Chapter 4

True and False Memories: Neuropsychological and Neuropharmacological Approaches

Regina Vieira Guarnieri,
Orlando Francisco Amodeo Bueno and
Ivanda de Souza Silva Tudesco

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.80918

Abstract

Some recent studies have explored the false memory and its mechanisms. True memories depend on draw in the past, retrieve of the information, remember past events plus recombine (reorganize) them with new information to finally re-encode these elements creating a new memory. But, sometimes failures in this system lead to memory errors collaborating to false memory formation. This chapter will address new neuropsychological tools to evaluate true and false memory performance. Some neuropharmacological aspects as possible mechanisms of agonist and antagonist modulation of false memory will be discussed.

Keywords: false memory, episodic memory, neuropsychology, neuropharmacology

1. Introduction

1.1. Memory

Memory can be described as the ability to acquire and retain new information and retrieve it in a conscious or unconscious way when necessary, being composed of a set of independent systems acting in a cooperative way [1]. Daily, we perform several numbers of tasks, such as reading a newspaper, calculating the tip at the restaurant, imagining a new layout of the furniture in our living room to fit a new sofa, comparing qualities and defects of apartments to choose the one that we will rent, and so on. Finally, tasks involving multiple steps that need to be kept mentally until a result is established [2].

1.2. Types of memory: short-term memory, working memory, and long-term memory

Memory is, in theory, fragmented into short-term memory, working memory, and long-term memory.

In 1890, James was the first one to propose the separation of memory in two systems: the primary memory, which nowadays could be equivalent to the concept of working memory, and the secondary memory that would be analogous to the long-term memory [3]. Atkinson and Shiffrin [4] proposed the model known as a modal model that would process information at three interconnected levels: (1) modal sensory register, (2) short-term memory, and (3) long-term memory, the latter being understood as a permanent storage of information (**Figure 1**). According to this model, information from external environmental stimuli are processed in different parallel sensorial registers, being stored in a short-term system (primary) with limited capacity and later in long-term memory (secondary). In this model, the role of short-term storage is crucial to achieve long-term storage, as well as to the retrieval of information contained in this system. The concept of short-term memory refers to the ability to process and store a few items, about four, for a very short period (seconds) decaying rapidly over time [5]. Despite this rapid forgetting rate, information can be kept longer in memory through rehearsal [4].

One of the most influential models of working memory is that of Baddeley and Hitch proposed in 1974 [6]. The model postulates two processing and manipulation loops: the phonological loop capable of maintaining and processing verbal information and the visuospatial sketchpad which similarly handles visual information. In addition, there is one more attentional component, the central executive, who coordinates all information from these subsystems. More recently, another integrator component has been incorporated into the model; the episodic buffer where information is temporarily held and manipulated before being definitively stored in long-term memory. The episodic buffer is a limited capacity storage system that temporarily keeps information under the control of the central executive [7]. Working memory is important in focusing attention, logic, reasoning, planning, strategy, and learning processes (**Figure 2**) [8].

Long-term memory is defined as the ability of the subject to acquire, retain, and retrieve information from events that occurred hours, days, months, or even years ago. According to Squire and

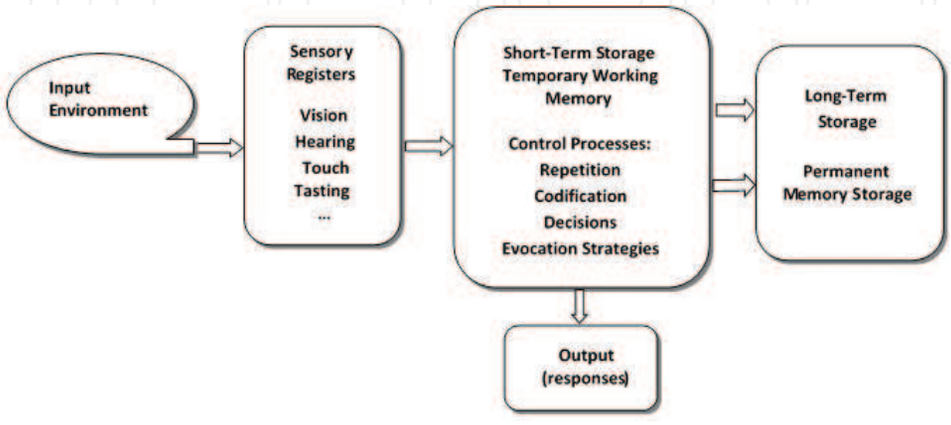

Figure 1. Modal model adapted from Atkinson and Shiffrin [4].

http://dx.doi.org/10.5772/intechopen.80918

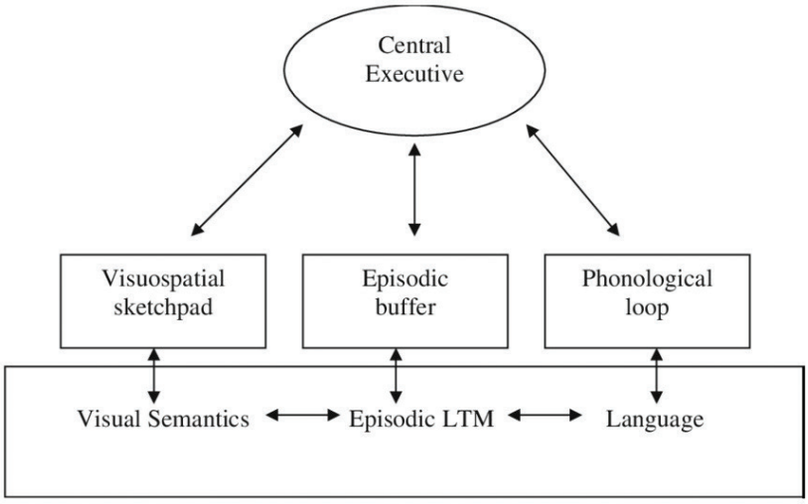

Figure 2. Model of working memory adapted from Baddeley.

Zola-Morgan [9], long-term memory can be subdivided into declarative (or explicit) memory and non-declarative (or implicit) memory. Explicit memory refers to the ability to store and consciously remember facts and events; otherwise, the implicit memory is independent of consciousness or intentional recollection and concerns learning, motor, and cognitive skills acquired gradually. Most memories stored in implicit memory are procedural memories. It involves several types of cognitive abilities, which can be measured through the performance of the individual. It occurs through the learning of a series of habits and abilities, making it easier to remember after exposure to specific stimuli, such as priming, classical and operant conditioning, and nonassociative learning [10].

Declarative memory depends on the integrity of medial temporal lobe structures including the hippocampus, parahippocampal gyrus, entorhinal and perirhinal cortices, fornix, and anterior and mediodorsal nuclei in the thalamus. Particularly, it is primarily dependent on mesial temporal lobe structures, especially the hippocampus [9]. Declarative memory is conceptually subdivided into semantic memory and episodic memory. The semantic memory is relative to the ability to acquire knowledge in general, such as knowledge of the world, concepts, and vocabulary, and does not depend on context for its evocation [11]. Episodic memory is a type of declarative memory that temporarily receives and stores information and its temporospatial relationships.

