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Cytokine dysregulation in age-dependent painful polyneuropathy in metabolic syndrome

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Metabolic syndrome is a prevalent condition that associates with painful polyneuropathy especially in the elderly population. However, little is known about how the aging process increases the peripheral pain sensitivity in metabolic syndrome. In the current study, we used high-fat-diet (HFD) to induce painful polyneuropathy in young (5 wk-old), mature (36 wk-old), and aged (72 wk-old) mice to study the age-related molecular mechanisms that lead to the development of painful polyneuropathy in metabolic syndrome. In HFD-treated mice, symptoms of metabolic syndrome, including increased body weight, fasting blood glucose, and plasma cholesterol levels were detected. In addition, age-dependent increasing degrees of painful neuropathy, presenting as hypersensitivity to mechanical (mechanical allodynia) and thermal (thermal hyperalgesia) stimuli as well as reduction of nerve conduction velocities were detected in HFD-treated mice. In parallel, increased proinflammatory tumor necrosis factor (TNF)- α , interleukin (IL)-6 and reduced anti-inflammatory IL-10 expressions in lumbar dorsal root ganglia (LDRG) were detected in mature and aged HFD-treated mice. Exogenous IL-10 (1 g/kg, i.p.) treatment significantly improved HFD-induced mechanical allodynia and thermal hyperalgesia as well as inhibited the upregulation of (TNF)- α , and IL-6 in LDRG of HFD-treated mice. In addition, IL-10 treatment reduced the activation of epidermal inflammatory Langerhans cells and macrophages in the hind paw skin of HFD-treated mice. These results suggest that there is age-dependent cytokine-mediated neurogenic inflammation that contributes to the development of painful polyneuropathy in metabolic syndrome. Targeting cytokine-mediated inflammation could be an effective approach for treating painful polyneuropathy in elderly patients with metabolic syndrome.

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