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# Effect of emotions on learning, memory, and disorders associated with the changes in expression levels: A narrative review

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**Abstract:**

Emotions, in general, have no scientific definition. Emotions can be denoted as the mental state because of the neurophysiological changes. Emotions are related to mood, personality, temperament, and consciousness. People exhibit different emotions in different situations causing changes in cognitive functions. One of the major cognitive functions is the ability to learn, to store the acquired information in the parts of the brain such as the hippocampus, amygdala, cortex, and cerebellum. Learning and memory are affected by different types of emotions. Emotional responses such as fear, depression, and stress have impaired effects on cognitive functions such as learning and memory, whereas optimistic and happy emotions have positive effects on long-term memory. Certain disorders have greater effects on the regions of the brain which are also associated with synaptic plasticity and Learning and Memory(LM). Neuroimaging techniques are involved in studying the changing regions of the brain due to varied emotions and treatment strategies based on the changes observed. There are many drugs, and in advancements, nanotechnology is also utilized in the treatment of such psychiatric disorders. To improve mental health and physical health, emotional balance is most important, and effective care should be provided for people with less emotional quotient and different types of disorders to inhibit cognitive dysfunctions. In this review, emotions and their varied effects on a cognitive function named learning and memory, disorders associated with the defects of learning due to emotional instability, the areas of the brain that are in control of emotions, diagnosis, and treatment strategies for psychiatric disorders dependent on emotions are discussed.

**Keywords:**

Emotions, health care, learning and memory, psychiatric disorders, regions of the brain, synaptic plasticity, treatment

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## Introduction

### Emotions

Emotions are general expressions that exhibit one's feelings. This involves fear, anger, happiness, eroticism, sadness, and tenderness. These all can be understood from the changes in the respiratory level, postural patterns, and facial expressions. Some feedback mechanisms in the brain are associated with changes in different emotions.[1] The influence of emotions in us and also in others refers to emotion regulation. This has become a popular subtopic in psychology, related to cognitive reappraisal, which is all about the thoughts of a person in a situation based on one's own emotions.[2,3] Emotions can also be evoked due to different art forms such as music, poetry, and dance.[4] One of the prevailing studies is the role of poetry in evoking an emotional response. There are different sorts of stimulation in studying the activity. The first sort of stimulation is understanding the natural language which can yield a mind-level model for stimulation. Prosody



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plays an important role in the second sort of stimulation of the emotional response. It helps in mimicking the emotional states of people and their characteristics. In the third sort of stimulation, we consider ourselves as a model and this helps to engage ourselves with the poetry and we start to cherish the emotion which leads to a condition named esthetic emotion.[5] Thus, emotions are involved in our daily activities, and they serve as a model for one's well-being.

### Emotions and regions of the brain

Many types of research are taking place to understand the areas of the brain that are responsible for emotional response, and in one such experiment with animal models, emotional learning and memory, the way emotions modulate memory, and the influence of emotion on attention and perception were studied. It is proven that the amygdala is involved in fear and other emotional activities.[6] The sensory input signals are received by the amygdala and these signals stop at the end of the lateral nucleus (LA). If there is any damage in the LA, it leads to fear conditions. There will be plasticity in the amygdala during the conditioning, and there might be some lesions that cause changes in cognitive functions.[7] There is a theory named the Need-Informational Theory of Emotions which signifies that there are different neural pathways for motivations, emotions, and intuition.[8] Some circuitries are involved in positive and negative emotional responses. The amygdala-neocortical circuitry explicitly shows the immediate consciousness of the implicit processing of emotions and the explicit processing of thoughts that are semantic based and are managed by the hippocampal-neocortical circuitry. The right hemisphere of the brain is responsible for regulating negative emotions. The left hemisphere is responsible for regulating positive emotions. The amygdala which is more involved in fear sensitization may lead to several phobias due to the increased sensitization-associated amygdala activity and these are proved through animal sensitization studies. This shows that there is a direct connection between emotions with learning and memory consolidation.[9]

### Learning and memory

Learning is an activity of acquiring knowledge or information which is followed by storing the acquired information. Memory has been qualitatively differentiated in ways of storing information as declarative and nondeclarative. The categories of memories are formulated according to time, and they are of three classes, immediate memory which can last for seconds, short-term memory which can last for seconds to minutes, and long-term memory which can remain for about days to years.[10] These memories are stored in the form of synaptic connections. There will be a change in the connections of neurons, and the stability of synapses is established to be the mechanism through which the memory is encoded and stored as different types in the regions such as the hippocampus, cortex, amygdala, and cerebellum. This mechanism is defined as the induction of appropriate synapses during the formation of memory, and the storage of information is dependent on the plasticity of synapses.[11] A study was carried out in the laboratory with mammals to monitor synaptic strength and activity-based changes in areas such as the hippocampus, amygdala, prefrontal cortex, and other cortical-related areas during the operant conditioning, and results showed long-term potentiation and striking differences in the localization of the synapses.[12] Plasticity has different forms and it has effects on learning and memory. NMDAR-Long Term Potentiation has effects on spatial learning and olfactory learning. Non-NMDAR-Long Term Potentiation affects working memory. The mGluR-Long-Term Depression affects the classical conditioning of motor responses.[13] Epigenetic mechanisms such as DNA methylation are also involved in regulating memory storage and retrieval, and there will be changes in the methylation of DNA that occur over experience.[14]

In this review, some of the emotion-based disorders have been studied and analyzed for their association with effects on learning and memory. Several treatment strategies and medications for each disease have been discussed and the nano-based approach with various types of nanoparticles that are used in treatment has been discussed in detail.

## Discussion

### Emotions and learning and memory

The emotions that arouse activate the neurobiological system, and this exhibits a major role in developing the strength of memories and reflecting emotional intelligence. The experiences that cause emotions are proven to create long-lasting memories.[15,16] The research was conducted to check the emotional learning affecting the source memory and item memory where trials had Pavlovian fear conditioning. From the results of this experiment, it is clearly understood that both emotional events and emotional learning have a role in the retrieval of memory.[17] Working memory is mainly focused on mood and emotions. The experiments have resulted in an understanding that negative emotions such as sadness, anxiety, and hopelessness have led to difficulty in performing complex tasks and reduced flow of activities, whereas positive emotions such as happiness and enjoyment have led to higher performance of complex tasks and improvement in the flow of activities.[18] Furthermore, stress, an adverse psychological condition, has been shown to either assist or impede learning and memory,