The episodic memory is the one who is most interested in the studies of false memories. Retrieval, also known as recall or remembering, is considered the reaccessing of events or information previously encoded and stored in our brain in the past. On the other hand, recognition is a subcategory of declarative memory, defined as the ability to recognize previously encountered events, objects, or people.

To test false memory, one can apply the word free recall task on subjects because it implies the recall of some words on a given occasion, that is, within a certain temporospatial context, but also recognition task is verily applied in several studies related to this topic (see items 2 and 3) (**Figure 3**).

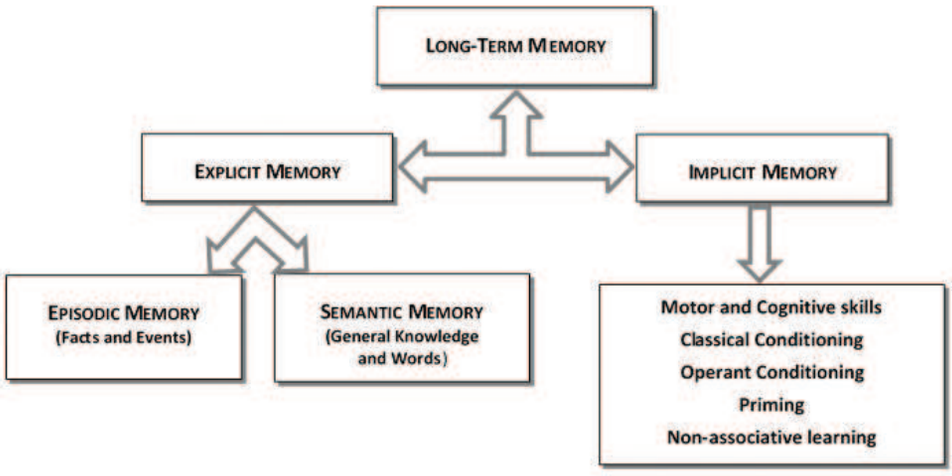

Figure 3. Long-term memory according to Squire and Zola's [9] definition.

So far, we have explored the types of memory: short-term memory, long-term memory, and working memory, which also clearly play a role in false memory processes. Now, we will present a very important type of memory in the formation of false memories, which is the emotional memory.

1.3. Emotional memory

Emotional reactions can be measured according to subjective reports (e.g., evaluation scales), objectives (e.g., physiological responses, such as heart rate and electrical conductance), and observation of behaviors (e.g., expressions) [12].

Human emotional experiences can be characterized by two main affective dimensions: valence and arousal. Valence refers to a continuous evaluation that varies from unpleasure (negative valence-unpleasant) to pleasure (positive valence-pleasant), passing through the neutral classification. The arousal refers to a continuous evaluation that varies from calm to stimulation. The emotional reaction to any stimulus (e.g., images and words) can be classified according to the valence and the arousal. In 1980, Lang developed a nonverbal pictographic measure for the subjective evaluation of valence and the arousal, the Self-Assessment Manikin (SAM) [13]. The SAM has the purpose of evaluating more objectively the affective dimensions of stimuli, used in studies on motivation, attention, and memory. At this task, usually, a stimulus that causes emotional reactions with low levels of valence is classified as negative, with medium levels as neutral, and with high levels as positive. Likewise, for the arousal, low-level stimuli are described as relaxing, with medium levels as non-stimulating and with high levels such as arousal.

Words and photographs classified as being of negative or positive valence present stimulating arousal level and are more likely to be correctly retrieved than similar stimuli classified as neutral and not stimulant [14]. Additionally, some studies have suggested that the arousal reinforces the encoding of central aspects of a stimulus through unintentional attention mechanisms while at the same time tends to decrease the encoding of peripheral details of stimuli [15]. For example, looking at a photo of an accident between two cars on a highway, people tend to remember more the central and significant aspects of the event (e.g., crumpled cars) than the

peripheral aspects of the event (e.g., a traffic board or advertisement billboards on the side of the road) [16]. Sometimes these circumstances facilitate the false memory formation once some peripheric details could not be well encoded and may be re-encoded in a wrong way and falsely retrieved in the future.

Several studies have shown that episodes that contain emotional relevance have a greater probability of being remembered than those that do not contain it: so, there are advantages in the retrieval of stimuli classified as stimulants compared to non-stimulating stimuli. The emotion promotes better encoding of the memory trace due to greater rehearsal, attention, and elaboration that it provides [17].

The amygdala is the primary orchestrator of emotional memory without which the emotional effects in memory do not occur. The amygdala is responsible for the incremental effect of emotion in declarative memory [18]. The amygdala affects the memory, whether in encoding as in storage, modulating, or increasing the activity of other brain regions, such as the hippocampus. On the other hand, the hippocampus influences the responses of the amygdala when emotional stimuli are involved [19]. A case study of a patient who had bilateral lesion of the amygdala related that he did not enjoy the typical benefit of emotion in increasing the memory for images of positive or negative emotional content [20]. Another interesting data come from a functional magnetic resonance study dependent on the blood oxygenation-level-dependent functional magnetic resonance imaging (BOLD fMRI)reporting that Parkinson's patients present abnormal activation of the amygdala that is associated with deficiencies in responses to emotional stimuli of fear [21].

There are two main effects of emotion in explicit memory, both mediated by the amygdala: *effect at the time of encoding*, including increased attention and elaboration, and the post-encoding effect that includes the release of cortisol and increased consolidation of memory trace. *At the time of memory consolidation*, the hormones released in the hypothalamus-pituitary-adrenal axis, under the influence of the amygdala, act in the hippocampus assisting the storage of stimuli, making them more resistant to forgetting and interference. In this way, it facilitates retrieval [22].

Emotional valence can affect explicit memory through its influence on the activity of the adeno-pituitary gland, modifying the release of stress hormones that interact with the amygdala. The modulation effect of emotional valence, through the amygdala action, acts specifically in the areas of memory consolidation such as the hippocampus. Studies have shown that the amygdala and hippocampus systems are independent. For example, one of these studies used the fear-conditioning paradigm where the emergence of a blue square on the screen is halted with a shock to the wrist. Patients with amygdala lesions did not show the normal physiological response of fear of dodging the shock, although they reported that they knew that the blue square preceded the same. That is, the prediction of what was going to occur, that is, the event itself, was intact, because it depends on the hippocampus, while the emotional link does not. Patients with damage to the hippocampus showed an opposite pattern [23]. There is evidence that the activation of the amygdala can be modulated by attention. The amygdala does not respond differently to faces with emotional content when attentional resources are being divided to another focus, which indicates that the emotional processing in the amygdala is susceptible to "top-down" control [24].

