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INVESTIGATION OF THE ASSOCIATION OF LEPTIN (LEP) –2548G/A (RS7799039) AND LEPTIN RECEPTOR (LEPR) 668A/G (RS1137101) GENE POLYMORPHISMS WITH CLINICAL PARAMETERS AND DISORDER SUBTYPES IN INDIVIDUALS WITH PANIC DISORDER

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BACKGROUND AND AIM: Panic disorder (PD) has a substantial genetic component, yet specific biological markers remain unclear.Leptin, a neuropeptide regulating energy balance, influences neuroplasticity and anxiety-related behaviors through limbic brain regions and interactions with the hypothalamic–pituitary–adrenal axis.Although LEP and LEPR variants have been linked to several psychiatric disorders, their role in PD has not been directly examined. This study compared the genotype and allele distributions of LEP–2548G/A (rs7799039) and LEPR 668A/G (rs1137101) polymorphisms between individuals with PD and healthy controls and evaluated associations with PD subtypes and clinical parameters.

METHODS: The study was approved by the Başakşehir Çam and Sakura City Hospital Ethics Committee (Protocol no: 2025.06.251). A total of 204 participants(102 PD patients;102 controls) were included. Diagnoses were established using SCID-5-CV.PDSS, PAS, HDRS, and STAI were administered. Genotyping was performed using PCR–RFLP.Categorical variables were analyzed using chi-square or Fisher's exact tests, and continuous variables using appropriate parametric or nonparametric tests.Odds ratios (OR) with 95% confidence intervals (CI) were calculated.A p value <0.05 was considered statistically significant.

RESULTS: For LEP –2548G/A, the AA genotype was more frequent in PD patients (OR=2.435; p=0.018), and the A allele frequency was also higher (p=0.046).For LEPR 668A/G, the AA genotype was less frequent (OR=0.396; p=0.001), whereas the AG genotype was more frequent (OR=2.238; p=0.006). Clinical variables and scale scores did not differ by genotype.No differences were observed for respiratory or nocturnal subtypes; however, patients with agoraphobia had higher frequencies of the LEPR AA genotype (OR=2.417; p=0.030) and A allele (OR=1.928; p=0.029).

CONCLUSIONS: LEP and LEPR gene polymorphisms were associated with PD in this sample.The LEP AA genotype was associated with increased PD risk, whereas the LEPR AA genotype was associated with reduced PD risk.Agoraphobia was also associated with the LEPR AA genotype and A allele. Replication in larger and independent samples is warranted.

Keywords: Panic disorder, leptin, leptin receptor, single gene polymorphism