

THE EFFECT OF SELECTED POLYMORPHISMS OF THE DOPAMINE RECEPTOR GENE DRD2 AND THE ANKK-1 ON THE PREFERENCE OF CONCENTRATIONS OF SUCROSE SOLUTIONS IN MEN WITH ALCOHOL DEPENDENCE

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SUMMARY

Background: The aim of the study was to determine the influence of DRD2 gene polymorphisms in exon 8 G/A (rs 6276) in the promoter region -141 C Ins/Del (rs1799732) and the influence of ANKK-1 gene Taq-1A polymorphism (rs 1800497) on the preference of increasing sucrose concentrations in men with alcohol dependence.

Subjects and methods: 63 male patients with alcohol dependence were genotyped for the above polymorphisms. Their preference for increasing sucrose concentrations was tested and their taste intensity perception of sucrose solutions was assessed. The patients were tested with the 'Sniffin' Sticks' olfactory test.

Results: We found a statistically significant association between some alleles of ANKK 1 gene Taq 1A polymorphisms and sucrose preference in the subjects. The A1 Taq 1A allele determined hedonistic response to the two highest concentrations of sucrose. No association was found regarding the other two polymorphisms (in the promoter region and in the exon 8 of the DRD2 gene).

Conclusions: Study results suggest Taq-1A polymorphism plays a role in the preference to high concentrations of sucrose and its potential association with alcohol dependence pathogenesis.

Key words: alcohol dependence - DRD2 gene polymorphisms - ANKK 1 gene polymorphisms - sucrose preference

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INTRODUCTION

Alcohol dependence (AD) is a clinically and etiologically varied medical condition. It is affected by both environmental and genetic factors. Population studies showed that the influence of genetic factors amounts to 40-50%, whereas the impact of environmental factors is assessed to be approximately 50-60% (Cloninger 1994, Merikangas et al. 1990, Grochans et al. 2011).

Ethanol principally affects CNS and particularly dopaminergic pathways which are directly involved in mediating the functioning of the reward system. The nucleus accumbens is activated and dopamine is released instantly once ethanol has been consumed. Nicotine and glutaminergic receptors are also involved in the process. Alcohol-induced effects of stimulation (talkativeness, being prone to social interaction) are therefore triggered by both dopaminergic and noradrenergic systems. By affecting the subpopulation of GABA A receptors, alcohol potentialises its effect on inhibiting GABAergic neurotransmission, hence its anxiolytic effects. In higher concentrations, ethanol has a wider effect causing ataxia and amnesia (Davis 2003).

Alcohol withdrawal symptoms are caused by reversing changes in the neurotransmitter GABAergic and glutaminergic systems occurring during repeated

exposure of alcohol intake. The activation of NMDA receptors during the cessation of drinking is caused by the neurotoxic effect of alcohol (Chandrasekar 2013, Grzywacz et al. 2013). Alcohol intake is directly responsible for increased concentration of endorphins in the blood. Laboratory studies demonstrated that the administration of opioid receptor antagonists to animals inhibited the reward effect (Chen, 2013). The serotonergic system regulates alcohol intake and affects the development of alcohol dependence and the preference of its intake. Alcohol impact on 5HT3 subpopulation also plays a role in its interactions with the gastrointestinal tract (Youssef et al. 2011). The endocannabinoid system plays a major role in regulating alcohol intake. Studies showed that the administration of CB1 receptor antagonists in laboratory animals significantly affected alcohol intake (Cwiek & Dyr 2007, Schmidt et al. 2002).

