Short Communication

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What is the Most Appropriate Animal Model for Experimental Diabetic Neuropathy Studies ?

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Dear Editor,

Neuropathies are the most common complication of type 1 and type 2 diabetes mellitus (DM), affecting up to 50% of patients, and they are associated with increased morbidity and mortality [1]. There are numerous experimental studies that try to find better ways to prevent or treat the neuropathy complication of the DM. However, an important limitation of these studies is that no animal model completely replicates the human condition of diabetic neuropathy.

The streptozotocin (STZ)-induced diabetic rat is the most commonly used experimental model, and it is regarded as being a type 1 model [1]. STZ is particularly toxic to the insulin-producing beta cell of the pancreas, and it causes a number of functional and biochemical abnormalities of the nervous system similar to those in human diabetic neuropathy. In contrast to functional abnormalities, like a marked reduction in motor and sensory conduction velocity, there are a mild degree of morphological changes, such as fiber density and diameter in the peripheral nerve of STZ-induced diabetic rats [2]. STZ mice may serve to be a better model of diabetes, since they developed severe hyperglycemia without the weight loss characteristic of STZ rats [3]. STZ-induced diabetic models have unpredictable degrees and fluctuations in their hyperglycemia.

The biobreeding diabetes-prone (BBDP) rat genetic model probably represents the best rodent model of human type 1 diabetes. The BBDP rat spontaneously develops type 1 diabetes through a T-cell-mediated autoimmune destruction of pancreatic beta cells [4]. Although underlying metabolic abnormalities are similar to

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those of the STZ rat, its advantage lies in the development of structural changes similar to those in human disease [1].

The most commonly used rodent models of type 2 DM include the Zucker diabetic fatty (ZDF) rat, the Otsuka Long Evans Tokushima fatty (OLETF) rat, and the db/db mouse, all of which exhibit obesity-associated insulin resistance and impaired beta-cell function, resulting in diabetes. ZDF type 2 diabetic rats develop a distal degenerative sensory neuropathy accompanied by a selective long-term pain syndrome [5]. The pathogenic diabetes mechanisms of these models do not correspond to the most human type 2 DM patients. The pathophysiology of type 2 DM in the UC Davis type 2 DM (UCD-T2DM) rat is more similar to humans, and this model may be a useful tool for investigating the pathophysiology of type 2 DM [6]. The Goto-Kakizaki (GK) rat has been widely used as a reliable animal model for type 2 DM, and it developed a mild neuropathy of large myelinated fibers, as reflected by decreased nerve conduction velocity [7].

Several animal models for the study of diabetic neuropathy have been used, and the studies that try to find the most appropriate model are proceeding. The researchers should select the most appropriate experimental diabetic neuropathy model, according to the aims of their studies, until an ideal experimental model that completely replicates the human condition of diabetic neuropathy is found.

Disclosure

The authors have no financial interests to declare in relation to the content of this article.

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