An Analytical Review of the Pharmacological Aspects of Using Zebrafish as an Animal Model in Cognitive Science

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ABSRACT

Creature models are essential to medical research because they help to synthesize our understanding of the causes of both deadly and non-mortal illnesses and facilitate the creation of novel treatments. Additionally, investigations on literacy and memory in the cognitive sciences reiterate findings pertinent to humans using relevant model species. In recent decades, the scientific community has embraced the use of the zebrafish (Danio rerio) model significantly, even though mice are still the most extensively used exploratory model worldwide.Zebrafish, a small tropical brackish teleost fish, shares significant genetic, anatomical, and physiological similarities with mammals. As a result, they are becoming increasingly recognized as one of the best models for studying neurological disorders. This is because they are easy and inexpensive to maintain, have a high reproductive rate, and can be easily genetically manipulated. Zebrafish is a highly suitable experimental model for studying behaviour, inheritance, and toxicology, particularly regarding several coloured fatal diseases. Zebrafish are more effective than other invertebrate models when simulating life-threatening scenarios, especially when it comes to studying large-scale inheritable mutations and conducting biological investigations involving restorative emulsion wireworks. The zebrafish is a highly sensitive species that can be affected by both changes in medication and environmental factors. These behavioural traits can be observed in both adult fish and larvae, making zebrafish a valuable tool for medical research and pre-clinical testing. This review specifically examines the use of zebrafish as an animal model for cognitive science research.

Keywords: Zebrafish (Danio rerio),biomedical research, neurodegenerative diseases, drug screenings, pre-clinical trials, cognitive science research.

I. INTRODUCTION

ZEBRA FISH (DANIO RERIO)

The zebrafish, also known as Danio rerio, is a small freshwater fish that belongs to the cyprinoid teleost family. This fish originates from rivulets in India and is commonly kept as an aquarium fish around the world. Keeping them in a Terraria is a simple task, almost as easy as taking care of guppies. These striped fish are available as graceful swimmers in most pet stores. The first zebrafish used in a classic screen were actually acquired from a pet store in Tubingen. Laboratory practices for their care and breeding have been well-established. The zebrafish has become a model organism for modern natural research, thanks to the pioneering work of George Streisinger and his colleagues, who recognized its numerous advantages as an experimental system. These advantages include its short generation time, the high number of eggs produced by each mating, and the fact that, because fertilization is external, all stages of development are easily accessible.

Embryo	Larva	Adult
• Rapid development	• Optical clarity	• Vertebrate neural structure
• Optical clarity	• Genetic malleability	• Low cost, easy maintenance
• Genetic malleability	• High throughput screening	• Genome comprises of several orthologs of human genes mutated in FAD
• External development		

A successful exploration program in cognitive social neuroscience requires two crucial conditions:
(1) The ability to explore the elaboration of social gestures and cognition using cladistics, to uncover how pre-existing cognitive modules may evolve quantitatively (such as an increase in memory storage capacity) and how networks may be reconfigured to solve adaptive problems in new ways; and
(2) The ability to explore the mapping of cognitive function onto neural networks using reductionism, which requires model organisms with applicable social gestures and an available "toolbox" for analysing neural circuits.

Studying cognitive capacities can be efficiently achieved by combining behavioural studies on named species with neuroethological exploration of a related model organism. Teleost fish models fulfil both requirements and offer an excellent opportunity for relative cognitive social neuroscience. Among various teleost fish models, zebrafish and medaka have gained popularity due to the availability of neurobiological and inheritable tools. Zebrafish, specifically, is a favourable model for social neuroscience research, as it displays relevant social behaviours and has suitable tools for studying brain function.

Studying the effects of environmental factors and drugs on zebrafish is relatively easy due to their well-developed and sensitive organs. These organs can detect different environmental stimuli and elicit well-defined behavioural responses. Zebrafish skin and gills provide a gateway for numerous soluble agents. This means that biologically active compounds can be administered non-invasively, simultaneously and with precise attention directly into the water surrounding hundreds of embryos, larvae, or adult zebrafish.

