

Attachment relationship and oxytocin among people addicted to alcohol – a literature review

Dawid Subocz

Abstract

Objective: This paper is aimed at reviewing the literature on oxytocin and attachment relationship among people addicted to alcohol. The paper describes in a holistic way their possible interactions with bio-psycho-social risk factors for the development of addiction. It also indicates the possible practical use of oxytocin in addiction therapy.

Material and method: The literature review was made with the use of the following databases: PsycINFO, PubMed and Google Scholar. Each database was searched using the following keywords: 'secure', 'disorganised', 'genetic', and 'therapy'. These keywords were combined with the terms "attachment style", "oxytocin" and each time with "alcohol addiction".

Results: The analysis of the literature confirms that people addicted to alcohol are more often characterised by relational problems than healthy people. The association of oxytocin with the attachment relationship is mediated by epigenetic, neurobiological, and environmental factors. Research also confirms that the use of oxytocin in addiction therapy brings positive effects for some patients.

Discussion and conclusions: The ability to build satisfactory interpersonal relationships is a protective factor against alcohol use. The article indicates the role that oxytocin plays in building interpersonal relationships and the possibility of its use in addiction therapy.

attachment style; alcohol addiction; oxytocin

INTRODUCTION

Oxytocin is a neurohormone, which is a 9-amino acid neuropeptide produced by the hypothalamus [1]. It is collected and released into the systemic circulation from the posterior pituitary gland [2]. Its secretion occurs in a reflexive way as a result of irritation of the nipple receptors or the receptors of the cervix and vagina. Increasing the secretion of oxytocin causes contraction

of the uterus, which accelerates the labour, while during sexual intercourse it enables the transport of sperm towards the fallopian tubes [3]. Therefore, it is used in medicine. It is used to accelerate the labour or inhibit postpartum bleeding [4]. Oxytocin, in addition to its role in the course of labour and lactation, also performs its function in the process of building bonds. It can therefore be concluded that the role of this neuropeptide – during sexual intercourse – is not limited only to uterine contractions, accelerating sperm transport, but also to building relationships between partners. This has evolutionary significance because the bond between the par-

Dawid Subocz: University of Szczecin, Institute of Psychology, Szczecin, Poland

Correspondence address: dawid.subocz@usz.edu.pl

ents increased the chances of the child's survival. Similarly, during breastfeeding, the secretion of oxytocin mediates building a safe bond between mother and child [5, 6]. Establishing a secure relationship with the mother is of paramount importance at this stage as the baby is completely dependent on her. Researchers call oxytocin a social neuropeptide [1]. This is because it is related to trust, which is a necessary factor in building complex interpersonal relationships of people [7]. Research also suggests that people addicted to alcohol have problems in building satisfying interpersonal relationships [8]. They are characterised by insecure attachment styles [9]. Today, addiction experts pay more and more attention to the role of individual factors in the development of addiction. A person caught in the chains of addiction is very often a lonely person, deprived of social support [10, 11]. This means that he/she does not build satisfactory social ties. The role of oxytocin – a social neuropeptide – in the pathogenesis of addiction is therefore theoretically justified. However, it should be emphasised here that people addicted to alcohol constitute a heterogeneous group. Different factors play a key role in the development of an alcohol problem in each patient. Biological, social and psychological factors can be distinguished here, as well as their interactions. These people are different in terms of personality traits, on the basis of which their alcohol problem develops. Whether relational problems are a significant factor in the pathogenesis of addiction requires an individual diagnosis of the patient. In this study, a reduced level of oxytocin

was presented as one of many risk factors for the development of alcohol dependence. The aim of this paper is to review the studies on oxytocin and attachment styles among people addicted to alcohol.

MATERIAL AND METHOD

The literature review was performed using the following databases: PsycINFO, PubMed and Google Scholar. Each database was searched using the following keywords: 'secure', 'disorganised', 'genetic', and 'therapy'. These keywords were combined with the terms "attachment style", "oxytocin" and each time with "alcohol addiction". During the database search, 74 publications were identified. Duplicates and articles unrelated to the purpose of this thematic review were excluded. Based on such selection, 53 publications were included in the qualitative analysis. The process of searching and selecting studies is presented in the PRISMA scheme (Figure 1).

