

# Effects of TSPO deletion on cardiac and metabolic phenotype in rats

Juliette BREHAT, Shirin LEICK, Jin-Bo SU, Lucien SAMBIN, Bijan GHALEH, Sandrine PONS, Didier MORIN

INSERM U955, IMRB, équipe 03, Créteil, France

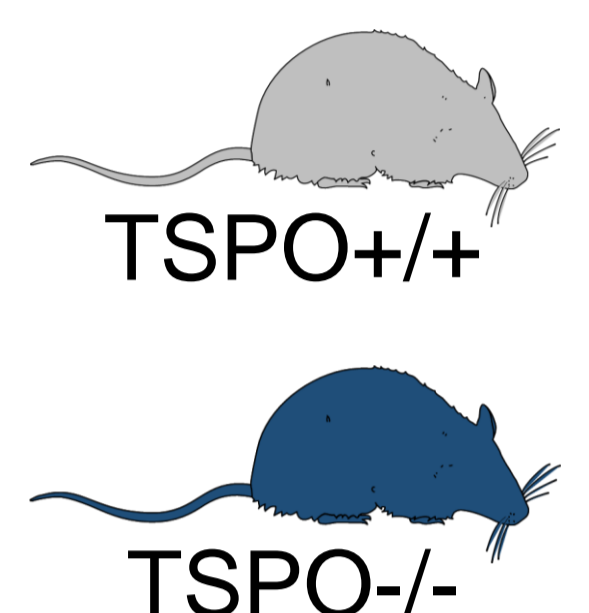
## INTRODUCTION

The translocator protein (TSPO) is involved in the transport of cholesterol across mitochondrial membranes in steroidogenic tissue. TSPO is widely distributed and is associated with multiple functions, such as steroid hormone or heme synthesis. This protein is also expressed in the heart but its role remains ill known. In this context, our laboratory demonstrated that 4'chlorodiazepam, a TSPO ligand, reduces infarct size following ischemia-reperfusion (IR). This cardioprotection was associated with the inhibition of cholesterol intake by cardiac mitochondria and less accumulation of cholesterol oxidized derivatives. In collaboration with Pr. Papadopoulos, our laboratory started a colony of rats deleted for *tspo* (TSPO<sup>-/-</sup>), providing an interesting tool to further investigate the role of TSPO in cardiac IR.

➤ The aim of this study was to investigate the metabolic and cardiac phenotypes of the rats deleted for *tspo*.

## METHODS

TSPO<sup>+/+</sup> and TSPO<sup>-/-</sup> rats were studied throughout their lives. The effects of the TSPO deletion on reproduction, morphology, cardiac phenotype (mitochondrial function, echocardiography and fibrosis), lipid phenotype and metabolic phenotype (insulin and glucose tolerance tests) were investigated.

