profiles with the psychotherapeutic effect are described. The analysis of the relationship of genetic predictors and psychological characteristics with the use of methods of cognitive behavioral therapy, therapy of PTSD, BPD, panic disorders, depression. **Discussion.** The analysis of modern scientific literature on the topic allows us to conclude that the DNA methylation index can be used as a predictor of effectiveness and an indicator of the response to psychotherapy. In the future, knowledge of the relationship between genetic predictors and psychological characteristics with the effectiveness of psychotherapy can be used to develop personalized programs aimed at providing psychological assistance.

Keywords

effectiveness of psychotherapy, epigenetics, DNA methylation, distress, cognitive behavioral psychotherapy, genes, neuroplasticity

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Introduction

Since the middle of the twentieth century, with the active development of genetics, researchers have begun to note the great role of heredity in the genesis of mental disorders. The question of the extent of the influence of genotype and environment on psychological characteristics and human behavior is still open. At the same time, recent discoveries in the field of neuroscience indicate the opposite effect of behavior on gene expression. The epigenetic approach allows us to take a different look at mental disorders and the available methods of their correction, such as medication, psychotherapy, and psychological correction. Epigenetic studies can play a key role in determining biomarkers associated with human vulnerability to psychopathologies, which can help improve the accuracy of diagnosis and expand opportunities for timely prevention of mental maladaptation and study the mechanisms of psychotherapy (Kumsta, 2019).

Psychotherapy is an interpersonal process that aims to change feelings, behaviors, attitudes, and cognitions that are problematic for the person seeking help (Strupp and

Binder, 1984). One of the goals of psychotherapy is the restoration of human social functioning, that is, the ability to maintain stable and productive interpersonal relationships that promote physical and emotional development. The most important change occurs with a person's ability to change their social environment (Fonagy et al., 2015).

To date, more than 400 types and methods of psychotherapy have been described, which relate to the main areas: psychodynamic, cognitive-behavioral, existential-humanistic (Roth and Fonagy, 2005). Recent studies indicate the effectiveness of therapy regardless of the direction, since common factors such as therapeutic alliance play the greatest role. The authors of the book "The Great Discussion about Psychotherapy. Evidence of what makes psychotherapy effective" Wampold and Imel give an example of a study of the effectiveness of group psychotherapy, in which an improvement in the psychoemotional state of members of the group receiving psychotherapeutic help was proved compared with the control group that did not receive such help, and with the placebo group (Wampold and Imel, 2015). The authors note that psychotherapy has fewer side effects than many conventional medical interventions and is more effective in terms of financial costs (if you take into account financial investments in the development and research of the effectiveness of medications). In the most common mental disorders, psychotherapy is comparable in effectiveness to drug treatment and has fewer adverse reactions. In addition, the psychotherapeutic process also has a preventive effect: the frequency of relapses is lower after its completion. There is no such effect in drug treatment (Wampold and Imel, 2015).

Considering the interdisciplinary problem of the relationship between genetics and psychotherapy, it is necessary to study the main modern concepts and discoveries of genetic neuroscience.

Some questions still remain open. For example, the question of which genes and their combinations affect susceptibility to stressful experiences, the genesis and manifestation of mental disorders (Gelernter, 2015). This scientific review is devoted to the search for answers to this and other designated questions.

Theoretical justification

Basic provisions of epigenetics

The human genome contains about 26 thousand genes encoding proteins, so the relationship between genotype and phenotype is incredibly complex. One gene can be associated with several phenotypes (the principle of multifinality), while one specific phenotype can be caused by mutations in several genes (the principle of equifinality). Consequently, one particular mutation can manifest itself differently in different people, which can be explained by a different profile of genetic variations and the influence of various environmental factors (Cicchetti and Rogosch, 1996).

The term "epigenetics" was first used by C. Waddington in the 1950s to refer to the mechanisms by which a genotype leads to a specific phenotype during embryonic development (Jamniczky et al., 2010). Currently, it is believed that an epigenetic trait is a stable and inherited phenotype resulting from chromosomal changes without any changes in the nucleotide sequence (Berger et al., 2009). Thus, epigenetics refers to all the mechanisms that regulate the genome by regulating gene expression - modifications that are not related to changing the DNA sequence.

