Chapter 8

Plasticity of Dendritic Spines. Not Only for Cognitive Processes

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Abstract

Excitatory synaptic transmission is associated with the input of "new" information at synaptic junctions established by dendritic spines. The role that each type of spine plays in the transmission of the synaptic impulses is different. Indeed, there is a close relationship between the shape of spines and the differential processing of the excitatory synaptic information that is relayed to them, influencing in turn the transmission of synaptic information related to several psychoneural processes.

The vast majority of the experimental evidence shows that specific plastic interchanges of dendritic spines' shapes are related to specific functional effects in the postsynapse, i.e., the acquisition or learning of new information (thin spines), or to the storage of information in memory (mushroom spines).

Several brain regions are involved in other functions different than those of a cognitive nature, and all projection neurons in these areas possess dendritic spines. However, the functional significance of the changes that the spines of these neurons express has not been studied. Thus, in this Chapter we will discuss experimental evidence supporting the claim that dendritic spines express plastic changes in some brain regions that are not directly related to cognition, and we will also preliminarily approach their possible functional meaning.

Keywords: plasticity, dendritic spines, synapse, cognition

1. Cognition and noncognition: basic concepts

Person A walks down the sidewalk alongside a fence when suddenly, a dog leaps out behind the fence and barks at Person A. Person A, caught off guard, jerks back and then kicks the fence. Coming to his sense, he realizes that the dog is a harmless little Chihuahua, still stuck behind the fence. Now conscious of the situation, he looks around and sees that various passers-by have been watching him and are laughing at his situation. Feeling exposed, Person A continues walking, now blushing furiously.

Looking at this situation, we might ask, if Person A was going to be embarrassed by his actions, why he reacted the way he did in the first place. Why he did not avoid the scare, and with it, the situation? Why did he kick an object without first working through what it was? This type of event—and Person A's type of reaction—is unrelated to cognition, which is the processing of information that permits the abstraction and manipulation of the environment by way of symbols (language and thought, for example) [1]. In this example, Person A could not place the origin of the stimulus nor relate it to as a previous experience, so his reaction had no cognitive component.

Certain *noncognitive* processes express themselves simultaneously with cognitive processes [2]. These processes arise consciously or unconsciously [3], automatically or implicitly [4]. These noncognitive processes do not require attention, perception, learning, memory, language, or thought for their integration; be that as it may, cognitive processes may be present for the regulation or modulation of those noncognitive ones [5].

Izdar [2] explores the role of noncognitive processes in emotional processing. He mentions that there exists a neural basis for the expression of the emotions that escape cognition and which precede the conscious experience of the stimulus. A series of experiments by LeDoux [6] provide experimental evidence for the two-way configuration for the expression of fear: one of them, the faster, permits the organism to generate a reaction to the stimulus without being fully aware of the situation. Person A's situation illustrates this case clearly.

Noncognitive processing has been the object of conceptual debate, since at one time it was thought that all nerve activity was aimed at the expression of processes related to cognition. Lazarus [7] writes that "cognition is the end of all cortical or subcortical activity." Likewise, Lazarus [8] defends that position by arguing that even simple perceptual phenomena (a type of which can be seen in Person A's case) depend on and create meanings or evaluations with respect to the stimulus. Frijda [9] argues that the nervous system is capable of generating emotions, but only when those emotions had been previously acquired through cognition. Frijda [10] argues that "emotions are the result of meaning, and that meaning is the result of inferences about causes and consequences." However, Zajonc [11] responds to Lazarus with experimental evidence wherein he illustrated the primacy of some noncognitive processes that do not themselves attribute meanings to stimuli. Zajonc mentions that even the integration of information from the retinohypothalamic tract is sufficient for the organism to produce a response, "leaving the attribution of the meaning of the stimulus a synapse away" [11].

Izdar [2] talks about the existing predisposition to argue that cognition is anything that goes hand in hand with learning, memory, and, in general, with "mental" life, leaving aside all

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those instinctive behaviors or those which present without cognitive acquisition or previous experience. An example of this type of behavior is the sucking reflex, the response to aversive stimuli that presents in infants even without prior cognitive processing to give it meaning. Likewise, the expression of circadian rhythms like the sleep-wake cycle. Some of these behaviors come from ancestral information accumulated in the course of a species' evolution, which shapes the brain architecture in the absence of experience with the environment [12] and that establishes itself in the absence of cognitive processing, serving the latter as a potentiator and moderator in later stages of life. It is worth mentioning that the processing of information can take place even in infants without previous experience or learning, that is, without cognitive processing [13]. The above leads to the argument that the processing of information has as much a noncognitive component as a cognitive one.