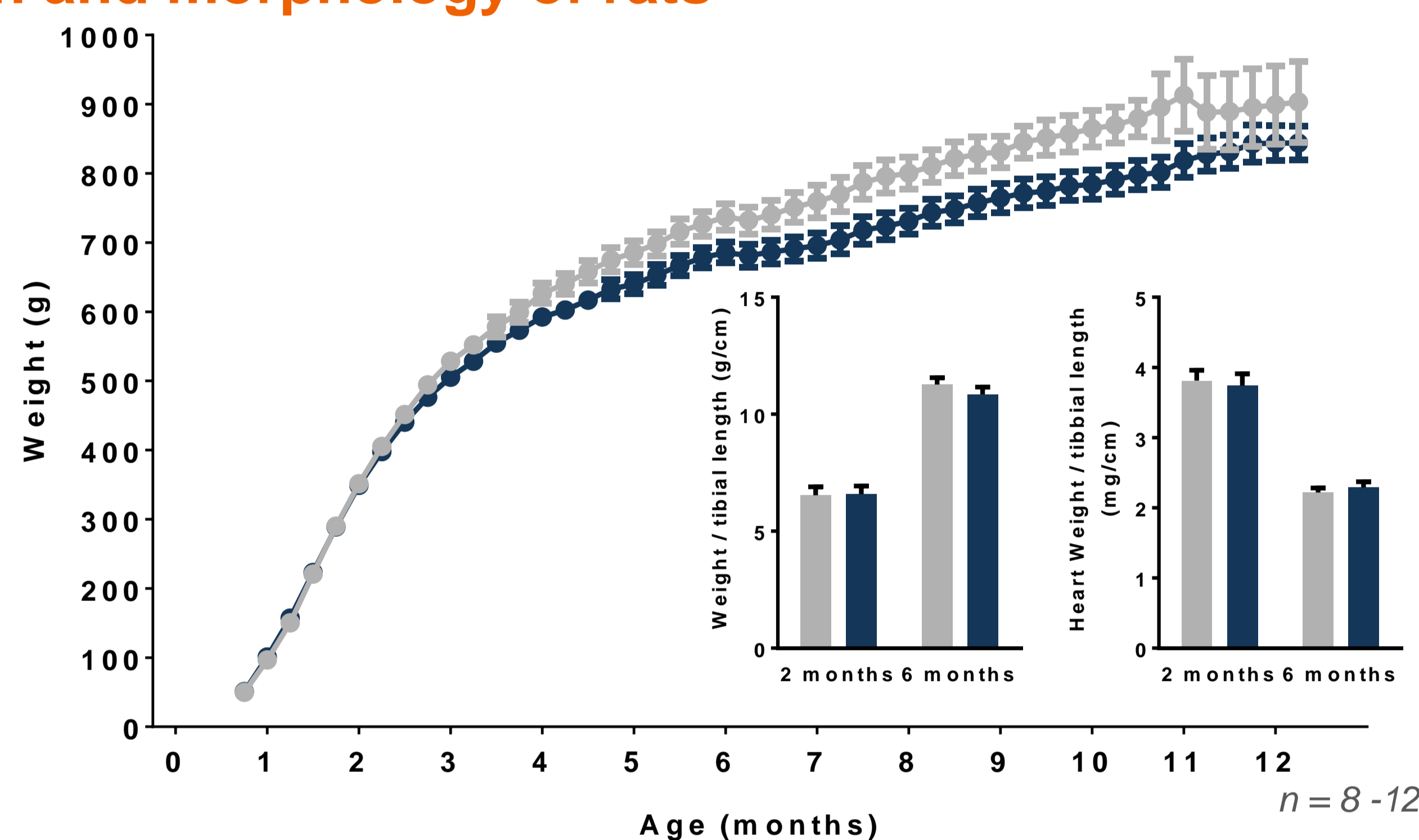
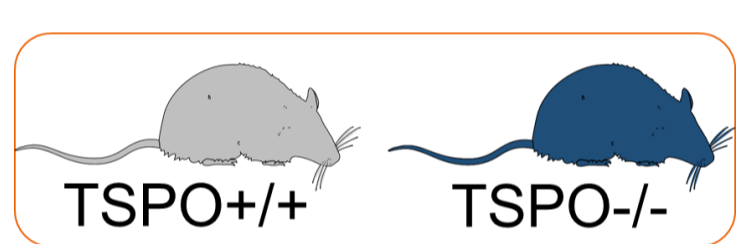