based on its intensity and length. More specifically, light and transient stress improves learning and cognitive ability, whereas excessive and chronic stress degrades learning and memory performance. Hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis causes a variety of deleterious outcomes, including decreased synaptic plasticity and learning ability. Activities that have both positive and negative emotions have several effects on learning and memory storage and retrieval. Emotions also influence retrieval-induced forgetting. In specific, negative mood reverses forgetting since it inhibits the spread of networks of memory that come under retrieval-induced forgetting while positive emotions facilitate and promote retrieval-induced facilitation as they improve the processing of information in relation that underlies facilitation. Therefore, it is understood that positive emotions are useful in learning coherent material and negative emotions to forgetting.[19] Epistemic beliefs play a role in evoking emotions, and it is observed that when the knowledge rendered is controversial, there are harmful effects on learning and performance. Hence, from the studies, it is clear that when there are aligned epistemic beliefs with complex learning tasks, there are positive emotions arousing in the individuals such as curiosity and motivation. On the contrary, the controversial knowledge brought negative emotions such as confusion causing impaired memory and led to the search for new information.[20,21] Serotonin is a neurotransmitter as well as a hormone. This is known for optimism and happiness. This is also involved in the retrieval of memory and forgetting. It is also noted that emotions such as anxiety, sadness, and depression release serotonin, and the drugs are prescribed to control the expression of serotonin which has effects examined in learning and memory.[22] Thus, emotions have a vital role in learning and memory storage and retrieval.

## Interactions of emotions and cognitive functions

The pleasant and unpleasant emotions are encoded in the form of memory by the amygdala. The amygdala is involved in the encoding of memory and the storage of that encoded memory is in the hippocampus.[23] The basolateral complex of the amygdala interacts with the regions of the brain such as the hippocampus, caudate nucleus, nucleus accumbens, and other cortical regions where there is a production of the feedback loop by the amygdala where it transmits signals and activates the cortical regions of the brain. This allows the enhancement of the attention mechanism and improves parallel processing.[24,25] It is also evident that there is an extensive release of adrenal stress hormones during emotional experiences leading to memory encoding following the release of epinephrine and glucocorticoids by activating the β-noradrenergic receptors present in the basolateral complex of the amygdala which consolidates memory of the specific event occurred. Hence, it is proved that memory has modulating effects due to the stress hormones released and the neurotransmitters that are activated due to stress in association with amygdala activation.[26] As a consequence, the impact of different types of stress is critical in the case of learning and memory. The emotions expressed and their regulation are important for enhanced learning.[27] As mentioned earlier, the prefrontal cortex region is observed to have a role in problem-solving, cognitive control, reasoning, and emotional responses. The prefrontal cortex region is interlinked with different regions of the amygdala and medial temporal lobe which have a major part in working memory, long-term memory retrieval, memory encoding, and emotional processing.[28] The prefrontal cortex has Brodmann areas (Brodmann area 11 for processing emotions and 46 for processing cognitive functions that include memory) which have associated cognitive and emotional centers. The anterior prefrontal cortex is involved in cognitive abilities such as problem-solving and reasoning. It also controls the working memory and the emotional activity involved in the control of the social-economic responses and disruption of this region leads to the loss of emotional control over certain situations.[29] Thus, from certain experiments, it is understood that long-term memory has enhanced effects because of pleasant emotions. The learning, memory, and execution of plans are controlled by the medial prefrontal cortex, and the regions of the medial prefrontal cortex are also implicated in the regulation of good and bad emotional responses.[30] Along with that, the orbital frontal cortex of the brain is involved in decision-making and the emotional activity of that region is social and emotional judgment, emotional processing, and responses. The researchers came up with the conclusion that the responses related to sexual arousal occur in the amygdala region, different areas of the prefrontal cortex, and anterior temporal lobe, and there will be an influence of different responses for images and words.[31] Anyway, a broad spectrum of studies showed that there will be differences in lateralization based on sex, mood, sleep, awareness of a person's situation, stress, and many other factors. Thus, these are all the variables that are in consideration for future studies.[32]

## Neuroimaging techniques

The associations of the brain regions about emotions-cognitive functions can be visualized with various imaging tools such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and functional near-infrared spectroscopy (fNIRs). The electrical stimulus and dynamics in the brain regions in response to emotional tasks and cognitive functions can be measured with the use of an electroencephalogram (EEG).[33] Various studies were done by providing certain stimuli and the different regions of the brain were examined. Each of these techniques has its advantages and disadvantages.

The fMRI was taken for the areas of the brain including the amygdala, prefrontal cortex, anterior temporal lobe, and temporo-occipital junction by providing words and pictures as stimuli. This led to the findings that the amygdala and areas of the prefrontal cortex had the same effects on pictures and words. Medial prefrontal cortex was highly activated to appreciative emotions, whereas ventrolateral prefrontal cortex was highly activated to liable emotions. Emotional pictures showed more sensitivity than words.[34] In another study, the faces of different individuals were provided as stimuli and the amygdala was studied based on the changing expression of faces and was recorded with an event-related fMRI. The results exhibited the activation of the amygdala located right side for all the emotional reactions such as fury, fear, and happiness. Therefore, it can be concluded that several other emotions can also be studied with fMRI.[35,36] In a study for assessing high negative emotions, fMRI was obtained for such as depression and anxiety. This had direct effects on the hippocampus and orbitofrontal cortex which results in poor cognition.[37]

The EEG was recorded for different behaviors such as aggressiveness, sadness, and neutrality when emotional film clips were provided as stimuli. The regions associated are the occipital, frontal, and temporal lobes of the brain. High EEG theta waves: aggressive type films in the occipital and frontal regions. EEG alpha waves: attention and habituation.[38]

The event-related potential was recorded in the centroparietal regions of the brain when the sentence stimulus was provided. The emotional verb processing while reading the short sentences was investigated. The results showed effects on late positive complex (LPC) for negative and high-arousal words. Thus, emotion-related words have effects on the regions of the brain.[39]

The auditory cortex in response to different sounds was investigated. The pleasant, unpleasant, and neutral sounds were provided, and response changes were recorded with fNIRs. This showed increased activation for the left and right cortices of auditory nerves in the case of pleasant and unpleasant sounds when compared to neutral sounds.[40]

PET is recorded for emotional self-generation of the varied regions of the brain (hippocampus, cingulate cortex, substantia nigra, and so on.) where emotional processing and cognitive functions can be determined. PET can show better activation in the regions – mesencephalon and brainstem in comparison with the fMRI.[41]

Thus, with the use of different imaging and spectroscopy techniques, the interactions of different brain regions associated with emotions and cognition concerning the stimuli can be observed.

