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Psychology goes molecular. Epigenetics of learning

Introduction

An organism's ability to learn and to memorize is essential for its behavioral adaptation to environmental changes. On a cellular level, learning and memory is mediated by structural and functional changes of in protein synthesis in the nervous system. These variations, also termed plasticity, modulate a neuron's response to external stimuli. Despite advances in methodologies applied, there are no objective methods to monitor learning and memory, mostly because psychology relies on symptoms as the basis of a diagnosis.

Process of learning

Learning is a result of past experience, permanent changes in the behavioral potential, thoughts and emotions of human being or an animal (Anderson, 2000; Sternberg, 2015). The foundation of that process is a lasting record of experiences, defined as memory, which allows to store products or effects of learning. Up to now, the process of learning has been analyzed from two perspectives. The first, nonmentalistic one concentrates on behavioral changes that are an effect of stimulating situations, and the second one, cognitive approach, which assume that learning is a reorganization of cognitive scheme in the individual that takes place due to active processing of information.

There are many approaches to describe the process of learning. The type of knowledge acquired by the student, the degree of engagement in the process, contextual circumstances of learning and other variables should be considered. Taking into a consideration the form of acquired knowledge, one can separate semantic knowledge (declarative, e.g., school knowledge) from acquired skills (the so-called procedural knowledge, e.g., manipulation activities). Analysis of the number of repetitions and the length of time between them, enables to identify cumulated learning (memorizing the

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entire material without breaks) and time distribution (memorizing the material which is exposed in several sessions of learning). When one considers the organization and the scope of the material, it is possible to identify holistic (total) learning (learning pertains to the entire material at once) and partial learning (dividing the material into smaller pieces and learning them one after the other). With respect to student's attitude, there are difference between voluntary learning (the student consciously concentrates on the process of learning) and involuntary learning (when the student comes in contact with the material, but has no intention of learning it), (Chlewiński, 1997).

The most up-to-date psychological dictionary claims that the definition and manner of applying the term learning has not acquired too much controversy among theoreticians, and it has been used with a relatively small ballast (in developmental, educational, cognitive psychology, behaviorism, et al.). Usually, it appears as a key word in titles of chapters in that meaning that does not diverge from its commonly accepted understanding. A problem arises, trying to define theoretical processes and mechanisms of learning (Reber, 2000). Currently, there are two issues, implicit and emotional learning (Kirsner, 1998: Elias, 2004). Implicit learning is a basic way of acquiring implicit knowledge (Reber, 1989). It enables building a deep representation of knowledge that takes into consideration abstract relationships between elements of the surrounding (environment) world. It functions without the participation of conscious learning strategies and without the intent to gain knowledge, and it is effortless. On the other hand, emotional learning is an extension of the construct of emotional intelligence (Mayer, Salovey, Caruso, & Sitarenios 2004), which is defined as an ability to perceive and express emotions, to understand and manage them in order to support the development of an individual. The authors describe emotional intelligence in terms of a collection of skills, wherein perception, appraisal and expression of emotions is considered to be the most basic skill, and within it, the ability to identify emotion in other people (Salovey, 2008). Emotional learning is gaining by the learning individual knowledge, attitudes and skills necessary to understand and manage emotions. The widely perceived emotional learning encompasses a set of 15 socio-emotional abilities, one of which is "the ability to identify emotion in oneself and in other people" (Jasielska, 2009). There are data that assume that, for example, the genetically conditioned attention and memory span can have an influence on the processes of learning (Colombo, 2004; Richards, 2004, Bauer, 2004). It has been shown that the temperamentally conditioned tendency to retreat in new situations is treated as one of the mechanisms that reduce the diversity of stimuli with which the individual comes into contact, and this, in turn, has an influence on the pace of learning. Fagen (1987) have demonstrated that tearfulness and associated with it lower level of exploratory activity in children, have a negative influence on the performance in cognitive tasks, whereas Colom (2007) has suggested

