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CLINICAL STUDY

Plasma nesfatin 1 level in patients with first attack psychosis

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ABSTRACT

OBJECTIVES: This study aimed to investigate the possible relationship between plasma concentrations of nesfatin 1 and first attack psychosis.

METHODS: Totally, 32 patients with the first episode psychosis and 33 randomly selected weight- and body mass index-matched healthy volunteers admitted to Mustafa Kemal University, Faculty of Medicine, Training and Research Hospital, Psychiatry outpatient clinic were included. Healthy control subjects were matched in terms of weight and body mass index (BMI). The Positive and Negative Syndrome Scale (PANNS) was applied to the patient group. The enzyme-linked immunosorbent assay (ELISA) method was used to measure plasma nesfatin 1 levels.

RESULTS: The mean nesfatin 1 level was lower in the patients with the first attack psychosis (0.60 ± 1.00 ng/mL) than in the control group (0.75 ± 1.07 ng/mL).However it did not reach statistical significance (t = –0.567, p = 0.573). There was no statistically significant correlation between plasma nesfatin 1 levels and total PANNS scores in the patient group (r = –0.262, p = 0.148).

CONCLUSION: Our study was the first to investigate the nesfatin 1 levels in patients with the first episode psychosis. Based on our study results, nesfatin 1 might be related to some central nervous system pathologies, including the severity of a psychiatric disorder; however, further large-scale studies are required to establish a conclusion *(Tab. 1, Ref. 21)*. Text in PDF *www.elis.sk.*

KEY WORDS: first attack psychosis, plasma nesfatin 1, body mass index.

Introduction

Nesfatin 1, which is involved in the regulation process of appetite and related metabolic conditions in hypothalamus is a recently discovered satiety molecule identified in various parts of the central nervous system (1).

Although impaired appetite and metabolic changes are common in psychotic disorders, the pathophysiology in psychosis and association with energy intake are not largely known. Energy regulation is managed by anorexigenic and orexigenic pathways; some neurotransmitters, such as neuropeptide Y, are orexigenic, while some others are anorexigenic, such as melanocyte stimulating hormone (MSH) and corticotropin-releasing factor (CRF) (2, 3). These neurotransmitters also play a role in the regulation of effect and stress reactions. Neuropeptide Y has an anxiolytic effect, while MSH and CRF have anxiety-producing properties (1, 3). Therefore, it can be suggested that these neurotransmitters may have actions both on appetite and on psychiatric states.

In addition, nesfatin 1 has similar findings for peptide, to some extent. Oh et al (1) reported that the administration of nesfatin 1 centrally reduced a food intake, such as antibody injection against an increased nutrition action. The study of Merali et al (3) also showed that intracerebroventricular (ICV) nesfatin 1 injection led to anxiety and fear-related behaviours in a rat model. In conclusion, nesfatin 1 may play a role in the process of emotional states, such as: anxiety and stress. However, these findings still need to be confirmed in further studies and more importantly, need to be supported by studies in the real-setting, which are still lacking in literature.

Nesfatin 1 is a neuropeptide, which plays a significant role in the reproductive processes, stress responses, and pathology of mental and neurological disorders (4, 5). Considering the anorectic properties of nesfatin 1, the presumption that it can display some characteristics of neuroprotective factors seems particularly intriguing. The study conducted by Ozsavci et al (6) is the only source for these suggestions. The authors examined the impact of nesfatin 1, administered intraperitoneally, on the profile of oxidative stress markers and the permeability of blood–brain barrier in rats with subarachnoid haemorrhage (SAH). The authors concluded that nesfatin 1 reduced the SAH-dependent histological structural changes of basilar arteries by inhibiting neutrophil infiltration. This research allows us to understand that nesfatin 1 can play the role of an anti-inflammatory and anti-apoptotic factor in the central nervous system.

In this study, we aimed to investigate the possible relationship between plasma nesfatin 1, a satiety peptide, level and the first attack psychosis.