Other important anatomical areas activated during emotional memory processing are the anterior cingulate cortex, nucleus accumbens, septum, ventral tegmental area, insula, somatosensory cortex, and brainstem. A study of functional neuroimaging demonstrated a correlation between the activation of the anterior cingulate cortex, emotion, and attention [25]. In 2000, Bush and collaborators published a review that cites several studies that evidence the involvement of the anterior cingulate cortex in a circuit involving attention in the regulation of cognitive and emotional processes [26]. Evidence suggests that this area is activated during the perception of emotion, affection, and pain, during the symptoms of post-traumatic disorder and the detection of errors [26, 27]. The anterior cingulate cortex is, in turn, related to the visceral, attentional, and emotional integration of the information involved with the regulation of affection and other forms of "top-down" control. It is also suggested that it is the key substrate for emotional awareness and the central representation of the autonomic arousal. These neuroimaging studies involving various types of emotional stimuli have determined the affective subdivision of the anterior cingulate cortex. It seems that this area is activated when the subject must monitor conflicts between the functional state of the organism and any new information that has relevant affective and emotional consequences. When such conflicts are detected, the areas of the anterior cingulate cortex project to the prefrontal cortex and nuclei of the base where options for responses will be evaluated. The prefrontal cortex plays an important role in emotion feedback; particularly, the ventromedial prefrontal cortex is active when decisions need to be made based on the emotional properties of the stimuli [30]. Generally, behavioral choices that require decision-making are influenced by the immediate affective consequence of a situation (e.g., a reward). In these situations, regions of the left prefrontal cortex are active when the target is related to appetitive situations, while the right prefrontal cortex is activated in negative [28, 29].

2. False memory

True memory is the real retrieval of an event of any nature, be it visual, verbal, or otherwise. True memories are constantly being rewritten (re-encoding). On the other hand, false memory is defined as the recollection of an event that did not happen or a distortion of an event that indeed occurred. Otherwise, confabulation is the formation of false memories, perceptions, or beliefs about yourself or the environment because of neurological or psychological dysfunction. During this process, confusion between imagination and memory or even confusion between true memories may occur.

Since the past decade, the phenomenon of false memories is drawing attention in the mental health area. Research in the field of mental health and legal area has suggested that emotion can influence the production of false memories. Some studies have indicated that certain psychotherapeutic techniques which are based on the retrieval of emotional memories in children can produce vivid memories of events that have not really occurred, for example, alleged cases of sexual violence suffered during childhood [30]. The memory of these children can be reconfigured in the wrong way. In the legal area, the impact of emotion on the functioning of memory may compromise the exercise of justice, since the person who has witnessed some crime, violation, and/or suffer if any kind of violence may be subject to distortion of their memories [31].

http://dx.doi.org/10.5772/intechopen.80918

The relationship between the emotion and the production of false memories, however, is difficult to test with autobiographical memories since a detailed comparison between the information retrieved and details of the original event is practically unfeasible [16, 32].

False memories can also occur in the ordinary day-to-day life (not necessarily in pathological or traumatic situations). For example, in this conversation, "Yesterday I met a friend on the street and said, 'Hi, Brad, how are you?' And he said, 'Thank you, but my name is Fred!'" This is the percentage of false memories we observe, for example, at control subjects during the performance of a task on trials about false memories.

False memories are a consequence of how memories are built in the brain. Since the pioneering studies of Milner and her colleagues [33] on H.M., an amnesic patient who after the surgical resection of a large part of his medial temporal lobe presented many specific changes in his memory, the idea of memory as a single entity has been losing support. What was thought to be unique engrams of lived experiences has since then been broken down in a series of pieces that must be joined together to give rise to the experience of retrieving memories. Each one of these pieces is acquired with different codes and stored in different locations in the brain, depending on the different contexts in which they were obtained and in which they are recollected later. That is, the retrieval operation depends on the external and internal conditions at encoding and at retrieval. Memory cues remind details of the input occasion and are a necessary condition to the retrieval. Other external inputs like feelings, thoughts, and the motivational state are also very important for a true retrieval but sometimes may be not like the original situation.

In agreement with the conception that memory is composed of several systems, Brainerd and Reyna [34] proposed the fuzzy-trace theory (FTT). According to FTT, episodic memory consists of two independent and parallel subsystems called the literal system and essence. These two subsystems encode information in the form of different representations, constituting literal memory and memory of essence. While literal memory stores the specific and detailed traits of the episodes, the essence memory stores the nonspecific sense, e.g., the meaning, and the general patterns of the episodes. For the FTT, true memories are mostly due to the retrieval of literal memories. False memories, therefore, would be arising from the retrieval of memories of essence [35].

Traditionally, false memories have been investigated through various types of experimental procedures that enhance their occurrence, using materials such as slides, films, and sentences.

In the last decade, a widespread methodology is the list of associated words. This procedure, known by the acronym DRM, was developed by Roediger and McDermott [36] based on previous studies done by Deese many years before (1959). DRM consists of lists of words that are presented to be memorized (study phase) and later recognized (test phase). For this, standardized verbal stimuli (word lists) with neutral and emotional content (positive and negative) are adopted in a way to evaluate if the recognition was true or false, even if it is familiar or not. This method of organizing stimuli into thematically related sets was inspired by the previous research with words, which produced robust false recognition effects (see item 3).

It is thought that such false memories arise from the automatic activation of conceptually related words or "gist" information [37]. Thus, when reading the words in the study phase, people encode the target words through literal representations (specific and detailed characteristics,

e.g., sound, spelling) and representations of essence (general characteristics and unspecific, e.g., the meaning). In the test phase, people recall or recognize the target words (true memory) by retrieving the literal and essence traces but recall or recognize the critical words (false memory) through retrieval only of essence traces. FTT has been widely used in interpreting results from research using the DRM procedure, for example, in studies that evaluated the effects of triazolam and scopolamine in the production of false memories for neutral words [38, 39].

In recognition tasks, in which the participants must distinguish items whose presentations are episodically remembered from those that seemed to be merely familiar that means they do not have a full memory. They recognize stimuli (words or images) previously presented (study phase) in a list that includes items that have not been presented before (recognition phase). Current models of recognition memory consider that recognition involves both familiarity and recollection. Familiarity seems to operate more quickly than the recollection, being defined as a quick decision of recognition. Some authors interpret the "remember" and "know" as responses that reflect different processes, of recollection and familiarity, respectively [40, 41].

The classification of stimuli in different emotional dimensions is also necessary, because some studies have shown that valence and the arousal influence the indexes of retrieval through different cognitive processes and neural mechanisms [42, 43]. It is assumed that valence and the arousal improve recollection, while the arousal increases familiarity [14]. On the other hand, true memories (events or thoughts) are often associated with retrieved experiences and feelings of familiarity, while false memories are characterized by feeling familiarity and no distinct state of consciousness [44]. During a recognition test, a decision-making process occurs whose participants give a "remember" answer when they recognize items that are accompanied by a conscious retrieval of their occurrence during an episodic memory study. On the other hand, they give a "know" answer to those items that do not evoke any detail, but which are recognized by other bases. The detailed instructions given to the participants for the "remember-know" trial can be obtained in previous studies [41, 45].