One can make a distinction between cognitive and noncognitive processes: a cognitive process depends on experience, learning, and memory, whose neural basis is the function of the areas of association of the cerebral cortex, changing stimuli into abstractions, meanings, and manageable symbols [14]. On the other hand, noncognitive processes have as their neural basis the function of subcortical structures such as the hypothalamus [15], the amygdala [6], and the functioning of primary areas of the cerebral cortex [14] that do not depend on learning, on memory, or on previous experience for the expression of certain behaviors, like sexual ones, those based on the emotional fast track [6], and the execution of voluntary movement; among others.

Noncognitive processing generates controversy within psychological epistemology. It creates a heuristic conflict that requires a solution not only from psychology but also from those sciences that provide evidence about the determinants of behavior.

This chapter presents experimental evidence about: the expression of behaviors that do not depend on cognition, as is the case in sexual behavior, which is expressed by virtue of neurophysiological changes in hypothalamic nuclei as well as in the ventromedial nucleus; about the formation of biological rhythms, like the sleep-wake cycle, which depend predominantly on the function of the preoptical area and the suprachiasmatic nucleus of the hypothalamus; about the execution of voluntary motor activity that depends on the function of the primary motor area; and about the expression of emotions through a fast track that is integrated in the nuclei of the amygdala even in the absence of the participation of the cerebral cortex and, therefore, of conscious experience.

2. Neuronal plasticity

The plastic capacity of the structures related to the expression of some of the previously mentioned behaviors that are usually related to cognition. However, as the experimental evidence presented in this chapter will show, the neural structures involved in those cognitive processes also form a part of the repertoire involved in the variable expression "noncognitive" processes through their plastic capacity.

Transmission of excitatory information between neurons is mediated by the activation of receptors located on dendritic spines. These neural substructures exist in all projection neurons, and by virtue of participating in the functional integration of the afferent information by those neurons, they "add" a psychoneural attribute to the conformation of functions integrated into the corresponding neural circuits.

The dendritic spines are cytoplasmic protrusions that cover varying portions of the tubular surface of the dendrites. Depending on the excitatory afferents, the spines show varying densities and distributions along the length of the dendrites. Although the spines generally translate the excitatory information, the way in which they process it depends on their geometric structure. According to their shape, six types of spines have been described: (1) thin; (2) mushroom; (3) stubby; (4) wide; (5) branched; and (6) double [16, 17].

The primary characteristic of these structural distinctions lies in the presence or absence of a neck and a head. The thin spines have a long, narrow neck that results in a bulbous structure, or "head," whose length is shorter than the neck. The mushroom spines have a short, narrow neck that leads to a head whose diameter and length are greater than those of its neck. Stubby spines are protoplasmic protrusions that show no difference between head and neck and whose length is less than their diameter. Similarly, wide spines show neither neck nor head, but their length is greater than their diameter. Branched spines, for their part, display a narrow neck that emerges from the dendrite and which divides into two similar necks before terminating in two similar heads. Double spines have a neck that emerges from the dendrite and forms a head, which then forms another neck, and which finally terminates in a second head.

Typically, the different types of spines show variable amounts between the neurons that host them, but their proportional density remains relatively similar in all neurons: thin > mushroom > fat > wide > branched > double.

Bioelectrically, thin spines have been linked to the rapid transmission of afferent information and are functionally related to the acquisition of new information (learning). Meanwhile, mushroom spines have been related to the slow transmission of afferent synaptic information and with the storage of the same (memory). The other types of spines have not been much studied. There is, however, evidence that suggests that stubby and wide spines could be related to the regulation of the excitability of postsynaptic neurons, while branched spines could be a transformation of other, larger spines (presumably mushroom spines) into two new (branched) spines—hypothetically thin ones. Finally, no functional evidence of the activity of the double spines has been uncovered, although their geometric structure suggests that they represent two independent sites of synaptic contact.

From this chapter's perspective, thin and mushroom spines are particularly relevant. According to the evidence, both are related to the processing of cognitive information: learning from thin spines and memory from mushrooms. However, it is clear that certain lines of projection neurons—like those located in the primary motor cortex, some nuclei of the amygdala, and certain hypothalamic nuclei, like the ventromedial, the preoptic, and the suprachiasmatic—possess dendritic spines that have shown plastic changes, which have been induced experimentally.

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3. Neuronal plasticity in cognitive and noncognitive processes

The hypothalamus is a structure that predominantly participates in the regulation of emotion/affective behavior, in the control of visceral functions, and in the maintenance of the body's homeostasis [18]. The hypothalamus is a structure associated with noncognitive functions. It is neuroanatomically divided into several nuclei, among which is the ventromedial nucleus, which participates in the regulation of sexual behavior in females [18–21]. This portion of the hypothalamus receives information primarily from the medial amygdala and passes the information along to other structures, like the periaqueductal gray and the medulla oblongata, provoking the display of female sexual behavior [21].