Oxytocin and attachment relationship

The basic task for the caretaker in the first year of the infant's life is to create a secure attachment with him / her [12]. It depends on the psychobiological synchronisation of the mother with the child's internal states of arousal. Through visual-facial, tactile-gesture and auditory-prosodic communication, the caretaker and the infant modify their behaviour to tune in to each other

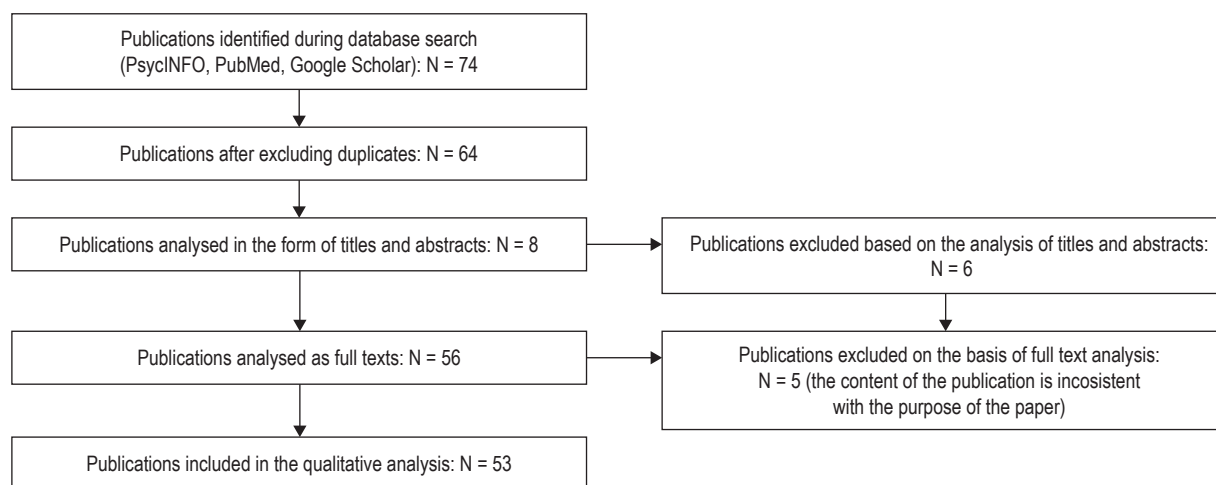


Figure 1. Summary of the research search and selection process in the PRISMA scheme

[12]. In this way, trusting attachment is created. It is a kind of emotional resonance, in which positive states may be strengthened. Good synchronisation has a positive effect on the postnatally maturing limbic system that processes and regulates socio-emotional stimuli and the autonomic nervous system responsible for the somatic aspects of emotions [13].

A child growing up in a secure attachment relationship learns to regulate his / her emotional states. This process is mediated by oxytocin. The mother calming the baby, supports the secretion of oxytocin through her behaviour. The beneficial anti-stress and anxiolytic effect of oxytocin occurs through the regulation of the hypothalamic-pituitary-adrenal axis (HPA) and the amygdala activities with its projection into the brainstem and hypothalamic centres [2]. It has been proven that microinjections of oxytocin to brain structures reduce the response to stress stimuli [14, 15]. In people who received oxytocin, a reduction in the level of anxiety, blood pressure and cortisol levels are observed [16]. This means that the production of oxytocin when interacting with the baby can be an important factor in emotional regulation. Breastfeeding mothers showed a reduced hormonal response to physical stress compared to bottle-feeding mothers [17]. The insecure attachment relationship and the low level of oxytocin accompanying this relationship prevent the child from developing competences in the field of modulating affective states. In the future, maladaptive coping strategies may lead to alcohol abuse, which, due to its sedative properties, suppresses over-stimulation. This is due to the influence of alcohol on enhancing the action of inhibitory neurotransmitters (e.g. GABA) and weakening of excitatory neurotransmitters (e.g. serotonin) [18].

The level of oxytocin is also associated with genetic factors. Oxytocin receptor genes exist as single copies in the human genome and are mapped to the 3p253p26.2 gene loci on the chromosome. However, this does not mean that oxytocin levels are only due to genetic differences. The oxytocin receptor may be sensitive to epigenetic regulation by CpG islands. These are regions of the genome that contain large amounts of guanine-cytosine dinucleotides [19]. Epigenetic processes are influenced, for example, by traumatic relational experiences. Epigenetic pro-

cesses are also associated with changes in neural structures. Some studies [20] suggest that methylation of the oxytocin receptor (OXTR) gene in abused children negatively correlates with the volume of grey matter in the left orbitofrontal cortex of the brain. Moreover, the grey matter volume in the left orbitofrontal cortex acts as a mediator of the negative relationship between oxytocin receptor gene methylation and insecure attachment style. This study showed for the first time that oxytocin receptor gene methylation in children who experienced attachment trauma in the past is associated with difficulties in interpersonal relationships in the future [20].

