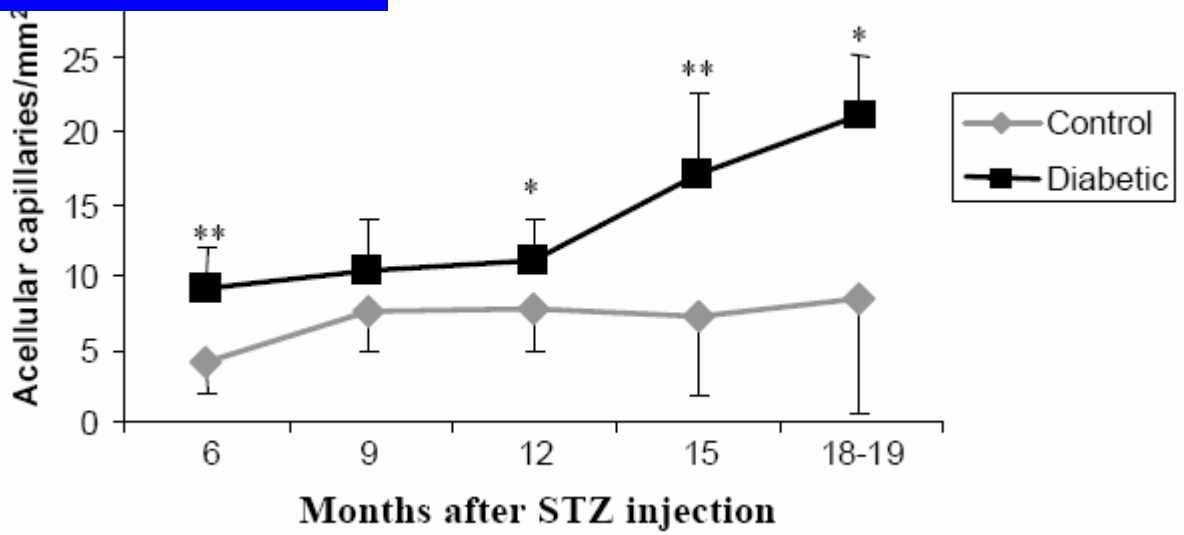
NONPROLIFERATIVE RETINOPATHY

- Vascular
  - Microaneurysms
  - Acellular (nonperfused) capillaries
  - Pericyte loss
  - Varicose, hypercellular capillaries (IRMA)
  - Thickening of capillary basement membrane
  - Hemorrhage
  - **Edema (especially macular)**
- Nonvascular
  - Death of neurons (and glia?)

