



# The Immunomodulating Effects of Morphine Dependence and Withdrawal in Rat Lung, Liver, Spleen and Blood

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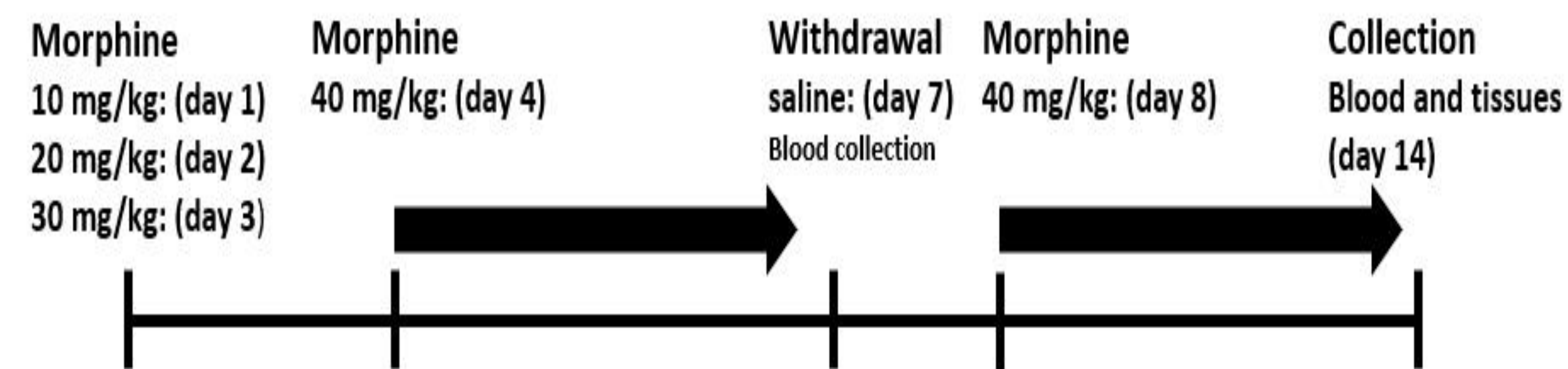
## Introduction

The opioid crisis continues to pose a significant health burden, as evidenced by increased opioid overdose reports during the COVID-19 pandemic and the years following. Opioids can modulate the immune response following acute and chronic administration; however, the effect of opioid withdrawal on immune function is limited, with variable results.

## Objective

Objectives of this experiment were to 1) measure the effects of morphine withdrawal on immune function, using IFN- $\gamma$  and TNF- $\alpha$ , 2) measure the change in expression of IFN- $\gamma$  in varying tissues, and 3) measure the change in expression of TNF- $\alpha$  in varying tissues.

## Methods



Morphine N=5  
Saline N=5

Figure 1. Opioid dependence and withdrawal. Escalating doses of morphine (10-40mg/kg) or saline (control group) were administered twice daily for three days and maintained by twice-daily injections of 40mg/kg morphine.

Enzyme-linked immunosorbent assay (ELISA) was utilized to examine the immunomodulatory properties of morphine dependence and withdrawal in the lungs, liver, spleen, and blood tissues.