A parallel study [21] showed that higher levels of neuropeptide oxytocin in plasma and lower levels of oxytocin receptor gene methylation are associated with lower levels of anxiety experienced in interpersonal relationships in young people (20-31 years; $M = 23.6$). However, no such relationships were found in the elderly (63-80 years; $M = 71.4$). Therefore, this study suggests that it is important to adopt a development perspective in order to verify the discussed relationships. The age of the subjects is related to maintaining and establishing interpersonal relationships. Other researchers [22] suggest that the avoidance of attachment relationships is associated with increased methylation of both the oxytocin receptor (OXTR) gene and the glucocorticoid receptor (NR3C1) gene.

The above studies therefore suggest that epigenetic factors and changes in the brain's neural structures mediate the relationship between the attachment relationship and the level of oxytocin. Researchers also suggest an association of the attachment relationship with genetic modifications in genes responsible for the regulation of social stress and for the functioning of the HPA axis related to the stress response [22]. From the point of view of the aetiology of problematic alcohol consumption development, these factors are significant, because reaching for alcohol or other depressants may be an attempt to suppress the state of arousal.

Attachment relationship and alcohol addiction

According to attachment theory [23], memories of interaction with a parent are the basis for the

development of the internal working model. Internal working models are cognitive structures based on generalised memories of past interactions with an attachment figure. Later attempts at bonding may modify them, but they are relatively stable over time [24]. Internal working models are defined as cognitive structures that are activated in relational situations. These structures define “myself”, ‘others’ and the relationship between them [25]. Today, attachment styles of adults are thus understood as personality traits developed on the basis of early attachment experiences. In the case of a secure attachment style, internal working models create an internal sense of the availability of help and encouragement from a loved one. In the case of insecure attachment, internal working models build the belief that the attachment figure will remain unavailable or that he / she will react negatively to a request for help [25]. This is the basis for creating complex emotion regulation strategies in many emotogenic situations [26]. Numerous empirical studies indicate the relationship between attachment styles and the mechanisms of emotional regulation [27, 28]. People with insecure attachment relationships often have problems with regulating emotions, which makes them more susceptible to difficult life events [25]. Both traumatic experiences and insecure attachment styles are significant risk factors for the development of alcoholism [18].

The lack of developed adaptive forms of arousal regulation – as part of a secure attachment relationship – may lead to tension reduction through alcohol consumption. Some studies [29] suggest that alcohol consumption in patients with anxiety disorders is motivated by them by the desire to suppress experienced anxiety and a sense of constant danger. The genesis of alcoholism may therefore be associated – in accordance with the concept of self-treatment – with the suppression of negative emotions in people who have not developed, as part of a secure attachment relationship, adaptive forms of emotional regulation. This thesis is supported by studies on attachment styles among alcohol abusers. The percentage distribution of insecure attachment styles in this group ranges from 66% to 94.6%, while the secure one ranges from 5.4% to 40% [30]. Studies conducted on adolescents shows that the intensity of anxious attach-

ment style is significantly correlated with risky alcohol drinking and the experience of more severe consequences of its use [31, 32]. Longitudinal studies among adolescents (1222 people) showed that, in addition to parental control, secure attachment may have a protective effect against drinking and getting drunk [33]. Studies [8] also show that people addicted to alcohol significantly less often show the pattern of trusting attachment than healthy people, while more often in interpersonal relationships they experience distrust, fear and avoid closeness. Such experiences affect the deficits in establishing close relationships with others. Consequently, alcohol can be used to reduce feelings of loneliness, pain and suffering. This process has a neurobiological background and is related to the dopamine reward system. Alcohol abuse can be explained as an attempt to replace endorphins (as endogenous opioids), which are naturally delivered through social attachment [34, 35]. Thus, it seems that alcohol in some cases acts as a means of alleviating the psychological pain that results from a lack of secure attachment.

Oxytocin and alcohol addiction

Studies suggest that alcohol consumption inhibits the release of oxytocin, the level of which usually returns to baseline after a decrease in blood alcohol content. Rats that were given alcohol showed a loss of neurones in the supraoptic nucleus and paraventricular hypothalamus, the areas responsible for the production of oxytocin. In addition to alcohol intoxication itself, the level of oxytocin is also influenced by genetic factors related to the tendency to overuse alcohol. Studies [36] have shown that men who were carriers of the AA allele in the oxytocin receptor gene polymorphism (rs53576) developed alcoholism more often at the age of 25. These men also used alcohol more often at the age of 15 and 18. However, this relationship has not been observed in women [36]. Other researchers [37] showed a significant relationship between alcohol dependence and the GG allele in the rs6133010 polymorphism of the oxytocin receptor gene. The researchers also point to the relationship between the rs4564970 polymorphism of the oxytocin receptor gene and the aggres-

sion experienced by the subjects under the influence of alcohol [38]. This means that genetic factors may be related not only to the tendency to use alcohol, but also to aggressive behaviour during social interactions in people under its influence [38].

