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The analysis of the polymorphic variations of the dopamine gen transporter (DAT 1) and the serotonin transporter (5-HTTLPR) in patients with Alcohol Dependence Syndrome with inclusion of the phenotypic feature of sweet liking preference

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Summary

Objectives. The purpose of this study was to determine the relationship between sweet-liking phenotype and the variation of the gene sequence of the dopaminergic and serotonergic system.

Methods. The study recruited 100 probands. The participants were interviewed for addiction (SSAGA-Semi Structured Assessment for the Genetics of Alcoholism) and assessed with the questionnaires: MMSE, Beck Depression Inventory and Hamilton Anxiety, Snaith-Hamilton Pleasure Scale. The taste was analyzed with tests to assess sensitivity to sweet taste and also smell tests were performed. Patients preferring the highest glucose volumes were called sweet likers. Statistical analyses were performed (SPSS - Statistical Package for the Social Sciences).

Results. Links between sweet liking phenotype and polymorphic variant of DAT1 gene were determined. The presence of DAT1 9/10 genotype increased three fold time sweet liking phenotype (p=0.015, odds ratio-3.00), the presence of DAT1 10/10 decreased two fold time the chance being sweet liker (p=0.051, odds ratio-0.43). Genotype 10/10 was significantly more common among sweet dislikers 10/10 (68.18% vs 47.92%) i 9/9 (6.82% vs 2.08%).

Conclusions. A genetically significant association between the presence of 9/10 DAT1 VNTR genotype and a sweet-liking phenotype in probands was determined.

Key words: Alcohol Dependence Syndrom, sweet liking phenotype, genetic study

Introduction

Alcohol Dependence Syndrome is a disease both clinically and etiologically varied. Numerous population studies showed that in its etiology genetic factors participate in about 40-50%, whereas environmental influence is estimated on the level of 50-60%.

Heterogeneous course of ADS causes that biological factors are difficult to identify. From this reason, not only crucial but also a necessary element of studies on biological causes of this disease is an isolation of so called homogeneous subgroups. Patients with ADS are assigned to similar, in respect of symptoms, the course of disease or and disposition of psychic groups.

Conducted scientific research should make it possible to develop uncomplicated diagnostic tests which will allow to recognize given type of disease. Thanks to this it will be possible to employ targeted therapy. ADS relations and sensation of tastes have been described in many reports. An interesting direction of researches are studies on recognition of a bitter taste and its association with an age of alcohol initiation, a preference of consumption of a particular kind of alcohol and a protective role in terms of ADS development [1]. In hereby study a subgroup of patients with ADS has been analyzed in respect of a sweet taste.

Legitimacy of considerations about preferences connection of the high sucrose concentration and alcohol consumption is the fact that both substances activate similar neurotransmitter systems: serotonin, dopamine and opioid [2-4] constituting a part of a reward systems. This correlation was observed in laboratory animals when after application sweet solutions there were activated dopaminergic ends in a limbic system like after alcohol application [2,5]. Dopaminergic receptors as well as mechanisms influencing on dopaminenergic transmission (dopamine transporter DAT) are responsible for regulations of preferences and consumption of sweet solutions in animals. Whereas selective reduction of consumption of sweet solutions in animals causes compounds blocking centrally D2 receptors or inhibiting dopamine reputake eg. Cocaine [6]. What's more consumption of sweet solutions can influence on D2 receptors density [7, 8].

There is a question whether a preference of the high sucrose density (>30%) can be a stable marker addiction to alcohol in a man. The one who answered it positively was Kampov-Polevoy [9] observing that in mens' group addicted to alcohol (keeping abstinence) from 46% to 65% preferred high sucrose density (0.83 M). In control group of people addicted, a preference concerned only 16% of examined. In the following studies he also showed correlation between a preference of the high sucrose density in adult alcoholics' sons and addiction of their fathers [10, 11].

Not all researchers, however, showed approval about this matter. Ścińska in her studies on underaged sons of fathers addicted to alcohol didn't show differences in comparison with control group [12]. Bogucka-Bonikowska showed that intensity and pleasure connected with a sucrose taste, which were evaluated on the scale of visual analogy (VAS) didn't differ alcoholics and control group [13]. Kampov-Polevoy in 2004 in the following study achieved also negative results [14].

The feature of „sweet liking" is not probably the alcohol addiction marker, however, it can be useful as an alcoholism indicator in conjunction with another features.

