

# The neuroscience of anxiety disorders

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# A clinical vignette

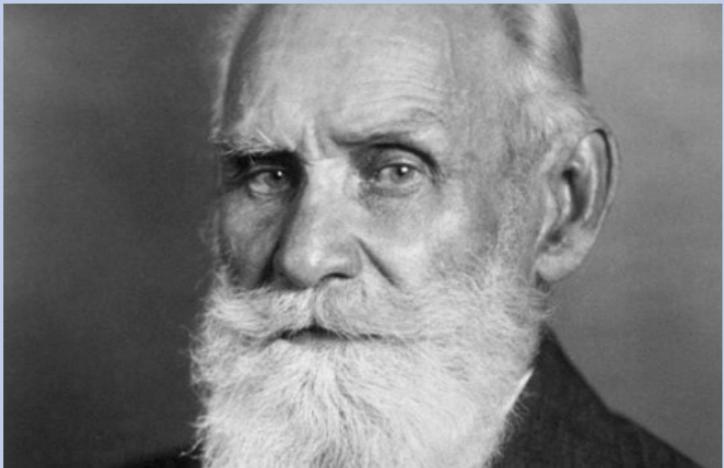


Credit: <http://www.x-rayscreener.co.uk>

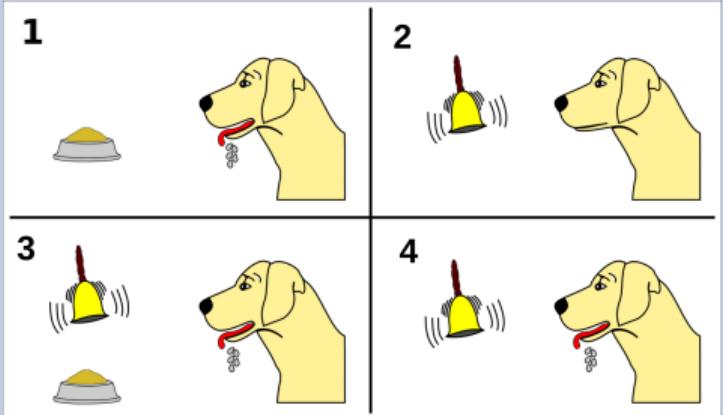
- USA combat veteran with PTSD
- Injured by explosion while on street patrol in Iraq
- Acquired fear reaction to a trash pile used to hide an improvised explosive device
- Trash piles along the street now trigger fear reaction