3. Neuropsychology as clinical tools to true and false memory: evaluation and rehabilitation

3.1. Evaluation

Some tests are classically used to evaluate false memory. One of them (cited above) is the *DRM*, a recognition test that associates words with neutral and emotional content. Each list contains 15 words (it may change depending on the study), and the words commonly chosen are those with the highest rates of false recognition. The word lists comprised some positive (e.g., music, fruit, sweet, and sleep), some neutral (e.g., chair, cold, pen, and high), and other negative contents (e.g., thief, trash, pain, and fear). The presentation order of the words is randomly generated and varied for each subject. The participants are instructed to encode all lists. The words of each list revolve around a theme in which it is strongly associated. These words were termed critical keywords [e.g., *smoke* (critical word), for which associated words that belong to a common theme are cigarette, puff, blaze, billows, pollution, ashes, cigar, chimney, fire, tobacco, stink, pipe, lungs, flames, and stain] that were the related lures. The critical

word, smoke, that translates the thematic essence of the list and is semantically associated with all other words of the list is not presented in the memorization stage (study phase). The word *smoke* is remembered or recognized many times in the same proportion as words from the list studied.

The recognition task is carried out immediately (hours, days, etc.) after presentation of lists. It consists of 90 words, of which 45 of them are targets, 15 related lures, and 30 unrelated lures. The targets are the studied words in the original material taken from positions 1, 8, and 10 of the lists (hit rates); the related lures are words not presented in the original material but represent the semantic essence of each of the lists (false alarm); and the unrelated lures are words not presented in the original material that have no semantic relationship with them (response bias measured by item intrusions). The subjects were asked to circle the words, presented in a sheet of paper that they thought to have seen before. If they circle a target, the measure is considered a "hit rate," and if they circle a related lure, it is considered a "false alarm."

Another task to evaluate visual false memory is the *DRM-IAPS*, developed according to the same criterion of DRM paradigm adapted for the construction of a set of associated images from the International Affective Picture System (IAPS) [46]. The IAPS in turn must be standardized according to each population studied since it may vary according to it. It evaluates the emotional memory, constituting an adequate task to evaluate false memories.

As the DRM task, the DRM-IAPS (**Figure 4**) consists of two phases: the study phase (encoding) and recognition phase (recognition). The study phase consisted of 20 blocks with 6 pictures

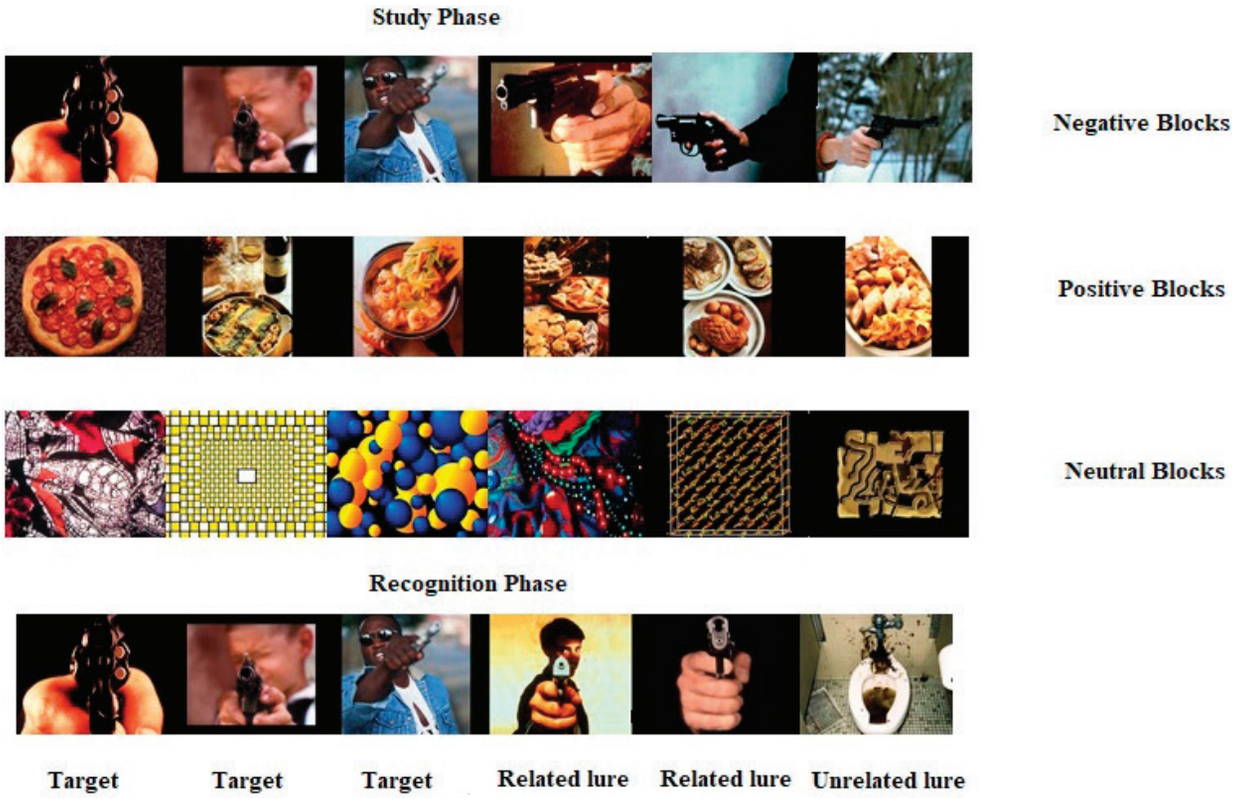

Figure 4. Example of DRM-IAPS task blocks (negative, positive, and neutral valences). Study and recognition phases.

that were elaborated, having a total of 120 photos (it may change according to the trial). The images are taken from the IAPS, which contains hundreds of color photographs capable of eliciting various emotional states. These images range from pleasant to unpleasant, arousal or relaxing, or neutral. The picture valence may be positive (e.g., food, sports, sex, etc.) or negative (e.g., guns, mutilated bodies, violence, and accidents). Each photograph, taken from the IAPS, showed a certain level of arousal and valence, whose average is calculated for each of the 20 blocks. These visual stimuli can induce various emotional states and represent many aspects of real life, sports, fashion, natural disasters, accidents, landscapes, pornography, violence, etc. and act as powerful generators of emotions easily presented in the experimental laboratory context, thus, allowing accurate control of their timing and exposure time.

So, usually most of the tasks aimed to study false memories consist of two phases: (1) the *encoding phase* (or study phase) and (2) *retrieval phase* (recognition or free recall phase test). During the recognition task, the subject may decide if they have seen the picture (stimulus) before or not. "Yes" responses to targets provided an index of true recognition, whereas "yes" responses to related lures provided an index of false recognition. During the recognition phase, it is also possible to evaluate the level of confidence of responses ("know/remember" answers). Physiological measures outcoming from emotional responses according to valence as well as arousal of the stimuli are commonly taken.

Other common tasks used on trials aimed to study false memories are as follows: emotional responses to pictures IAPS, personality trait of words, recognition of facial emotions, or films [46–50].

3.2. Neuropsychology and neuropsychological rehabilitation

The main role of neuropsychology is the evaluation of cognitive functions and their relation to behavior, which means to investigate the cerebral changes and their impact on the behavior of the individual. Neuropsychology is, in a broad sense (latus), the study of the relations between the brain and the behavior and, in a strict sense (strictum), is the professional field of research that investigates the cognitive and behavioral alterations associated with brain lesions [51].

Neuropsychology involves various types of knowledge such as neuroanatomy, neurophysiology, neurochemistry, and neuropharmacology, which contributes to the professional performance of the psychologist in the application of resources such as psychometry, clinical psychology, experimental psychology, psychopathology, and cognitive psychology. It is aimed to investigate cognitive functions such as memory, language, attention, executive function, perception, praxis, gnosis, mood, and personality disorders [52].