Genetic background was confirmed in epidemiological studies (Cloninger et al. 1981, Gurling et al. 1981, Luthar et al. 1992, McGue et al. 1992). In the association studies of so-called candidate genes, the focus is placed on polymorphisms that might be associated with neurotransmitter systems involved in AD development (Grzywacz et al. 2008, Grzywacz et al. 2012, Finckh et al. 1997, Preuss et al. 2011, Samo-

chowiec et al. 2000, Sander et al. 1996), including dopaminergic, serotonergic, noradrenergic, glutaminergic and GABAergic systems. Since dopamine is a major neurotransmitter that helps control the brain's reward and pleasure centers, involved in the development of addiction, it is hardly surprising that genes involved in its synthesis, decomposition and transport as well as genes coding dopaminergic receptors are also candidate genes in research on AD. The D2 dopamine receptor gene (DRD2) is located on the chromosome 11q22.3-q23. Research on AD genetic association usually focuses on two DRD2 gene polymorphisms; in the promoter region -141 C/I/D (rs1799732) and in exon 8 G/A (rs 6276) and on ANKK 1 gene Taq 1A polymorphism (rs 1800497) which was earlier regarded as DRD2 gene polymorphism (Matsumoto et al. 2001). Nowadays, while AD heritability is known to have a multi-gene mechanism. Therefore, homogenous subgroups are identified for research purposes, e.g. groups characterised by early-onset, severe alcohol withdrawal syndromes with other comorbid mental disorders, family history of AD, to find so-called endophenotypes, i.e. measurable distinguishing characteristics associated with AD of a stable character, heritable, present in family members, both unaffected and those with AD, with higher intensity in the affected members of a family (Samochowiec 2008). Endophenotypes must be easy to assess and should fit the criteria of addiction pathophysiology (Turetsky 2007). Taste perception was selected in the present study as a potential endophenotype.

Some researchers focused on the association between bitter taste detection and AD (Pelchat et al. 1992). Response changes to salt and sour tastes in patients with a family history of AD were also studied (Ścińska et al. 2001). Sweet taste is one of the phylogenetically oldest "rewards" for the man and other mammals. Facial reactions of human newborns to sucrose and glucose solutions are not basically different from those of monkeys (Berridge 2000). The preference for sweet solutions is an in-born trait which remains unchanged throughout the whole life. While children prefer higher concentrations of sweet solutions than adults (Desor et al. 1987), Stevens demonstrated decreased taste acuity in the elderly (Stevens et al. 1995). Environmental factors may be conducive to changes of taste preferences. This is particularly the case in pathological social groups suffering from malnutrition or consuming homogeneous monotonous diets. Based on the differences in sweet taste preferences, the general human population can be divided into those who prefer a high concentration of sucrose, the so-called sweet likers (s.l) and a low concentration, the so-called sweet dislikers (s.d). People who preferred highest concentrations of sucrose (0.88 M) were defined as sweet likers (Bogucka-Bonikowska et al. 2001, 2002).

The association between preference of sucrose high concentrations and alcohol consumption is based on the fact that both substances have similar (serotonergic, opioid and dopaminergic) neurotransmitter systems. Central dopaminergic pathways, which make up a part of the reward system, play a special role affecting preference and consumption of sweet solutions in animals (Di Chiara et al. 1988, Johann et al. 2005, Small et al. 2003). Consumption of sweet solutions by animals leads to dopaminergic nerve ending activation in the limbic system. A similar phenomenon was observed after administration of small doses of alcohol (Di Chiara et al. 1988, Mark et al. 1991). Substances blocking central receptors D2 (pimozide) or dopamine reuptake inhibitors (cocaine) can selectively reduce sweet solution consumption in animals (Leeb et al. 1991). Sweet solution consumption can also affect DAT density in the nucleus accumbens and ventral tegmental area (Bello et al. 2003). Based on research conducted by Kampov-Polevoy et al. (Kampov-Polevoy et al. 1997), a hypothesis was put forward that preference for sucrose high concentrations (>10%) may be a stable AD marker in humans. They demonstrated that in a group of AD men (abstaining from alcohol) 65% preferred high concentrations of sucrose (0.83 M), compared to 16% in the control group. The same research team revealed a distinct association between preference for sucrose high concentrations (expressed as the percentage of "sweet likers" in a group) in adult sons of AD fathers and AD of their fathers (Kampov-Polevoy 2001, 2003). Those findings were not consistently replicated in subsequent studies. A study by Ścińska (Ścińska et al. 2001) on minor sons of AD fathers did not find any differences between them and controls regarding sweet taste preference. Those results were later replicated by Kranzler et al. (2001) on a group of adult offspring (of both genders) of AD fathers. Another study by Bogucka-Bonikowska et al. (2001) demonstrated that the intensity and pleasure combined with sucrose taste, measured with Visual Analogue Scale (VAS), was similar in alcoholics and controls. Successive studies by Kampov-Polevoy (Kampov-Polevoy et al. 2004) also revealed negative results. Interestingly, Kampov-Polevoy's research suggest that an association between sweet liking and paternal alcoholism may be a predictor of development of AD in an adult son (Kampov-Polevoy et al. 2001, 2004). It is, therefore, fair to say that sweet liking is not AD marker. However, it can be used as AD indicator combined with other traits. Consequently, sucrose solution acuity tests were conducted on AD men. Family history of alcoholism was considered. Consistent with previous observations, based on sweet taste assessment scores in the dimension "pleasant - unpleasant", it is impossible to differentiate alcoholics from controls. It was found that the percentage of sweet likers and a hedonistic response to the highest concentration of sucrose (30%) was markedly higher in AD group consisting of sons of AD fathers (Wroński et al. 2007).

