EFFECT OF PSYCHONEUROBICS AND DIET ON THE LEVEL OF DOPAMINE

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Abstract

The ability to resist the urge to eat requires the proper functioning of neuronal circuits involved in top-down control to oppose the conditioned responses that predict reward from eating the food and the desire to eat the food. Imaging studies show that obese subjects might have impairments in dopaminergic pathways that regulate neuronal systems associated with reward sensitivity, conditioning and control. It is known that the neuropeptides that regulate energy balance (homeostatic processes) through the hypothalamus also modulate the activity of dopamine cells and their projections into regions involved in the rewarding processes underlying food intake. It is postulated that this could also be a mechanism by which overeating and the resultant resistance to homoeostatic signals impairs the function of circuits involved in reward sensitivity, conditioning and cognitive control.

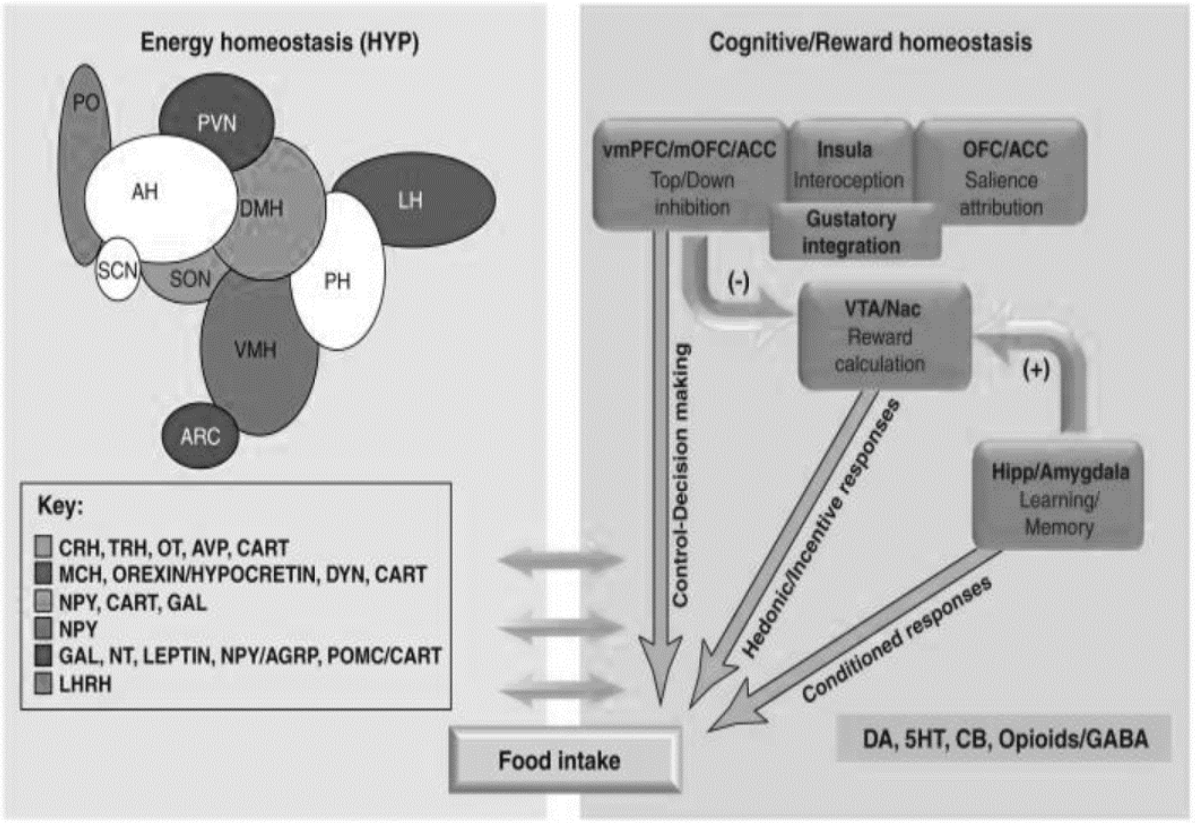
Introduction

Regular physical exercise has been proved to have therapeutic benefit, such as treating psychiatric illnesses supporting brain injury recovery, and resisting neurodegenerative diseases. The advantageous effects of exercise on brain functions have been attributed to increased capacities of metabolism reserve and antioxidation. Furthermore, regulations of the secretion of neurotrophic factors, vasculotropic factors, inflammatory mediators, and neurotransmitters are also involved in exercise's influence on brain function. Among these effects, secretion of neurotransmitters, especially monoamines, have been linked to the exercise-induced neuronal adaptation. Interplay between exercise and monoamines was initially derived from the "Central Fatigue Hypothesis", in which increased brain 5-HT release was found to be associated with central fatigue. 5-HT is linked to fatigue because of its known effects on sleep, lethargy, and loss of motivation. The hypothesis prompted

