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Review Article

A Review On The Effect Of Anxiety In Rat Using Hole Board Apparatus

Nilesh Pawar*[1], Prasanna Bachhav[2], Sanskruti Sarode[3], Sanjivni Bachhav[4]

[1-4] *Bachelors, Department of Pharmacology, K. B. H. S. S. Trust's Institute of Pharmacy & Research Centre, Bhayegaon, Malegaon, Nashik, Maharashtra, India.*

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ABSTRACT

Anxiety disorders are biosocial conditions that involve systemic or situational responses to perceived threats. Childhood anxiety affects one in four children between the ages of 13 and 18. The average age of onset is 11 years. Overall prevalence in children under 18 years of age ranges from 5.7% to 12.8%. Anxiety disorders are usually treated with medication, some form of psychotherapy, or both. The main medications used for anxiety disorders are antidepressants, anxiolytics, and beta blockers to control physical symptoms. Behavioral studies in animal subjects (mice) are important to understand this disease and introduce new treatments from a translational perspective. The Hole-board apparatus has emerged as a widely used test for studying anxiety-related behavior in relationships. We focused on the Hall apparatus as an advanced tool to measure research activity in laboratory mice. Other behavioral control mechanisms (eg, emotional responses, risk assessment, active coping) may play an additional role in shaping the animal's activity on the Hole-board apparatus.

INTRODUCTION

Anxiety disorders are biosocial conditions involving systemic or situational responses to perceived threats [1]. Anxiety disorders have historically attracted considerable research attention [1,2]. Anxiety disorders are one of the most common mental disorders. They usually appear early in life and share features with other psychiatric disorders, but with a more progressive evolution and severe functional consequences. The global security epidemic poses a serious threat to the well-being and quality of human life [2]. Anxiety disorders have different clinical manifestations. For some people, certain environmental stimuli are linked to the cause of the phobia [3]. Some people experience serious problems like panic disorder [4,5]. If left untreated, chronic anxiety can lead to a number of health problems, including high blood pressure, cardiovascular disease, and dementia [6]. Current treatments for anxiety usually include pharmacotherapy and psychotherapy. Although

***Corresponding Author:** Nilesh Pawar
Address: *Bachelors, Department of Pharmacology, K. B. H. S. S. Trust's Institute of Pharmacy & Research Centre, Bhayegaon, Malegaon, Nashik, Maharashtra, India.*
Email : sakshivyavahare25@gmail.com

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physical reactions associated with anxiety can be treated with medication, the mental memory and causes of anxiety require mental resolution. There is a lot of evidence that psychological therapy, such as educational therapy, is more beneficial for people with anxiety disorders. Researchers need to understand the epidemiological nature of anxiety to identify trends related to demographic factors and to aim for better prevention and control in the population [7]. 20% of adults experience an anxiety disorder each year. Generalized anxiety disorders cause feelings of fear, anxiety, and worry. Generalized anxiety disorder is characterized by persistent, excessive, and unrealistic worry about everyday things. These problems can take many forms, including financial, family, health, and future problems. The disease is characterized by persistent mental and physical symptoms that are difficult to control and often non-specific. Excessive worry is one of the main symptoms of generalized anxiety disorder [8-10]. Childhood anxiety affects one in four children between the ages of 13 and 18. The average age of onset is 11 years. However, among children aged 13-18 years, the prevalence of severe anxiety disorders is around 6%. Overall prevalence in children under 18 years of age ranges from 5.7% to 12.8%. The prevalence in women is twice that of men [11-13].

Symptoms:

Sleep disturbances and the psychological experience of difficulty concentrating, concentrating, and/or functioning are common symptoms of many anxiety disorders. Despite their similarities, these disorders often have different symptoms, course, and treatment. Patients often report worsening physical health as their main concern. This can distract you from the main symptoms of anxiety temporarily. This is usually accompanied by short-term intense fear and panic with physical symptoms such as chest pain, dizziness and shortness of breath. In addition to agoraphobia, personal fear can lead to panic attacks and the inability to escape. As a result, patients avoid such situations and eventually become depressed [14]. The ancient word "agoraphobia" is translated from Greek as "fear of the free market". Modern agoraphobia is a strong and violent reaction to situations where escape is difficult or impossible, such as being alone outside the home, traveling in a car, bus, or plane, or in crowded places with a lot of attention [15].