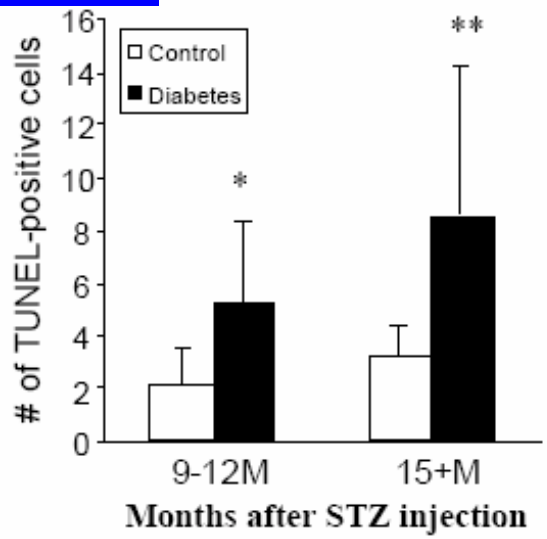
PROLIFERATIVE RETINOPATHY

- **Neovascularization**

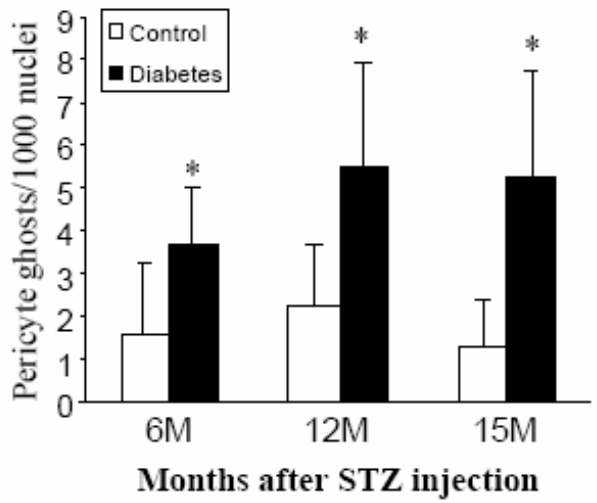
Acellular capillaries



TUNEL



Pericyte ghosts

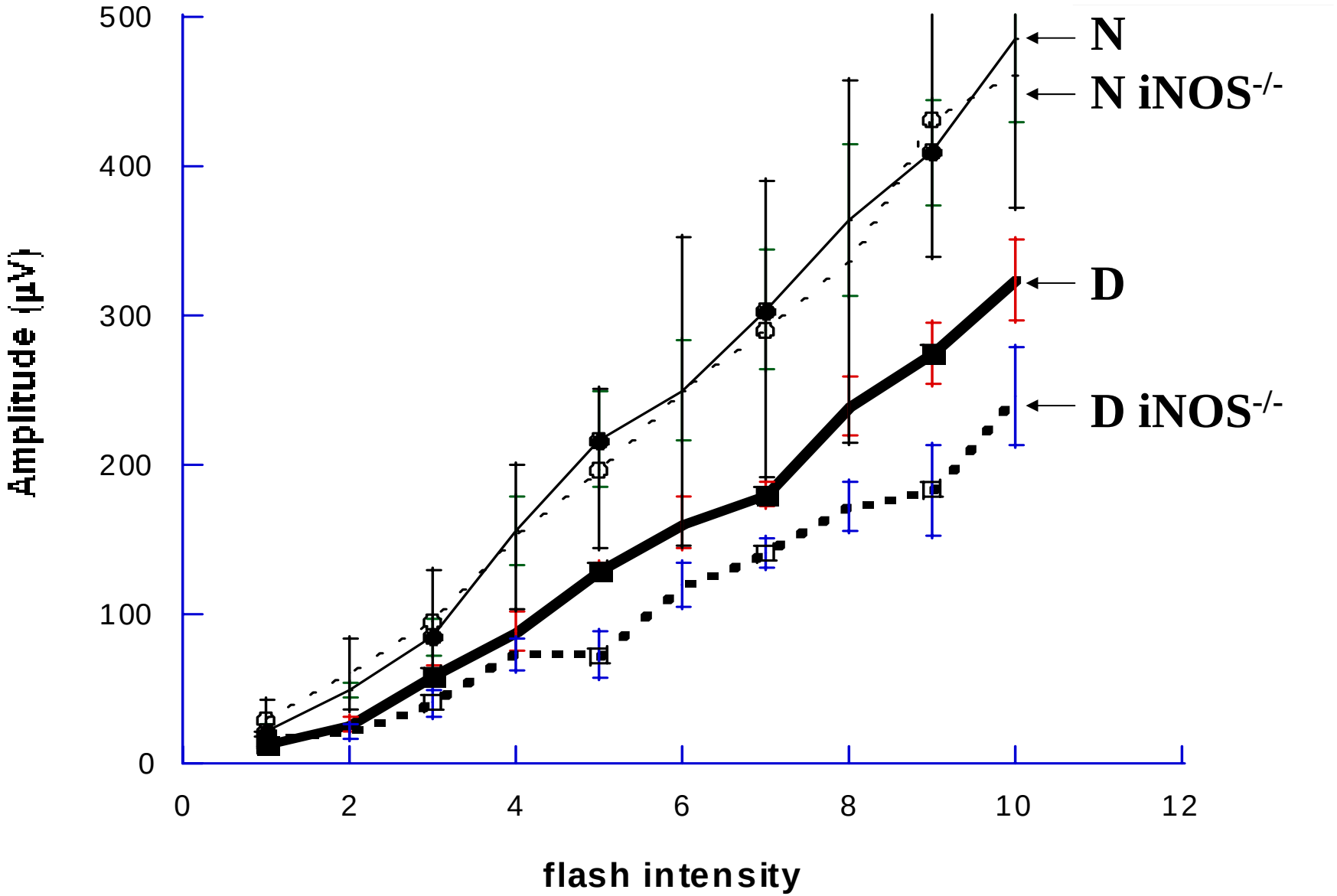


Diabetic C57Bl/6J mice develop vascular lesions of early stages of diabetic retinopathy