Cognitive impairment is a common issue in several brain disorders such as epilepsy, Alzheimer's disease, schizophrenia, Huntington's disease, and autism. Epileptic patients experience electric discharge in the brain affecting areas like the temporal lobe, hippocampus, medial frontal brain regions, bilateral superior temporal, and sub-thalamus brain regions. It can be argued that recurrent seizures and seizure-induced neuronal modelling during epilepsy can cause continuous neuronal reorganization.

Zebrafish possess a complex nervous system that is capable of sophisticated behaviours and is susceptible to seizures. Adult zebrafish offer a full range of mature geste for study, which makes them particularly desirable for model development. Over time, the use of zebrafish has become popular as an alternative to rodents and other experimental creatures for studying the molecular mechanisms associated with cognition deficiency and for developing potential therapeutic compounds. There is significant scientific evidence demonstrating the benefits of creatures like zebrafish as a more humane and effective animal model for drug discovery. The genetic makeup of zebrafish is similar to humans, with around 70% of genes being associated with humans and about 84% of genes known to cause human disorders also being expressed in zebrafish.

Zebrafish (Danio rerio) are commonly used in cognitive science as experimental animal models due to their high success rate in yielding accurate results, according to several studies.
A list of cognitive science studies using zebrafish as an animal model is provided below.

1. **Exposure to sodium arsenite affects the behavior, ultrastructure, and gene expression of adult zebrafish brains (Danio rerio).**

Arsenic is a type of metallic element that is considered an environmental poison and can be found in nature. It has been classified by the International Agency for Research on Cancer (IARC) as a Group I human carcinogen, which means that it poses a significant threat to human health. The main way that the general public gets exposed to arsenic is through drinking water, particularly in the form of inorganic arsenic. The World Health Organisation recommends that drinking water should not have an arsenic concentration of more than 10 μg/L. Unfortunately, in more than 100 countries, epidemiological

surveys have found that the levels of arsenic in groundwater are higher than the acceptable limits, putting approximately 296 million people at risk of possible arsenic exposure.

Scientific research indicates that concentrations of arsenic exceeding 50 μg/L in water can lead to damage to the central nervous system in children. In adults, high levels of arsenic in water may also cause harm to the central nervous system. While arsenic-induced peripheral neuropathy can eventually heal, damage to the central nervous system may be irreversible. Studies on mice show that exposure to arsenic can cause neurobehavioral abnormalities, often accompanied by histological damage to the brain and an increase in anxiety-like behaviours. Rats treated with arsenic have shown neuronal atrophy and worse spatial memory, possibly due to changes in the hippocampal ultrastructure. At present, there is limited research on arsenic-induced histopathological brain damage in aquatic animals like zebrafish. However, studies on carp have found a variety of structural abnormalities in the brain tissue after 30 days of exposure to sodium arsenite, including micro thrombosis, a decrease in cell quantity, disarray in arrangement, and loosening of structure.

Arsenic is a metal-like substance that can potentially harm human and rodent health and cause behavioural changes. However, the long-term neurotoxic effects of arsenic on aquatic life are still unknown. A study was conducted to investigate the effects of arsenic exposure on adult zebrafish. The experiment involved exposing three-month-old zebrafish over 30 days to three different sodium arsenite water concentrations. The control group had 0 μg/L, test group 1 had 50 μg/L, and test group 2 had 500 μg/L. To assess the risks of arsenic exposure in aquatic environments, the study employed behavior analysis, transmission electron microscopy techniques, and quantitative real-time PCR. Adult zebrafish behavior was evaluated using six different tests, including the mirror biting test, shoaling test, novel tank test, social preference test, social recognition test, and T maze. After the behavioural tests, the zebrafish brains were dissected and collected for ultrastructural study and gene expression analysis.
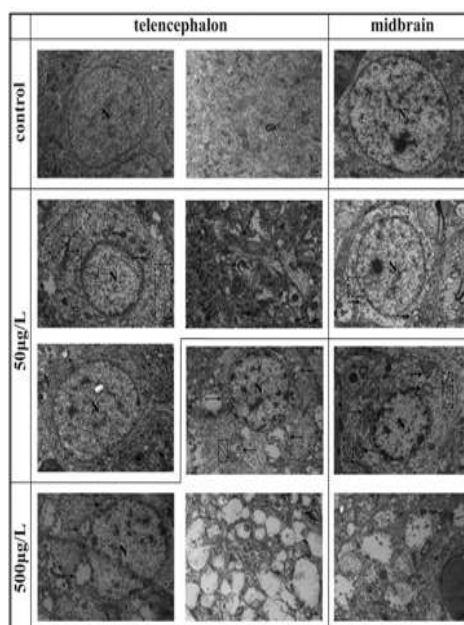
According to the research, when zebrafish are exposed to sodium arsenite, it leads to a significant reduction in their levels of aggression, cohesiveness, social ability, social cognition ability, learning, and memory. Moreover, this exposure causes damage to the ultrastructure and genes that control the behavior in the brain of zebrafish.