researchers to investigate the role of 5-HT in exercise-induced central fatigue. Results suggest that exercise-induced central fatigue is more complex and depends on the intensity and duration of exercise. Overtraining exercise may stimulate hyperactivation of the monoamine systems which could cause fatigue. Rodents that receive exhaustive treadmill exercise have higher 5-HT in the midbrain, striatum, hypothalamus and hippocampus. The levels of dopamine are increased only in the striatum, although the levels of DOPAC, the major DA metabolite, are increased in both midbrain and striatum. On the other hand, exhaustive treadmill exercise reduces NE levels in the hypothalamus and brain stem. Chronic moderate exercise is also known to stimulate the monoamine systems, but exercise of this sort does not induce central fatigue. Instead, chronic moderate exercise has been recognized as one of the most effective ways to enhance the adaptation/plasticity of the central nervous system (CNS). In addition, clinical studies suggest that monoamine systems play central roles resistance and recovery induced by chronic moderate exercise from various diseases like mental disorders and Parkinson's disease (PD). This article reviews recent studies that emphasize the effects of exercise on brain functions due to monoamine systems.

Social and cultural factors undoubtedly contribute to this epidemic. Specifically, environments that promote unhealthy eating habits (ubiquitous access to highly processed and junk foods) and physical inactivity are believed to have a fundamental role in the widespread problem of obesity. However, individual factors also help determine who will (or will not) become obese in these environments. Based on heredity studies, genetic factors are estimated to contribute between 45% and 85% of the variability in BMI. Although genetic studies have revealed point mutations that are over-represented among obese individuals, for the most part, obesity is thought to be under polygenic control. Indeed, the most recent whole genome-wide association analysis study (GWAS) conducted in 249,796 individuals of European descent identified 32 loci associated with BMI. However, these loci explained only 1.5% of the variance in BMI. Moreover, it was estimated that GWAS studies with larger samples should be able to identify 250 extra loci with effects on BMI. However, even with the undiscovered variants, it was estimated that signals from common variant loci would account for only 6–11% of the genetic variation in BMI (based on an estimated heritability of 40–70%). The limited explanation of the variance from these genetic studies is likely to reflect the complex interactions between individual factors (as determined by genetics) and the way in which individuals relate to environments where food is widely available, not only as a source of nutrition, but also as a strong reward that by itself promotes eating.

The hypothalamus [via regulatory neuropeptides such as leptin, cholecystokinin (CCK), ghrelin, orexin, insulin, neuropeptide Y (NPY), and through the sensing of nutrients, such as glucose, amino acids and fatty acids] is recognized as the main brain region regulating food intake as it relates to caloric and nutrition requirements. In particular, the arcuate nucleus through its connections with other hypothalamic nuclei and extra-hypothalamic brain regions, including the nucleus tractus solitarius, regulates homeostatic food intake and is implicated in obesity. However, evidence is accumulating that brain circuits other than those regulating hunger and satiety are involved in food consumption and obesity. Specifically, several limbic [nucleus accumbens (NAc), amygdala and hippocampus] and cortical brain regions [orbitofrontal cortex (OFC), cingulate gyrus (ACC) and insula] and neurotransmitter systems (dopamine, serotonin, opioids and cannabinoids) as well as the hypothalamus are implicated in the rewarding effects of food. By contrast, the regulation of food intake by the hypothalamus appears to rely on the reward and motivational neurocircuitry to modify eating behaviors.