Both early attachment experiences as well as genetic factors have an impact on building relationships among addicted people. Susceptibility to aggressive behaviour under the influence of alcohol may be a significant risk factor for the development of addiction and deepening the deficits in building interpersonal relations of patients. Both alcohol intoxication and traumatic attachment experiences may affect the expression of genes responsible for the level of oxytocin [20, 36], which is the basis for further escalation of the alcohol problem.

An important area of research explaining the role that oxytocin plays in building interpersonal relationships are studies on social cognition of people addicted to alcohol. Social cognition can be defined as the ability to construct mental representations about others, oneself, and one's relationships with others. The scope of social cognition includes cognitive processes involved in understanding, perceiving and interpreting the social world. Nasally-delivered oxytocin improves skills related to social cognition, and social contacts are a factor determining its release [39]. The studies on social cognition include papers devoted to the ability to recognise the expression of facial emotions. A meta-analysis of studies confirms that people who abuse alcohol show worse recognition of emotions on the face compared to healthy people [40]. It turns out that intranasal administration of oxytocin improves the ability to recognise the expression of facial emotions. This is confirmed by two meta-analyses [41, 43]. The first meta-analysis [41] included 13 studies with a total of 408 participants. The second meta-analysis [42] included 7 studies. 381 people took part in them. The ability to read emotions from the face performs many important functions, such as reading the intentions of another person. Reading intentions, on the other hand, helps to build social ties. The relationship of oxytocin with the recognition of emotions may explain the mechanism linking the deficit level of oxytocin in people addicted to alcohol with their failure to build inter-

personal relationships. The factor mediating in this process may be problems in the field of social cognition of patients. Therefore, interventions focused on psychoeducation in the field of social cognition for addicted people who exhibit insecure attachment styles seem to be promising. The above review also shows that the effectiveness of such interventions could be higher when supported using oxytocin.

Oxytocin therapy

The presented review of studies suggests that the lack of secure attachment relationships may result in a decreased level of oxytocin, which in turn is associated with problems in the regulation of affective states [25, 27, 28]. A way to suppress negative emotions and provide positive reinforcements in some people is alcohol abuse. Accepting this argument, one should expect that the administration of oxytocin may bring positive effects in addiction therapy. Indeed, studies [43] confirm that intraperitoneal administration of oxytocin blocks the motivation to drink alcohol in addicted rats. It also reduces withdrawal symptoms in rodents and people addicted to alcohol [44]. Regular intake of oxytocin also reduces alcohol tolerance [45, 46].

There are interesting discoveries on the influence of oxytocin on the effect of alcohol intoxication itself. Even moderate doses of alcohol impair motor coordination. Oxytocin has been shown to selectively alleviate ethanol-induced motor disorders. Researchers [47] conducted an experiment on rats. They estimated how long rats could hang on a metal mesh. The study was conducted in sober rats, rats given ethanol (1.5 g/kg) and a group of rats which were injected with oxytocin (1 µg/5 µL) prior to ethanol administration. Rats from the control group continued on the mesh about 10-15 seconds, rats under the influence of ethanol for about 2 seconds, and those previously treated with oxytocin for about 10 seconds. This means that oxytocin reverses the effect that alcohol has on motor coordination in rodents. The behaviour of rodents in cages was also observed in the experiment. Drunken rats sat silent in the corner of the cage, while sober rats walked around the cage. Interestingly, rats given oxytocin prior to alcohol in-

toxication were as mobile as sober animals. Alcohol has a toxic effect on gamma aminobutyric acid (GABA) receptors. Researchers suggest that oxytocin blocks the delta subunits of GABA-A receptors. At higher doses, however, alcohol binds to GABA receptors in the synapses, where oxytocin does not reach. Thus, its influence on motor efficiency depends on the dose of alcohol consumed [47]. The results of these studies are promising. The decrease in sensations under the influence of alcohol may weaken the motivation to take alcohol and thus increase the effectiveness of addiction therapy.