## Emotions and brain disorders

It is evident that emotions have a strong influence on regulating learning and memory, and it has been proved with the use of neuroimaging and neuropsychological techniques. This has provided great insight into several types of disorders that alter learning and memory and change synaptic plasticity. These disorders include posttraumatic stress disorder (PTSD), schizophrenia, major depression disorder, Alzheimer's disease (AD)[42], facial paresis, Kluver–Bucy syndrome, and Schmahmann syndrome. These neuropsychiatric disorders will be further discussed [Figure 1].

### *Posttraumatic stress disorder*

PTSD arises due to the tragic experiences encountered by an individual, and this leads to negative emotions, changes in mood, and hyperarousal symptoms. This is associated with several mental and physical health consequences. Sleep will also be affected leading to drastic effects in the amygdala. The hippocampus of the brain which has a major role in learning and memory undergoes structural and functional changes when affected by PTSD. It might lead to difficulty in the retrieval of memory.[43] To examine the mechanisms that are involved in the development of this disorder, A neuroimaging technique was carried out, and multimodal neuroimaging is one of the techniques used to study the hidden patterns and can be used to investigate the changes in the neural processes and the effects of PTSD. This would be useful for the improvement of therapeutic strategies.[44] For the treatment of PTSD, certain drugs are involved. One such drug is propofol. This is the most widely used anesthetic administered intravenously and shown to have protective effects in human and animal disease models. A study was conducted where the fear memory was examined in which mice were taken and divided into three groups with providing shock as stimuli for the saline group, propofol administered group, and sham control. Those were administered and then investigated for different behavior tests that included a contextual test, Morris water maze test, and a sucrose preference test. Along with that, the hippocampus was also examined for synaptic plasticity, long-term potentiation, and long-term depression. From this study, they have obtained the results that the propofol group shows an improved response and it rescues by reserving the plasticity of synapses in the mice and provided a great insight into the treatment of PTSD.[45]

Drug-assisted psychotherapy is an emerging treatment strategy for PTSD. MDMA (3,4,-methylenedioxymethamphetamine), a potential drug is used for this therapy. This facilitated the user to

recall the fear memories without the overwhelmingly negative effects of such memories.[46]

### *Schizophrenia*

The behavioral disruptions that involve sensorimotor gating deficits, alterations in emotional processing, and cognitive impairments are the characteristics of schizophrenia. There is an observed impairment in attention, concentration, reasoning, and judgment.[47] A study was conducted in which Fifty-seven percent of the patients with schizophrenia and 83% of the control individuals without the schizophrenic condition were shown to display autonomic responsivity during the learning phase of fear, and there was observed increase in skin conductance responses to the stimulus in patients in compared to control. There was no significant difference in the levels of learning deficit between the patients and control subjects in the responder group; however, recalling the memory was significantly worse in the patients with schizophrenia compared to the control subjects. In addition, hallucination was high in the patients and had a link with skin conductance levels in the baseline. Another research suggests that psychosis and schizophrenia are shown to have increased levels of arousal. The discovery of impairment in memory recall in schizophrenic patients who had problem learning raises the possibility that the disorder had been accompanied by a disruption in the brain mechanisms underlying emotional memory.[48] There is a piece of evidence provided by neurotrophins such as Brain Derived Neurotropic factor (BDNF) for the explanation of the framework. In addition, the dopaminergic and gamma-aminobutyric acid (GABA) systems, which are traditionally involved in the pathophysiology of schizophrenia, may be altered by synaptic changes brought on by issues with BDNF production. BDNF plays a major role in regulating learning and memory which causes changes in the molecular and cellular levels of learning and memory. There are some biomarkers at the gene and protein levels that act as a current therapeutic strategy. However, there is no such conclusion to prove that BDNF acts as a main component in this type of illness, starting from neurodegenerative changes to the molecular causes of cognitive failure in schizophrenia patients.[49]

The dopaminergic antagonists and stabilizers, glutamatergic agents, serotonin agents such as lurasidone, GABA allosteric modulators such as benzodiazepines, cholinergic agonists, neuropeptides, and genetic-based approaches such as the coding of a gene named serine racemase are used for treatment. There are certain genes that also play a role which involves DISC1, NOS1, NOS1AP, GRM, Pdxdc1, or ZNF804A that are used as a part of therapy and anti-inflammatory approaches.[50] Antipsychotic drugs play a huge role in schizophrenia treatment, but certain studies have established that the relapsing rate or the reoccurrence of the disease is high and has severe symptoms.[51,52]

### *Major depression disorder*

One of the most crippling illnesses with symptoms such as depression, reduction in interest, and impairment in cognitive function is major depressive disorder (MDD). There is a statistical study that exhibits that one in six people suffer from MDD at a certain level at any stage of their lifetime, where the analysis shows that women experience twice higher as men. Certain environmental situations, sexual assault in childhood, physical problems, or emotional abuse are mainly related to the cause of having MDD.

Brain circuits are being affected and tend to have functional abnormalities due to MDD, leading to changes in the cognitive control network, and causing variations in the brain sizes of brain regions, particularly the hippocampus. In addition, MDD has characteristic abnormalities in the neurobiological stress-responsive systems, such as the immunological systems and the HPA axis.[53]

There is a rough estimation of 37% which is much lower in comparison with other disorders, suggesting that the studies have a comparison based on concordance among monozygotic and dizygotic twins. Although heredity has an equivalent role in depression, some other elements are heritable and have contributing factors to depression. Depression at an early stage with severe symptoms and recurrence is considered to be more heritable than other kinds of depression. Studies were done at the family level that showed the complexity of the traits that have no attribution to a single gene in the case of depression. There is no replication observed in the regions of chromosomes in each family that had been studied for any genetic linkage in the case of depression and there is a presence of loci that are replicated in more studies. There is evidence linking chromosome 15q25-q26 to recurrent, early-onset depression, but the population-attributable risk was minimal.[54]

Drugs such as citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline are selective serotonin reuptake inhibitors (SSRIs); drugs such as maprotiline and trimipramine are tricyclic antidepressants (TCAs); bupropion is a norepinephrine–dopamine reuptake inhibitors, these all are considered to be effective drugs in the treatment of MDD.[55] Antidepressants have certain effects on cytokines for the cure of the disease. The anti-inflammatory properties of selective serotonin and noradrenaline inhibitors, SSRIs, and TCAs are useful in the reduction of depression.[56]