2. The effects of heavy metal exposure on brain and gut microbiota.

Heavy metals are a group of dense elements that occur naturally in the earth's crust in varying amounts. However, human activities such as mining, farming, burning, and industrial processes also contribute to their release into the environment. Heavy metals can persist in the ecosystem for extended periods and accumulate within the food chain, posing a significant environmental threat, especially to groundwater sources. Human exposure to heavy metals occurs through contaminated food, water, inhalation, or skin contact. These elements can cross the blood-brain barrier (BBB) and interfere with the biological processes of the central nervous system (CNS), which can lead to neurological diseases and cerebral damage. Children and infants are particularly vulnerable to the toxic effects of heavy metals due to their developing brains and prolonged growth period from pregnancy through adolescence. The gut microbiota has a significant role in regulating numerous physiological functions such as digestion, the synthesis of proteins and amino acids, energy metabolism, modulation of the

immune system, growth, neurodevelopment, and behavior. Studies on rats have shown that the microbiota plays a crucial role in the development of the brain during the early stages of life as well as in the neurogenesis of the adult hippocampus. It is also strongly involved in modulating learning, memory, and behavioural responses to stress.

In this study, we investigated the impact of gut microbiota on the neurotoxic effects caused by exposure to heavy metals. We evaluated various neuropsychological domains, including changes in behavior and cognitive aspects that occur after exposure to heavy metals (i.e., neuropsychological outcomes). Additionally, we reviewed alterations such as neurotoxicity and neurochemical or morphological changes in brain areas (molecular outcomes) affected by heavy metals exposure. Only studies that examined the gut microbiota composition, cognitive and/or molecular consequences, and heavy metal exposure simultaneously were considered for evaluation.

The PECO approach - Population, Exposure, Comparison, and Outcomes - was utilized to establish selection criteria for research inclusion and exclusion.

The studies primarily focused on investigating the impact of heavy metals on gut microbiota changes in animal models and various brain-related outcomes. The studies that did not measure biomarkers indicative of neurological function, assess morphological changes at the cellular and tissue levels in the brain (molecular outcomes), or examine cognition or behavior (neuropsychological results) were excluded. Additionally, studies that did not investigate changes in the gut microbiota were also disqualified.

The gut-brain axis is an important link between the gut microbiota and the central nervous system. Recent studies have shown that exposure to environmental pollutants, such as heavy metals, can cause an imbalance in gut microbiota. This can affect communication between the gut and the brain, impacting aspects of brain function and behavior. The purpose of this systematic literature review is to assess whether the altered gut microbiota profiles may act as a mediating factor in the harmful effects of heavy metal exposure on brain function.

To conduct this review, researchers evaluated animal studies that included heavy metal exposure and compared them with a control group. They assessed cognitive and/or molecular results, in addition to microbiota composition analysis. The authors used the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) approach for preclinical investigations to independently evaluate papers for inclusion, extract data, and assess the risk of bias.

