

The relationship between alcohol dependence and prodynorphin gene polymorphisms among Turkish men

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Aim: It is a known fact that Prodorphin (PDYN) binds to kappa-opioid receptors and regulate dopaminergic tone, making this system important for the reinforcing and rewarding properties of drugs of abuse such as heroin, cocaine, and last but not least alcohol (1-5). The present study's purpose was to evaluate potential association between alcohol dependence and four single nucleotide polymorphisms (SNPs) of PDYN gene (rs35286281 in promoter region and rs1022563, rs2235749, rs910080 in 3'UTR) among Turkish men.

Method: The Ethical Committee of the University approved the study and then the study was conducted alcohol dependent (n=68, %43.3) at Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Alcohol and Drug Research, Treatment and Training Center (AMATEM). Voluntary Turkish healthy control group (n=89, %56.7) was included in the study by Turgut Ozal University Faculty of Medicine Department of Psychiatry. The peripheral blood samples were obtained from patients and healthy controls were collected in EDTA tubes and 25 µl PCR mixture was prepared for amplification from the DNA samples. Genomic DNA was extracted from samples using a DNA isolation kit (Qiagen: Puregene Blood Core Kit B) according to the manufacturer's instructions and then stored at -20°C until polymerase chain reaction (PCR) was performed. The genotypic analysis of the PDYN gene polymorphisms were performed using PCR-RFLP, whereas only PCR was used for VNTRs on PDYN gene. Sociodemographic features, Genotype and allele frequencies and difference between two groups were analysed by Chi-square.

Results : Smoking cigarette, suicidal attempts, self-harming behavior, prison and police station experience were higher in alcohol dependence group (table 1). Moreover, there is a significant frequency of the PDYN 68bp VNTR (rs35286281) Genotype and allele frequencies in between two groups, but statistical significance of PDYN polymorphism 68bp VNTR (1022563) Genotype (p=0.053) and allele (p=0.057) frequencies are the limit. However, the PDYN 68bp VNTR (rs2235749 and rs910080) Genotype and allele frequencies did not differ between the groups (table 2).

Conclusion: The present study's main finding is a significant higher frequency of the PDYN 68bp VNTR (rs35286281) L allele in alcohol-dependent subjects than in controls. Previous studies that have examined the relationship between PDYN polymorphism and substance use disorders (SUDs) but results are controversial, with some studies showing that high PDYN expressing alleles are more common among people with SUDs (3,5), some showing low expression alleles in association with SUDs (6) and others reporting no association (7,8). The inconsistent results across studies can be attributed to a variety of factors such as sample sizes, ethnic diversity, culture, drug availability, legislation and the examination of different SUDs or alcohol dependence since gene polymorphisms is not the only etiological factor for addiction. Thus, further research is required.

Table 1

	Control group		Alcohol dependence		χ^2	P
	n=89	%	n=68	%		
Suicidal attempts	0	0.0	9	13.4	12.69	<0.001
Self-harming behavior	2	2.2	9	13.4	7.30	0.007
Prison experience	0	0.0	12	17.6	17.01	<0.001
Police station experience	2	2.2	34	50.0	49.74	<0.001
Smoking cigarette	24	27.0	60	88.2	58.17	<0.001

Table 2

Position	Genotyping	Control (n=89, % 56.7)		Alcohol dependence (n=68, % 43.3)		χ^2	p
68bp VNTR Genotype	12	0	0	0	0	18.09	0.11
	13	0	0	0	0		
	22	4	4.5	12	17.6		
	23	32	36.0	24	35.3		
	24	3	3.4	0	0		
68bp VNTR Allele	33	46	51.7	30	44.1	5.56	0.06
	34	4	4.5	2	2.9		
	4	7	4.0	2	1.5		
68bp VNTR Genotype	LL	4	4.5	12	17.6	7.32	0.026
	LH	35	39.3	24	35.3		
	HH	50	56.2	32	47.1		
68bp VNTR Genotype	LL	4	4.5	12	17.6	7.29	0.007
	LH+HH	85	95.5	56	82.4		
68bp VNTR Allele	L	43	24.4	48	35.3	4.38	0.036
	H	133	75.6	88	64.7		
rs1022563 Genotype	CC	66	74.2	38	59.4	3.85	0.15
	CT	21	23.6	23	35.9		
	TT	2	2.2	3	4.7		
rs1022563 Genotype	CC	66	74.2	38	59.4	3.74	0.053
	CT+TT	23	25.8	26	40.6		
rs1022563 Allele	C	151	85.8	99	77.3	3.62	0.057
	T	25	14.2	29	22.7		
rs2235749 Genotype	AA	0	0	1	1.6	1.42	0.492
	AG	42	47.7	29	46.0		
	GG	46	52.3	33	52.4		
rs2235749 Allele	A	42	24.1	31	24.6	0.009	0.93
	G	132	75.9	95	75.4		
rs910080 Genotype	AA	83	93.3	62	92.5	0.958	0.62
	AG	1	1.1	0	0		
	GG	5	5.6	5	7.5		

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