SUBJECTS AND METHODS

The protocol of the study was approved by the Bioethics Committee of the Pomeranian Medical University of Szczecin. A cohort of 62 adult men who fulfilled the ICD-10 alcohol dependence criteria was studied. All the subjects abstained from alcohol for a minimum of 7 days prior to the study. No withdrawal symptoms were observed. Patients diagnosed with mental diseases or addictions other than AD (apart from nicotine addiction) were excluded from the study. Individuals who within 30 days prior to the study suffered from psychotic disorders, smell and/or taste impairments, exacerbation of somatic disease that required a change of treatment or hospitalisation were also excluded. Prior to the study, all the subjects were fully informed about the aims and the methodology of the research and all of them expressed their written informed consent.

Genetic tests

10 ml venous blood samples from the elbow area were obtained from the subjects. The samples were placed in EDTA anticoagulant tubes. Genomic DNA was extracted using salting-out method based on Miller et al. (1998). The following polymorphisms were investigated with PCR method: the ANKK-1 gene Taq-1A polymorphism (Grandy et al. 1989) and two polymorphisms of D2 dopamine receptor gene DRD2: in promoter region -141 C Ins/Del (Arinami et al. 1997) and within exon 8 A/G (Finckh et al. 1997). Visualization of PCR product and DNA fragments was conducted by agarose gel electrophoresis using ethidium bromide staining of agarose gels.

Gustatory tests

Taste perception tests were conducted between 10 a.m. and 1 p.m. in a quiet, well-ventilated room. The subjects were asked to refrain from eating, drinking and smoking cigarettes for a minimum of 1 h before the testing. Prior to the study, all the subjects were fully informed about the procedure and assessment scales (Bogucka-Bonikowska et al. 2001, 2002, Wroński et al. 2007). The procedure was validated at the Institute of Psychiatry and Neurology, Warsaw, Poland, indicating good test-retest reliability (correlation coefficient values for scores using VAS scales >0.9; Bienkowski et al., unpublished data). At the beginning of the study subjects received distilled water in disposable cups to wash their mouths to adopt themselves to water taste, i.e. neutral stimulus. Using 1 ml disposable syringes 8 samples of sucrose solutions were placed directly in the middle of the tongue. Then, subjects spread samples within their mouths and using VAS rated their intensity (from "0" = very weak to "100" = very strong) and pleasantness (from "-50" = very unpleasant to "50" = very pleasant). Samples were administered every 60-90 s. During the breaks subjects were asked to fill their answer sheets, spit out