Ścińska and et al carried out susceptibility testing on sucrose solutions in addicted men keeping at least the period of 7 days abstinence [12].

On the basis of the evaluation of a sweet taste it was impossible to distinguish addicted men from control group. It was claimed that the proportion of „sweet likers"

and the evaluation of 30% of sucrose density was higher than in alcoholics subgroup - sons of addicted fathers [15]. People qualified as „sweet likers" are 77,3% in alcoholic group - sons of alcoholic fathers, whereas 57,6% in control group and merely 47,8% in alcoholic group - sons of nonalcoholic fathers.

Jabłoński at al 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 [16].

On the basis of analyzed literature in hereby study there were studied two polymorphisms of the DAT 1 dopamine gen transporter as well as 5-HTT serotonin gen transporter in patients group with Alcohol Dependence Syndrome - differentiated on the group of „sweet liking" and „sweet disliking".

Dopamine transporter plays a crucial role through the influence of amine reputake in the regulation of dopaminergic activity. Encoding gen: transporter is located on 5p15.3. There was described polymorphism involving 3-11 repetition 40pz in the area of 3'. There is also mentioned allele 14 VNTR. Individuals homozygous for the 10 VNTR allele show the lowest ability of the neurotransmitter binding than individuals possessing 9 VNTR allele.

Serotonin transporter is directly connected with the regulation of serotonergic activity in CNS through the influence on serotonin reputake from a synaptic connection. It is encoded by a single SLC6A4 gen on 17q12 chromosome [17]. In the area of the gen promoter mentioned above, there was discovered functional polymorphism involving on insertion or 44pz deletion in the region of gen promoter what results in emergence of allele L (long) or allele s (short) [18]. Allele s results in transporter emergence with a lower activity than allele L, what causes lower reputake serotonin [17]. Allele s is connected with anxiety [19], affective disorders [20] and severe suicidal attempts [21].

Studies of young adult individuals showed association of 5HTT short allele gen with high tolerance of ethanol. It indicates to the possibility of participation of serotonin carrier variant with lower activity in neural mechanisms of response to alcohol and dependences development [22]. There was found a relation between polymorphism in the region of gen promoter of serotonin carrier and increased risk of alcoholism connected with antisocial impulsive personality, including willingness to suicidal attempts [23-25]. The larger frequency of short allele 5HTT was claimed in alcoholics in comparison with control group (45%vs29%) [26].

Materials and methods

The study recruited 100 probands. The participants were interviewed for addiction (SSAGA) and assessed with the questionnaires: MMSE, Beck Depression Inventory and Hamilton Anxiety, Snaith-Hamilton Pleasure Scale. Mean of age was 33.58+/-8.47 years. The taste was analyzed with tests to assess sensitivity to sweet taste and also smell tests were performed.

Gen polymorphism of the serotonin carrier - (SLC6A4):5-HTT

This polymorphism characterizes insertion or deletion of the fragments' size 44 alkali pairs (pz) in the region containing variable number tandem repeat. DNA isolation from leukocytes from peripheral blood was conducted by salting out method PCR-VNTR. The following starters were used to amplification: F:5' GGC GTT GCC GCT CTG AAT GC 3', R: 5' GAG GGA CTG AGC TGG ACA ACC AC 3'. On the basis of the results of electrophoretic separation in the presence of DNA weight markers were received fragments with a length of: 44 nad 528 bp. A fragment with a length of 484 bp was called a short allele - s, whereas fragment 528 bp was defined as a long allele l.

Gen polymorphism of the dopamine carrier - (SLC6A3):DAT

This polymorphism characterizes a repeatable number 40 bp of tandems in 3' non translational region of the gen dopamine carrier. Analysis was carried out using method PCR - VNTR. The following starters were used to amplification: : F: 5'- TGT GGT GTA GGG AAC GGC CTG Ag 3', R: 5'- CTT CCT GGA GGT CAC GGC TCA AGG 3'Obtained results were different in size dependent on a VNTR number repeats which are characteristic for each allele with a size: 410 bp (9 repeats), 450 bp (10 repeats) and 490 bp (11 repeats).

