

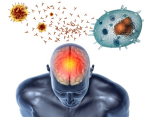


## Teach the T cells: How Learning Can Shape Immunity

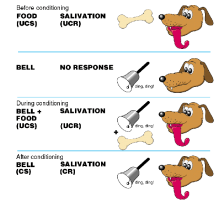
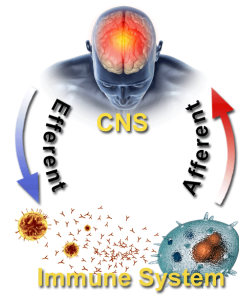
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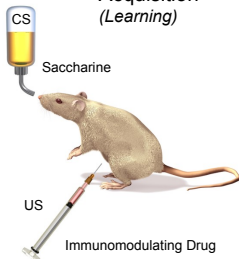


## Learned Placebo Effects on Immune Functions

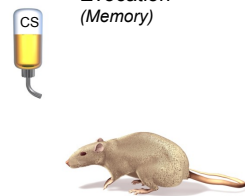


## Conditioned Taste Aversion

### Acquisition (Learning)



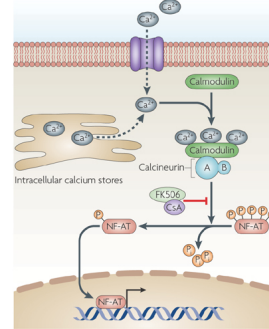
### Evocation (Memory)



**Conditioned Response:**  
• Taste Aversion  
• Immunological Changes



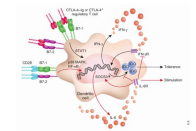
## Model of Action of Cyclosporine A



### Cyclosporine A (CsA)

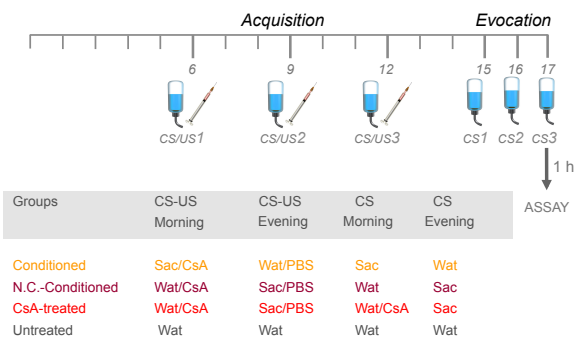
Calcineurin activity ↓  
IL-2 ↓

→ No T cell proliferation

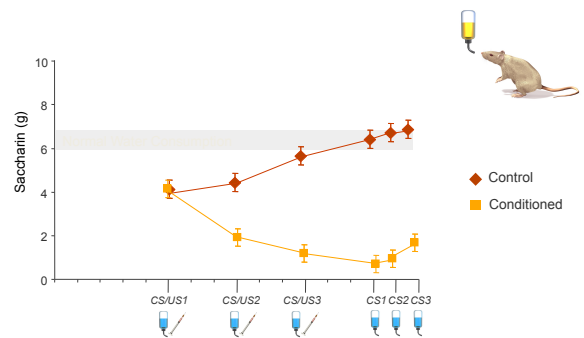


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## Conditioning Protocol

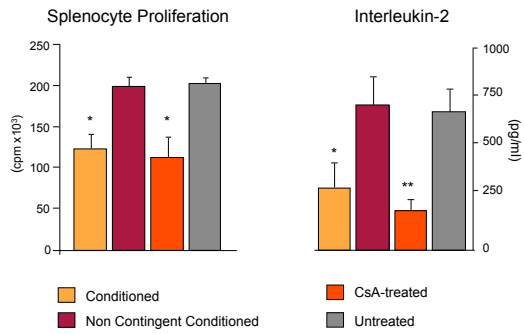


## Behaviorally Conditioned Response Taste Aversion





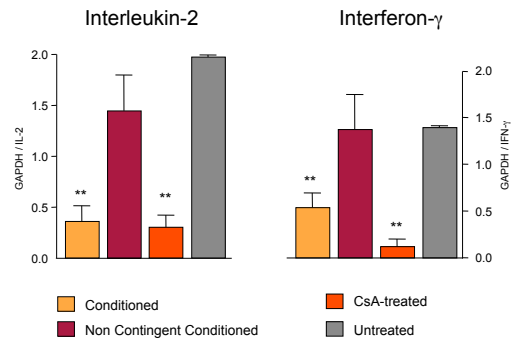
### Teach the T cells Splenocyte Proliferation, Cytokine Production