## Results

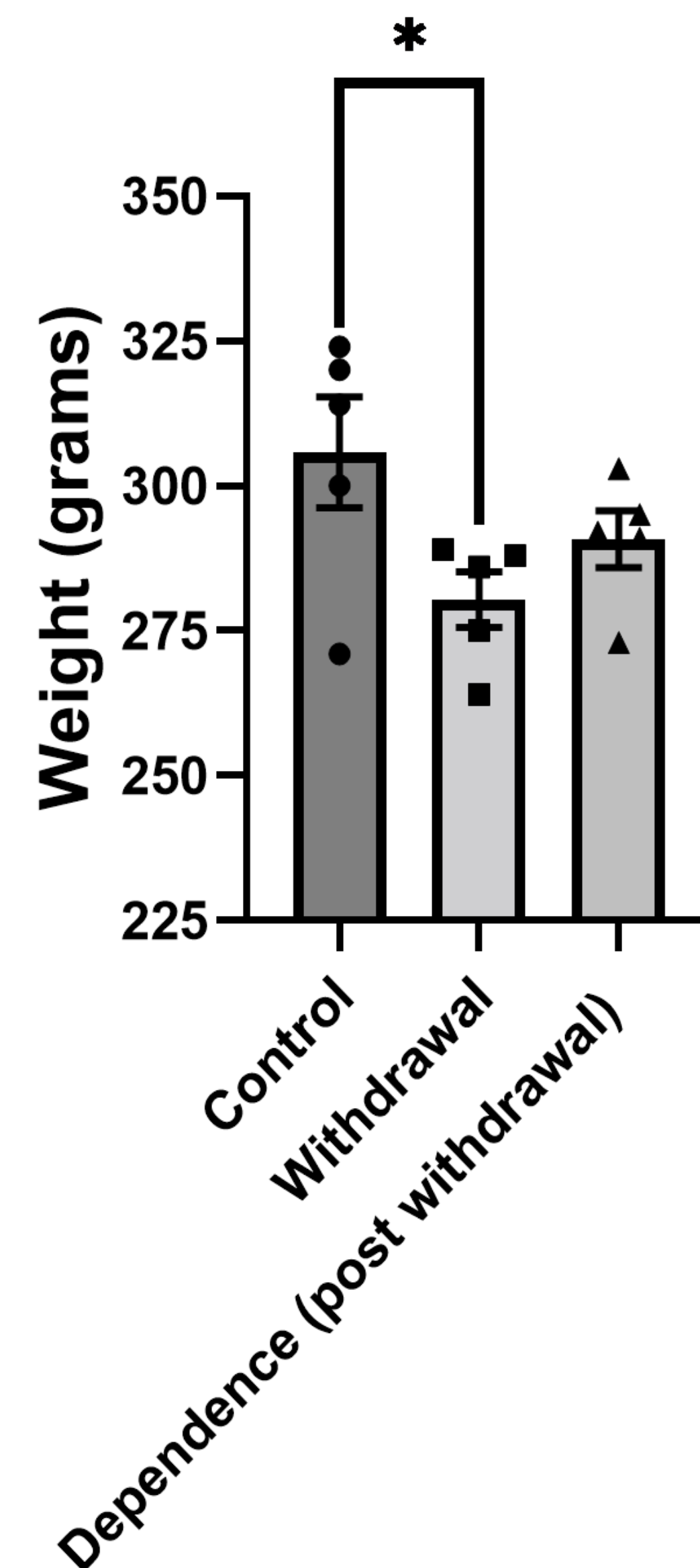


Figure 2. Weight in grams. Rat weight decreased approximately 10% in morphine-dependent and withdrawn rats. Weight returned to baseline approximately 7 days post withdrawal.

