Psychiatr. Pol. 2014; 48(3): 541–551
PL ISSN 0033-2674
www.psychiatriapolska.pl

An interaction between a polymorphism of the serotonin transporter (5HTT) gene and the clinical picture of adolescents with combined type of ADHD (hyperkinetic disorder) and youth drinking

Izabela Gorzkowska[1], Grzegorz Gorzkowski[2], Agnieszka Samochowiec[1,3], Aleksandra Suchanecka[1], Jerzy Samochowiec[1].

[1] Department of Psychiatry, Pomeranian Medical University, Szczecin, Poland
[2] Department of Dental Prosthetics Pomeranian Medical University, Szczecin, Poland
[3] Department of Clinical Psychology, University of Szczecin, Poland

Summary

Introduction: The combined type of ADHD and alcohol dependence are two different disorders. Research demonstrate that 45-55% of patients diagnosed with ADHD also suffer from comorbid substance abuse, and 11-55% of patients diagnosed with substance abuse suffer from undiagnosed ADHD. Alcohol is by far the most widely used psychoactive substance in the European culture. The serotonin transporter *(5HHT)* gene has been implicated as one of the candidate genes in both disorders in recent molecular genetic research.

Aim: The aim of the present study was to seek a common clinical and biological marker for hyperkinetic disorder and youth drinking.

Methods: The study was conducted between 2008 and 2012. The sample consisted of 100 combined type ADHD patients: 51 adolescents youth drinking and 100 individuals without mental disorders or addiction in a population-based group. The *5HHT* gene polymorphism was examined using PCR *(Polymerase Chain Reaction)*. Statistical analysis was conducted with STATISTICA.PL software (version 5.0.97) licensed by StatSoft, Inc. USA.

Results: A preferential trend for the "s" short allele of the investigated *5HHT* gene polymorphism was observed in all the groups of adolescents compared to the population-based group of adults without alcohol dependence (p=0.01).

Conclusion: Based on the conducted study a provisional conclusion may be drawn that the presence of the short "s" allele of the *5HTT* gene polymorphism may be a prognostic factor of impulsivity in ADHD and of predisposition to alcohol dependence.

Key words: ADHD, alcohol, 5-HTT polymorphism

Introduction

Symptoms which, diagnosed mainly in childhood ADHD, persist at 33-66% of adult patients, causing multiple issues related to health (recklessness, anxiety, depressive and personality disorders) and social functioning (work-related issues, marital difficulties, legal problems) [1, 2]. While hyperkinetic disorder is thought to be the most genetically conditioned mental disorder, the concordance rates in twins diagnosed with it reach 80% [3, 4]. However, the identification of specific genes involved in etiopathogenesis is difficult due to the multifactorial nature of the etiology. Genes of the serotonergic system have been implicated as the candidate genes for the disorder [4, 5].

Alcohol dependence remains a major cause of social degradation and is instrumental in the etiology of both many mental disorders and somatic diseases. AD is considered to be conditioned by both genetic and environmental factors and their comorbidity [6, 7]. The role of genetic factors in causing addiction is estimated at 40-50%. Serotonergic system genes have also been named as the candidate genes for AD [8].

A Swedish follow-up study on a sample of 50,000 people revealed that early alcohol initiation is to be considered an important predictor of subsequent work-related problems and potential exclusion from the labour market [9]. Patients with primary ADHD have shorter transition periods from adverse substance experiences to addiction [10-12]. Jester et al. analysed the trajectory from childhood aggression and inattention/hyperactivity symptoms to differences in initiation methods and ways of developing substance, including alcohol. Children aged 2 to 5 were qualified for the study and were followed over 10 years. At the time of the first examination the children were 3-5 years old. Environmental factors (familial problems, paternal alcoholism) were also considered. According to observation and CBCL *(Child Behavior Checklist)* and TRF*(Teacher Rating Scales Report)* scale scores demonstrated that hyperactive adolescents with attention deficit and aggression behaviour were most at risk of early alcohol initiation. The researchers also emphasized the relevance of genetic factors which they related to paternal alcoholism and legal problems [13].