Literature Review

Mark S Gold (2014) Obesity as a result of overeating as well as a number of well described eating disorders has been accurately considered to be a world-wide epidemic. Recently a

number of theories backed by a plethora of scientifically sound neurochemical and genetic studies provide strong evidence that food addiction is similar to psychoactive drug addiction. Our laboratory has published on the concept known as Reward Deficiency Syndrome (RDS) which is a genetic and epigenetic phenomenon leading to impairment of the brain reward circuitry resulting in a hypo-dopaminergic function. RDS involves the interactions of powerful neurotransmitters and results in abnormal craving behavior. A number of important facts which could help translate to potential therapeutic targets espoused in this focused review include: (1) consumption of alcohol in large quantities or carbohydrates binging stimulates the brain's production of and utilization of dopamine; (2) in the meso-limbic system the enkephalinergic neurons are in close proximity, to glucose receptors; (3) highly concentrated glucose activates the calcium channel to stimulate dopamine release from P12 cells; (4) a significant correlation between blood glucose and cerebrospinal fluid concentrations of homovanillic acid the dopamine metabolite; (5) 2-deoxyglucose (2DG), the glucose analog, in pharmacological doses is associated with enhanced dopamine turnover and causes acute glucoprivation. Evidence from animal studies and fMRI in humans support the hypothesis that multiple, but similar brain circuits are disrupted in obesity and drug dependence and for the most part, implicate the involvement of DA-modulated reward circuits in pathologic eating behaviors. Based on a consensus of neuroscience research treatment of both glucose and drug like cocaine, opiates should incorporate dopamine agonist therapy in contrast to current theories and practices that utilizes dopamine antagonistic therapy. Considering that up until now clinical utilization of powerful dopamine D2 agonists have failed due to chronic down regulation of D2 receptors newer targets based on novel less powerful D2 agonists that up-regulate D2 receptors seems prudent. We encourage new strategies targeted at improving DA function in the treatment and prevention of obesity a subtype of reward deficiency.

Nora D Volkow (2011) The ability to resist the urge to eat requires the proper functioning of neuronal circuits involved in top-down control to oppose the conditioned responses that predict reward from eating the food and the desire to eat the food. Imaging studies show that obese subjects might have impairments in dopaminergic pathways that regulate neuronal systems associated with reward sensitivity, conditioning and control. It is known that the neuropeptides that regulate energy balance (homeostatic processes) through the hypothalamus also modulate the activity of dopamine cells and their projections into regions involved in the rewarding processes underlying food intake. It is postulated that this could

also be a mechanism by which overeating and the resultant resistance to homoeostatic signals impairs the function of circuits involved in reward sensitivity, conditioning and cognitive control.

Michaelides et al. (2012) Certainly, the compulsion and the loss of control observed in the drug taking behaviors of drug-addicted subjects is similar to overeating by obese individuals. Although not well understood the mechanisms of these behaviors were studied utilizing PET in drug-addicted subjects. Reductions in striatal DA D2 receptors were documented. In pathologically obese subjects, the same researchers found striatal DA D2 receptors reductions similar to those found in drug-addicted subjects. Moreover, DA D2 receptor levels were inversely related to the BMI of the obese subjects. Postulated that decreased DA D2 receptors levels predisposed subjects to search for reinforcers; drug of choice in the case of drug-addicted subjects and food in the case of the obese subjects to compensate temporarily for a decreased sensitivity of reward circuits regulated by the activity of DA D2 receptors.

Avena et al. (2008) using microdialysis found an increase in extracellular Ach and a decrease in dopamine release, in the NAc shell, in rats undergoing withdrawal from sugar binging. This finding suggests that a state, that involves anxiety, an altered accumbens dopamine and Ach balance is induced by intermittent binging on sucrose and chow followed by fasting. This is similar to withdrawal from opiates following naloxone and may be a feature of some eating disorders.

Yu Min Kuo (2013) The beneficial effects of exercise on brain function have been demonstrated in animal models and in a growing number of clinical studies on humans. There are multiple mechanisms that account for the brain-enhancing effects of exercise, including neuroinflammation, vascularization, antioxidation, energy adaptation, and regulations on neurotrophic factors and neurotransmitters. Dopamine (DA), noradrenaline (NE), and serotonin (5-HT) are the three major monoamine neurotransmitters that are known to be modulated by exercise. This review focuses on how these three neurotransmitters contribute to exercise affecting brain function and how it can work against neurological disorders.

Methods

Physiological Properties of DA

DA is synthesized from L-dihydroxyphenylalanine (L-DOPA), which is catalyzed from amino acid tyrosine by enzyme tyrosine hydroxylase. L-DOPA is then converted to DA by the

catalysis of enzyme DOPA decarboxylase (or aromatic amino acid decarboxylase). In the CNS, dopaminergic neurons mainly reside in two nuclei of the midbrain: substantia nigra and ventral tegmental nucleus. Axons of the dopaminergic neurons in the substantia nigra project to the striatum (nigrostriatal pathway) which in turn is responsible for movement behavior. Axons of the ventral tegmental nucleus dopaminergic neurons project to the entire cortex (mesocortical pathway) and nucleus accumbens (mesolimbic pathway), which are involved in cognition and reward responses, respectively.