This investigation of the relationship between brain functions and behavior begins with neuropsychological evaluation, thenceforth due to neuropsychological and cognitive rehabilitation to be taken. Cognitive and neuropsychological rehabilitation are part of the field of psychology, first aimed to enable both patients and family members to minimize or overcome the cognitive deficits resulting from neurological disorders (acquired or congenital) and then the search for strategies for treatment of cognitive impairments, dealing with behavioral, social, and emotional changes in a way to improve quality of life of the patient [51]. There are many cognitive intervention technologies used as an aid to neuropsychological rehabilitation of the patient with different disorders

http://dx.doi.org/10.5772/intechopen.80918

such as temporal lobe epilepsy, schizophrenia, and stroke, among others. Varied from the simple the use of notes that help, for example, a patient with schizophrenia to remind their activities and commitments, until memory training, brain training, computerized exercises, and so on.

Just recently the researchers began to analyze false memories in pathological conditions (e.g., schizophrenia, post-traumatic stress disorder, and dementia) [53–56]. There are still many doubts to be elucidated in this fascinating area, and therefore the rehabilitation interventions are still to be defined in the next years.

4. Neuropharmacology on memory and false memories (dopaminergic modulation and other systems)

4.1. Dopaminergic modulation of true memories

The prefrontal cortex plays an essential role in the mediation of working memory, which has been observed in neuroimaging and neurophysiology studies, in monkeys and humans [57, 58]. Studies have demonstrated dopaminergic modulation of executive functions, working memory, and emotion [59, 60]. Studies with monkeys have shown that activation of dopamine D_1 receptors in the prefrontal cortex is necessary for the expression of working memory [57, 61]. Also, in humans, there is evidence of the predominant role of dopamine D_1 receptor with working memory [57, 62]. However, other studies with dopaminergic D_2 receptor antagonists and agonists have shown that they are also implicated in working memory in humans and monkeys [63–65]. According to Takahashi and colleagues, hippocampal D_2 receptors also influence frontal lobe functions, such as executive functions and verbal fluency [66]. Studies have particularly demonstrated the involvement of dopamine D_2 receptors in working memory, executive functions, working memory capacity, selective attention, and shifting [67–69]. Studies suggest that dopaminergic D_1 and D_2 receptors have complementary functions [70, 71].

Dopaminergic modulation of episodic memory was observed in humans [72]. Decreased binding to D_2 dopaminergic receptors in the hippocampus has been implicated in impairment of memory performance and learning impairments in Alzheimer's patients [73–75] and in experimental animals [76, 77]. There are many studies in humans and animals aimed to verify the involvement of dopamine in attentional mechanisms, executive functions, and working memory. Although the literature involving dopamine and emotion when referring to reward and addiction mechanisms is ample, few studies have evaluated the influence of dopaminergic receptors on emotional episodic memory.

Some neurological and psychiatric pathologies such as Parkinson's disease, schizophrenia, autism, attention deficit, Huntington's disease, and lesions of the frontal lobe present emotional process impairments. All these pathologies involve the dopaminergic system that suggests the participation of dopamine in emotion [78–83]. Moreover, emotional processes depend on different structures; many of them comprise the limbic system that has dopaminergic innervation. Many biochemicals, pharmacological, and neuroimaging studies reinforce the idea of dopaminergic contribution in emotion. A study with Parkinson's disease suggests that an abnormal state

of the dopaminergic system compromises the normal operation of the amygdala) [21]. Some studies suggest the participation of dopaminergic D_2 receptors in emotional memory [84, 85].

The evaluation of the effect of specific drugs acting on several neurotransmitter systems on the functioning of memory for emotional stimuli is relevant, since healthy people process emotional episodes differently from episodes without emotional content. This often results in a higher probability of emotional events being retrieved than neutral ones [14, 86, 87]. The finding that emotions impact the performance of episodic memory has led some researchers to investigate the influence of emotions on the production of false memories. Although these researches present different results, perhaps stemming from a variety of methods employed, they all suggest that emotion interferes with the indices of false memories.

4.2. Dopaminergic and other neurotransmitter system modulation of false memories

Two studies using antipsychotics haloperidol and sulpiride, both dopamine D_2 receptor antagonists, set up to evaluate the dopaminergic modulation of false memories observed that the drugs increased false memory rates but had no effect on true memory [88, 89].

Other neurotransmitter system effects on the production of false memories were studied in trials with dextroamphetamines, Δ(9)-tetrahydrocannabinol (THC), and benzodiazepines (diazepam and lorazepam). The effect of caffeine and of alcohol on true and false memories was also investigated.

Ballard observed that dextroamphetamine (AMP) increases errors during memory retrieval [90]. The same author in another study found that AMP increases true, but not false, memory relative to placebo, but AMP increases false memory compared to THC [91]. In 1999, Blair and Curran observed that diazepam selectively impaired subjects' ability to recognize angry expressions but did not affect recognition of any other facial emotional expression [92]. A study demonstrated that diazepam and lorazepam impair conscious recollection associated with true, but not false, memories [93]. Caffeine appears to intensify the strength of connections among the list words and critical lures, thereby enhancing both true and false memories [94].

In 2012, another study observed more false-positive responses of ecstasy/polydrug users than nonusers [95]. Increased long-term frequency of ecstasy use was positively associated with memories when ingested before encoding. But differently it verified an increased false recognition when amphetamine was ingested before retrieval. On the contrary, alcohol appears to decrease semantic activation leading to a decline in false memories and decrease in rejection of false memories, commonly observed in placebo. The latter effect of alcohol may be due to its ability to impair monitoring processes established at encoding [96]. Milani and Curran compared the effect of low dose with high dose of alcohol on recollective experience of illusory memory [97]. They found high levels of false recall and recognition across both treatments and verified that a small dose of alcohol did not change too much measures of false memory but modifies the pattern of recollective experience in terms of remember and know responses. Specifically, it increased the level of remember responses for false recognitions (critical lures).

An autobiographical study reported that compared to placebo, lorazepam increased levels of conscious recollection, as assessed by "remember" responses, for both true and false memories and induced an overestimation of the personal significance and emotional intensity of past events [98].

Emotion facilitates true memory performance in comparison to neutral content events. However, in situations with negative emotional content, where the level of stress and cortisol released is high, the opposite must occur; that is, there is an impairment in the performance of processes such as perception and memory. This mechanism can be represented in a graph by one of the inverted "U" curves. These situations of high stress would be represented in the descending part of the curve, which means that the emotion has a facilitating effect on the encoding, but if the level of emotion is exaggerated, the effect is the contrary [99]. Possibly, at extreme stressful circumstances, with a high level of attention and arousal, an exaggerated processing of the relevant stimuli of the event (the central aspects) in detriment of the processing of peripheral (irrelevant) stimuli occurs. This unbalance during encoding could facilitate the formation of false memories through errors during the re-encoding of some memory traces.

