Positive Reinforcement Training Reduces Stress in SIV-Infected Macaque Models of HIV Infection

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Selena M. Guerrero-Martin[1, 2, 3], Bess W. Carlson[1], Samuel A. Brill[1, 3], Erin N. Shirk[1], Suzanne Queen[1], Leah H. Rubin[1], Melanie J. Graham[4], Lydia M. Hopper[1], Lucio Gama[1], Christine Zink[1], Joseph Mankowski[1], Janice E. Clements[1], **Kelly A. Metcalf Pate[1, 2]**

[1]Johns Hopkins School of Medicine, Baltimore, MD, [2]Massachusetts Institute of Technology, Cambridge, MA, [3]Colorado State University College of Veterinary Medicine, Fort Collins, CO, [4]IUniversity of Minnesota, Minneapolis, MN, USA

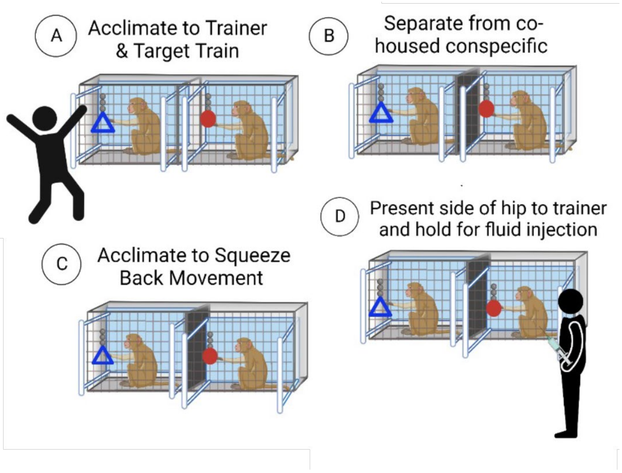
BACKGROUND

Work with SIV infected macaque models is essential to HIV pathogenesis, vaccine development and cure research. Positive reinforcement training (PRT) may be used rather than restraint or sedation to facilitate administration injectable antiretroviral therapy (ART) or obtain blood samples. In addition to these practical benefits, PRT may reduce physiologic stress in infected animals. Other means of reducing physiologic stress such as social housing affect the immune response and viral load in SIV-infected macaques.

We hypothesized that PRT would reduce physiologic stress in SIV-infected macaques, ultimately resulting in a less pronounced decline in CD4+ T cells and lower viral loads.

METHODS

- Compared untrained to PRT trained macaque subjects:
  - Juvenile male rhesus macaques (Macaca mulatta) infected IV with SIVmac251 (8 untrained vs 24 trained)
  - Juvenile male pigtailed macaques (Macaca nemestrina) dual infected IV with SIV17E/Fr and SIV delta B670 (29 untrained vs 6 trained)



- Blood and CSF collected under ketamine sedation for 3 pre-infection measurements, followed by timepoints indicated in figures, for CD4 T cell counts and viral load.
- Macaques treated with ART to suppress viral replication.
- All analyses completed with Mixed Effects Models.

- SIV infection is stressful.
- Providing macaques with control over their environment through positive reinforcement training buffers that stress.
- Positive reinforcement training affects the course of infection, including CD4 T cell counts & viral load, in some animals.

RESULTS

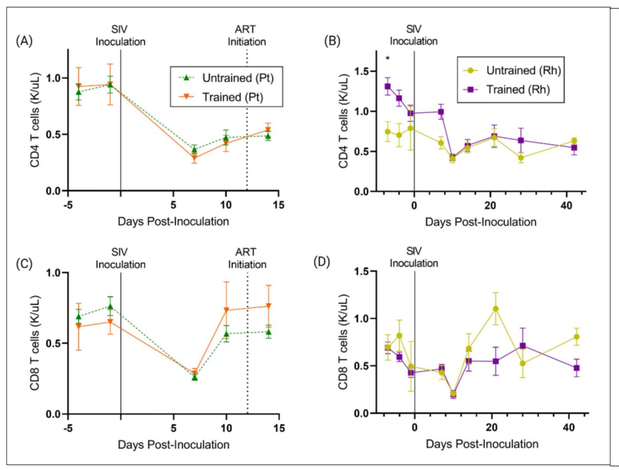


Figure 1: CD4 (A & B) and CD8 (C & D) T cell counts in pigtailed (A & C) and rhesus (B & D) macaques as measured by flow cytometry normalized to CBC.