Material and methods

This study included totally 32 patients with the first episode psychosis and 33 randomly selected weight- and body mass index

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(BMI)-matched healthy volunteers admitted to Mustafa Kemal University, Faculty of Medicine, Training and Research Hospital, Psychiatric outpatient clinic. Individuals with any other chronic diseases such: as diabetes mellitus, hypertension, hyperlipidemia, or neurological disorders, who were under 18 years of age and those over 65 years of age and pregnant women were excluded from the study. Before enrolment, the relationship between plasma nesfatin 1 levels and socio-demographic characteristics was examined. Nesfatin 1 levels of the patients were compared to the healthy controls. A written informed consent was obtained from each participant. The study protocol was approved by the institutional Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Socio-demographic data, such as age, sex, educational level, marital status, occupational status, mental status, smoking, height and weight and BMI index, were collected. The severity of schizophrenia symptoms in the patients was evaluated using the Positive and Negative Syndrome Scale (PANSS) (7). Physical and neurological examinations were performed in all participants.

From the patients' forearm, a venous blood sample was taken after 12 hours of fasting at 08.00 A.M. Routine psychiatric examination, PANNS and CGI scale were applied on the blood collection day. All collected bloods were centrifuged for 15 min (3000xg) over two hours, and sera were stored at –70 °C. After the blood collection, plasma nesfatin 1 level was measured by enzyme-linked immunosorbent assay (ELISA) method using the nesfatin 1 ELISA kit (Bio Vendor Laboratory Medicine Inc., Czech Republic).

Statistical analysis

Statistical analysis was performed using the NCSS version 2007 software (Number Cruncher Statistical System) (Kaysville, Utah, USA). Descriptive data were expressed as the mean, standard deviation, frequency, and rate. The independent sample t-test for the inter-group comparison of normally distributed quantitative variables was used. Normally distributed qualitative variables were compared using the Pearson's chi-square and Pearson correlation tests. P values of <0.05 were considered statistically significant.

Results

Both groups had similar demographic characteristics. The demographic and biochemical characteristics are shown in Table 1. The BMI was 25.22 ± 5.24 kg/m^2 in patients and 25.11 ± 4.41 kg/m^2 in healthy controls, indicating no statistically significant differences between the groups (p = 0.931, t = 0.086).

The mean plasma nesfatin 1 level in patients with the first attack psychosis was 0.60 ± 1.00 ng/mL, whereas it was 0.75 ± 1.07 ng/mL in the control group. Lower mean plasma nesfatin 1level was found in patients with the first attack psychosis, compared to the control group; however, nesfatin 1 level was not statistically significantly different between the groups (t = –0.567, p = 0.573).

In addition, there was no statistically significant correlation between the plasma nesfatin 1 levels and total PANNS scores in the patient group (r = –0.262, p = 0.148). There was no statistically significant difference in sociodemographic variables in terms of the mean plasma nesfatin 1 level between both groups. Nesfatin 1 plasma levels of both groups were not statistically significantly associated with BMI and smoking (p > 0.05).

Tab. 1. Comparison of the mean values of study variables in the first attack psychosis group and the control group.

Variables	First attack psychosis group (n=32)	Control group (n=33)	t or x^2	p
Age (X±SS)	31.15±12.20	34.78±12.00	–1.209*	0.231
Sex (female/male)	12/20	15/18	0.423**	0.515
BMI (kg/m^2)	25.22±5.24	25.11±4.41	0.086*	0.931
Nesfatin 1 (ng/ml)	0.60±1.00	0.75±1.07	–0.567*	0.573
Total PANNS	100.31±16.79	–	–	–

BMI – body mass index; PANSS – Positive and Negative Syndrome Scale. * Independent Sample t-Test, ** Pearson's chi-square test, p < 0.01 and p < 0.05.

Discussion

In the present study, we found lower mean plasma nesfatin 1 levels in patients with the first attack psychosis, compared to the healthy controls; however, it did not reach statistical significance. Similarly, in the study, the pre-treatment of manic episodes of serum nesfatin 1 levels were lower than the control group; however, after the treatment including electroconvulsive therapy + antipsychotics, plasma nesfatin 1 levels significantly increased (8). In another study, plasma nesfatin 1 levels were found to be lower in men with generalized anxiety disorder with different psychiatric conditions (9). In the study including patients with restrictive type of anorexia nervosa, serum nesfatin 1 levels were significantly lower in the patients, compared to the controls (10). Consistent with previous findings, we found lower nesfatin 1 levels in some psychiatric disorders.

Chen et al (11) reported that the ventral tegmental area (VTA) showed a decline in the nesfatin 1 injection and the food intake excitability of neurons in the ventral tegmental area was inhibited by nesfatin 1. The authors also reported that nesaftin 1 inhibited dopamine released by the nucleus accumbens. Therefore, nesfatin 1 was the activity on dopaminergic pathways and reduced food intake led to the development of such an effect.