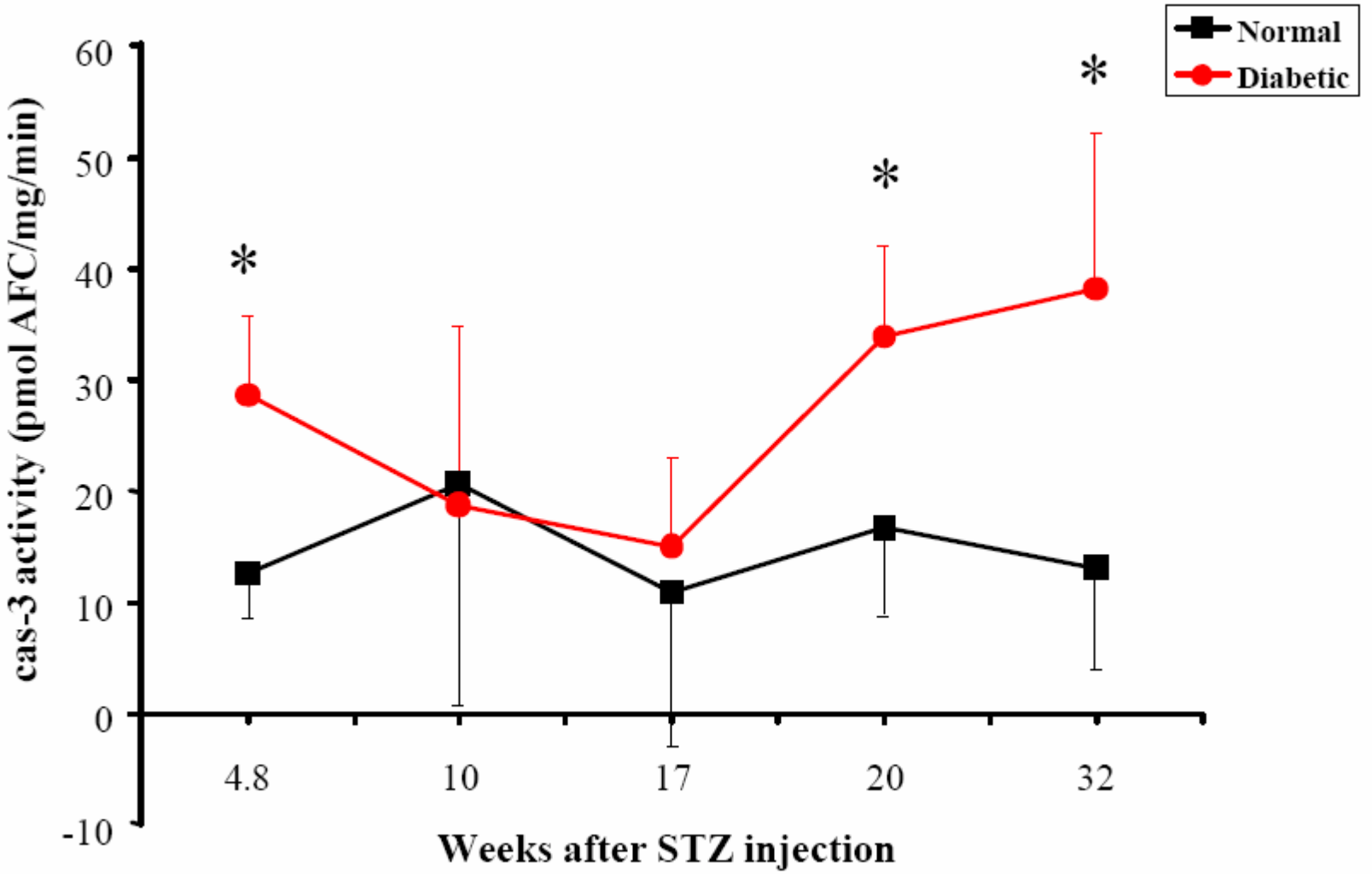
Relation of vascular lesions and neurodegeneration in diabetes: C57BL/6J mouse:

