

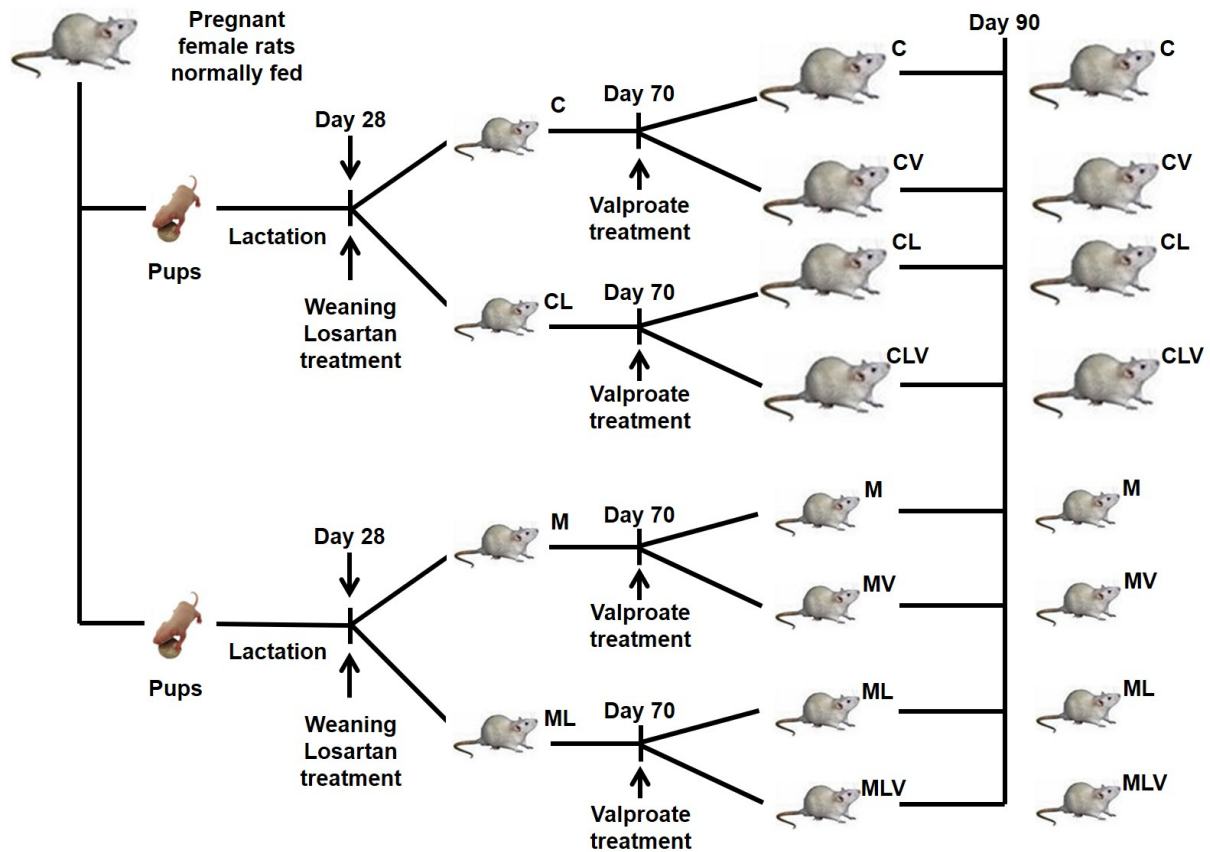
Supplementary Material

Histone Deacetylase Activity and the Renin-Angiotensin-Aldosterone System: Key Elements in Cardiorenal Alterations Provoked by Chronic Malnutrition in Male Adult Rats

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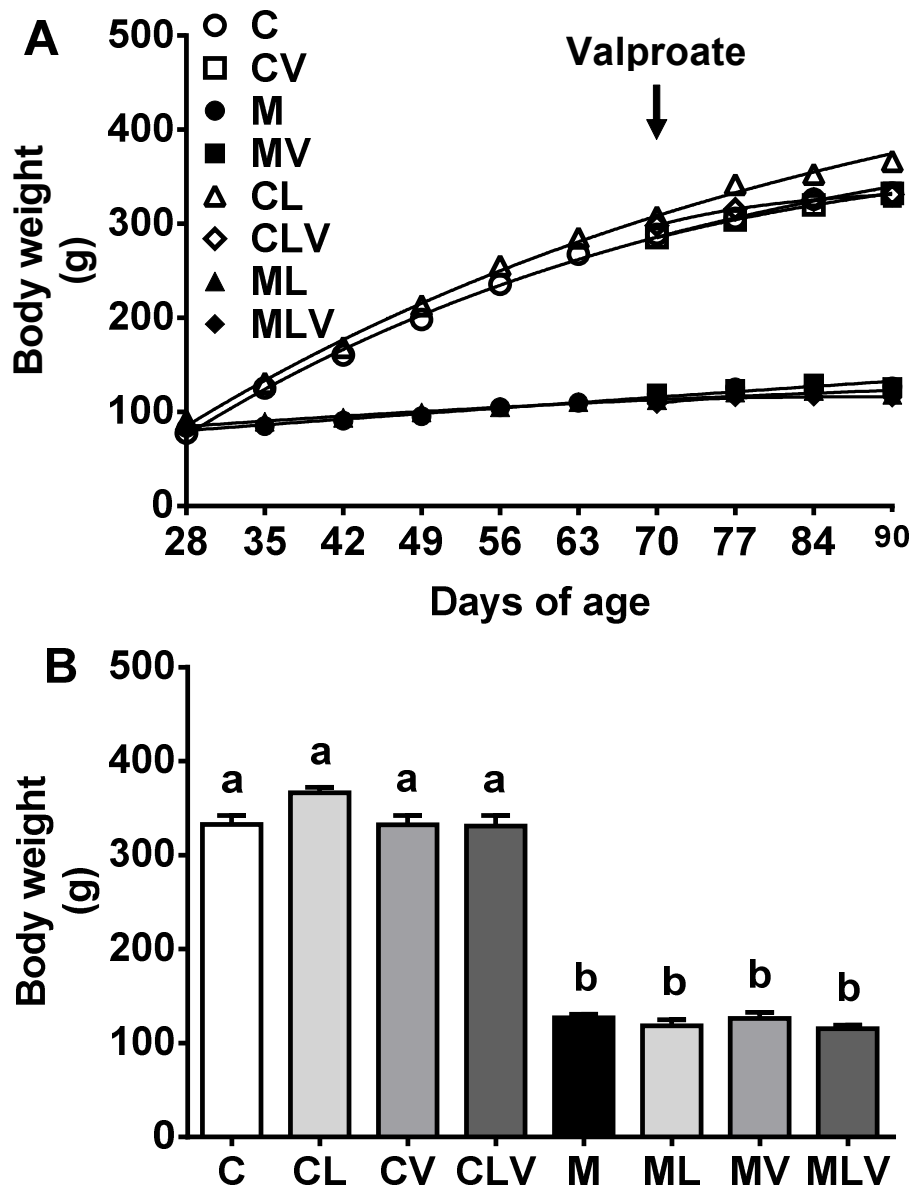
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Supplementary Fig. 1



