



Pathological features of diabetic retinopathy in unilaterally nephrectomized Spontaneously Diabetic Torii fatty rats given 0.3% saltwater

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BACKGROUND

- We previously reported on the Spontaneously Diabetic Torii (SDT) rat, which is an animal model of spontaneous type 2 diabetes with severe diabetic ocular complications.¹⁻⁴
- The SDT fatty rat, established by introducing the *fa* allele (obesity gene) of the Zucker fatty rat into the SDT rat genome, is a new model of obese type 2 diabetes.⁵⁻¹¹
- We reported that the SDT fatty rats developed more severe diabetic retinopathy (DR) earlier than the SDT rats.^{12,13}
- It was reported recently that unilateral nephrectomy (Nx) and salt supplementation in Spontaneously Diabetic Torii (SDT) fatty rats expedite kidney disorders.¹⁴

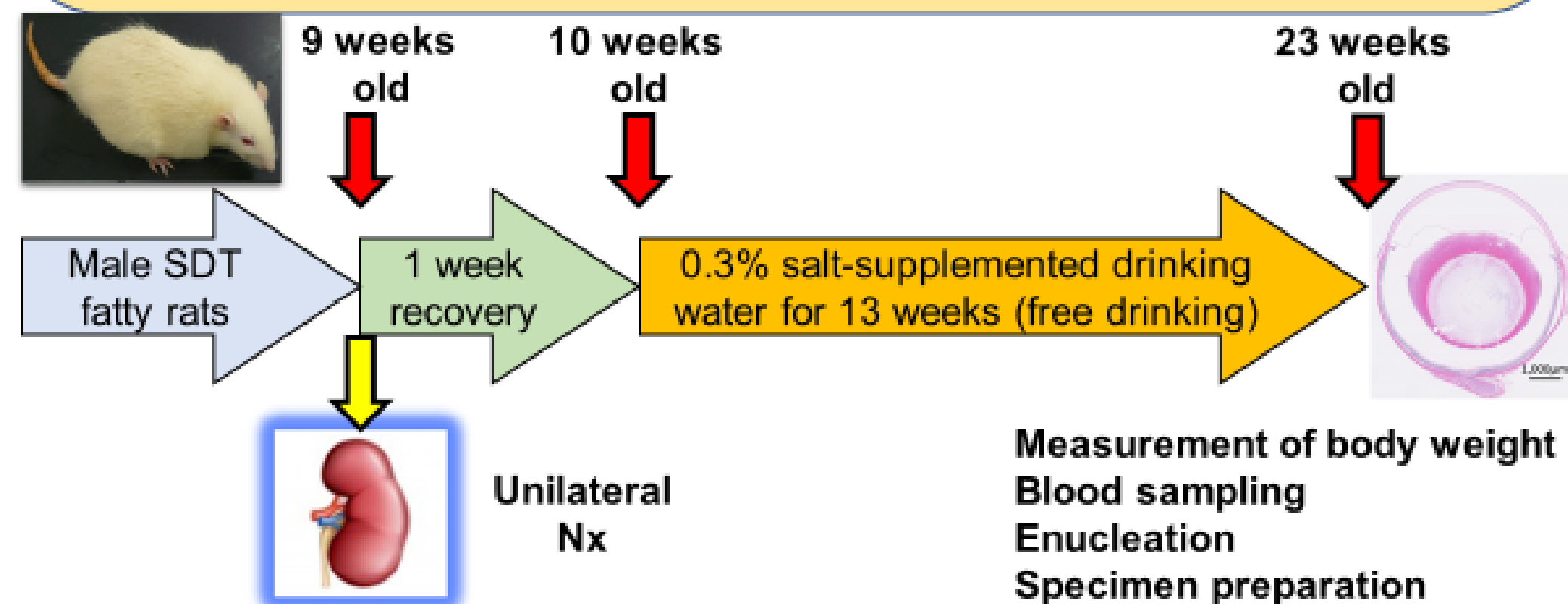
PURPOSE

To clarify the pathological features of DR in unilaterally nephrectomized SDT fatty rats given 0.3% saltwater

METHODS

Animals

- Nx+0.3% salt SDT fatty rats: n=6
With unilateral Nx/0.3% saltwater (study group)
- SDT fatty rats: n=6
Without Nx/water without salt (control group)
- SD rats: n=6
Without Nx/water without salt (normal control group)