### *Alzheimer's disease*

AD is one of the neurodegenerative diseases that impair memory and lessen the functioning of cognition. Most cases show that dementia leads to AD. AD has a level of

proteinopathy (amyloid and tau) usually incorporated with other age-related diseases that are cerebrovascular disease and Lewy body disease have the complicating effort to create efficient diagnosis techniques and therapeutics for modifying the diseases.[57] According to the amyloid theory, the foremost pathological process in AD is the collection of pathological aspects of Aβ, which are produced by consecutive cleavage of the Amyloid Precursor Protein (APP) by the β- and γ-secretase enzymatic reactions in the brain. This imbalance between Aβ production and Aβ clearance causes AD. It is believed that neurofibrillary tangle production is followed by neuronal damage and neurodegeneration, possibly driven by inflammation.[58] Genetics provides compelling evidence that Aβ plays a key role in disease: all fAD mutations affect Aβ generation and cause a relative overproduction of hazardous forms of amyloid. AD is treated by decreasing APP in the form of a missense mutation (A673T), which causes a permanent reduction in APP breakdown by β-secretase. ApoE and several other risk genes participate in amyloid clearance in sporadic illness.[59,60] In a study with 49 subjects, it was observed that the subjects with AD Stage 1 showed learning disabilities, and long-term memory was affected significantly after 3 months.[61]

The pillars of symptomatic treatment are acetylcholinesterase inhibitors (AChEIs) such as donepezil, galantamine, and rivastigmine, which increase acetylcholine availability by preventing the breakdown of the synapse. The majority of the data for such positive effects of AChEIs are in the mild-to-moderate stage of AD. Memantine is a different symptomatic medication approved to treat less severe levels of AD. Memantine which is a lower-level antagonist of the NMDA receptor aims to decrease the neurotoxicity because of the glutamate without causing any changes in the physiological effects of the molecule. AChEIs and memantine combo therapy are now supported by some data. In moderate-to-severe AD, a current meta-analysis found indications of enhanced behavioral symptoms but minimal evidence of improved cognition with dual therapy. The use of nonpharmacological methods is preferred; these methods include training in person-centered care, music therapy, and communication skills.[62]

### *Facial paresis*

A weakening of emotionally triggered facial movements, such as grinning, combined with natural volitional activation is known as emotional facial paresis (EFP). Unilateral EFP, in addition to postencephalitic parkinsonism, can also be seen associated with lesions of the contralateral supplementary motor region, thalamus, subthalamus, and dorsal midbrain. Volitional facial paresis (VFP) is the term for face muscles that become weak when used voluntarily, yet emotional movements are still there. More frequently than EFP 13, unilateral VFP is more frequently a complication of cortical lesions and subcortical lesions.[63,64] Independently, the fibers named corticopontine control voluntary movement and involuntary smiling emerge from the medial prefrontal cortex and fall through the interior capsule's anterior limb, thalamus, and the brain stem. The network that controls the emotionally triggered facial expressions heavily relies on the mesial temporal lobe, especially the amygdala. To exclude pathology of the focal brain, as, like a stroke, tumor, or multiple sclerosis, EFP is therefore seen as a unique and little-studied neurological symptom that might be included in a clinical evaluation.[65] The patients who recovered from a stroke with facial paresis also show fewer facial emotions and recognition of emotions, and this was assessed by facial feedback hypothesis.[66] The data obtained from meta-analyses of random clinical studies act as support for using glucocorticoid as a therapeutic agent.

The viral theory (HSV type 1 virus reactivation as the etiology) suggests that glucocorticoid and virostatic medication co-treatment may be advantageous. In the acute stage of the condition, decompression surgery is not recommended since there is insufficient evidence to support its benefits and because its risks can be serious.[67]

### *Kluver–Bucy syndrome*

Many people believe that Klüver–Bucy syndrome (KBS) is uncommon and only occurs in those who have bilateral amygdala damage. Several other reasons might be at play, necessitating investigation into the presentation, pathogenesis, prognosis, and treatment of the illness. Damage or malfunction of the hippocampal-amygdaloid complex system and its projections are symptoms of the syndrome. Human KBS does not happen on its own; instead, it usually occurs with amnesia as well as aphasia, and this may also accompany dementia along with seizures and affecting attention.[68] KBS receives a challenging and frequently inadequate level of care.[69] The research was conducted, where animal studies were done to understand the significance of the inadequate impulses, from all of these senses, although the disease was characterized by impairment of intelligence and memory after the adaptation of animals to the current environment. The animals thoroughly investigated, touched, smelt, and tasted, as when inspecting something completely foreign, but far more slowly and thoughtfully even the most familiar objects. Again but, after only a short while, upon discovering the same object, the same examination process would be repeated, as if no memory of it existed and the animals showed impaired memory.[70]

KBS therapy entails a mix of environmental and pharmaceutical interventions and has a variable outcome.

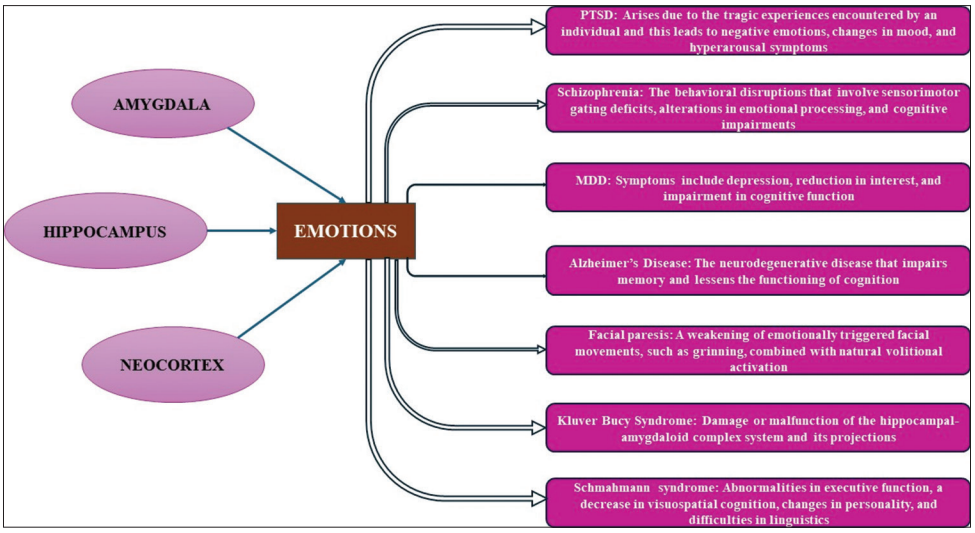


**Figure 1:** Regions of the brain associated with emotions (right) and disorders/diseases related to emotions (left)

In some people with KBS, carbamazepine is helpful. If carbamazepine is ineffective or not recommended, it is worth trying other alleged medication-mood stabilizers such as valproic acid and gabapentin. People with KBS who have suffered a tragic injury in the brain may benefit from medications called SSRIs. Leuprolide and propranolol were used as combinatorial therapy strategies for patients with both KBS and dementia; leuprolide eliminated the latter symptoms. Propranolol decreased linguistic and nonconsensual physical aggression but not sexual aggression or inappropriate behaviors. Many antipsychotic medications, including haloperidol, haloperidol decanoate, and thiothixene, have been tested with varying degrees of success; nevertheless, these medications can occasionally be effective in treating related psychosis and violence.[71]

