Chronic renal failure worsens ischemic stroke severity and neurological consequences in mice

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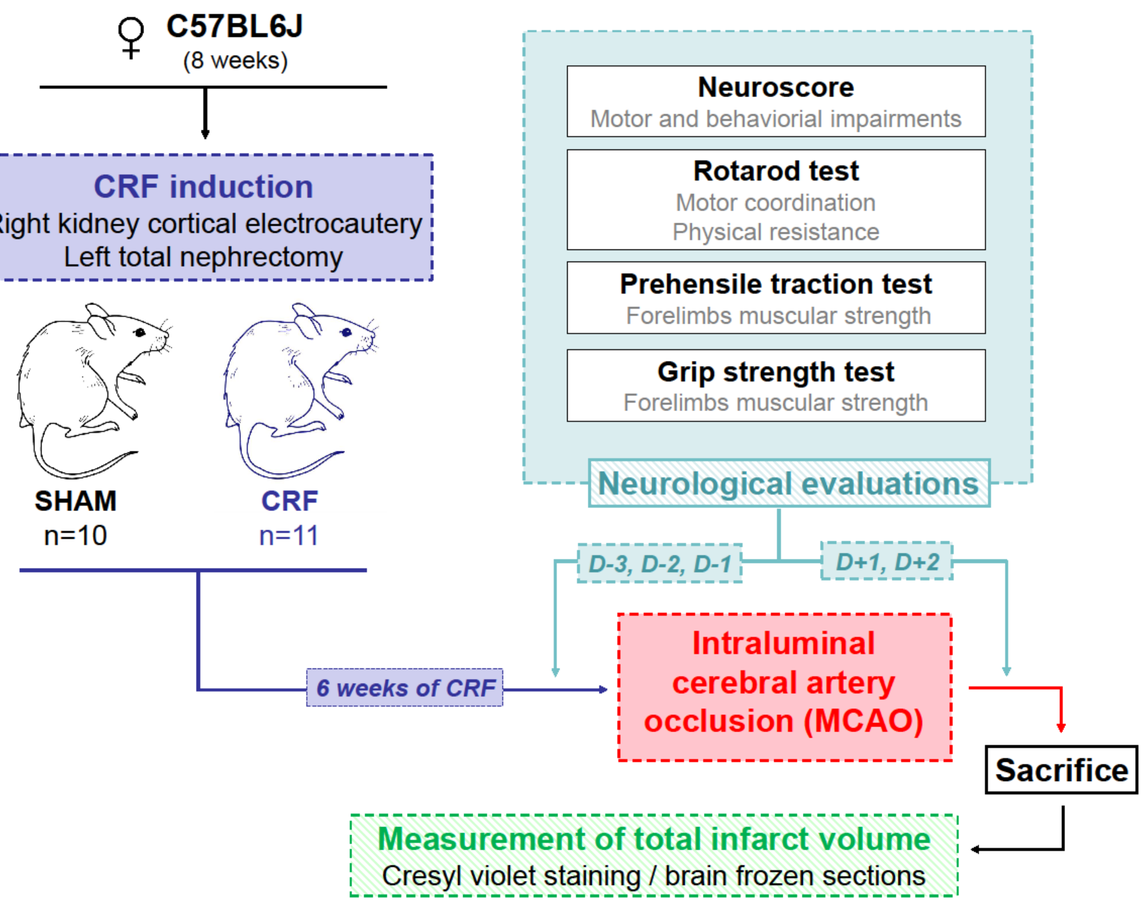
INTRODUCTION AND AIM