Epigenetic changes have three key features:

4. they depend on the environment (Zhang, Meaney, 2010);
5. they are hereditary, that is, they can be transmitted to at least the first three generations of descendants (Daxinger, Whitelaw, 2012);
6. dynamic throughout life and potentially reversible (Szyf et al., 2008).

There are several mechanisms of epigenetic regulation. The most studied are: 1) DNA methylation, 2) histone modification, 3) chromatin conformation, 4) microRNA regulation (Graff et al., 2011).

DNA methylation is a process of activation and suppression of gene activity, which plays an important role in cell differentiation and provides a mechanism by which the genome can express multiple phenotypes in a multicellular organism. It can also serve as a form of biological adaptation to an ever-changing environment, especially in the early years of life (Szyf, 2012).

Histones are proteins that pack and organize DNA, and are also involved in the regulation of chromatin condensation.

MicroRNAs are widely activated in neurons and are associated with the processes of neurogenesis and neuroplasticity. They may play a role in the pathogenesis of depression (Dwivedi, 2014).

The "diathesis-stress" model

There are different models of the origin of mental disorders. According to the "diathesis-stress" model (Monroe, Simons, 1991; Patten, 2013), psychopathology arises as a result of the interaction of premorbid genetic vulnerability or organic predisposition (diathesis) and environmental aggression (stress).

In recent years, another assumption has been discussed, according to which, instead of diathesis, people have different susceptibility to environmental influences; they may not only be more vulnerable to the negative effects of an unfavorable environment, but also sensitive to beneficial influences (Belsky et al., 2007), that is, the effect of a particular polymorphism will be reflected in the phenomenon of plasticity. Thus, the transformation of the environment into a resource environment at the individual (for example, by encouraging prosocial behavior and psychotherapeutic interventions) or sociocultural level (a favorable environment for the population) can have positive results. Therefore,

the understanding of the role of prevention, diagnosis and treatment of mental disorders and maladaptations will change.

Currently, two ways of linking genes with the environment have been described (Caspi and Moffitt, 2006; Kendler, 2011):

7. Gene-environment correlation (rGE);
8. Gene-environment interaction (GxE).

Correlations between genes and the environment are divided into three types (Kendler and Eaves, 1986):

- passive, where children not only inherit genes, but also share with their parents the environment in which they grow and develop. For example, they inherit an athletic physique and family sports habits (Plomin et al., 1997);
- reactive or provocative — refers to the tendency of certain genetically determined temperamental behavior to cause certain types of reactions in people around them. For example, a child with a "difficult" temperament is more likely to provoke negative parental behavior;
- active or selective — defined as the active generation of certain environments based on genetically determined behavioral tendencies. This refers to the relationship between a person's genetic characteristics and the niches in the environment that a person chooses or creates. For example, an intellectually inquisitive child will tend to find an intellectually rich environment, while a child with a behavioral disorder will look for peers with similar behavior and related interests (Plomin et al., 1997).

The gene-environment interaction explains why people react differently to environmental factors (for example, why some people are more prone to depression after exposure to negative life events; why some people with genetic risk are less prone to depression if they were influenced by a favorable environment). So in the study of Heils et al. (1996) it was shown that the risk of depression increases due to the interaction between the genotypes of the 5-HTTLPR gene and the number of stressful life events experienced (Heils et al., 1996): individuals with one or two copies of the short allele of the 5-HTTL promoter polymorphism have more pronounced depressive symptoms and suicidal tendencies due to stressful life events, compared with carriers of the homozygous variant of the long allele (Caspi et al., 2003).

Correlation and interaction models are not mutually exclusive. Genetic polymorphism may be associated with certain traits that cause changes in the environment and interact with the environment to determine the phenotype. An example of such an indirect model is the detection of the correlation of a short polymorphic allele in the promoter region of the serotonin transporter gene (5HTTLPR) with neuroticism (Greenberg et al., 2000; Sen et al., 2004), which, in turn, is associated with a tendency to negatively interpret life events and with higher rates of depression (John and Gross, 2004).

Thus, it can be concluded that psychosocial interventions (environmental effects) are reflected in biological changes; therefore, psychotherapy is a type of treatment/support

that involves learning from the environment determined by therapeutic relationships and can lead to certain changes in behavior, well—being, quality of life, etc., which are also reflected in biological shifts.