that impulsiveness, sensation seeking, and a lower level of anxiety are connected with the level of an academic performance. In line with the theory of activation (Gray, 1964), people differ from one another in terms of the level of activation (arousal) that determines both the direction and intensity of behavior. According to Gray (1964), differences in the level of activation depend on an individual trait that can be coined arousability, i.e. the level of activation characteristic of the particular person, depends, in turn, on the individually diversified reactivity of biological mechanisms that underlie particular temperament traits. Arousability is considered to be a more or less stable tendency to react to stimuli, which is conditioned by adequate biological mechanisms that are responsible for its level (Strelau, 2014). Irrespective of the manner of operationalization of the construct of arousability (extraversion and emotional stability in the concept of H. J. Eysenck, sensation seeking in M. Zuckerman's concept, or novelty seeking, harm avoidance and reward dependence in the concept of R. Cloninger), it can be assumed that "there exist more or less stable individual differences in physiological and/or biochemical mechanisms, which explain individual differences in respect of temperament traits" (Stelau, 2014). These mechanisms can also effect the process of learning. At the bottom of the psychobiological model of personality developed by Cloninger (1993,1994a, 1994b, Hauser, 2003; Hornowska, 2003a,b, 2006) there is an assumption about an influence of the genetically controlled neurotransmitters on the expression of particular traits of human personality. In line with that model, personality is composed of the genetically conditioned temperament and environmentally determined character. It is worth to add, that phenotypical manifestation of the personality structure may differ from its biogenetical basis due to the process of interaction that takes place between genes and environmental influences (Cloninger, 1993). Temperament, which is to a large extent conditioned genetically and can be understood as an individual set of emotional reactions and skills manifested in response to stimuli present in the surrounding environment, constitutes the biological foundation for the development of personality traits (Cloninger, 1993). Individual differences in temperament are associated with minor differences in the structure and connections within cerebrum, such as amygdala, hypothalamus, striatum and structures of the limbic system (Cloninger, 1994a,b). Particular dimensions of temperament are also connected with the diversification of procedural memory functioning. Procedural memory is limited to simple, unconscious cognitive functions. It refers to our life experience in respect of operational conditioning of habits with the use of presemantic processes that code particular spatio-visual information and affective states. When it comes to dimensions that describe temperament in the discussed model, there are, novelty seeking (NS), i.e., the tendency to react actively to new stimuli, harm avoidance (HA), i.e., the tendency to inhibit actions in response to negative stimuli, reward dependence (RD),

i.e., the tendency to maintain behavior in response to positive reinforcement, and persistence(P), i.e., the ability to independently maintain the given kind of activity (Hornowska, 2011). According to Cloninger (1993) three out of four dimensions of temperament, i.e., sensation seeking, harm avoidance and reward dependence, possess a precisely determined biological foundation. The author assumes that the novelty of seeking remains in a relation with the dopaminergic system. Harm avoidance is connected with the serotonin synthesis, and reward dependence with noradrenaline production.

Psychologists are strung ling to establish a simple and direct predictor of academic success. Instead of many small factors, one big thing can explain everything is urgently needed. After excitement with a potential changes of gene expression induced by social processes, it turned out that such fast processes as learning and memory do not provide a good perspective for this type of studies (Hornowska, 2013).

Molecular psychology

Early studies of long-term storing in memory showed that both the protein synthesis and gene transcription are the key players of that process (Barondes, 1964; Cohen, 1966). Further studies have shown that the formation of long-term memory is a complex process that requires the engagement of many independent signal paths and regulation of numerous genes (Robertson, 1999; Selcher, 2002; Levenson, 2004). However, they are not so clear and are difficult to interpret.

