EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Coden USA: EJBPBO
Volume: 12
Issue: 11
Year: 2025

DECODING AMNESIA: NEURAL MECHANISMS, ANIMAL MODELS, AND TRANSLATIONAL INSIGHTS

***Shalini Sharma, [1]Dr. Deovrat Kumar**

*College of Pharmacy Roorkee(Haridwar Unuiversity).
[1]Roorkee College of Pharmacy Roorkee.

***Corresponding Author: Dr. Deovrat Kumar**

College of Pharmacy Roorkee(Haridwar Unuiversity)

DOI: https://doi.org/10.5281/zenodo.17473913

How to cite this Article: *Shalini Sharma, 1Dr. Deovrat Kumar. (2025). Decoding Amnesia: Neural Mechanisms, Animal Models, And Translational Insights. European Journal of Biomedical and Pharmaceutical Sciences, 12(11), 19–32.

Article Received on 28/09/2025 **Article Revised on 18/10/2025** **Article Published on 01/11/2025**

ABSTRACT

Amnesia is a multifactorial neurological disorder that is marked by loss in encoding, consolidation, and retrieving memories. This review examines the clinical subtypes of amnesia- such as anterograde, retrograde, transient global and dissociative amnesia-and the neural basis underlying these subtypes especially the hippocampus, medial temporal lobe and the network of associated cortices. We emphasize such important molecular processes as the disruption of synaptic plasticity, the neurotransmitter imbalance, and neuro inflammatory signalling. The animal models have played an invaluable role in explaining the pathophysiology of amnesia. CREB, BDNF, and NMDA receptor pathway models Chemically induced models (e.g., scopolamine, muscimol) and genetic manipulations have provided important understanding of the dysfunction of memory and therapeutic targets. Rodent and zebrafish models can be used to complement each other in the study of molecular cascades and behavioural phenotypes. The cross-species comparisons are highlighted in order to increase translational relevance, to make the difference between preclinical results and human clinical outcomes. New treatment options, such as pharmaceutical intervention, neuromodulation and gene therapy, are addressed in terms of mnemonic recovery. This review aim to cover the horizon of animal models used to study amnesia and its related complication.

KEYWORDS: Amnesia, muscimol, Phenotypes, neuroinflammatory, therapeutics.

Memory and Learning

Ayurveda defines intelligence as a mixture of three mental faculties: (a) gathering and analysing knowledge, (b) retaining that information and (c) recalling that information. However, the degree of readiness of these mental facilities does not always remain constant. For a variety of reasons, memory might deteriorate over time. The intelligence mainly depends upon the memory and the learning ability of brain. [1] Learning and memory are crucial processes. Learning is the process of modification within the behaviour of an organism by acquiring new knowledge or characteristics. Memory is the process by which knowledge is stored for future use and retrieval. It is important to retain information for immediate use, to form learning process easier and to retain learned material for a protracted time.[2] As the findings on the learning and memory enhancing, there were establishment of factors and disease that affecting the brain badly. The effect produce by these factors affects the person in such a way that the person is unable to recall some events and sometime he may completely lost his presence with surrounding world.[3] These factors cause the abnormalities in brain and recognizing behaviour, which is associated with involvement of neuronal discharge of impulses. The majority of recognizing behaviour of brain occurs inside Hippocampus. Whenever there is disorders in brain there will be an imbalance of neurohumoral transmission. This imbalance often associated with other factors, which triggers either pre synaptic transmission or post synaptic transmission.[4]

Types of neurons associated with memory and learning disorders

Various types of neurons affected by the disorders of brain cells with respect to learning are as follow

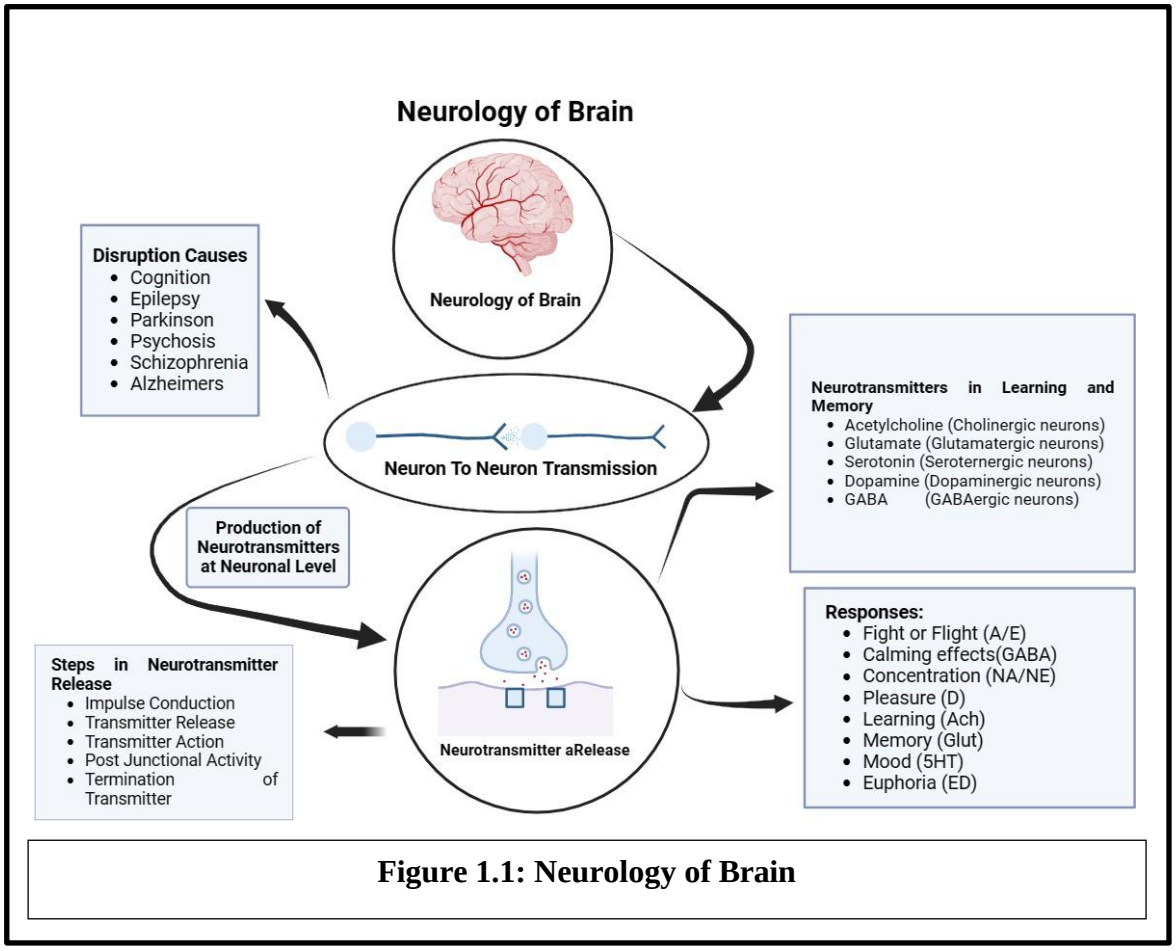


Figure 1.1: Neurology of Brain

Process of Learning and Memory

There are four stages of learning and memory which plays magnificent role in memorizing all kind of information which is stored in brain as showed in fig. 1.2. The major parts of brain which involved in these processes are Hippocampus, Prefrontal cortex and Cortex as showed in Fig. 1.3.[5]

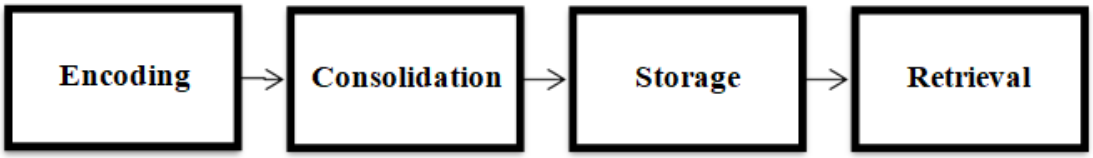


Figure 1.2: Process of Learning in Normal

The process of learning involve **Encoding** (first stage of learning process which occurs in prefrontal cortex by which individual recognize any object by sense).**Consolidation** (second stage of learning which occurs in Hippocampus by which it encoded information linked to existing memory), **Storage** (third stage which occurs in cortex part of brain).**Retrieval** (forth and most important stage in which occurs in three brain regions (prefrontal cortex, Hippocampus and