Supplementary Fig. 1. Timeline of pharmacological interventions with Losartan and Valproate in normonourished and malnourished male rats. Rats received a control diet for rodents (4 upper branches) or a multideficient diet (Regional Basic Diet/RBD) (4 lower branches); see details in the main text. The experimental 8 groups are identified as: C, control; CL, control + Losartan (Los); CV, control + Valproate (Val); CLV, control + Los + Val; M, malnourished; ML, malnourished + Los; MV, malnourished + Val; MLV, malnourished + Los + Val (see also Supplementary Table 1). The right vertical line indicates the day of sacrifice (90 days of age). Protocols 007/16 and 012/19 were approved by the Ethics Committee on Animal Use, Health Sciences Center/Federal University of Rio de Janeiro (see also main text).

Supplementary Fig. 2



Supplementary Fig. 2. (A) Body mass evolution in control and malnourished rats treated either with or without Losartan (Los) or Valproate (Val) (alone or in combination), from weaning (28 days of age) to young adult age (90 days). Los administration began immediately after weaning. The body-mass of the 4 normonourished groups was different from the 4 malnourished groups ($p < 0.0001$) from the first week (35 days of age), as assessed by two-way ANOVA followed by Bonferroni's test. (B) Body mass of normonourished and malnourished rats aged 90 days, which were treated with or without Los, Val or both drugs. Abbreviations of groups are described in Materials and Methods section and Supplementary Table 1. The data are mean \pm SEM ($n = 9-19$). Different lowercase letters above the bars indicate different mean values ($p > 0.05$; two-way ANOVA followed by Bonferroni's test).

Supplementary Table 1. Identification of the experimental groups. Groups are as follows: C, control; CL, control + Los; CV, control + Val; CLV, control + Los + Val; M, malnourished; ML, malnourished + Los; MV, malnourished + Val; MLV, malnourished + Los + Val.

Group	Nutritional status	Losartan starts at day	Valproate starts at day
C	Control		
CV	Control		70
CL	Control	28	
CLV	Control	28	70
M	Malnourished		
MV	Malnourished		70
ML	Malnourished	28	
MLV	Malnourished	28	70

Supplementary Table 2. Renal and cardiac masses and indexes from normonourished and malnourished rats treated or not with Los and/or Val (90 days of age).

Organ masses	Groups of normonourished rats				Groups of malnourished rats			
	C	CL	CV	CLV	M	ML	MV	MLV
Renal mass (g)	2.23±0.05 ^a	2.26±0.07 ^a	2.20±0.06 ^a	2.17±0.05 ^a	0.90±0.02 ^b	0.89±0.03 ^b	0.92±0.03 ^b	0.92±0.02 ^b
Renal index (mg/g)	6.82±0.10 ^a	6.88±0.08 ^a	6.87±0.07 ^a	6.77±0.09 ^a	7.06±0.10 ^a	8.28±0.26 ^b	7.12±0.19 ^a	8.29±0.16 ^b
Cardiac mass (g)	1.07±0.02 ^a	1.02±0.03 ^a	1.02±0.02 ^a	1.00±0.03 ^a	0.57±0.02 ^b	0.40±0.02 ^c	0.54±0.02 ^b	0.40±0.01 ^c
Cardiac index (mg/g)	3.25±0.04 ^a	3.10±0.05 ^a	3.20±0.06 ^a	3.09±0.06 ^a	4.42±0.08 ^b	3.76±0.12 ^c	4.17±0.10 ^b	3.62±0.12 ^c

Groups are indicated as shown in Materials and Methods section and Supplementary Table 1. The data are mean ± SEM (n = 9–19). Mean values within a line with different lowercase superscript letters were significantly different ($p < 0.05$; two-way ANOVA followed by Bonferroni's test).