Hallikainen et al. in their study on the *5HHT* gene polymorphism found an association between the short "s" allele and a risk of early onset alcoholism with violent, impulsive behaviours [14]. Research to date has been focusing on analysing concurrent genetic and environmental factors pointing out to associations between the *5HHT* gene polymorphisms and psychosocial/familial moderators [15, 16, 17, 18, 19, 20] as well as to the relevance and ways of executing impulsive behaviours. Researchers maintained that while some ADHD adolescents respond with aggression combined with behaviour disorders (which was later referred to as 'impulsive aggression'), others make quick, inadequate decisions or are unable to wait for gratification (later known as cognitive impulsiveness) [18, 21]. The long allele of the *5HTTLPR* polymorphism was associated with cognitive impulsiveness symptoms, the short allele with ADHD accompanied by mood disorders, aggression and compulsive behaviour disorders [17, 18].

A study on 366 families that categorised 1167 genotypes demonstrated an association between the *5HTT* short "s" allele and aggression in children, which was the strongest in 9-year olds. The behaviour of children was assessed by their parents and teachers using CBCL diagnostic tools [22].

Materials and methods

The protocol of the study was approved by the Bioethics Committee of the Pomeranian Medical University of Szczecin number BN-001/76/2007. Written informed consent was obtained from all subjects and their legal guardians. Diagnostic examination of 100 patients with combined type of ADHD was conducted at Private Specialist Medical Practice (92 males, 8 females, average age of 12.7). The tests of 51 patients who early experimented with alcohol were performed in randomly selected junior high schools in Zachodniopomorskie province and at the Detoxification Unit of the Nephrology Ward of a public health care institution for mother, children and young people in Szczecin (30 males, 21 females, average age of 14.3). A population-based cohort of 100 controls (90 males, 10 females, average age of 38.5) was examined at the Department of Psychiatry, Pomeranian Medical University, Szczecin to determine possible associations between some genetic polymorphisms and personality profiles of individuals without any mental disorders [23].

Questionnaire Testing Methods

All adolescents were clinically tested using standardized rating scales for ADHD screening and assessment of the disorder's symptoms' severity and for behaviour disorders according to ICD-10 criteria [24]. Guardians completed ADHD Diagnostic Parent Rating Scale – an experimental diagnostic tool for parents [25] and CBCL *(Child Behavior Checklist)* in Polish adaptation [26]. Young patients reflected on their own behaviour by filling YSR *(Youth Self Report)* in Polish adaptation [26] and *Beck Youth Inventories of Emotional and Social Impairment* in Polish adaptation [27]. Adolescents and their guardians also completed our own survey forms on early experiments with alcohol. The inclusion criteria during the study were as follows: age between 11 and 18. Patients with hyperkinetic disorder (combined type of ADHD) were diagnosed according to ICD-10 criteria [28]. Adolescents early experimenting with alcohol were 11-18 years of age and regularly consumed alcohol, i.e. at least once per month.

Laboratory methods

Genetic material was extracted from saliva using Oragene OG-500 set according to the manufacturer's instruction. PCR *(Polymerase Chain Reaction)* was used to identify the 5HHT gene polymorphism (insertion/deletion variations). The following primer sequences were used: F: 5'- ggC gTT gCC gCT CTg AAT gC; R: 5'- gAg ggA CTg AgC Tgg ACA ACC AC. Products were visualised on 3% agarose gel [29].

Statistical analysis

Statistical analysis was conducted with statistica.pl software (version 5.0.97) licensed by StatSoft, Inc. USA. A comparison of measurable values with normal distribution for three and more groups (a grouping variable has more than two values) was conducted by analysis of variance on ANOVA platform and by Laeven variance analysis of homogeneity. For variables with abnormal distribution, the Kruskal-Wallis test was used.

Discussion

Owing to negligible differences in results obtained from male and female adolescent patients, it was decided that no gender-related analysis would be presented in the paper.

Results are presented in tables and as graphs.