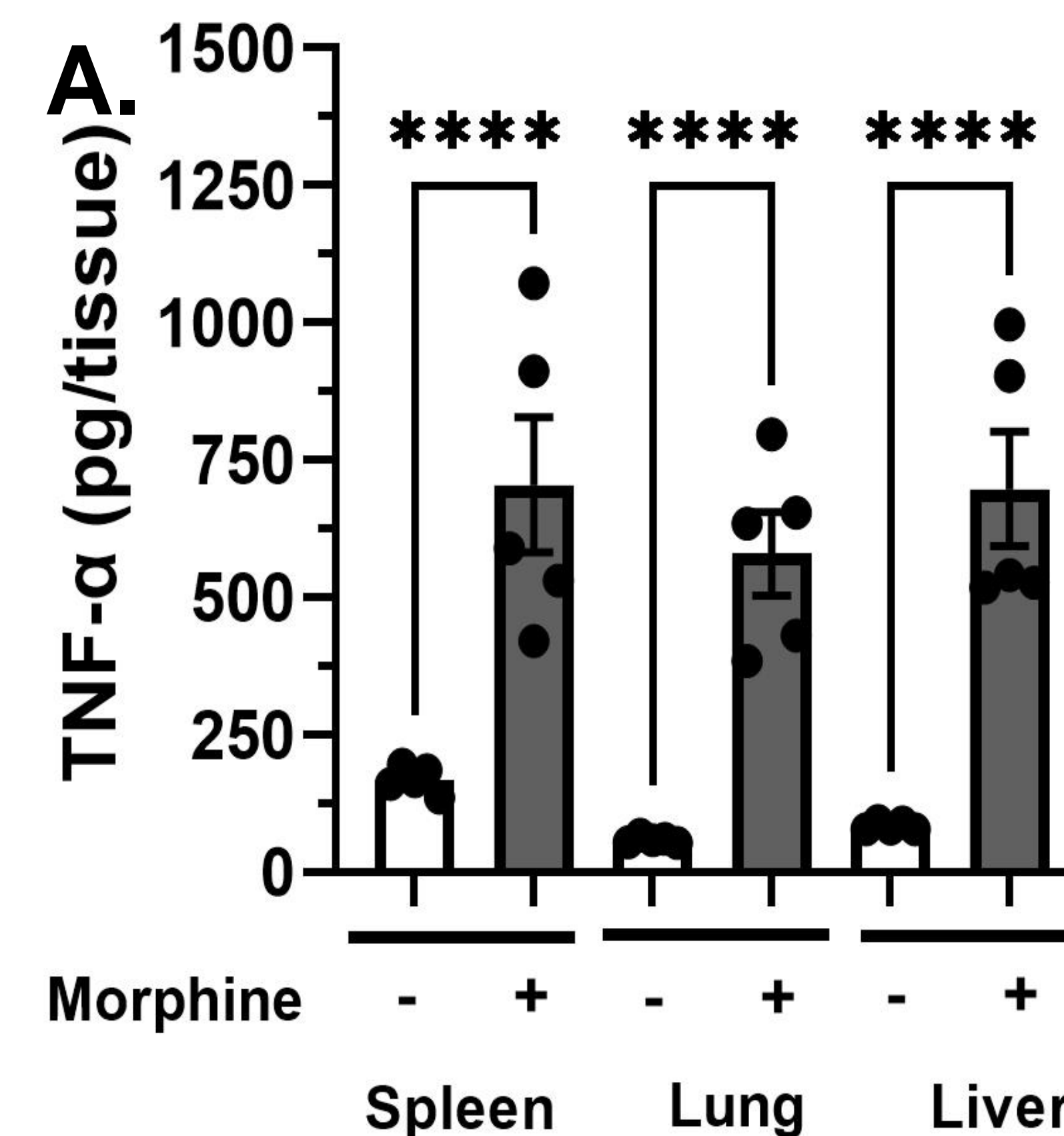


Figure 3. Tissue TNF- $\alpha$  (A) and IFN- $\gamma$  (B) levels. Tissue collected on day 14. Homogenized lysate for spleen, lung, or liver were tested with ELISA