### *Schmahmann syndrome*

Observable cognitive abnormalities were reported in 20 patients who suffered isolated cerebellar injuries by Schmahmann and Sherman in 1998. The cerebellar cognitive affective syndrome (CCAS), which is found to have abnormalities in executive function, a decrease in visuospatial cognition, changes in personality, and difficulties in linguistics, was introduced by them. This syndrome causes an overall loss in intellectual performance.[72] It is widely believed that CCAS is caused by injury to the pathways of the proximal efferent cerebellum such as the dentate nucleus and superior cerebellar peduncles, which results in a cerebello-cerebellar diaschisis and hypofunction of supratentorial cortical regions. The existence of reverse diaschisis was investigated with single-photon emission computed tomography (SPECT) and perfusion MRI investigations.[73] Ten studies, mostly observational cohorts that included elderly sufferers with isolated cerebellar lesions were found as a consequence of the systematic search. Within a year of diagnosis, neuropsychological testing was conducted on patients and matched them to healthy controls. In a meta-analysis of the 12 assessments used in two or more research, it was discovered that patients with cerebellar dysfunction significantly underperform on phonemic proficiency, semantic language skills, Stroop tests such as naming, reading, and interference, block design test, and WMS-R visual memory tests. Visuospatial, linguistic, and executive function abnormalities are prominent and pertinent in cerebellar patients. Therefore, the analysis that was mentioned highlights the significance of Schmahmann and Sherman and this study described the affecting conditions in the cognitive activities of the cerebellum.[74]

Only when taking the dose of one mg of risperidone, it made the mood and behavior show a noticeable stabilization. 400–800 mg of carbamazepine and aripiprazole (30 mg) are involved in the stabilization of alterations in mood. 50 mg of nortriptyline and valproic acid (1,200 mg) are involved in the stabilization of behavior and attitude. 400 mg of carbamazepine with paroxetine (30 mg) is involved in the stabilization of attitude and conduct. Pipamperone (600 mg ) along with carbamazepine (120 mg) is involved in partial mood and behavior stabilization. Quetiapine (600 mg) helps in the remission of chronic depression symptoms and psychosis (0.8 mmol/L) of lithium helps in the stabilization of attitude and conduct.[75]

## Treatment strategies

Research on medications for neurodegenerative diseases is still ongoing. Even though there are several chemotherapeutic strategies, the proper and complete cure is still in vain. Psychiatric sessions with medical professionals might be a cure in the long term, but the

recurrence of the disease is still possible. To provide an effective cure in the treatment of neuro-based disorders, nano-based therapy has been introduced and research has been done to enhance the effectiveness.

### *Nano-based therapy*

Nanoparticles have the potential to significantly enhance drug delivery by increasing blood–brain barrier (BBB) permeability, pharmacodynamics, and bioavailability. It is believed that nanotechnology will help treat psychiatric diseases more successfully than current medication by combining different treatment techniques. Inorganic nanoparticles, polymeric, and lipid nanocarriers are different types of nanocarriers for which their benefits and drawbacks are highlighted. There are three major categories into which the processes of NPs transit across BBB can be divided:

A stimulus from the bioactive elements on the surface of nanoparticles or the "nano effects" or "nanotoxicity" of nanoparticles causes the BBB to temporarily open. The adsorption of nanocarrier conjugates by BBB makes it easier for the drug to be released from carriers on the cell surface of capillary endothelium cells; this opening encourages drug conjugates' diffusion into the brain tissue. Nanocarriers pass through mechanisms named transcytosis, endocytosis, and exocytosis through the capillary endothelial cells in the brain, drugs can directly penetrate brain tissue, increasing the drug's concentration gradient and promoting diffusion into the brain.[76]

On account of great biocompatibility and less toxicity, Poly Lactic Acid and poly (lactic-co-glycolic acid)-based nanoparticles have been developed to serve as an alternate route for delivering medications to the brain. Various synthetic processes, such as emulsification, evaporation, solvent replacement, and solvent diffusion, were used for the preparation of nanoparticles. Their sizes range from 100 to 200 nm, and they are biodegradable.

Polymer nanoparticles pass through the BBB across endocytosis. Polymer nanoparticles have been demonstrated to improve drug delivery to the brain in *in vitro* investigations. For instance, curcumin administration is more efficient at lowering plaque load, oxidative stress, and inflammation.[77]

Monodisperse symmetrical macromolecules called dendrimers have an inner nucleus surrounded by a succession of branching blocks. Dendrimers have a spherical structure that is made up of a central core, layers of repetitive, branched building blocks, and an outer layer with functional end groups. Dendrimers that include polyamidoamine are the most frequently employed for treating brain disorders. One study looked at the application of encapsulated carbamazepine, an antiepileptic medication, to treat AD.[78]

Amphiphilic block copolymers make micelles. They combine in aquatic solutions to create stable, hydrophobic-cored spheroidal nanostructures with hydrophilic surfaces. The micelles are effective drug delivery systems for the brain. This is made feasible by the hydrophobic nucleus area's ability to dissolve poorly soluble compounds and its capacity to combine with specific target ligands. Liposomes, solid lipid nanoparticles (SLNs), nanoemulsions, and exosomes are lipid-based nanoparticles.