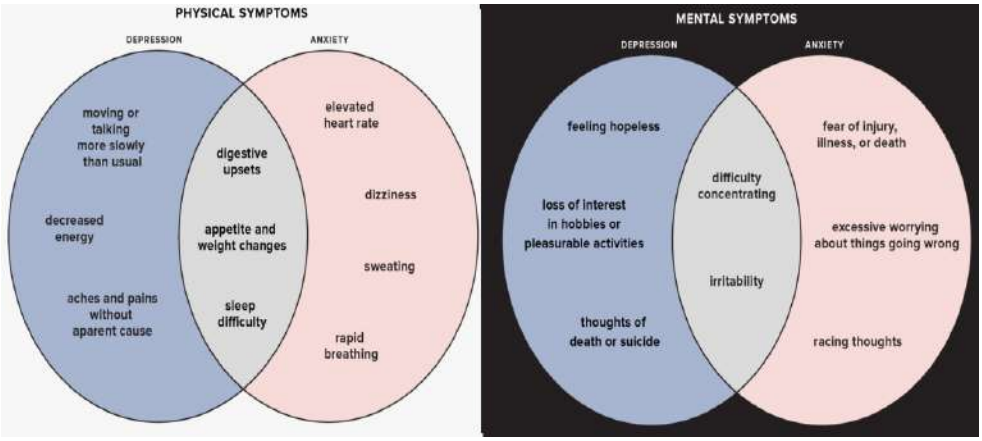

Figure 1: Sign and symptoms of Anxiety vs Depression

Pathophysiology of Anxiety:

Important mediators of anxiety in the central nervous system (CNS) are norepinephrine, serotonin, dopamine, and gamma aminobutyric acid (GABA). The autonomic nervous system, especially the sympathetic nervous system, mediates many of these symptoms. The amygdala plays an important role in reducing fear and anxiety [16]. In patients with anxiety disorders, the amygdala is more sensitive to anxiety. Amygdala

and prefrontal cortex structures are connected to prefrontal cortex regions, and abnormal prefrontal cortex activation can be reversed by psychological or pharmacological interventions [17].

Treatments of anxiety disorder:

Anxiety disorders are usually treated with medication, some form of psychotherapy, or both. The choice of treatment depends on the problem and your personal preferences. Before starting treatment, the doctor must perform a thorough diagnostic examination to determine whether the patient's symptoms are related to an anxiety disorder or a physical illness. When an anxiety disorder is diagnosed, the type of disorder or type of disorder and comorbidity such as depression or substance abuse must be specified. In some cases, alcoholism, depression, or other disorders are present, so treatment for anxiety can wait until treatment is under control [18]. People with anxiety disorders who are currently being treated should discuss the details of their treatment with their current doctor. If you take medication, you should tell your doctor what medication you are taking, the initial dose, if the dose has been increased or decreased during treatment, if you have had any side effects, and if the medication has helped to reduce anxiety. If you receive psychotherapy, you should describe the therapy you received, how often you attended sessions, and how the therapy benefited you. Many people believe that the treatment has failed or is ineffective, when in fact they are not given enough time or the treatment is wrong. In some cases, you may have to try different treatments or combinations of treatments until you find one that works for you [19,20]. Medication cannot cure anxiety disorders, but psychotherapy can help manage them. Medication must be prescribed by a doctor (usually a psychiatrist). Doctors may provide psychotherapy alone or work as a team with a psychologist, social worker, or counselor who provides psychotherapy. The main medications used for anxiety disorders are antidepressants, anxiolytics, and beta blockers to control physical symptoms. With appropriate treatment, many people with anxiety disorders can lead normal, normal lives [20].

Table 1: The main types of medications used for anxiety disorders are different [21,22]

Classes	Used for	Mode of Action	Advantages
Anticonvulsants	Social anxiety disorder	Affects GABA	Usually effective in 2-4 weeks
Azaspirones	Generalized anxiety disorder	Increases serotonin activity	Less sedative than benzodiazepines
Benzodiazepines	Generalized anxiety disorder, Social anxiety disorder Panic disorder	Increases GABA activity	Moving quickly, some people feel better on their first day
Beta Blockers	Social anxiety disorder	Decreased ability to produce adrenaline	To move quickly; It does not form a habit
Monoamine oxidase inhibitors (MAOIs)	Social anxiety disorder Panic disorder, Post Traumatic stress disorder	It blocks the action of brain enzymes by preventing the release of serotonin and noradrenaline.	For most people, especially patients who have not responded to other treatments, 2-6 weeks is effective until improvement
Serotonin reuptake inhibitors (SSRIs)	Disorder, Obsessive compulsive disorder, Generalized anxiety disorder, Social anxiety disorder.	Serotonin Concentration	Fewer side effects than other drugs. 4-6 weeks until healing

Tricyclic antidepressants (TCAs)	Panic disorder, Obsessive compulsive disorder, Post Traumatic stress disorder	It regulates serotonin and/or noradrenaline in our brain	Effective for most people, improvement can take 2-6 weeks

For people with anxiety disorders, general behavior is characterized by avoiding activities, people, things, places, and situations that cause anxiety and, rarely, excessive use of drugs or alcohol. These maladaptive behaviors persist over time and lead to harmful outcomes such as poor relationships, reduced interpersonal functioning, and an unwanted "decrease" in quality of life. Not surprisingly, the socioeconomic burden of anxiety disorders is severe. As a result, this problem has been observed to increase continuously in the last decades [23,24]. In this context, it is not difficult to believe that detailed studies using animal models play an important role in better understanding the behavioral characteristics of anxiety disorders [25]. Several research centers have investigated anxiety-related behavior in rats by manipulating anxiety levels using board devices (HB) and various behavioral techniques. The HB is basically an open space with a pre-defined hole where the rat can poke its head. The HB is a simple tool to explore different aspects of the behavioral repertoire of rodents related to exploration and anxiety [26,27].