The study of the effect of carrying "plasticity alleles" on the effectiveness of psychotherapy has contradictory results. Thus, Bryant et al. (2010) demonstrated that respondents diagnosed with post-traumatic stress disorder with a short 5HTTPLR allele reacted worse to cognitive behavioral therapy (CBT) compared with patients with a homozygous variant of the long allele. In another study, it was found that in patients with post-stroke depression with a short 5HTTPLR allele, psychosocial rehabilitation had a significant effect that was not obvious for patients with homozygous carriers with a long allele (Kohen et al., 2011). Eley et al. (2012) showed that children with anxiety disorder who have two short alleles in the genotype (SS) show more pronounced success in cognitive behavioral therapy than children with a long allele (SL/LL). In a study by Bockting et al. (2013) the relationship between the serotonin 5HTTLPR transporter gene and the response to cognitive behavioral therapy in patients with recurrent depression has not been identified.

The relationship between the genotype of the 5HTTLPR gene and the effectiveness of cognitive behavioral therapy could not be replicated in childhood anxiety disorder. The authors reported that children homozygous for the short allele showed more positive treatment results, but with minor effects that did not reach the level of statistical regularity (Lester et al., 2016).

It is important to note that in recent years, research in this area has shifted from low-productivity studies of genetic associations in which one or more genetic loci (candidate genes) are simultaneously genotyped to high-performance full-genome associative studies that include thousands of gene variants (GWAS) (CONVERGE consortium, 2015; Hou et al., 2016; Power et al., 2017).

The study of the complex relationships between genes and the environment has led to the development of epigenetic models that go beyond the classical paradigm of vulnerability to stress. Let's turn to a more detailed consideration of them.

Research on the relationship between social and (epi)genetic factors

Several social environmental factors, such as parental care in infancy and distress, can have a significant impact on neurobiological development by altering epigenetic programming, causing long-term consequences for mental health. It is known that the quality of parental care can determine the activation of certain genes in offspring associated with the development of certain areas of the brain, such as the hippocampus, which are involved in the regulation of stress response (Meaney, 2001). Thus, chronic and unpredictable separation from the mother causes depressive behavior in offspring in adulthood, changing the DNA methylation profile, which is passed on to the next generation with subsequent changes in gene expression (Franklin et al., 2010). For

example, a study of rat development has shown that abuse at an early age leads to persistent changes in the methylation profile of the BDNF gene and, consequently, in its expression in the prefrontal cortex, which in turn is observed in subsequent offspring (Fumagalli et al., 2004, Roth et al., 2009). Prenatal stress in rats and social stress in mice reduced BDNF levels in the hippocampus and prefrontal cortex (Luoni et al., 2014). As for humans, patients with depression had decreased levels of BDNF in serum and plasma, as well as in the hippocampus, during pathoanatomic studies (Lee and Kim, 2010). Thus, BDNF can be associated with adaptation to environmental conditions.

Other studies have shown that exposure to an acute stressor activates several effects, including enhanced danger memory, adaptive immunity, and metabolic changes that prepare the body to deal with the threat (Rubin et al., 2014). On the other hand, more intense and/or longer periods of stress have negative consequences, including memory impairment, cardiovascular disease, and metabolic syndrome (McEwen, 2007).

Transcriptomic studies in animal models have shown that both acute and chronic stressors cause behavioral changes in high anxiety, changes in hippocampal function and gene expression, although these effects vary depending on the type of stressor. For example, the transcription profile of the hippocampus in response to acute stress differs depending on whether the animal was previously subjected to chronic stress, even if a recovery period followed (Verhagen et al., 2010). Thus, each stressful situation that arises can change the initial set level, which also depends on the stage of development at which the stressor is affected.

In humans, prenatal exposure to depressed/anxious maternal mood was associated with increased methylation of the GR (NR3C1) gene in the fetus, which, in turn, led to an increased salivary cortisol response to stress in the child 3 months after birth (Oberlander et al., 2008). In addition, in patients with a high risk of suicide and a history of sexual violence, researchers observed an increase in methylation of exon 1F NR3C1 and a decrease in its expression in the hippocampus (McGowan et al., 2009). This suggests that the intergenerational transmission of vulnerability to psychopathology in adulthood may be mediated by early epigenetic modifications (due to an unfavorable environment) associated with the regulation of stress response.

Let us turn to the study of the relationship between genetic and epigenetic factors with the effectiveness of psychotherapy.