If there is any interruption in process of learning, it can lead to neurodegenerative disorder because learned information which is stored in memory are linked with these processes. Whenever there are any Neurodegenerative disorders they affect the whole process directly or indirectly by which mentally disabled person are not socializing due to unrecognized environment.[6]

Cognitive State or Memory Loss

Recognition abnormality of braindue to brain trauma, stroke, tumour, depression, etc is termed as a Cognitive state which includes temporary or permanent deficits. Cognitive state is often termed as amnesia which was taken from ancient Greek term "Forgetfulness". This can impair daily activities of patient and also burdens to theassociated caretakers.[7] Memory loss always associated with major risk so, it is very important to understand the molecular mechanism of Learning and memory. The studies available on learning and memory shows, whenever our brain is learning the information is passed by regulation of tuning in neural network. These information's then stored as in form of memory in our hippocampus.[8]

Amnesia

Amnesia is neurological disorders in which patient experience memory loss. The disease may arise due to physical cause, such as an injury, infection, or other trauma that impairs brain function. Amnesia often arises from oxidative stress that impairs neuron functions. Along with cognitive decline patients also experiences behavioural and psychological related disorders such as psychosis, aggression, agitation, and depression. These symptoms are related to dementia.[9]

Depending on the cause, amnesia can be temporary in which the patient eventually regains lost memories and have the ability to create new memories. If Amnesia is caused by physical damage to the brain, the memory loss may be permanent. Amnesia and dementia are different but sometime the term used together which is irrelevant because dementia associated with memory loss but patient also suffers from other cognitive problems which are not seen in Amnesia.[10]

Neurology of Amnesia

learning and memory processes have the exact mechanism ofstructural and functional modification of neurons . The alteration of signal transmission describes the stability of excitatory synapses to activity driven for long lasting changes. These alteration can be classified either long term potentiation (LTP) or long term depression (LTD). If the alteration of neuronal signalling lasts longer than usual, the symptoms associated with memory loss will started to appear. In neurons the dendrites play majority of role in neurohummoral transmission.[11]

The dendrites activity in its function is regulated by actin cytoskeleton. The actin cytoskeleton is essential for neurohummoral transmission from pre synaptic cleft to post synaptic cleft. Usually in normal cases when the impulse is generated, it is passed from one neuron to other. However there is a small gap between the neuron known as junction or synapse. When the impulse reaches to the end of neuron there is release of chemical mediators known as neurotransmitters. These neurotransmitters than binds to post synaptic neuron. In case of Cognitive deficit the whole process is interrupted either by internal factor such as Oxidative stress or by external factors.[12]

Cognitive deficit in Amnesia is linked with many factors which include Nogo-A, deregulation of acetylcholine or hyper activation of cholinesterase.[13] Most interestingly, actin polymerization is regulated by many molecules and Nogo-A is the recently identified candidate molecule. It plays a vital role within the regulation of filamentous-actin dynamics. Studies on Nogo-A started within the year 1988 by Caroni and Schwab and it was identified as a neurite outgrowth inhibitory protein.[14] Subsequent reports showed its involvement in other brain functions like brain development and synaptic plasticity. Its expression has been detected in plastic regions of the brain- cerebral mantle and hippocampus. It's down-regulation during both activity induced neuronal activity or drug induced neuronal activity. When this protein is over-expressed, memory is impaired.[15]

In hippocampal slice culture, if this protein is externally supplied, decrease in dendritic spine density which leads to decrease in LTP. Conversely, when function blocking antibody is applied to hippocampal slices, increase in dendritic spine density leads to increase LTP is reported. Additionally, Nogo-A has been studied in memory related brain disorders like Alzheimer's disease. These studies suggested that the role of Nogo-A in memory and related disorders, though its involvement in amnesia and memory recovery, is still unknown.[16]

To study the molecular mechanism of amnesia and its recovery, animal models with disrupted cholinergic neurotransmission are commonly used. Scopolamine induced amnesic model is frequently used model to check amnesia.[17] Scopolamine is an alkaloid derived from plants of Solanaceae family like Belladonna, Mandrake, Datura and Henbane. it's non-selective muscarinic receptor antagonist that blocks the results of acetylcholine, impairs LTP and induces amnesia in mammals as is revealed by several behavioral paradigms including water maze, passive avoidance latency test, novel visual perception test, etc.[18]

The recent focus of researchers is to unfold the molecular mechanism of amnesia using animal models and determine the recovery approaches. The use of muscarinic antagonist scopolamine hydrobromide for generating amnesic rodent models became popular after the postulation of cholinergic hypothesis for memory dysfunction.[19]

Genrally age-related decline in cognitive functions is primarily because of the decrease within the integrity of cholinergic neurotransmission. Scopolamine-induced amnesic condition is analogous to those occurring during neurodegenerative pathologies like Alzheimer disease (AD). On the other hand, synaptic

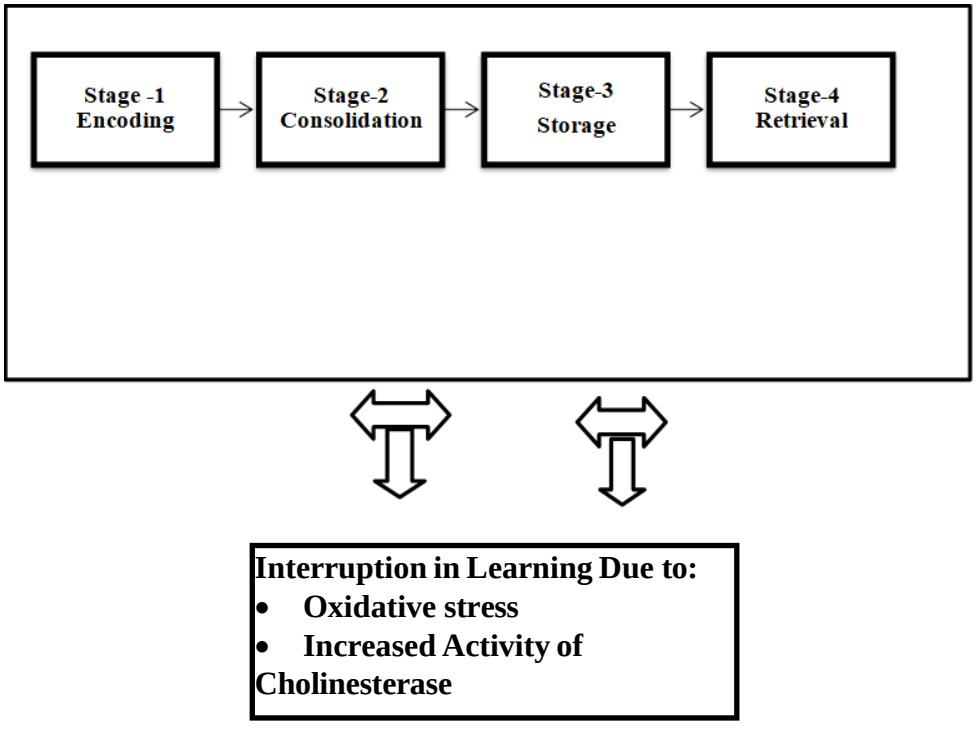
plasticity is integral to memory formation and exhibits changes within the expression of huge numbers of molecules, multitude of intracellular signalling cascades, synaptic strength and neural networks and provides essence to the individual existence.[20] Interestingly, numerous studies have implicated the importance of acetylcholine in higher brain functions like learning and memory. Acetylcholine level is under the dynamic regulation of an enzyme AChE at the synapse. Alterations within the acetylcholine metabolism are also involved in various neuropathological conditions like mild cognitive impairment (MCI), AD and dementia. Decreased levels of acetylcholine at the synaptic cleft are implicated within the loss of synaptic architecture resulting in state of amnesia in rodents.[21]