Taste studies

Taste studies were conducted between 10:00 am and 1:00 pm in a silent, ventilated room. The examined were restrained from drinking, eating, smoking cigarettes at least 1 hour before an examination. Participants before an examination were familiarized with a research procedure and scales [15, 27]. This procedure was subjected to validation in Institute of Psychiatry and Neurology showing the high level of solidity. At the beginning of the examination each participant was given distilled water in a cup to bathe mouth with an aim to getting used to the water taste - a neutral stimulus „reference". In the next step samples of sucrose solutions (n=8) were given from the disposable syringes directly on the tongue. Examined people distributed samples in an oral cavity, then they evaluated VAS on scales, intensity (from „0"= very weak to „100"= very strong) and pleasure (from „-50" = very unpleasant to „50" = very pleasant) which is connected with it. Samples were given every 60-90 s. At that time examined people were filling in answers sheets, spitting out samples and bathing an oral cavity with distilled water. Between first and second series (between samples no 4 and 5) examined people were resting about 5 minutes [15]. Examined were not informed about an order and a content of a particular samples. Another one millimeter samples: 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. Sets of syringes were prepared in Institute of Psychiatry and Neurology according to previously prepared scheme [13], they were stored in the

temperature of - 4°C. An hour before a sample examination they were taken to room temperature. Density of sucrose solutions were selected on the basis of previous studies [10,13, 15]. Individuals preferring the highest sucrose solution (average hedonic evaluation from the two series) were classified as „sweet likers" (s.l), other individuals as „sweet dislikers" (s.d). Furthermore, values from VAS scales were subjected to analysis. Evaluation of intensity of sucrose solutions (among both s.l. as well as s.d) serves to exclusion of sensory deficits, which could influence on evaluation of sucrose solutions in terms of hedonistic.

Table 1. **Data concerning the course ADS at probands**

Data	Alcoholics N (average ± standard deviation)
Age of first contact with alcohol (years)	15.18 ± 2.43 (n=100)
Age of the loss control under drinking	21.17± 5.41 (n=100)
Age of first abstinence symptoms	23.64 ± 11.31 (n=92)
The lasting time of abstinence symptoms	4.04 ± 6.79 (n=92)
Individuals who experienced delirium tremors (% people)	15%
Age of emergence the first delirium tremor event	29.25 ± 6.17 (n=15)
Individuals who experienced withdrawal seizures (%people)	16.0 %
Individuals who experienced withdrawal seizures (years)	30.81 ± 4.78 (n=16)
Average daily amount of consumed vodka during drinking period	584.51 ± 341.73 (n=100)
Age of first alcohol treatment	24.73 ± 13.58 (n=100)
Individuals with suicidal attempts in an interview	37.0%

Table 2. **Sucrose preference among probands**

Sucrose preference			Overall	Overall
	Number	Percent	Number	Percent
SWL -	48	48.00	48	48.00
SWL +	52	52.00	100	100.00

SWL+:"sweet likers", hedonistic response to the highest concentrations of sucrose
SWL-: „sweet dislikers", hedonistic lack of response to the highest concentrations of sucrose

Laboratory studies

The study of selected gen polymorphisms was conducted in the Laboratory of Psychiatric Genetics PUM in Szczecin. The study design was approved by the institutional review board committees PUM. Whole blood was collected from an elbow vein and DNA was isolated using salting out method.

Results

Table 3. **Correlation between the distribution of allelic polymorphisms in the dopamine transporter gene DAT1 and 5HTT serotonin and sucrose preference at probands**

	SWL -		SWL+		
DAT1	number	share %	number	share %	Sum
9	17	19.32%	26	27.08%	43
10	71	80.68%	70	72.92%	141
Sum	88		96		184
Chi² Pearsona	1.55		df=1		p=0.21374
Chi² NW	1.56		df=1		p=0.21213
	SWL -		SWL+		
5HHT	number	share %	number	share %	Sum
L	58	60.42%	56	56.00%	114
S	38	39.58%	44	44.00%	82
Razem	96		100		196
Chi² Pearsona	0.39		df=1		p=0.53091
Chi² NW	0.39		df=1		p=0.53080

In the conducted studies, statistical significance was not shown between occurrence of certain alleles of the dopamine transporter gene polymorphisms in DAT1 and 5HTT serotonin transporter gene and sucrose preference in probands.

