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Review Article

Reproductive System Abnormalities Accompanied By Environmental Factors Alterations in Rat Model

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Abstract

Rat is one of the most commonly used model animals for biological research. The organs and systems of human being are somewhat similar to that of rat in structure as well as functions, making it a valuable choice for research experimentation in biological sciences. A number of studies have been conducted to evaluate the potential risks and toxicity of different elements on the physiology and histology of rats. There is need to address certain environmental factors affecting rats condition during experimentation. Reproduction along with its pathologies is under investigation on larger scale throughout the world, being central for the existence of a species. These studies focus on the major factors that influence reproductive function. Review of literature clearly indicated the unwanted consequences of over nutrition, malnutrition, high or low temperature, non-enriched housing, improper handling, intense or poor light exposure and environmental pollution on histology and hormonal profile of reproductive system of rats.

KEYWORDS: Rats; Biological research; Environmental conditions; Stress; Handling

INTRODUCTION

Human beings are always fighting with a number of environmental factors to maintain steady state health condition failure to adopt environmental insults, cause abnormalities and disease. For treat a certain disease, we must have the basic knowledge about its cause, mode of action, sign and symptoms, risk factors etc. To get the relevant information we used different animals making feasible to carry out experiments on human itself due to a variety of concerns. These model animals share great structural and functional resemblance with human beings. Moreover, they behave much similar to humans in various pathological conditions also and about 90% of veterinary medicines are either identical or similar with medicine used to treat humans. A number of vaccines have been developed using animal models [1].

Wistar laboratory rats (Rattus norvegicus) are one of the experimental models being extensively used in scientific research across the globe owing to multiple similarities with most of the human physiological phenomena. The practice goes centuries back to the ancient times of Greeks [2]. They also respond much likely in most of the complications along with retaining the ability to modify them in response to environmental factors. Their genome has been sequenced presented 90% homology with human [3]. Additionally, they are less expensive with shorter life span and high reproduction rate. Their handling and feeding is relatively easier. They have the ability to learn a wider variety of tasks. Dissection is comparatively easier. But, they require carefully monitored living conditions to survive; e.g. proper diet, optimum ambient temperature, peaceful environment, standard housing facilities, careful handling and appropriate exposure to light. Therefore, vigilant consideration is required during experimentation on these animals to avoid any possible alterations in the biological systems. Environmental fluctuations, even minor in nature may lead to ambiguous outcomes. The core objective of this review is to comprehensively discuss factors that may influence the results and data interpretation during reproductive physiology studies of rats.

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DIET

It is generally accepted that a balanced diet with appropriate concentration of all essential ingredients is necessary for proper growth and maintenance of an organism. Any modification in feed constituents even at minute quantities that may administer for prolonged time period may lead to abnormal physiological functioning of particular organism. Commercially available Rodent pellets usually contain about 55% carbohydrates, 20% proteins, 8% fats and 17% others in their routine diet. It has been indicated that high carbohydrate diet (91%) or high protein diet (75%) result in prolongation and even cessation of estrous cycle. High protein and low carbohydrate diet also caused reduction in weight gain [4]. Diet containing high lactose content was proved to retard growth and lower serum progesterone, a key hormone of pregnancy [5]. A study of combined high sugar and high fat diet resulted irregularities in reproductive cycle, disruption in the levels of estradiol, progesterone (P), testosterone (T) and luteinizing hormone. Any imbalance in the P/T ratio is associated with the development of ovarian cyst [6].

High fat diet is major cause of obesity that may elevate apoptosis of luteal cells [7], infertility and various other endocrine and metabolic problems like low metabolic rate, hyperinsulinemia, and overproduction of progesterone [8]. Further studies support the claim that high fat diet causes reduction in estradiol and LH surge and elevation in leptin level [9]. Moreover, number of pregnancies declines and pup's mortality rate went up [10]. Females suffer with an-ovulatory ovaries and exhibit either delayed breeding or no breeding at all, accompanied by higher serum Insulin and lower adiponectin levels [11]. Likewise, either a general reduction in feed intake or decrease in percentage of any constituent results lower body weight along with reduction in weight of important reproductive endocrine glands and organs (pituitary, ovaries, and uterus). In chronic situations, it affects ovulation rate, cyclic behavior and reproductive receptivity. In addition, serum levels of reproductive hormones like Testosterone and Luteinizing Hormone were lower with a larger corpus luteum containing fibrous tissue in center [12]. Effecting directly, reproduction capabilities are diminished linearly with increasing restrictions [13]. Interestingly, these abnormalities get vanished after switching back to balanced diet to the affected animals. These studies clearly indicated the importance of properly maintained diet for normal reproductive physiology of rats.