A study [48] on alcohol-dependent Americans showed that 0.9 µg of oxytocin administered 3 times a day (for a period of 12 weeks) significantly reduced both the number of days of heavy drinking and the amount of alcohol consumed per day. Other researchers [42] showed that intranasal administration of oxytocin twice a day (in a dose of 24 IU) for a period of 3 days among alcohol-dependent people resulted in a decrease in alcohol withdrawal symptoms. These patients underwent detoxification with lorazepam. The decrease in withdrawal symptoms in the oxytocin group was significantly greater compared to the placebo group at the same time. Studies [49] indicate that symptoms such as anxiety during abstinence and relapse of heavy drinking are associated with a weakened corticosteroid response and dysregulation of the hypothalamic-pituitary-adrenal axis. The therapeutic effect of oxytocin on withdrawal symptoms may be related to its anxiolytic properties. It regulates the activity of the hypothalamic-pituitary-adrenal axis [2].

It turns out, however, that the therapeutic effect of oxytocin is not limited to its calming properties and blocking the delta subunits of GABA-A receptors. Its effectiveness also depends on such individual characteristics as the subjects' attachment styles. The administration of oxytocin in the dose of 0.8 µg/kg in people abusing alcohol with a high level of anxious attachment style resulted in a decrease in the severity of symptoms of alcohol craving. In people with a low level of anxious attachment style, the symptoms of craving for alcohol became more severe [50]. These results suggest that the level of anxiety experienced in the attachment relationship is related to the effectiveness of ox-

ytocin-based treatment. This is significant because it indicates that oxytocin is not the therapeutic agent itself, but its interaction with the subjects' relational schemas. Probably its action may support the creation of adaptive relational behaviour in people who are characterised by an anxious attachment style. Trust is essential to building secure relationships. It has been proven that intranasal administration of oxytocin increases the level of trust in the subjects, which resulted in the transfer of larger sums of money in the expectation that the interaction partner would pay back with a similarly high transfer [7]. The subjects who were administered oxytocin also assessed the faces exposed to them as more friendly than the subjects from the control group [51]. Thus, an increase in trust in others favours building social ties. The level of oxytocin in adult life is related to seeking support from other people and the ability to use the help offered [52]. On the other hand, social support helps to maintain abstinence from drinking alcohol [53]. Future studies should consider the influence of oxytocin on the effectiveness of therapy aimed at building satisfactory interpersonal relationships of addicted people. The results of the cited study [50] also explain why some studies do not confirm the effectiveness of oxytocin in the treatment of alcohol addiction [54, 55]. In addition to attachment styles, genetic factors can also affect attachment effectiveness. This is an area for future research that should explain the reasons for these discrepancies in more detail.

CONCLUSIONS

The current state of knowledge suggests that insecure attachment relationships and deficit of oxytocin are risk factors for the development of alcohol addiction [31, 32, 33]. However, the exact role these factors play in the development of addiction is not known. The analysis of studies suggests that this process is mediated by several groups of factors. The first group includes genetic factors and epigenetic modifications of the oxytocin receptor gene, manifested in changes in the neuronal structures responsible for its production [20, 22]. The second group of factors are environmental factors – influencing epige-

netic modifications – such as the relationship between mother and child. It allows – with the mediating role of oxytocin – for the emotional regulation of the child and, in the future, for his / her more adaptive strategies of coping with emotions [16, 17]. The third group of factors are future adversities, especially in adolescence. Lack of social support and competence in the field of emotional regulation may result in a lower adaptation capacity to future difficult experiences [25]. In early adulthood, this may lead to coping with difficult emotions through the use of alcohol, which is a risk factor for the development of addiction in adulthood [56]. At a later stage, problematic alcohol consumption, including aggressive behaviour under its influence, result in building-up relational problems, which perpetuates maladaptive patterns of regulating negative emotional states by continuing to drink alcohol.

Paying attention to the relational aspect of the development of the alcohol problem is important due to its practical implications. While therapeutic interactions aimed at building satisfying relationships and rebuilding trust in people are a priority, it is also worth paying attention to the role that oxytocin plays in this process. Addiction therapy can be supported by the use of oxytocin. Its administration not only increases the sense of trust in other people and supports the building of stable interpersonal relationships, but also increases the effectiveness of addiction therapy [7, 44, 51]. Studies confirm that it reduces alcohol withdrawal symptoms and motivation to continue drinking [43, 44]. The use of oxytocin may also prove useful in building a therapeutic relationship. It is defined as a mutual and emotional bond between the therapist and the patient [57]. Researchers confirm the association between the therapeutic relationship and the effectiveness of addiction treatment [57]. Regardless of the adopted psychotherapeutic orientation, the use of oxytocin may prove useful in the therapy of people with insecure attachment styles. The association between the level of oxytocin and the quality of the therapeutic relationship, as well as the importance of this association in the process of therapeutic change, require further research. There is no doubt, however, that the continuation of research in this area is of great practical importance. In a broader perspective, this research serves to understand the

role that interpersonal relationships play for human mental health.