Table 1. **The number of symptoms necessary to diagnose combined type of ADHD (group A – patients with combined type of ADHD, group B – adolescents early experimenting with alcohol)**

Variable	Number of symptoms necessary to meet ICD-10 criteria	average	average	standard deviation	standard deviation	p
		Group A n=99	Group B n=51	Group A	Group B	p value
N_AD_S	6-9	8.11111	5.78431	0.935566	2.48446	p < 0.001
N_H_S	3-5	4.38384	3.09804	0.650072	1.45952	p < 0.001
N_I_S	1-4	3.59596	2.72549	0.698675	1.38677	p < 0.005

N_AD_S (number of attention deficit symptoms); N_H_S (number of hyperactivity symptoms); N_I_S (number of impulsive symptoms)

Table 2. **A comparison of average number of symptoms of combined type of ADHD between group A (patients with hyperkinetic disorder) and group C (teenagers with combined ype of ADHD singled out from adolescents early experimenting with alcohol)**

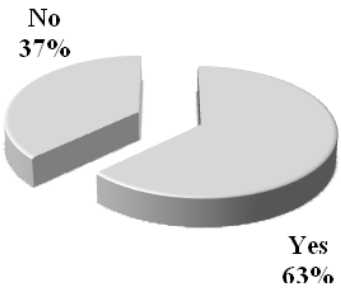
Variable	Number of symptoms necessary to meet ICD-10 criteria	average	average	standard deviation	standard deviation	p
		Group A n=99	Group C n=32	Group	Group C	p vaule
N_AD_S	6-9	8.11111	7.43750	0.935566	1.04534	ns
N_H_S	3-5	4.38384	3.96875	0.650072	0.78224	ns
N_I_S	1-4	3.59596	3.34375	0.698675	1.03517	ns

N_AD_S (number of attention deficit symptoms); N_H_S (number of hyperactivity symptoms); N_I_S (number of impulsive symptoms)

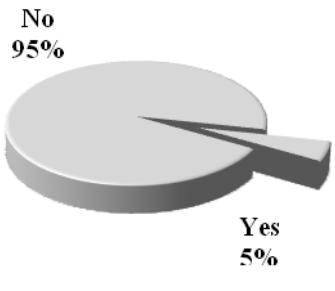
Although the number of symptoms required to diagnose hyperkinetic disorder was statistically significant (Table 1), 63% of adolescents youth drinking fulfilled

the criteria of combined type of ADHD (Graph 1). Given this kind of disorder distribution, a third group of adolescents was defined for further analysis – group C (teenagers with combined type of ADHD singled out from adolescents early experimenting with alcohol). Table 2 presents a comparison of the number of symptoms required to diagnose hyperkinetic disorder in groups A and C. The results are not statistically significant.

Graph 1. **Disorder distribution in investigated adolescents**



Adolescents early experimenting with alcohol meeting hyperkinetic disorder criteria



Adolescents with hyperkinetic disorder meeting criteria of alcohol abuse

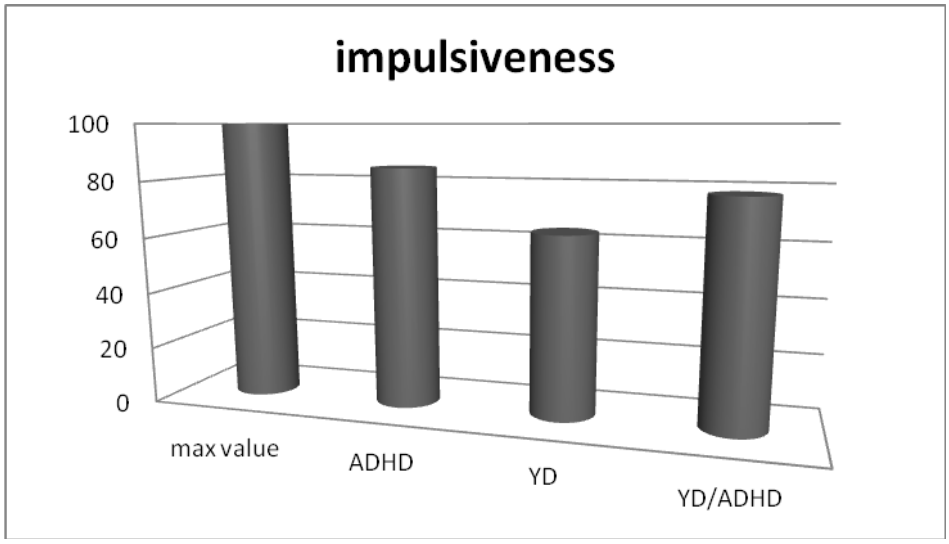
Whereas 12-13-year-old adolescents in Poland are typically pupils in the 6th form of a primary school, adolescents who are 14-15 years of age attend the 2nd form of a junior high school (middle school). According to ESPAD *(The European School Survey Project on Alcohol and Other Drugs)* survey data collected from young people until the 2nd form of a junior high school, adolescent alcohol initiation in Poland typically occurs in the 2nd form of a junior high school (middle school). Our study showed that 5% of ADHD patients confirmed they had consumed alcohol. Since the average age of adolescents with hyperkinetic disorder was lower, it is possible they had not gone through alcohol initiation yet [30, 31].