Lissek and Van Meurs 2015

# Learning by association

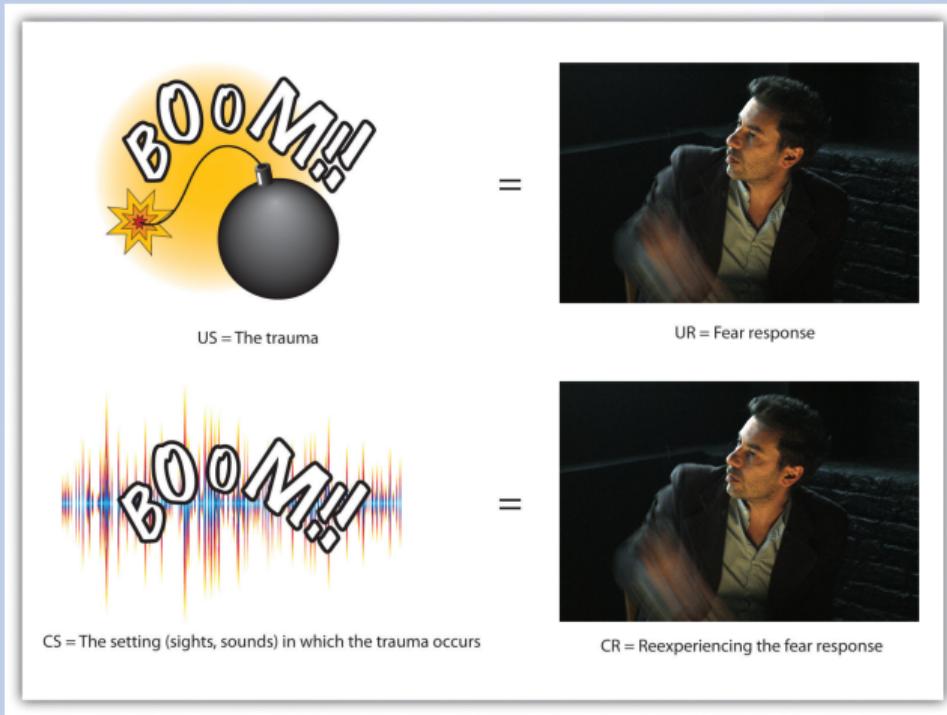


Ivan Pavlov (1849 - 1936)



Credit: <https://www.psychestudy.com>

# Pavlovian fear conditioning



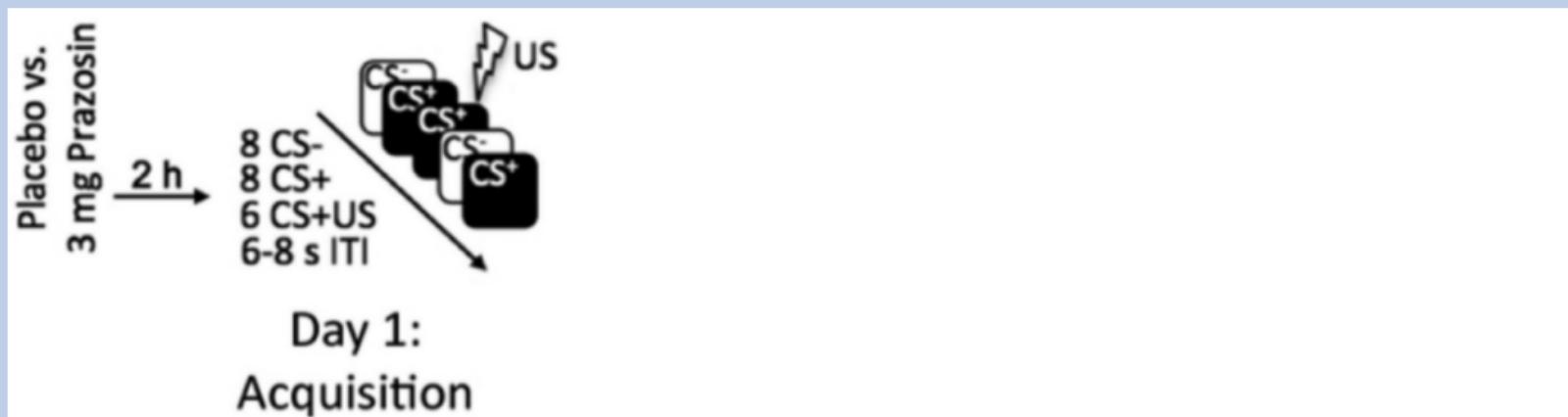
Credit: <http://open.lib.umn.edu>



# Objectives

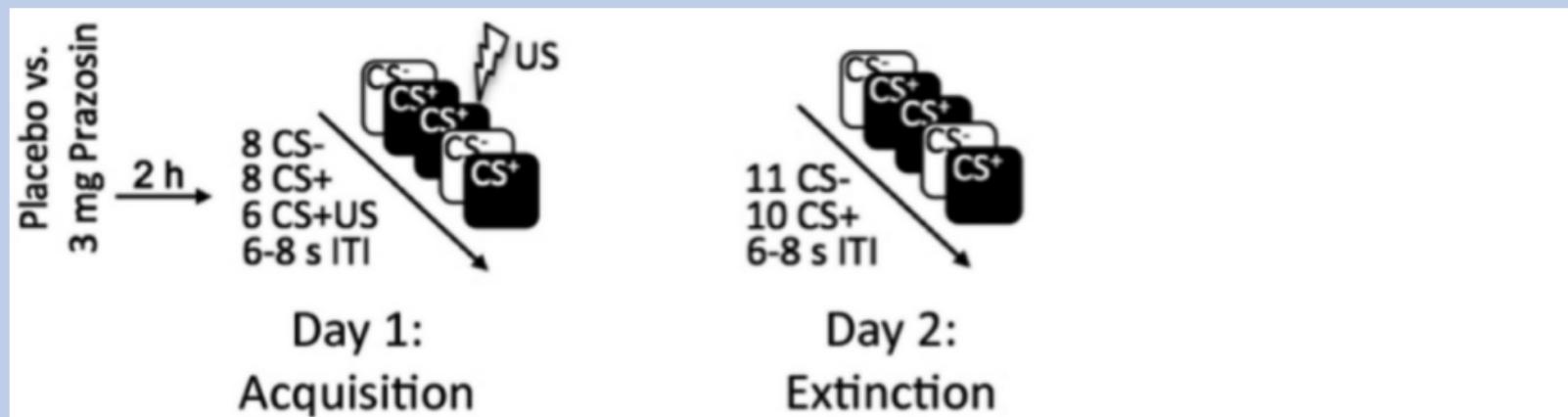
1. Give an example of Pavlovian conditioning that is relevant for anxiety disorders.
2. Name the key brain areas implicated in fear conditioning.
3. Explain what prediction error means and where in the brain it is computed.