the administered samples and rinse their mouths. Samples were distributed in two series. Between the series, i.e. between samples 4 and 5, the subjects could rest for 5 min. No information about the order and content (water - sucrose) of successive samples was given. Distilled water was used as a neutral stimulus (0% sucrose solution). Successive, 1 ml samples included: sample 1 =0% sucrose solution, sample 2 =1% sucrose solution, sample 3 =10% sucrose solution, sample 4 =30% sucrose solution, sample 5 =0% sucrose solution, sample 6 =1% sucrose solution, sample 7 =10% sucrose solution, sample 8 =30% sucrose solution. Syringe sets were prepared at the Institute of Psychiatry and Neurology using methodology developed earlier (Bogucka-Bonikowska et al. 2001, 2002), stored at a temperature below 0°C, and transported in thermos flasks filled with ice. 1h before the test the samples were placed in room temperature. The concentrations of sucrose solutions were selected based on earlier studies (Bogucka-Bonikowska et al. 2001, 2002, Kampov-Polevoy et al. 2001, Wroński et al. 2007). Subjects who preferred the highest sucrose concentration (mean hedonistic scores in two series) were defined as sweet likers and the remainder as sweet dislikers. VAS scores were analysed. The assessment of taste intensity perception (both for s.l and s.d) was performed to exclude sensory deficits that could have affected hedonistic scores of sucrose solutions.

Olfactory tests

Olfactory tests were conducted to check for possible differences in general sensory sensitivity of the investigated groups (Jones et al. 1978). There is a distinct correlation between a hedonistic score, an intensity score and normal olfactory function. A battery of Sniffin' Sticks, a smell identification test, was used for testing purposes (Sniffin' Sticks-Olfactory Test manufactured by Burghardt, Wedel, Germany). The test is a standardised method of assessing the ability to identify smells (Hummel et al. 1997, Hummel et al. 2001, Kobal et al. 1996). Each subject was asked to identify 16 pens of various smells. Norms for smell identification are age-related; for adult Caucasians below 50 years of age the norm is 14.7±1.2, and for adults over 50 13.7±1.5. The random score of smell identification in anosmia is 4 out of 16 samples (Hummel et al. 1997 Kobal et al. 1996). It is, therefore, fair to assume that scores below 10 are tantamount to olfactory dysfunction and scores below 4 to complete anosmia.

Statistical methods

Statistica.Pl (StatSoft) and SPSS 9.0 for Windows (SPSS 9.0 for Windows) were used in the statistical analysis of results. The differences between genotype and allele frequency distributions were determined using the Pearson-Fisher chi-squared test or the Fisher's

exact test. P-values of 0.05 or less were considered to be statistically significant. SAS statistical package (SAS 6.03 Edition for Windows) was used for the assessment of Hardy–Weinberg equilibrium.

RESULTS

We examined 62 alcoholics, 32 of them were sweet likers and 30 were sweet dislikers. Proband who met inclusion criteria did not have any olfactory disorders that might have affected their hedonistic response or their perception of the intensity of sucrose solutions. HWE test showed no statistically significant changes of genotype distribution.

Polymorphism analysis was conducted. A statistically significant association was found between the presence of some alleles of the ANKK 1 gene Taq 1A polymorphism and sucrose preference in AD subjects ($p=0.00161$); A1 alleles occurred more frequently in sweet likers compared to sweet dislikers (76.67% vs 23.33%), A2 alleles occurred more frequently in sweet dislikers compared to sweet likers (56.38% vs. 43.62%). Since there were only four patients with A1A1 genotype, it was decided that a comparison between A1A2 and A2A2 would be conducted (to estimate the effect of the A1 allele). An association between the presence of the ANKK1 gene Taq-1A polymorphism and the preference of sucrose in

alcoholics was statistically demonstrated ($p=0.017$). The A2A2 genotype was found more frequently in sweet dislikers compared to sweet likers (76.67% vs 40.63%), whereas the A1A2 genotype was found more frequently in sweet likers compared to sweet dislikers (46.87% vs. 23.33%). To produce a more comprehensive estimation, the A1A1 and A1A2 genotypes were summed and compared with the A2A2 genotype. An association between the presence of the ANKK1 gene Taq-1A polymorphism and the preference of sucrose in alcoholics was statistically demonstrated ($p=0.0041$). The summed A1A1 and A1A2 genotypes were found more frequently in sweet likers compared to sweet dislikers (59.37% vs. 23.33%) (Table 1).

