

# Significance of renal autonomic nerves for weight-reduction by SGLT2 inhibitors.



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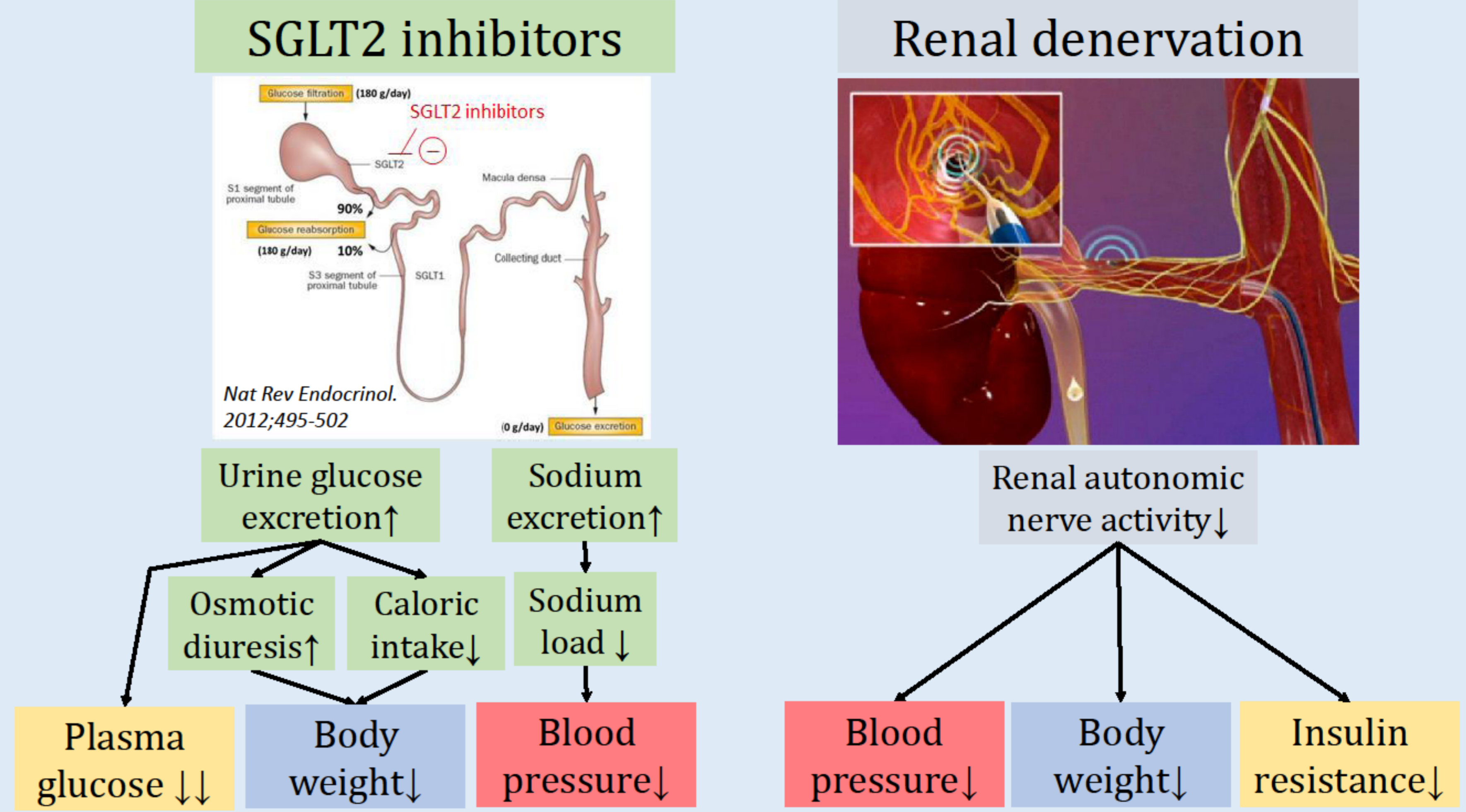
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## Introduction

- ▶ Sodium-glucose co-transporter (SGLT) 2 inhibitors decrease not only serum glucose level but also the body weight significantly.
- ▶ It is reported that renal denervation (RDN) similarly decreases not only blood pressure but also body weight.
- ▶ The urine glucose may have some relation with the renal autonomic nerve in the control of body weight. However, that relation has not been elucidated.
- ▶ The present study examined the roles for renal autonomic nerves in the weight reduction by SGLT2 inhibitors through performing RDN on mice fed on a high-fat diet.



