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Review Article

A Review on Spatial Memory, Psychosis and Cognitive Dysfunction Screening Methods in Rat models

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ABSTRACT

Assessment of memory and learning in animal models has been extensively employed in scientific research. Among many disorders, in this article, we emphasise an overall review of memory-related problems like those representing diseases with primary processes of affected memory – such as amnesia, dementia, brain ageing, neurodevelopment, trauma, epilepsy and neuropsychiatric disorders, etc. Toxic effects of specific drugs and other exploring are often responsible for these conditions. There is a diversification of experimental methods assessing animal learning and memory skills. We have many memories assessment models today to test memory along with maze in rodents; there are also other several types of them, but their real usefulness, advantages and applications stay to be completely settled and rely upon the specific variation chosen by the experimenter. The point of the current article is first, to momentarily audit the collected information concerning spatial memory tasks; second, to welcome the reader data on the various types of memory diseases in rodents; and third, to elucidate the usefulness and limitations of different available plant sources to treat memory and learning disorders.

Keywords: Animal Model, Scientific Research, Amnesia

INTRODUCTION

A psychotic disorder is a mental disorder that causes abnormal thinking and perceptions. It affects the way the brain processes information. Marked disturbances in personality in social, interpersonal, judgment & occupational functioning and spatial working memory ability is a marker of risk-for-psychosis, In both humans and animals, spatial memories can be synced.[1] Spatial memory is a form of memory responsible for the recording and recovery of information needed to plan a course to a location and to recall the location of an object or the occurrence of an event.[2] Spatial memory is indispensable for direction in space.[3,4] Spatial memory can be separated into egocentric and all centric spatial memory.[5] A person's spatial memory is expected to investigate around a recognizable city. A rat's spatial memory is expected to become familiar with the area of food toward the end of a maze. Spatial memory has representations in short-term memory long-term

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memory and working. Research indicates that there are specific areas of the brain associated with spatial memory like the hippocampus, prefrontal cortex and amygdala[2] Psychotic disorders are the group of illnesses that affect the mind. They make it difficult to think, react inwardly, convey adequately, make great decisions get reality, and act appropriately.

At the point when indications are serious, individuals with psychotic problems experience difficulty keeping in contact with the real world and can't deal with their routine. Yet, even extreme psychotic problems normally can be dealt with.

TYPES OF PSYCHIC DISORDERS:[3]

Schizophrenia: Patients with this illness have changes in behaviour and other symptoms such as delusions and hallucinations

Delusional disorder: having a delusion involving a real-life situation that could be true but isn't, such as being plotted against, having a disease or being followed.

Shared psychotic disorder: This is observed when one person in a relationship has a delusion then the other person in the relationship adopts it, too.

Substance-initiated psychotic disorder: This condition is for the most part brought about by the utilization or withdrawal of medications, such as crack cocaine, that cause hallucinations, delusions, or confused speech.

Psychotic disorder due to another medical condition and Paraphrenia are some of the psychic disorders.

Difference between spatial memory and cognitive mapping:

It is the spatial memory that records information about one's environment and spatial orientation whereas cognitive mapping uses spatial memory.[4]

SYMPTOMS:

Disorganized and incoherent speech, confused thinking, hallucinations, delusions, strange and dangerous behaviour, slowed movements, less interest in personal hygiene, poor interest in activities, issues at the everyday schedule and with connections, cold, withdrew away with the failure to communicate the feelings, mood swings or other disposition side effects, for example, discouragement and lunacy are the most generally noticed manifestations in psychotic problems.[5]

DIFFERENT SCREENING METHODS FOR SPATIAL MEMORY:

A) POLE CLIMBING TEST (WITH TRAINED RAT)

Pole Climbing Test: Cook's Pole Climbing Apparatus is used to study cognitive function, mainly a response to conditioned stimuli during learning & its retention. Mixed shock (6mA) is conveyed to the grid floor of the chamber made out of treated steel poles. A pole, 2.5 cm in diameter, hangs inside the chamber through a hole in the upper centre of the chamber. The review rat was put in the chamber and permitted to investigate the chamber for 45 seconds. Conditioned stimulus (CS) for example bell signal was turned on and unconditioned Stimulus (US) i.e. electric shock delivered through grid floor for 45 Sec. Creature figured out how to connect the bell with the approaching foot shock and was equipped for keeping away from the foot shock by climbing the post after the bell signal. Avoidance response was defined as climbing reaction time 10 Sec.[6]

B) T MAZE ALTERATION TEST

T Maze is used to assess the cognitive ability of rodents. It is an elevated or enclosed apparatus in the form of a T placed horizontally. Animals are started from the base of the T Maze and allowed to choose a goal arm. When given two trials, in the second trial the rodent tends to choose the arm not visited before, it is called spontaneous alternation. If this tendency is reinforced by rewarding animals in the preferred food is called rewarding alteration. Both spontaneous and rewarded alterations are very sensitive to dysfunction of the hippocampus.