Exton et al. 2002, J Neuroimmunol



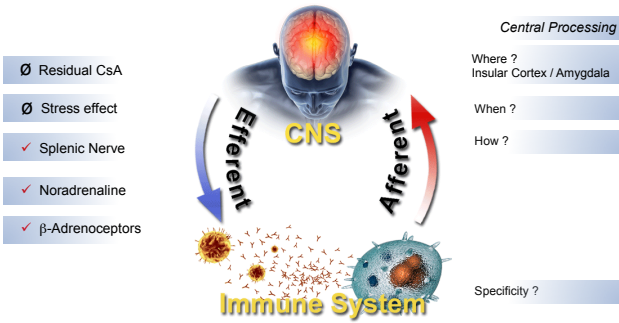
### Behaviorally Conditioned Response Cytokine mRNA-Expression



Exton et al. 2002, J Neuroimmunol



### Teach the T cells Mechanisms

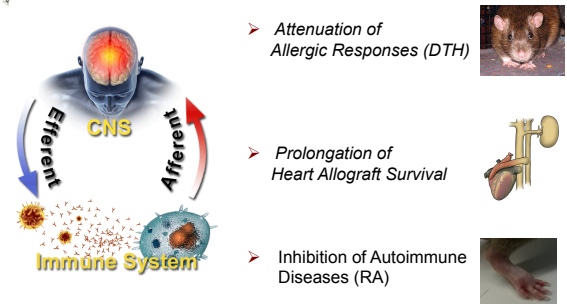


Exton et al. 1998, J Neuroimmunol  
von Hörsten et al. 1998, J Neuroimmunol  
Exton et al. 1999, Ann J Physiol  
Exton et al. 2002, J Neuroimmunol  
Pacheco-Lopez et al. 2009, FASEB J

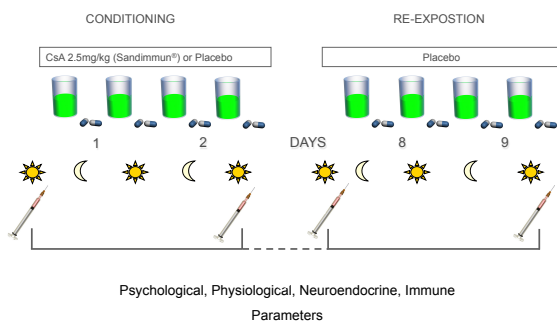
Pacheco-Lopez et al. 2005, J Neurosci  
Doeniers et al. 2011, Proc Biol Sci  
Pacheco-Lopez et al. 2012, Int J Neuropsychopharmacol  
Pacheco-Lopez et al. 2009, FASEB J  
Reither et al. 2010, Brain Behav Immun



### Teach the T cells Clinical Relevance



### Teach the T Cells: Human Studies Study Design



Goebel et al. 2002, FASEB J

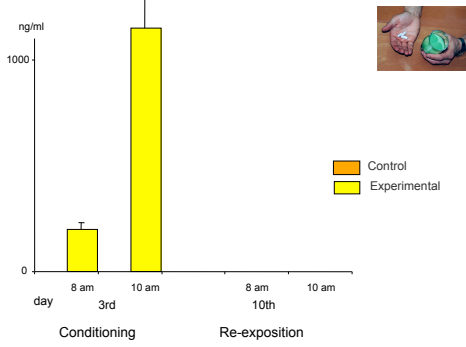


### Teach the T Cells: Human Studies Study Design





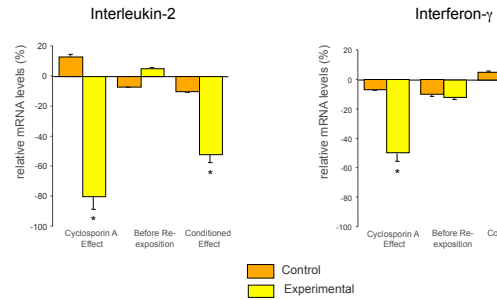
### Behaviorally Conditioned Immunosuppression in Humans Cyclosporine A Levels



Goebel et al. 2002, FASEB J



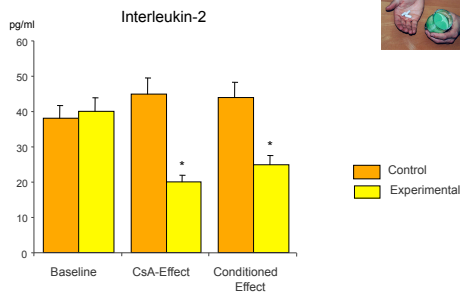
### Teach the T Cells: Human Studies Cytokine mRNA Expression



Goebel et al. 2002, FASEB J



### Behaviorally Conditioned Immunosuppression in Humans Interleukin-2 Production



Goebel et al. 2002, FASEB J



### Teach the T Cells: Human Studies

Rodents

Humans

Open Questions ?