TEMPERATURE

Optimum temperature is mandatory for maintaining normal reproductive functions in rats as they are very sensitive to temperature variations. Standard room temperature for rats is 65-75°F with 40-60% humidity. Raised ambient temperature possesses harmful effects like increased gestational period, number of neonatal deaths, decreased litter size, disturbed implantation with less number of implantation sites and unusual delay in parturition [14]. High temperature affects a number of reproductive abilities as oocyte maturation, early embryonic development, fetal growth and lactation. It also induces oxidative stress by producing reactive oxygen species [15].

High temperature causes production of heat shock proteins in the body to compensate the change however chronic exposure to high temperature leads to abnormalities in reproduction functions [16]. Elevation is not merely harmful, lower temperature also has noxious effects. Although animals strive to normalize the fluctuations gradually but still they suffer by the alterations like decrease in weight and production of Reactive Oxygen Species [17]. These studies clearly specify the importance of proper temperature maintenance during the experimentation especially in hot and dry season.

HOUSING

Every living organism in the world has its own territory and way of living, forcing animals to habitat incompatible condition lead to negative physiological and behavioral responses. This negativity could result poor enrichment, social isolation, grid flooring and absence of proper bedding material [18]. They should be placed in an environment allowing them to perform their natural behaviors like hiding, climbing and standing upright resembled their wild habitat. Devoid of natural mimicking habitat compromised their welfare [19].

ENVIRONMENTAL ENRICHMENT

Rats residing in an open place with an opportunity for a number of social activities are usually confined in small, barren cages placed in a windowless room except some research laboratories. Various studies revealed that enriched environment (environment with improved living conditions) significantly impacts on reproductive performance, weight gain and better survival proportion [20]. It brings positive change on the quality of oocytes as well as reduces the chances of cannibalism [21]. Enriched environment provides improvement in reproductive performance, boost up immunity, reduce behavioral abnormalities and stress [21,22]. Moreover, linked with suppressed release of stress hormone corticosterone and aging neurotransmitters (Acetylcholine and Dopamine) from prefrontal cortex region of brain [23].

It's believed that rats experience stress and cardiopathies when they are kept individually lacking enriched environment [24]. Additionally, it can illicit feeding, behavior changes, neuronal changes and poor functioning of hypothalamic-pituitary-adrenocortical axis [25]. Enrichment is supposed to be an alternative neuro-rehabilitation approach for traumatic brain injury [26]. It can also restore neurogenesis in aged rats refreshing their cognitive abilities [27]. Generally, laboratory rats are kept in cages during research experimentation, maximum efforts should be made to ensure the provision of enriched environment.

POLLUTION FREE AND PEACEFUL LOCATION

Every living being is constantly under the direct influence of environment. Any disturbance or discomfort in the environment affects organism's biological systems. Air pollution (mainly Carbon Monoxide) is involved in the disruption of neural development [28]. About 4000 dangerous chemicals have been identified in cigarette smoke. In males they alter semen quality, plasma level of reproductive hormones, spermatogenesis and morphology of spermatozoa. Moreover, associated with generation of ROS leading to DNA fragmentation [29], and death of germ cell diminishing male fertility [30,31]. Airborne particulate matter (includes dust, dirt, soot, smoke, and liquid droplets) is genotoxic to male germ cells [32], while in females it leads to declined fetal weight, dysfunctioning of placenta [33], oxidative stress, deprived oocyte morphology [34], unprompted abortion and significant reduction in placental vascularization [35]. Environmental pollution by pesticides has proven hazardous for living beings as it minimizes life span by damaging vital body organs by generation of potential oxidative stress [36].