C) LOCOMOTOR ACTIVITY

The creature locomotor action was observed utilizing Actophotometer furnished with an advanced counter, photocell and a light source was utilized to quantify locomotor action (horizontal movement) of creatures. Every creature was put in Actophotometer for 5 minutes and a basal action score was recorded for all creatures. Each animal was treated with the respective drug and the activity score was recorded after 30 min to 1hr. Decreased movement score was taken as a list of CNS depression Depending on the particular arrangement, one can inspect horizontal action, vertical action, time spent in different areas of the enclosure, and all-out distance travelled.

Improvements of an open-field water-maze method in which rats figure out how to escape from misty water onto a hidden platform are depicted. These incorporate a technique (A) for naturally following the spatial area of a hooded rat without the utilization of connected light-emitting diodes; (B) for concentrating on various parts of spatial memory (for example working memory); and (C) for concentrating on non-spatial separation learning. The speed with which rats learn these tasks suggests that they may lend themselves to a variety of behavioural investigations, including pharmacological work and studies of cerebral function.

PLANTS THAT IMPROVE MEMORY AND CONCENTRATION:

Huperzia, Beans, Ginkgo Biloba, Kale, Rosemary, Thyme, Peppermint, Bacopa Monnieri, Ashwagandha, Sweet Flag (Vacha), Gotu Kola, Reishi Mushroom, Holy Basil, Ginseng, Periwinkle, Blueberries, Yerba Maté.[7]

Eugenol has great potential against ***oxidative stress, inflammation, pain management (dental analgesic)*** which was reported in previous studies**.**

DISORDERS OF SPATIAL MEMORY:

Topographical disorientation, Hippocampus damage and schizophrenia, GPS (Global Positioning System), NEIL1 are some of the spatial memory disorders.

Hippocampus damage and schizophrenia

Research with rats showed that spatial memory can be unfavourably impacted by harm to the hippocampus so that it intently takes after schizophrenia. Shortly after birth schizophrenia is thought to stem from neuro-developmental problems.

The most commonly used models of schizophrenia patients are rats. During experimentation lesions in the ventral hippocampus area are created shortly after birth, a procedure known as neonatal ventral hippocampus lesioning (NVHL). Adult rats with NVHL show typical indicators of schizophrenia such as hypersensitivity, psychosis, impaired prepulse inhibition, working memory reduced social interactions and set-shifting. Like schizophrenia, impeded rats neglect to involve natural settings in spatial learning undertakings, for example, showing trouble finishing the spiral arm maze and the Morris water maze.[8]

NEIL1

Endonuclease VIII- NEIL1 is a DNA repair enzyme that is mostly expressed throughout the brain. NEIL1 is a DNA glycosidase that starts the initial phase in base extraction fix by severing bases that are harmed by responsive oxygen species and afterwards presenting a DNA strand break by a related lyase response. This catalyst perceives and eliminates oxidized DNA bases including formamidopyrimidine, thymine glycol, 5-hydroxyuracil and 5-hydroxycytosine. NEIL1 works by promoting short-term spatial memory retention. The mice lacking NEIL1 have impaired short-term spatial memory retention in a water maze test.[9]

PATHOPHYSIOLOGY OF PSYCHOSIS:

Psychosis is linked to the neurotransmitter dopamine. To be more precise, the dopamine hypothesis of psychosis is very much influential and states that an over-activity of dopamine function in the brain results in psychosis, particularly in the mesolimbic pathway. The dopamine-blocking drugs (i.e. antipsychotics) tend to decrease the intensity of psychotic symptoms, and those drugs which boost dopamine activity (such as cocaine) in some people can trigger psychosis, these pieces of evidence support the above theory. However, in recent times increasing evidence has pointed to a possible dysfunction of the excitatory neurotransmitter glutamate, in particular, with the activity of the NMDA receptor. This theory is reinforced by the fact that dissociative NMDA receptor antagonists such as ketamine, PCP and dextromethorphan/ dextrorphan (at large overdoses) induce a psychotic state more rapidly than dopaminergic stimulants, even at recreational doses.[10]

TREATMENT:

Treatment includes a combination of medication and counselling. Drugs that are effective in reducing the symptoms are Aripiprazole, Asenapine, Brexpiprazole, Clozapine, Iloperidone, Lurasidone, Cariprazine, Olanzapine, Paliperidone and its palmitate, Quetiapine.[11] New antipsychotic drugs which act on glutamate and its receptors are currently undergoing clinical trials.

Epigenetic and pathophysiology

Epigenetic mechanisms are basic biological processes that have been studied extensively in many areas of behavioural neuroscience, and growing evidence suggests that epigenetics play an important role in the complex pathophysiology of psychotic disorders. Mainly three epigenetic mechanisms serve to regulate function and chromatin structure i.e., DNA methylation, post-translational histone modification, and RNA interference.