Some possible mechanisms of dopaminergic modulation of false memories proposed by this chapter's authors would be (1) the dopamine effect on working memory/executive functions through corticostriatal as well as hippocampus-prefrontal D_2 dopaminergic modulation, (2) through D_2 dopaminergic modulation of the response of the amygdala to emotionally loaded stimuli, and (3) dopaminergic modulation of decision-making process (via striatum). Other possible failures in post-encoding through other neurotransmitters may also contribute to false memory formation. But the exact mechanisms as well as the role of other neurotransmitter systems on the production of false memories remain still to be clarified in the future.

5. Conclusions

The activation (agonism) or blockade (antagonism) of receptors may have different effects on emotional judgment of the stimulus and may stimulate or impair true or false memories depending on the drug and system studied. The study of false memories is a challenging area of neuroscience that is extraordinarily fascinating with many questions yet to be clarified in a way that in the future new methods and tools of neuropsychological rehabilitation can be proposed.

Conflict of interest

There is no conflict of interest.

Author details

Regina Vieira Guarnieri[1]*, Orlando Francisco Amodeo Bueno[1]
and Ivanda de Souza Silva Tudesco[1,2]

*Address all correspondence to: vguarnieri@uol.com.br

1 Department of Psychobiology, Universidade Federal de São Paulo, São Paulo, SP, Brazil

2 Psychology-Psychosomatics of Universidade Ibirapuera, São Paulo, SP, Brazil

References

[1] Squire LR, Kandel ER. Brain system from declarative memory. In: Scientific American Library, editor. Memory: From Mind to Molecules. New York; 1999. pp. 83-107

[2] Miyake A, Shah P, editors. Models of Working Memory: Mechanisms of Active Maintenance and Executive Control. New York: Cambridge University Press; 1999

[3] James W. The Principles of Psychology. Dover Publications; 1890 (1950, Vol. 1: ISBN: 0-486-20381-6, Vol. 2: ISBN 0-486-20382-4)

[4] Atkinson RC, Shiffrin RM. The control of short-term memory. Scientific American. 1971; **225**:82-90

[5] Cowan N. The magical number 4 in short-term memory: A reconsideration of mental storage capacity. Behavioral and Brain Sciences. 2000;**24**:87-185

[6] Baddeley AD, Hitch GJ. Working memory. In: Bower GA, editor. The Psychology of Learning and Motivation. New York: Academic Press; 1974. pp. 49-79

[7] Baddeley AD. Short-term and working memory. In: Tulving E, Craik FIM, editors. The Oxford Handbook of Memory. New York: Oxford University Press; 2000. pp. 77-92

[8] Baddeley AD, Della Sala S. Working memory and executive control. In: Roberts AC, Robbins TW, Weisenkrantz L, editors. The Prefrontal Cortex. Oxford: Oxford University Press; 1998. pp. 9-21

[9] Squire LR, Zola-Morgan S. The medial temporal lobe memory system. Science. 1991;**253**: 1380-1386

[10] Squire LR. Memory systems of the brain: A brief history and current perspective. Neurobiology of Learning and Memory. 2004;**82**:171-177

[11] Tulving E. Elements of Episodic Memory. New York: Oxford University Press; 1983

[12] Bradley MM, Lang PJ. Measuring emotion: The self-assessment manikin and semantic differential. Journal of Behavioral Therapy and Experimental Psychiatry. 1994;**25**(1):49-59

[13] Lang PJ. Behavioral treatment and bio-behavioral assessment: Computer applications. In: Sidowski JB, Johnson JH, Williams TA, editors. Technology in Mental Health Care Delivery Systems. Norwood, NJ: Ablexs; 1980. pp. 119-137

[14] Kensinger EA, Corkin S. Memory enhancement for emotional words: Are emotional words more vividly remembered than neutral words? Memory & Cognition. 2003;**31**(8): 1169-1180

[15] Burke A, Heuer F, Reisberg D. Remembering emotional events. Memory & Cognition. 1992;**20**:277-290

[16] Reisberg D, Heuer F. Memory for emotional events. In: Reiberg D, Hertel P, editors. Memory and Emotion. New York: Oxford University Press; 2004. pp. 3-41

[17] Hamann S. Cognitive and neural mechanisms of emotional memory. Trends in Cognitive Sciences. 2001;**5**:394-400

[18] Hamann SB, Cahill I, McGaugh JL, Squire IR. Intact enhancement of declarative memory for emotional material in amnesia. Learning & Memory. 2009;**4**:301-309

[19] Phelps EA. The human amygdala awareness: Interactions between emotion and cognition. In: Gazzanica MS, editor. The Cognitive Neuroscience III. Cambridge, MA: MIT press; 2004. pp. 1005-1016

[20] Hamann SB, Lee GP, Adolphs R. Impaired declarative emotional memory but intact emotional response following human bilateral amygdalobotomy. Society for Neuroscience. 1999;**25**:99 (abstract)

[21] Tessitore A, Hariri AR, Fera F, Smith WG, Chase TN, Hyde TM, et al. Dopamine modulates the response of the human amygdala: A study in Parkinson's disease. The Journal of Neuroscience. 2002;**22**(20):9099-9103

[22] Mcgaugh JL. The amygdala modulates the consolidation of memories of emotionally arousing experiences. Annual Review of Neuroscience. 2004;**27**:1-28

[23] Bechara A, Tranel D, Damasio H, Adolphs R, Rockland C, Damasio AR. Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. Science. 1995;**269**:1115-1118

[24] Pessoa I, Mckenna M, Gutierrez E, Ungerleider IG. Neural processing of emotional faces requires attention. Proceedings of the National Academy of Sciences of the United States of America. 2002;**99**:11458-11463

[25] Lane RD, Reiman EM, Axelrod B, Yun LS, Holmes A, Schwartz GE. Neural correlates of levels of emotional awareness: Evidence of an interaction between emotion and attention in the anterior cingulate cortex. Journal of Cognitive Neuroscience. 1998:525-535

[26] Bush G, Luu P, Posner MI. Cognitive and emotional influence of anterior cingulated cortex. Trends in Cognitive Sciences. 2000;**4**:215-222

[27] Rauch SI, Van der Kolk BA, Fisler RE, Alpert NM, et al. A symptom provocation study of posttraumatic disorder using positron emission tomography and script-driven imagery. Archives of General Psychiatry. 1996;**53**:380-390

[28] Damasio AR. The somatic markers hypothesis and the possible functions of the prefrontal cortex. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences. 1996;**351**:1413-1420

[29] Davidson RJ, Lewis DA, Alloy IB, Amaral DG, et al. Neural and behavioral substrates of mood and mood regulation. Society of Biological Psychiatry. 2002;**52**:478-502

[30] Lindsay DS. Contextualizing and clarifying criticisms of memory work in psychotherapy. Consciousness and Cognition. 1994;**3**:426-434

[31] Eisen MI, Quas JA, Goodman GS. In: Eisen MI, Quas JA, Goodman GS, editors. Memory and Suggestibility in the Forensic Interview. Mahwah (NJ): Lawrence Erlbaum; 2002

[32] Berntsen D. Tunnel memories for autobiographical events: Central details are remembered more frequently from shocking than from happy experiences. Memory & Cognition. 2002;**30**(7):1010-1020