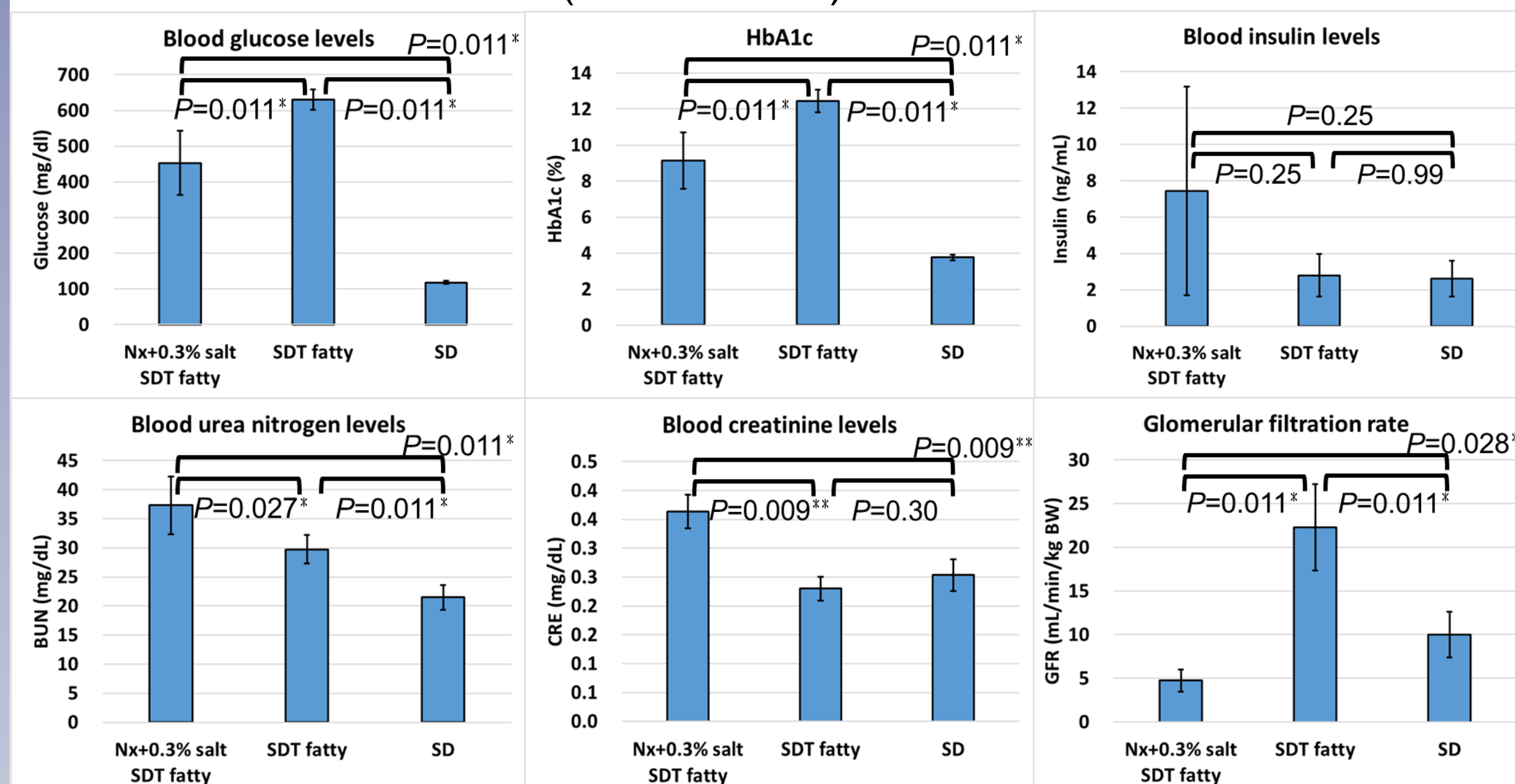
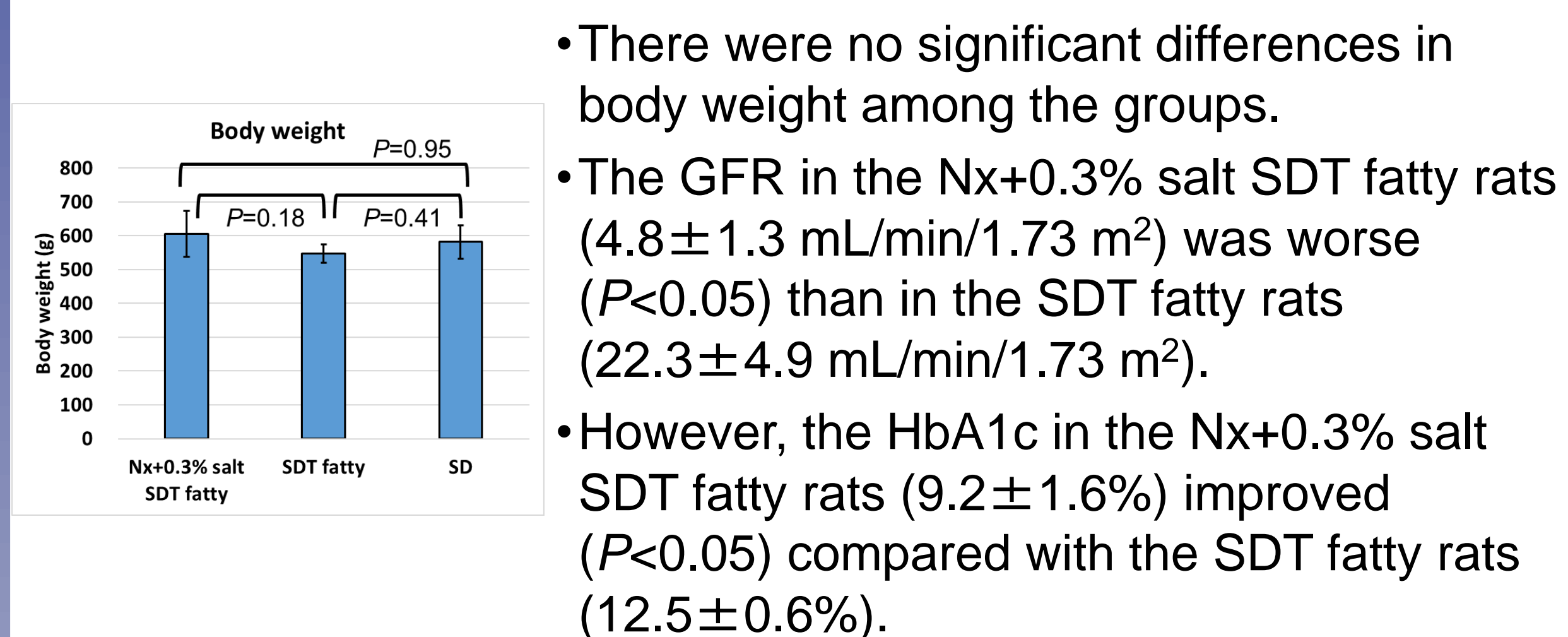