Genetic and epigenetic correlates of psychotherapy effectiveness

Patients diagnosed with borderline personality disorder (BPD) were treated with dialectical behavioral therapy for 4 weeks. The Beck Depression Questionnaire II, the Beck Hopelessness Scale (BHS) were used to assess negativity and pessimism about the future, the Barratt impulsivity Scale (BIS-10), the trauma questionnaire (CTQ). DNA extraction was performed from blood leukocytes. Before and after the psychotherapeutic intervention, the percentage of CpG methylation of exons I and IV of the brain neurotrophic factor

(BDNF) gene protein was measured. The study showed that, compared with the control group, the level of methylation (directly proportional to the number of traumatic events in childhood) in both areas of BDNF was significantly higher in people diagnosed with PRL. In addition, a positive association was found between BDNF methylation status and levels of depression, hopelessness, and impulsivity. In patients with PRL, BDNF methylation increased significantly after psychotherapeutic intervention, especially in those who demonstrated pharmacoresistance. In patients who noted the effectiveness of drug treatment, a decrease in the severity of the DNA methylation process was recorded. Changes in methylation status were largely associated with changes in symptoms of depression, hopelessness, and impulsivity (Perroud et al., 2013).

In another study, patients with post-traumatic stress disorder underwent psychotherapy for 12 weeks. At the end of the course of psychotherapy and after 3 months of follow-up, the level of methylation of DNA isolated from blood lymphocytes was measured before treatment. Methylation of the NR3C1 gene predicted a response to treatment, but did not change significantly over time. Patients who had higher methylation levels before treatment responded better to the intervention. Methylation of the FKBP51 gene is not a predictor of treatment success, although it tends to decrease in patients who have experienced the effectiveness of drug treatment (Yehuda et al., 2013).

After undergoing cognitive behavioral therapy for 6 weeks, patients with panic disorder had lower DNA methylation, compared with the control group, in the monoamine oxidase A (MAOA) gene. An increase in methylation of MAOA correlates with a decrease in the intensity of symptoms of agoraphobia (Ziegler et al., 2016).

After undergoing cognitive behavioral therapy for 12 weeks, children with anxiety disorder showed a decrease in the level of methylation of CpG IV FKBP5. The analysis showed that a change in the methylation of CpG4 FKBP5 DNA was largely associated with a "good" response to treatment (Roberts et al., 2015).

An increased level of GLUT1 methylation, compared with conditionally healthy people, was found in patients with depression. In addition, patients with depression in remission after treatment (6 weeks of inpatient treatment, cognitive behavioral therapy and taking antidepressants) had significantly lower levels of GLUT1 methylation compared to patients without remission (Kahl et al., 2016).

In total, some disorders (for example, borderline personality disorder and panic disorder) exhibit characteristic patterns of gene methylation associated with neurotransmission or neuroplasticity functions. Preliminary data indicate that these methylation profiles may mitigate the effect of psychotherapy or vary depending on the patient's response to it. In this regard, epigenetic changes, for example, the level of methylation, can be used as predictors and indicators of response to psychotherapy (Jiménez J. P. et al. 2018).

Thus, the study of epigenetic mechanisms that may underlie psychotherapeutic changes is a promising area of research. At the same time, scientists emphasize the need

to control mixed environmental factors and whether methylation variations are caused by a simple passage of time (Jiménez J. P. et al. 2018). Also, studies on the relationship between epigenetics and psychotherapy did not exceed 12 weeks in duration, which may not be enough to cause persistent changes in personality functioning (Lindfors et al., 2015).

Discussion

Children inherit not only genes from their parents, but also significant environmental influences encoded in them. Given that there is some evidence of the transmission of epigenetic modifications in people who have been subjected to traumatic situations, it can be assumed that epigenetic changes caused by psychotherapy can also potentially be transmitted to offspring. In addition, the fact that epigenetic changes are reversible may serve as an argument in favor of the use of psychotherapy (Yehuda et al., 2016).

The transfer of knowledge from one generation to another is another mechanism for the transfer of information necessary for survival, in parallel with the transfer of genetic material (Fonagy and Allison, 2014), where epigenetic modifications play an important role.