[33] Scoville WB, Milner B. Loss of recent memory after bilateral hippocampal lesions. Journal of Neurology, Neurosurgery and Psychiatry. 1957;**20**:11-21

[34] Brainerd CJ, Reyna VF. Theorical explanation of false memories. In: Brainerd CJ, Reyna VF, editors. The Science of False Memory. Oxford: New York; 2005. pp. 59-96

[35] Brainerd CJ, Reyna VF. Fuzzy-trace and false memory. Current Direction in Psychological Science. 2002;**11**(5):164-168

[36] Roediger HI, Mcdermott KB. Creating false memories: Remembering words not presented on lists. Journal of Experimental Psychology: Learning, Memory, and Cognition. 1995;**21**(4):803-814

[37] Schacter DL, Slotnick SD. The cognitive neuroscience of memory distortion. Neuron. 2004;**44**:149-160

[38] Mintzer MZ, Griffiths RR. False recognition in triazolam-induced amnesia. Journal of Memory and Language. 2001;**44**:475-492

[39] Mintzer MZ, Griffiths RR. Acute dose-effects of scopolamine on false recognition. Psychopharmacology. 2001;**153**:425-433

[40] Conway MA, Dewhurst SA. Remembering, familiarity and source monitoring. Quarterly Journal of Experimental Psychology. 1995;**48A**:125-114

[41] Gardiner JM. Functional aspects of recollective experience. Memory & Cognition. 1988; **16**:309-313

[42] Kensinger EA. Remembering emotional experiences: The contribution of valence and arousal. Reviews in the Neurosciences. 2004;**15**:241-251

[43] Kensinger EA, Corkin S. Two routes of emotional memory: Distinct neural processes for valence and arousal. Proceedings of the National Academy of Sciences of the United States of America. 2004;**101**(9):3310-3315

[44] Conway MA, Collins AF, Gathercole ES, Anderson SJ. Recollections of true and false memories. Journal of Experimental Psychology, General. 1996;**125**(1):69-95

[45] Rajaram S. Perceptual effects on remembering: Recollective processes in picture recognition memory. Journal of Experimental Psychology: Learning, Memory, and Cognition. 1996;**22**:365-377

[46] Lang PJ, Bradley MM, Cuthbert BN. International affective picture system (IAPS): Inst ruction manual and affective ratings. Technical Report A-4. The Center for Research in Psychophysiology, University of Florida. 1997

[47] Anderson NH. Likableness ratings of 555 personality-trait words. Journal of Personality and Social Psychology. 1968;**9**:272-279

[48] Ekman P, Friesen WV. Pictures of Facial Affect [Slides]. Palo Alto, CA: Consulting Psychologists Press; 1976

[49] Harmer CJ, Shelley NC, Cowen PJ, et al. Increased positive versus negative affective perception and memory in healthy volunteers following selective serotonin and norepinephrine reuptake inhibition. American Journal of Psychiatry. 2004;**161**:1256-1263

[50] Quevedo J, Sant'Anna MK, Madruga M, Lovato I, de-Paris F, Kapczinski F, et al. Differential effects of emotional arousal in short and long-term memory in healthy adults. Neurobiology of Learning and Memory. 2003;**79**(2):132-135

[51] Hamdan AC, Pereira APA, Riechi TIJS. Avaliação e reabilitação neuropsicológica: desenvolvimento histórico e perspectivas atuais. Interação em Psicologia. 2011;**15**:47-58

[52] Lezak MD, Howieson DB, Loring DW. Neuropsychological Assessment. 4th ed. New York: Oxford University Press; 2004

[53] Fairfield B, Altamura M, Padalino FA, Balzotti A, Di Domenico A, Nicola Mammarella N. False memories for affective information in schizophrenia. Frontiers in Psychiatry. 2016; **7**(191):1-9. DOI: 10.3389/fpsyt.2016.00191

[54] Moradi AR, Heydari AH, Abdollahi MH, Rahimi-Movaghar V, Dalgleish T, Jobson L. Visual false memories in posttraumatic stress disorder. Journal of Abnormal Psychology. 2015;**124**(4):905-917. DOI: 10.1037/abn0000109

[55] Hayes JP, LaBar KS, Nasser J, Dolcos F. Reduced hippocampal and amygdala activity predicts memory distortions for trauma reminders in combat-related PTSD. Journal of Psychiatry Research. 2011;**45**(5):660-669. DOI: 10.1016/j.jpsychires.2010.10.007

[56] Phillipps C, Kemp J, Jacob C, Veronneau A, et al. Comparative study of false memory in dementia with Lewy bodies and Alzheimer's disease. Geriatrie et Psychologie Neuropsychiatrie du Vieillissement. 2016;**14**(3):332-340. DOI: 10.1684/pnv.2016.0620

[57] Sawaguchi T, Goldman-Rakik PS. D1 dopamine receptors in prefrontal cortex: Involvement in working memory. Science. 1991;**251**:947-950

[58] Arnsten AFT, Cai JX, Murphy Bl, Goldman-Rakic PS. Dopamine D1 receptor mechanisms in the cognitive performance of young adult aged monkeys. Psychopharmacology. 1994;**11**:143-151

[59] Floresco SB, Magyar O. Mesocortical dopamine modulation of executive functions: Beyond working memory. Psychopharmacology. 2006;**188**:567-555

[60] Nieoullon A, Coquerel A. Dopamine: A key regulator to adapt action, emotion, motivation and cognition. Current Opinion in Neurology. 2009;**16**(Suppl 2):S3-S9

[61] Wang K, Hoosain R, Yang RM, et al. Impairment of recognition of disgust in Chinese with Huntington's or Wilson's disease. Neuropsychologia. 2003;**41**:527-537

[62] Müller U, Yves von Cramon D, Pollmann S. D1- versus D2-receptor modulation of visuospatial working memory in humans. The Journal of Neuroscience. 1998;**18**(7):2720-2728

[63] Arnsten AFT, Cai JX, Steere JC, Goldman-Rakik PS. Dopamine D2 receptors mechanisms contribute to age-related cognitive decline: The effects of quinpirole on memory and motor performance in monkeys. Journal of Neuroscience. 1995;**15**:3429-3439

[64] Luciana M, Depue RA, Arbisi P, Leon A. Facilitation of working memory in humans by a D2 dopamine receptor agonist. Journal of Cognitive Neuroscience. 1992;**4**:58-67

[65] Mehta MA, Hinton EC, Montgomery AJ, Bantick RA, Grasby PM. Sulpiride and mnemonic function: Effects of a dopamine D_2 receptor antagonist on working memory, emotional

memory and long-term memory in healthy volunteers. Journal of Psychopharmacology. 2005;**19**:29-38

[66] Takahashi H, Kato M, Hayashi M, Okubo Y, Takano A, Ito H, et al. Memory and frontal lobe functions; possible relations with dopamine D2 receptors in the hippocampus. NeuroImage. 2007;**34**:1643-1649

[67] Mehta MA, Manes FF, Magnolfi G, Sahakian BJ, Robbins TW. Impaired set-shifting and dissociable effects on tests of spatial working memory following the dopamine D2 receptor antagonist sulpiride in human volunteers. Psychopharmacology. 2004;**176**:331-334