Measurements

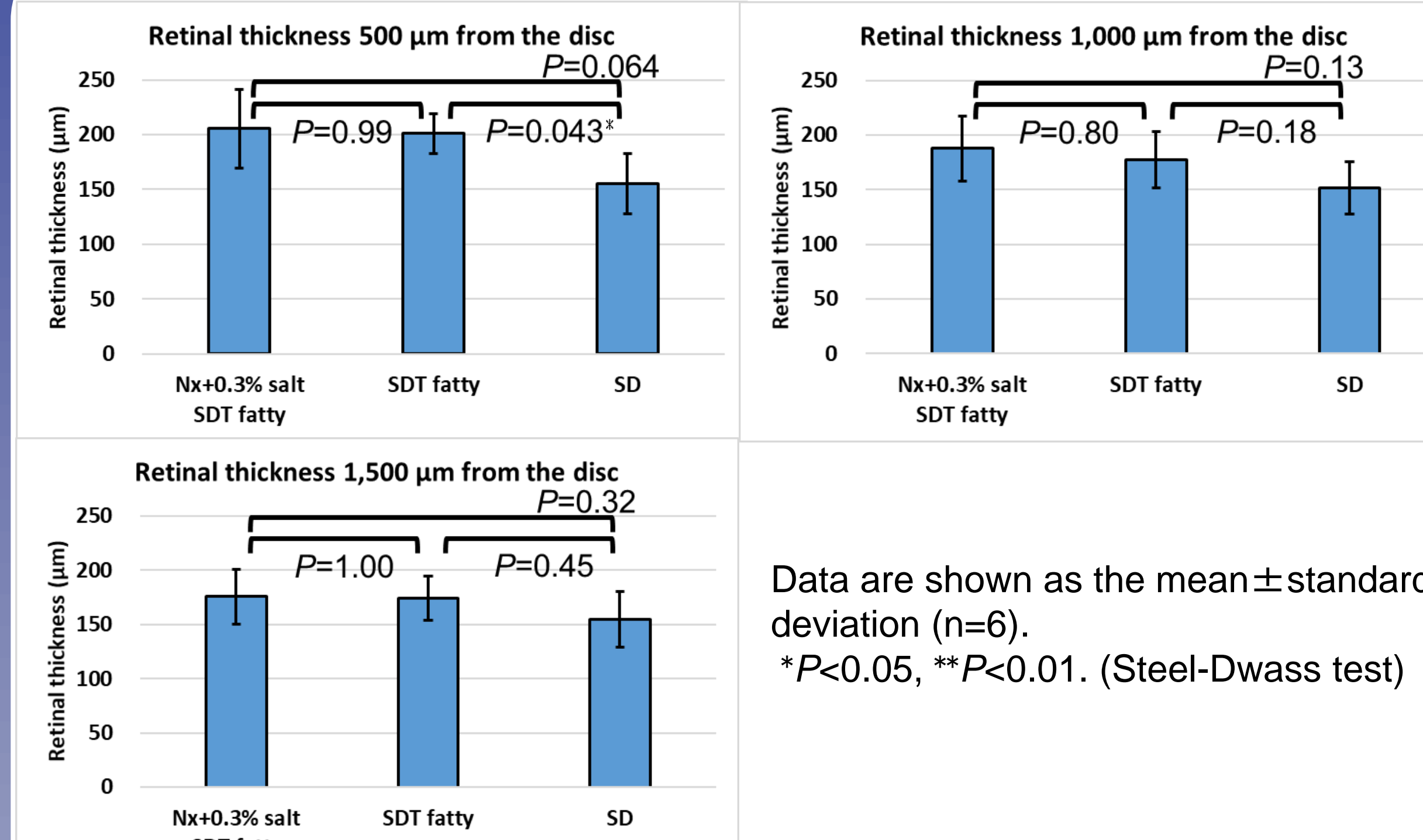
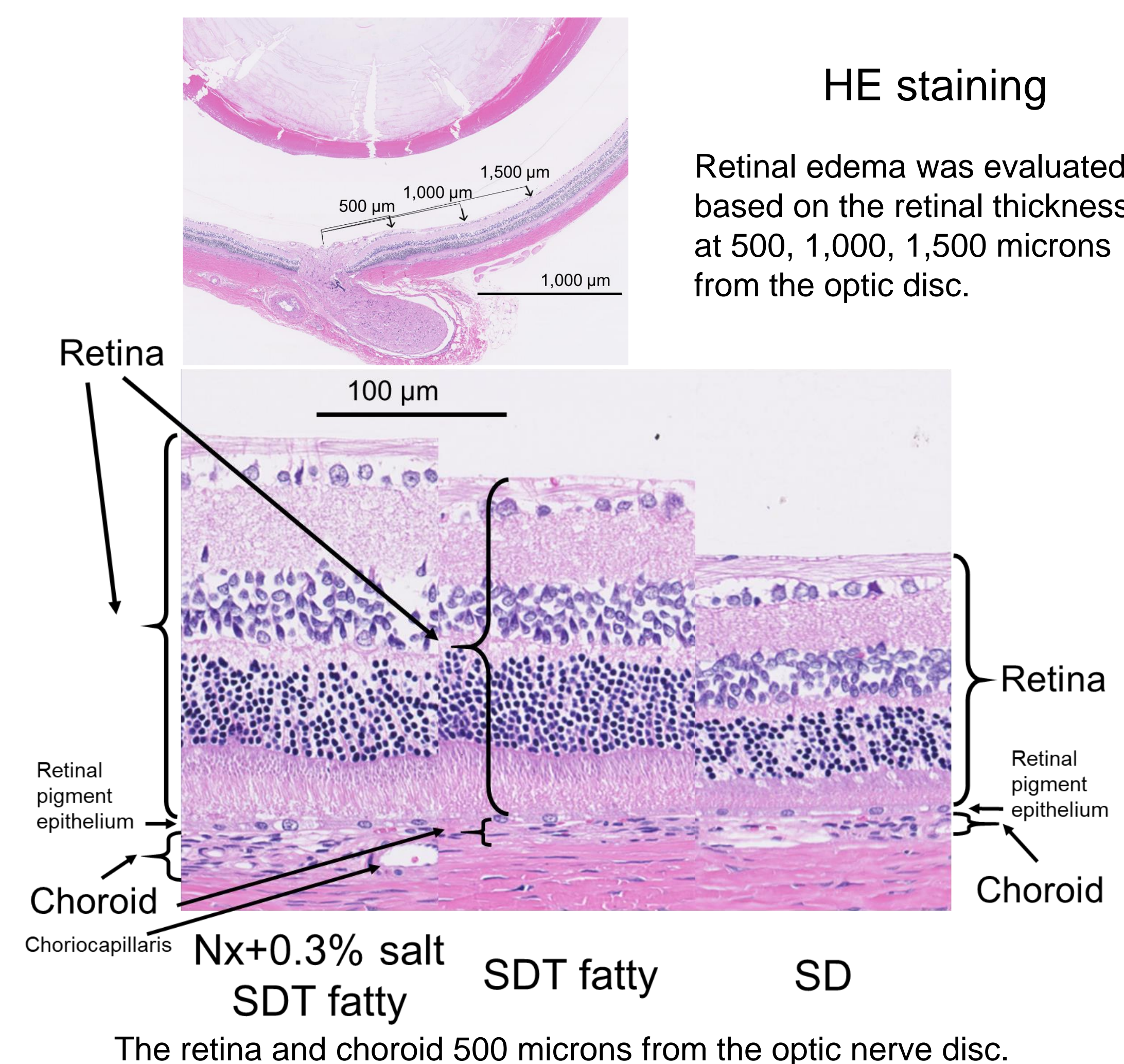
- Body weight
- Blood samples: Glucose, hemoglobin (Hb) A1c, insulin, blood urea nitrogen (BUN), creatinine (CRE), glomerular filtration rate (GFR)
- Retinal thickness (hematoxylin and eosin [HE] staining):
The retinal thicknesses were measured 500, 1,000, and 1,500 microns from the optic nerve disc.
- Retinal folds (HE staining):
The numbers of retinal folds, defined as deformation from the outer nuclear layer to the photoreceptor layer, were measured within 1,500 microns of the optic nerve disc.
- Immunostaining for glial fibrillary acidic protein (GFAP) and vascular endothelial growth factor (VEGF):
Quantitative analyses of the immunopositive regions were performed within 1,000 microns of the optic nerve disc using the Hybrid Cell Count Module (Keyence, Tokyo, Japan).