HOLE BOARD APPARATUS:

Hole board (HB) Boissier et al. [28] is a widely used behavioral test to assess behaviors such as exploration and anxiety in rats and mice [28–30]. A punch board is a typical host (picture 2). Therefore, approaches to prevent the simple consequences of open space and competition can be combined to address various ecological issues, such as soil erosion [31,32]. Depending on the number and size of the holes in the soil, there are different types of HB. The dimensions of the holes are varied between mice and rats with 4 holes (eg one hole in each corner of the field or 4 holes in a row) and 16 holes per hole (eg four holes in the corner of the field). . even a row), or a hole board with 36 holes (ie 6 holes with the same space) or a hole board with 36 holes (ie 6 holes with the same space each). On the one hand, these holes offer the possibility to measure the exploratory behavior of rats or mice, and on the other hand, they reveal unknown signals that can cause a conflict between approach and avoidance [34,35].

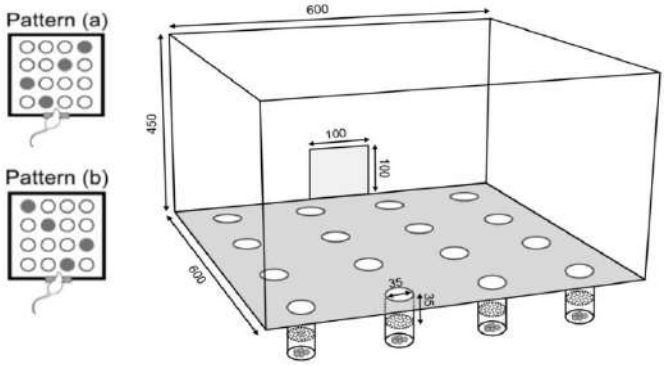

Figure 2: Schematic representation of the hole-board apparatus

Therefore, it is argued that this device is designed to prevent difficulties in interpreting natural locomotor movements, which are difficult in the open field, and many studies have shown that head diving and motor movements are different from each other. [36]. In general, a large number of animals is interpreted as a sign of neophilia, while a small number of animals may indicate the absence of neophilia or a severe anxiety state in the animal. The whole board challenge is now considered a test for neophilia in many areas of behavioral pharmacology [38]. The researchers tried to confirm head dipping as a measure of neophilia by comparing different genetic strains of mice using different drugs. For example, if head diving is a nootropic response that is suppressed by an anxiety-like response, treatment with an anxiolytic drug would be expected to improve head diving. Such studies have yielded conflicting evidence. For example, the treatment of anxiety with benzodiazepines, which are anti-anxiety drugs, has been reported [39]. A recent study showed that the effects of anti-anxiety drugs on head-tossing behavior were independent of head-tossing associated with general behavioral changes. Whether brain clearing can be interpreted as a valid measure of neophilia remains an open question [40].

PROCEDURE:

Animals are placed on the floor in a crate with a series of holes. We then measured the frequency and duration of spontaneous activity emitted over short periods of time. This test also provides a simple way to assess anxiety in an unfamiliar environment in rats. In this context, the use of hole boards is based on the assumption that the behavior of animals in novel situations is the result of competition between exploratory and withdrawal instincts. Therefore, a high level of anxiety reduces head moisture and vice versa, a low level of anxiety increases head moisture. Other behaviors such as grooming, standing, and locomotion can also be assessed during the board test [39,41].

The Head-Dip/Edge-Sniff Ratio:

When evaluating anxiety-related behavior and the effects of certain psychoactive substances, head tilt, especially the relationship between head and posture, should be taken into account. increased significantly (Figure 3). The current results are in good agreement with previous results showing that the use of diazepam and FG7142 decreased and increased anxiety in the opposite direction, respectively [42]. The explanation lies in the strong emotional value of the relationship that links these two hole-seeking behaviors. Edge brushing is when the animal cleans the edge of the hole. Confusion occurs when the animal's head is placed in the hole. Of course, why the animal closes its head after sniffing depends on its motivation, and this motivation has a great influence on the change in its emotional state. Therefore, if the animal bends its head several times without washing the edge, as the ratio increases, the speed of tilting the head also increases. This is due to wear and tear. For example, the level of anxiety after the administration of diazepam [41]. Conversely, when the offset increases, the main slope ratio decreases, except for some edges with a slight slope. This is what it looks like after construction. For example, FG7142 [42] has received little attention. After TPA, the image will be sharper, with fewer edges and a more distinctive character architecture with curves and edges. By identifying and analyzing T-patterns, it is possible to assess quality characteristics that cannot be determined by conventional analysis. Indeed, the synergistic use of quantitative and qualitative approaches in research provides a broader explanation for observed phenomena than is easily accepted by the human eye [43,44].