Researchers suggest that adolescents with hyperkinetic disorder start alcohol experiments by approximately 1.5 years earlier than their peers in the control group [32]. Attention deficit disorder symptoms and hyperactivity are the most significant predictors of subsequent alcohol-related crime [33]. Patients with primary ADHD have shorter transition periods from adverse substance experiences to addiction [10-12]. Analysis of results obtained in the present study demonstrates that intensive preventive measures geared at stopping adolescents with combined type of ADHD from conducting alcohol experiments should be undertaken by the 5th form of primary school at the latest.

Table 3. **A comparison of average severity of (combined type) ADHD symptoms between group A (patients with combined type of ADHD), group B (adolescents early experimenting with alcohol) and group C (teenagers with combined type of ADHD singled out from adolescents early experimenting with alcohol)**

Variable	Maximum severity of combined type ADHD symptoms	average	average	average	P
		Group A n= 99	Group B n=51	Group C n=32	Kruskal–Wallis test
S_AD_S	27	22.54545	16.01961	19.59375	0.00001
N_H_S	15	11.84849	8.39216	10.59375	0.0031
S_I_S	12	10.17172	7.64706	9.40625	ns

S_AD_S (severity of attention deficit symptoms); N_H_S (number of hyperactivity symptoms); S_I_S (severity of impulsive symptoms)



Graph 2. A comparison of impulsive symptom severity compared to maximum scores in group A (patients with combined type of ADHD), group B (adolescents early experimenting with alcohol) and group C (teenagers with combined type of ADHD singled out from adolescents early experimenting with alcohol)

Meta-analysis of different effects of genetic and environmental factors on ADHD symptoms (attention deficit disorders, hyperactivity/impulsiveness disorders) revealed that both dimensions, i.e. attention deficit disorders as well as hyperactivity/impulsiveness disorders, are hereditary (71% – attention deficit disorders; 73% – hyperactivity/impulsiveness disorders). Interestingly, they probably follow different mechanisms of hereditary pathways [17]. In Sonuga-Brake's model of delay aversion, attention deficit is associated with executive function deficit disorders (anatomically associated with the prefrontal cortex). Hyperactivity is more connected with the problems

of motivation and a way to respond to the prize (anatomically related to striatum and nucleus accumbens which are thought to be critical components of the reward system) [17, 21].

The examination of patients early experimenting with alcohol seems to implicate early alcohol initiation with impulsiveness, poor emotion regulation skill, tendency to externalised behaviour and potential development of dissocial personality. Neurobiological research shows that those at risk of early alcohol initiation, e.g. due to family history of alcohol abuse, have reduced volume of prefrontal cortex, which is also involved in mediating emotional behavior [34].

In the present study, the number of impulsive symptoms necessary to fulfil diagnostic criteria was statistically different only between group A (patients diagnosed with combined type of ADHD) and B (adolescents early experimenting with alcohol) p=0.005. Groups A and C (teenagers with combined type of ADHD singled out from adolescents early experimenting with alcohol) did not statistically differed in this respect (Tables 1 and 2). High impulsivity scores of 75% (relative to the possibly highest score in a symptom rating scale) were recorded in all the sample. In groups A, B and C the severity of impulsivity was at a similar level and no statistically significant differences were found (Table 3). Detailed analysis revealed the highest severity of impulsive symptoms in group A, compared to group B. A comparison of group A vs group C did not find any significant differences (Graph 2). It is fair to state that group B adolescents experimenting with alcohol who did not meet diagnostic criteria for hyperkinetic disorder displayed lower impulsivity than ADHD teenagers and those who met (combined type) ADHD criteria singled out from adolescents who early experimented with alcohol (group C).