RESULTS

Body weight, Blood samples

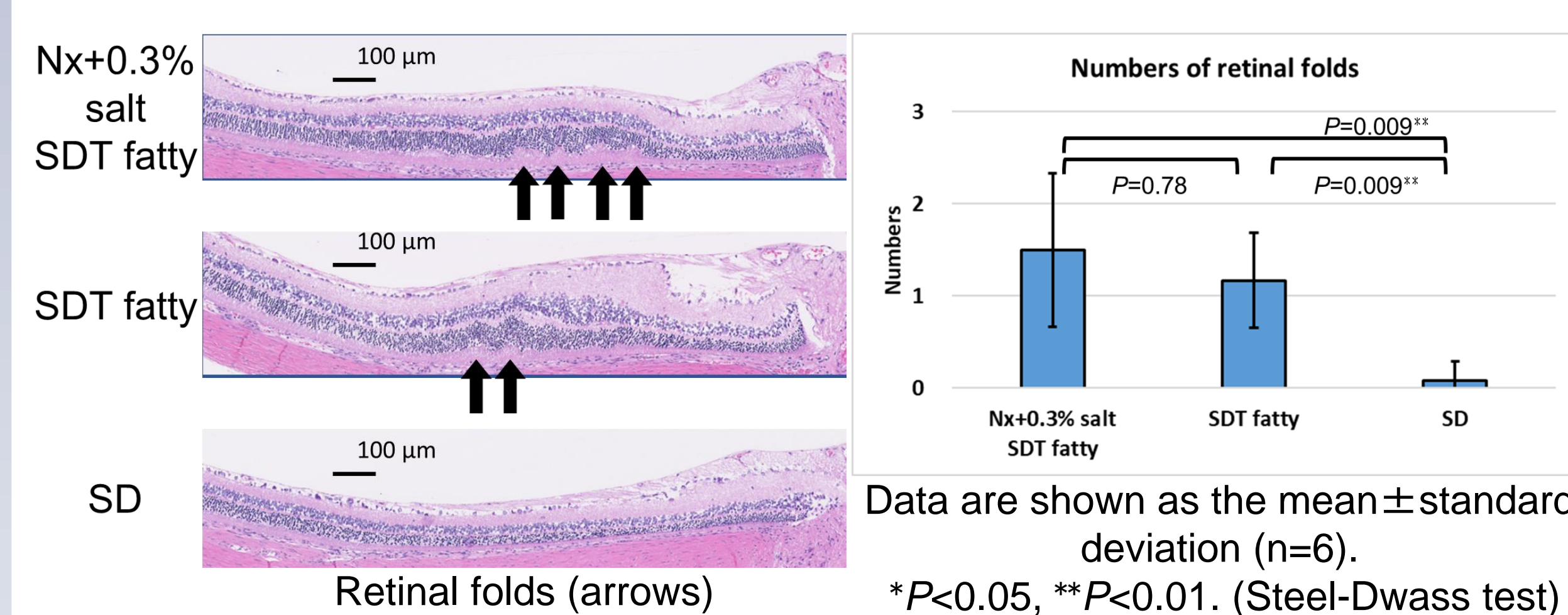


Retinal thickness



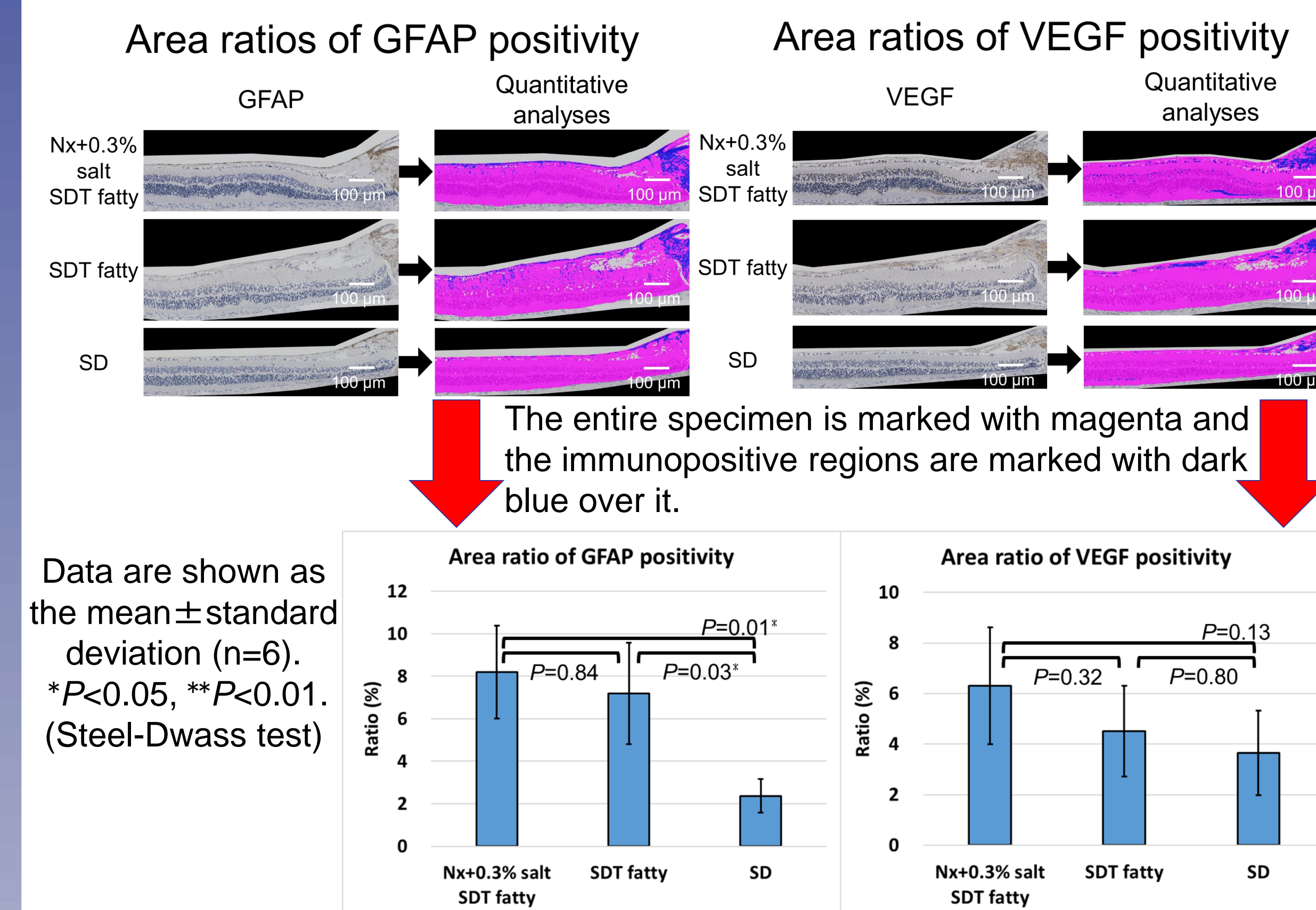
- The mean retinal thicknesses 500 microns from the optic nerve disc were:
 - Nx+0.3% salt SDT fatty rats 205.7 \pm 35.9 microns
 - SDT fatty rats 201.1 \pm 18.4 microns
 - SD rats 155.6 \pm 27.5 microns(Nx+0.3% salt SDT fatty rats vs. SDT fatty rats, $P = 0.99$; Nx+0.3% salt SDT fatty rats vs. SD rats, $P = 0.064$; SDT fatty rats vs. SD rats, $P = 0.043^*$) (Steel-Dwass test)
- The retinas were thicker in the SDT fatty rats than in the SD rats.
- However, the retinal thicknesses did not differ significantly between the Nx+0.3% salt SDT fatty rats and the SDT fatty rats.

