A REVIEW ON ANIMAL MODEL OF OBESITY, PATHOGENESIS AND METABOLIC DYSREGULATION OF OBESITY.

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Abstract: Obesity is a convoluted biochemical disorder which has reached uncontrollable proportions globally. Learning about the operations which help cause obesity is crucial to establishing useful prevention and care plans. Animal models are of major assistance in analyses of obesity, permitting the observation of genetic, ecological and physiological variables that assume a part in the genesis and growth of such an illness. The contents of this overview are a thorough appraisal of the distinct animal models that are utilized in obesity investigation. Rodents, in particular mice and rats, are the most frequently applied animal models due to their genetic likeness to humans, simple control, and convenience of genetic alteration techniques. Diet-prompted obesity models need animals to be given a high-fat or high-sugar diet with the purpose of producing obesity and metabolic disorders. Genetic models of obesity consist of changing certain genes that are involved in regulating appetite, energy expenditure or fat metabolism. Nonhuman primates can be utilized to provide detailed insight into the pathophysiology of obesity because of their physical similarities to humans, however, their use is restricted mainly by ethical and cost complications. Other animal models, for example, dogs, cats, pigs, and zebrafish, assist in recognizing the comorbidities and genetic cadres linked with obesity. Dogs and cats permit existing obesity-related conditions such as osteoarthritis and cardiovascular disease to be studied. Pigs are ideal for inspecting diabetes and hypertension while zebrafish offer one-of-a-kind advantages for examining the genetic and molecular operations which underlie obesity. This assessment examines the advantages and difficulties with each animal model and demonstrates their positive influence on learning obesity pathogenesis, metabolic disruption. Through a variety of animal models, scientists are getting useful perspectives into the intricate mechanisms behind obesity, leading to novel approaches in handling this pandemic medical problem.

Index Terms - Obesity, Biochemical disorder, Animal models, Genetic variables, Pathogenesis, Metabolic dysregulation.

I. INTRODUCTION

Obesity is a very serious physical ailment that has become pandemic, affecting people worldwide. The prevalence of overweight or obese adults has soared in recent years, with over 1.9 billion individuals afflicted. Moreover, obesity is linked to a host of illnesses such as diabetes, cardiovascular disease, and certain types of cancer[1].

Animal models have been absolutely essential in deepening our comprehension of the physiology of obesity and evaluating potential remedies. Such models supply an advantage over lone studies since they enable us to manage genetic and ecological conditions, monitor nourishment consumption, and examine the long-term

ramifications of obesity. They have made a tremendous contribution deepen our insight into obesity and spurring on innovative therapeutic strategies[2].

Scientists have developed different animal models to study (being very overweight), including rodents, non-human (monkeys, apes, etc.), dogs, cats, pigs, and zebra fish. Among these, rodents are the most commonly used models in research. This is because they are small in size, have a shorter (length of time something is alive.), and are easier to handle compared to other animals[3].

Two distinct types of rodent models are used to investigate obesity - diet-induced obesity (DIO) models and genetically induced obesity models. In DIO models, rodents are fed diets that are high in sugar or fat, which quickly leads them to become overweight and comprehend metabolic problems[4].

These models are highly beneficial for uncovering how environmental parameters factor into obesity and metabolic derangement. Genetic obesity models, meanwhile, manipulate particular genes responsible for regulating hunger, energy utilization, or lipid metabolism to comprehend the molecular pathways leading to obesity and metabolic difficulties[5].

Non-human primates are a precious animal model for studying obesity. They have similar physiological and metabolic characteristics to humans, making them the ideal model for understanding the development and progression of obesity. Still, conducting studies with non-human primates can be expensive, time-consuming and require technical facilities and expertise[6].

In addition to rodents and non-human primates, other animal models like dogs, cats, pigs, and zebrafish have been employed in obesity study. Dogs and cats are particularly beneficial for studying obesity- related conditions like osteoarthritis and cardiovascular disease[7].

Pigs are indeed precious models for studying obesity-related co-morbidities like hypertension and diabetes. On the other hand, zebrafish are useful models for researching the inheritable and molecular mechanisms involved in the development of obesity[8].

In this examination, we will survey the numerous creature models utilized in heftiness research. We'll analyze the advantages and disadvantages of each model and feature their advantages for understanding the causes of weight, metabolic abnormalities, and potential cures. Likewise, we will investigate ongoing developments in the field of creature models of weight and address a portion of the unresolved inquiries that hold on. The reason for this survey is to furnish a thorough comprehension of the unique creature models utilized in weight research and their importance in forming new therapeutic approaches.