Summarizing the above, we can conclude that the origin of mental illness is related to the interaction of the environment and the genome, and that this interaction also depends on epigenetic mechanisms. On the other hand, we also know that the effectiveness of psychotherapy largely depends on a number of factors related to both interpersonal processes and biological changes in the central nervous system. Also, differentiating genetic polymorphisms of variability, one can assume the presence of susceptibility to positive environmental stimuli, which may be useful as an indicator of response and prognosis for psychotherapy.

References

Belsky, J., Bakermans-Kranenburg, M., & van Ijzendoorn, M. (2007). For better and for worse: Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, *16*(6), 300–304. https://doi.org/10.1111/j.1467-8721.2007.00525.x

Berger, S. L., Kouzarides, T., Shiekhattar, R., & Shilatifard, A. (2009). An operational definition of epigenetics. *Genes & Development*, *23*(7), 781–783. https://doi.org/10.1101/gad.1787609

Bockting, C. L., Mocking, R. J., Lok, A., Koeter, M. W., & Schene, A. H. (2013). Therapygenetics: The 5HTTLPR as a biomarker for response to psychological therapy? *Molecular Psychiatry*, *18*(7), 744–745. https://doi.org/10.1038/mp.2012.92

Bryant, R. A., Felmingham, K. L., Falconer, E. M., Pe Benito, L., Dobson-Stone, C., Pierce, K. D., et al. (2010). Preliminary evidence of the short allele of the serotonin transporter gene predicting poor response to cognitive behavior therapy in posttraumatic stress disorder.

Biological Psychiatry, *67*(12), 1217–1219. https://doi.org/10.1016/j.biopsych.2010.03.016

Caspi, A., & Moffitt, T. E. (2006). Gene–environment interactions in psychiatry: joining forces with neuroscience. Nature Reviews Neuroscience, 7(7), 583-590. https://doi.org/10.1038/nrn1925

Caspi, A., Sugden, K., Moffitt, T. E., Taylor, A., Craig, I. W., Harrington, H., et al. (2003). Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science*, *301*(5631), 386–389. https://doi.org/10.1126/science.1083968

Cicchetti, D., & Rogosch, F. A. (1996). Equifinality and multifinality in developmental psychopathology. *Development and Psychopathology*, *8*(4), 597–600. https://doi.org/10.1017/S0954579400007318

CONVERGE consortium. (2015). Sparse whole-genome sequencing identifies two loci for major depressive disorder. *Nature*, *523*(7562), 588–591. https://doi.org/10.1038/nature14659

Daxinger, L., & Whitelaw, E. (2012). Understanding transgenerational epigenetic inheritance via the gametes in mammals. *Nature Reviews Genetics*, *13*(3), 153–162. https://doi.org/10.1038/nrg3188

Domschke, K., Zavorotnyy, M., Diemer, J., Nitsche, S., Hohoff, C., Baune, B. T., ... & Zwanzger, P. (2010). COMT val158met influence on electroconvulsive therapy response in major depression. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 153(1), 286-290. https://doi.org/10.1002/ajmg.b.30949

Dwivedi, Y. (2014). Emerging role of microRNAs in major depressive disorder: diagnosis and therapeutic implications. Dialogues in clinical neuroscience, 16(1), 43-61. https://doi.org/10.31887/DCNS.2014.16.1/ydwivedi

Eley, T. C., Hudson, J. L., Creswell, C., Tropeano, M., Lester, K. J., Cooper, P., et al. (2012). Therapygenetics: the 5HTTLPR and response to psychological therapy. *Molecular Psychiatry*, *17*(3), 236–237. https://doi.org/10.1038/mp.2011.132

Fonagy, P. (2003). The interpersonal interpretive mechanism: The confluence of genetics and attachment theory in development. In V. Green (Ed.), *Emotional development in psychoanalysis, attachment theory and neuroscience: Creating connections* (pp. 107–126). New York, NY: Brunner-Routledge.