Stages of Amnesia

The memory loss involved in amnesia is often started in brain with the learning stages specifically stage 2,3 and stage 4. Stage 2 includes the consolidation part of memory which can be impaired either by head injury or by disruption in cholinergic neurons by which individual are unable to recall existing memory in hippocampus. Stage 3 includes Storage which is impaired by oxidative stress and it can be associated due to loss of cholinergic neurons. It is occurs in cortex in which usually the unwanted information is removed in normal but in amnesic patient they were unable to recognize what is important and what is not. The process of learning complete at stage 4 which is retrieval. In this all the stages of learning is repeated in prefrontal Cortex, Hippocampus and in Cortex which have important role in learning. In amnesic patient the first 2 stages are impaired which ultimately leads to interruption of stage 4[22]

These interruptions are due to

- **Oxidative stress:** In our body there are many enzymes which performs there specified work as per there nature so, in case of stress condition there is question about cell survivality. The oxidative stress involves various enzymes such as activity of superoxide dismutase, catalase, glutathione peroxidase and lipid peroxidase.[23]
- **Increased Activity of Cholinesterase:** The acetylcholine is the main neurotransmitter in involved in memory and learning. Whenever there is impulse generation in learning and memory the Acetyl CoA is binded with choline to form Acetylcholine which is stored in vesicles then released to synapse.[24] The Acetylchloline binds to M_1-M_5in postsynaptic neuron. After the completion of process the excess of Acetylcholine is taken by cholinesterases which hydrolyse it to Choline+ Acetate. In case of low acetylcholine production and more cholinesterase activity the neurohumoral transmission is interrupted which further impairs the learning and recognizing ability.[25]
- **Interruption by Nogo-A in Neurohummoral Transmission:** The studies showed that in brain there is a protein involved in storage and consolidation stage. When the interruption of Nogo-A is less it will lead to temporaory memory loss but it was severe then permanent memory loss may observed.[26]



Types of Amnesia

Amnesia can be identified by seeing inability of individual to recall information, event and experiences[27]

- If patient is unable to recall past events that occurred before the beginning is called
- **retrograde amnesia.**
- If patient has remembering new information or event that occur after beginning of amnesia is called
  anterograde amnesia.
  If Amnesia is caused by traumatic events is called dissociative amnesia which is further categorized into**:**
- **Generalized amnesia:** In this patient forget everything about themselves including their identities and life history.
- **Localized amnesia:** In these cases patients suffers memory loss for particular event.
- **Selective amnesia:** In this patient forget only some part of specific event.
- **Systematized amnesia:** The patient loses specific information such as memories of particular person.
- **Continuous amnesia:** In this case patient is not able to form new memory**.**
- **Dissociative fugue:** These cases involve generalized amnesia, and the patient leaves his or her previous routine after losing his own identity.[28]

Factors Involved in Amnesia

Some factors as described in figure 1.5 might increase the chances of developing amnesia.

- **Age Related Memory Changes:** Earlier clinical trials on memory loss showed that the loss of memory is progressed with aging which may be due to oxidative stress conditions. Our body has self-damaging and its prevention function in which when the cell faces high oxidative stress they try to change morphologically for the survival but these changes are also self-damaging in nature which leads to cell death.[29] In neuronal cell death (apoptosis and necrosis) associated with protein release in form of granules likely β amyloid in case of Alzheimer's and Nogo-A in case of Cognitive deficits. In both the cases the Neurohumoral transmission is impaired. Aging is also associated with loss of cholinergic neuron or lack of enough acetylcholine which also leads to memory loss.[30]

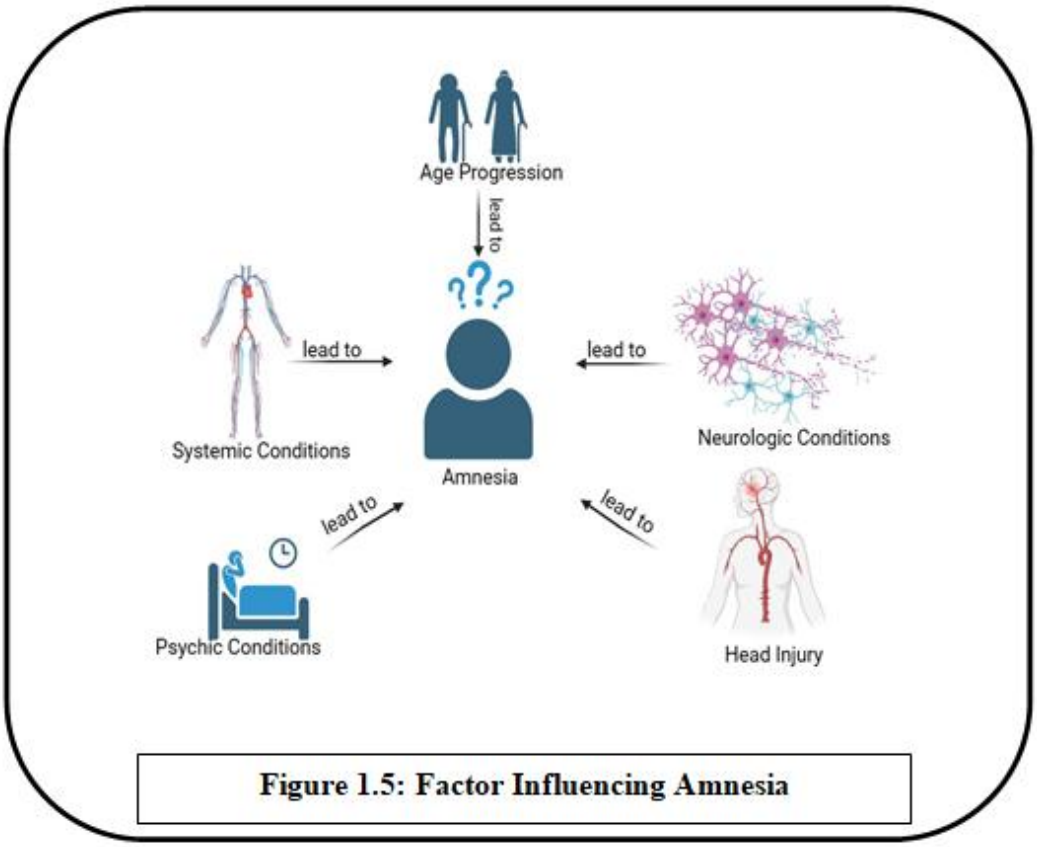


Figure 1.5: Factor Influencing Amnesia

- **Neurologic Disorders:** These include Alzheimer's disease, Picks disease, Parkinson's disease and Huntington's disease in which the memory loss start after the neurologic transmission interruption. The individual can recall the memory in flashback or whenever they unable to recall information in systemic presentation may help. However in other neurologic disorder like Picks disease the frontal and temporal lobes are predominantly affected which leads to prominent memory loss.[31]
- **Head Injury:** Head injury has been described from decade for the cause of memory loss. The clinical trials on patients with least affected and most affected were observed. In which it was found that in least affected patient have been responding quickly recalling everything has problem solving skills while in most affected they were suffering from delayed response. The head injury induced memory loss is often classified as retrograde amnesia to the period of post traumatic period of anterograde amnesia.[32]
- **Psychiatric Condition:** The disorders like episodes in depression, manic and schizophrenia cause individual to impair attention and concentration. In depressive episodes the pseudo dementia is showed in which concrete thinking is impaired which is related to problem-solving ability. The ones with psychiatric condition also have multiple personality disorder which make the individual to learn new things faster and these conditions often seen in short term amnesia.[33]
- **Systemic Condition:** Memory loss is most often seen in systemic diseases. This is due to impaired memory consolidation in temporal lobe or inability to recall memory at retrieval process which affects thalamus.[34] The systemic condition often occurs due to hypoxia in which brain is affected by shortage of oxygen. Hypoxia affects the hippocampus and permanent impairment in consolidation part of memory. Hypoxia induced memory loss often seen in the patient with Asthma and patient with poorly controlled diabetes mellitus. Sometime systemic memory loss is also termed as pure amensetic syndrome.[35]