It is possible to access a genetic factors like single DNA nucleotide polymorphisms (SNPs). Although the largest effect sizes of the associations between SNPs and behavioral traits are very small, it is possible to aggregate the effects of thousands of SNP associations, ranked by effect size, into a SNP genotypic score for a particular trait or as a genome-wide polygenic score (GPS). Many different labels have been ascribed to polygenic scores that usually include the word risk. It highlights the genome-wide nature of these polygenic scores and encompasses positive as well as negative effects implied by the normal distribution of polygenic scores. Recently a genome-wide polygenic score (GPS) has been used to predict behavior all traits from DNA alone. Some GPS are more strongly associated with a particular trait, but others are less strongly associated. The effects of these variants are weighted by the strength of association and then summed to a score, so that people with many variants related to academic achievement will have a higher polygenic score and higher academic achievement, whereas people with fewer associated variants will have a lower score and lower level of academic achievement or success. To get that, one should carry out genome-wide association studies (GWAs), which identify specific genetic variants linked to particular traits. Over the last several years genome wide association (GWA) research across the life sciences

has revealed that there are almost no genetic variants with large effects on complex traits and common disorders. This suggests that the heritability of behavioral traits is due to many genetic variants of small effect. GWA studies of behavioral traits began to be successful as their sample sizes increased sufficiently to detect associations of very small effect size between single-nucleotide polymorphisms (SNPs) and outcome.

GWAs look at traits such as capability to learning, as a means of defining personalized educational achievement. Identifying the genetic variants responsible for the ubiquitous heritability of behavioral dimensions and disorders is transforming genetic research in the social and behavioral sciences by making it possible to predict genetic strengths and weaknesses of individuals from DNA alone. Assessment of individuals educational strengths and weaknesses from their DNA, provide information about whether a student may develop learning problems (Selzam, 2016).

Currently physiology is seeking for new approaches to analyze and evaluate learning and memory processes. It seemed that molecular biology could provide an answer. It seems that at the molecular level, the acquisition and maintenance of memory require not only genetic component but also epigenetic variations as DNA methylation, histone modifications, non-coding RNAs and chromatin remodeling. It is understandable that beyond the two-dimensional genetic universe there is the three dimensional epigenetic universe which is subtler, shiftier, but still chartable. In fact, this is a 3D object, folded in hierarchical way, and affect how to think about many aspects of human development, health and disease.

Epigenetics

In the last decade one can observe an exponential increase in the study of epigenetics, which is stable chemical modifications that occur on, over, near, or at (but not in) to the gene (DNA) primary structure (nucleotide sequence) by both heritable and non-heritable influences that does not alter the gene sequence. It serves to activate and silence genes, and to incorporate a layer of information onto the backbone of DNA, thus controlling gene expression and behavior traits. The DNA sequence of the human genome is identical in all cells of the body, but cell types, such as heart, brain or skin cells have specific characteristics and are uniquely susceptible to various diseases. By guiding how genes are expressed, epigenomes allow cells carrying the same DNA to differentiate into the more than 200 types in the human body. The term epigenetics has been in common usage since 1942 when the Conrad Waddington (1905-1975) defined it as a part of molecular biology that studies the causal interactions between genes and their products, which ultimately bring the phenotype into being. More recently, the term has gained varied additional meanings dependent upon whether it is used in developmental, molecular or evolutionary biology. The underlying concept

is that across these disciplines, those biological processes may be described as epigenetic if they are not the result of direct changes to the sequence of DNA, but to changes in how genes are expressed. A good example is cellular differentiation. Every cell in an organism contains the same genetic material, but different cell lines become specialized as development proceeds, becoming part of the liver, skin, heart etc. This is achieved through the epigenetic silencing or activation of specific genes within each cell line, with these modifications inherited by daughter cells. Indeed, another common usage of epigenetic is the inheritance of characteristics of an individual from one generation to the next through nongenetic mechanisms. Epigenetics is the study of traits inherited by daughter cells that are not directly caused by DNA sequence alterations. Epigenetics is concerned with modifications to genetic material that affect whether genes are expressed (Loi, 2013; McGuinness, 2012). The role of epigenetics is functionary and the biological study is dual. It is about gene regulation (histone modification through acetylation and methylation, DNA methylation, and non-coding RNAs); and about transgenerational inheritance – cellular memory. Epigenetics describes heritable changes affected by the environment. What is surprising that after all, for decades we have all been told, you are what you eat, you are what you drink, you are how much, or how little, you exercise, you are whatever toxic material you imbibe or inhale. But as health experts have cautioned us repeatedly, we are a product of our own lifestyle choices. Environment signals come from nutrition, exercise, toxins, ecological conditions, stress, trauma, nurturance, and personal beliefs. A biomarker should be a quantitative compound, specifically relevant that can be applied to monitor of a problem studied. There is a wealth of data which exemplify that some biomolecules are on different level relative to their normal counterparts and their altered level could be measured in order to find a correlation with current organism state. Such markers, can have high prognostic and prediction values.