Fonagy, P., & Allison, E. (2014). The role of mentalizing and epistemic trust in the therapeutic relationship. Psychotherapy, 51(3), 372–380. https://doi.org/10.1037/a0036505

Franklin, T. B., Russig, H., Weiss, I. C., Graff, J., Linder, N., Michalon, A., et al. (2010). Epigenetic transmission of the impact of early stress across generations. *Biological Psychiatry*, *68*(5), 408–415. https://doi.org/10.1016/j.biopsych.2010.05.036

Fumagalli, F., Bedogni, F., Perez, J., Racagni, G., & Riva, M. A. (2004). Corticostriatal brain-derived neurotrophic factor dysregulation in adult rats following prenatal stress. *European Journal of Neuroscience*, *20*(6), 1348–1354. https://doi.org/10.1111/j.1460-9568.2004.03592.x

Gelernter, J. (2015). Genetics of complex traits in psychiatry. *Biological Psychiatry*, *77*(1), 36–42. https://doi.org/10.1016/j.biopsych.2014.08.005

Graff, J., Kim, D., Dobbin, M. M., & Tsai, L. H. (2011). Epigenetic regulation of gene expression in physiological and pathological brain processes. *Physiological Reviews*, *91*(2), 603–649. https://doi.org/10.1152/physrev.00012.2010

Greenberg, B. D., Li, Q., Lucas, F. R., Hu, S., Sirota, L. A., Benjamin, J., et al. (2000). Association between the serotonin transporter promoter polymorphism and personality traits in a primarily female population sample. *American Journal of Medical Genetics*, *96*(2), 202–216. https://doi.org/10.1002/(SICI)1096-8628(20000403)96:2<202::AID-AJMG16>3.0.CO;2-J

Gusev, S. A., & Skirtach, I. A. (2019). Psychological characteristics of people with high levels of anxiety and the possibility of its correction through CBT training. *Innovative science: psychology, pedagogy, defectology, 2*(2), 16–33. (in Russ.).

Heim, C., & Binder, E. B. (2012). Current research trends in early life stress and depression: Review of human studies on sensitive periods, gene–environment interactions, and epigenetics. *Experimental Neurology*, *233*(1), 102–111. https://doi.org/10.1016/j.expneurol.2011.10.032

Hou, L., Bergen, S. E., Akula, N., Song, J., Hultman, C. M., Landen, M., et al. (2016). Genome-wide association study of 40,000 individuals identifies two novel loci associated with bipolar disorder. *Human Molecular Genetics*, *25*(15), 3383–3394. https://doi.org/10.1093/hmg/ddw181

Jamniczky, H. A., Boughner, J. C., Rolian, C., Gonzalez, P. N., Powell, C. D., Schmidt, E. J., et al. (2010). Rediscovering Waddington in the post-genomic age: Operationalising Waddington's epigenetics reveals new ways to investigate the generation and modulation of phenotypic variation. *BioEssays*, *32*(7), 553–558. https://doi.org/10.1002/bies.200900189

Jiménez, J. P., Botto, A., Herrera, L., Leighton, C., Rossi, J. L., Quevedo, Y., ... & Luyten, P. (2018). Psychotherapy and genetic neuroscience: An emerging dialog. Frontiers in Genetics, 9, 257. https://doi.org/10.3389/fgene.2018.00257

John, O. P., & Gross, J. J. (2004). Healthy and unhealthy emotion regulation: Personality processes, individual differences, and life span development. *Journal of Personality*, *72*(6), 1301–1333. https://doi.org/10.1111/j.1467-6494.2004.00298.x

Kahl, K. G., Georgi, K., Bleich, S., Muschler, M., Hillemacher, T., Hilfiker-Kleinert, D., et al. (2016). Altered DNA methylation of glucose transporter 1 and glucose transporter 4 in patients with major depressive disorder. *Journal of Psychiatric Research*, *76*, 66–73. https://doi.org/10.1016/j.jpsychires.2016.02.002

Kendler, K. S., & Eaves, L. J. (1986). Models for the joint effect of genotype and environment on liability to psychiatric illness. *American Journal of Psychiatry*, *143*(3), 279–289. https://doi.org/10.1176/ajp.143.3.279

Kohen, R., Cain, K. C., Buzaitis, A., Johnson, V., Becker, K. J., Teri, L., et al. (2011). Response to psychosocial treatment in poststroke depression is associated with serotonin transporter polymorphisms. *Stroke*, *42*(7), 2068–2070. https://doi.org/10.1161/STROKEAHA.110.611434

Kovsh, E. M., Ermakov, P. N., & Vorobyeva, E. V. (2015). Association of the polymorphic marker Val158Met of the COMT gene with the level of aggression and conflict behavior strategies in girls aged 18-24. *North Caucasian Psychological Bulletin, 13*(3), 15–21. (in Russ.).