Animal Model Used in Amnesia

The amnesia is cognitive deficit which affect everyone in their life however it can be short term. The safer drug testing in human is important to study amnesia. The researchers provide various investigations on the disease by using humans and animals. The drug investigation directly on humans challenges the guideline of Helsinky and to avoid that animal testing is needed.[36]

The animal models used in amnesia are

- **Monkeys (*Macaca fascicularis*):** *Macaca fascicularis*have significantly contributed to expanding our knowledge of various neurological and cognitive functions, including memory and amnesia. Employing monkeys as models for amnesia research provides valuable insights into the fundamental mechanisms of memory creation, consolidation, and retrieval. This research also holds promise for developing potential treatments for memory-related disorders in humans. Monkeys share a remarkable level of anatomical, physiological, and cognitive resemblance with humans. Their brain structures and functions closely parallel those of humans more than other animal models. This likeness positions monkeys as apt subjects for investigating intricate cognitive processes like memory and amnesia, which are deeply pertinent to human brain activities.[37] Researchers can establish controlled experimental settings with monkeys, enabling meticulous manipulation of variables and standardized testing protocols. This facilitates the focused examination of factors contributing to memory impairment or amnesia, allowing scientists to methodically explore their impacts. Monkeys engaged in memory-related tasks can be monitored using cutting-edge neuroimaging methods like functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). Additionally, invasive techniques like neural recordings offer real-time insights into the firing patterns of individual neurons involved in memory processes. Targeted brain lesions, such as those in the hippocampus or prefrontal cortex, can be induced in monkeys to replicate specific memory deficits. Controlled experiments involving pharmacological interventions, including drugs that modulate memory functions, permit the exploration of potential therapeutic avenues for amnesia. The relatively lengthy lifespans of monkeys, along with their extended cognitive development, enable researchers to conduct longitudinal studies. This approach facilitates the observation of memory changes over extended periods, proving especially useful in studying age-related memory decline and neurodegenerative conditions.[38] Monkeys can be trained to perform diverse memory-related tasks, such as spatial memory challenges, object recognition tests, and delayed response exercises. These tasks closely mirror the cognitive demands of similar tasks in humans, offering researchers valuable insights into the mechanisms underlying memory formation and retrieval. Insights gained from studies involving monkeys can be extrapolated to human conditions, aiding in the formulation of potential therapies for memory disorders like Alzheimer's disease, traumatic brain injuries, and other forms of amnesia. The structural and functional similarities between monkey and human brains enhance the reliability of extrapolation.[39]

Limitations

Cynomolgus monkeys, specifically Macaca fascicularis, have been a prominent fixture in biomedical research due to their genetic and physiological proximity to

humans.[40] However, the utilization of these primates in research endeavours presents multifaceted limitations and ethical considerations. The inclusion of cynomolgus monkeys in research precipitates ethical concerns regarding animal welfare. Particularly in cases of invasive experiments, these animals may endure pain, stress, and suffering. Notably, the social nature of monkeys renders them susceptible to distress and behavioral disturbances when subjected to isolation or placed in non-natural group settings, which amplifies the ethical discourse surrounding their research use, especially in situations involving harm or suffering.[41]

Despite their genetic resemblance to humans, discernible genetic disparities subsist, necessitating validation of findings from monkey studies prior to extrapolation to human biology. The financial cost associated with housing and attending to monkeys in research facilities is considerable, and the intricate task of breeding and sustaining monkey populations entails substantial time and financial investments. The availability of cynomolgus monkeys for research purposes frequently falls short of the demand, further exacerbating the constraints.[42] The potential carriage of zoonotic diseases by monkeys introduces plausible risks to researchers and handlers. Furthermore, the generalizability of research outcomes from one monkey species to other monkey species or to humans is constrained, underscoring the complexity of translating findings across these groups. To mitigate these challenges, progressive advancements in alternative research methodologies, such as in vitro cell culture models and non-invasive imaging techniques, are diminishing the imperative for animal testing. Simultaneously, the application of monkeys in research is subject to exacting regulatory and ethical oversight, culminating in logistical hurdles and delays.[43] Their extended lifespans can elongate study durations and introduce intricacies into long-term experiments. The potential need for invasive procedures in certain research scenarios may inflict pain and distress upon these animals. Additionally, akin to humans, monkeys exhibit inter-individual variability in their responses to treatments or interventions, compounding the complexity of deriving definitive conclusions from limited sample sizes. Researchers and institutions engaging cynomolgus monkeys in biomedical research are frequently compelled to adhere to stringent guidelines and ethical tenets to minimize harm and uphold the animals' welfare. Concurrently, continuous endeavors persist in the development of alternative methodologies and technologies aimed at diminishing reliance on animal models, including monkeys, in the realm of scientific research.[44]

- **Rodents:** Rodents, notably mice and rats, have proven to be indispensable models within the realm of neuroscience, particularly in the study of memory and amnesia. The extensive application of rodents in research is owed to their biological parallels with humans, their well-established genetic backgrounds, and their cost-effectiveness. These creatures offer unparalleled insights into the underlying mechanisms governing memory formation, consolidation, and retrieval, along with the potential interventions for conditions linked to amnesia. Mice and rats share substantial genetic homology with humans, enabling researchers to manipulate specific genes linked to memory processes. This genetic likeness positions rodents as potent tools for investigating the roles of diverse genes and molecular pathways in memory creation and amnesia.[45] Laboratory settings provide researchers with meticulous control over environmental variables, allowing for the manipulation of factors that impact memory function. This controlled environment facilitates methodical examinations of the effects of particular interventions, substances, or circumstances on behaviors associated with memory. Rodents can be trained to execute a spectrum of memory-related tasks, such as the Morris water maze for spatial memory or fear conditioning for associative memory. These tasks offer insights into the intricacies of learning and memory processes, facilitating the assessment of memory impairment due to experimental alterations. Rodents serve as a platform for administering drugs that influence memory processes, enabling the evaluation of their effects on memory formation and amnesia. This approach aids in the identification of potential targets for therapeutic interventions targeting memory disorders and in gauging the efficacy of drug-based approaches. Invasive techniques like electrophysiological recordings permit the observation of neuronal activity during memory-related tasks.[46] These recordings offer real-time glimpses into the firing patterns of neurons within specific brain regions associated with memory processing. Advanced imaging methods, including functional MRI (fMRI) and two-photon microscopy, empower researchers to visualize and analyze alterations in brain activity and connectivity correlated with memory tasks in rodents. Discoveries derived from rodent studies can inform the development of potential treatments for memory disorders, encompassing conditions like Alzheimer's disease and traumatic brain injuries.[47] The ability to manipulate genes and assess the consequences of various interventions in rodents contributes to understanding their potential effects on human conditions. While rodents offer profound insights, ethical considerations pertinent to animal research must be addressed. Researchers and institutions are committed to upholding stringent animal welfare standards, ensuring responsible and ethical utilization of these models.[48]

Limitations

The utilization of mice and rats, collectively referred to as rodents, has become pervasive in biomedical research due to their pragmatic attributes, cost-effectiveness, and

genetic affinities with humans across various dimensions. Nevertheless, there exist a cadre of constraints intricately associated with their application in this domain. Rodents, notwithstanding shared physiological and anatomical congruities with humans, manifest considerable idiosyncrasies.[49]

These variances engender restrictions upon the direct transference of research findings from rodents to the human context. Of particular import is the relatively truncated lifespan of rodents vis-à-vis humans, a factor that begets constraints in the investigation of protracted effects or chronic maladies whose emergence unfolds over extended temporal frames in the human sphere. The metabolic variances and pathways exhibited by rodents in comparison to humans precipitate ramifications for drug metabolism dynamics and responses to therapeutic modalities. The diminutive physical dimensions of rodents impart constraints upon certain research realms, particularly those necessitating elaborate surgical interventions or comprehensive scrutiny of specified anatomical structures.[50]

Concurrently, the behavioral and cognitive dispositions delineated in rodents are disparate from those of humans, thereby posing methodological challenges in the precise exploration of intricate neurological or behavioral pathologies. Divergences in the immunological apparatus between rodents and humans wield discernable impacts upon their responses to infectious agents, vaccination regimens, and immune-mediated afflictions. Not all maladies that afflict humans can be faithfully recapitulated within the confines of rodent models. A subset of diseases, notably those that are intrinsically human or inherently tied to larger mammalian physiology, eludes faithful emulation within rodent models.