# A mechanism we can study in the lab



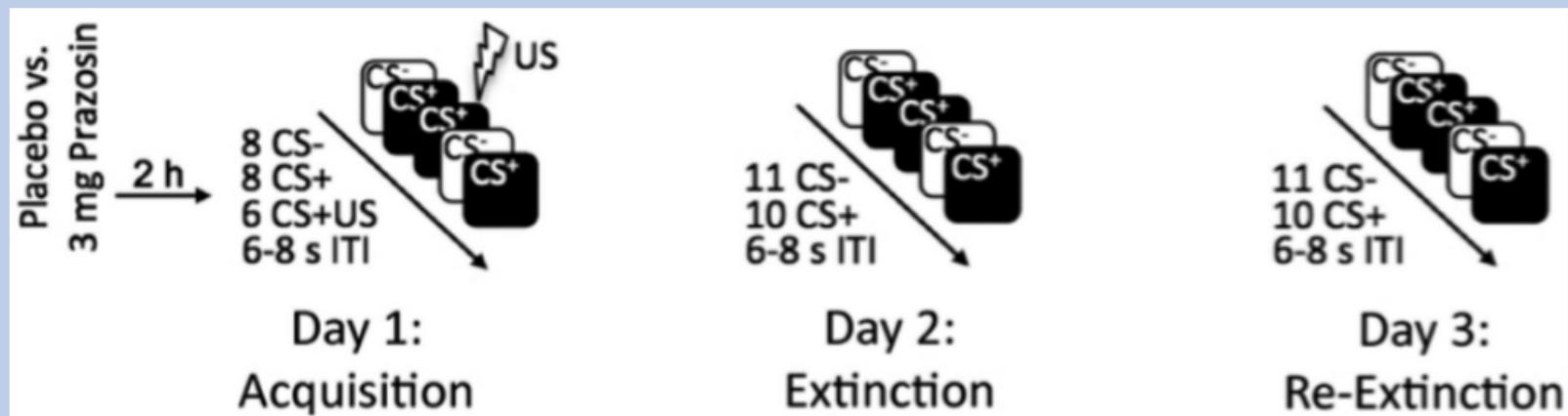
Homan et al. 2017, Learn Mem

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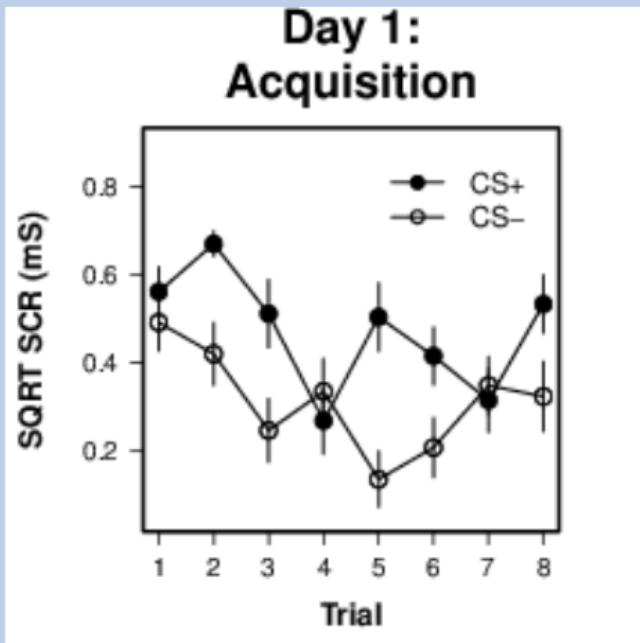
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Homan et al. 2017, Learn Mem