[68] Ward R, Duncan J, Shapiro K. The slow time-course of visual attention. Cognitive Psychology. 1996;**30**:79-109

[69] Kimberg DY, D'Esposito M, Farah MJ. Effects of bromocriptine depends on working memory capacity. Neuroreport. 1997;**8**(16):3581-3585

[70] Barone P, Palma V, DeBartolomeis A, Tedeschi E, Muscettola G, Campanella G. Dopamine D1 and D2 receptors mediate opposite functions in seizures induced by lithium-pilocarpine. European Journal of Pharmacolology. 1991;**195**:157-162

[71] Bo P, Soragna D, Marchioni E, Candeloro E, Albergati A, Savoldi F. Role of dopamine D-1 and D-2 antagonists in a model of focal epilepsy induced by electrical stimulation of hippocampus and amygdala in the rabbit. Progress in Neuropsychopharmacology and Biological Psychiatry. 1995;**19**:917-930

[72] Schott H, Seidenbercher C, Fenker DB, Lauer CJ, Bunzeck N, Bernstein H-G, et al. The dopaminergic midbrain participates in human episodic memory formation: Evidence from genetic imaging. Journal of Neuroscience. 2006;**26**:1407-1417

[73] Joyce JN, Kaeger C, Ryoo H, Goldsmith S. Dopamine D2 receptors in the hippocampus and amygdala in Alzheimer's disease. Neuroscience Letters. 1993;**154**:171-174

[74] Kemppainen N, Laine M, Laakso MP, Kaasinen V, Nagren K, Vahlberg T, et al. Hippocampal dopamine D2 receptors correlate with memory functions in Alzheimer's disease. European Journal of Neuroscience. 2003;**18**:149-154

[75] Reeves S, Mehta M, Howard R, Grasby P, Brown R. The dopaminergic basis of cognitive and motor performance in Alzheimer's disease. Neurobiology of Disease. 2010;**37**:477-482

[76] Fujishiro H, Umegaki H, Suzuki Y, Oohara-Kurotani S, Yamaguchi Y, Iguchi A. Dopamine D2 receptor plays a role in memory function: Implications of dopamine-acetylcholine interaction in the ventral hippocampus. Psychopharmacology. 2005;**182**:253-261

[77] Umegaki H, Munoz J, Meyer RC, Spangler EL, Yoshimura J, Ikari H, et al. Involvement of dopamine D2 receptors in complex maze learning and acetylcholine release in ventral hippocampus of rats. Neuroscience. 2001;**103**:27-33

[78] Dujardin K, Blairy S, Defrebve L, et al. Subthalamic nucleus stimulation induces deficits in decoding emotional facial expressions in Parkinson's disease. Journal of Neurological Neurosurgery Psychiatry. 2004;**75**:202-208

[79] Bryson G, Bell M, Lysaker P. Affect recognition in schizophrenia: A function of global impairment or a specific cognitive deficit. Psychiatry Research. 1997;**71**:105-113

[80] Volkmar FR. Pharmacological intervention in autism: Theoretical and practical issues. Journal of Clinical Child Psychology. 2001;**30**:80-87

[81] Rapport LJ, Friedman SR, Tzelepis A, et al. Experienced emotion and affect recognition in adult attention-deficit hyperactivity disorder. Neuropsychology. 2002;**16**:102-110

[82] Backman L, Farde L. Dopamine and cognitive functioning: Brain imaging findings in Huntington's disease and normal aging. Scandinavian Journal of Psychology. 2001;**42**: 2870-2296

[83] Lee MJ, Swann AC, Dafny N. Methylphenidate sensitization is prevented by prefrontal cortex lesion. Brain Research Bulletin. 2008;**76**:131-140

[84] McDowell S, Whyte J, D'Esposito M. Differential effect of a dopaminergic agonist on prefrontal function in traumatic brain injury patients. Brain. 1998;**121**:1155-1164

[85] Powell JH, al-Adawi S, Morgan J, et al. Motivational deficits after brain injury: Effects of bromocriptine in 11 patients. Journal of Neurology, Neurosurgery, and Psychiatry. 1996; **60**:416-421

[86] LaBar KS, Phelphs EA. Arousal-mediated memory consolidation: Role of the medial temporal lobe in humans. Psychological Science. 1998;**9**(6):490-493

[87] Ochsner KN. Are affective events richly recollected or simply familiar? The experience and process of recognizing feelings past. Journal of Experimental Psychology: General. 2000; **129**(2):242-261

[88] Guarnieri RV, Buratto LG, Gomes CFA, Ribeiro RL, deSousa AAL, Stein LM, et al. Haloperidol increases false recognition memory of thematically related pictures in healthy volunteers. Human Psychopharmacology: Clinical and Experimental. 2016;**32**:e2563. DOI: 10.1002/hup.2563

[89] Guarnieri RV, Ribeiro RL, De Souza AA, Galduróz JF, Covolan L, Bueno OFA. Effects of sulpiride on true and false memories of thematically related pictures and associated words in healthy volunteers. Frontiers in Psychiatry. 2016;**7**:28. DOI: 10.3389/fpsyt.2016.00028

[90] Ballard M, Gallo D, de Wit H. Amphetamine increases errors during episodic memory retrieval. Journal of Clinical Psychopharmacology. 2014;**34**:85-92. DOI: 10.1097/ JCP.000 0000000000039

[91] Ballard M, Gallo D, de Wit H. Psychoactive drugs and false memory: Comparison of dextroamphetamine and delta-9-tetrahydrocannabinol on false recognition. Psychopharmacology. 2012;**219**:15-24. DOI: 10.1007/s00213-011-2374-5

[92] Blair RJR, Curran HV. Selective impairment in the recognition of anger induced by diazepam. Psychopharmacology. 1999;**147**:335-338

[93] Huron C, Servais C, Danion JM. Lorazepam and diazepam impair true, but not false, recognition in healthy volunteers. Psychopharmacology. 2001;**155**:204-209. DOI: 10.1007/s00 2130100683

[94] Capek S, Guenther RK. Caffeine's effects on true and false memory. Psychological Reports. 2009;**104**:787-795. DOI: 10.2466/PR0.104.3.787-795

[95] Gallagher DT, Fisk JE, Montgomery C, Judge J, Sarita J, Robinson SJ, et al. Effects of ecstasy/polydrug use on memory for associative information. Psychopharmacology. 2012;**222**: 579-559. DOI: 10.1007/s00213-012-2652-x

[96] Garfinkel SN, Dienes Z, Duka T. The effect of alcohol and repetition at encoding on implicit and explicit false memories. Psychopharmacology. 2006;**188**(4):498-508. ISSN 0033-3158

[97] Milani R,·Curran HV. Effects of a low dose of alcohol on recollective experience of illusory memory. Psychopharmacology. 2000;**147**:397-402

[98] Pernot-Marino E, Danion JM, Hedelin G. Relations between emotion and conscious recollection of true and false autobiographical memories: An investigation using lorazepam as a pharmacological tool. Psychopharmacology. 2004;**175**(1):60-67

[99] Lupien SJ, Fiocco A, Wan N, Maheu F, Lord C, Schramek T, et al. Stress hormones and human memory function across the lifespan. Psychoneuroendocrinology. 2005;**30**:225-242