REFERENCES

1. Talarowska ME, Maruszewska P, Staroń E, Galecki P. Oxytocin – a social neuropeptide. Is it important in the developmental theory of depression? *Neuropsychiatry and Neuropsychology*. 2018; 13(2): 65-74.
2. Kania BF, Wrońska D, Balchut M. Neurobiology of oxytocin in humans and Animals. *Veterinary life*. 2014; 89(7): 583-587.
3. Konturek S. Wydzielanie wewnętrzne. In: Traczyk W, Trzebiński A, editors. *Fizjologia człowieka z elementami fizjologii stosowanej i klinicznej*. Wydanie III. Warszawa: PZWL; 2007. p. 343-345.
4. Śmieja K, Kamińska A, Ziętek M, Grzymała-Figura A, Celewicz Z. Postpartum haemorrhage causes, prevention, pharmacotherapy. *Gin. Perinat. Prakt.* 2018; 3(4): 137-142.
5. Insel TR, Young LJ. The neurobiology of Attachment. *Nat. Rev. Neurosc.* 2002; 2: 129-136.
6. Ross HE, Young LE. Oxytocin and the neural mechanism regulating social cognition and affiliative behavior. *Front. Neuroendocrinol.* 2009; 30: 534-547.
7. Kosfeld M, Heinrichs M, Zak PJ, Fischbacher U, Fehr E. Oxytocin increases trust in humans. *Nature*. 2005; 436(7042): 673-676.
8. Wyrzykowska E, Głogowska K, Mickiewicz K. Relacje przywiązania u osób uzależnionych od alkoholu. *Alkoholizm i Narkomania*. 2014; 27(2): 127-143.
9. De Rick A, Vanheule S. Attachment styles in alcoholic inpatients. *Eur. Addict. Res.* 2007; 13: 101-108.
10. Akerlind I, Hornquist JO. Loneliness and alcohol abuse: A review of evidences of an interplay. *Social Science & Medicine*. 1992; 34(4): 405-414.
11. Groh DR, Jason LA, Davis MI, Olson BD, Ferrari JR. Friends, Family, and Alcohol Abuse: An Examination of General and Alcohol Specific Social Support. *American Journal of Addictions*. 2007; 16(1): 49-55.
12. Schore AN. Attachment Trauma and the Developing Right Brain: Origins of Pathological Dissociation. In: Dell PF, O'Neil JA, editors. *Dissociation and the dissociative disorders*. New York: Routledge Taylor & Francis Group; 2009. p. 107-141.
13. Bankiewicz J, Werner M. Wpływ wczesnodziecięcych doświadczeń życiowych na rozwój układu nerwowego i wzorców reakcji z perspektywy potencjalnych zagrożeń. Jak naprawiać szkody – czy psychoterapia zmienia mózg? *Neurokognitywistyka w patologii i zdrowiu*. 2013; 1: 135-140.
14. Cohen H, Kaplan Z, Kozlovsky N, Gidron Y, Matar MA, Zohar J. Hippocampal microinfusion of oxytocin attenuates the behavioural response to stress by means of dynamic interplay with the glucocorticoid-catecholamine responses. *J. Neuroendocrinol.* 2010; 22: 889-904.

