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Schwann cells contribute to demyelinating diabetic neuropathy and nerve terminal structures in white adipose tissue

***Aim*:** Willows and colleagues aimed to evaluate the presence and distribution of Schwann cells (SCs) within subcutaneous white adipose tissue (scWAT), particularly how they associate with adipose nerve structures. They also aimed to understand phenotypic changes of adipose-resident SCs in response to altered energy balance states, including diabetes.
***Methods*:** The authors first characterized the relative proportions of myelinated and unmyelinated nerves in inguinal scWAT in mice that endogenously express a pan-neuronal (PGP9.5) GFP reporter using immunohistochemistry, transmission electron microscopy (TEM), and fluorescence-activated cell sorting. They also examined the impact of changing energy balance, including diabetes, on adipose-resident SCs using the BTBR *ob/ob* mice as a model of diabetic peripheral neuropathy. They further validated the clinical relevance of their animal findings in scWAT biopsies from obese patients.
***Results*:** Under normal conditions, both myelinating and unmyelinating SCs were detected in mouse scWAT, which suggests a role for SCs in adipose nerve support and function. scWAT of BTBR *ob/ob* mice had a significant downregulation of pan-SC marker *Sox10*, myelin-specific marker *Mpz*, and neurotrophin receptor p75 (*p75*). However, BTBR *ob/ob* scWAT displayed an upregulation of *Krox20*, a key regulator of myelination, which was similarly increased in obese human adipose. These alterations in SC markers were associated with small fiber demyelination and a loss of small fiber innervation density in the scWAT of BTBR *ob/ob* mice.
***Conclusions*:** These findings suggest that SCs maintain adipose nerve health and innervation under homeostatic conditions, and become dysregulated in impaired metabolic states, including diabetes.

Comments. Research in the neuropathy field has mostly focused on the role of SCs in large peripheral nerves, including sciatic and sural nerves. However, the contribution of SCs to nerve and adipose function in physiological and pathophysiological conditions has been largely overlooked. This study provides the first evidence on the association of adipose-resident SCs with myelinated and unmyelinated adipose nerve structures. The data also highlight changes in SC marker gene expression and myelin profiles, suggesting that adipose-resident SC injury may exacerbate metabolism, energy balance, and thermogenesis in the context of diabetes.

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Reference. Willows JW, Gunsch G, Paradie E, Blaszkiewicz M, Tonniges JR, Pino MF, Smith SR, Sparks LM, Townsend KL. Schwann cells contribute to demyelinating diabetic neuropathy and nerve terminal structures in white adipose tissue. iScience. 2023 Feb 13;26(3):106189. doi: 10.1016/j.isci.2023.106189. PMID: 36895649; PMCID: PMC9989657.
https://www.cell.com/action/showPdf?pii=S2589-0042%2823%2900266-3