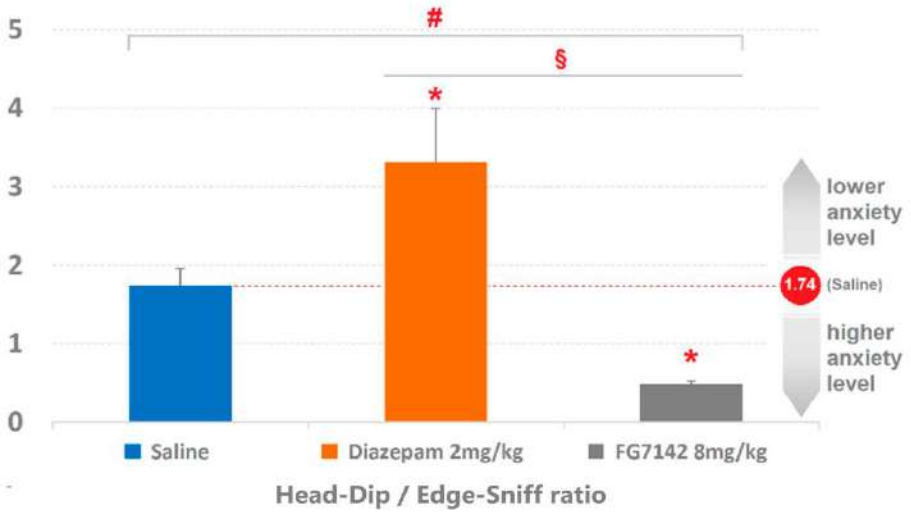

Figure 3: Effects of saline, diazepam, and FG7142 on head tilt velocity and edge-to-edge ratio [45].

Modified hole board apparatus:

A modified Hole-board apparatus can be used to assess a variety of unconditioned behaviors, particularly in rats and mice. It includes conventional pit equipment and open field testing, overcoming some of the weaknesses of experimental batteries, such as reducing the number of animals used, reducing time efficiency, and reducing costs. The main advantage is that there is no need to feed the animal to increase its willingness to solve the problem. This tool has been validated in mice and rats. The modified Hole-board device can be used to conduct a variety of behavioral tests including risk assessment, avoidance, arousal, exploration, habituation, learning, social desirability, locomotor activity, social stress tests, and object recognition tests [46].

Other studies have shown that pinhole devices can be used to measure preference and avoidance properties for biological odors. Various samples were placed in the hole, including female urine, predator urine sample, permanent urine sample and plant urine sample. Observations show that they completely avoid holes containing prey samples and prefer holes containing female urine samples. Treatment of rats with buspirone (an anxiolytic drug) completely abolished the inhibition of urine sampling, which shows the anxiolytic effect of predator urine samples [47]. However, this test is not suitable for evaluating highly reactive compounds. In another study, oral administration of a methanolic extract of Holoptera integrifolia increased head-dipping latency when tested in interventional rats, suggesting anxiolytic effects. Pause has been shown to increase mental immersion [48]. Previous studies have reported that dopaminergic transmission is enhanced by blocking D3 receptors, which are commonly found in the cortical and striatal systems. Studies have shown increased inhibition of monoamine oxidase, which breaks down catecholamines and serotonin in our brain. Therefore, research in the Hall paradigm and research on anti-anxiety drugs have intensified [49]. Currently, the use of transgenic animals is encouraged because of their high accuracy and efficiency. Therefore, transgenic mice can also be used to assess the behavioral effects of changes in specific types of metabolotropic serotonin and glutamate neurochemical receptors [50]. Anti-anxiety medication is expected to encourage movement, concentration, and resolution. If the animal does not show this behavior, it becomes more anxious [46].

CONCLUSION:

Anxiety disorders are a serious problem that carries a significant social and economic burden in modern society. Behavioral studies in animal

subjects (mice) are important to understand this disease and introduce new treatments from a translational perspective. In this regard, the drinking apparatus has emerged as a widely used test to study anxiety-related behavior in rats.

Based on a review of previous experimental literature on exploratory behavior in low-stress environments, we conclude that the pit apparatus is the most advanced tool for measuring exploratory behavior in laboratory rats. Other behavioral control mechanisms (threat assessment, emotional response, active resistance) may play a greater role in shaping pig activity.

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