The congruence in gene expression profiles shared by rodents and humans is tempered by substantive genetic disparities that may, in turn, delimit the translational scope of rodent-derived research findings.In the pursuit of experimental consistency, a preponderance of rodent investigations leans upon inbred strains.[51] However, this stratagem may falter in adequately mirroring the spectrum of genetic heterogeneity witnessed within the human population, potentially circumscribing the extensibility of research outcomes. Ethical considerations germane to animal welfare, with heightened pertinence in studies involving pain, distress, or invasive procedures, underscore the ethical discourse within rodent research.The ubiquity of rodent models engenders a propensity toward their overreliance, thereby bearing the risk of introducing biases into scientific conclusions. Issues germane to the reproducibility of outcomes have surfaced in select rodent investigations. Environmental variables, encompassing dietary regimens, housing conditions, and stressors, wield the capacity to exert influential effects upon research outcomes, thereby inserting confounding elements. Intriguingly, significant inter-species disparities may exist even within the broader class of rodents, culminating in the situational inapplicability of findings derived from one species to others. In efforts to surmount these constraints, investigators commonly employ a hybridized investigative paradigm integrating diverse animal models, including larger mammalian organisms and non-human primates, in concert with in vitro experimentation and computational modeling. In tandem, the ethical treatment of rodents within the research milieu assumes paramount significance as a corollary to animal welfare preservation. The concomitant limitations imprinted upon rodent models underscore the imperativeness of a judicious and meticulously orchestrated framework for result interpretation and validation.[52] In this context, the synergistic amalgamation of multiple model systems, when deemed feasible, ascends as a pivotal stratagem for the augmentation of scientific research's dependability and translational relevance within the sphere of biomedicine.

- **Zebrafish:** Zebrafish (Danio rerio) have risen to prominence as a valuable model organism across diverse scientific domains, including the exploration of memory and amnesia. Despite their evolutionary distance from mammals, zebrafish possess distinct advantages that make them exceptional candidates for delving into memory processes. Their genetic manipulability, transparent embryos, and well-characterized behavioral responses contribute to their role in amnesia research, offering insights into the core mechanisms of memory formation, impairment, and prospective therapeutic interventions. The genetic makeup of zebrafish can be easily altered, empowering researchers to target specific genes linked to memory functions. Despite the genetic disparity from mammals, conserved genes and pathways associated with memory between zebrafish and higher organisms allow for investigations into the molecular foundations of memory and amnesia.[53] Zebrafish showcase a spectrum of behaviors that can be quantitatively assessed, rendering them amenable to efficient high throughput screening. Automated behavioral assays enable the evaluation of learning and memory-related behaviors, providing effective means to study memory in large groups of fish. The transparency of zebrafish embryos facilitates direct observation of brain development and neural activity. This unique trait proves particularly beneficial for imaging techniques like calcium imaging, enabling the visualization of neuronal responses associated with memory tasks. Zebrafish can be trained in various memory-related tasks, including fear conditioning, novel object recognition, and spatial learning. These tasks yield insights into associative and spatial memory processes, facilitating the exploration of memory impairment resulting from genetic modifications

or experimental interventions. Zebrafish can be exposed to pharmacological agents that influence memory processes, offering a platform to scrutinize the impact of drugs on memory formation and amnesia. The relatively small size and aquatic habitat of zebrafish make drug administration and monitoring a practical endeavor.[54] Advanced imaging techniques, encompassing two-photon microscopy and confocal imaging, can be employed to visualize neural activity during memory tasks in zebrafish. These methodologies permit the tracking of neuronal and neural circuit dynamics associated with memory processing. Despite notable differences from mammals, specific brain regions and processes linked to memory exhibit evolutionary conservation in zebrafish. This positions zebrafish as a pertinent model for uncovering the fundamental principles of memory, with potential implications for comprehending similar processes in diverse species. In comparison to mammalian models, zebrafish research entails fewer ethical complexities due to their lower position on the phylogenetic scale. Nevertheless, ethical mindfulness regarding their care and utilization remains essential throughout research endeavors.[55]

❖ **Limitations**

Zebrafish (Danio rerio) have gained popularity as a model organism in biomedical research due to their genetic resemblance to humans, transparent embryonic development, and the ease with which their genetics can be modified. Nonetheless, there are several limitations associated with their utilization in research.[56] Despite sharing certain genetic and anatomical traits with humans, zebrafish also exhibit significant disparities. These distinctions can curtail the direct relevance of research findings from zebrafish to humans. Zebrafish are ectothermic, meaning their body temperature is influenced by their environment. This can impact how they respond to specific drugs and environmental factors, which may not directly correlate with human physiology. Zebrafish possess less intricate organ systems compared to humans, rendering them less suited for investigating complex human diseases or systems involving intricate organ interactions.[57] Zebrafish have a relatively brief lifespan, limiting their utility in the study of chronic diseases and research focused on aging. Zebrafish tissues are less complex than those of mammals, which constrains the study of certain diseases and tissue-specific functions. Differences in the zebrafish immune system compared to humans affect their responses to infections and immune-related diseases. Zebrafish have limited cognitive and behavioral complexity compared to mammals, which can hinder the study of specific neurological and behavioral disorders. Differences in drug and chemical metabolism between zebrafish and humans can complicate drug development studies.[58]

While zebrafish are seen as a more ethically acceptable model organism due to their small size and relatively simple nervous system, concerns about animal welfare persist, particularly in studies involving pain, suffering, or invasive procedures. Variations in environmental conditions, such as water quality and temperature, can influence research outcomes and introduce potential sources of error. As with any model organism, issues related to the reproducibility of results have been observed in some zebrafish studies, especially when genetic backgrounds are not precisely defined. Genetic variations can exist even among zebrafish populations, and findings in one population may not necessarily apply to others. Despite these constraints, zebrafish research has contributed valuable insights into various biological processes and diseases. Researchers often employ zebrafish in conjunction with other model organisms, in vitro experiments, and computational modeling to complement their findings. Additionally, ongoing efforts to enhance genetic manipulation techniques and broaden the utility of zebrafish as a model organism in biomedical research continue to progress.[59]

DEVLOPMENT OF AMNESIA IN ANIMAL MODELS

Amnesia can be developed by interfering cholinergic neuronal conduction in which acetylcholine major role. The conduction can be stop by either damaging cholinergic neurons, increasing activity of acetyl cholinesterase or by using anticholinergic drugs.