## RESULTS

### Effect of *tspo* deletion on reproduction and morphology of rats

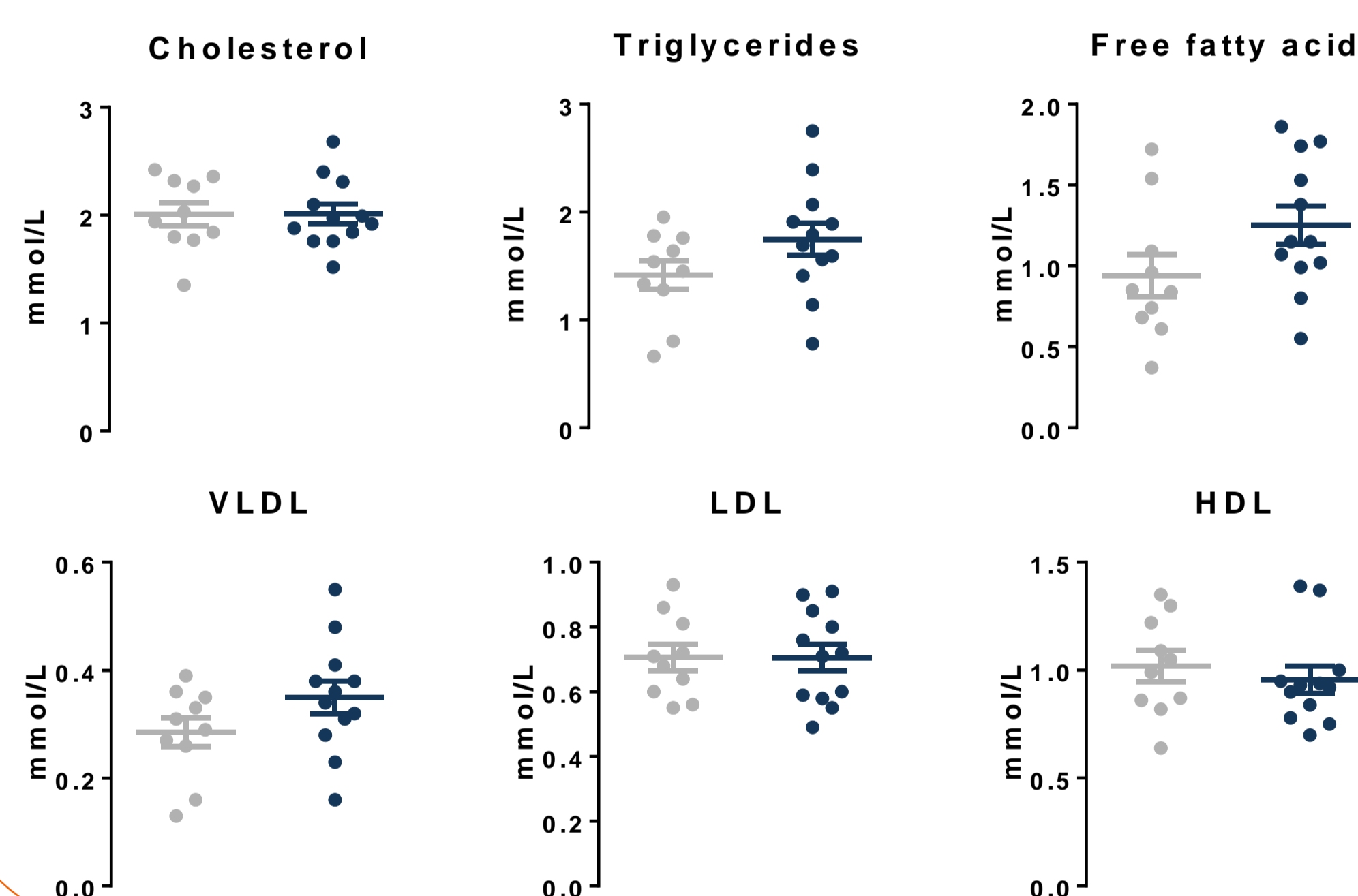
Breeding	Pups per litter	Sexe		Genotype		
		Female	Male	TSPO <sup>+/+</sup>	TSPO <sup>+/-</sup>	TSPO <sup>-/-</sup>
Homozygous TSPO <sup>+/+</sup>	11	60%	40%	100%	x	x
Homozygous TSPO <sup>-/-</sup>	12	55%	45%	x	x	100%
heterozygous TSPO <sup>+/-</sup>	10	50%	50%	27%	47%	26%