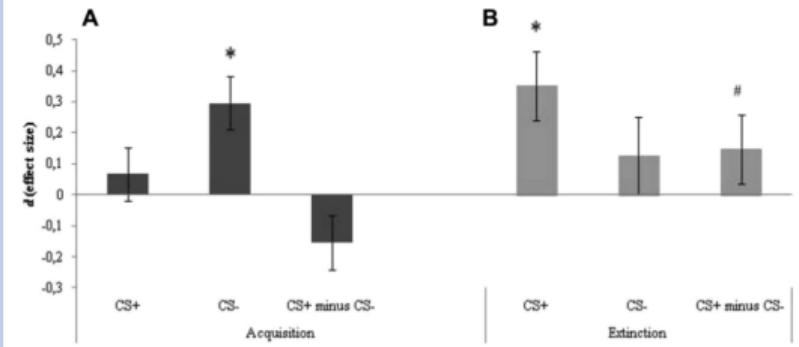
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Homan et al. 2017, Learn Mem

# Fear conditioning and extinction in anxiety disorders

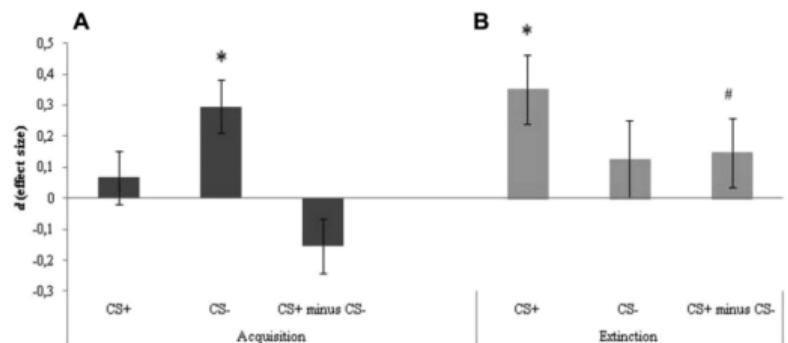
Review: Updated Meta-Analysis of Fear Conditioning in Anxiety Disorders



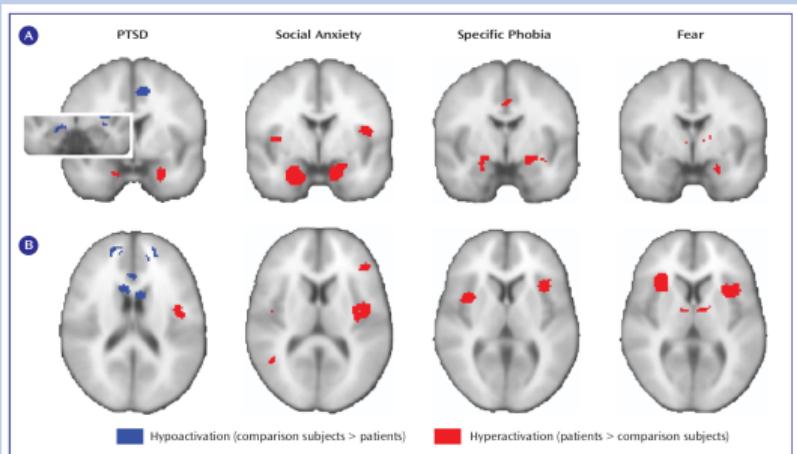
Duits et al. 2015, Depress Anxiety

# Fear conditioning and extinction in anxiety disorders

*Review: Updated Meta-Analysis of Fear Conditioning in Anxiety Disorders*



Duits et al. 2015, *Depress Anxiety*



Ektin and Wager 2007, *Am J Psychiatry*



# Why anxiety matters

- About 12% of people are affected by an anxiety disorder in a given year
- 5% - 30% are affected at some point in their life
- Twice as often in females as males
- Generally begin before the age of 25
- Most common: specific phobia and social anxiety disorder