Research conducted on the ventromedial nucleus of the hypothalamus has shown the presence of adaptive plastic changes in the neurons of this structure. There is evidence that estrogenic activity reduces the density of dendritic spines on the projection neurons of the ventromedial hypothalamus, thereby facilitating lordosis behavior in female rats [22]. Studies in our laboratory [15] have shown plastic changes in projection neurons in the ventrolateral area of the ventromedial nucleus during different stages of the estrous cycle. Among other plastic changes in the neurons, we observed changes in the densities of spines and in the proportional densities of thin and mushroom spines. The density of spines was greater in diestrus, proestrus, and estrus with respect to metestrus, which was reflected in the greater proportional density of thin and mushroom spines in those stages in which the circulating levels of estradiol are higher. We suggest that these changes are associated with neuroendocrine mechanisms, and that they do not respond to any kind of activity related to cognition. Furthermore, these findings evidence that the functional role of the types of spines that have been classically linked to learning (thin spines) and memory (mushroom spines) would also be linked to other neuropsychophysiological events, beyond those related to the expression of cognitive functions.

The largest number of thin spines in stages like those above could be related to the rapid transmission of synaptic information that is, in fact, mediated by spines with the same geometric characteristics as the thin spines [23–25]. Thus, thin spines would then mediate those changes that in the short term influence female behavior in the shorter phases of the reproductive cycle. Meanwhile, the largest proportion of mushroom spines could be related to the changes that may occur slowly in the formation of patterns of sexual behavior by virtue of the fact that the transmission mediated by this type of spine triggers responses mediated by secondary messengers that, when transmitted to the nucleus, generate the synthesis of proteins [16, 17, 26] capable of modifying the psychophysiology of sexual behavior. Thus, the plasticity of dendritic spines in this region unrelated to cognitive activity might be more related to patterns of synaptic activity. Yes, like those related to cognition, but whose functional significance should be associated with the bioelectric activity that is most fundamental to synaptic activity. Consequently, the interpretation of the plastic changes mediated by dendritic spines should be attributed to the very psychophysiological activity of the noncognitive region in question.

Sensory input is of great importance in the deployment of sexual behavior. Olfactory information that has passed through regions such as the olfactory lobe, the amygdala, the stria terminalis, and the medial preoptic area or the hypothalamus has not yet been involved in nervous

centers that give that olfactory information a cognitive character. In all of these structures, it has been seen that exposing rodents to the smell of the opposite sex results in an increase in *fos*-protein, which is related to the corresponding increase in metabolic and cellular activity [27]. Thus, the brain generates a plastic response at the molecular level in the presence of relevant sexual stimuli. Studies of brain lesions have shown that massive damage to the medial preoptic area eliminates sexual behavior of male rates throughout the entire life of the individual [28]. In the case of females, the same occurs when the ventromedial hypothalamus is injured [29], a site that, as has already been mentioned, relates to the organization of female sexual behavior.

Despite those findings, there exists in the literature a vast quantity of work, which mentions the role of the prefrontal cortex—an area clearly associated with cognition—in relation to sexual behavior [30–32]. A study by Agmo et al. [33] reported that injuries to the prefrontal cortex and particularly to regions that receive information from the amygdala considerably delay the onset of sexual behavior. However, that same study reported that once male sexual behavior does begin, it then develops normally despite the injury. These data suggest that the prefrontal cortex could be playing an important role in the integration of the information necessary to initiate the approach during sexual arousal. Moreover, other structures participate in the emergence of sexual behavior as sensory receptors, as well as in the expression of copulatory behavior. It is important to highlight that there exists significant gender dimorphism in humans and rodents related to the structures involved in the expression of sexual behavior [27]. This might mark some tendencies about the way processes not directly associated with cognition could differ with the gender of the individuals.

There is experimental evidence that shows a direct relationship between good and bad performance in cognitive tasks and varying levels of hormones such as estradiol and progesterone during the menstrual cycle. It has been observed that in the execution of cognitive tests involving verbal fluency, perceptual speed, fine motor skills, verbal memory, and working memory, performance is higher during the follicular phase, when the greatest amount of estradiol is present in blood plasma. Likewise, when plasma progesterone levels reach their peak in the cycle—halfway through the luteal phase—performance improves on tests of visual memory, in comparison with the menstrual phase [34, 35]. This suggests that there is a differential modulation of cognitive processes by some ovarian hormones, depending on the variation of their concentrations throughout the menstrual cycle. Fernández et al. [36] conducted a longitudinal study that used fMRI to observe the brain activity of young women as they completed cognitive tests focused on language use during different phases of their menstrual cycle. They obtained data that suggested that the neural recruitment necessary to carry out such tasks is very sensitive to the hormonal fluctuations—progesterone and estradiol—of the menstrual cycle. The results likewise showed that the activity of the cortical areas associated with language varies through the different stages of the cycle, and that both progesterone and estradiol were capable of modulating neuronal plasticity of certain areas during the tests. The influence that hormones—which do not imply any cognitive process—have on tasks that are entirely associated with cognition is remarkable.