Table 4. **Correlation between the distribution of genotypes studied polymorphisms of dopamine transporter gene DAT1 and 5HTT serotonin transporter gene and sucrose preference in probands**

	SWL+		SWL -		
DAT1	number	share%	number	share%	Sum
10/10	23	47.92%	30	68.18%	53
9/10	24	50.00%	11	25.00%	35
9/9	1	2.08%	3	6.82%	4
Razem	48		44		92
Chi² Pearsona	6.59		df=2		p=0.03704
Chi^2 NW	6.75		df=2		p=0.03429
	SWL+		SWL-		
5HTT	number	share%	number	share%	Sum
LL	16	32.00%	18	37.50%	34
LS	24	48.00%	22	45.83%	46
SS	10	20.00%	8	16.67%	18
Sum	50		48		98
Chi² Pearsona	0.39		df=2		p=0.82441
Chi² NW	0.39		df=2		p=0.82425

There was a statistical significant correlation between the occurrence of genotype 9/10 polymorphism of the dopamine transporter gene DAT1 and sucrose preference among probands (p = 0.03704). It has been shown more frequent occurrence of 10/10 (68.18% vs. 47.92%) and 9/9 (6.82% vs. 2.08%) in probands SWL-, and more frequent occurrence of 9/10 from probands SWL + (50.00% vs 25.00%).

There was no correlation between the occurrence of a particular genotype of the studied polymorphism of the serotonin transporter gene, 5HTT and sucrose preference among probands.

Table 5. **Analysis of the genotype distribution of 10/10 and 9/10 40-bp VNTR DAT1 dopamine transporter gene group probands and SWL+ and SWL -**

	SWL +		SWL -		
DAT1	number	share%	number	share%	Sum
other	25	52.08%	14	31.82%	39
10/10	23	47.92%	30	68.18%	53
Sum	48		44		92
Chi^2 Pearsona	3.86		df=1		p=0.04944
Chi^2 NW	3.90		df=1		p=0.04834
	SWL +		SWL -		
DAT1	number	share%	number	share%	Sum
other	24	50.00%	33	75.00%	57
9/10	24	50.00%	11	25.00%	35
Sum	48		44		92
Chi^2 Pearsona	6.09		df=1		p=0.01362
Chi^2 NW	6.20		df=1		p=0.01278

Based on the obtained results of the analysis it was showed significantly more frequent occurrence of DAT1 9/10 VNTR SWL + group compared to the SWL- (50.00% vs. 25.00%) (p = 0.01362).

It has also been more frequent occurrence of significant DAT1 10/10 VNTR SWL- group compared to the SWL + (68.18% vs. 47.92%) (p = 0.04944).

The presence of the DAT 1 9/10 VNTR 3 x increase the chances of occurrence of features „sweet liking" (p = 0.015, odds ratio - 3.00) in the studied group.

The presence of DAT1 10/10 VNTR at probands than 2 x decreased chance of occurrence SWL + (p = 0.051, odds ratio - 0.43).

Discussion

It is widely accepted that both constitutional and environmental factors have a considerable influence on the development, course and prognosis in ADS.

Current state of knowledge about alcohol dependence allows to claim that this term involves heterogeneous group of patients which differ in terms of predisposing factors, different clinical course of the disease and prognosis.

A study described here was planned in order to verify hypothesis given in literature as well as to familiarize with phenotypic - genotypic association of ADS in associative studies in unrelated individuals (sweet liking phenotype).

There was analyzed gen polymorphism of the dopamine transporter **DAT (SLC6A3),** invloving variable number repeats (3-11) 40 pz in the noncoding region 3' [28].

Heinz and et al claimed that individuals heterozygous 9/10 VNTR DAT1 have reduced availability of DAT 1 protein on average 22% in the striatum as compared to subjects homozygous 10/10 VNTR. His results suggest that VNTR polymorphism of the DAT gen has an impact on protein translation. It can explain the multitude of clinical relations of the above carrier [29].

In independent associative studies there was confirmed correlation of 10 VNTR with Attention. Deficit Hyperactivity Disorder (ADHD) [30, 31, 32].

Ueno and et al identified SNP polymorphism at the end of 3 - UTR DAT 1 gen. Allele A 2319 of this polymorphism occurred only in individuals with one allele 10-, 11-,14- VNTR. There was showed its relation to ADS. Haplotype A 2319 and 10 VNTR DAT l is associated with alcoholism, there was no correlation in the case of haplotype G 2319 and 10 VNTR DAT1 [33].

Wernicke and et al neither claimed any differences in frequency of G2319A polymorphism in the whole group which was studied by them nor in separated subgroups. They proved, however, that A 2319 allele of the SNP polymorphism occurred also in patients with 9 VNTR allele, however, more frequently it was related to 10 VNTR allele [34].