After a thorough search across three databases, the researchers found 16 relevant papers on heavy metal exposure. Of these, 10 were on lead, 1 was on cadmium, 3 were on mercury, 1 was on manganese, and 1 was on combined exposure of lead and manganese. The animal species utilized for the research included zebrafish, rats, mice, carp, and fruit flies.

Heavy metal exposure has been shown to alter the abundance of essential bacterial phyla like Firmicutes and Proteobacteria, which are crucial to gut health. These changes have been linked in several studies to mood disorders, deficits in memory and learning. The relationship between heavy metals, gut microbiota, and the brain implies that heavy metals may cause direct changes in the brain and indirect effects via the microbiota. This can lead to neurotoxicity and the emergence of neuropsychological problems.

Studying the impact of heavy metals on the gut microbiota of zebrafish can help us comprehend the possible direct changes in the brain and indirect effects via the microbiota. This may result in neurotoxicity and the emergence of neuropsychological problems. The same applies to humans.

3. In Zebrafish, Obesity Reduces Cognitive Performance but Has No Effect on Anxiety-Like Behaviour.

There is currently a growing body of research focusing on the effects of metabolic disorders on cognitive and neurodegenerative processes. Alzheimer's disease has been proposed as "type III diabetes" due to the high risk of dementia associated with type II diabetes and the evidence suggesting the existence of insulin resistance in the brain during Alzheimer's disease. Additionally, diet and nutrition are closely linked to mood disorders, including anxiety and depression, as well as other neuropsychiatric conditions. Obesity, a global concern, poses a challenge to the health systems in Western societies and is a major factor in metabolic syndrome, which has significant negative effects on brain structure that impair cognitive function and emotional states. This exacerbates the development of learning and

memory dysfunction and promotes anxiety-related responses.

Zebrafish have become a crucial model organism for the study of neurological disorders, metabolic diseases, and behaviour in the last decade. They provide an exciting model for examining the effects of energy disturbance on behavioural features. High-fat and/or carbohydrate diets have been shown to impact cognitive function and anxiety-like behaviour in neurobehavioral tests that resemble those conducted on mammals. However, there is controversy surrounding the behavioural effects of obesity, depending on the method used to promote it. High-fat-induced diet-induced obesity results in hyperglycaemia, ectopic lipid accumulation, and adipocyte hypertrophy, leading to increased visceral adipose tissue depots and the expression of genes related to inflammation, fibrosis, and lipid metabolism. Overfeeding with regular diets promotes obesity while maintaining metabolic health. However, it harms brain homeostasis and neural plasticity, which makes zebrafish more prone to anxiety-like behaviours. Despite this, overfeeding-induced obesity in zebrafish did not result in variations in aversive learning assays or generate anxiety-like reactions in some trials. To address this controversy, researchers explored the effects of overfeeding-induced obesity on anxiety-like behaviour and short- and long-term memory using aversive learning tests in zebrafish.

In this study, two groups of fish were used, with 24 fish in each group. One group was fed a normal diet (2% food), while the other group was overfed (8% food) for a period of 8 weeks to induce obesity. The anxiety-like behaviour of the fish was assessed using a novel tank diving test (NTDT). Before the test, the fish were trained for four days to measure their long-term memory, and then tested for short-term memory. After the trial, the fish were dissected to obtain their biometric samples and analyse their total lipid content and triglycerides. The brains of eight fish from each group were also dissected to study the monoamines using HPLC.

An increase in total lipid content indicates faster growth and obesity caused by overfeeding. However, overfeeding-induced obesity does not affect behaviours resembling anxiety. To assess the cognitive function (memory and learning) of animals, researchers used the unpleasant learning test in Zantik AD units. The study found that zebrafish with obesity have cognitive functions. Although both overfeeding-induced obesity and control animals were able to associate the unpleasant stimulus with the conditioned stimulus (conditioned learning), overfeeding-induced obesity decreased short-term memory, independently of fish sex. The study also quantified the total brain levels of serotonin and dopamine, as well as their metabolites, which showed that obese fish did not exhibit a decrease in monoaminergic transmission.