As in the case of the female reproductive cycle, other hypothalamic structures play a key role in the establishment of some biological rhythms. The suprachiasmatic nucleus and preoptic

area of the hypothalamus are associated with the expression of the sleep-wake cycle. This cycle is regulated by the activity of a number of genes, such as the *per*, *clock*, and *tim* genes, which are transcribed cyclically [37, 38]. From the viewpoint of synaptic plasticity, a study from Girardet et al. [39] on rats showed an increase of afferent glutamatergic synapses toward the suprachiasmatic nucleus of the retina, a phenomenon regulated by the input of photic information [40]. That working group also associated with the synaptic arrangements and the configuration of the glia in the suprachiasmatic nucleus with the entrance of photic information that regulates the sleep-wake cycle.

The suprachiasmatic nucleus is comprised of general bipolar small neurons whose dendrites may branch or not. Those dendrites display the presence of dendritic spines whose distribution is irregular [41] and which establish synaptic contact with 33% of all of the synapses in the said nucleus [42]. Despite the relevance of the eventual synaptic plasticity that could implicate the circadian regulation of the sleep-wake cycle, there are no studies that show variations in the synaptology of the suprachiasmatic nucleus, which strongly suggests that investigations ought to be performed.

Some studies discussed the relevance of the use of diverse techniques to establish which circuits are involved in insomnia in human adults [43, 44]. However, it seems clear that the participation of structures associated with cognition (like the prefrontal cortex) is also linked with the adequate establishment of those circuits that govern the sleep-wake cycle. Among these structures, it has been reported that the medial prefrontal cortex reduces its functional connectivity with the medial temporal cortex [45].

It has also been reported that the medial and inferior prefrontal cortex showed a decrease in activity when performing fMRI [46], and, particularly, it has been shown that pyramidal neurons from the infralimbic cortex layer III experience alternating plastic changes during both phases of the cycle: in the nocturnal phase, neurons show a pattern of dendritic arborization that is more profuse, and a greater density of spines in comparison with the diurnal phase, which could relate to the cyclical activity of the liberation of different neurotransmitters, growth factors, and corticosterone, in association with the afferent activities of the fibers of the suprachiasmatic nucleus [47]. Another study showed a decrease in the gray matter of the orbitofrontal cortex and in the parietal cortex [48]. In these studies, the results were associated with the presence of insomnia. Together, these investigations suggest that the sleep-wake cycle, although it is a biological rhythm, could also be regulated by structures associated with cognition.

Voluntary motor activity is the result of a series of mostly cognitive processes in which certain areas of the neocortex such as the prefrontal cortex, the premotor cortex, the parietal posterior cortex, and the primary motor cortex, as well as subcortical areas such as the basal ganglia, the thalamus, and the cerebellum participate [49, 50]. All these structures form different circuits for programming and establishing the commands necessary for the execution of movement. The information that is processed in them is sent through the spinal cord by the pyramidal tract from the Betz pyramidal neurons in the primary motor cortex. These last neurons perform the final step in circuits, integrating all the information that has been processed previously.

The pyramidal neurons in layer V of the primary motor cortex do not perform cognitive processing of the information they receive, but rather represent the final necessary filter for that information before motor function [49–51]. Little has been studied about the plastic capacity of these neurons. However, there is research that shows that after behaviors with a cognitive component, such as motor learning [52] and self-stimulation [53, 54], changes occur in the dendritic arborization of pyramidal neurons in layer V of the primary motor cortex. At the same time, preliminary studies conducted in our laboratory (submitted to publication) showed a greater density of dendritic spines (thin, mushroom, and branched spines) on neurons in the layer V of the motor cortex of mice subjected to forced motor activity over a week under differing levels of intensity using a treadmill device. The increase in branched spines corresponded directly to the increase in thin spines, a phenomenon that could be interpreted as a circumstantial demand for the integration of information coming to those neurons due to the increased demand for motor performance. For its part, the greater proportion of mushroom spines could be interpreted as the establishment of patterns of motor activity, which adjusted throughout the study to meet the increasing demand for physical effort on the part of the rats.