❖ **Chemically induced Amnesia:** The chemically induced amnesia involve the use of anticholinergic drugs to stop the binding of acetylcholine on cholinergic neurons. Scopolamine is anticholinergic drug which produce its effect by cholinergic receptor blocking activity.[60] The different studies have been established till now that contain use of scopolamine to induce amnesia in mice as well as in zebrafish. For inducing amnesia by using scopolamine is non-invasive procedure simply involves immersing zebrafish in scopolamine aqueous solution for 30 min.[61]

Scopolamine and benzodiazepine are the drugs of choice for cognitive deficit. The most commonly animals preferred for this method are mice, rat and zebrafish with Scopolamine induced memory deficit. The dose of the drug varies for each model for mice and rat the scopolamine concentration used 3m/kg by *i.p.* administration.[62] The zebrafish model involves the immersion of zebrafish in 100mM concentration of scopolamine for 30 minute.[63]

❖ **High fat induced:** High fat induced amnesia involve development of diabetes to induce amnesia. For the development of this method 22 days the mice are fed with high fatty diet and glucose level is regularly monitored. After the development of diabetes the mice were tested on Morris maize test for memory recognition and for further investigation acetylene cholinesterase level were measured.[64]

- **Hypoxia Induced:** Hypoxia involves lowering the oxygen level in animal body. The animal is subjected to inhale pure nitrogen and the oxygen levels were kept to 3.5%.Oxygen plays crucial role in consolidation part of learning phase so if there is hypoxia then process of learning will be stopped. As a result of it the process of learning will fail the recognition.[65]
- **Brain injury Induced:** Concussive head trauma includes striking a weight (30mg) directly on the skull. The weight is placed over the head of rat at 80cm distance. Then the rat were analysed for memory loss by behavioural analysis.[66]
- **Electroshock induced:** The Han's variable-intensity electroshock seizure apparatus is used to deliver electroshock. The electroshock involves use of electrode to deliver shock in alternative manner. The time and duration of shock is 0.10 sec. to 6sec. at a 0.10 sec. interval with 60cps a.c.waveform.[67]
- **Thiamine Deficiency Induced:** The thiamine deficiency result in cognitive deficit which involve feeding mice or rat with thiamine deficient chow. The method allows continuation of therapy for up to 11month to 22months. The further evaluation is done by behavioural analysis.[68]

ASSESSMENT OF AMNESIA

The development of amnesia can be confirmed by behavioral analysis, biochemical estimation and histopathology analysis. The behavioral testing involves the light-dark test, shoaling test and Y maze test; biochemical estimation involve recognition of enzyme superoxide dismutase, nitric oxide synthase and histopathological analysis shows neurological changes in brain cell.[69]

Behavioral Analysis

Behavioral analysis involves analyzingthe animal for behavior after administration of negative control, test drug and standard drug. Behavioral test involve Novel Tank Diving Test, Y- maze test and Novel object recognition test.

Table 1.2: Test for Behavioural Analysis.

Apparatus Name	Parameters Observed
Novel tank diving test	• The tank is divided into two zones • No. of entries and time spent in each zone is recorded.
Shoaling.	• Group of animal is added to Novel tank • The mean distance in each member is recorded.
Y maize Test	• Y maze divided into three zone • No. of entries and time spent in each zone is observed.
Plus Maze test	• Test contain three zone • Each zone is numbered accordingly • On side of plus the animal is irritated while other side animal is provided with some rewards like feed. • No. of entries in both zone at Plus is counted.

Biochemical Estimation

The biochemical estimation involves enzymatic estimation related to specific disease. These involve the diagnostic parameters or protein involvement in disease progression. Usually in Neural disease progression, there are certain enzymes whose level either increased or decreased. At initial steps of neural disease there is oxidative stress by which cell tried to change their structure internally and morphologically for survival. During the change process the level of enzymes like superoxide dismutase (SOD), Glutathione peroxidase (GPX) and lipid peroxidase will change. Acetylcholinesterase (AchE), Catalase (CAT) and Malondialdehyde (MDA) enzyme has major involvement in cognitive deficit with respect to learning and memory, which is related to acetylcholine.[70]

Table 1.3: Enzymatic estimation of normal and diseased condition.

BIOCHEMICAL ENZYME ESTIMATION					
Enzyme	**Reagent**	**Inference**	**Normal**	**Diseased**	**Reference**
AchE	• Sodium Phosphate buffer solution 0.25mM • 5,5-dithiobis-2- nitrobenzoic acid 1mM • Acetylcholine chloride 5mM • Acetone	Yellow colour due to formation of 2-nitrobenzoate-5-thiobenzoate anion at 412nm.	Decreased	Increased	[71]
SOD	• Nitro Blue Tetrazonium 1.5mM • Potassium Phosphate buffer	Blue color due to formazan which is analyse at 560nm.	Increased	Decreased	[72]

	0.067mM • Riboflavin 0.12mM				
PX	• Sodium Phosphate Buffer 0.25M • EDTA 25mM • Sodium trinitrite 0.4M • GSH 50mM • DTNB 0.04%	Yellow color due to glutathione which is analyse at 412nm.	Decreased	Increased	[73]
CAT	• Sodium Hydroxide 3M • Sulphuric Acid 0.5M • TCA 20% • Monopotassium	Greeencolorappear ance like chromic acetate analyse at 570nm.	Increased	Decreased	[74]
	phosphate 30mM				
MDA	• Sodium Hydroxide 3M • Sulphuric acid 0.5M • TCA 20% • TBA 0.335% • Monopotassium phosphate	Formation of pink color due to 1,1,3,3 tetraethoxypropane analyse at 532nm with HPLC uv detector.	Decreased	increased	[75]

Histopath Analysis

TheHistopath analysis involves extraction of organ like brain and its fixation with 10% formalin. The 10um slides were made and embedded in paraffin and stained with staining reagents like hematoxylin and eosin staining to evaluating cell decays for e.g. neuronal loss in hippocampus. The prepared slide were analysed under stereomicroscope at different resolution. The presence of dead cell related to necrosis and cell population is counted.[76]

CONCLUSION

In conclusion, amnesia represents a cognitive deficit that can impact individuals across their lifespan, with both short-term and chronic manifestations. This prevalent condition affects more than 5% of the global population, and its repercussions are felt even among those dealing with other neurological disorders. Extensive research by scientists, employing both human subjects and animal models, has shed light on the clinical manifestations of amnesia. However, direct drug testing on humans challenges the ethical guidelines set by the Helsinki Declaration, making animal models crucial for preliminary investigations.

The investigation of amnesia spans various animal models, each offering unique advantages. Monkeys provide insights into complex cognitive functions due to their resemblance to humans, rodents bridge genetic gaps, and zebrafish offer innovative opportunities for research. These models collectively contribute to the advancement of our understanding of memory processes and the development of potential interventions for memory-related disorders.

REFERENCES

1. Bhangare, A. N., Lahange, S. M., Bhatnagar, V., & Bhatnagar, S. (2016). A REVIEW STUDY ON THE CONCEPT OF MANOVAHA SROTAS IN AYURVEDA AND ITS CLINICAL IMPORTANCE
2. Okano, H., Hirano, T., & Balaban, E. (2000). Learning and memory. Proceedings of the National Academy of Sciences, 97(23): 12403-12404.
3. Thompson, R. F. (1986). The neurobiology of learning and memory. Science, 233(4767): 941-947.
4. Leblanc, H., & Ramirez, S. (2020). Linking Social Cognition to Learning and Memory. The Journal of neuroscience:the official journal of the Society for Neuroscience, 40(46): 8782–8798. https://doi.org/10.1523/JNEUROSCI.1280-20.2020
5. Teyler, T. J.,&Discenna, P. (1984). Long-term potentiation as a candidate mnemonic device. Brain Research Reviews, 7(1): 15-28.
6. Nicoletti, F., Meek, J. L., Iadarola, M. J., Chuang, D. M., Roth, B. L., & Costa, E. (1986). Coupling of inositol phospholipid metabolism with excitatory amino acid recognition sites in rat hippocampus. Journal of neurochemistry, 46(1): 40-46.
7. McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. Psychological review, 102(3): 419–457. https://doi.org/10.1037/0033-295X.102.3.419
8. Janowsky, J. S., Shimamura, A. P., Kritchevsky, M., & Squire, L. R. (1989). Cognitive impairment following frontal lobe damage and its relevance to human amnesia. Behavioral neuroscience, 103(3): 548.
9. Brun, A. (1994). Pathology and pathophysiology of cerebrovascular dementia: pure subgroups of obstructive and hypoper fusive etiology. Dementia and Geriatric