A spherical-shaped nanostructure along with the lipid bilayer is the primary characteristic of the class of nanostructures known as liposomes. The range of ideal diameters is 100–200 nm. Doxil, a liposome-based formulation, was the first Food and Drug Administration (FDA)-approved nano-drug in 1995.[79] High biocompatibility, biodegradability, increased bioavailability, and stability of medicines are often characteristics of liposomes. They can also alter the surfaces to allow for active targeting. The structure of nanoparticles enables the insertion of supplementary lipids like cholesterol or dioleoylphosphatidylethanolamine (DOPE). When DOPE is exposed to low pH, it can conjugate with other lipids, which increases the efficiency of loading into the cytosol and favors the formation of endosomes.[80] Liposomes are altered to target transcytosis via the central nervous system endothelium by adding biologically active ligands to the liposomal surface, such as peptides, antibodies, or small molecules. Another technique for changing the liposomal surface is G-Technology® (technology authorized by the FDA). It is a method for employing glutathione-PEGylated liposomes, which can attach to glutathione transporter.[81]

SLNs are hydrophile–lipophile-balanced bioactive compounds that are stable nanoscale suspensions of physiologically suitable lipids such as triglycerides, fatty acids, or waxes. Nanoemulsions, which are stabilized by surfactants, are composed of heterogeneity in dispersions of the compositions "oil in water" or "water in oil." In such nanosystems, the interior phase's diameter is scaled down to the nanometer. Drugs delivered by nanoemulsions enter cells by receptor-mediated endocytosis. The advantage of those nanoemulsions for BBB penetration over other nanocarriers is their capacity to use secure oils. In addition, because these oils contain necessary omega-3 as well as omega-6 acids, the use of these nanoparticles has several beneficial biological features.[82]

Solid nanoparticles made of silicon dioxide, carbon nanotubes, metal, or metal oxide are known as inorganic nanoparticles. They are coated with a variety of polymers, including polysaccharides, polyacrylamide, poly(vinyl alcohol), poly(N-vinyl-2-pyrrolidone), PEG, and copolymers including PEG, to help them penetrate the BBB. PEG is the covering polymer that is most frequently utilized. These surface alterations increase the stability of nanoparticles, increase water solubility, and enable vector molecules to modify the particle surface. Inorganic nanoparticles also have their physical characteristics altered to maximize their penetration through the BBB in addition to chemical alteration. $Fe_3O_4$ nanoparticles, for instance, show that they can become magnetized because of the magnetic field that exists. It has been demonstrated that human brain microvascular endothelial cells can be crossed by superparamagnetic iron oxide nanoparticles that comprise magnetite ($Fe_3O_4$) and maghemite (c-$Fe_2O_3$). Gold nanoparticles can cross the BBB and be supplied for therapy for neuropsychiatric disorders in addition to iron nanocarriers.[83]

## Conclusion

Emotions that are denoted as the mental state are because of neurophysiological changes. Different kinds of emotions that are expressed about mood, personality, temperament, and consciousness have several effects on different regions of the brain. Different emotions based on different situations are exhibited, and this leads to changes in cognitive functions. One of the major cognitive functions is the ability to learn and to store the acquired information in the areas of the brain like the hippocampus, amygdala, cortex, and cerebellum. Learning and memory are affected by different types of emotions. Emotional responses such as fear, depression, and stress have impaired effects on cognitive functions such as learning and memory, whereas some other emotions have some positive effects on long-term memory. Certain disorders have greater effects on the regions of the brain which are also associated with synaptic plasticity and LM and some of those disorders were discussed along with their current treatment strategies. Neuroimaging techniques are involved in studying the changing regions of the brain due to varied emotions and the treatment strategies are carried out based on the changes observed which need to be improved for the welfare of people. There are many drugs, and in advancements, nanotechnology is also utilized in the treatment of such psychiatric disorders. In this review, emotions and their varied effects on a cognitive function named learning and memory, disorders associated with the defects of learning due to emotional instability, the areas of the brain that are by emotions, diagnosis, and treatment strategies for psychiatric disorders dependent on emotions were discussed.

### Ethical statement
Not applicable.

### Data availability statement
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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### Conflicts of interest
There are no conflicts of interest.

## References

1. Kalawski JP. The Alba Method and the Science of Emotions. Integrative Psychological and Behavioral Science 2020;54: 903–19.
2. McRae K, Gross JJ. Emotion regulation. Emotion 2020;20:1-9.
3. Dennison J. Emotions: functions and significance for attitudes, behaviour, and communication. Migration Studies 2024;12: 1-20.
4. Zaidel DW. Art and brain 2013. p. 217-33. doi: 10.1016/B978-0-444-63287-6.00011-7.
5. Johnson-Laird PN, Oatley K. How poetry evokes emotions. Acta Psychologica 2022;224:103506. doi: 10.1016/j.actpsy.2022.103506.
6. Phelps EA, LeDoux JE. Contributions of the amygdala to emotion processing: From animal models to human behavior. In Neuron 2005;48:175-87.
7. LeDoux J. The emotional brain, fear, and the amygdala. Cellular and Molecular Neurobiology 2003;23:727-38.
8. Simonov PV. Brain mechanisms of emotions. Neuroscience and Behavioral Physiology 1997;27:405-13.
9. Min J, Nashiro K, Yoo HJ, Cho C, Nasseri P, Bachman SL, *et al*. Emotion Downregulation Targets Interoceptive Brain Regions While Emotion Upregulation Targets Other Affective Brain Regions. The Journal of Neuroscience 2022;42:2973-85.
10. Squire LR. Memory systems of the brain: A brief history and current perspective. Neurobiology of Learning and Memory 2004;82:171-7.
11. Martin SJ, Grimwood PD, Morris RGM. Synaptic Plasticity and Memory: An Evaluation of the Hypothesis. Annual Review of Neuroscience 2000;23:649-711.
12. Barco A, Brambilla R, Rosenblum K. Editorial. Neurobiology of Learning and Memory 2015;124:1-2.
13. Baudry M. Synaptic Plasticity and Learning and Memory: 15 Years of Progress. Neurobiology of Learning and Memory 1998;70:113-8.
14. Abel T, Klann E. Molecular and cellular cognition: Neurobiology of Learning and Memory Special Issue 2013. Neurobiology of Learning and Memory 2013;105:1-2.
15. McGaugh JL. Consolidating Memories. Annual Review of Psychology 2015;66:1-24.
16. Kensinger EA. Remembering the Details: Effects of Emotion. Emotion Review 2009;1:99-113.
17. Hennings AC, Lewis-Peacock JA, Dunsmoor JE. Emotional learning retroactively enhances item memory but distorts source attribution. Learning and Memory 2021;28:178-86.
18. Pekrun R. Emotions as Drivers of Learning and Cognitive Development. In New Perspectives on Affect and Learning Technologies. Springer New York. 2011. p. 23-39. doi: 10.1007/978-1-4419-9625-1_3.
19. Pekrun R. Emotions as Drivers of Learning and Cognitive Development. In New Perspectives on Affect and Learning Technologies. Springer New York. 2011. p. 23-39. doi: 10.1007/978-