Table 4. **Frequency distribution of genotypes and alleles of the 5HTT gene in group A (patients with combined type of ADHD), group B (adolescents early experimenting with alcohol) and group C (teenagers with combined type of ADHD singled out from adolescents early experimenting with alcohol) compared to population-based group (PBG)**

Group	Genotypes				p	Alleles			p
	n	l/l n %	l/s n %	s/s n %		n	L n %	s n %	
PBG	100	48 (48)	43 (43)	9 (9)	-	200	139 (69.5)	61 (30.5)	-
A+B+C	175	56 (32)	94 (53.7)	25 (14.3)	0.043	300	206 (58.9)	144 (41.1)	0.01
A	96	39 (40.6)	46 (47.9)	11 (11.5)	ns	192	124 (64.6)	68 (35.4)	ns
B	49	10 (20.4)	31 (63.3)	8 (16.3)	0.00475	98	51 (52)	47 (48)	0.048
C	30	7 (23.3)	17 (56.7)	6 (20)	0.035	60	31 (51.7)	29 (48.30)	ns

Associations between a polymorphism of the serotonin transporter *(5HTT)* gene and impulsive behaviour and early experiments with alcohol by adolescents were discussed in the introduction. It is worth mentioning a study conducted by Retz who found that in a population of young offenders the *5HTT* gene polymorphism was associated with ADHD [35]. Regression analysis for Retz study revealed an association between ADHD that survived into adulthood and *HTTLPR l/l* genotype. Additionally, individuals with the short "s" allele were more susceptible to environmental factors [19]. A difference of polymorphic variants of the *5HTT* gene was observed in the present study between the population-based group and the whole sample for the "s" allele in s/s and l/s combinations. This distribution of the polymorphism may suggest its pleiotropic character. The short "s" allele of the *5HTT* gene is clinically associated with increased severity of impulsive and risk-seeking behaviour. The severity of impulsive behaviour was substantially high throughout all the groups of our sample. l/s and s/s genotypes occurred significantly more frequently in all the sample. Genotypes with the short "s" allele in both l/s and s/s forms were more frequent in groups B and C. It was particularly noticeable in group B of adolescents early experimenting with alcohol. ADHD patients had a distribution of "s" and "l" alleles similar to that of the controls (Table 4).

Conclusions

Based on the conducted study, a tentative conclusion can be drawn that the presence of the short "s" allele of the *5HTT* gene polymorphism may be a prognostic predictor of impulsive behaviour in ADHD and may be implicated in susceptibility to alcohol dependence.

