Contribution of animal models to the understanding of the metabolic syndrome
a systematic overview

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Contribution of animal models to the understanding of the metabolic syndrome: a systematic overview

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Introduction

The metabolic syndrome (MetS) is often defined as clustering of abdominal obesity, hypertension, dyslipidaemia, insulin resistance, and impaired glucose tolerance. Although both definition and clinical relevance of the MetS are highly debated, there are numerous animal experiments conducted in this field.

Animal models of MetS, such as leptin deficient obese mice or Göttingen minipigs have contributed to our understanding of the pathophysiological basis and the development of novel therapies. For a complex disease syndrome, no animal model can be expected to serve all needs of research.

AimS

- To collect and analyze information about the animal models used in the field,
- To present the benefits of animal research in the field,
- To gain a better understanding of the role of animal models in this area.

References

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Methods

Keywords for PubMed search: "insulin resistance syndrome" OR "Metabolic Syndrome X"[Mesh] limited for animals, original papers and for articles published in English AND "Disease Models, Animal"[Mesh] limited for original papers and for articles published in English.
Number of articles: 137 original article, 50 reviews
Nvivo8, qualitative analyzer software (QSR International Pty Ltd, Doncaster Victoria, Australia)

Results

Experimental studies with these models addressed questions in etiology (e.g. role of genetic factors, role of fetal programming, role of obesity), pathophysiology (role of insulin resistance, role of adipose tissue, role of hormones and role of inflammation), treatment (pharmaceuticals, effect of diets and exercises) and associated diseases (atherosclerosis, hypertension, vascular wall abnormalities).

In this review we collected data about 78 animal models from 11 species (dog, guinea pig, horse, Syrian golden hamster, Psammomys obesus, monkey, mouse, pig, rabbit, rats and sheep .

Rodent models are the main pillars of MetS research. However, there are significant differences (from human) in their lipid metabolism .

Reviews compared 43 mouse strains on the basis of MetS-related parameters and suggested CAST/EiJ, CBA/J, and MSM/Ms as particularly suitable. A similar approach for rats suggest male obese ZDF, obese Koletsky, obese SHHF/Mcc-facp, and obese ZSF1 rats. The Rat Genome Database indicates nine potentially useful strains but does not allow a detailed comparison.

Monogenic rodent models are frequently used but they represent rare and extreme obesity in human subjects.

Large animal models including pigs (Ossabaw female swine), dogs, and certain non-human primates are good alternatives and offer better opportunities for translation of the results. However, they are expensive, difficult to handle and less characterized.

Benefits and obstacles of animal research on MetS

In MetS research animal models are used to test new hypotheses (e.g. pollution theory), discover basic patomechanisms (free fatty acids in insulin resistance) and to develop new treatment (PPAR-gamma knockout mouse in thiazolidinedione insulin-sensitisings). Specifically for animal use in MetS research, we see three main factors difficulting translation : 1) interspecies differences in physiology (e.g. lipoprotein metabolism in herbivores differs from human), 2) inappropriate choice of animal models (e.g. the use of leptin-deficiency models with a different obesity etiology) and 3) the uncertainties about MetS in the clinical practice (e.g. MetS definition and treatment debate).

Conclusions

There are two main alternatives for selecting the most suitable animal model for a particular MetS related study.
•If a single specific aspect of the MetS is concerned then the use of monogenic models is a better choice.
•When the research is focusing on general aspects of the syndrome, polygenic models that phenotypically resemble the human situation more closely are better suited.
Animal studies undoubtedly helped to understand basic pathophysiological mechanisms of MetS, but the translation of their results into effective preventive or intervention therapies, especially in case of the most commonly used rodent models are highly complicated.