Selective biomarkers in medicine can identify susceptibility risks and be helpful for diagnosis and for proper time therapeutic interventions and effective treatment. To date, there are no good biomarkers in blood and serum for detection and follow up. Therefore new markers are needed for more detailed human characterization, better prognosis and selection of efficient treatment. It has been known for long time that genetic variants associated with subjective psychological wellbeing have a genetic component and only a few specific genetic variants related to this traits have been identify. However it seems that genetics is only one factor that influences psychological traits. The environment (epigenetics) is at least as important, and it interacts with the genetic effects.

Epigenetic mechanisms play a central role in the regulation of cellular processes by influencing genomic activity. DNA methylation, defined as the covalent bonding of

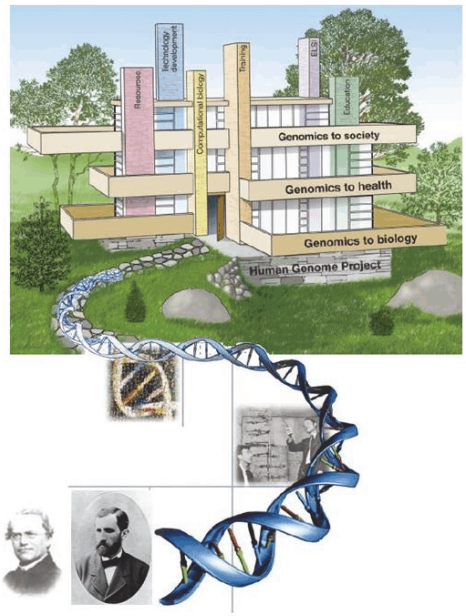

Fig. 1. DNA as basis for learning and memory assessment

a methyl group to a cytosine in the context of a CpG dinucleoside, is an important component of these mechanisms in mammals. Basically DNA methylation represses transcription, which can occur by inhibiting the binding of transcription factors or by recruting binding proteins that remodel chromatin structure. The establishment and maintenance of DNA methylation patterns are crucial for normal cellular function and developmental processes and, these patterns are highly heterologous at different life stages and between different tissue types.

Genome scale DNA methylation can be considered to be a large set of traits in which variation can arise from environmental, stochastic or genetic changes and there is welch of data that DNA methylation could mediate the links between these processes in influencing complex diseases (Gaunt et al. 2016).

So, now comprehensive appreciation of the integrated genomics and epigenomics is urgently needed for better understanding of the multiple cellular pathways involved in development, and establish markers of resistance to traditional therapies as well as contributing to the development of new treatment modalities. It is now clear that epigenetic changes in histone and DNA modifications can alter gene expression, affect their function and contribute to well-being, learning and memory.

The assessment of epigenetic alterations is one of the most promising means of marker identification for the early detection of current status of an individual. The best characterized epigenetic mark is a methyl group at the fifth position of cytosine (m5C). The methylation of gene promoters is associated with gene silencing and thus the distribution of methyl groups within the genome defines regions of varying transcriptional