Tan et al (12) demonstrated that it could give back the rotenone-induced neurotoxicity and the related studies were saved by the mitochondrial transmembrane potential collapse of rotenone-induced and the function of mitochondrial respiratory chain complex. It is also known that the release of rotenone-induced mitochondrial cytochrome C by nesfatin 1 blocks the production of ROS and inhibition caspase-3 activation (12). Nesfatin 1 is found to be improving and neuroprotective for dopaminergic cells of mitochondrial dysfunction induced by rotenone and inhibiting the activity of the anti-ptotic (12). It has also the potential for prevention of Parkinson disease (12).

In the present study, we found no statistically significant correlation between the plasma nesfatin 1 levels and total PANNS scores in the patient group. Therefore, we concluded that there was no relationship between the severity of the disease and plasma nesfatin 1 levels.

On the other hand, in the study including patients with depression and healthy controls, nesfatin 1 levels were found to be significantly higher in the patient group (13). Similarly, in an-

other study, plasma nesfatin 1 levels of patients with a diagnosis of obsessive-compulsive disorder were higher, compared to the healthy controls. This suggests that the condition is associated with anxiety component (14).

In our study, there was no statistically significant correlation between plasma nesfatin 1 levels and BMI. Stengel et al (15) reported that nesfatin 1 reduced food intake and obesity. Another study showed a negative correlation between the cerebrospinal fluid plasma levels of nesfatin 1 and obesity (16). Increased BMI values indicate reduced orexigenic ghrelin; however, increased anorexigenic nesfatin 1 has been also shown (17). In another study, BMI and weight and nesfatin 1 were reported to be associated with various genetic variations (18). An opposite phenomenon was displayed in healthy men with normal BMI values, in whom the fasting nesfatin 1 concentration was negatively correlated with BMI (19). Due to the presence of controversial results in literature, we conclude that the relationship between plasma nesfatin 1 levels and BMI produces different results.

An increased BMI in psychiatric patients taking anti-psychotics, anti-depressants, and other psychotropic medications is an important clinical issue. In the majority of obese patients, a substantial reduction of sensitivity to leptin or some other adipokines may occur in various hypothalamic centers (20). It seems that, in these cases, the use of nesfatin 1 can cause a substantial clinical improvement. Based on experimental studies, an intraperitoneal administration of nesfatin 1 has significantly reduced food intake in leptin resistant animals. In addition, nesfatin 1 has been found to reduce an elevated body mass of experimental animals.

Furthermore, nesfatin 1 levels are not only related to psychiatric disorder, but also to neurological diseases, such as generalized epilepsy. In the study conducted by Aydin et al (21) a significant decrease in plasma nesfatin 1 levels of primary generalized epileptic patients was found following an anti-epileptic treatment. The authors concluded that nesfatin 1 level might be related to pathophysiology of some central nervous system problems, such as epilepsy. Recently, it has been also confirmed that nesfatin 1 can exert its neuroprotective effect against subarachnoid hemorrhage-induced injury via its anti-apoptotic and anti-inflammatory properties (6). However, whether it has a neuroprotective effect on dopamine neurons remains largely unknown.

Nonetheless, there are some limitations to this study. First, this is a cross-sectional study with a small sample size. Second, blood samples collected only once from the patients with the first attack psychosis complicated the interpretation and generalization of the findings. Third, the absence of data relating to the duration of the first attack psychosis in psychotic patients is another limitation. We believe that the analysis of other parameters such as ghrelin and leptin as well as nesfatin 1 would better elucidate the complex relationship between them.

In conclusion, to our knowledge, this study was the first which investigated the plasma nesfatin 1 levels in patients with the first episode psychosis. Based on these study results, nesfatin 1 may be related with some central nervous system pathologies, including the severity of a psychiatric disorder. However, further large-scale studies are required to establish a conclusion.

References

1. Oh I, Shimizu H, Satoh T, Okada S, Adachi S, Inoue K et al. Identification of nesfatin 1 as a satiety molecule in the hypothalamus. Nature 2006; 443: 709–712.

2. Erlanson-Albertsson C. How palatable food disrupts appetite regulation. Basic Clin Pharmacol Toxicol 2005; 97 (2): 61–73.