No such associations were observed for DRD2 gene polymorphisms.

An association with borderline significance ($p=0.0666$) was found between the probability of A1A2 Taq-1A genotype occurring in the ANKK-1 gene and sucrose preference in AD probands; the frequency of A1A2 genotype was almost three-fold greater in sweet likers compared to sweet dislikers. A statistically significant association was found between the presence of A2A2 Taq-1A genotype of the ANKK-1 gene and sucrose preference in AD probands; the probability of A2A2 occurrence is five-fold smaller in sweet likers compared to sweet dislikers (Table 2). No such associations were found in DRD2 gene polymorphisms.

Table 1. Association between allele and genotype distribution of the ANKK 1 gene Taq 1A polymorphism and sucrose preference in alcoholics

Allele	Sweet likers (n=32)		Sweet dislikers (n=30)		
	Number	%	Number	%	
A1	23	76.67%	7	23.33%	
A2	41	43.62%	53	56.38%	
χ^2	9.95		df=1		$p=0.00161$
Genotype	Sweet likers (n=28)		Sweet dislikers (n=30)		
	Number	%	Number	%	
A1A2	15	46.87%	7	23.33%	
A2A2	13	40.63%	23	76.67%	
χ^2	5.62				$p=0.017$
Genotype	Sweet likers (n=32)		Sweet dislikers (n=30)		
	Number	%	Number	%	
A1A2+A1A1	19	59.37%	7	23.33%	
A2A2	13	40.63%	23	76.67%	
χ^2	8.26				$p=0.0041$

n - number of patients; p - p value; χ^2 - chi-squared

Table 2. Association between the probability of a specific genotype occurring in the ANKK 1 gene Taq 1A polymorphism and sucrose preference in probands

Sucrose preference	Taq 1A	Odds ratio	95% Conf	Interval	Fisher exact
sl vs sd					
sl vs sd	A1A2	2.90	0.99	8.47	$p=0.0666$
sl vs sd	A1A1	0.00	1.05	0.00	$p=0.1136$
sl vs sd	A2A2	0.21	0.07	0.62	$p=0.0051$

sl - sweet liking; sd - sweet disliking

Table 3. Sensation of pleasure for 0%, 1%, 10% and 30% sucrose solutions with a comparison of Taq 1A genotypes of the ANKK 1 gene

Proband's genotype		Mann-Whitney test			
		Concentration of sucrose solution %	N1	N2	p
A1A1	A2A2	0	4	36	0.868
A1A2	A2A2	0	22	36	0.187
A1A2	A1A1	0	22	4	0.252
A1A1	A2A2	1	4	36	0.716
A1A2	A2A2	1	22	36	0.494
A1A2	A1A1	1	22	4	0.521
A1A1	A2A2	10	4	36	0.064
A1A2	A2A2	10	22	36	0.051
A1A2	A1A1	10	22	4	0.499
A1A1	A2A2	30	4	36	0.029
A1A2	A2A2	30	22	36	0.017
A1A2	A1A1	30	22	4	0.355

N1 - number in the first column, N2 - number in the second column, p - p value

Table 4. Hedonistic response to sucrose solutions depending on the ANKK 1 gene Taq1A polymorphism found in probands. The table presents average, median, minimum and maximum values as well as the standard deviation