There are five types of DA receptors (D1 to D5), which are simply categorized in two families of GPCR: D1-like and D2-like receptors. The D1-like receptor family contains D1 and D5 receptors that are coupled with G_s and G_q protein. The D2-like receptor family comprises of D2, D3 and D4 receptors which couple with the G_i proteins to inhibit adenylyl cyclase. D2-like receptors can be found on both pre- and post-synaptic terminals, while D1-like receptors are mainly located at post-synaptic sites. The actions of DA receptors on membrane excitability are well defined in the striatal neurons. Both D1 and D2 receptors are capable of modulating long-term depression; activation of D1 receptor enhances long-term depression, while activation of D2 receptor inhibits long-term depression. Furthermore, D1 and D2 receptors modulate motor functions by modifying the excitatory transmission between the presynaptic cortical glutamatergic neurons and the post-synaptic striatal GABAergic neurons. Certain foods are considered to enrich the dopamine levels in the body.

- Dairy foods such as milk, cheese and yogurt
- Omega-3 rich food
- Green Tea
- Fruit and vegetables, in particular bananas
- Nuts such as almonds and walnuts
- Dark chocolate

Psychoneurobics system of neuro - muscular exercises have been used to elevate the dopamine levels in the brain. These exercises are successful in elevating the mood of the participants and as well improve the concentration of an indivisual.

The Psychoneurobics exercises used were as follows -:

1. Neurobic Spa : Spa is a 27 min. visual video meditation practice. It does 7 Chakras cleaning, healing & it's strengthening. Delta Healing Music has been used in this, which users do in Apana Vayu Mudra & this is done only by seeing the video. So, that no other thoughts will disturb. Through this visualization process, each and every chakra is healed.

Mudra- Apan Vayu Mudra

2. Blissful Neurobics: The seventh major chakra is found near the inside of the top of the head and looks like a ceiling fan colored in vivid royal violet. It's essential to clear cognizance or "clear knowing", which is the ability to receive thoughts, information & ideas from the Divine mind or collective can tap into the wealth of creativity & inventions that abound in the spiritual plane.

Procedure : Step I: Sit down comfortably either cross-legged or in a chair. Ensure your back is straight and your hands are in Gyan Mudra .

Step II: Touch the palate with your tongue and close your mouth.

Step III : Visualize that you are inhaling

violet color gas slowly and deeply. Now feel violet - colored showers entering through your Crown Chakra and spreading through your entire body to fully relax all cells and tissues of the body.

Step IV : Exhale with a ' humming sound and feel all black toxic gases being released . Also feel inner bliss with the humming sounds.

Step - V : Do the above steps for a minimum of 10 minutes. Practice slowly so as to achieve one act of respiration in one minute.

Note: In case of arthritis / joints pain the above should be done in Vayu Mudra.

Exercise:

Mudra- Mahaveer Mudra

Colour- Violet

Sound Chanting- “Humming”

3. ENLIGHTENING NEUROBICS: The sixth major chakra is located between the two eyes. We often call it the Brow or the Ajna Chakra. However, we most commonly call it the Third Eye, and for good reason. If your eyes, take a few deep breaths, and place your attention on the area between your eyes, you will begin to see you close or feel an oval-shaped object lying on one side. This is your third eye; it is the eye of your true self or your higher self. The reason why the eye is turned towards you is because everything is what is in There is nothing else within except you. Heart your and mind. It is only an illusion that a material world exists outside and separate from you.

Procedure: Step I: Sit down comfortably either cross-legged or in a chair. Ensure your back is straight and your hand is in Pran Mudra .

Step II : Take a deep breath and visualize indigo-colored pas slowly and deeply

Step III : Roll your lips in ' O shape .

Step IV : Breathe out slowly and completely with ' Ooood sound. While exhaling feel all the black - colored toxin gues in being released.

Step V : Do the above steps for a minimum of 10 minutes every day.