References

1. Biederman J, Petty C, Fried R, Fonatanella J, Doyle AE, Seidman LJ i wsp. *Impact of psychometrically defined deficits of executive functioning in adults with attention deficyt hyperactivity disorder*. Am. J. Psychiatry 2006; 163(10): 1730–1738.
2. Kooij SJ, Bejerot S, Blackwell A, Caci H, Casas-Brugué M, Carpentier PJ i wsp. *Europejskie wspólne stanowisko dotyczące rozpoznawania i leczenia dorosłych z ADHD. The European Network Adult ADHD.* Med. Prakt. Psychiatr. 2011; 4(21): 18–46.
3. Biederman J, Faraone SV. *Current concepts on the neurobiology of Attention-Deficit/Hyperactivity Disorder*. Atten. Disord. 2002; 6(1): 7–16.
4. Faraone SV, Perlis RH, Doyle AE. *Molecular Genetics of attention-deficit/hyperactivity disorder.* Biol. Psychiatry 2005; 57: 1313–1323.
5. Williams NM, Franke B, Mick E, Anney RJ, Freitag CM, Gill M i wsp. *Genome-wide analisis of copy number variants in attention deficit hyperactivity disorder: the role of rare variants and duplications at 15q13.3. Am*. J. Psychiatry 2012; 169(2): 195–204.
6. Samochowiec J. *Molekularno-biologiczne mechanizmy zespołu zależności alkoholowej*. Aachen: Shaher Verlag; 1999.
7. Galèra C, Bouvard MP, Lagrade E, Michel G, Touchette E, Fombonne E i wsp. *Chilhood attention problems and socioeconomic status in adulthood: 18-year follow-up*. Br. J. Psychiatry 2012; 201(1): 20–25.
8. Grochans E, Grzywacz A, Małecka I, Samochowiec A, Karakiewicz B, Samochowiec J. *Badania asocjacyjne wybranych polimorfizmów genów DRD2, 5HTT, GRIK3, ADH4 u pacjentów z zespołem zależności alkoholowej*. Psychiatr. Pol. 2011; 45(3): 325–335.
9. Sidorchuk A, Hemmingsson T, Romelsjö A, Allebeck P. *Alcohol use in adolecence and risk of disability pension: a 39 year follow-up of population-based conscriptionsurvey*. PloS One 2012; 7(8). e42083. doi:10.1371/journal.pone.0042083
10. Biederman J, Wilens TE, Mick E, Faraone SV, Spencer T. *Does attention deficit hyperactivity disorder impact the developmental course of drug and alcohol abuse and dependence?* Biol. Psychiatry 1998; 44: 269–273.
11. Wilens TE, Prince JB, Biederman J, Spencer TJ, Frances RJ. *Attention-deficit hyperactivity disorder and comorbid substance use disorders in adults*. Psychiatr. Serv. 1995; 46: 761–763, 765.
12. Wilens TE, Upadhyaya HP. *Impact of substance use disorder on ADHD and its treatment.* J. Clin. Psychiatry 2007; 68(8): e20.
13. Jester JM, Nigg JT, Buu A, Puttler LI, Glass JM, Heitzeg MM i wsp. *Trajectories of childhood aggresion and inattention/hyperactivity: differential effects on substance abuce in adolescente*. J. Am. Acad. Child Adolesc. Psychiatry 2008; 47(10): 1158–1165.
14. Hallikainen T, Saito T, Lachman HM, Volavka J, Pohjalainen T, Ryynänen OP i wsp. *Association between low activity serotonin transporter promoter genotype and early onset alcoholism with habitual impulsive violent behavior*. Mol. Psychiatry 1999; 4(4): 385–388.
15. Acher T, Oscar-Berman M, Blum K. *Epigenetics in Developmental Disorder: ADHD and Endophenotypes.* J. Genet. Syndr. Gene Ther. 2011; 2(104): 1000104.
16. Nigg J, Nikolas M, Burt SA. *Measured gene-by-environment interaction in relation to attention hyperactivity disorder*. J. Am. Child Adolesc. Psychiatry 2010; 49(9): 863–873.
17. Nikolas MA, Burt SA. *Genetic and environmental influences on ADHD symptom dimensions of inattention and hyperactivity: a meta-analysis*. J. Abnorm. Psychol. 2010; 119(1): 1–17.