Hence, this research provides a better understanding of the effect of metabolic diseases on cognitive and behavioural science using zebrafish. This approves it as a superior animal model for understanding cognitive and behavioural neuroscience.

4. A semi-automated method and procedure to explore associative learning in adult zebrafish in a home-tank setting

Zebrafish offer a balance between biological complexity and pragmatic simplicity, making them a potential paradigm in brain research. Their simple but evolutionarily conserved brain, coupled with a variety of genetic tools, allows exploration of molecular mechanisms underlying brain function and behaviour. With nucleotide sequences highly homologous to those of human genes, zebrafish are considered an excellent translational tool with potential for modelling various human CNS dysfunctions and underlying disease mechanisms. In recent years, researchers have mainly exploited these qualities of the zebrafish in studies exploring toxicology, behavioural processes, pharmacology, and cognitive abilities.

The use of zebrafish for studying learning and memory has been successful. It has been found that adult zebrafish are capable of displaying both types of associative learning present in higher-order animals. They can associate a single stimulus (known as conditioned stimulus or CS) with a reinforcer (known as unconditioned stimulus or US) that can be either appetitive (rewarding) or aversive (punishing). The number of zebrafish learning paradigms is rapidly increasing, which allows researchers to quantify similar learning phenomena using different methods. For instance, researchers were able to achieve one-trial learning in zebrafish by using an electric shock inhibitory avoidance task in a small aquarium that contained a black-and-white section. Another similar learning regimen was used in different settings, where the fish learned to associate electric shocks with the side of the aquarium that had a green light.

Assessing behaviour is important in various domains, and new techniques and frameworks have been developed to examine learning and memory in mature zebrafish. However, human handling can be a significant obstacle in these techniques. To overcome this, automated learning paradigms have been created with varying degrees of effectiveness. In this study, a semi-automated home tank-based learning and memory test paradigm was used to quantify classical associative learning performance in zebrafish. The paradigm utilized visual cues and showed that zebrafish could successfully learn to associate coloured light with food reward. The apparatus and software used in the task are simple to purchase, affordable, and easy to set up. Test fish can stay in their home tank for several days without any disturbance from the experimenter, reducing stress caused by handling or human interaction.

Researchers have developed an inexpensive and simple technology to test and train zebrafish memory without human intervention. The system involves observing the actions of solitary zebrafish in their "home tank" for seven days. During this time, the fish showed no signs of stress or sedation, and they were able to develop associative memory. The learning task required discriminating between reinforced and unreinforced stimuli, or creating a link between a single stimulus and the response. This method eliminates confounding effects of human interference and is cost-effective, expandable, and easy to use. It is expected to be popular among those studying the psychological and neurobiological mechanisms of learning and memory in zebrafish.

The researchers have successfully developed inexpensive and straightforward automated home-tank-based learning paradigms for zebrafish. These paradigms will aid in comprehending various cognitive and mnemonic traits of zebrafish; such as element and configural learning and memory.

Hence, zebrafish is a superior model organism for researching neural mechanisms involved in memory and learning.

5. Zebrafish can be used as a model organism to study the effects of flavonoids on neurodegenerative diseases.

Over the past decade, scientific studies have shown a great interest in flavonoids, a large family of polyphenolic secondary metabolites. Flavonoids are known to regulate the expression of multiple genes and modulate many molecular pathways involved in various biological mechanisms. They can reduce the formation of reactive oxygen species (ROS) and limit the expression of some inflammatory mediators, resulting in their anti-inflammatory properties. By doing so, flavonoids can prevent the onset of pathological processes such as aging, cancer, cardiovascular diseases, inflammation-related diseases, and neurodegenerative diseases.

There is increasing evidence that a diet rich in flavonoids can improve cognitive abilities at the neurological level. Flavonoids appear to impact the signalling pathways that are involved in neuronal plasticity, learning, and memory, such as cAMP response element-binding protein/extracellular signal-regulated kinase/brain-derived neurotropic factor (CREB/ERK/BDNF) or serine/threonine-specific protein kinase/protein kinase B (Akt/PKB). Additionally, some flavonoids are beneficial as adjuvants in preventing and treating neurodegenerative diseases like Alzheimer's and Parkinson's.