Concentration %	0%	0%	0%	0%	0%	0%	0%	0%
Genotype	N	Average	Median	Minimum	Maximum	Q25	Q75	SD
A1A2	22	-2.48	0.00	-23.46	5.52	-1.38	0.00	6.70
A1A1	4	0.17	0.00	0.00	0.69	0.00	0.35	0.35
A2A2	36	0.23	0.00	-22.08	24.84	-0.35	0.69	8.40
Concentration %	1%	1%	1%	1%	1%	1%	1%	1%
Genotype	N	Average	Median	Minimum	Maximum	Q25	Q75	SD
A1A2	22	3.64	1.04	-10.35	23.46	0.00	9.66	7.99
A1A1	4	2.07	0.00	-2.07	10.35	-1.04	5.18	5.61
A2A2	36	1.32	1.38	-23.46	19.32	-0.35	7.25	9.43
Concentration %	10%	10%	10%	10%	10%	10%	10%	10%
Genotype	N	Average	Median	Minimum	Maximum	Q25	Q75	SD
A1A2	22	16.78	17.25	-14.49	37.26	8.97	28.29	13.01
A1A1	4	23.46	23.12	8.28	39.33	15.18	31.74	12.71
A2A2	36	11.04	12.42	-15.87	35.19	1.73	21.05	11.44
Concentration %	30%	30%	30%	30%	30%	30%	30%	30%
Genotype	N	Average	Median	Minimum	Maximum	Q25	Q75	SD
A1A2	22	21.45	25.53	-33.12	46.92	12.42	37.26	21.27
A1A1	4	31.57	30.36	17.25	48.30	22.77	40.37	12.86
A2A2	36	7.88	3.45	-37.95	49.68	-7.94	18.98	21.06

A difference with borderline significance in sensory pleasure between A1A1 and A2A2 probands ($p=0.064$) and A1A2 and A2A2 probands ($p=0.051$) was found for 10% sucrose solutions.

A statistically significant difference in sensory pleasure between A1A1 and A2A2 probands ($p=0.029$) and A1A2 and A2A2 probands ($p=0.017$) was found for 30% sucrose solutions (Table 3).

DISCUSSION

There are many reports that address the problem of associations between abnormalities of dopaminergic transmission and (alcohol and nicotine) addiction and

obesity (Nisoli et al. 2007, Preuss et al. 2007, Suchanecka et al. 2011). Klein et al. used neuroimaging techniques to investigate the role of dopamine in error-correction learning. They demonstrated that people with A1 allele of Taq 1A polymorphism (with a lower density of D2 receptors) were less effective in learning how to avoid actions with negative consequences compared to people with A2 allele. A lower number of D2 receptors seems to reduce sensitivity to negative consequences which can account for an increased risk of developing addiction in A1 allele carriers. Stice et al. (2008) demonstrated that obese people have a reduced number of dopamine receptors in the striatum compared to thin people. Excessive consumption may be a way of

compensating striatal dopaminergic hypofunction which ultimately leads to obesity. Both alcohol and sweet substances elicit activation in dopaminergic nerve endings in the limbic structures of laboratory animals and thus increase dopamine concentration in the brain. Rats repetitively fed 0.3 M glucose solution had increased dopamine turnover compared to rats fed water only (Hajnal et al. 2004). The authors note that dopamine receptor antagonists may selectively suppress consumption of sweet solutions in animals (Leeb et al. 1991). Consequently, it is fair to hypothesise that genetic-related changes in dopaminergic transmission (mutations of genes involved in dopaminergic pathways) may affect changes in the rewarding effects of alcohol and sweet substances. The present study demonstrated an association between several genotypes in the ANKK 1 gene Taq 1A polymorphism and sucrose preference in AD probands (Table 1) which is consistent with the above mechanism. The presence of A1 Taq 1A allele was the determinant of sweet taste response. Every additional A1 allele enhanced hedonistic response to the two highest sucrose concentrations while every additional A2 allele suppressed it (Table 4, Figure 1). It is, however, to be noted that the statistical significance of this association only applies to A1A1, A1A2 and A2A2 genotypes. The role of A1 allele can be the consequence of two reasons. First, Reward Deficiency Syndrom (RDS) might be involved (Comings et al. 2000). Consequently, since the reward system mediates several modulation systems, a certain combination of protein-coding gene polymorphisms involved in neurotransmission may be damaging to the process. The mechanism may lead to inadequate stimulation caused by natural rewards, such as food or sex, and following on from that to sensation-seeking and ultimately to drug-seeking behaviour and addiction.