Another necessary component for the performance of voluntary movement is the adjustment of patterns of motor execution at the cerebellar level, a characteristic that, it has been suggested, is not associated with the processing of cognitive information. In this sense, it has been shown that Purkinje cells of the simple lobe of the cerebellum present plastic changes at the level of their dendritic spines during the performance of moderate motor activity. Such modifications consist of an increase in the stubby dendritic spines, which could be due to the input of excessive afferent synaptic information—inherent in the requirements of motor activity—which stimulates the postsynaptic components (the dendritic spines), thus causing the formation of the type of spines that would regulate the hypothetical hyperexcitability of the Purkinje neurons involved [55].

The role of the cerebellum during motor learning, a cognitive process, has also been approached. Those studies have investigated metabolic activity in the cerebellar cortex [56] and the plastic changes of the dendritic spines on the Purkinje neurons, particularly in the region that corresponds with the paramedian lobe [57]. In keeping with the role attributed to the spines in paradigms involving cognitive activity, the study found that there was a particular increase in thin spines (acquisition of new information, or learning) and in mushroom spines (consolidation of acquired information, or memory).

Overall, the results of research related to the functional activity of the cerebellum suggest that differential regions of this brain structure work in concert as much in cognitive processing—motor learning—as in noncognitive processing—motor adjustments. In both cases, there is evidence of plastic events at dendritic spines level underlying these processes.

As mentioned in a previous section, there exists a debate over the role of cognition in the emotions. There are certain brain structures involved in the neural circuits that lead to the expression of emotions, including the amygdala and the prefrontal cortex. In the noncognitive

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processing of emotion, the amygdala plays a key role. This structure participates in two distinct ways. In the more direct way, the amygdala receives thalamic sensory afferents that provide the information necessary to generate emotional responses and, given their connections with the hypothalamus, that induce autonomic activation. Moreover, the connections of the amygdala with the periaqueductal gray matter and the medulla give way to the responses of "freezing" or fight/flight, respectively. The slower way for the amygdala to participate is an indirect route in which the prefrontal cortex processes information associated with the emotional significance of experiences, providing the amygdaloid complex with the information necessary to trigger the appropriate response [6].

From the above, it can be concluded that the expression of emotions depends on structures that are related both to the organization of cognitive functions—the prefrontal cortex, in the indirect route—and with noncognitive functions—the amygdala, in the direct route. It has been reported that chronic stress induces an increase in dendrite length, in dendritic arborization, and in the density and length of the spines of the neurons in the nuclei of the basolateral amygdala. In turn, acute stress provokes an increase in the density of spines, which could be associated with an increase in elevated circulating levels of glucocorticoids [58], and it is clear that the neuronal cytoarchitecture of the amygdala related to noncognitive processes is also subject to plastic changes.

It is common to think of us processing emotions either "consciously" or "unconsciously" [2]. From a neuroscientific point of view, these two terms are what we have in this chapter referred to as "cognitive" and "noncognitive." A recent review of Lee et al. [59] discusses the importance of the noncognitive processing of information necessary for the expression of emotions, particularly in individuals diagnosed with anxiety disorders, schizophrenia, bipolar disorder, and stress. This paper makes a clear distinction between the perception of the emotions without the involvement of a cognitive process and the analysis of emotion that involves the assignation of meaning and emotional valence. It establishes that the perception of emotion that would involve structures such as the amygdala, the insular cortex, the anterior cingulate, and the primary visual cortex [60, 61] is a phenomenon in which information is processed about the stimulus that provoked an emotion without cognitive attribution [62] almost like an automatic processing of emotions without being aware of their meaning.

Although conflicting data regarding the structures that participate in this first step of the recognition of emotions [63] exists, it seems clear that the set of brain processes that involve emotional processing are not only limited to cognition, but that there exist other structures and previous, noncognitive processes that lead to emotional experience [2, 11, 13].

4. Conclusions

It should be clear that the processing of synaptic information in distinct regions of the brain is independent of the conceptual aspects of the neuropsychological process in question. Thus, the plastic events that underlie the functional organization of "cognitive" and "noncognitive" processes appear to present common neurophysiological and neuromorphological

bases. That is, they consist of adaptive changes in different levels of behavioral organization that, more than depending on the plastic events at a cellular level, depend on the structures involved and on the circuits that they establish among themselves in order to result in the expression of behavior.

Based on that, we would propose the following:

1. The intensification of experimental studies of neuronal plasticity related with "noncognitive" processes.

2. The broadening of the criteria of interpretation with regard to the functional significance of such plastic events.

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References

[1] Gardner, H., (1987). The Mind's New Science: A History of the Cognitive Revolution. Basic Books. New York.

[2] Izdar, C., (1993). Four systems for emotion activation: cognitive and noncognitive processes. Pychol. Rev. 100, (1) 68-90.

[3] Kihlstrom, J.F., (1987). The cognitive unconscious. Science. 237, 1445-1452.