Recent research has shown that adult vertebrates, including humans, exhibit significant neurogenic activity in certain areas of their brains throughout life, despite previously held beliefs that adult neurogenesis was impossible. This discovery has significant implications for combating neurodegenerative and psychiatric illnesses, which have been associated with changes in the neurogenic niches responsible for the synthesis of new neurons or loss of equilibrium between apoptosis and new neuron genesis. Flavonoids, a group of phytochemical compounds, have emerged as a promising candidate for fighting these diseases. They have been found to inhibit pro-apoptotic mechanisms and enhance neuronal plasticity, making them ideal for neuroprotection and regeneration. Furthermore, flavonoids have been found to reduce neuroinflammation by modulating the release of inflammatory cytokines by mixed glial cells (astrocytes and microglia). They also alter the activity of oxidative stress-related enzymes, including SOD, COX-1, and COX-2, which makes them effective in treating neurodegenerative diseases. Additionally, some flavonoids interfere with the formation and accumulation of neurotoxic proteins, such as amyloid-protein 42 (A 42) and synuclein, which are responsible for the progression of neurodegenerative diseases. Therefore, flavonoids have become a promising area of research for the development of new neuroprotective and neuroregenerative strategies.

Zebrafish are an ideal model for studying human neurodegenerative disorders. This is because they share many genetic and neuroanatomical similarities with humans. Additionally, the adult zebrafish brain has a high level of neurogenic activity, which helps researchers understand how flavonoids can protect and regenerate neurons. Flavonoids have been found to have neuropharmacological properties and may be used as adjuvants in managing and preventing neurodegenerative diseases. This research offers potential support for the development of natural and alternative therapies against these illnesses.

Studying the potential positive effects of flavonoids on neurodegenerative illnesses may become easier with the use of zebrafish, which is an intriguing model organism. Zebrafish are valuable for researching human neurodegenerative diseases and understanding the role of flavonoids in those disorders because they share a high degree of genome homology—70% compared to humans. Zebrafish also have a brain organization that is similar to the human brain, as well as similarities in neuroanatomical and neurochemical processes. Additionally, zebrafish maintain high levels of neurogenic activity in adult brains.

This study confirms zebrafish as an appropriate animal model for cognitive science research.

6. Protein dynamics and molecular tools in zebrafish are used to study learning and memory formation.

Memory and learning play an essential role in our daily lives. During learning and memory, molecular modifications occur, which lead to behavioural and cognitive changes. Most of these modifications are specific to each species. Despite substantial advancements in understanding the molecular mechanisms of learning and memory and identifying key protein components essential for plasticity, the precise molecular pathways responsible for these processes have not been completely characterised.

The brain is a highly complex organ that poses a significant challenge to researchers who seek to unravel the intricate neuronal networks and chemical processes involved in learning and memory formation. To overcome this challenge, scientists have turned to model organisms with relevant behavioural repertoires, such as simple-nervous invertebrates and vertebrates with well-preserved central nervous system areas. Among these model organisms, zebrafish stand out as an excellent choice for investigating memory consolidation due to their unique characteristics that are highly useful for studying the general and conserved principles of vertebrate nervous system activities, including learning and memory.

Zebrafish are genetically tractable vertebrates with a small, easily accessible, and translucent brain that exhibits several characteristics of vertebrate-conserved brain organization. They also exhibit sophisticated behaviours, such as learning and memory functions, making them a complementary vertebrate model that is highly suitable for high-throughput investigations. Zebrafish are particularly useful for exploring the molecular and neurological foundations of learning and memory, owing to their translucent nature from ovum to mature larvae and their suitability for genetic manipulation. As a result, they have long been a favourite model organism among developmental biologists and geneticists.