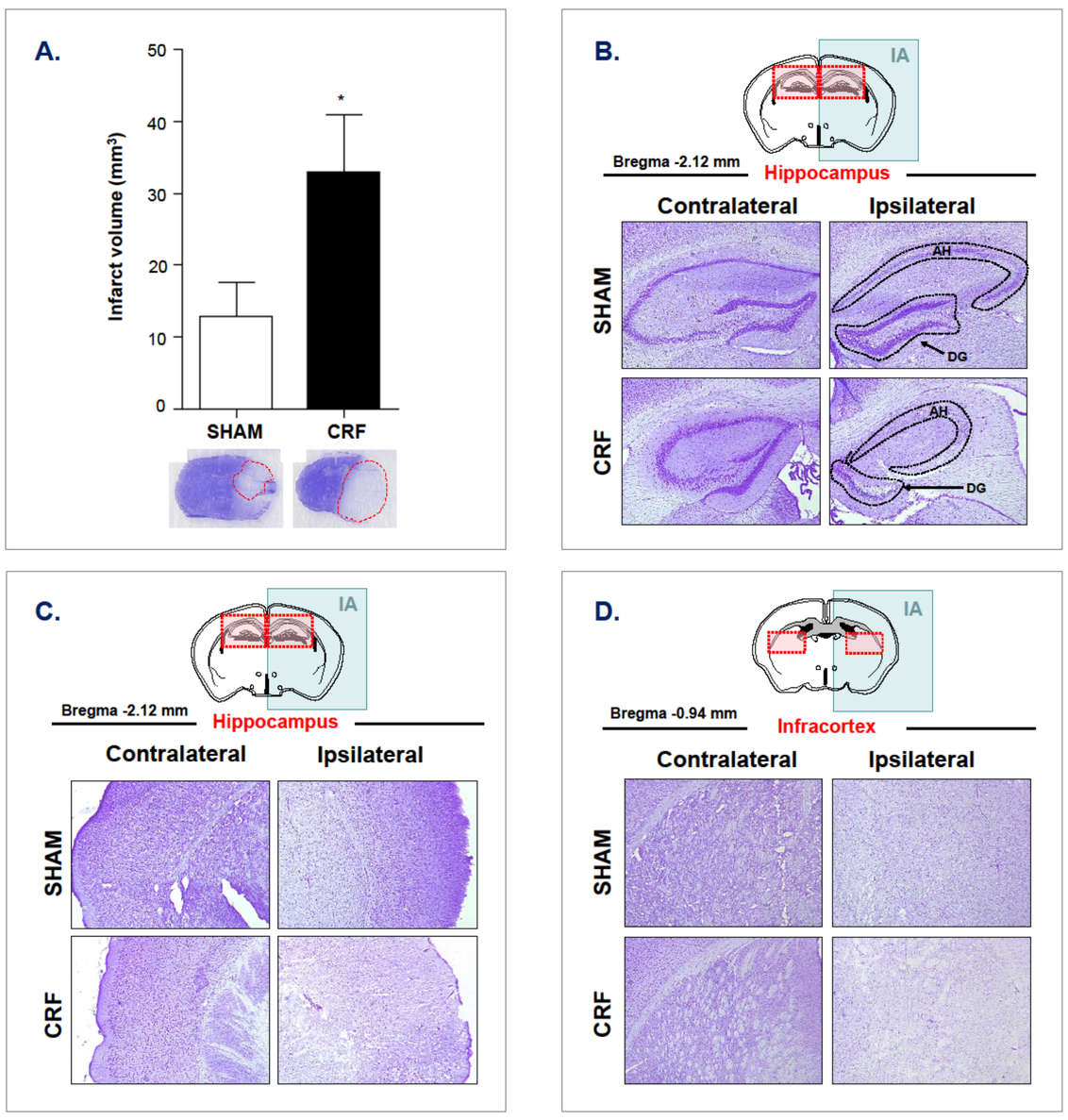
Stroke is the **third most common cause of cardiovascular death in patients with chronic renal failure (CRF)**. To date, data on the impact of CRF on the cerebral circulatory system are scarce and identification of underlying causes and successful medical treatments remains a major challenge. **The present study sought to evaluate the impact of CRF on the severity of ischemic stroke 6 weeks after CRF installation.**