n = 18-21 litters per breeding

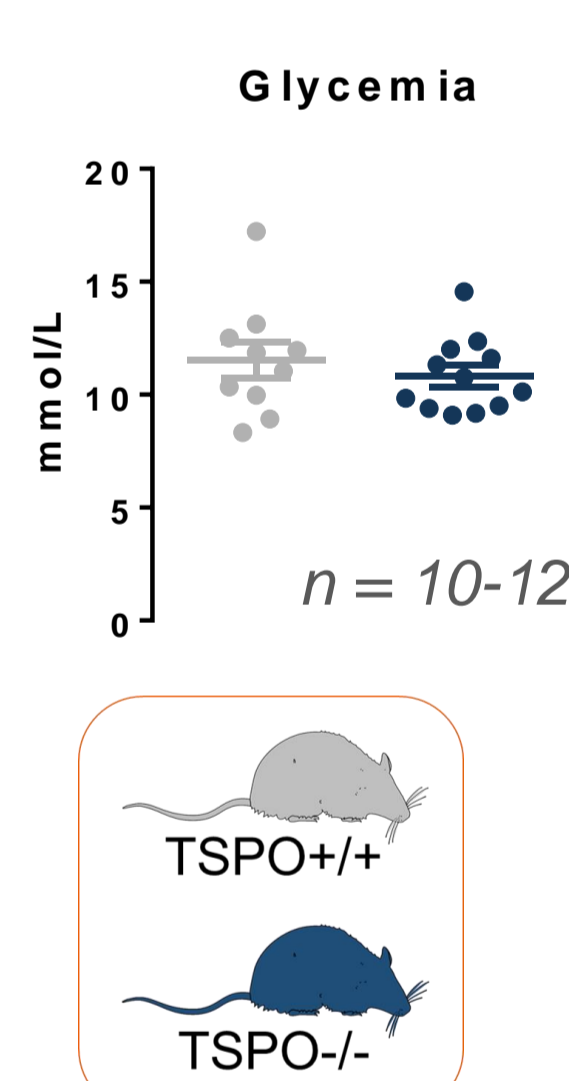


### *tspo* deletion does not alter rat metabolic phenotype

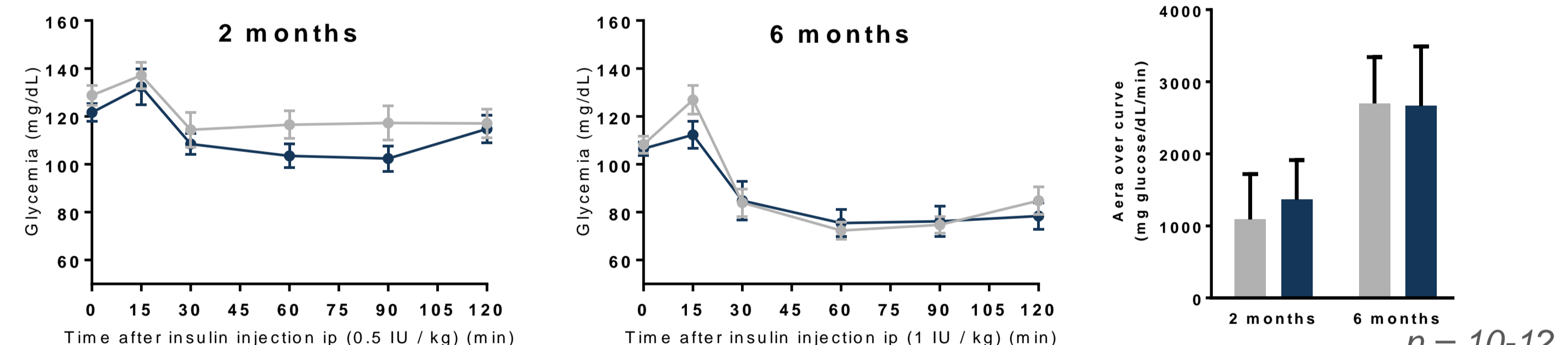
#### Lipid phenotype n = 10-12



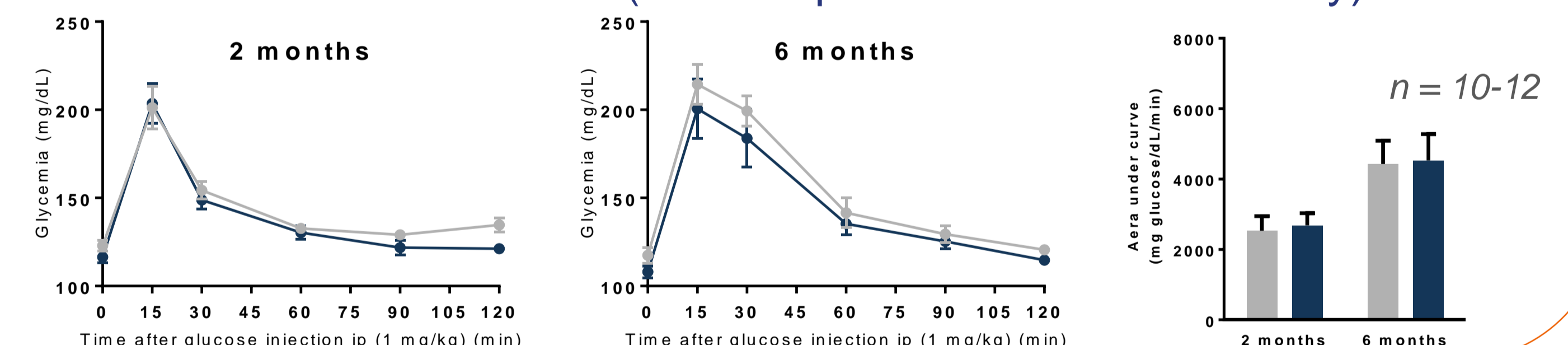