Kumsta, R. (2019). The role of epigenetics for understanding mental health difficulties and its implications for psychotherapy research. *Psychology and Psychotherapy: Theory, Research and Practice*, *92*(2), 190–207. https://doi.org/10.1111/papt.12227

Lee, B. H., & Kim, Y. K. (2010). The roles of BDNF in the pathophysiology of major depression and in antidepressant treatment. *Psychiatry Investigation*, *7*(4), 231–235. https://doi.org/10.4306/pi.2010.7.4.231

Lester, K. J., Roberts, S., Keers, R., Coleman, J. R., Breen, G., Wong, C. C., et al. (2016). Non-replication of the association between 5HTTLPR and response to psychological therapy for child anxiety disorders. *British Journal of Psychiatry*, *208*(3), 182–188. https://doi.org/10.1192/bjp.bp.114.154997

Lindfors, O., Knekt, P., Heinonen, E., Harkanen, T., Virtala, E., Helsinki Psychotherapy, et al. (2015). The effectiveness of short- and long-term psychotherapy on personality functioning during a 5-year follow-up. *Journal of Affective Disorders*, *173*, 31–38. https://doi.org/10.1016/j.jad.2014.10.039

Luoni, A., Berry, A., Calabrese, F., Capoccia, S., Bellisario, V., Gass, P., et al. (2014). Delayed BDNF alterations in the prefrontal cortex of rats exposed to prenatal stress: Preventive effect of lurasidone treatment during adolescence. *European Neuropsychopharmacology*, *24*(7), 986–995. https://doi.org/10.1016/j.euroneuro.2013.12.010

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiological Reviews*, *87*(3), 873–904. https://doi.org/10.1152/physrev.00041.2006

McGowan, P. O., Sasaki, A., D'alessio, A. C., Dymov, S., Labonté, B., Szyf, M., ... & Meaney, M. J. (2009). Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nature neuroscience, 12(3), 342-348. https://doi.org/10.1038/nn.2270

Meaney, M. J. (2001). Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annual Review of Neuroscience*, *24*(1), 1161–1192. https://doi.org/10.1146/annurev.neuro.24.1.1161

Monroe, S. M., & Simons, A. D. (1991). Diathesis-stress theories in the context of life stress research: Implications for the depressive disorders. *Psychological Bulletin*, *110*(3), 406–425. https://doi.org/10.1037/0033-2909.110.3.406

Oberlander, T. F., Weinberg, J., Papsdorf, M., Grunau, R., Misri, S., & Devlin, A. M. (2008). Prenatal exposure to maternal depression, neonatal methylation of human glucocorticoid receptor gene (NR3C1) and infant cortisol stress responses. *Epigenetics*, *3*(2), 97–106. https://doi.org/10.4161/epi.3.2.6034

Patten, S. B. (2013). Major depression epidemiology from a diathesis-stress conceptualization. BMC psychiatry, 13, 1-10.

Perroud, N., Salzmann, A., Prada, P., Nicastro, R., Hoeppli, M. E., Furrer, S., et al. (2013). Response to psychotherapy in borderline personality disorder and methylation status of the BDNF gene. *Translational Psychiatry*, *3*(3), e207. https://doi.org/10.1038/tp.2012.140

Plomin, R., DeFries, J., McClearn, G., & Rutter, M. (1997). *Behavioral genetics*. New York, NY: W. H. Freeman.

Power, R. A., Tansey, K. E., Buttenschon, H. N., Cohen-Woods, S., Bigdeli, T., Hall, L. S., et al. (2017). Genome-wide association for major depression through age at onset stratification: Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium. *Biological Psychiatry*, *81*(4), 325–335. https://doi.org/10.1016/j.biopsych.2016.05.010

Roberts, S., Keers, R., Lester, K. J., Coleman, J. R., Breen, G., Arendt, K., et al. (2015). HPA axis related genes and response to psychological therapies: Genetics and epigenetics. *Depression and Anxiety*, *32*(11), 861–870. https://doi.org/10.1002/da.22430

Roth, A., & Fonagy, P. (2005). *What works for whom? A critical review of psychotherapy research* (2nd ed.). New York, NY: The Guilford Press.