potential. It may lead to genomic instability, affect tissue specific differentiation and finally influences well-being. The genome of cell individuals under different kind of external stimuli are generally characterized by a global loss of methylation (hypomethylation). That can happen through oxidative stress. It results from a cellular imbalance in the production of reactive oxygen species (ROS) and antioxidant enzyme activities. It is generally accepted that environmental influence on a human genome has been linked to the disruption of red-ox balance. Furthermore stressed cells are characterized by enhanced ROS generation, which deregulate the red-ox homeostasis and promote an aberrant induction of signaling networks that effect of well-being. ROS are formed during normal metabolic processes. Under physiological conditions the balance exists among ROS production and scavenging, oxidative alteration of cellular components and their repair. An imbalance between ROS production and scavenging potential (oxidative stress), leads to an accumulation of oxidative damaged cellular macromolecules that is associated with abnormal behavior. Among these macromolecules that are covalently modified by ROS are nucleic acids. ROS, particularly hydroxyl radical (·OH), may cause a wide range of DNA lesions including canonical and odd bases, deletions, strand breakage, and chromosomal rearrangements. Oxidative damaged DNA has been blamed for the physiological changes associated with as cancer. One of the best studied DNA damage product is 8-oxo-7,8-dihydroguanine (8-oxoGua), a marker of oxidative stress, which is formed in DNA via a direct reaction of guanosine with ·OH. The same random radical reaction can take place with all normal and modified DNA constituents. Eukaryotic DNA contains only 5-methyldeoxycytosine (m5C) as a modified nucleoside. It is assumed that ca. 5% of all cytosine residues or 1% of bases in the mammalian genomes are methylated. Although DNA methylation has been viewed as a stable epigenetic mark, studies in the past decade have revealed that is not the case. m5C demethylation occurs through action of ROS. 5-methylcytosine (m5C), along with other DNA bases are targets for hydroxyl radical (·OH), the most reactive ROS. Radical oxidation of m5C leads to its modification and degradation. The oxidized derivatives are unstable and release formaldehyde, what results in loss of the methyl group from m5C and decrease of global (genomic) m5C contents in DNA (hypomethylation), (Haigis, 2012). To determine a minute content of mC in limited amount of blood, we will apply the postlabeling with 32P] ATP of DNA hydrolysate and identification of m5C with two dimensional thin layer chromatography (TLC). We expect to find changes of m5C and direct correlation of global m5C content in blood DNA with well-being. We have already found hypomethylation in DNA isolated from peripheral blood of patient with pain. That observation prompted us to use m5C demethylation as a probe for psychological studies. Oxidative damage can lead to the formation of a variety of modified bases in DNA, including oxidation of guanine to 8-oxoguanine and the oxidation of m5C to 5-hydroxy-

methylcytosine, which leads to the demethylation of m5C. Oxidative deamination of m5C was also observed. For aberrant DNA methylation various reasons have been proposed, mostly changes in DNA methyltransferases, but never radical demethylation. Methylation of cytosine is established in epiblast and maintained in the later stages of the cell development. It creates a pattern specific and characteristic to every organism (Esteller, 2007). This is the only one modification involving the formation of covalent carbon-carbon bond between the C5 of cytosine and methyl group. 5-methyl cytosine (m5C) is present in the genomes of all vertebrates and flowering plants and some fungi, invertebrates and bacteria. The total amount of m5C in the genome of mammals is ~1% which means that about 5% of all cytosines are methylated. Methylated are primarily dinucleotides CpG, CpNpG and CpNpN (where N – adenosine, cytidine or thymidine). In the stem cells of embryos almost 25% of all methylated cytosines are located within the last two sequences which are lost as a result of differentiation of embryonic stem cells. CpG sequences are not evenly distributed throughout the genome, they create so-called "CpG islands" consisting 0.5-4 kbp and are located mainly within the gene promoters made in 60-70% of these dinucleotides. In the remainder part of the genome, their number is estimated at less than 20%. The promoters of human genes are divided into two distinct classes of CpG content. The first which is hypermethylated has a low CpG content and a second group of genes undergoing continuous transcription has a high content of CpG and low methylation levels. There are three groups of epigenetic enzymes as DNA methyltransferases, histone methylase and histone deacetylase. Cytosine methylation causes silencing, while demethylation, activation of gene expression. Methylated cytosines bind methyl-binding proteins (MBD), which prevent the transcription factors accessing the gene promoter or interact with histone deacetylases, which induce chromatin condensation. Thus cytosine methylation determines specific at a given stage of the development, gene expression leading to tissue differentiation. DNA methylation in mammalian cells is catalysed by four enzymes: DNMT1, and DNMT3b and DNMT3a DNMT3L (Goll, 2008; Enlago, 2008; Yoo, 2006; Cheng, 2008; Brown, 2007). DNA methyltransferases 3a, 3b and 3L catalyse methylation de novo during early embryonic development, while DNMT1 maintains the methylation pattern in subsequent DNA replication. Methylation of the daughter strand of DNA during the synthesis according to the pattern from maternal strand takes place in the S phase of the cell cycle. Lack of DNMT1 in the replication complex causes an imbalance leading cell to the one of the many pathways of apoptosis. For example, in colon cancer cell line with a knockout of DNMT1 gene a reduct ion in total methylation of the genome was observed, which decreased more in the case of a double knockout of DNMT1 and 3b. Deletion of the coding sequence or DNMT3a DNMT1 and 3b leads to the lethality of murine embryos. DNMT1 activity allows the progenitor cells to multiple