#### Carbohydrate phenotype n = 10-12



#### Insuline tolerance test (insuline sensitivity) n = 10-12

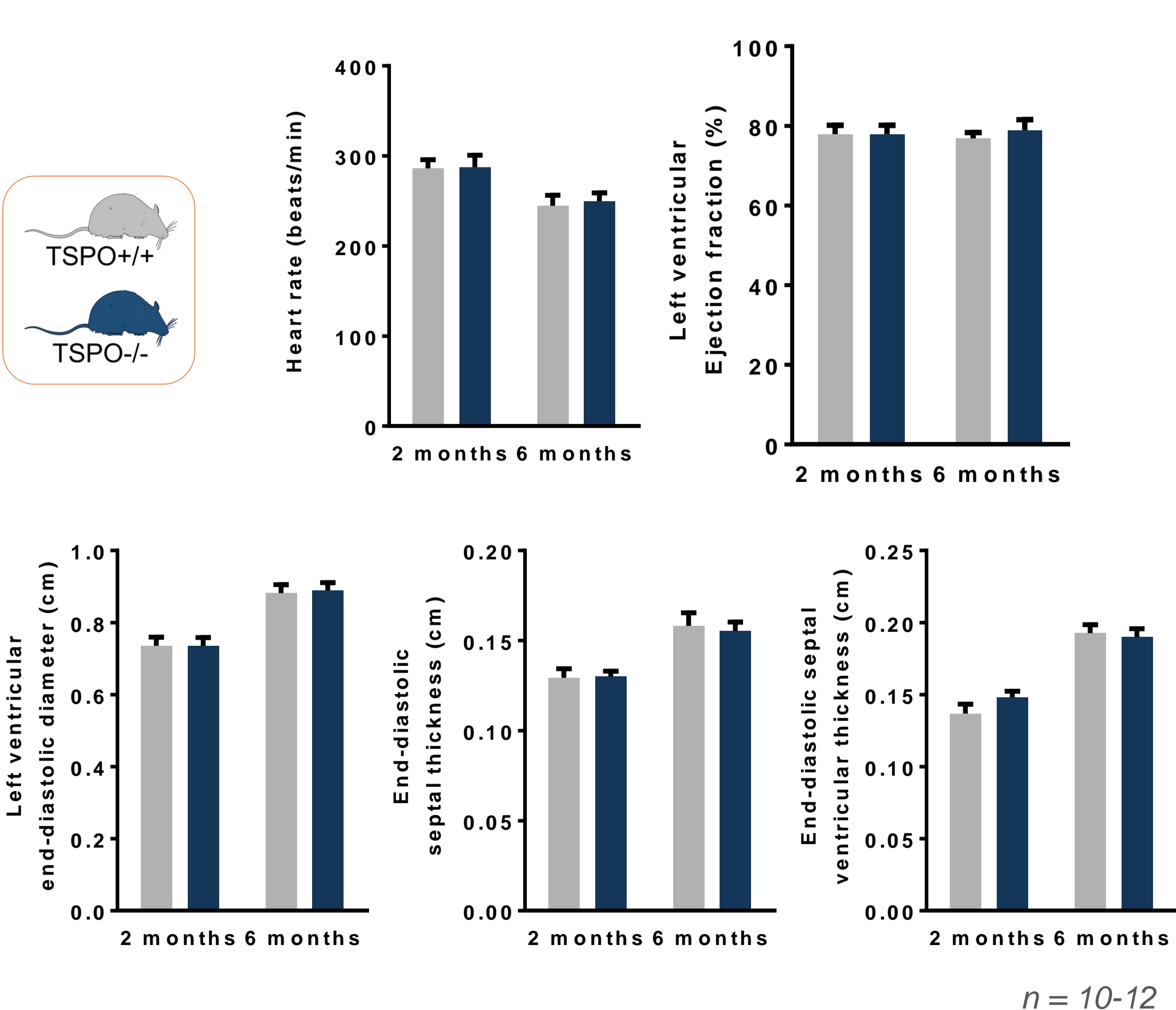


#### Glucose tolerance test (insuline production and sensitivity) n = 10-12

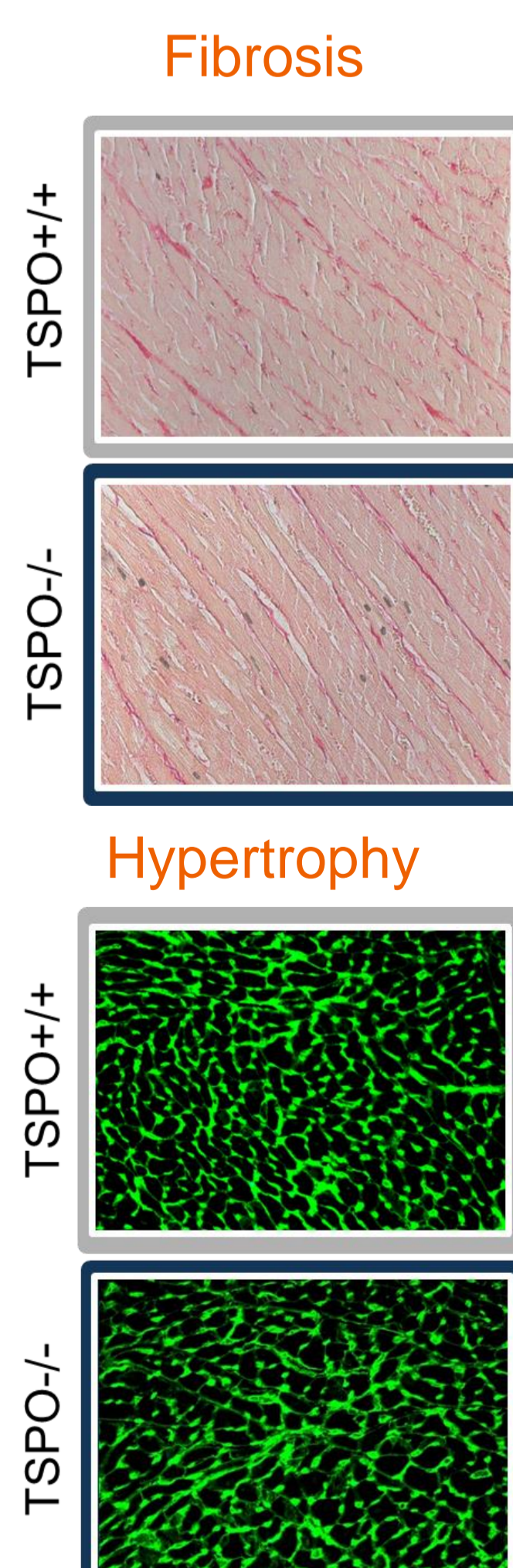