Collaboration with DongFen Chen, Schepens Eye Research Institute, Boston

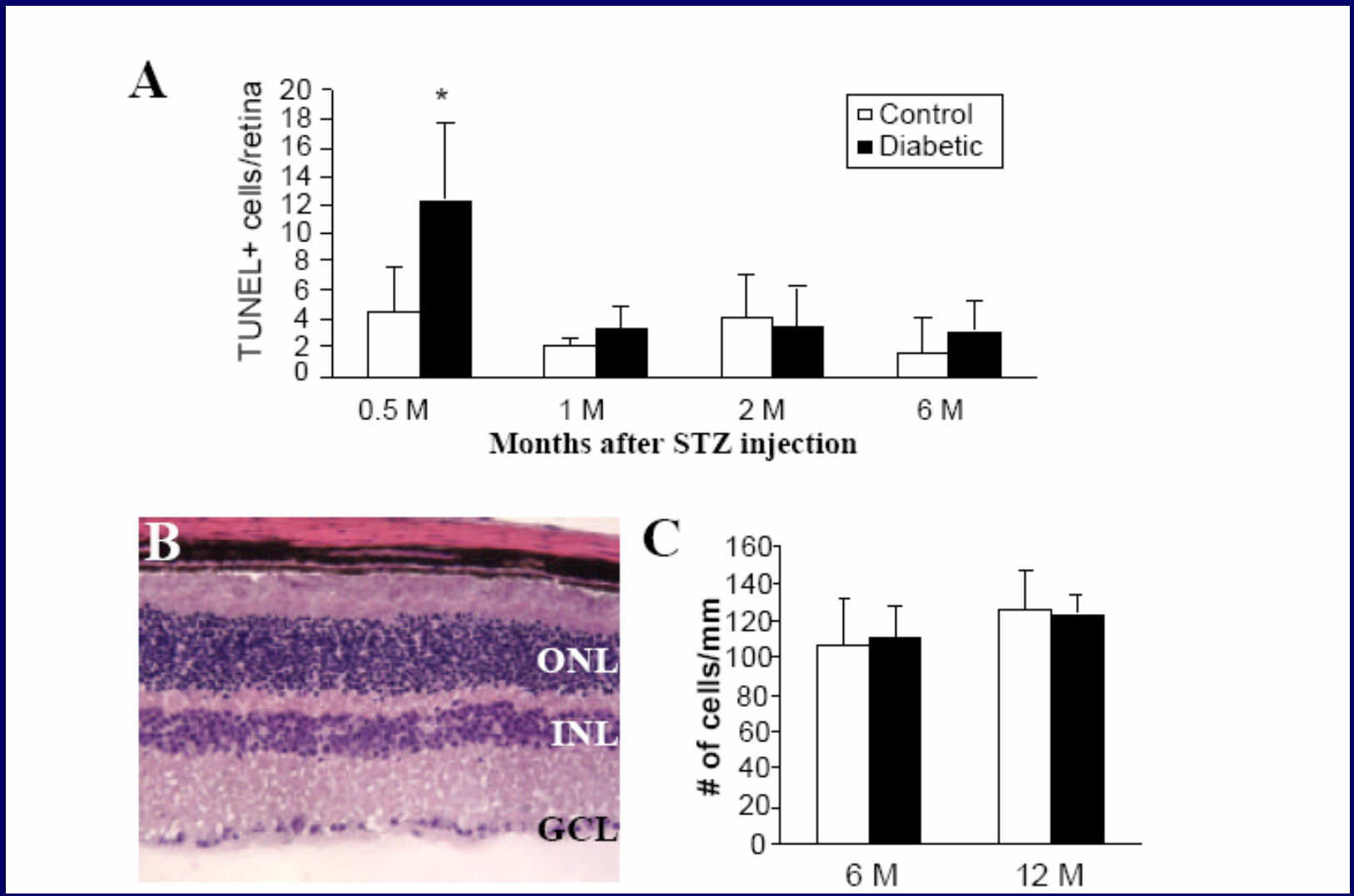
Diabetes-induced decrease in retinal function in C57Bl/6 mice (8 mos diabetes)