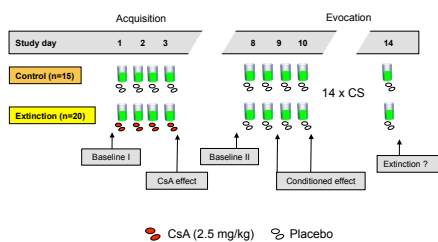
- How much „conditioning is needed“ ? ✓ ✗
- Can immune responses be induced by mere **expectation** ?
- Predict **Responder** vs. **Non-Responder** of learned immune response ✓
- The learned immune response can be **re-produced** ✓
- Prevent extinction of learned immunosuppression ?

Wirth et al. 2011, Brain Behav Immun  
Albring et al. 2012, Plos One  
Ober et al. 2012, Clin Pharmacol Ther  
Albring et al. 2014, Clin Pharmacol Ther



### Teach the T Cells: Human Studies Preventing Extinction

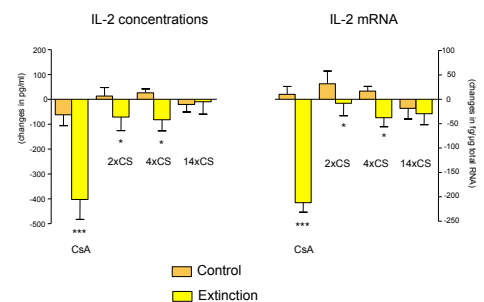
➔ When does extinction of the learned immunosuppression occurs ?



Albring et al. 2014, Clin Pharmacol Ther



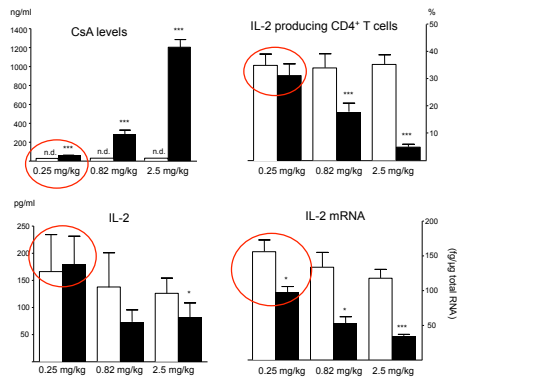
### Teach the T Cells: Human Studies Preventing Extinction



Albring et al. 2014, Clin Pharmacol Ther



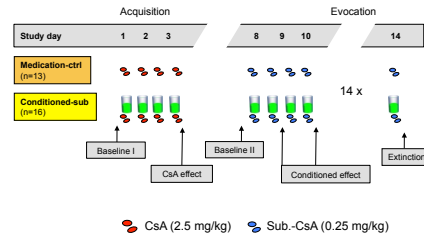
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Albring et al. 2014, Clin Pharmacol Ther



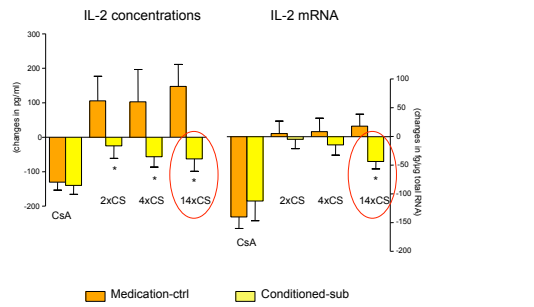
### Teach the T Cells: Human Studies Preventing Extinction



Albring et al. 2014, Clin Pharmacol Ther



### Teach the T Cells: Human Studies Preventing Extinction



Albring et al. 2014, Clin Pharmacol Ther



### Teach the T Cells

#### Implementing Learning Protocols as Supportive Therapy in Immunopharmacological Treatment Strategies

- Reducing the dose of medication required
- Limiting unwanted drug side effects
- Maximizing therapeutic effects