In 1998 similar results were achieved by Schmidt and et al. According to the researchers 9 allele of the dopamine gen transporter connected with severe complications of alcohol withdrawal seizures, what is probably possible due to compensating of the effect of long-term effects of ethanol on cerebral function [35].

Franke and et al in associative studies of families didn't claim the existence of significant correlation between 9 allele VNTR SLC6A3 and ADS in both the whole studied addicted group as well as in a homogeneous group of severe withdrawal symptoms [36].

Chen and et al in Chinese population and inhabitants of Taiwan didn't prove correlation between DAT gen VNTR polymorphism and ADS [37].

Muramatsu and Higuchi showed in their studies higher frequency of DAT 1 7 VNTR allele in alcoholic group with lower activity of aldehyde dehydrogenase II than in control group [38].

In a presented study a statistical significance wasn't demonstrated between the existence of certain alleles of the dopamine transporter gene polymorphisms DAT1 and 5HTT serotonin transporter gene and sucrose preference in probands (Table 3).

We found a statistically significant correlation between the presence of genotype 9/10 polymorphism of the dopamine transporter gene DAT1 and sucrose preference among probands (50.00% vs 25.00%) (Table 4), in a more detailed analysis (Table 5).

We also found more frequent occurrence of genotype 10/10 (68.18% vs 47.92%) i 9/9 (6.82% vs 2.08%) in probands SWL - (Table4).

As it clearly results from literature, reports in this field are contradictory and undoubtedly they require studies on larger populations. Unequal frequency of the occurrence of allele A9: 4.2-6.2% in Japanese control group, to 16-28% in American control group indicates to significant impact on the prevalence of different alleles in the studied populations [39]. Presented study indicated to statistically significant differences in terms of genotypes emergence and alleles of the dopamine transporter gene polymorphism DAT 1. It can be linked to the fact that dopaminergic system is responsible for the regulation of the preferences and consumption of sweet solutions and mechanisms influencing dopaminergic transmission.

Selective reduction of consumption of fresh solutions cause compounds that block centrally D2 receptors or inhibit the reuptake of dopamine. Repeatability and objectification results require testing large, ethnically homogeneous groups of patients.

Gen polymorphism of the serotonin transporter 5 HTT (SLC6A4)

There are a lot of reports describing associative studies 5 HTT gen polymorphism studied people who abused alcohol, with the genotype s/s or l/s [40] there were found greater number of serotonin binding carrier.

There was proved correlation of the high ethanol tolerance in young adults with s allele of the 5HTT gen. It is possible that serotonin transporter with a lower activity takes part in mechanisms of neuronal response to ethanol and the development of tolerance alcohol [41].

Kranzler reported also about lack of correlation 5 HTT polymorphism with alcoholism with the earlier loss control under drinking [42]. Hammoumi and et al proved greater frequency of a short allele of 5 HTT gen in alcoholics in relation to control group (45.5% vs 29%) [43].

There was also found correlation between polymorphism in the region of gen promoter of serotonin transporter and increased risk of alcoholism connected with antisocial personality, impulsive [44-46].

Johnson suggested in his studies alcoholism correlation with the earlier loss control under drinking with a greater frequency of L allele [47].

The correlation of s allele with alcohol dependence was not confirmed by Gorwood and et al, however, they proved on the relation to repeating, more serious suicidal attempts [48].

Grzywacz and al did not find significant differences in the case-controlled study. The alleles and genotypes distribution of the DAT1 polymorphism did not differ significantly between the alcoholics and the controls in the case-control study.They found significant differences in allele transmission in the case group - families like trios. Allel 10 VNTR was more frequently transmitted [49].

Grochans et al did not find significant differences in the alleles and genotypes distribution of the 5HTT polymorphism in patients with alcohol dependence and control [50].

In a presented study there wasn't found association between control group and marked polymorphism of the serotonin transporter 5HTT. Undoubtedly, a significant impediment was a low number in a group as it was a pilot study. It is planned not only to carry on studies but also to enlarge a group, to construct haplotypes as well as to conduct analysis of haplotype transmission disequilibrium of alleles in families trios type.

Conclusions

Association between sweet liking phenotype and polymorphic variant of DAT1 gene was determined. In addition, it is advisable to examine studied probands once again in a few years time interval with an aim to verifying whether SWL+ feature is a constant feature during the influence of such factors as MMSE result, or treatment in a hospital because of the somatic complications may suggest, that the feature can bind with more severe course of addiction and accompanying degradation process within the NS (which may be a secondary effect of the disclosure of the features of SWL +).