II. Rodent Models:

Table No. 1: Different animal models used in obesity:-

Animal Model	Method of Induction	Advantages	Limitations
Diet-Induced Obesity (DIO)	High-fat diet feeding	Simulates excessive calorie intake and lack of physical activity similar to humans.	Does not completely replicate the genetic factors involved in obesity[9,10].
Genetic Obesity Models (e.g., ob/ob mice, db/db mice)	Genetic mutations	Includes specific genes linked to obesity.	May not completely represent the characteristics of obesity in humans[11,12].
Zucker Diabetic Fatty (ZDF) Rat	Leptin receptor mutation	Leads to obesity, insulin resistance, and type 2 diabetes.	Less accessible and more expensive compared to mouse models[13].
OLETF Rat	Defect in cholecystokinin receptor	Shows increased appetite, obesity, and impaired	Not as widely available and more expensive than mouse models[14,15].

		glucose metabolism.	
High-Fat Diet (HFD) Fed Rat	High-fat diet feeding	Enables study of metabolic changes caused by diet.	Not as frequently used as mouse models[16,17].

2.1 Small Rodents: -

The rodents, such as rats and mice, are often employed as preclinical animal models for the analysis of metabolic disorders[18]. These kinds of rodent models are widely used in research concerning obesity to study its causes and results. They have a major role in assisting scientists in comprehending the background of obesity and assessing potential treatment methodologies[19].

A commonly used rodent model for examining adiposity is the diet-induced obesity (DIO) model. Through this approach, rodents are supplied a high sugar or high fat diet causing them to gain weight, increase body fat, and create insulin resistance, which is analogous to human obesity[20]. The ob/ob mouse is another typical model used, which derives its obesity from a hereditary mutation of the leptin gene resulting in leptin insufficiency[21].

Fresh rodent models of obesity include the Zucker rat, which has an inheritable predilection to obesity due to a mutation in the leptin receptor gene. Another model is the diet resistant (DR) rat, which has a unique metabolic phenotype that makes it resistant to diet- convinced obesity[22,23].

III.   Diet-Induced Obesity (DIO) Model:

The diet-induced obesity (DIO) model is based on feeding rodents a high-sugar diet or high-fat diet, performing in increased body weight, obesity, and insulin resistance, similar to human obesity. This model facilitates the examination of how diet influences the development of obesity and its metabolic changes[19].

IV.   Genetic Models:

4.1 Leptin-Deficient ob/ob Mouse:

The ob/ob mouse is an inheritable model of obesity where mutation in the leptin gene causes an absence of leptin hormone production. Leptin plays a role in regulating appetite and energy expenditure, so the insufficiency of leptin in these mice leads to increased appetite, obesity, and various metabolic abnormalities[21].

4.2 Leptin Receptor-Deficient db/db Mouse:

The db/db mouse is another inheritable model of obesity where mutation in the leptin receptor gene causes incapability to respond to leptin. Like the ob/ob mouse, the db/db mouse exhibits increased appetite, obesity, and various metabolic abnormalities[11].

4.3 Zucker rat, ZDF rat, Koletsky rat:

The Zucker rat model is characterized by a mutation in the leptin receptor gene, which causes hyperplasia, obesity, and metabolic dysregulation[23]. Also to the Lepdb /Lepdb mouse, certain rat models with leptin-resistant obesity have mutations in the leptin receptor. The fat Zucker (fa/fa or "adipose " rat) and the Koletsky rat have mutated forms of the leptin receptor's extracellular domain. These models share common features similar to increased appetite and reduced energy expenditure, leading to severe adiposity[24].

ZDF rats are deduced from a specific group of fat Zucker adipose rats that experience early disruptions in glucose metabolism. When given a high-fat diet, these rats develop diabetes at an early stage. This increased vulnerability to diabetes may be related to changes in the expression of the glucose transporter GLUT4 in cadaverous muscle[25].

4.4 Wistar Kyoto fatty rat (WDF rat):-

The Wistar kyoto fatty (WDF) rat model was created by breeding Zucker (fa/fa) rats with Wistar-Kyoto (WKY) rats. Similar to the Zucker (fa/fa) rat, the WDF rat displays obesity and associated features like insulin resistance, elevated insulin levels, and high lipid levels. Male WDF rats also develop early-onset high blood sugar levels and glucose in the urine. Insulin resistance in this model is connected to reduced insulin binding in the brain and peripheral organs, particularly the liver[26,27].

V.   Monogenic Models:

Monogenic models of obesity are rodent models that have been genetically engineered to contain a particular gene mutation which provokes obesity. These models are of great value in comprehending the molecular mechanisms prompting the development of obesity as well as exploring understood remedies[28].

5.1 Melanocortin-4 Receptor (MC4R) Mutant Mouse:

This model involves an alteration in the MC4R gene, involved in managing energy balance and appetite. MC4R mutant mice demonstrate enormous appetite, greater body weight, and obesity[29].

5.2 Agouti-Related Protein (AGRP) Neuron Ablation Model:

The Agouti-Related Protein (AGRP) Neuron Ablation Model is a testing technique used to probe the effect of AgRP neurons on adiposity. AgRP neurons comprise a special type of neuron in the hypothalamus and are responsible for regulating eating habits and upholding energy balances[30].