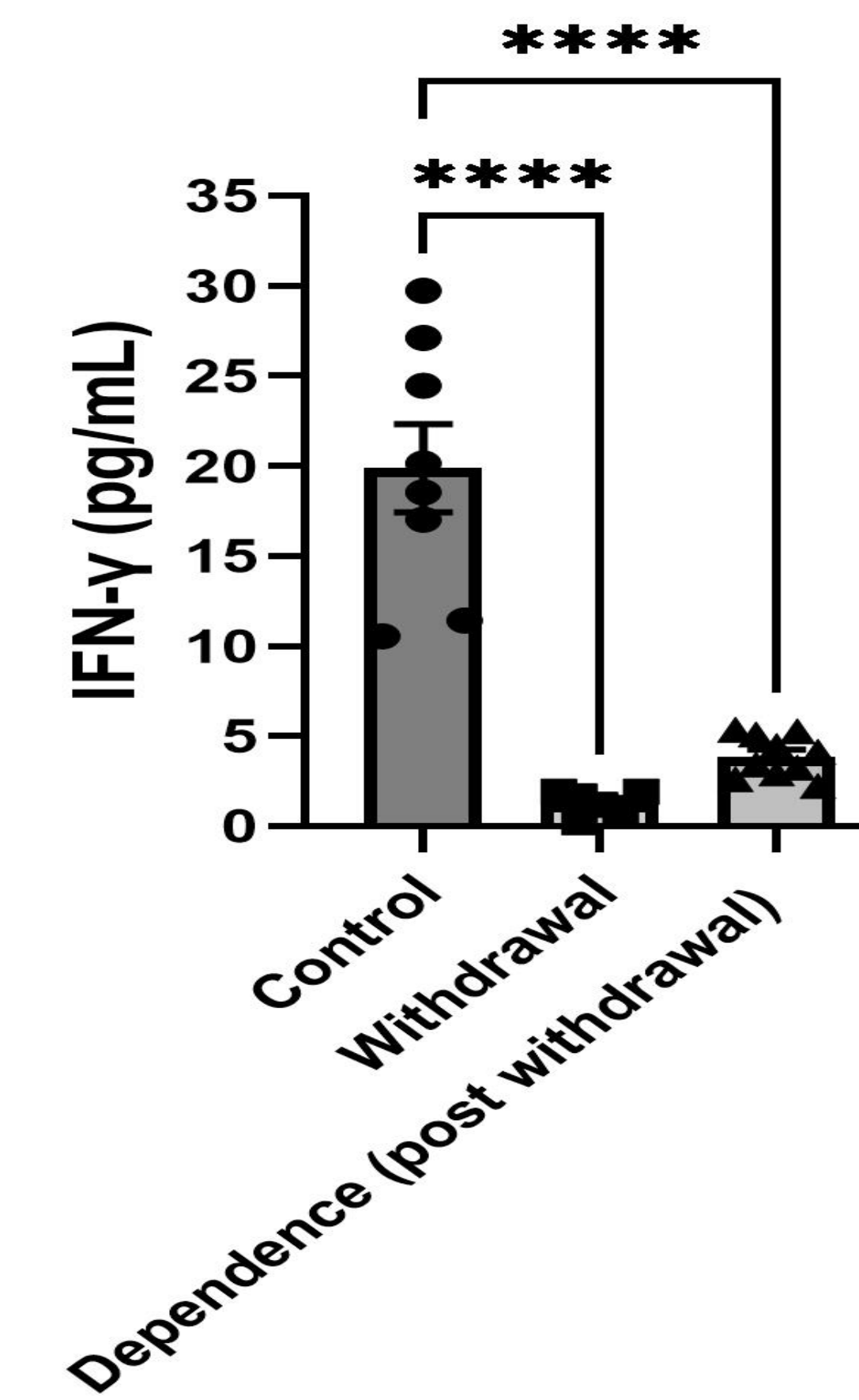
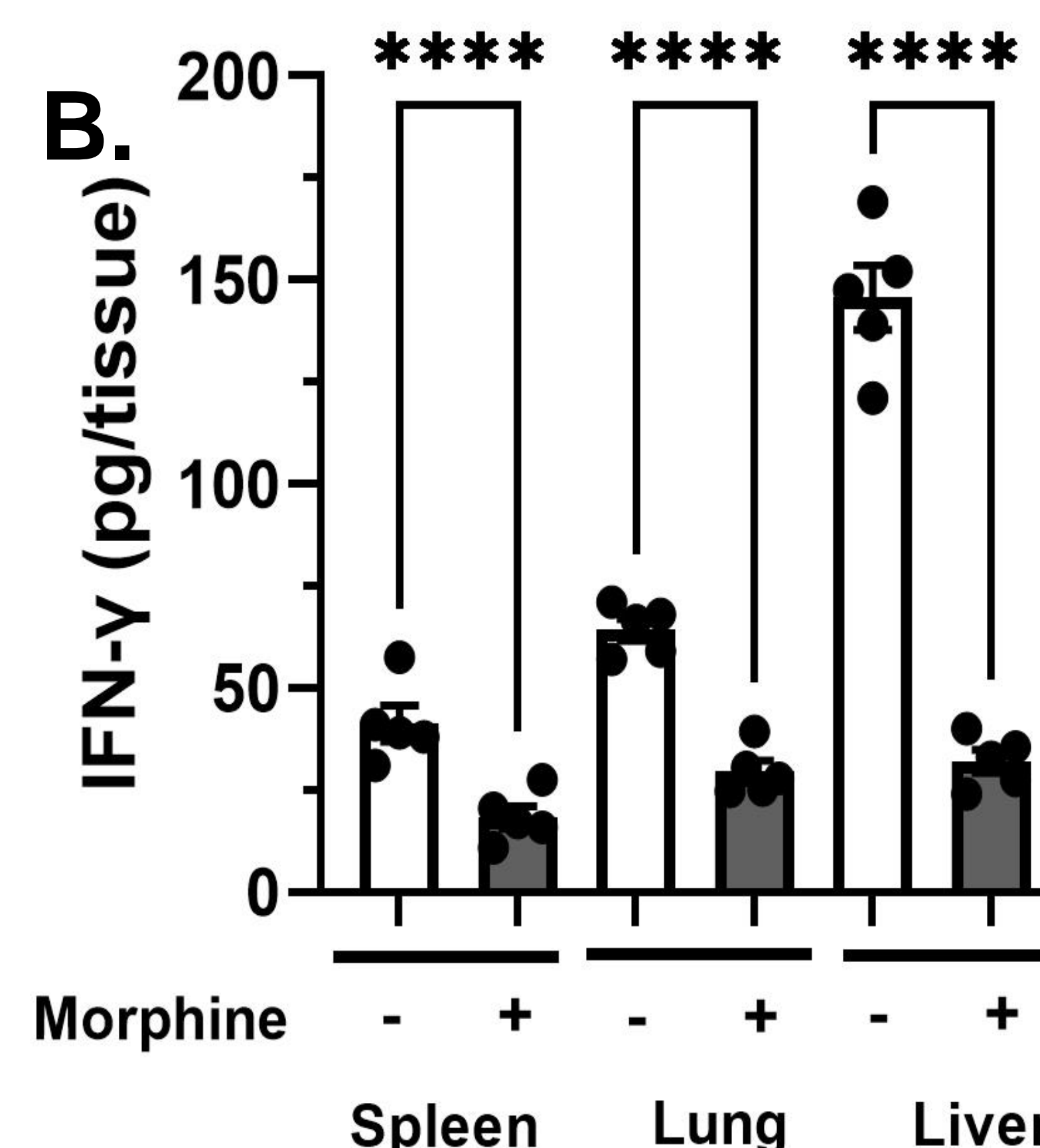


Figure 4. Blood IFN- $\gamma$  levels. Blood collected during morphine dependent and withdrawn state. Control indicates saline administered rats.

## Significant findings and Conclusion

Morphine dose and regimen established dependence; withdrawal was observed by weight loss and somatic signs.

TNF- $\alpha$  levels in spleen, lung, and liver remained elevated above control at day 14 (7 days post withdrawal).

IFN- $\gamma$  levels in blood and spleen, lung, and liver remained decreased compared to control at day 14 (7 days post withdrawal).

Withdrawal may induce a T-cell related immune dysfunction

## Future Directions

Test long term opioid use ( $\geq 30$  days) and the effects on immunomodulation and cellular function.

Test cyclic withdrawal events and the effects on immune profile and cellular function.

Expand cytokine analytes and include IgM and IgG profile.

## Acknowledgments

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