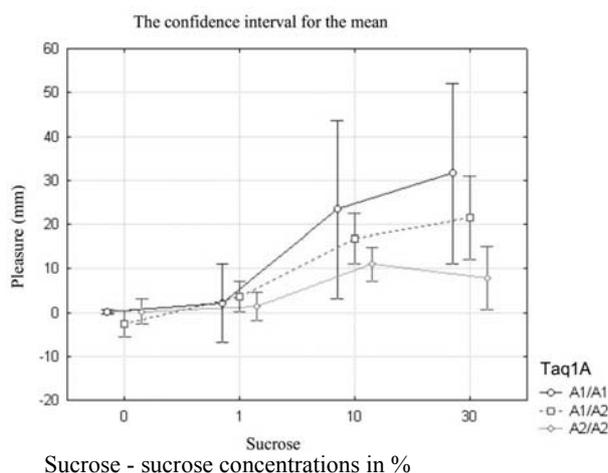


Figure 1. Association between hedonistic response to increasing sucrose concentrations and certain Taq 1A genotypes in the probands

Let us examine another scenario with no neurotransmitter deficiencies, but a situation in which increased sucrose concentrations enhance perception of pleasure. Experiments on rats demonstrated a linear dependence

between administration of solutions with increasing sucrose concentrations and elevated flow and concentration of dopamine in the nucleus accumbens (Hajnal et al. 2004). If alcohol had the same mediating effect on the amount of dopamine as sucrose, it would incessantly increase the amount of alcohol consumption stripping a patient of any motivation to stop drinking and leading to severe health and social problems.

We found no association between the polymorphic variants in the promoter region of the DRD2 gene (-141 Ins/Del) and the preference for sweet taste. Although there are findings on an association between the polymorphism and AD, results seem to be inconclusive (Blomqvist et al. 2000, Parisan et al. 2000). In a study by Ishiguro conducted on a sample of 209 Japanese alcoholics, the allele (-141 C Ins) was found to be more frequently present in alcoholics compared to controls (Ishiguro et al. 1998). However, Sander did not replicate this finding in his study of AD patients with family history of alcoholism and severe alcohol withdrawal syndromes (Sander et al. 1999). Johann et al investigated a group of alcoholics of German descent who were divided, according to a genotype-phenotype research strategy, into alcoholics suffering from severe withdrawal complications such as seizure or delirium, family history positive (FH+) alcoholics, alcoholics with an antisocial personality disorder (ASPD), alcoholics with an ADHD, and type 1 or type 2 alcoholics according to Cloninger's typology. They found a significant excess of the -141C Del allele in alcoholics with a paternal and grandpaternal history of alcoholism and in subgroups of suicidal alcoholics. There are no available data in the literature on the association between the above polymorphism and sucrose preference.

Finally, we investigated polymorphisms in the DRD2 gene exon 8. Finckh et al. (1997) found an association between exon 8 A/A genotype and exacerbation of anxiety and depression symptoms in an observational study conducted in a detoxification ward. The genotype was associated with an increased number of suicide attempts, a tendency to exacerbate the severity of withdrawal symptoms, earlier relaps and a reduced response to apomorphine (Finckh et al. 1997). Kucharska et al. (2012) conducted haplotype analysis of DRD2 (-141 C Ins/Del, exon 8 (A/G), intron 2 STRP) and ANKK1 (Taq1A (A1/A2)) and demonstrated that the I-A2-A-6 and D-A2-A-7 haplotypes were found more frequently in the subgroup of alcoholics with withdrawal complications. Interestingly, no association with withdrawal seizures was observed. No association between the above polymorphisms as well as the -141C Ins/Del polymorphism in the dopamine D2 receptor gene promoter region and sucrose preference was found. The literature provides no data on the topic.

Although the authors' own research was conducted on a relatively small sample, the statistical power of the study was sufficient to draw valid conclusions. Naturally, an independent replication study on a different sample of AD patients would have led to a broader understanding of the problem.

CONCLUSIONS

Study results suggest Taq-1A polymorphism plays a role in the preference to high concentrations of sucrose and its potential association with alcohol dependence pathogenesis.

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