MATERIALS AND METHODS



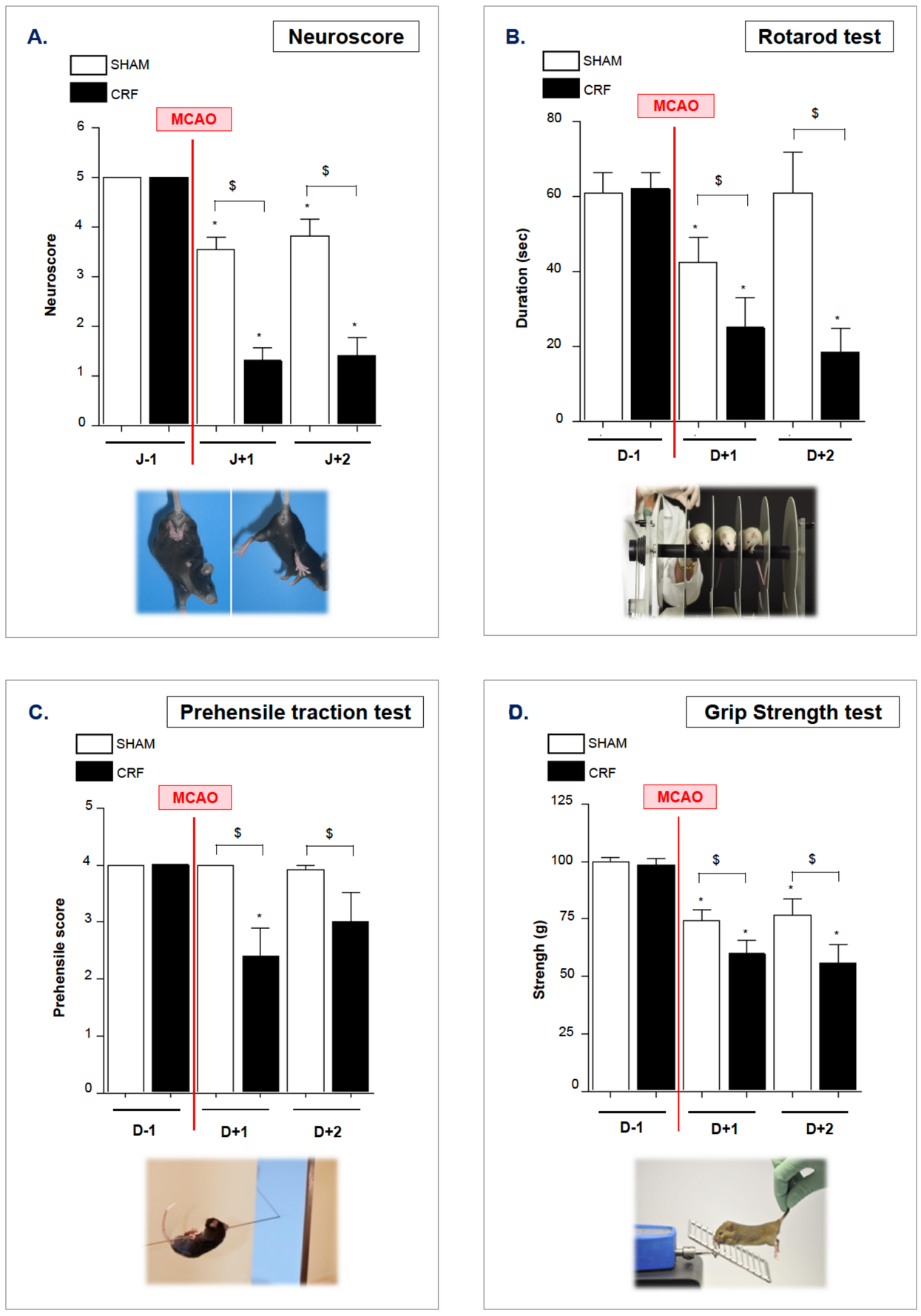
RESULTS

Figure 1. *CRF worsens stroke-induced brain ischemia and hippocampal, cortical and infracortical loss of neurons as compared to SHAM operated mice.*



A. Evaluation of total brain infract volume in SHAM (n=10) and CRF (n=11) mice. Results are expressed as mean ± SEM. *: p<0.05 CRF *versus* SHAM operated mice (Student t test). **B., C., and D.** Contra- and ipsilateral **evaluation of neuronal loss** in the hippocampus (B.), cortex (C.) and infracortex (D.) of CRF and SHAM operated mice (Cresyl violet staining, Gx25). AH: Ammon's horn; DG: Dentate gyrus; IA. Ischemic Area.

Figure 2. *CRF amplifies stroke-induced decrease in mice neuroscore (A), resistance to tiredness (B) and muscular strength (C,D) as compared to SHAM operated mice.*



Neurological evaluations. All evaluations were performed on SHAM and CRF mice 1 day before (D-1) and 1 and 2 days (D1 / D2) after stroke induction. **A. Neuroscores** (2 ways ANOVA: CRF/SHAM: p < 0.0001, days: p = 0.5439, interaction: p = 0.7781). **B.** Duration for which mice remained on the device during the **rotarod test** (2 ways ANOVA: CRF/SHAM: p = 0.0009, days: p = 0.4850, interaction: p = 0.1461). **C. Prehensile scores** (2 ways ANOVA: CRF/SHAM: p = 0.0008, days: p = 0.4648, interaction: p = 0.3226). **D. Forelimbs muscular strength** (2 ways ANOVA: CRF/SHAM: p = 0.0103, days: p = 0.8870, interaction: p = 0.6217).). Results are expressed as mean ± SEM. *: p<0.05 D1 or D2 *versus* D-1 within each group; $: p<0.05 CRF *versus* SHAM mice

CONCLUSIONS

The present model appears to be suitable to investigate CRF-associated neurological disorders in mice. We showed that **CRF increases stroke-induced brain ischemia** and **amplifies cortical, infracortical and hippocampal loss of neurons** as compared to SHAM operated mice. CRF worsens stroke-induced motor and behavioral impairments, by **decreasing mice muscular strengh**, **motor coordination** and **physical resistance to tiredness** as compared to SHAM operated mice. Supplemental experiments are currently ongoing in order to identify the molecular mechanisms by which CRF worsens stroke-induced alteration of brain tissue integrity. The potential roles of specific and non-specific uremic toxicity in the genesis of these neurological abnormalities will soon be investigated.

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