## Methods

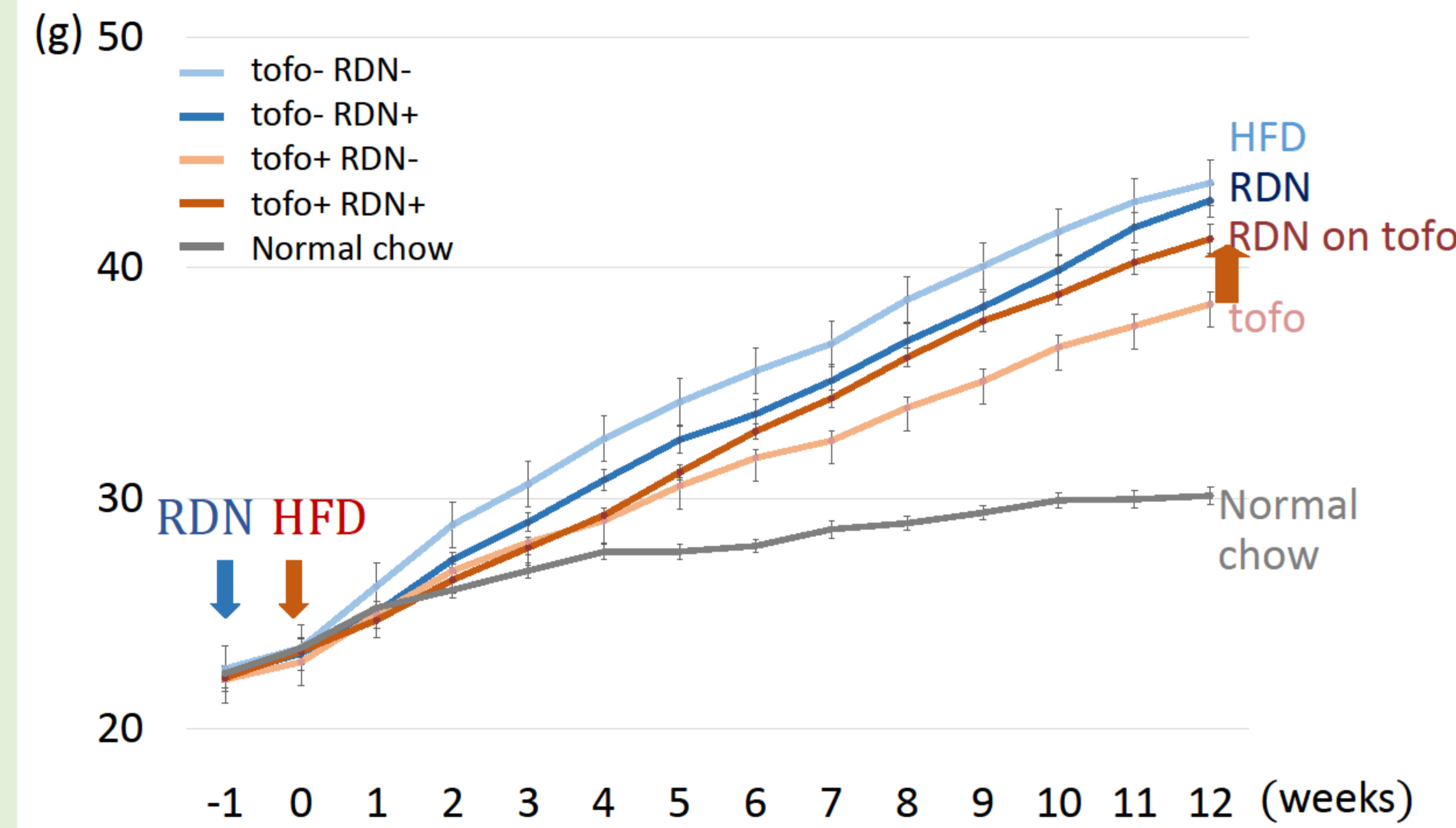
- ▶ The C57BL/6 mice fed on a high-fat diet were divided into 4 groups; control, RDN, SGLT2 inhibitor and SGLT2 inhibitor with RDN group.
- ▶ Measurements: the body weight, glucose tolerance, tissue weights and hormone sensitive lipase.
- ▶ The SGLT2 inhibitor was administered to mice from 8 weeks old by mixing it in the high-fat diet (tofogliflozin 5 mg/g pellet, 60 %Kcal fat).
- ▶ RDN was performed at 7 weeks old by surgically stripping the renal arteries and coating the vessels with a solution of 10% phenol in ethanol.