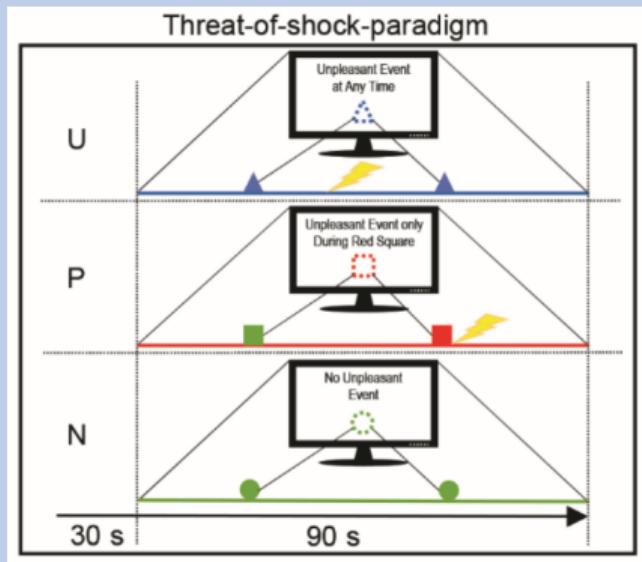


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# Fear vs. anxiety

- Fear: reaction to something specific (has an object)
- Anxiety: more generalized