18. Oades RD, Lasky-Su J, Christiansen H, Faraone SV, Sounga-Barke EJ, Banaschewski T i wsp. *The influence of serotonin-and other genes on impulsive behavioral aggresion and cognitive impulsivity in children with attention-deficit/hyperactivity disorder (ADHD): Findings from a family-based association test (FBAT) analysis*. Behav. Brain Funct. 2008; 4: 48.
19. Retz W, Freitag CM, Retz-Junginger P, Wenzler D, Schneider M, Kissling C i wsp. *A functional serotonin transporter promoter gene polymorphism increases ADHD symptoms in delinquents: interaction with adverse childhood environment*. Psychiatry Res. 2008; 158(2): 123–131.
20. Stolle M, Sack PM, Thomasius R. *Binge drinking in childhood and adolescence: epidemiology, consequence, and interventions*. Dtsch. Arztebl. Int. 2009; 106(19): 323–328.
21. Sonuga-Barke EJ. *Causal models of attention-deficit/hyperactivity disorder: from common simple deficits to multiple developmental pathways*. Biol. Psychiatry 2005; 57(11): 1231–1238.
22. Haberstic BC, Smolen A, Hewitt JK. *Family based association test of the 5HTTLPR and aggressive behavior in general population sample of children*. Biol. Psychiatry 2006; 59(9): 836–843.
23. Pełka-Wysiecka J, Ziętek J, Grzywacz A, Kucharska-Mazur J, Bieńkowski P, Samochowiec J. *Association of genetic polymorphisms with personality profile in individuals without psychiatric disorders.* Prog. Neuropsychopharmacol. Biol. Psychiatry 2012; 39(1): 40–46.
24. Wolańczyk T, Kołakowski A. *Kwestionariusz do diagnozy ADHD i zaburzeń zachowania.* Warszawa: Janssen-Cilag; 2005.
25. Święcicka M. *Skale szacunkowe dla rodziców i nauczycieli jako narzędzia diagnozy w psychologii klinicznej dziecka*. W: Święcicka M. red. *Metody diagnozy w psychologii klinicznej dziecka i rodziny*. Warszawa: Paradygmat; 2011. s. 112–120.
26. Wolańczyk T. *Zaburzenia emocjonalne i behawioralne u dzieci i młodzieży.* Warszawa: Academia Medica Varsoviensis; 2002.
27. Mathiak KA, Karzeł K, Oscypa M, Seget A, Mathiak K, Ostaszewski P. *Kwestionariusz Becka dla Dzieci do oceny zaburzeń emocjonalnych i społecznych – polska adaptacja i walidacja kwestionariusza Beck Youth Inventories of Emotional and Social Impairment*. Psychiatr. Pol. 2007; 41(3): 387–399.
28. *Klasyfikacja zaburzeń psychicznych i zaburzeń zachowania w ICD-10. Badawcze kryteria diagnostyczne*. Rozdział V. Kraków–Warszawa: Uniwersyteckie Wydawnictwo Medyczne „Vesalius", Instytut Psychiatrii i Neurologii; 1998.
29. Miller S, Dykes D, Plesky H. *A simple salting out procedure for extracting DNA from human nucleated cells*. Nucl. Acids Res. 1988; 16: 1215.
30. ESPAD 2011; http://www.cinn.gov.pl/portal?id=15&res_id=392521 [dostęp 27.09.2012]
31. Sierosławski J. *Używanie alkoholu i narkotyków przez młodzież szkolną. Raport z ogólnopolskich badań ankietowych zrealizowanych w 2011 r. Europejski Program Badań Ankietowych w Szkołach*. Warszawa; 2011. http://www.cinn.gov.pl/portal?id=15&res_id=392519 [dostęp: 27.09.2012]
32. Langley K, Flower T, Thapar AK, van den Bree M, Harold G, Owen MJ i wsp. *Adolescent clinical outcomes for young people with attention – deficit hyperactivity disorder.* Br. J. Psychiatry 2010; 196(3): 235–240.
33. Eklund JM, Klinteberg BA. *Childhood behaviour as related to subsequent drinking offences and violent offending: a prospective study of 11 – to 14-year-old youths into their fourth decade*. Crim. Behav. Ment. Health 2003; 13(4): 294–309.
34. Lejuez CW, Magidson JF, Mitchell SH, Sinha R, Stevens MC, de Wit H. *Behavioral and biological indicators of impulsivity in the development of alcohol use, problems, and disorders.* Alcohol. Clin. Exp. Res. 2010; 34(8): 1334–1345.

35. Retz W, Freitag CM, Retz-Junginger P, Wenzler D, Schneider M, Kissling C i wsp. *A functional serotonin transporter promoter gene polymorphism increases ADHD symptoms in delinquents: interaction with adverse childhood environment*. Psychiatry Res. 2008; 158(2): 123-131

Corresponding author:
Izabela Gorzkowska
Department of Psychiatry, Pomeranian Medical University, Szczecin, Poland Broniewskiego 26 71-460 Szczecin, Poland
e-mail: gorzkowskaiza@gmail.com Phone number: +48914541507