1-4419-9625-1_3.
20. Lewandowsky S. Future Global Change and Cognition. Topics in Cognitive Science 2016;8:7-18.
21. Trevors GJ, Muis KR, Pekrun R, Sinatra GM, Muijselaar MML. Exploring the relations between epistemic beliefs, emotions, and learning from texts. Contemporary Educational Psychology 2017;48:116-32.
22. Meneses A, Liy-Salmeron G. Serotonin and emotion, learning and memory. Reviews in the Neurosciences 2012;23:543-53.
23. Richter-Levin G, Akirav I. Amygdala-Hippocampus Dynamic Interaction in Relation to Memory. Molecular Neurobiology 2000;22:011–020.
24. Amaral DG, Behniea H, Kelly JL. Topographic organization of projections from the amygdala to the visual cortex in the macaque monkey. Neuroscience 2003;118:1099-120.
25. Vuilleumier P. How brains beware: neural mechanisms of emotional attention. Trends in Cognitive Sciences 2005;9:585-94.
26. McGaugh JL, Roozendaal B. Role of adrenal stress hormones in forming lasting memories in the brain. Current Opinion in Neurobiology 2002;12:205-10.
27. Vogel S, Schwabe L. Learning and memory under stress: implications for the classroom. Npj Science of Learning 2016;1:16011. doi: 10.1038/npjscilearn.2016.11.
28. Blumenfeld RS, Ranganath C. Prefrontal Cortex and Long-term Memory Encoding: An Integrative Review of Findings from Neuropsychology and Neuroimaging. The Neuroscientist 2007;13:280-91.
29. Volman I, Roelofs K, Koch S, Verhagen L, Toni I. Anterior Prefrontal Cortex Inhibition Impairs Control over Social Emotional Actions. Current Biology 2011;21:1766-70.
30. Etkin A, Egner T, Kalisch R. Emotional processing in anterior cingulate and medial prefrontal cortex. Trends in Cognitive Sciences 2011;15:85-93.
31. Pegna AJ, Khateb A, Lazeyras F, Seghier ML. Discriminating emotional faces without primary visual cortices involves the right amygdala. Nature Neuroscience 2005;8:24-5.
32. Palomero-Gallagher N, Amunts K. A short review on emotion processing: a lateralized network of neuronal networks. Brain Structure and Function 2022;227:673-84.
33. Tyng CM, Amin HU, Saad MNM, Malik AS. The influences of emotion on learning and memory. In Frontiers in Psychology Frontiers Media S.A. 2017;8. doi: 10.3389/fpsyg.2017.01454.
34. Kensinger EA, Schacter DL. Processing emotional pictures and words: Effects of valence and arousal. Cognitive, Affective, & Behavioral Neuroscience 2006;6:110-26.
35. Pegna AJ, Khateb A, Lazeyras F, Seghier ML. Discriminating emotional faces without primary visual cortices involves the right amygdala. Nature Neuroscience 2005;8:24-5.
36. Liu C, Wang Y, Sun X, Wang Y, Fang F. Decoding six basic emotions from brain functional connectivity patterns. Science China Life Sciences 2023;66:835-47.
37. Zhang L, Bai Y, Cui X, Cao G, Li D, Yin H. Negative emotions and brain: Negative emotions mediates the association between structural and functional variations in emotional-related brain regions and sleep quality. Sleep Medicine 2022;94:8-16.
38. Krause CM, Viemerö V, Rosenqvist A, Sillanmäki L, Åström T. Relative electroencephalographic desynchronization and synchronization in humans to emotional film content: an analysis of the 4–6, 6–8, 8–10 and 10–12 Hz frequency bands. Neuroscience Letters 2000;286:9-12.
39. Bayer M, Sommer W, Schacht A. Reading emotional words within sentences: The impact of arousal and valence on event-related potentials. International Journal of Psychophysiology 2010;78: 299-307.
40. Plichta MM, Gerdes ABM, Alpers GW, Harnisch W, Brill S, Wieser MJ, *et al*. Auditory cortex activation is modulated by emotion: A functional near-infrared spectroscopy (fNIRS) study. NeuroImage 2011;55:1200-7.
41. Choudhary M, Kumar A, Tripathi M, Bhatia T, Shivakumar V, Beniwal RP, *et al*. F-18 fluorodeoxyglucose positron emission tomography study of impaired emotion processing in first-episode schizophrenia. Schizophrenia Research 2015;162:103-7.
42. Dere E, Pause BM, Pietrowsky R. Emotion and episodic memory in neuropsychiatric disorders. Behavioral Brain Research 2010;215:162-71.
43. Wang Z, Zhu H, Yuan M, Li Y, Qiu C, Ren Z, *et al*. The resting-state functional connectivity of amygdala subregions associated with post-traumatic stress symptom and sleep quality in trauma survivors. European Archives of Psychiatry and Clinical Neuroscience 2021;271:1053-64.
44. Harnett NG, Goodman AM, Knight DC. PTSD-related neuroimaging abnormalities in brain function, structure, and biochemistry. Experimental Neurology 2020;330:113331.
45. Niu W, Duan Y, Kang Y, Cao X, Xue Q. Propofol improves learning and memory in post-traumatic stress disorder (PTSD) mice via recovering hippocampus synaptic plasticity. Life Sciences 2022;293. doi: 10.1016/j.lfs.2022.120349.
46. Sessa B. MDMA and PTSD treatment. Neuroscience Letters 2017;649:176-80.
47. Lewis DA, Lieberman JA. Catching Up on Schizophrenia. Neuron 2000;28:325-34.
48. Holt DJ, Lebron-Milad K., Milad MR, Rauch SL, Pitman RK, *et al*. Extinction Memory Is Impaired in Schizophrenia. Biological Psychiatry 2009;65:455-63.
49. Nieto R, Kukuljan M, Silva H. BDNF and schizophrenia: From neurodevelopment to neuronal plasticity, learning, and memory. In Frontiers in Psychiatry 2013;4. doi: 10.3389/fpsyt.2013.00045.
50. Yang A, Tsai SJ. New Targets for Schizophrenia Treatment beyond the Dopamine Hypothesis. International Journal of Molecular Sciences 2017;18:1689.
51. de Boer JN, Voppel AE, Brederoo SG, Wijnen FNK, Sommer IEC. Language disturbances in schizophrenia: the relation with antipsychotic medication. Npj Schizophrenia 2020;6:24.
52. Kim J, Ozzoude M, Nakajima S, Shah P, Caravaggio F, Iwata Y, *et al*. Insight and medication adherence in schizophrenia: An analysis of the CATIE trial. Neuropharmacology 2020;168:107634. doi: 10.1016/j.neuropharm.2019.05.011.
53. Wang K, Hu Y, Yan C, Li M, Wu Y, Qiu J, *et al*. Brain structural abnormalities in adult major depressive disorder revealed by voxel- and source-based morphometry: evidence from the REST-meta-MDD Consortium. Psychological Medicine 2023;53:3672-82.
54. Belmaker RH, Agam G. Major Depressive Disorder. New England Journal of Medicine 2008;358:55-68.
55. Kupfer DJ, Frank E, Phillips ML. Major depressive disorder: new clinical, neurobiological, and treatment perspectives. The Lancet 2012;379:1045-55.
56. Mosiołek A, Pięta A, Jakima S, Zborowska N, Mosiołek J, Szulc A. Effects of Antidepressant Treatment on Peripheral Biomarkers in Patients with Major Depressive Disorder (MDD). Journal of Clinical Medicine 2021;10:1706.
57. DeTure MA, Dickson DW. The neuropathological diagnosis of Alzheimer's disease. Molecular Neurodegeneration 2019;14:32.
58. Scheltens P, de Strooper B, Kivipelto M, Holstege H, Chételat G, Teunissen CE, *et al*. Alzheimer's disease. The Lancet 2021;397:1577-90.
59. Jonsson T, Atwal JK, Steinberg S, Snaedal J, Jonsson PV, Bjornsson S, *et al*. A mutation in APP protects against Alzheimer's disease and age-related cognitive decline. Nature 2012;488:96-9.
60. Trejo-Lopez JA, Yachnis AT, Prokop S. Neuropathology of Alzheimer's Disease. Neurotherapeutics 2022;19:173-85.
61. Tort-Merino A, Valech N, Peñaloza C, Grönholm-Nyman P, León M, Olives J, *et al*. Early Detection of Learning Difficulties when Confronted with Novel Information in Preclinical Alzheimer's Disease Stage 1. Journal of Alzheimer's Disease