A job for chromatin elements in every individual neuron's genomic reaction to that cell's exceptional climate inside the mind (an example of synaptic information and result, openness to neurotrophic factors, and extracellular matrix) is beginning to emerge.[12] Neuronal activation has long been associated with increased expression of c-fos [13,14] and brain-derived neurotrophic factor (BDNF).[15]

Contextual fear conditioning is a typical trial worldview in the investigation of learning and memory, where creatures figure out how to relate a generally harmless occasion or climate with an aversive improvement. Learning in this context leads to the induction of BDNF exons I, IV, VI, and DC and decreased DNA methylation of these regions through an NMDA receptor-dependent mechanism.[16] Animal models of addiction have been utilized to exhibit neuronal movement subordinate phosphorylation of methyl-cytosine

restricting protein 2 (MeCP2), a "reader" of DNA methylation that enlists extra chromatin modifiers to a locus, mediated by calcium flood.[17] An itemized comprehension of how the intricate arrangement of chromatin guideline capacities in the sound cerebrum creates neuronal plasticity, and how it is broken in the development of mental infection, is a terrific test in the field.

Epigenetic mechanisms are rapidly expanding fields and basic biochemical pathways essential to every cell function and cell type, which offers great hope for improved understanding and interventions in virtually all areas of medicine. The field of psychiatry, which has since a long time ago looked for a thorough logical comprehension of the interaction among genome and climate, or nature and support, stands to benefit particularly from the investigation of epigenetics. Epigenetics is at present being applied to an extraordinary number of mental diseases across the whole broadness of the field. One region that loans itself particularly well to epigenetic examination is enslavement research, which at its centre is the investigation of how a particular gathering of ecological exposures (medications of abuse) prompts enduring changes in the construction and capacity of the cerebrum, at last coming about in relentless social pathology.[18] While examination of epigenetic is proving to be fruitful in various spaces of psychopathology, the current discussion will focus on late work applying the thoughts of epigenetic to the examination of psychotic disorders.

In the affected individual's brains the Molecular analysis of psychotic disorders has documented many specific changes like diagnosis, neuronal circuitry, and cell type which are specific to the changes in gene expression.

CHALLENGES

Despite huge progress in the study of behavioural neuroscience, several significant challenges remain. The brain is a complex organ composed of a large number of neurons, glial cells, and vascular and other supportive cells. The particular neuronal subtypes assume discrete parts in the cerebrum work in wellbeing, and neurotic changes relevant to sickness processes are not dispersed similarly across all neuronal subtypes. The majority of biochemical studies of the brain up to date have been performed by the homogenized cortex, which is problematic for homogenizing the brain tissue discards wealthy information concerning the cellular and subcellular distribution of the molecules of interest, making it impossible to determine which subpopulations of cells are host to the findings of the study. Consequently, further developed innovation fit for testing homogenous subpopulations of neurons from brain tissue for biochemical investigation is required. At present exciting work using fluorescence-activated cell sorting (FACS) 93 and microfluidic cell, sorting is on its way in pursuit of this goal. Another way to this problem is an analysis of isolated single neurons, but this approach has limited sensitivity of the downstream analytic technique and will need to overcome significant limitations of throughput. Also, psychopathology is delivered not by the modified capacity of single cells but rather by pathologic changes in the behaviour of neuron groups particular to perform specific tasks in discrete areas inside neuronal circuits.

Problem is that human brain tissue for the direct study is inaccessible. Epigenetic mechanisms are reversible and metastable, and having access to our brain only at post-mortem time makes it difficult or impossible to completely understand how these mechanisms are involved in disease progression, treatment response, relapse, remission, and so on.

Many groups are trying to solve this problem from a living subject by identifying other issues that can be sampled to offer insight into epigenetic processes which is relevant to brain function. Lymphocytes that are isolated from peripheral blood are most commonly sampled for this purpose. epigenetic mechanisms act in a tissue-specific manner highly, and while changes in DNA methylation patterns are correlated between cortex and the peripheral blood of an individual significantly, differences in patterns of DNA methylation between cortical tissue of separate subjects is significantly exceeded by the variation observed between cortex and blood within a specific single subject.[19] It has been shown that many aspects of the human neuronal epigenome are unique to neurons and are not present in glial also they are unique to humans. Due to the complex architecture of the cortex the examination of human brain tissue was limited as it is, and will be essential to further investigate our understandings of the role of epigenetic mechanisms in the pathophysiology of psychosis.[20] Also, investigations of human peripheral tissues and animal models are necessary at the same time and hopefully, it will lead to the identification of biomarkers for the susceptibility of disease, progression, and response to pharmacotherapy. The consolidated endeavours of numerous groups exploring post-mortem human brain, peripheral human tissues and cultured cells, and creature models will ideally be fruitful in fashioning a way ahead.

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