divisions, by maintaining the proliferative activity and inhibition of differentiation of these cells, thus providing the ability to self-renewal of tissue. Loss of methylation during differentiation leads to the activation of inhibitors of cyclin-dependent kinases – p15INK4B and p16INK4A, belonging to the tumour suppressor protein and regulating the cell cycle. Mechanism of active DNA methylation was quite satisfactory explained. But the reverse process – DNA demethylation very important on the stage of cleaning the genomic slate during embryogenesis still become mysterious. Moreover the mechanism of DNA demethylation proposed in response to rapid activation of silence genes, which requires the multistage oxidation methyl group catalysed Tet proteins also raises reasonable doubts. According to that mechanism methyl group is oxidized in three step reaction through subsequent formation of 5-hydroxymethyl-, 5-formyl- and 5-carboxycytosine catalysed by Tet1-3 protein followed by base excision. Other method of removing of methyl group proceed through cytosine deamination, leading to uracil formation with subsequent base excision with repair enzymes (Ito, 2010). The other two genes which methylone will be studied are histone methyltransferase and histone deacetylase. In epigenetic analysis of individuals we will measure global DNA methylation level as well as specific methylome DNA methyltransferase.

Psychology epigenetics

Psychology, social psychology, economics and sociology represent the scientific disciplines dealing with human behavior, but epigenetics helps to explain how nurture shapes nature, where nature refers to biological heredity, but nurture refers to virtually everything that occurs during the life-span (e.g., social-experience, diet and nutrition, and exposure to environment). Epigenetics in psychology can provide a framework for understanding how the expression of genes is influenced by experiences and the environment to produce individual differences in behavior, cognition, personality, and mental health.

The goal of Epigenetics Psychology is the study and practical application of knowledge gained from epigenetics and from behavioral standpoints. It asks what can be done by man to influence or obtain the desired functions? The effective management of any human behavior requires a diagnosis at an early stage, which specifies the need for specific and sensitive biomarkers.

The recent studies (Levenson, 2004) show that same processes that lead to the formation of long-term memory also lead to the epigenetic characterization of the genome. It has been assumed that changes in methylation are a response of the organism to acquired experiences, and consequently transformations within long-term memory (Lester, 2011). The studies on learning in animals suggested that DNA methylation is dynamically regulated within the central nervous system (CNS) of adult individuals

upon the influence of experience, and that molecular mechanism is crucial for memory formation (Blaze, 2013). In laboratory animal models, where the classical paradigms of fear conditioning by an aversive stimulus were applied, it has been proven that the epigenetic molecular mechanism that involves DNA methylation and demethylation leads to long-term changes in behavior through active transcription of genes in CNS (e.g., Lattal, 2013).