Retinal folds



- The numbers of retinal folds within 1,500 microns of the optic nerve disc were:
 - Nx+0.3% salt SDT fatty rats 1.50 \pm 0.84
 - SDT fatty rats 1.16 \pm 0.52
 - SD rats 0.08 \pm 0.20(Nx+0.3% salt SDT fatty rats vs. SDT fatty rats, $P = 0.78$; Nx+0.3% salt SDT fatty rats vs. SD rats, $P = 0.009^{**}$; SDT fatty rats vs. SD rats, $P = 0.009^{**}$) (Steel-Dwass test)
- Retinal folds developed infrequently in the SD rats.
- No significant differences in the retinal folds were seen between the Nx+0.3% salt SDT fatty rats and the SDT fatty rats.

Immunostaining for GFAP and VEGF



- Area ratios of GFAP positivity
 - Nx+0.3% salt SDT fatty rats 8.2 \pm 2.2%
 - SDT fatty rats 7.2 \pm 2.4%
 - SD rats 2.4 \pm 0.8%(Nx+0.3% salt SDT fatty rats vs. SDT fatty rats, $P = 0.84$; Nx+0.3% salt SDT fatty rats vs. SD rats, $P = 0.01^*$; SDT fatty rats vs. SD rats, $P = 0.03^*$) (Steel-Dwass test)
- Area ratios of VEGF positivity
 - Nx+0.3% salt SDT fatty rats 6.3 \pm 2.3%
 - SDT fatty rats 4.5 \pm 1.8%
 - SD rats 3.7 \pm 1.7%(Nx+0.3% salt SDT fatty rats vs. SDT fatty rats, $P = 0.32$; Nx+0.3% salt SDT fatty rats vs. SD rats, $P = 0.13$; SDT fatty rats vs. SD rats, $P = 0.80$) (Steel-Dwass test)
- There were no significant differences in the quantitative analyses of the GFAP- and VEGF-positive regions in the retinas between the Nx+0.3% salt SDT fatty rats and SDT fatty rats.

CONCLUSIONS

- Severe DR developed in both the Nx+0.3% salt SDT fatty and SDT fatty rats compared with the SD rats.
- However, the progression of DR in the Nx+0.3% salt SDT fatty rats was not marked compared with the SDT fatty rats.
- The progression of DR may have been suppressed by the improvement in the blood glucose level despite development of kidney dysfunction due to unilateral Nx and salt supplementation.
- Further analysis and examination are needed.

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