Анализ полиморфных вариантов гена транспортера допамина ДАТИ и транспортера серотонина 5-ХТТЛПР у пациента с Синдромом алкогольной зависимости с учетом фенотипной черты употребления сладостей

Содержание

Задание. Заданием работы было определение зависимости между фенотипом „сладкий" (любовь к сладостям) пациентов с Синдромом алкогольной зависимости и некоторых полиморфных вариантов гена транспортера допамина ДАТИ и транспортера серотонина 5-ХТТЛПР (serotonin-transporter-linked-polimorphic-region).

Материал и методы. В исследование включено 100 пациентов зависимых от алкоголя, исполняющих критерии зависимости по классификации ЦИД-10. Расспрос, относящийся к течению зависимости собран при использовании польской версии глоссария ССАГА (Semi Structured Assesment for the Genetics of Alcoholilism). Выбор употребления сладостей определен при помощи состава пробирок, содержащих растворы сахарозы. Лица с наибольшими склонностями к сладостям с наибольшей концентрацией сахарозы были определены как „сладкий ликер", „очень сладкий". Материал для генетических исследований собран из венозной крови, ДНК изолирована методом высаливания. Проведен анализ появления полиморфных вариантов гена транспортера допамина ДАТИ и транспортера серотонина 5-ХТТЛПР. Для статистического анализа использована программа СПСС.

Результаты. В предложенном исследовании не отмечено зависимости между появлением определенных аллели полиморфизмов гена транспортера допамина ДАТИ и гена транспортера 5-ХТТЛПР и преференцией сахарозы у пробантов (пациентов с алгогольной зависимостью). С другой стороны, статистически существенность найдена между появлением генотипа 9/10 полиморфизма гена транспортера допамина ДАТИ и преференцией сахарозы среди пробантов (p=0,0370). Присутствие этого ДАТИ 9/10 ВНТР в три раза увеличивает шанс появления черты „очень сладкий (p=0,015, отклонение собрания =3,00) в исследованной гвуппе. Отмечено также более частое присутствие генотипа 10/10 (68,18% до 47,92% и 9/9 (6,82 до 2,08%) у пробантов без преференции сладкого вкуса. Присутсивие ДАТИ 10/10 ВНТР у пробантов более двух раз уменьшало шанс к появлению потребности сладкого продукта (p =0,051, отклонение собрания = 0,43).

SWL – sweet liking (–) без преференции сладкого вкуса

SWL – sweet liking (+) преференция сладкого вкуса

Выводы. Подтвержена связь фенотипа „сладкого вкуса" с генотипом транспортера допамина ДАТИ.

Ключевые слова: синдром алкогольной зависимости, фенотип „очень сладкий", генетические исследования

Analyse der Variationen von Genpolymorphismus des Dopamintransporters (DAT1) und Serotonin - Transporters (5-HTTLPR) bei Patienten mit Alkoholabhängigkeitssyndrom mit Berücksichtigung von phänotypischen Eigenschaft der Präferenz für Süßes

Zusammenfassung

Ziel. Das Ziel der Arbeit war die Feststellung der Abhängigkeit zwischen dem Phänotyp „sweetliking")Präferenz für Süßes) der Patienten mit dem Alkoholabhängigkeitssyndrom und dem Auftreten der bestimmten der Variationen von Genpolymorphismus des Dopamintransporters DAT1 und Serotonin - Transporters 5-HTTLPR (serotonin-transporter-linked-polymorphic-region).

Material und Methoden. Zur Studie wurden 100 alkoholabhängige Männer eingeschlossen, die die Kriterien der Abhängigkeit nach ICD-10 erfüllten. Die Anamnese zur Abhängigkeit wurde mit Hilfe der polnischen Version des Fragebogens SSAGA (Semi Structured Assesment for the Genetics of Alcoholism) durchgeführt. Die Präferenz für süßen Geschmack wurde mit Hilfe der Reagenzgläser mit Saccharoselösung bestimmt. Die Personen, die die höchste Konzentration der Saccharose bevorzugten, wurden als „sweet likers" bezeichnet. Das Material für die genetischen Untersuchungen wurde aus dem Blut isoliert, RNA wurde mit dem Aussalzen isoliert. Es wurden die Variationen des Genpolymorphismus des Dopamintransporters DAT1 und Serotonin – Transporters 5-HTTLPR analysiert. Zur statistischen Analyse wurde der SPSS Programm eingesetzt.