' Om ' or ' Aum ' is the most widely chanted syllable across religions and cultures. Some popular chants resonating w Om are Tibetan mantra Namo Arihantanam Namo Namo the Sikh mantra

"Ek Omkar Satnam ' and ' Allah - O - Akbar Islam. This is the basic trinity of sounds and the whole music of life grows out of this.

Step IV : Concentration on Indigo color 3D plate.

Exercise:

Mudra- Pran Mudra

Colour- Indigo

Sound Chanting- “O”

Exercise and DA System

Exercise is known to change the DA system in the CNS. Using a radioenzymatic assay followed by a thin-layer chromatography, the concentrations of DA are found to be upregulated in brain homogenates of rats subjected to eight weeks of food-reinforced running-wheel exercise, while a compensatory down-regulation of DA receptor densities is evident in these animals. Upregulation of DA in the brain has been linked to exercise-induced higher levels of serum calcium, which is transported into the brain and affects calcium/calmodulin-dependent DA synthesis by activating the tyrosine hydroxylase enzyme. Furthermore, the binding affinity between DA and DA receptor, determined by [3H]spiroperidol binding, is also increased by exercise training.

Table of Observed value of Psychoneurobics

Variables	Change in Dopamine level	No Change in Dopamine level	Total
Psychoneurobics Exercise	42	8	50
No Psychoneurobics	8	50	58
Total	50	58	108

Table of Expected Value Psychoneurobics

Variable	Change in Dopamine level	No Change in Dopamine level
Psychoneurobics Exercise	50*50/108 = 23.14	50*58/108 = 26.85
No Psychoneurobics Exercise	50*58/108 = 26.85	58*58/108 = 31.14

Observed Value	Expected Value	(O-E)	$(O-E)^2$	$(O-E)^2/E$
42	23.14	18.86	$(18.86)^2$	8.461
8	26.85	-18.85	$(-18.85)^2$	13.23
8	26.85	-18.85	$(-18.85)^2$	13.23
50	31.14	18.86	$(18.86)^2$	11.422

$X^2 = \sum(O-E)2/E$

=8.46 + 13.23+ 13.23 + 11.422 = 46.34

Hence $x^2 = 46.34$

To find out tabular value

Degree of freedom (v) = (Column -1) (Row -1)

V = (2-1)(2-1)

V=1

Hence V = Degree of freedom = 1

When no value of significance is mentioned, we by default take 5 as the value of significance

Hence = x^2 0.05 = 3.84 and x2 calculated = 46.34

We observe that when calculated value is > tabulated value

46.34 > 3.84

Therefore, the null hypothesis is failed

And alternative hypothesis passes successfully.

This indicates that psychoneurobic is effective in balancing the dopamine level

Conclusion

An overwhelming majority of studies accredit that the monoamine systems mediate the exercise-induced enhancement of various brain functions. It is noteworthy that DA, NE and 5-HT receive reciprocal regulation from each other. For instance, 5-HT enhances DA release through the 5-HT_4 receptors in the striatum. Activation of locus coeruleus induces DA secretion either directly through firing on the ventral tegmental nucleus dopaminergic neurons, or indirectly through the local glutamatergic neuron to activate neurons in the ventral tegmental nucleus. Therefore, the cooperative effects of the monoamine family should also be taken into consideration, while studying the effects of exercise on brain function.

The stimulation of the monoamine system is dependent on exercise intensity. Mandatory treadmill exercise and voluntary wheel running are the two most common forms of exercise in rodent models with different exercise intensities. Treadmill exercise is more effective in enhancing the muscle aerobic capacity and in increasing the serum corticosterone level than that of wheel-running exercise. The exercise-associated stress level could be an underlying modulating factor for their differential effects on brain monoamine systems. Different exercise intensities between treadmill exercise and wheel running may induce different degree of feedback in the hypothalamus-pituitary gland-adrenal gland axis. Furthermore,

treadmill exercise is much more effective in activating the BDNF signaling pathway than that of wheel running in hippocampus and amygdala. The effects of BDNF cannot be neglected and should be taken into consideration when studying the effects of exercise on monoamine systems.