Group	n	HFD	tofo	RDN
Group1	15	HFD	-	-
Group2	15	HFD	-	+
Group3	15	HFD	+	-
Group4	15	HFD	+	+
Group5	5	Normal chow	-	-

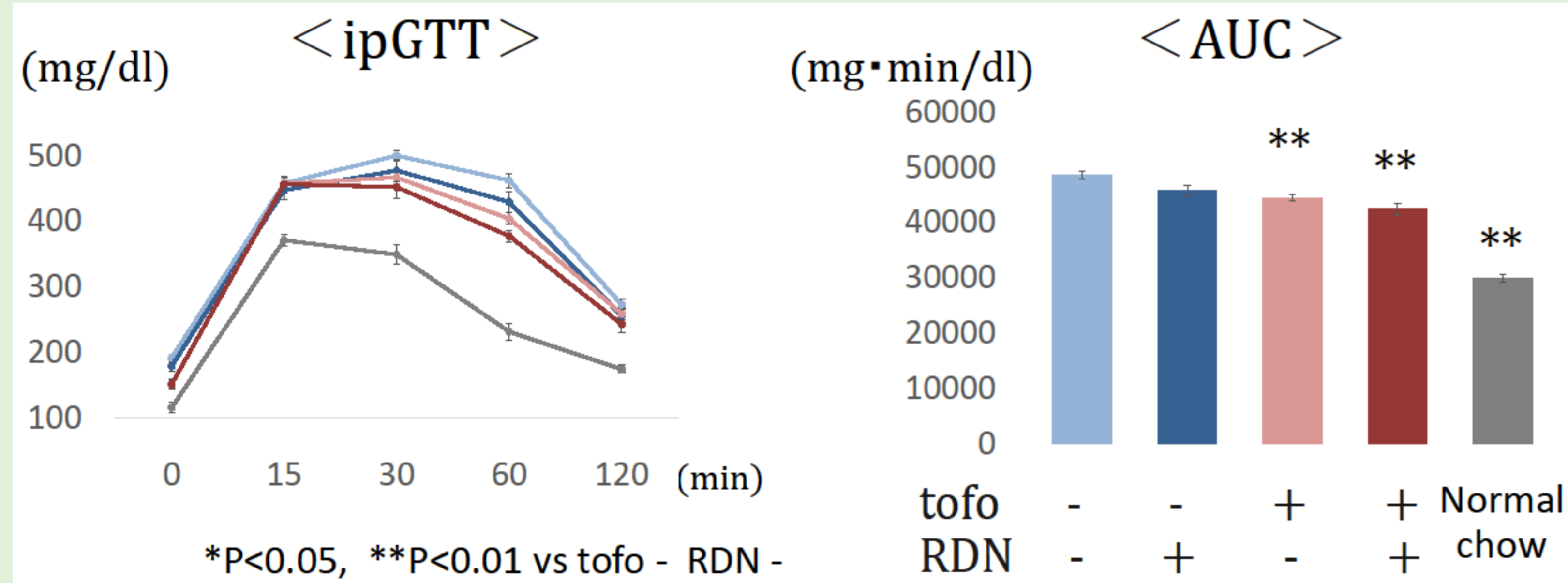
tofo: tofogliflozin (SGLT2 inhibitor)  
RDN: renal denervation  
HFD: high fat diet (60%Kcal)