In this experimental strategy, researchers removed AgRP neurons in Lab animals, including mice, to assess the effect on their body mass, food consumption, and metabolism. By removing these neurons, scientists were able to research the clear role they have in obesity. A further study demonstrated that, by eliminating AgRP neurons, there was an improved energy expenditure and resistance to obesity stemming from nutrition, which provides additional evidence of the involvement of AgRP neurons in obesity progression[31].

Various studies have employed the agrp neuron elimination approach to investigate the correlation between AgRP neurons and corpulence. As an example, one investigation ascertained that when AgRP neurons were taken out, mice exhibited reduced food intake and defended against obesity caused by a high-fat food regimen. This indicates that AgRP neurons are crucially involved in augmenting overeating and body weight increase[32].

VI.   Pathogenesis: -

The development of obesity various factors, including genetics, environment and behavior. Here are some key factors that contribute to obesity:

6.1 Genetics:

Genetics plays a significant role in obesity; with examination indicating that over to 70% of the variation in body weight can be attributed to inheritable factors. Multitudinous genes are involved in regulating body weight, including those related to appetite control, energy expenditure and lipid metabolism[33,34].

6.2 Environmental factors:-

A diet high in calories, fat and sugar, coupled with an inactive lifestyle, can produce an inequity between energy intake and expenditure, leading to weight increase. Environmental factors, including a physical exercise, stress, and diet, also play a role in obesity development. A diet high in calories, fat, and sugar, coupled with an inactive lifestyle, can produce an inequity between energy intake and expenditure, leading to weight increase. Pressure can contribute to overeating and weight increase by activating the release of cortical, a hormone that promotes fat storage[35,36].

6.3 Gut microbiota:

The microbiome existing in the digestive canal, which encompasses trillions of minuscule microorganisms, has been associated with obesity development. Research has indicated that differences in the composition of the gut microbiota can affect metabolic equilibrium and energy utilization and exist between overweight and lean subjects[37].

6.4 Hormones:

A handful of hormones have a role in controlling body weight, including leptin, ghrelin, insulin and glucagon-like peptide-1 (GLP-1). Leptin is created by adipose tissue and communicates with the brain to influence hunger and energy consumption. Ghrelin is secreted by the stomach and encourages appetite. Insulin is conceived by the pancreas and regulates glucose breakdown. GLP-1 is manufactured in the gut and impacts glucose metabolism and hunger[38,39].

VII.   Metabolic Dysregulation:-

7.1 Insulin resistance:

Obesity is strongly connected with insulin resistance, a condition in which the body's cells responding less to insulin, the hormone that regulate glucose metabolism. Insulin resistance can lead to high blood sugar leveland advanced risk of developing type 2 diabetes[40].

7.2 Dyslipidemia:

Obesity is also associated with dyslipidemia, which is an irregular lipid profile characterized by high levels of triglycerides and low levels of HDL cholesterol. Dyslipidemia increases the threat of developing cardiovascular conditions[41].

7.3 Inflammation:

Obesity is associated with chronic low-grade inflammation, which can contribute to insulin resistance, dyslipidemia, and other metabolic disorders. Inflammatory cytokines produced by adipose tissue and immune cells can weaken insulin signaling and promote lipid accumulation in tissues[42].

7.4 Non-alcoholic fatty liver disease (NAFLD):

Weight problems are a major predisposing factor to the onset of NAFLD, wherein there is an excessive aggregation of fat in the liver. Prolonged NAFLD can then progress to non-alcoholic steatohepatitis (NASH), a more serious liver illness that may lead to cirrhosis and failing of the organ[43].

7.5 Sleep apnea:

Being overweight is a contributor to the development of sleep apnea, a disorder in which one's breathing pattern pauses and resumes intermittently during sleep. Consequences include daytime drowsiness, hypertension, and other detrimental health issues[44].

These metabolic alterations linked to obesity prompt the development of multiple chronic conditions and stress the importance of managing a healthy weight.

VIII. CONCLUSION

In conclusion, The Uses of animal models to study the phenomena of obesity (genetic, physiological, epigenetic and environmental) and to investigate possible therapies. animals have provided a huge amount of information which had both direct and indirect effects on the state of our understanding. In this review describe about the animal models such as Rodents model, genetic and monogenetic models. This review also contains pathogenesis and metabolic dysregulation factors (Insulin resistance, Dyslipidemia, Inflammation, Non-alcoholic fatty liver disease (NAFLD), Sleep apnea) of obesity. The pathogenesis of obesity involves a dysregulation of energy balance, which leads to an excessive growth of adipose tissue. This dysregulation is containes the various factors, such as genetics, physical activity, diet, and the gut microbiota.

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