Roth, T. L., Lubin, F. D., Funk, A. J., & Sweatt, J. D. (2009). Lasting epigenetic influence of early-life adversity on the BDNF gene. *Biological Psychiatry*, *65*(9), 760–769. https://doi.org/10.1016/j.biopsych.2008.11.028

Rubin, T. G., Gray, J. D., & McEwen, B. S. (2014). Experience and the ever-changing brain: What the transcriptome can reveal. *Bioessays*, *36*(11), 1072–1081. https://doi.org/10.1002/bies.201400095

Sen, S., Burmeister, M., & Ghosh, D. (2004). Meta-analysis of the association between a serotonin transporter promoter polymorphism (5-HTTLPR) and anxiety-related personality traits. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 127(1), 85-89. https://doi.org/10.1002/ajmg.b.20158

Shushanikova, A. A., & Lukyanov, O. V. (2016). adaptation of instruments developed to study the effectiveness of psychotherapeutic processes. Psychology in Russia: State of the art, 9(2), 69-79. https://doi.org/10.11621/pir.2016.0206

Strupp, H. H., & Binder, J. L. (1984). *Psychotherapy in a new key: A guide to time-limited dynamic psychotherapy*. New York, NY: Basic Books.

Szyf, M., McGowan, P., & Meaney, M. J. (2008). The social environment and the epigenome. Environmental and molecular mutagenesis, 49(1), 46-60. https://doi.org/10.1002/em.20357

Verhagen, M., van der Meij, A., van Deurzen, P. A., Janzing, J. G., Arias-Vasquez, A., Buitelaar, J. K., et al. (2010). Meta-analysis of the BDNF Val66Met polymorphism in major depressive disorder: Effects of gender and ethnicity. *Molecular Psychiatry*, *15*(3), 260–271. https://doi.org/10.1038/mp.2008.109

Wampold, B. E., & Imel, Z. E. (2015). *The great psychotherapy debate: The evidence for what makes psychotherapy work* (2nd ed.). New York, NY: Routledge.

Yehuda, R., Daskalakis, N. P., Bierer, L. M., Bader, H. N., Klengel, T., Holsboer, F., & Binder, E. B. (2016). Holocaust exposure induced intergenerational effects on FKBP5 methylation.

Biological psychiatry, 80(5), 372-380. https://doi.org/10.1016/j.biopsych.2015.08.005

Yehuda, R., Daskalakis, N. P., Desarnaud, F., Makotkine, I., Lehrner, A. L., Koch, E., ... & Bierer, L. M. (2013). Epigenetic biomarkers as predictors and correlates of symptom improvement following psychotherapy in combat veterans with PTSD. Frontiers in psychiatry, 4, 118. https://doi.org/10.3389/fpsyt.2013.00118

Zhang, T. Y., & Meaney, M. J. (2010). Epigenetics and the environmental regulation of the genome and its function. *Annual Review of Psychology*, *61*, 439–466. https://doi.org/10.1146/annurev.psych.60.110707.163625

Ziegler, C., Richter, J., Mahr, M., Gajewska, A., Schiele, M. A., Gehrmann, A., et al. (2016). MAOA gene hypomethylation in panic disorder: Reversibility of an epigenetic risk pattern by psychotherapy. *Translational Psychiatry*, *6*(4), e773. https://doi.org/10.1038/tp.2016.41

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Emotion Dysregulation and its Neurophysiological Basis in People with Autism Spectrum Disorders

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Abstract

Introduction. Emotion dysregulation is a characteristic of autism spectrum disorders (ASDs). This study aims to systematize and analyze data on the specificity of emotion dysregulation in children and adults with autism spectrum disorders (ASDs) and their neurophysiological correlates. **Emotion regulation in ASDs.** Typical manifestations of emotion dysregulation in different age groups with ASDs, the relationship between efficient and inefficient regulatory mechanisms and concomitant disorders, external and internal problems, and key symptoms of autism are described. The emotion regulation system in ASDs shows a developmental delay. **Neurobiological mechanisms of disorders in the emotional sphere and social interactions in ASDs.** Data on the neurobiological mechanisms of emotion dysregulation in ASDs show a number of structural, functional, and molecular characteristics in the brain regions associated with the processing of social information, as well as an imbalance of excitation and inhibition processes, which obviously decreases stress resistance. Due to the increase in avoidance behavior and reduction in social experience, low stress resistance to social stimuli creates secondary obstacles to the formation of effective self-regulation strategies. **Neurobiological mechanisms of emotion dysregulation in ASDs.** There is a single neurophysiological basis for disturbances in the processing of emotional and social signals and in emotion dysregulation in ASDs.