### Cardiac phenotype is not modified by *tspo* deletion

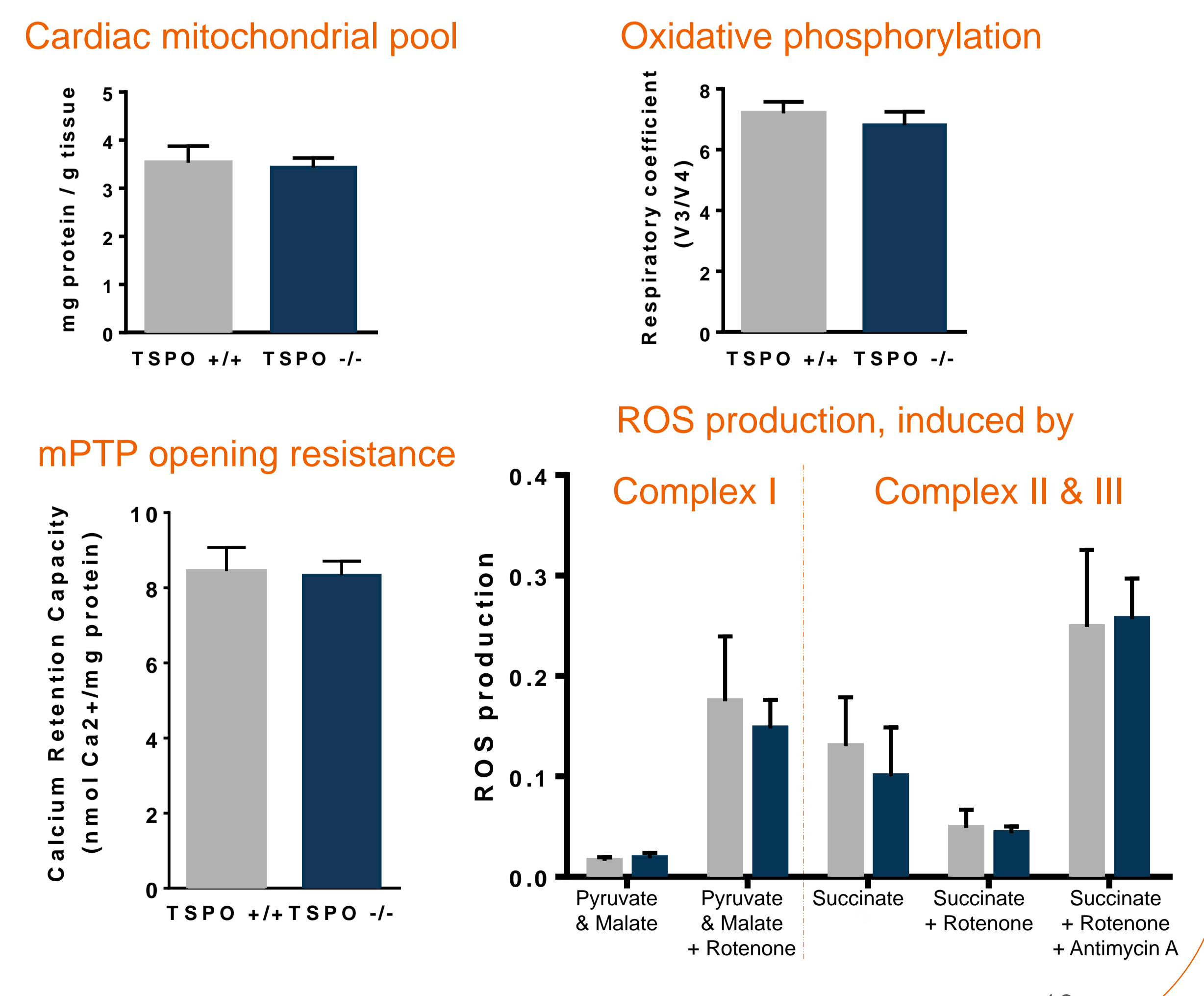
#### Cardiac echography n = 10-12



#### Cardiac histology 6 months



#### Mitochondrial functions 2 months



## CONCLUSION

All experiments performed with rats from our colony revealed that, despite the ubiquitous expression of TSPO and its implications in various biological functions, the deletion of *tspo* did not modify the cardiac and metabolic phenotype in young rats (2 and 6 months). The follow up of these animals will provide further data at older stages (1 and 1,5 year).