## Results

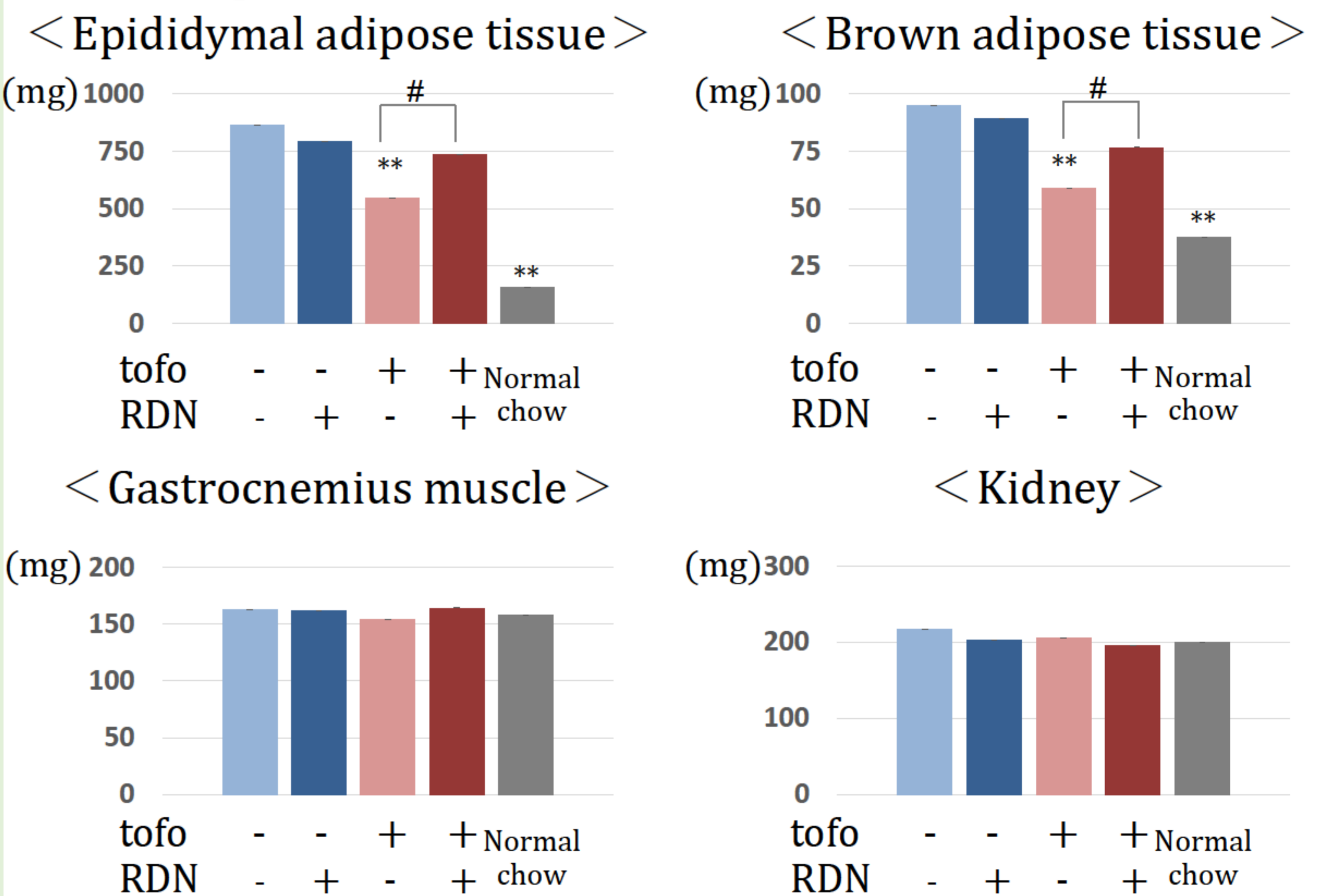
### Body weight



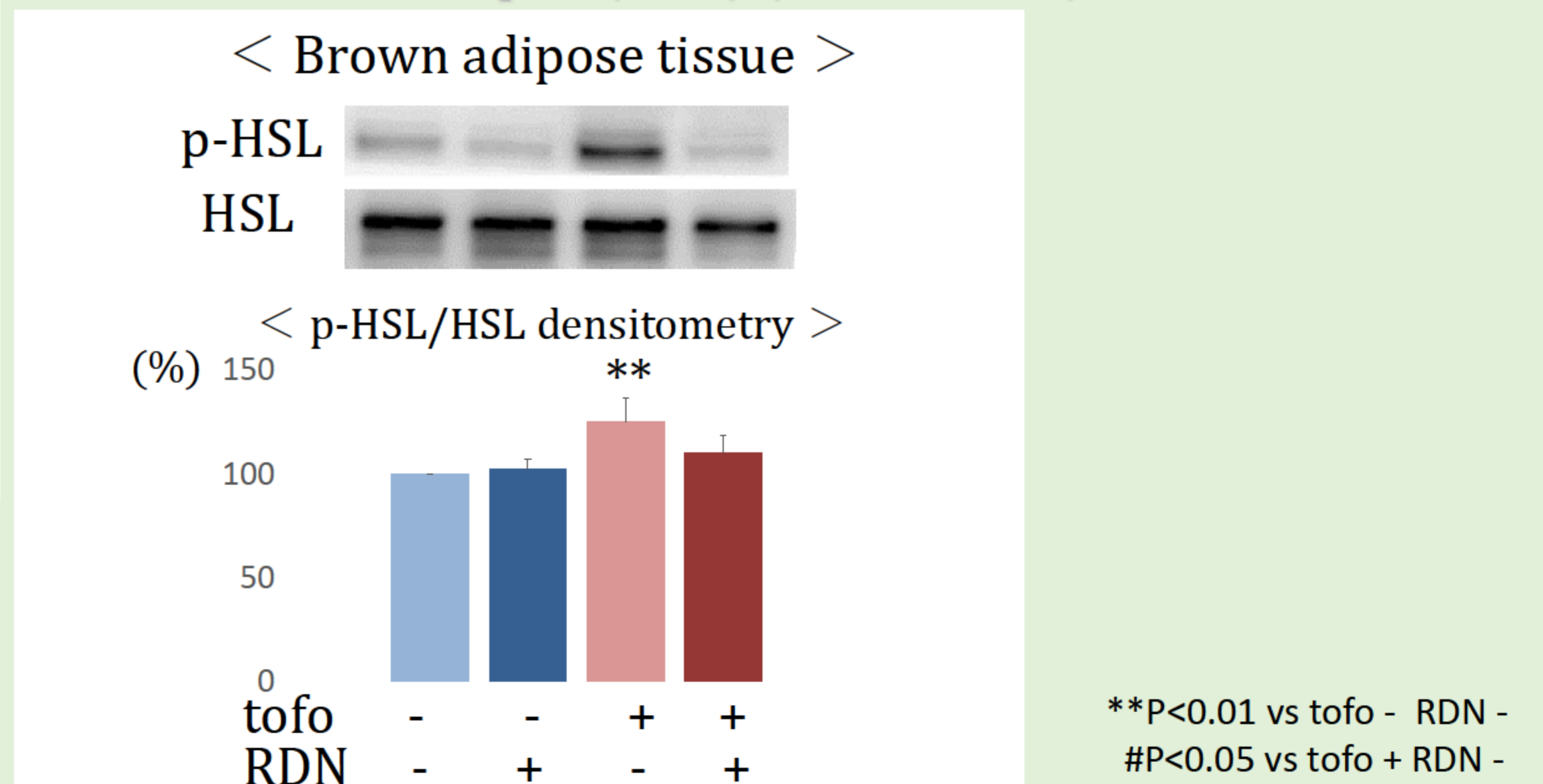
### Glucose tolerance



### Tissue weights



### Hormone sensitive lipase(HSL) (western blot)



## Conclusions and Discussion

HFD mice	RDN	SGLT2i	RDN on SGLT2i
Body weight	↓	↓↓	↑
ipGTT AUC	↓	↓	↓
Fat tissue weight	→	↓↓	↑
Skeletal muscle weight	→	→	→
Fat tissue p-HSL/HSL	→	↑	↓

- ▶ These results indicate that HSL activation in the adipose tissue mediated by the renal autonomic nerves were involved in the mechanism of weight-reduction by SGLT2 inhibitors.
- ▶ The renal autonomic nerves were suggested to have a role in the control of body weight.

