The Genetically Epilepsy-Prone Rat
A Valuable Model for the Study of the Epilepsies

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ABSTRACT

In order to develop a rational clinical treatment for any pathological state, the molecular bases for that state must be understood. As simple and logical as that statement appears, it remains the major obstacle to effective treatment of the family of neurological disorders collectively called the epilepsies.

Under the term, the epilepsies are grouped as several types of seizure processes that undoubtedly have multiple pathophysiological causes. Thus, the search to elucidate the molecular bases for the epilepsies has as one of its fundamental components the careful selection of an appropriate model system. The search for an "ideal" seizure model has essentially followed two paths. In the first, animals are rendered "epileptic" by artificial methods and then the pathophysiological, electrophysiological, and pharmacological changes are evaluated. In the second, animals are developed with a genetic predisposition to seizures and used to evaluate the molecular bases for the seizure-prone state. Work using both types of models have provided valuable information about the epileptic state.

This review describes an epilepsy model developed using the second approach, namely, the Genetically Epilepsy-Prone Rat (GEPR). These animals represent a valuable model for the study of the inborn neurological defect that predisposes these animals to seizures. A brief description of the work done in several laboratories characterizing the model is presented. Finally, the value of the GEPR as a model for studying the pathophysiology of the epilepsies will be described.
INTRODUCTION

The search for an effective treatment for the family of seizure disorders collectively categorized under the rubric, the epilepsies, continues unabated. In part, this is owing to the search for anticonvulsant agents with greater selectivity and efficacy. However, the ultimate goal is to gain knowledge of the molecular bases for the epileptic state that would permit the development of a logical and potentially curative clinical therapy. Toward this goal, research has progressed using two basic approaches to gain insights into the epileptic state. The first approach is to artificially create an "epileptic-like" state in the normal animal and the pathophysiological and pharmacological consequences are evaluated. In the second, animals with a genetic predisposition to seizures are developed, and the molecular bases for the seizure state are studied (Laird and Jobe, 1987). A wealth of valuable information has been and will continue to be obtained using both of these approaches. Nevertheless, it is important that the researcher carefully evaluate the experimental questions being asked so that the most appropriate epilepsy model can be selected. For example, questions on the pathophysiology of the seizure-prone state are more likely to be answered using genetic models of epilepsy. By comparison, information on the mechanisms of seizure initiation and/or propagation may be sought using either artificial or genetic epilepsy models.

In the following paragraphs, a short review of the Genetically Epilepsy-Prone Rate (GEPR) will be presented. This presentation is an updated version of a recent detailed review on this model (Laird and Jobe, 1987). This review will be restricted to the GEPR. Furthermore, Jobe and Laird (1987a) have compared the neurochemical and pathophysiological characteristics of the more frequently used genetic and artificial models of epilepsy. The interested reader is referred to this later source for presentations on other genetic epilepsy models (Jobe and Laird, 1987b).

HISTORY OF THE GEPR MODEL

The GEPR has been referred to by various names over the years. The most frequently used terminology was the audiogenic seizure-susceptible (AGS) rats since the animals were selectively bred based on their susceptibility to sound-induced seizures (Jobe, Picchioni, and Chin, 1973; Consroe, Picchioni, and Chin, 1979). The original colony of Spraque-Dawley-derived AGS rats were developed by A. L. Picchioni.