15. Onaka T. Neural pathways controlling central and peripheral oxytocin release during stress. *J. Neuroendocrinol.* 2004; 16: 308-312.
16. Uvnäs-Moberg K. Oxytocin may mediate the benefits of positive social interaction and emotions. *Psychoneuroendocrinol.* 1998; 23(8): 819–835.
17. Altemus M. Suppression of hypothalamic-pituitary adrenal axis responses to stress in lactating women. *J. Clin. Endocrinol. Metab.* 1995; 80: 2954-2959.
18. Cierpiakowska L, Chodkiewicz J. Uzależnienie od alkoholu. Oblicza problemu. Warszawa: Wydawnictwo Naukowe PWN; 2020.
19. Levin R, Edelman S, Shalev I, Ebstein P, Heresco-Levy U. The role of oxytocin in neuropsychiatric disorders: concepts and mechanisms. In: MS Ritner, editors. *Brain Protection in Schizophrenia, Mood and Cognitive Disorders.* New York: Springer Science+Business Media; 2010. p. 611-634.
20. Fujisawa TX, Nishitani S, Takiguchi S, Shimada K, Smith AK, Tomoda A. Oxytocin receptor DNA methylation and alterations of brain volumes in maltreated children. *Neuropsychopharmacology.* 2019; 44(12): 2045-2053.
21. Ebner NC, Lin T, Muradoglu TL, Weir DH, Plasencia GM, Lillard TS, Cohen RA, Connelly JJ. Association between oxytocin receptor gene (OXTR) methylation, plasma oxytocin, and attachment across adulthood. *International Journal of Psychophysiology.* 2019; 136: 22-32.
22. Ein-Dor T, Verbeke WJM, Mokry M, Vriticka P. Epigenetic modification of the oxytocin and glucocorticoid receptor genes is linked to attachment avoidance in young adults. *Attachment & Human Development.* 2018; 20(4): 439-454.
23. Bowlby JA. *Secure Base: Clinical Applications of Attachment Theory.* London: Routledge; 1988.
24. Main M, Hesse E, Kaplan N. Predictability of attachment behaviour and representation processes at 1, 6, and 19 years of age: the Berkeley longitudinal study. In: Grossmann KE, Grossmann K and Waters E, editors. *Attachment from Infancy to Adulthood: The Major Longitudinal Studies.* New York: The Guilford Press; 2005. p. 245-304.
25. Liotti G. Trauma, Dissociation, and Disorganized Attachment: Three Strands of a Single Braid. *Psychotherapy: Theory, research, practice, training.* 2004; 41: 472-486.
26. Wearden AJ, Lambertson N, Crook N, Walsh V. Adult attachment, alexithymia, and symptom reporting: An extension to the four category model of attachment. *Journal of Psychosomatic Research.* 2005; 58(3): 279-288.
27. Besharat MA, Salimian MM. The relationship between attachment styles and alexithymia: Mediating role of self-regulation. *International Journal of Research Studies in Psychology.* 2014; 3(4): 89-98.
28. Fossati A, Acquarini E, Feeney JA, Borroni S, Grazioli F, Laura E, Giarolli LE. Alexithymia and attachment insecurities in impulsive aggression. *Attachment & Human Development.* 2009; 11(2): 165-182.
29. Turner S, Mota N, Bolton J, Sareen J. Self-medication with alcohol or drugs for mood and anxiety disorders: A narrative review of the epidemiological literature. *Depression & Anxiety.* 2018; 35: 851-860.
30. Wojtyńkiewicz E. Uzależnienie od alkoholu z perspektywy teorii przywiązania – stadium przypadku. *Psychoterapia.* 2016; 2(177): 69-82.
31. Molnar D, Sadava S, DeCourville N, Perrier C. Attachment, motivations, and alcohol: testing a dual path model of high-risk drinking and adverse consequences in transitional clinical and student samples. *Canadian Journal of Behavioral Science.* 2010; 42(1): 1-13.
32. Kassel JD, Wardle M, Roberts JE. Adult attachment security and college student substance use. *Addictive Behaviors.* 2007; 32: 1164-1176.
33. Danielsson A, Romelsjoo A, Tengstrom A. Heavy episodic drinking in early adolescence: gender-specific risk and protective factors. *Substance Use and Misuse.* 2011; 46(5): 633-643.
34. Hofler DZ, Kooyman M. Attachment transition, addiction and therapeutic bonding – an integrative approach. *J. Subst. Abuse. Treat.* 1996; 13(6): 511-519.
35. Fontagy P, Luyten P, Bateman A, Gergely G, Strathearn L, Target M. Przywiązanie a patologia osobowości. In: Clarkin JF, Fontagy P, Gabboard GO, editors. *Psychoterapia psychodynamiczna zaburzeń osobowości. Podręcznik kliniczny.* Kraków: Wydawnictwo Uniwersytetu Jagiellońskiego; 2013. p. 61-117.
36. Vaht M, Kurrikoff T, Laas k, Veidebaum T, Harro J. Oxytocin receptor gene variation rs53576 and alcohol abuse in a longitudinal population representative study. *Psychoneuroendocrinology.* 2016; 74: 333-341.
37. Yang L, Wang F, Wang M, Han M, Hu L, Zheg M, Kang Y, Wang P. Association between oxytocin and receptor genetic polymorphisms and aggression in northern Chinese Han population with alcohol dependence. *Neurosci. Lett.* 2017; 636: 140-144.
38. Johansson A, Bergman H, Corander J, Waldman ID, Karrani N, Salo B, Jern P. Alcohol and aggression behavior in men: moderating effects of oxytocin receptor gene (OXTR) polymorphism. *Genes Brain Behav.* 2012; 11: 214-221.
39. Deuse L, Wudarczyk O, Rademacher L. Peripheral Oxytocin Predicts Higher Level Social Cognition in Men Regardless of Empathy Quotient. *Pharmacopsychiatry.* 2019; 52(3): 148-154.
40. Castellano F, Bartoli F, Crocarno C, Gamba G, Tremolada M, Santambrogio J, Carra G. Facial emotion recognition in alcohol and substance use disorders: A meta-analysis. *Neuroscience & Biobehavioral Reviews.* 2015; 59: 147-154.
41. Van Ijzendoorn MH, Bekermans-Kranenburg MJ. A sniff of trust: meta-analysis of the effects of intranasal oxytocin