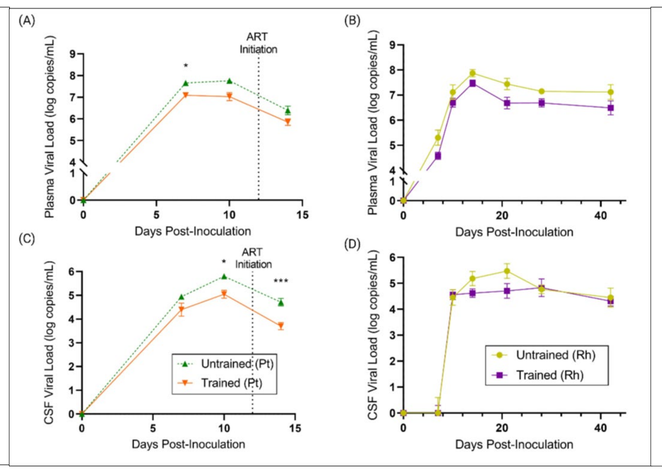


Figure 2: Plasma (A & B) and cerebral spinal fluid (C & D) viral loads throughout acute infection in pigtailed (A, C) and rhesus (B, D) macaques, measured by qRT-PCR.

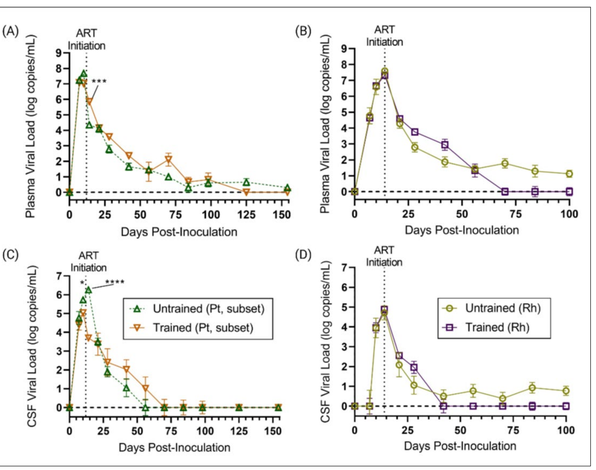


Figure 3: Plasma (A & B) and cerebral spinal fluid (C & D) viral loads throughout infection in pigtailed (A, C) and rhesus (B, D) macaques pre- & post-ART.

CONCLUSIONS

PRT buffers the physiologic stress associated with SIV infection in macaques, as evidenced by a less pronounced cortisol response to infection. Further work needs to be completed to understand the extent to which PRT may affect viral load and immune parameters, and caution should be exercised when comparing data from animals that have engaged in PRT compared to untrained macaques.

For further information on this work, contact Kelly Metcalf Pate: kpate@mit.edu

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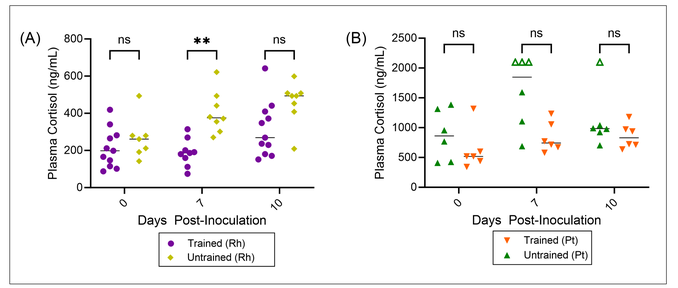


Figure 4: Plasma cortisol level, as measured by ELISA.