[4] Shiffrin, R.M. & Schneider, W., (1977). Controlled and automatic human theory. Psychol. Rev. 84, 127-190.

[5] Izdar, C.E. & Kobak, R.R., (1991). Emotions system functioning an emotion regulation. In: Garber, J. & Dodge, K.A., (Eds). The Development of Emotion Regulation and Dysregulation. Cambridge University Press. England. pp. 303-321.

[6] LeDoux, J., (2000). Emotion circuits in the brain. Annu. Rev. Neurosci. 23, 155-184.

[7] Lazarus, R.S., (1984). On the primacy of cognition. Am. Psychol. 39, 124-129.

[8] Lazarus, R.S., (1991). Cognition and motivation in emotion. Am. Psychol. 46, 352-367.

[9] Frijda, N.H., (1986). The Emotions. Cambridge University Press. England.

[10] Frijda, N.H., (1988). The laws of emotion. Am. Psychol. 43, 349-358.

[11] Zajonc, R.B., (1984). On the primacy of affect. Am. Psychol. 39, 117-123.

[12] Gonzalez-Burgos, I., (2015). Functional neuroanatomy of the memory systems. In: González-Burgos, I. (Ed). Psychobiology of memory: an interdisciplinary view. Bios Médica. México. pp. 15-49.

[13] Izdar, C.E. & Malatesta, C.Z., (1987). Perspectives on emotional development: I. Differential emotions theory of early emotional development. In: Osofsky, J.D., (Ed). Handbook of Infant Development. Second ed. Wiley-Interscience. New York, U.S.A. pp. 494-554.

[14] Olson, C. & Colby, C., (2013). The organization of cognition. In: Kandel, E., et al. (Eds). Principles of Neural Sciences. Fifth ed.. McGraw and Hill. U.S.A. pp. 318-411.

[15] González-Burgos, I., Velázquez-Zamora, D.A., González-Tapia, D., & Cervantes, M., (2015). A golgi study of the plasticity of dendritic spines in the hypothalamic ventromedial nucleus during the estrous cycle of female rats. Neuroscience. 9, (298) 74-80.

[16] González-Burgos, I., (2009). Dendritic spines plasticity and learning/memory processes: theory, evidence and perspectives. In: Baylog, L.R. (Ed). Dendritic Spines. Biochemistry, Modelling and Properties. Neuroscience research progress series. Nova Science Publishers, Inc. New York. pp. 163-186.

[17] González-Burgos, I., (2012). From synaptic transmission to cognition: an intermediary role for dendritic spines. Brain Cogn. 80, (1) 177-183.

[18] Horn, J.P. & Swanson, L.W., (2013). The autonomic motor system and the hypothalamus. In: Kandel, E., Schwartz, J., Jessell, T., Siegelbaum, S., Hudspeth, A.J. (Eds). Principles of Neural Science. Fifth ed. McGraw Hill Professional. U.S.A. pp. 1055-1078.

[19] Rubin, B.S. & Barfield, R.J., (1980). Priming of estrous responsiveness by implants of 17 beta-estradiol in the ventromedial hypothalamic nucleus of female rats. Endocrinology. 106, (2) 504-509.

[20] Rubin, B.S. & Barfield, R.J., (1983). Induction of estrous behavior in ovariectomized rats by sequential replacement of estrogen and progesterone to the ventromedial hypothalamus. Neuroendocrinology. 37, (3) 218-224.

[21] Guillazo, G., Redolar, D.A., Torras, M., Vale, M., (2007). Fundamentals of neuroscience. Soriano, C. (coord.); UOC, Barcelona.

[22] Calizo, L.H. & Flanagan-Cato, L.M., (2002). Estrogen-induced dendritic spine elimination on female rat ventromedial hypothalamic neurons that project to the periaqueductal gray. J. Comp. Neurol. 447, (3) 234-248.

[23] Harris, K.M., Jensen, F.E., Tsao, B., (1992). Three-dimensional structure of dendritic spines and synapses in rat hippocampus (CA1) at postnatal day 15 and adult ages: implications for the maturation of synaptic physiology and long-term potentiation. J. Neurosci. 12, (7) 2685-2705.

[24] Koch, C., Zador, A., Brown, T.H., (1992). Dendritic spines: convergence of theory and experiment. Science. 256, (5059) 973-974.

[25] Koch, C., Zador, A., (1993). The function of dendritic spines: devices subserving biochemical rather than electrical compartmentalization. J. Neurosci. 13, (2) 413-422.

[26] González-Burgos, I., González-Tapia, D., Feria-Velasco, A., (2015). Neuronal plasticity associated to learning and memory. In: González-Burgos, I. (Ed). Psychobiology of memory: an interdisciplinary view. México. Bios Médica. pp. 159-190.