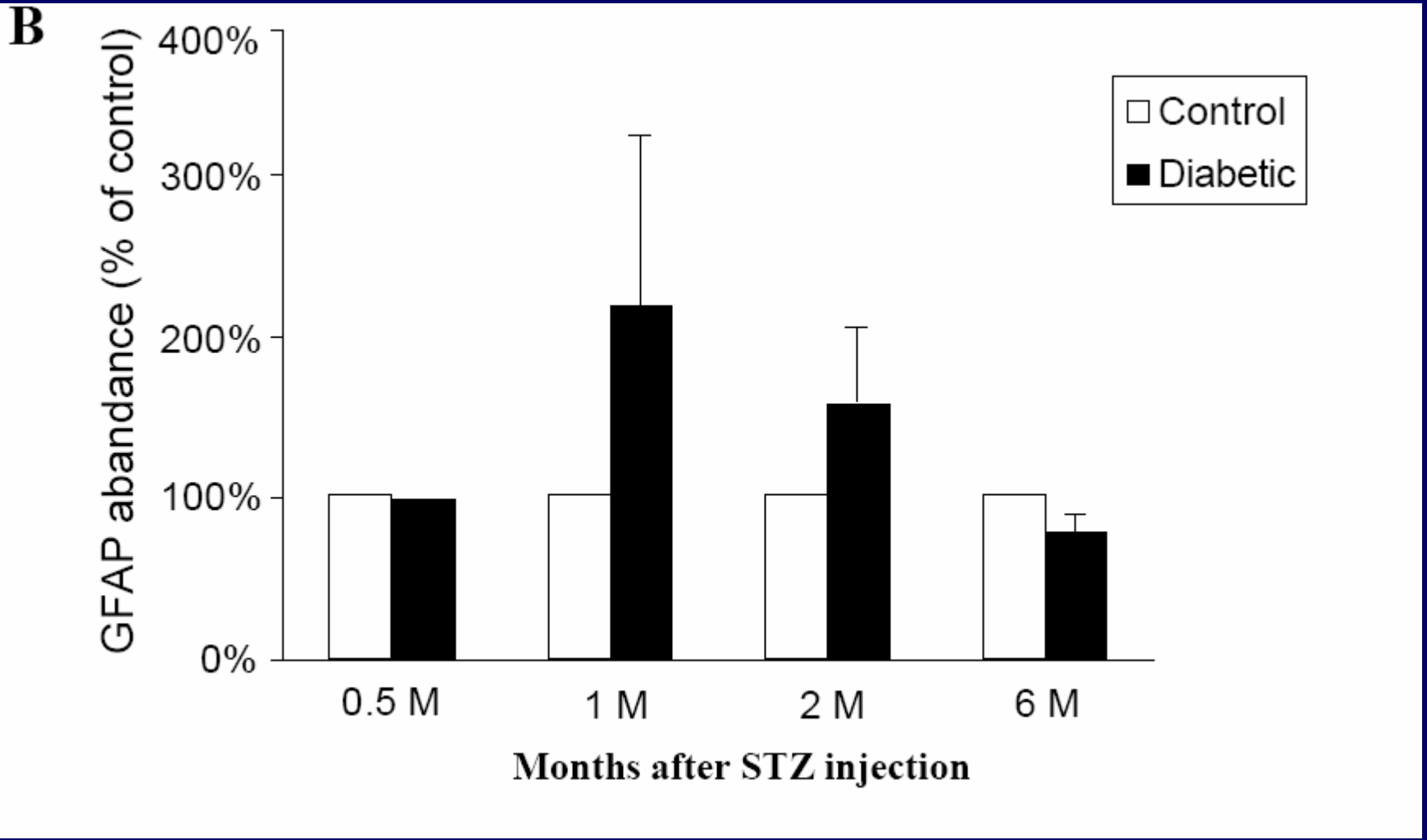
Pro-apoptotic signals occur in multiple phases in retina of diabetic C57Bl/6J mice



Apoptotic signals in retinal ganglion cells are not maintained in diabetic mice



Glial activation is transient in retina of diabetic mice



In contrast to rats, diabetic C57Bl/6J mice develop vascular lesions consistent with the early stages of diabetic retinopathy, in the apparent absence of neuronal degeneration or glial activation.