3. Merali Z, Cayer C, Kent P, Anisman H. Nesfatin 1 increases anxiety- and fear-related behaviors in the rat. Psychopharmacology 2008; 201: 115–123.

4. Könczöl K, Bodnar I, Zelena D et al. Nesfatin 1/NUCB2 may participate in the activation of the hypothalamic-pituitary-adrenal axis in rats. Neurochem Int 2010; 53: 189–197.

5. Ogiso K, Asakawa A, Amitani H et al. Plasma nesfatin 1 concentrations in restricting-type anorexia nervosa. Peptides 2011; 32: 150–153.

6. Ozsavci D, Ersahin M, Sener A et al. The novel function of nesfatin 1 as an anti-inflammatory and antiapoptotic peptide in subarachnoid hemorrhage-induced oxidative brain damage in rats. Neurosurgery 2011; 68: 1699–1708.

7. Kay SR, Flszbein A, Opfer LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophrenia Bull 1987; 13 (2): 261.

8. Emul M, Karamustafalioglu N, Kalelioglu T et al. The nesfatin 1level in male patients with manic episode and alterations of nesfatin 1 level after antipsychotic and electroconvulsive treatment. J Affect Dis 2013; 151: 849–853.

9. Gunay H, Tutuncu R, Aydin S, Dag E, Abasli D. Decreased plasma nesfatin 1 levels in patients with generalized anxiety disorder. Psychoneuroendocrinol 2012; 37: 1949–1953.

10. Ogiso K, Asakawa A, Amitani H et al. Plasma nesfatin 1 concentrations in restricting-type anorexia nervosa. Peptides 2011; 32 (1): 150–153.

11. Chen X, Shu X, Cong ZK, Jiang ZY, Jiang H. Nesfatin 1 acts on the dopaminergic reward pathway to inhibit food intake. Neuropeptides 2015; 53: 45–50.

12. Tan Z, Xu H, Shen X, Jiang H. Nesfatin 1 antagonized rotenone-induced neurotoxicity in MES23.5 dopaminergic cells. Peptides 2015; 69: 109–114.

13. Ari M, Ozturk OH, Bez Y, Oktar S, Erduran E. High plasma nesfatin 1 level in patients with major depression. Progr Neuropsychopharmacol Biol Psychiat 2011; 35 (2): 497–500.

14. Bez Y, Ari M, Ozturk OH, Oktar S, Can Y. Increased Plasma Nesfatin 1 Levels in Patients with Obsessive Compulsive Disorder. Bull Clin Psychopharmacol 2012; 22: 1.

15. Stengel A, Tache Y. Minireview: Nesfatin 1. An Emerging New Player in the Brain-Gut, Endocrine, and Metabolic Axis. Endocrinology 2011; 152 (11): 4033–4038.

16. Tan BK, Hallschmid M, Kern W, Lehnert H, Randeva HS. Decreased Cerebrospinal Fluid/Plasma Ratio of the Novel Satiety Molecule, Nesfatin 1/NUCB-2 in Obese Humans: Evidence of Nesfatin 1/NUCB-2 Resistance and Implications for Obesity Treatment. J Clin Endocrinol Metab 2011; 69: 4.

17. Stengel A, Hofmann T, Goebel-Stengel M et al. Ghrelin and NUCB2/nesfatin 1 are expressed in the same gastric cell and differentially correlated with body mass index in obese subjects. Histochem Cell Biol 2013; 139: 909–918.

18. Zegers D, Beckers S, Mertens IL et al. Association between polymorphisms of the Nesfatin gene, NUCB2, and obesity in men. Mol Genet Metab 2011; 103(3): 282–286.

19. Tsuchiya T, Shimizu H, Yamada M et al. Fasting concentrations of nesfatin 1 are negatively correlated with body mass index in non-obese males. Clin Endocrinol 2010; 73: 484–490.

20. Heymsfield SB, Greenberg AS, Fujioka K et al. Recombinant leptin for weight loss in obese and lean adults: a randomized, controlled, doseescalation trial. JAMA 199; 282: 1568–1575.

21. Aydin S, Dag E, Ozkan Y, Erman F, Dagli AF, Kilic N et al. Nesfatin 1 and ghrelin levels in serum and saliva of epileptic patients: hormonal changes can have a major effect on seizure disorders. Mol Cell Biochem 2009; 328 (1–2): 49–56.

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