A decline in fetal growth and rise in weight gain after birth has been noted following neonatal exposure to high traffic pollution [37]. Long term exposure to noise (mainly of traffic) is observed to be related with cardiovascular abnormalities [38], such as heart failure, BP problems, ischemic stroke and myocardial infarction [39]. Noise can reduce sleep duration and quantity, increases food intake and weight gain [40]. Animals can even suffer from vestibular system damage, balance problems and consequently hearing loss [41]. It is evident from the mentioned facts, requirement of a clean, fresh and disturbance free environment for experimental rats.

HANDLING

Like all others, rats are sensitive animals, require proper and delicate handling and standard laboratory procedures. Improper and careless handling causes long lasting changes in behavior and hormonal profile like estradiol, progesterone, luteinizing hormone, follicle-stimulating hormone and gonadotropin releasing hormone progressing towards an-ovulation. Handling of neonates has much deeper impacts on their reproductive performance even progress to the cessation of estrous cycle [42]. It has been found that improper handling of neonates induces long lasting behavioral and hormonal irregularities [41], underscoring the importance of proper handing during experimental work.

STRESS

Stress is a major factor affects brain activity and alters all physiological and behavioral functions. Stress may provoke due to a variety of physical, psychological and environmental factors. Rats are very susceptible to their surroundings and strongly react no noise as someone enters into room, pick them up or replace their cage. Different animals of the same species even respond differently towards different stimuli, hence stress is the prominent example in animal handling [43]. Scientific studies reported that stress causes weight loss, increased adrenal gland weight [44], and elevated levels of stress hormones like corticosterone [45]. Stress during the gestational age deregulates the production of progesterone hormone; the central regulator of pregnancy along with the disturbance in central nervous system activities [46].

Gonadal hormones enhance the production of stress causing factors especially in females as they are more prone due to high levels of circulating estradiol [47,48]. Maternal stress is then responsible for underdevelopment of reproductive axis of males prenatally [49]. If they face stress in pregnancy their pups show depressed behavior and increased amounts of lymphocytes and interleukin 1β. But with enriched housing most of the immunological alterations were reverted [22]. Neonatal handling can cause long lasting hormonal and behavioral changes [41]. Repeated stress can lower appetite and trigger anxiety, anhedonia and ultimately depression [50].

LIGHT

Light is an essential part of life for all organisms, so increased or decreased light intensity and duration of exposure exert a profound effect on various physiological and behavioral functions. Generally, a 12-hour light/ dark period is preferred. Studies have shown that the female rats kept under bright light for a period of 14 hours for only one cycle either failed to ovulate or showed abnormalities in hormonal profile and behavior [51].

Aother study reported that continuous exposure to bright light (at least 2 months) induced polycystic ovarian syndrome in rats; an endocrine and metabolic disorder of female reproductive system [52]. On the other hand, exposure for less than 10 hours resulted in diminished growth, food intake and reproduction, while exposure for more than 14 hours stimulated these events [53]. Further decline in photoperiod (6 hours) resulted irregularity in estrous cycle [54]. Prolonged exposure to dim light during night resulted reduced diurnal rhythms and food intake along with induction of obesity and diabetes [55-58]. These studies indicated that light dark cycle of 1:1 should be maintained during experimental period.

CONCLUSION

Conclusively present review described concisely the potential factor that could influence reproductive physiology and experimental outcomes. It is evident from a number of researches that (1) under- or over- nutrition of any dietary constituent, (2) temperature above or below from tolerable range, (3) poor housing facilities, (4) lack of proper environmental enrichment, (5) improper or careless handling and (6) prolonged exposure to light / dark cycle, impart profound effects on reproductive performance of normal and healthy rats. So considering all the relevant outcomes, the present review emphasizes on the provision of balanced diet, average temperature, enriched and peaceful housing, stress free handling, needful exposure to light and the use of most compatible procedures to get maximum accuracy of commonly employed experimental findings. Further studies are required to overcome these effects by optimization of environmental and experimental conditions to get standardize outcomes.

Author contributions

MAB wrote the manuscript, searched the literature and wrote the manuscript, MA reviewed and edited the manuscript. All authors have read and approved the final manuscript.

Availability of data and materials

All data generated or analyzed was obtained from original papers and review articles cited from Google scholar, Science direct and PubMed.

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