References

1. Meeusen R. Exercise and the brain: Insight in new therapeutic modalities. *Ann. Transplant.* 2005;10:49–51.
2. Knochel C., Oertel-Knochel V., O'Dwyer L., Prvulovic D., Alves G., Kollmann B., Hampel H. Cognitive and behavioural effects of physical exercise in psychiatric patients. *Prog. Neurobiol.* 2012;96:46–68. doi: 10.1016/j.pneurobio.2011.11.007.
3. Dinas P.C., Koutedakis Y., Flouris A.D. Effects of exercise and physical activity on depression. *Ir. J. Med. Sci.* 2011;180:319–325. doi: 10.1007/s11845-010-0633-9.
4. Tordeurs D., Janne P., Appart A., Zdanowicz N., Reynaert C. Effectiveness of physical exercise in psychiatry: A therapeutic approach? *Encephale.* 2011;37:345–352. doi: 10.1016/j.encep.2011.02.003. Carek P.J., Laibstain S.E., Carek S.M. Exercise for the treatment of depression and anxiety. *Int. J. Psychiatry Med.* 2011;41:15–28. doi: 10.2190/PM.41.1.c.
5. Alsuwaidan M.T., Kucyi A., Law C.W., McIntyre R.S. Exercise and bipolar disorder: A review of neurobiological mediators. *Neuromolecular Med.* 2009;11:328–336. doi: 10.1007/s12017-009-8079-9.
6. Al-Eitan L. N. 1., Jaradat S. A., Hulse G. K., Tay G. K. (2012). Custom genotyping for substance addiction susceptibility genes in Jordanians of Arab descent. *BMC Res.* 5:497 10.1186/1756-0500-5-497
7. Archer T. Influence of physical exercise on traumatic brain injury deficits: Scaffolding effect. *Neurotox. Res.* 2012;21:418–434. doi: 10.1007/s12640-011-9297-0.

8. Anitha M., Abraham P. M., Paulose C. S. (2012). Striatal dopamine receptors modulate the expression of insulin receptor, IGF-1 and GLUT-3 in diabetic rats: effect of pyridoxine treatment. *Eur. J. Pharmacol.* 696 54–61 10.1016/j.ejphar.2012.09.006
9. Wolff E., Gaudlitz K., von Lindenberger B.L., Plag J., Heinz A., Strohle A. Exercise and physical activity in mental disorders. *Eur. Arch. Psychiatry Clin. Neurosci.* 2011;261:S186–S191. doi: 10.1007/s00406-011-0254-y.
10. Adler C. M., Elman I., Weisenfield N., Kestle L., Pickar D., Breier A. (2000). Effects of acute metabolic stress on striatal dopamine release in healthy volunteers. *Neuropsychopharmacolgy* 22 545–550 10.1016/S0893-133X(99)00153-0
11. Ariza A. J., Hartman J., Grodecki J., Clavier A., Ghaey K., Elsner M., et al. (2013). Linking pediatric primary care obesity management to community programs. *J. Health Care Poor Underserved* 24 158–167 10.1353/hpu.2013.0112
12. Avena N. M., Kobaissy F. H., Borcarsly M. E., Yang M., Hoebel B. G., Gold M. S. (2010) "Poster: binge eating sucrose activates gene pathways involved in substance abuse," in Proceedings of the *49th Annual Meeting* (Miami, FL: American College of Neuropsychopharmacology).
13. Avena N. M., Murray S., Gold. M. S. (2013a). Comparing the effects of food restriction and overeating on brain reward systems. *Exp. Gerontol.* 48 1062–1067 10.1016/j.exger.2013.03.006
14. Beaver K. M., Belsky J. (2012). Gene-environment interaction and the intergenerational transmission of parenting: testing the differential-susceptibility hypothesis. *Psychiatr. Q.* 83 29–40 10.1007/s11126-011-9180-4

15. Bergen A. W., Yeager M., Welch R. A., Haque K., Ganjei J. K., van den Bree M. B., et al. (2005). Association of multiple DRD2 polymorphisms with anorexia nervosa. *Neuropsychopharmacology* 30 1703–1710 10.1038/sj.npp.1300719
16. Blum K., Bailey J., Gonzalez A. M., Oscar-Berman M., Liu Y., Giordano J., et al. (2011a). Neuro-genetics of reward deficiency syndrome (rds) as the root cause of "addiction transfer": a new phenomenon common after bariatric surgery. *J. Genet. Syndr. Gene. Ther.* 23 S2-001.
17. Chen D., Liu F., Shang Q., Song X., Miao X., Wang Z. (2011a). Association between polymorphisms of DRD2 and DRD4 and opioid dependence: evidence from the current studies. *Am. J. Med. Genet. B Neuropsychiatr. Genet.* 156B, 661–670 10.1002/ajmg.b.31208