Ergebnisse. In der besprochenen Untersuchung wurden keine Abhängigkeiten zwischen den Allelen von Genpolymorphismus des Dopamintransporters DAT1 und des Serotonintransporters 5-HTT und der Präferenz für Saccharose bei den Probanden (Patienten mit diagnostiziertem Syndrom der Alkoholabhängigkeit) nachgewiesen. Es wurde aber die statistisch signifikante Abhängigkeit zwischen dem Genotyp 9/10 des Genpolymorphismus des Dopamin-Transporters DAT1 und der Präferenz für Saccharose unter den Probanden nachgewiesen (p=0,0370). Die Anwesenheit von DAT1 9/10 VNTR steigerte dreimal das Auftreten der Eigenschaft „sweet liking" (p=0,015, odds ratio = 3,00) in der untersuchten Gruppe. Es wurde auch häufigeres Auftreten des Genotyps 10/10 (68,18% vs. 47,92%) und 9/9 (6,82% vs. 2,08%) bei den SWL- - Probanden nachgewiesen. Die Anwesenheit von DAT1 10/10 VNTR bei den Probanden minderte fast zweimal das Auftreten von SWL+ (p=0,051, odds ratio = 0,43).

SWL- „sweet liking" ohne Präferenz für Süßes

SWL+ „sweet liking" mit Präferenz für Süßes

Schlussfolgerungen. Der Zusammenhang des Phänotyps „sweet liking" wurde bestätigt.

Schlüsselwörter: Alkoholabhängigkeitssyndrom, Phänotyp „sweet liking", genetische Untersuchung

L'analyse des variations polymorphiques du gène transporteur de dopamine DAT1 et du gène transporteur de sérotonine 5-HTTLPR chez les patients avec le syndrome de la dépendance à l'alcool en prenant en considération aussi la particularité phénotypique de la préférence du goût doux

Résumé

Objectif. Déterminer les relations du phénotype « sweet liking » (préférence du goût doux) des patients avec le syndrome de la dépendance à l'alcool et les variations polymorphiques du gène transporteur de dopamine DAT1 et du gène transporteur de sérotonine 5-HTTLPR (serotonin-transpoter-linked-polymophic-region).

Matériel et Méthodes. On examine 100 hommes dépendant à l'alcool (les probands), diagnostiqués d'après ICD-10. On les examine avec les questionnaires : SSAGA (Semi Structured Assessment for the Genetics of Alcoolism), MMSE, Beck Depression Inventory and Hamilton Anxiety, Snaith-Hamilton Pleasure Scale. Pour déterminer la préférence du goût doux les probands goûtent les solutions de saccharose. Les personnes préférant la plus grande concentration de saccharose sont définies comme « sweet likers ». Pour les examens génétiques on use leurs échantillons sanguins. On analyse les variations polymorphiques du gène transporteur de dopamine DAT1 et du gène transporteur de sérotonine 5-HTTLPR avec le programme SPSS (Statistical Package for the Social Sciences).

Résultats. Ces examens n'attestent pas de relations des allèles choisis des polymorphismes du gène transporteur de dopamine DAT1 et du gène transporteur de sérotonine 5-HTT et de la préférence de saccharose des probands. On note pourtant la relation valable statistiquement du génotype 9/10 du polymorphisme du gène transporteur de dopamine DAT1 et la préférence de saccharose des probands (p=0,0370). La présence de DAT1 9/10 VNTR augmente trois fois la possibilité de la particularité « sweet liking » (p=0,015, odds ratio =3,00) dans le groupe examiné.

On observe aussi la plus grande fréquence du génotype 10/10 (68,18% vs 47,92%) et du génotype 9/9 (6,82% vs 2,08% chez les probands SWL - . La présence de DAT1 10/10 VNTR diminue deux fois la possibilité se SWL + (p=0,051, odds ratio =0,43).

SWL - = « - sweet liking » = sans la préférence du goût doux

SWL + = « + sweet liking » = avec la préférence du goût doux

Conclusions. On confirme la relation du phénotype « sweet liking » avec le génotype du transporteur de dopamine DAT1.

Mots clés : syndrome de la dépendance à l'alcool, phénotype « sweet liking », étude génétique

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