Cognitive Disorders, 5(3-4): 145-147.
10. Neergaard, P. M., &Mairson, H. G. (2004). Types, potency, and idempotency: why nonlinearity and amnesia make a type system work. ACM SIGPLAN Notices, 39(9): 138-149.
11. Baddeley, A., & Wilson, B. (1988). Frontal amnesia and the dysexecutive syndrome. Brain and cognition, 7(2): 212-230.
12. Muhammad, T., Ali, T., Ikram, M., Khan, A., Alam, S. I., & Kim, M. O. (2019). Melatonin rescue oxidative stress-mediated neuroinflammation/neurodegeneration and memory impairment in copolamine-induced amnesia mice model. Journal of Neuroimmune Pharmacology, 14(2): 278-294.
13. Flores, J., Noël, A., Foveau, B., Beauchet, O., & LeBlanc, A. C. (2020). Presymptomatic Caspase-1 inhibitor delays cognitive decline in a mouse model of Alzheimer disease and aging. Nature communications, 11(1): 1-14.
14. Pace-Schott, E. F., Germain, A., & Milad, M. R. (2015). Effects of sleep on memory for conditioned fear and fear extinction. Psychological bulletin, 141(4): 835–857. https://doi.org/10.1037/bul0000014
15. HAINA, Q. (2011). Studies on structures, Dynamics and Interactions with small molecules of CNS regeneration Inhibitory components associated with Nogo-A and EphA4.
16. Mingorance, A., Fontana, X., Solé, M., Burgaya, F., Ureña, J. M., Teng, F. Y., ... & del Río, J. A. (2004). Regulation of Nogo and Nogo receptor during the development of the entorhino-hippocampal pathway and after adult hippocampal lesions. Molecular and Cellular Neuroscience, 26(1): 34-49.
17. Endress, A. D., Slone, L. K., & Johnson, S. P. (2020). Statistical learning and memory. Cognition, 204: 104346. https://doi.org/10.1016/j.cognition.2020.104346
18. Hsieh, M. T., Lin, Y. T., Lin, Y. C., & Wu, C. R. (2000). Radix Angelica Sinensis extracts ameliorate scopolamine-and cycloheximide-induced amnesia, but not pchloroamphetamine-induced amnesia in rats. The American journal of Chinese medicine, 28(02): 263-272.
19. Yoo, A. H., & Collins, A. G. E. (2022). How Working Memory and Reinforcement Learning Are Intertwined: A Cognitive, Neural, and Computational Perspective. Journal of cognitive neuroscience, 34(4): 551–568. https://doi.org/10.1162/jocn_a_01808
20. Wagman, A. S., Johnson, K. W., & Bussiere, D. E. (2004). Discovery and development of GSK3 inhibitors for the treatment of type 2 diabetes. Current pharmaceutical design, 10(10): 1105-1137.
21. Lopez, C. M., Govoni, S., Battaini, F., Bergamaschi, S., Longoni, A., Giaroni, C., & Trabucchi, M. (1991). Effect of a new cognition enhancer, alphaglycerylphosphorylcholine, on scopolamine-induced amnesia and brain acetylcholine. Pharmacology Biochemistry and Behaviour, 39(4): 835-840.
22. Rotenberg, V. S. (1992). Sleep and memory I: The influence of different sleep stages on memory. Neuroscience &Biobehavioral Reviews, 16(4): 497-502.
23. Kim, H. J., Baek, S. Y., Sok, D. E., Lee, K. J., Kim, Y. J., & Kim, M. R. (2020).
24. Neuroprotective activity of polyphenol-rich ribesdiacanthum pall against oxidative stress in glutamate-stimulated ht-22 cells and a scopolamine-induced amnesia animal model. Antioxidants, 9(9): 895.
25. Herszage, J., & Censor, N. (2018). Modulation of Learning and Memory: A Shared Framework for Interference and Generalization. Neuroscience, 392: 270–280. https://doi.org/10.1016/j.neuroscience.2018.08.006
26. Umukoro, S., Adeola, A. H., Ben-Azu, B., & Ajayi, A. M. (2018). Lemon grass tea enhanced memory function and attenuated scopolamine-induced amnesia in mice via inhibition of oxidative stress and acetyl-cholinesterase activity. Journal of Herbs, Spices & Medicinal Plants, 24(4): 407-420.
27. Pavon, M. V., Navakkode, S., Wong, L. W., &Sajikumar, S. (2022, April). Inhibition of Nogo-A rescues synaptic plasticity and associativity in APP/PS1 animal model of Alzheimer's disease. In Seminars in Cell & Developmental Biology. Academic Press.
28. Shandurina, A. N., Kambarova, D. K., &Kalyagina, G. V. (1982). Neuropsychological and neurophysiological analysis of different types of amnesia. Human Physiology. Russell, W. R., & Nathan, P. W. (1946). Traumatic amnesia. Brain, 69: 280-300.
29. Weber, D., Richter, V., Rohwedder, A., Großjohann, A., & Thum, A. S. (2023). Learning and Memory in Drosophila Larvae. Cold Spring Harbor protocols, 2023(3): .https://doi.org/10.1101/pdb.top107863
30. Spiteller, G. (2001). Lipid peroxidation in aging and age-dependent diseases. Experimental gerontology, 36(9): 1425-1457.
31. Strupp, M., Teufel, J., Zwergal, A., Schniepp, R., Khodakhah, K., & Feil, K. (2017). Aminopyridines for the treatment of neurologic disorders. Neurology: Clinical Practice, 7(1): 65-76.
32. Ahmed, S., Bierley, R., Sheikh, J. I., & Date, E. S. (2000). Post-traumatic amnesia after closed head injury: a review of the literature and some suggestions for further research. Brain Injury, 14(9): 765-780.
33. Smith, J. P., & Smith, G. C. (2010). Long-term

