

ストレプトゾトシン誘発糖尿病モデルマウスにおける 感覚性ニューロパチーの発症機序

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Brain and behavior, **3** (1), 35-41 (2013)

Development of sensory neuropathy in streptozotocin-induced diabetic mice

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ABSTRACT: Diabetic polyneuropathy is a major complication of diabetes and the most common cause of peripheral neuropathy. Sensory-dominant neuropathy is the most common type. We previously used streptozotocin (STZ)-induced diabetic ddY mice with sensory neuropathy to evaluate the therapeutic effects of vascular endothelial growth factor and placental growth factor isoforms. In this study, to characterize the development of diabetic sensory neuropathy, electrophysiological, behavioral, and histopathological studies were performed in these diabetic mice. A significant difference in sensory conduction velocity in the tail nerve was observed between healthy and diabetic mice at 1 week after STZ injection. Diabetic mice developed hypoalgesia at 5 weeks after STZ injection. Axon area and myelin thickness of the myelinated fibers were increased in 17-week-old healthy mice compared with those in 8-week-old healthy mice. However, these increases were retarded in 17-week-old diabetic mice. In unmyelinated fibers, axon area was significantly reduced in 17-week-old diabetic mice compared with 8- and 17-week-old healthy mice. These findings suggest that both impaired maturation of myelinated fibers and atrophy of unmyelinated fibers simultaneously occur in the early stage of diabetes in these mice. Our mouse model may be useful for studying the pathogenesis of and therapies for diabetic sensory neuropathy.

抄録 STZ 誘発性糖尿病マウスの感覚性ニューロパチー発症機序を解明するため、行動学的、電気生理学的、病理組織学的に検討した。正常マウスでは13週齢まで尾神経の感覚神経伝導速度は上昇したが、8週齢でSTZを投与した糖尿病マウスではその上昇は抑制された。また、糖尿病マウスではSTZ投与5週後において痛覚鈍麻が発現した。17週齢の正常マウスにおける有髄神経線維と髄鞘の面積は8週齢のものより増大したが、糖尿病マウスではその増大は抑制された。17週齢糖尿病マウスの無髄神経線維の面積は8週齢および17週齢正常マウスに比べて有意に低下していた。これらの結果は、STZ誘発性糖尿病マウスのニューロパチーでは有髄神経線維の成熟遅延および無髄神

経線維の委縮がその初期段階で生じていることを示している。

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