One should remember that learning or memorizing is differentiated from acquiring knowledge (Nęcka, 2006). If we look at the process of learning in terms of a mechanism thanks to which a human being is able to adjust to the dynamically changing environment, then the critical element of this process will be the application of the acquired knowledge in new circumstances. A characteristic trait of this process is detaching the knowledge from the primary context of learning and applying it in many situations. It is believed that only such a procedure makes it possible to check the actual adaptiveness of the process of learning. Studies indicate that remembering the knowledge created as a result of solving problems is the more difficult, the more time has passed since the moment of its processing (Phyne, 1990).

For that reason, it is believed that the essence of the process of learning is transferring the acquired knowledge or skill to situations outside the situation in which it has been acquired. For this process to take place, there has to occur the phenomenon of transfer, i.e., the application of the acquired knowledge in new situations (Greeno, 1996). The probability of transfer increases due to de contextualization of learning which consists in loosening the relationship between the content of learning and the non-significant aspects of the context of learning (Perkins, 1989; Salomon, 1989).

Additionally, it has been assumed that emotional memory, which is created as a result of fear conditioning in animals, (Day, 2010) can contribute to the explanation of PTSD in humans (Zovkic, 2012). Learning of coping with stress in a situation of sudden danger in the form of a defense reaction, specifically the reaction of conditioned defensive burying (CDB) has also been investigated (Ahmadiyeh, 2005). Also, studies of recognizing new objects and the formation of spatial memory e.g., with the use of Morris water maze, (Sweat, 2009) have been conducted. Very interesting in this respect are studies of psychopathology that take into consideration the mediational influence of epigenetic factors in schizophrenia (Roth, 2009; Toyokawa, 2012). In the process of learning we can observe a change of behavior that corresponds to an alleged mental change. Thus, mental change is identified with a memory record, which is identified with changes in neuronal activity (Kandel, 1991). It has been assumed that short-term memory is probably based upon slight changes in the strength of synaptic connections, which result from the amount of the released neurotransmitter, whereas long-term memory requires structural changes in synapses. These processes are ac-

companied by various molecular phenomena: in the case of short-term memory – modification of proteins that already exist, and in the case of long-term memory–synthesis of new proteins thanks to gene expression (Squire, 2000). For many decades now, it has been assumed that protein synthesis is crucial for the formation of long-term memory through strengthening synaptic connections (Davis, 1984). With reference to that, perhaps the epigenetic mechanism is engaged in the regulation of synaptic variability that is required for the formation of long-term memory (Bird, 2007; Dulac, 2010; Levenson, 2005). In psychology, there has prevailed an opinion that learning is to a large extent a well-investigated area, described in a way that does not raise too many doubts (Anderson, 2000; Jagodzińska, 2008).

There are evidences that epigenetic modifications, specifically histone acetylation and methylation as well as DNA methylation, might be a molecular correlate of long-term memory by modulating the stimulus dependent activation of learning-relevant genes in memory-forming cellular networks. In addition, epigenetic modifications might be functionally important during cellular and systems consolidation. Although this theoretical framework highlights the potentially dual role of chromatin modifications in learning and memory processes, the extent of DNA methylation and histone changes and their functional implications remain unclear. So, DNA methylation plays a roles in learning and memory.

DNA modification is changing during memory acquisition and correlated with variations in gene expression. Although long-lasting changes were almost exclusive to neurons, learning-related epigenetic changes can occur in non-neuronal cell types, suggesting a functional role for non-neuronal cells in epigenetic learning. In a molecular framework of memory acquisition and maintenance, DNA methylation alters the expression and splicing of genes involved in functional plasticity and synaptic wiring.

Epigenetic changes, especially during memory consolidation, strongly suggest a functional role of non-neuronal cells during memory formation. Although the exact role of these changes in learning and memory processes requires further investigation, it is quite unlikely that they represent a cellular correlation of memory, as their timing, specificity and location. Nevertheless, these results imply that chromatin modification changes are not necessarily of neuronal origin and provide further rationale for the cell type-specific analysis of epigenetic modifications in the brain, especially in the emerging field of neuroepigenetics.

