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## **Influence of tacrolimus on brain-derived neurotrophic factor expression in the hippocampus in diabetic rats**

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**Objectives:** Approximately one-third of organ transplant recipients experience neurologic alterations as a complication. The neurotoxicity of immunosuppressive agents and diabetes mellitus are known risk factors of neurological complications in kidney transplant recipients. The aim of the present study was to investigate the influence of tacrolimus on brain-derived neurotrophic factor (BDNF), the critical protein for maintenance of neuronal functions, in the hippocampus in a diabetic condition.

**Methods:** A diabetic rat model was established by a single streptozotocin injection (60 mg/kg). Control and diabetic rats then received tacrolimus (1.5 mg/kg per day) injection for 6 weeks. BDNF expression in the hippocampus was examined in the dentate gyrus (DG) and CA3 region using immunohistochemistry.

**Results:** There was a significant decrease of BDNF expression in the DG and CA3 region in tacrolimus-treated or diabetic rats compared with that of the control group injected with vehicle only. However, there was no difference in BDNF expression between the two experimental groups. Tacrolimus treatment in diabetic rats further decreased the BDNF expression in the CA3 region but not in the DG region. Interestingly, mossy fiber sprouting, demonstrated by prominent punctate immunolabeling of BDNF with synaptopodin, was observed in the diabetic group treated with tacrolimus, which localized at the stratum oriens of the CA3 region.

**Conclusions:** Tacrolimus treatment or a diabetic condition decreases BDNF expression in the hippocampus, and that tacrolimus treatment in the diabetic condition further injures the CA3 region of hippocampus. This finding suggests that tacrolimus treatment may cause further psychiatric and neurological complications for patients with diabetes, and should thus be used with caution.