- administration on face recognition, trust to in-group, and trust to out group. *Psychoneuroendocrinology*. 2012; 37(3): 438-443.
42. Shahrestani S, Kemp AH, Gustella AJ. The impact of a single administration of intranasal oxytocin on the recognition of basic emotions in humans: a meta-analysis. *Neuropsychopharmacology*. 2013; 38(10): 1929-1936.
 43. Tunstall BJ, Kirson D, Zallar LJ, McConnell SA, Vendruscolo JCM, Ho CP, Oleata CS, Khom S. Oxytocin blocks enhanced motivation for alcohol dependence and blocks alcohol effects on GABAergic transmission in the central amygdala. *PLOS Biol*. 2019; 17(4): 1-28.
 44. Pedersen CA, Smedley KL, Leserman J, Jarskog LF, Rau SW, Kampov-Polevoi A. Intranasal oxytocin blocks alcohol withdrawal in human subjects. *Alcohol Clin. Exp. Res*. 2013; 37: 484-489.
 45. Szabo G, Kovacs GL, Szekeli S, Telegdy G. The effects of neurohypophyseal hormones on tolerance to the hypothermic effect of ethanol. *Alcohol*. 1985; 2: 567-574.
 46. Szabo G, Kovacs GL, Telegdy G. Intraventricular administration of neurohypophyseal hormones interferes with development of tolerance to ethanol. *Acta Physiol Hung*. 1989; 73: 97-103.
 47. Bowen MT, Peters ST, Absalom M, McGregor IS. Oxytocin prevents ethanol actions at δ subunit-containing GABA_A receptors and attenuates ethanol induced motor impairment in rats. *Proc Natl Acad Sci USA*. 2015; 112(10): 3104-3109.
 48. Pedersen CA. Oxytocin, tolerance, and the dark side of addiction. *Int. Rev. Neurobiol*. 2017; 136: 239-274.
 49. Sinha R, Fox HC, Hong KI, Hansen J, Tuit K, Kreek MJ. Effects of adrenal sensitivity, stress and cue induced craving, and anxiety on subsequent alcohol relapse and treatment outcomes. *Arch. Gen Psychiatry*. 2011; 68: 942-952.
 50. Mitchell JM, Arcuni PA, Weinstein D, Woolley JD. Intranasal oxytocin selectively modulates social perception, craving, and approach behavior in subjects with alcohol use disorder. *J. Addict. Med*. 2016; 10: 182-189.
 51. Theodoridou A, Rowe AC, Penton-Voak IS, Rogers PJ. Oxytocin and social perceptions; oxytocin increases perceived facial trustworthiness and attractiveness. *Horm Behav*. 2009; 56(1): 128-132.
 52. Thomas S, Larkin T. Plasma cortisol and oxytocin levels predict help-seeking intentions for depressive symptoms. *Psychoneuroendocrinology*. 2018; 87: 159-165.
 53. Jakubik J, Kowaluk B. Wsparcie społeczne a utrzymywanie abstynencji u mężczyzn uzależnionych od alkoholu. *Alkoholizm i narkomania*. 1997; 1(26): 89-103.
 54. Melby K, Grawe RW, Aamo TO, Skovlund E, Spigset O. Efficacy of Self-Administered Intranasal Oxytocin on Alcohol Use and Craving After Detoxification in Patients With Alcohol Dependence. A Double-Blind Placebo-Controlled Trial. *Alcohol and Alcoholism*. 2021; 56(5): 565-572.
 55. Melby K, Grawe RW, Aamo TO, Salvesen O, Spigset O. Effect of intranasal oxytocin on alcohol withdrawal syndrome: A randomized placebo-controlled double-blind clinical trial. *Drug and Alcohol Dependence*. 2019; 197: 95-101.
 56. Hawkins JD. Exploring the effects of age of alcohol use initiation and psychosocial risk factors on subsequent alcohol misuse. *Journal of Studies on Alcohol*. 1997; 58(5): 280-290.
 57. Martin DJ, Garske JP, Davis KM. Relation of the Therapeutic Alliance with Outcome and Other Variables: A Meta Analytic Review. *Journal of Consulting and Clinical Psychology*. 2000; 68: 438-450.