[27] Agmo, A., (2015). Brain circuits relevant to sexual behavior. In: Hernández-González, M., Sanz-Martin, A., & Guevara-Pérez, M.A. (Eds). Brain circuits involved in cognition and behavior. University of Guadalajara. México. pp. 17-46.

[28] Heimer, M. & Larsson, K., (1966). Impairment of mating behavior in male rats following lesions in the preoptic-anterior hypothalamic continuum. Brain Res. 3, 248-263.

[29] Agmo, A., (2007). Functional and Dysfunctional Sexual Behavior. A Synthesis of Neuroscience and Comparative Psychology. Academic Press: San Diego. E.U.A.

[30] Agmo, A., (2015). The role of the prefrontal cortex in male sexual behavior. In: Hernández-González, M., Chacón-Gutiérrez, L., Barradas-Bribiesca, J.A., Guevara-Pérez, M.A. (Eds). Prefrontal cortex. Cognition and behavior. University of Guanajuato. México. pp. 295-328.

[31] Davis, J.F., Loos, M., Di Sebastiano, A.R., Brown, J.L., Lehman, M.N., & Coolen, L.M., (2010). Lesions of the medial prefrontal cortex cause maladaptive sexual behavior in male rats. Biol. Psychiatry. 67, (12) 1199-1204.

[32] Balfour, M.E., Brown, J.L., Yu, L., & Coolen, L.M., (2006). Potential contributions of afferents from medial prefrontal cortex to neural activation following sexual behavior in the male rat. Neuroscience. 137, (4) 1259-1276.

[33] Agmo, A., Villalpando, A., Picker, Z., & Fernández, H., (1995). Lesions of the medial prefrontal cortex and sexual behavior in the male rat. Brain Res. 696, 177-186.

[34] Hausmann, M., (2010). Hormonal effects on the plasticity of cognitive brain functions. Wiley Interdiscip. Rev. Cogn. Sci. 1, (4) 607-612.

[35] Cervantes, J.M., Velázquez-Zamora, D., González-Burgos, I., (2015). Estrogenic modulation of cognitive functions during the menstrual cycle and menopause. In: González-Burgos, I. (Ed). Psychobiology of memory: an interdisciplinary view. México. Bios Médica. pp. 263-290.

[36] Fernández, G., Weis, S., Stoffel-Wagner, B., Tendolkar, I., Reuber, M., Beyenburg, S., Klaver, P., Fell, J., de Greiff, A., Ruhlmann, J., Reul, J., & Elger, C.E., (2003). Menstrual cycle-dependent neural plasticity in the adult human brain is hormone, task, and region specific. J. Neurosci. 23, (9) 3790-3795.

[37] Fort, P., Bassetti, L., & Luppi, T.H., (2009). Alternating vigilance state: new insights regarding neuronal networks and mechanisms. Eur. J. Neurosci. 29, 1741-1753.

[38] King, P. & Takahashi, S., (2000). Molecular genetics of circadian rhythms in mammals. Annu. Rev. Neurosci. 23, 713-742.

[39] Girardet, C., Blanchard, M.P., Ferracci, G., Lévêque, C., Moreno, M., François-Bellan, A.M., Becquet, D., Bosler, O., (2010). Daily changes in synaptic innervation of PVI neurons in the rat suprachiasmatic nucleus: contribution of glutamatergic afferents. Eur. J. Neurosci. 31, (2) 359-370.

[40] Girardet, C., Becquet, D., Blanchard, M.P., François-Bellan, A.M., & Bosler, O., (2010). Neuroglial and synaptic rearrangements associated with photic entrainment of the circadian clock in the suprachiasmatic nucleus. Eur. J. Neurosci. 32, (12) 2133-2142.

[41] Millhouse, O.E., (1979). A Golgi anatomy of the rodent hypothalamus. In: Morgane, P.J., Panksepp, J. (Eds). Handbook of the Hypothalamus. Marcel Dekker. USA. pp. 221-265.

[42] Güldner, F.H., (1976). Synaptology of the rat suprachiasmatic nucleus. Cell Tissue Res. 165, (4) 509-544.

[43] O'Bryne, J.N., Berman-Rosa, M., Gouin, J.P., & Dang-Vu, T.T., (2014). Neuroimaging findings in primary insomnia. Pathol. Biol. Paris. 62, (5) 262-269.

[44] Desseilles, M., Dang-Vu, T., Schabus, B., Sterpenich, V., Maquet, P., & Schwartz, S., (2008). Neuroimaging insights into the patophysiology of sleep disorders. Sleep. 31, (6) 777-794.

[45] Nie, X., Shao, Y., Liu, S.Y., Li, H.J., Wan, A.L., Nie, S., Peng, D.C., & Dai, X.J., (2015). Functional connectivity of paired default mode network subregions in primary insomnia. Neuropsychiatr. Dis. Treat. 11, 3085-3093.