economic costs of psychological problems during childhood. Social science & medicine, 71(1): 110-115.
34. von der Goltz, C., & Kiefer, F. (2009). Learning and memory in the aetiopathogenesis of addiction: future implications for therapy?. European archives of psychiatry and clinical neuroscience, 259 Suppl 2,
35. S183–S187. https://doi.org/10.1007/s00406-009-0057-6
36. Schroyens, N., Alfei, J. M., Schnell, A. E., Luyten, L., & Beckers, T. (2019). Limited replicability of drug-induced amnesia after contextual fear memory retrieval in rats. Neurobiology of learning and memory, 166: 107105.
37. Roland, J. J., Mark, K., Vetreno, R. P., & Savage, L. M. (2008). Increasing hippocampal acetylcholine levels enhance behavioral performance in an animal model of diencephalic amnesia. Brain research, 1234: 116-127.
38. Kumar, N., van Vugt, F. T., & Ostry, D. J. (2021). Recognition memory for human motor learning. Current biology : CB, 31(8): 1678–1686.e3. https://doi.org/10.1016/j.cub.2021.01.097
39. Barco, A., Brambilla, R., & Rosenblum, K. (2015). Neurobiology of Learning and Memory.
40. Editorial. Neurobiology of learning and memory, 124: 1–2. https://doi.org/10.1016/j.nlm.2015.08.001
41. Russchen, F. T., Amaral, D. G., & Price, J. L. (1987). The afferent input to the magnocellular division of the mediodorsal thalamic nucleus in the monkey, Macaca fascicularis. Journal of Comparative Neurology, 256(2): 175-210.
42. Mumby, D. G. (1999). Animal models of global amnesia: What can they tell us about memory?.
43. Markowska, A. L., Olton, D. S., Murray, E. A., & Gaffan, D. (1989). A comparative analysis of the role of fornix and cingulate cortex in memory: rats. Experimental Brain Research, 74: 187-201.
44. Sodhi, R. K., Jaggi, A. S., & Singh, N. (2014). Animal models of dementia and cognitive dysfunction. Life Sciences, 109(2): 73-86.
45. Anand, A., Banik, A., Thakur, K., & L Masters, C. (2012). The animal models of dementia and Alzheimer's disease for pre-clinical testing and clinical translation. Current Alzheimer Research, 9(9): 1010-1029.
46. Yokoyama, M., Kobayashi, H., Tatsumi, L., & Tomita, T. (2022). Mouse models of Alzheimer's disease. Frontiers in Molecular Neuroscience, 15: 912995.
47. Bucci, D., & Stanton, M. (2017). The ontogeny of learning and memory. Neurobiology of learning and memory, 143, iv. https://doi.org/10.1016/j.nlm.2017.07.012
48. Squire L. R. (2004). Memory systems of the brain: a brief history and current perspective. Neurobiology of learning and memory, 82(3): 171–177. https://doi.org/10.1016/j.nlm.2004.06.005
49. Abel, T., & Klann, E. (2013). Molecular and cellular cognition: Neurobiology of Learning and Memory Special Issue 2013. Neurobiology of learning and memory, 105: 1–2. https://doi.org/10.1016/j.nlm.2013.08.005
50. Kabir, Z. D., Lee, A. S., & Rajadhyaksha, A. M. (2016). L- type Ca2+ channels in mood, cognition and addiction: integrating human and rodent studies with a focus on behavioural endophenotypes. The Journal of Physiology, 594(20): 5823-5837.
51. Milad, M. R., & Radulovic, J. (2014). Introduction to the special issue of Neurobiology of Learning and Memory on fear extinction. Neurobiology of learning and memory, 113: 1–2. https://doi.org/10.1016/j.nlm.2014.04.004
52. Bermúdez-Rattoni, F., & McGaugh, J. L. (2017). Memory reconsolidation and memory updating: Two sides of the same coin?. Neurobiology of learning and memory, 142(Pt A), 1–3. https://doi.org/10.1016/j.nlm.2017.05.002
53. Capatina, L., Todirascu-Ciornea, E., Napoli, E. M., Ruberto, G., Hritcu, L., & Dumitru, G. (2020). Thymus vulgaris essential oil protects zebrafish against cognitive dysfunction by regulating cholinergic and antioxidants systems. Antioxidants, 9(11): 1083.
54. Jang, H., Buhrman, D., Burton, J., Joshi, B., Mumert, M., Price, P., ... &Cattelin, F. (1997). Single and multiple dose pharmacokinetics of a pharmaceutical compound in elderly subjects. Drug information journal, 31(4): 1227-1235.
55. Way, G. P., Ruhl, N., Snekser, J. L., Kiesel, A. L., & McRobert, S. P. (2015). A comparison of methodologies to test aggression in zebrafish. Zebrafish, 12(2): 144- 151.
56. Verma, S., Rathia, S., Chandravanshi, L., & Gupta, P. K. (2022). Swarna Prashana– faith in the embrace of research. Journal of Complementary and Integrative Medicine, 19(2): 161-172.
57. Sodhi, R. K., Jaggi, A. S., & Singh, N. (2014). Animal models of dementia and cognitive dysfunction. Life Sciences, 109(2): 73-86.
58. Yokoyama, M., Kobayashi, H., Tatsumi, L., & Tomita, T. (2022). Mouse models of Alzheimer's disease. Frontiers in Molecular Neuroscience, 15: 912995.
59. Aravind, A., Ravula, A. R., Chandra, N., & Pfister, B. J. (2020). Behavioral deficits in animal models of blast traumatic brain injury. Frontiers in neurology, 11: 990.
60. Ngoupaye, G. T., Yassi, F. B., Bahane, D. A. N., Pahaye, D. B., & Bum, E. N. (2020). Antidepressant and anti-amnesic effects of the aqueous lyophilisate of the leaves of Leptadenia arborea on an animal model of cognitive deficit associated depression. Biomedicine & Pharmacotherapy, 130: 110603.
61. Brinza, I., Raey, M. A. E., El-Kashak, W., Eldahshan, O. A., & Hritcu, L. (2022).

Sweroside Ameliorated Memory Deficits in Scopolamine-Induced Zebrafish (Danio rerio) Model: Involvement of Cholinergic System and Brain Oxidative Stress. Molecules, 27(18): 5901.
62. Manzione, M. G., Herrera- Bravo, J., Sharifi- Rad, J., Kregiel, D., Sevindik, M., Sevindik, E., &Pezzani, R. (2022). Desmodiumadscendens (Sw.) DC.: A magnificent plant with biological and pharmacological properties. Food Frontiers.
63. Van Dam, D., & De Deyn, P. P. (2011). Animal models in the drug discovery pipeline for Alzheimer's disease. British journal of pharmacology, 164(4): 1285-1300.
64. Anand, A., Banik, A., Thakur, K., & L Masters, C. (2012). The animal models of dementia and Alzheimer's disease for pre-clinical testing and clinical translation. Current Alzheimer Research, 9(9): 1010-1029.
65. Pachter, A. Zebrafish as a Reliable Model for Alzheimer's Disease. Welcome from the Editor, 104.
66. Wang, J., & Cao, H. (2021). Zebrafish and medaka: Important animal models for human neurodegenerative diseases. International journal of molecular sciences, 22(19): 10766.
67. Giurgea, C., Lefevre, D., Lescrenier, C., & David-Remacle, M. (1971). Pharmacological protection against
Hypoxia induced amnesia in rats. Psychopharmacologia, 20(2): 160-168.
68. Tashlykov, V., Katz, Y., Volkov, A., Gazit, V., Schreiber, S., Zohar, O., & Pick, C. G.
(2009). Minimal traumatic brain injury induce apoptotic cell death in mice. Journal of molecular neuroscience, 37(1): 16-24.
69. Dorfman, L. J., & Jarvik, M. E. (1968). A parametric study of electroshock-induced retrograde amnesia in mice. Neuropsychologia, 6(4): 373-380.
70. Pitkin, S. R., & Savage, L. M. (2004). Age-related vulnerability to diencephalic amnesia produced by thiamine deficiency: the role of time of insult. Behavioural Brain Research, 148(1-2): 3-105.
71. Nishimura, Y., Okabe, S., Sasagawa, S., Murakami, S., Ashikawa, Y., Yuge, M., ... & Tanaka, T. (2015). Pharmacological profiling of zebrafish behavior using chemical and genetic classification of sleep-wake modifiers. Frontiers in pharmacology, 6: 257.
72. Ghumatkar, P. J., Patil, S. P., Jain, P. D., Tambe, R. M., & Sathaye, S. (2015). Nootropic, neuroprotective and neurotrophic effects of phloretin in scopolamine induced amnesia in mice. Pharmacology Biochemistry and Behavior, 135: 182-191.
73. Sabaliauskas, N. A., Foutz, C. A., Mest, J. R., Budgeon, L. R., Sidor, A. T., Gershenson, J. A., & Cheng, K. C. (2006). High-throughput zebrafish histology. Methods, 39(3): 246-254.
74. Winterbourn, C. C., Hawkins, R. E., Brian, M., & Carrell, R. W. (1975). The estimation of red cell superoxide dismutase activity. The Journal of laboratory and clinical medicine, 85(2): 337-341.
75. Salbitani, G., Vona, V., Bottone, C., Petriccione, M., & Carfagna, S. (2015). Sulfur deprivation results in oxidative perturbation in Chlorella sorokiniana (211/8k). Plant and Cell Physiology, 56(5): 897-905.
76. Sinha, A. K. (1972). Colorimetric assay of catalase. Analytical biochemistry, 47(2): 389-394.
77. Fujihara, K., Suzuki, H., Sato, A., Kodama, S., Heianza, Y., Saito, K., ... & Shimano, H. (2015). Circulating malondialdehyde-modified LDL-related variables and coronary artery stenosis in asymptomatic patients with type 2 diabetes. Journal of Diabetes Research, 2015.