu Rev Public Health* 2008; 29:273-95.
4. Renato P, and Valentina. Obesity and hormonal abnormalities. *International textbook of obesity* 17; 2001: 225- 239.
5. Wilborn C, Beckham J, Campbell B, Harvey T, Galbreath M, Bounty P, Nassar E, Wismann J , and Kreider R. Obesity: Prevalence, Theories, Medical consequences, Management, and Research directions. *Journal of the International society of sports Nutrition* 2(2) ; 2005: 4-31.
6. Lewin GR, and Barde WA. Physiology of the neurotrophins. *Annu Rev Neurosci.* 1996;19:289-317.
7. Aydemir C, Yalcin ES, Aksaray S, Kisa C, Yildirim SG, Uzbay T, and Goka E. Brain-derived neurotrophic factor (BDNF) changes in the serum of depressed women. *Prog Neuropsychopharmacol Biol Psychiatry.* 2006 Sep 30;30(7):1256-60
8. Phillips C, Baktir MA, Srivatsan M, and Salehi A. Neuroprotective effects of physical activity on the brain: a closer look at trophic factor signaling. *Front Cell Neurosci.* 2014 Jun 20;8:170
9. Kubota N, Yano W, Kubota T, Yamauchi T, Itoh S, Kumagai H, *et al.* Adiponectin stimulates AMP-activated protein kinase in the hypothalamus and increases food intake. *Cell Metab.* 6; 2007: 55–68.
10. Yoshii A, and Constantine- Paton M. Postsynaptic BDNF-TrkB signaling in synapse maturation, plasticity, and disease. *Dev Neurobiol* 70 ; 2010:304- 322.

11. Monteleone P, Tortorella A, Martiadis V, Serritella C, Fuschino A, and Maj M. Opposite Changes in the Serum Brain-Derived Neurotrophic Factor in Anorexia Nervosa and Obesity. *Psychosomatic Medicine* 66; 2004:744–748.
12. Jacob C, and Katherine M. Assessing obesity: classification and epidemiology *British Medical Bulletin* 53(2) ; 1997: 238- 252.
13. Chumlea WC, Guo SS, Kuczmarski RJ, Flegal KM, Johnson CL, Heymsfield SB, *et al*. Body composition estimates from NHANES III bioelectrical impedance data. *Int J Obes Relat Metab Disord*. 2002 Dec;26(12):1596-609.
14. National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI). Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults. The evidence report. *Obes Res* 6(suppl2); 1998: 51S-209.
15. Janssen I, Heymsfield SB, Allison DB, *et al*. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. *Am J clin Nutr* 2002 Apr;75(4):683-8.
16. Yamamoto H, and Gurney ME. Human platelets contain brain- derived neurotrophic factor. *J Neurosci* 1990 Nov;10(11):3469-78.
17. Nakahashi T, Fujimara H, Altar CA, Li J, Kambayashi J, *et al*. Vascular endothelial cells synthesize and secrete brain-derived neurotrophic factor. *FEBS Lett*. 2000 Mar 24;470(2):113-7.
18. Lyons WE1, Mamounas LA, Ricaurte GA, Coppola V, Reid SW, Bora SH, Wihler C, Koliatsos VE, Tessarollo L. Brain –derived neurotrophic factor – deficient mice develop aggressiveness and hyperphagia in conjunction with brain serotonergic abnormalities. *Proc Natl Acad Sci U S A*. 1999 Dec 21;96(26):15239-44.
19. Burkhalter J, Fiumelli H, Allaman I, Chatton JY, and Martin JL. Brain-derived neurotrophic factor stimulates energy metabolism in developing cortical neurons. *J Neurosci* 23; 2003: 8212-8220 .
20. Suwa M, Kishimoto H, Nofuji Y, Nakano H, Sasaki H, Radak Z, and Kumagai S. Serum brain- derived neurotrophic factor level is increased and associated with obesity in newly diagnosed female patients with type 2 diabetes mellitus. *Metabolic clinical and experimental* 55; 2006: 852- 857 .
21. Hristova M, Aloe L .Metabolic syndrome–neurotrophic hypothesis. *Med. Hypotheses* 66; 2006:545– 549 .
22. Levinger I, Goodman C, Matthews V, Hare DL, Jerums G, Garnham A, and Selig S. BDNF, Mtabolic Risk Factors, and Resistance Training in Middle-Aged Individuals. *Med Sci Sports Exerc*, 40(3) ; 2008:535–541 .
23. Camhi SM, Bray GA, Bouchard C, Greenway FL, Johnson WD, Newton RL, Ravussin E, Ryan DH, Smith SR, Katzmarzyk PT. The Relationship of waist circumference and BMI to visceral, Subcutaneous, and total body fat: Sex and Race Differences. *Obesity (Silver Spring)*. 2011 Feb;19(2):402-408.
24. Kopelman PG, Caterson ID, and Dietz WH. *Clinical obesity in adults and children*. Third edition; chapter 2 ;2010: 15-24.
25. Míguez-Burbano MJ, Espinoza L, Cook RL, Mayra M1, Bueno D, Lewis JE, Asthana D.. Alcohol, Brain Derived Neurotrophic Factor and Obesity among People Living with HIV. *J AIDS Clin Res*. 2013 Sep 20;4:245.
26. Rios M. BDNF and the central control of feeding: accidental bystander or essential player. *Trends Neurosci*. 2013 Feb;36(2):83-90.
27. Nakagomi A, Okada S, Yokoyama M, Yoshida Y, Shimizu I, Miki T, Kobayashi Y, and Minamino T. Role of the central nervous system and adipose tissue BDNF/ TrkB axes in metabolic regulation. *npj Aging and Mechanisms of Disease*.15009; 2015: 763- 770.
28. Yeo GS, Connie Hung CC, Rochford J, Keogh J, Gray J, Sivaramakrishnan S, Orahilly S, and Farooqi IS. A de novo mutation affecting human TrkB associated with severe obesity and developmental delay. *Nat Neurosci*. 2004 Nov;7(11):1187-1189
29. Kernie SG, Liebl DJ, and Parada LF. BDNF regulates eating behavior and locomotor activity in mice. *EMBO J*. 2000 Mar 15;19(6):1290-1300.