Ground-breaking research on the requirement for protein synthesis during the establishment of long-term memory has utilized puromycin and other non-specific protein synthesis inhibitors. These inhibitors can be administered by injection to a specific area of the brain or added to the water bath of zebrafish, causing global inhibition. While these inhibitors cannot be limited to a particular cell type, they can be directly applied to specific brain regions at different stages of long-term memory formation. However, they are unable to differentiate between the roles played by glial cells and neuronal subtypes in memory consolidation, even though glia's have been shown to function in memory. Therefore, new tools have been developed, including a toxin from Maize that can be expressed in a cell-type-specific manner, enabling cell-type-specific drug-inducible inhibition of protein synthesis. Another approach involves altering the kinase activity of elf2a, which influences memory consolidation in mice, to regulate the translation of proteins linked to memory consolidation in a cell-type-specific fashion.

Young juvenile zebrafish (2–4 weeks post-fertilization) have smaller, easier-to-access brains than adult zebrafish, making them a suitable tool for future studies. Although comparatively underutilized, the combination of early juveniles and innovative techniques, such as labelling with NCAAs in a cell-type-specific manner, is beginning to be employed to examine the

developing proteome during different forms of learning and memory. With the potential for increased application and improvement of the zebrafish model, including new approaches, researchers anticipate a better understanding of the molecular mechanisms underlying conserved long-term memory development in vertebrates.

7. **Glaucosciadiumcordifolium's (Boiss.) promnesic, anxiolytic, and antioxidant effects Essential Oil of Burtt & Davis in a zebrafish Model of Cognitive Impairment**

Alzheimer's disease (AD) is a brain disease that causes dementia, and it progressively deteriorates over time. It damages neurons in the brain that are responsible for memory, language, and thinking. This damage leads to symptoms such as memory loss, difficulty with thinking, language, and problem-solving, as well as neuropsychiatric symptoms such as anxiety, apathy, and depression.

Beta-amyloid plaques, tau protein neurofibrillary tangles, loss of cholinergic neurons in the forebrain, and a significant decrease in acetylcholine (ACh) levels are significant indicators of Alzheimer's disease.

Cholinergic transmission plays a crucial role in memory, learning, attention, and other complex cognitive processes in the brain. Alzheimer's disease affects two types of receptors important in cognition: the nicotinic acetylcholine receptors (nAChRs) and muscarinic acetylcholine receptors (mAChRs).

Scopolamine (SCOP) is a mAChR antagonist that mimics dementia in Alzheimer's disease by causing cognitive impairment in test animals. Zebrafish, a small freshwater fish originating from India, is an excellent complementary model for neurodegenerative research due to its simplicity and robust behavior forms. It shares similarities with humans in psychological, emotional, and social behavioral patterns, as well as neuroanatomical and neurochemical pathways.

Glycosciadiumcardifolium, a plant belonging to the family Umbelliferae, has been used in traditional medicine for stomach ailments and as an aphrodisiac and appetizer. Researchers aimed to characterize Glaucosciadiumcordifolium (Boiss.) essential oil from the aerial parts and evaluate its potential in a SCOP-induced zebrafish model of cognitive impairment.

The study found that GCEO alleviated memory impairment and anxiety-like responses caused by SCOP and lessened oxidative damage. It enhanced cholinergic system activity by reducing the activity of acetylcholinesterase (AChE) after exposure to GCEO. Together, GCEO improves memory impairment by re-establishing the brain's antioxidant state and cholinergic dysfunction.

The results of this study demonstrate that zebrafish are a suitable model for conducting tests on various kinds of cognitive science-related topics.

8. **Utilising zebrafish as a Research Instrument for Sleep and Memory-Associated Disorders**

Sleep is a fundamental part of life that is observed in several animal species. In humans, the amount of sleep required varies from person to person, but it is generally estimated that 7 to 8 hours of sleep per night are needed for the body to function optimally. Despite ongoing debates about its underlying causes and functions, sleep is an essential biological need that plays a crucial role in a wide range of processes, including learning, memory consolidation, emotional stability, and cerebral homeostasis maintenance. When you sleep, the brain exhibits two distinct types of electrical activity: slow-wave activity, which is characterized by Non-Rapid Eye Movement (NREM) sleep, and desynchronized brain wave activity, which is indicative of wakeful brain activity and rapid eye movement (REM) sleep.