2017;58:855-70.
62. Lane CA, Hardy J, Schott JM. Alzheimer's disease. European Journal of Neurology 2018;25:59-70.
63. Hopf HC, Hopf NJ. Localization of emotional and volitional facial paresis. Neurology 1992;42:1918.
64. Blom S S, Aarts H, Kunst HP, Wever CC, Semin GR. Facial emotion detection in Vestibular Schwannoma patients with and without facial paresis. Social Neuroscience 2021;16:317-26.
65. Miele G, Lavorgna L, Marrapodi MM, Abbadessa G. Emotional facial palsy: an unusual and rarely explored neurological sign. Neurological Sciences 2022;43:6305-7.
66. Kuttenreich AM, von Piekartz H, Heim S. Is There a Difference in Facial Emotion Recognition after Stroke with vs. without Central Facial Paresis? Diagnostics 2022;12:1721.
67. Heckmann JG, Urban PP, Pitz S, Guntinas-Lichius O, Gágyor I. The Diagnosis and Treatment of Idiopathic Facial Paresis (Bell's Palsy). Deutsches Ärzteblatt International 2019. doi: 10.3238/arztebl.2019.06924].
68. Ruiz-García RG, Chacón-González J, Bayliss L, Ramírez-Bermúdez J. Neuropsiquiatría del síndrome de Susac: a propósito de un caso. Revista Colombiana de Psiquiatría 2021;50:146-51.
69. Caro MA, Jimenez XF. Mesiotemporal Disconnection and Hypoactivity in Klüver-Bucy Syndrome. The Journal of Clinical Psychiatry 2016;77:e982–8.
70. Sharpey-Schäfer EA. Royal College of Surgeons of England. Experiments on special sense localisations in the cortex cerebri of the monkey. In Medical Heritage Library. [Printed by William Clowes and Sons]. 1888.
71. Lanska DJ. The Klüver-Bucy Syndrome 2018.p.77-89. doi: 10.1159/000475721.
72. Gok-Dursun E, Gultekin-Zaim OB, Tan E, Unal-Cevik I. Cognitive impairment and affective disorder: A rare presentation of cerebellar stroke. Clinical Neurology and Neurosurgery 2021;206:106690. doi: 10.1016/j.clineuro.2021.106690.
73. Schmahmann J. The cerebellar cognitive affective syndrome. Brain 1998;121:561-79.
74. Ahmadian N, van Baarsen K, van Zandvoort M, Robe PA. The Cerebellar Cognitive Affective Syndrome—a Meta-analysis. The Cerebellum 2019;18:941-50.
75. Egger JI, Zwanenburg RJ, van Ravenswaaij-Arts CM, Kleefstra T, Verhoeven WM. Neuropsychological phenotype and psychopathology in seven adult patients with Phelan-McDermid syndrome: implications for treatment strategy. Genes, Brain and Behavior 2016;15:395-404.
76. Li X, Tsibouklis J, Weng T, Zhang B, Yin G, Feng G, *et al*. Nanocarriers for drug transport across the blood–brain barrier. Journal of Drug Targeting 2017;25:17-28.
77. Mathew A, Fukuda T, Nagaoka Y, Hasumura T, Morimoto H, Yoshida Y, *et al*. Curcumin Loaded-PLGA Nanoparticles Conjugated with Tet-1 Peptide for Potential Use in Alzheimer's Disease. PLoS ONE 2012;7:e32616.
78. Igartúa DE, Martinez CS, Temprana CF, Alonso S, Del V, Prieto MJ. PAMAM dendrimers as a carbamazepine delivery system for neurodegenerative diseases: A biophysical and nanotoxicological characterization. International Journal of Pharmaceutics 2018;544:191-202.
79. Barenholz Y. (Chezy). Doxil® — The first FDA-approved nano-drug: Lessons learned. Journal of Controlled Release 2012;160:117-34.
80. Hattori Y, Suzuki S, Kawakami S, Yamashita F, Hashida M. The role of dioleoylphosphatidylethanolamine (DOPE) in targeted gene delivery with mannosylated cationic liposomes via the intravenous route. Journal of Controlled Release 2005;108:484-95.
81. Lindqvist A, Rip J, van Kregten J, Gaillard PJ, Hammarlund-Udenaes M. *In vivo* Functional Evaluation of Increased Brain Delivery of the Opioid Peptide DAMGO by Glutathione-PEGylated Liposomes. Pharmaceutical Research 2016;33:177-85.
82. Tapeinos C, Battaglini M, Ciofani G. Advances in the design of solid lipid nanoparticles and nanostructured lipid carriers for targeting brain diseases. Journal of Controlled Release 2017;264:306-32.
83. Frigell J, García I, Gómez-Vallejo V, Llop J, Penadés S. 68 Ga-Labeled Gold Glyconanoparticles for Exploring Blood–Brain Barrier Permeability: Preparation, Biodistribution Studies, and Improved Brain Uptake via Neuropeptide Conjugation. Journal of the American Chemical Society 2014;136:449-57.