This suggests that neurodegeneration does not play a critical role in the development of vascular lesions of diabetic retinopathy

Strain comparison of rates at which lesions of retinopathy develop

- Induced diabetes
  - C57Bl/6J
  - 129P3J
  - DBA/1LacJ
  - MRL/MpJ
  - A/J
- Spontaneous diabetes
  - KK.Cg-A^{y}/J
  - Akita

All animals killed at 6 mos diabetes

Models that would be predicted to accelerate development of diabetic retinopathy:

increased capillary occlusion
(ICAM transgenic)
increased rate of capillary degeneration
increased oxidative stress
increased aging
increased lipid concentration (LDLr KO)

Eye collection for evaluation of retinopathy

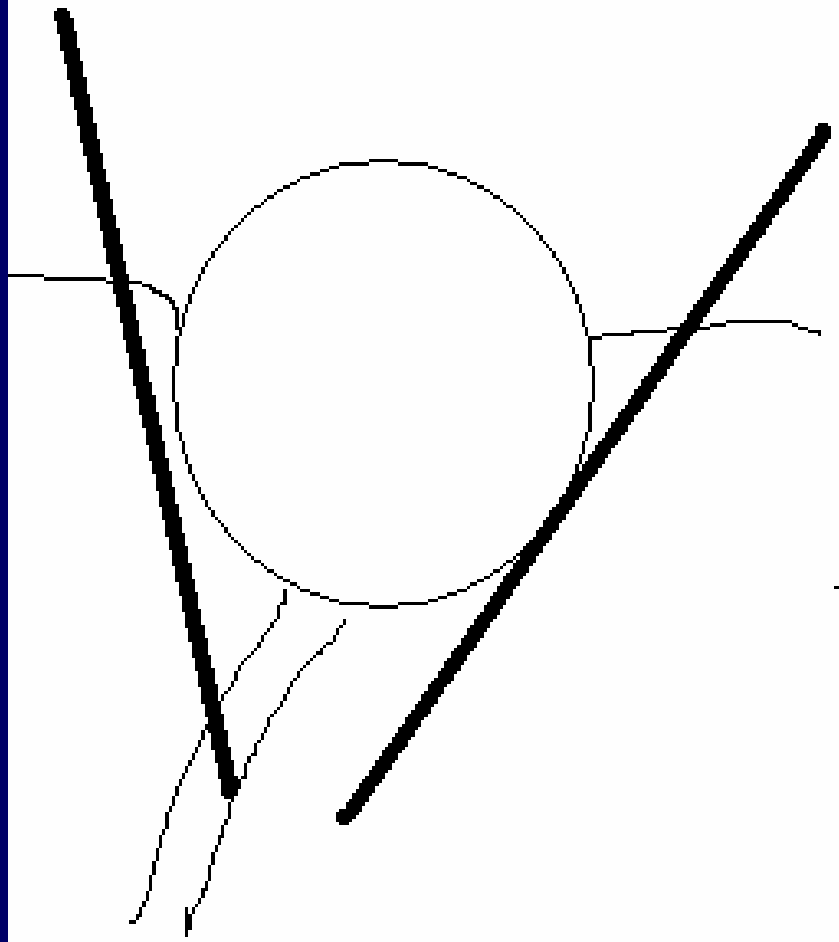
At least 5 animals per experimental group (include age-matched nondiabetic and diabetic controls). The longer the duration of diabetes, the better (C57bl/6 mice require at least 6 mos diabetes before retinal microvascular lesions can be detected).

Enucleate eye. Tissue needs to be collected fresh. Be careful not to push or compress the eye.

Fix both eyes into 10% buffered formalin (pH 7.4) in a microfuge tube. pH seems to be important.

To enucleate the eye:

DO cut deep into the socket



DO NOT cut across the socket