Learning as one of many social and individual issues has significant sociological, economical, psychological as well as biological dimensions. In the past scholars tended to focus on the simple and direct interaction between the genome and the environment in the etiology of such phenomenon. What is highlighted nowadays it is the need for considering and study the meditating role of the epigenome. It is postulated that diffe-

rent environmental exposures can impact epigenetic pattern, with important implications for individuals' well-being (McGowan, 2010). For example; in his '4Rs' model of nutritional epigenomics John Mathers shows how dietary experience over time is received and recorded by the human body, remembered during tissue regeneration and revealed in patterns of gene expression. In other words, each individual has a fixed genotype, but human's phenotype is plastic in response to environmental factors, and this plasticity is meditated, at least to some extent, by epigenetics mechanism (Mathers, 2015). Only in recent years scholars appreciated that individuals' life experiences affect DNA methylation pattern, which is only one a kind of epigenetic mechanism that modulates gene expression. Epigenetics is a study of semi-stable molecular states that are sensitive to environmental clues rather than being exclusively endogenously determined and that have the capability to "learn" (Loi, 2013). Although there are some striking examples of the ways in which environment modulate phenotype via epigenetic mechanism, the epigenetics-based research is in its infancy (Mathers, 2015)

Perspectives

We would like to coin a new scientific discipline psychology epigenetics. It is located on the border of social sciences, particularly psychology and molecular biology. Two general questions are of special interest in psychology of epigenetics: i) how various, environmental conditions affect individual's biologically embedded learning and ii) whether the epigenetic markers reflect change of different conditions that affect individual's learning and memory capacity? It would be of special interest to:

1) Combining the global DNA methylation changes in human epigenome with variety of learning.
2) Understanding the epigenetic mechanisms of how individuals' react to different modes of learning.
3) Identifying the differences in methylation level in individuals' reactions to different learning modes.
4) Understanding the limitations of experimental and survey studies of learning.
5) Identifying the biological mechanisms that affect various factors of subjective learning.

We think that it is possible to combine the methods of analysis of psychological studies with epigenetic markers as global DNA methylation changes to get better understanding of the human being. This is a very first application of epigenetics in psychological studies.

Generally, by linking social with molecular life sciences it is possible to establish the constructive and a perspective interdisciplinary dialogue. Shortly, we can say that molecular biology meets social sciences.

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Abstract

The challenge for psychology is to integrate findings from genetics and environmental (social, biological, chemical) factors, into the study of human behavior and deep understanding of the emergence of different changes in the anatomy, physiology, and chemistry of the nervous system that influence the mental health. Currently, cognitive abilities associated with learning and memory, reasoning, problem solving, and developing relationships are in scope of molecular psychology, which is the study of behavior and its underlying brain systems using the tools of molecular biology. However, studies have demonstrated that DNA sequence variations and rare mutations account for only a small fraction of the risk for inheritance of personality traits and mental illness. The large unaccounted heritability of personality traits and mental health suggest that additional molecular and cellular mechanisms are involved. Various complex gene-environment interactions can lead to different phenotypes. These structural changes may be crucial for the development of mature neural networks that support emotional, cognitive, and social behavior. The generation of different morphology, physiology, and behavioral outcomes from a single genome in response to changes in the environment forms the basis for phenotypic plasticity, which is fundamental to the way organisms cope with environmental variation, navigate the present world, and solve future problems. Epigenetics has major implications for psychology and gives the new answer for the old question- what is the biochemical basis of learning. It is bringing back the leading role of environment and behavior, by including their effects on genome function. In addition, it opens up the possibility of memory being stored in the epigenome, so that our experiences may be embedded in our genome by epigenetic mechanisms. Epigenetics can be described as the study of the complex interactions underlying the development of an organism over its lifetime.

Key words: behavioral epigenetics, cognitive functions, DNA methylation, epigenetic inheritance, epigenetics, gene-environment interplay, learning, memory