[46] Altena, E., Van Der Werf, Y.D., Sanz-Ariquita, E.J., Voorn, T.A., Rombouts, S.A., Kuijer, J.P., & Van Someren, E.J., (2008). Prefrontal hypoactivation and recovery in insomnia. Sleep. 31, (9) 1271-1276.

[47] Perez-Cruz, C., Simon, M., Flügge, G., Fuchs, E., Czéh, B., (2009). Diurnal rhythm and stress regulate dendritic architecture and spine density of pyramidal neurons in the rat infralimbic cortex. Behav. Brain Res. 205, (2) 406-413.

[48] Altena, E., Vrenken, H., Van Der Werf, Y.D., van den Heuvel, O.A., & Van Someren, E.J., (2010). Reduced orbitofrontal and parietal gray matter in chronic insomnia: a voxel-based morphometric study. Biol. Pshychiatry. 67, (2) 182-185.

[49] Amaral, D, (2013). The functional organization of perception and movement. In: Kandel, E., Schwartz, J., Jessell, T., Siegelbaum, S., Hudspeth, A.J. (Eds). Principles of Neural Science. Fifth ed. McGraw Hill Professional. U.S.A. pp. 356-369.

[50] Kalaska, J.F. & Rizzolatti, G., (2013). Voluntary movement: the primary motor cortex. In: Kandel, E., et al. (Eds). Principles of Neural Sciences. Fifth ed. McGraw and Hill. U.S.A. pp. 835-864.

[51] Noback, R. & Demarest, R., (1975). The Human Nervous System. Basic Principles of Neurobiology. McGraw-Hill. EUA.

[52] Gloor, C., Luft, A.R., & Hosp, J.A., (2015). Biphasic plasticity of dendritic fields in layer V motor neurons in response to motor learning. Neurobiol. Learn. Mem. 125, 189-194.

[53] Rao, B.S., Desiraju, T., Meti, B.L., & Raju, T.R., (1994). Plasticity of hippocampal and motor cortical pyramidal neurons induced by self-stimulation experience. Indian J. Physiol. Pharmacol. 38, (1) 23-28.

[54] Shankaranarayana Rao, B.S., Raju, T.R., & Meti, B.L., (1999). Self-stimulation rewarding experience induced alterations in dendritic spine density in CA3 hippocampal and layer V motor cortical pyramidal neurons. Neuroscience. 89, (4) 1067-1077.

[55] González-Burgos, I., González-Tapia, D., Zamora, D.A., Feria-Velasco, A., & Beas-Zárate, C., (2011). Guided motor training induces dendritic spine plastic changes in adult rat cerebellar purkinje cells. Neurosci. Lett. 491, (3) 216-220.

[56] Ramnani, N., Tini, I., Passingham, R.E., & Haggard, P., (2001). The cerebellum and the parietal cortex play a specific role in coordination: a PET study. Neuro Image, (14) 899-911.

[57] González-Tapia, D., González-Ramírez, M.M., Vázquez-Hernández, N., & González-Burgos, I., The fast period of motor learning is associated with an increase in thin spines on rat cerebellar Purkinje cells. Behav. Brain Res. Submitted to publication.

[58] Leuner, B., Shors, T.J., (2013). Stress, anxiety, and dendritic spines: what are the connections? Neuroscience. 251, 108-119.

[59] Lee, S.A., Kim, C.Y., & Lee, S.H., (2016). Non-conscious perception of emotion in psychiatric disorders: the unsolved puzzle of psychopathology. Psych. Inv. 13, (2) 165-173.

[60] Suslow, T., Kugel, H., Ohrmann, P., Stuhrmann, A., Grotegerd, D., Redlich, R., Bauer, J., Dannlowski, U., (2013). Neural correlates of affective priming effects based on masked facial emotion: an fMRI study. Psychiatry Res. 211, (3) 239-245.

[61] Brooks, S.J., Savov, V., Allzén, E., Benedict, C., Fredriksson, R., Schiöth, H.B., (2012). Exposure to subliminal arousing stimuli induces robust activation in the amygdala, hippocampus, anterior cingulate, insular cortex and primary visual cortex: a systematic meta-analysis of fMRI studies. Neuroimage. 59, (3) 2962-2973.

[62] Tamietto, M., de Gelder, B., (2010). Neural bases of the non-conscious perception of emotional signals. Nat. Rev. Neurosci. 11, (10) 697-709.

[63] Pessoa, L., Japee, S., Sturman, D., Ungerleider, L.G., (2006). Target visibility and visual awareness modulate amygdala responses to fearful faces. Cereb. Cortex. 16, (3) 366-375.