One of the primary theories behind the need for sleep is synaptic homeostasis restoration. The process of learning, creating new memories while awake, and synaptogenesis throughout development all increase synaptic strength, which upsets the balance of synaptic homeostasis. This results in higher energy consumption and a greater demand for cellular supply, leading to cellular stress. Additionally, there may be a decrease in the selectivity of neural responses and difficulties in learning. During sleep, reduced plasticity in neurons and other cells facilitates memory consolidation and integration by regaining neural selectivity and learning capacity, as well as restoring synaptic strength.

Wakefulness and sleep patterns differ among different animal species. These patterns are likely influenced by the environment in which they live, and the neural mechanisms underlying these processes are likely developed to adjust brain functions to each environment, enhancing performance, sustaining nervous system health, and promoting behaviour. The state of wakefulness is liable for behaviours that are directly linked to motivation and ability, such as reproduction,

foraging, and parental nurturing. Similarly, sleep is a quiescent state that is thought to be essential for the neurological system's upkeep, as well as the body's immune system, learning, memory, and consciousness systems. Certain birds and marine mammals exhibit what is known as one-hemisphere sleep, in which one side of the brain maintains alertness while the other produces activity resembling NREM sleep, enabling the animals to fly or swim while they sleep.

As a robust model for biomedical research, particularly in neuroscience, zebrafish (Danio rerio) has garnered attention. This species has genetic and physiological similarities to other vertebrates, including humans, as it exhibits 70% homology with human genes. Zebrafish has an integrated central nervous system, with homologous brain structures showing a high degree of similarity in neuroanatomical and neurochemical pathways, presenting organizational conservation between zebrafish and human brains. The zebrafish brain comprises four structural structures: the telencephalon, diencephalon, midbrain, and hindbrain. The hippocampus, isocortex, and amygdala of vertebrates exhibit resemblances to the lateral, dorsal, and medial pallium of zebrafish, respectively. Zebrafish contain neurotransmitter networks that are exactly like those in the human brain, including noradrenergic, serotonergic, dopaminergic, histaminergic, and aminergic systems.

Sleep tests have already been standardized in zebrafish. In a study, larvae were subjected to a light and dark cycle of 14 L:10 D. The test involved a 14-hour light adjustment period beginning at 8 am, followed by a 6-hour dark evaluation period beginning at 10 pm after the larvae were moved to the Zebrabox at 4 pm. The distance travelled and high activity was analysed as well as the average inactivity to determine the period of sleep at night. Cognitive tasks have previously been used in adult animals to evaluate the effects of various sleep deprivation regimens in zebrafish. Animals subjected to sleep deprivation procedures have been shown to have impaired affective spatial memory related to school, object discrimination, and unpleasant memory through electric shock. These studies highlight the value of utilizing zebrafish as a model for sleep disorders study, both in the larval and adult stages, using a variety of behavioural activities.

In conclusion, a deeper comprehension of the molecular and neural mechanisms of sleep regulation will help expand our knowledge of sleep. Further studies on sleep in various species, including zebrafish, may provide new perspectives on the fundamental roles and conserved genetic mechanisms underlying sleep regulation.

II. CONCLUSION

Through the study of research conducted using zebrafish as an animal model, we can understand its importance in contributing to different aspects of cognitive science. Zebrafish share up to 70% genetic resemblance with humans, making them an important animal model for biomedical research in studying cognitive behaviour.

The use of zebrafish as an animal model in cognitive behaviour research promotes the investigation of a wide range of pharmacological interventions. This includes conducting behavioural assays, drug screening, and neuropharmacological studies. These approaches provide valuable insights into the effects of drugs on learning, memory, attention, and other cognitive functions. As a result, they offer potential avenues for therapeutic interventions in cognitive disorders.

Overall, these findings have a positive impact and encourage the utilization of zebrafish in conducting different pharmacological studies in the field of cognitive science.

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