# Modeling fear vs. anxiety



Schmitz & Grillon 2012, Nat Protoc  
Grieder\*, Homan\* et al., under review

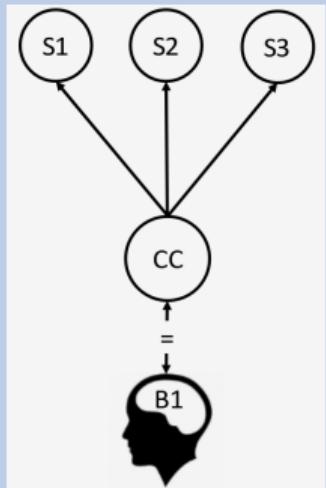


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# A fragile balance

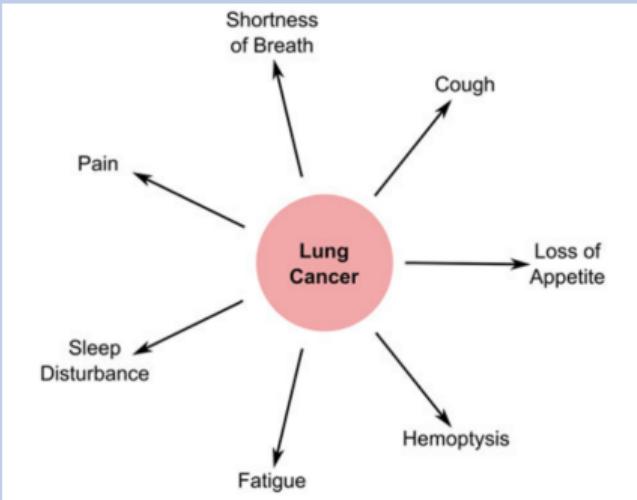


# A common way to think about anxiety disorders



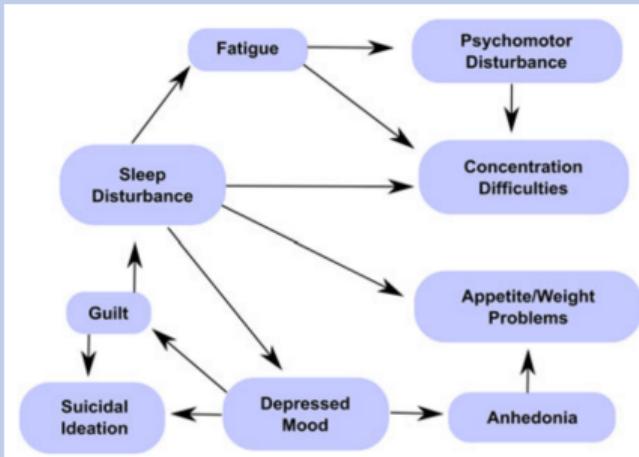
Borsboom et al. 2018, Behav Brain Sci

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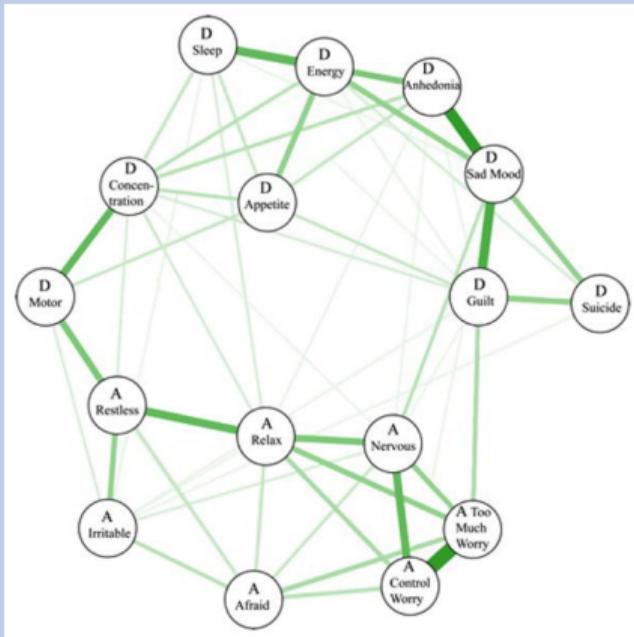
Guloksuz et al. 2017, Psychol Med

# But do we really need a hidden cause?



Guloksuz et al. 2017, Psychol Med

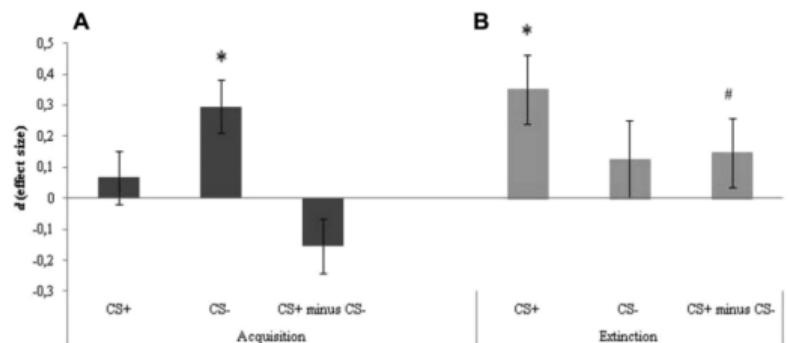
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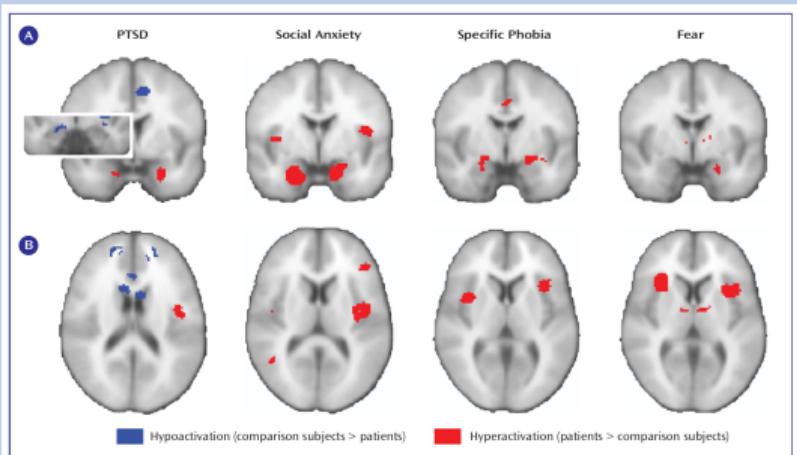
Beard et al. 2016, Psychol Med

# Fear conditioning and extinction in anxiety disorders

*Review: Updated Meta-Analysis of Fear Conditioning in Anxiety Disorders*

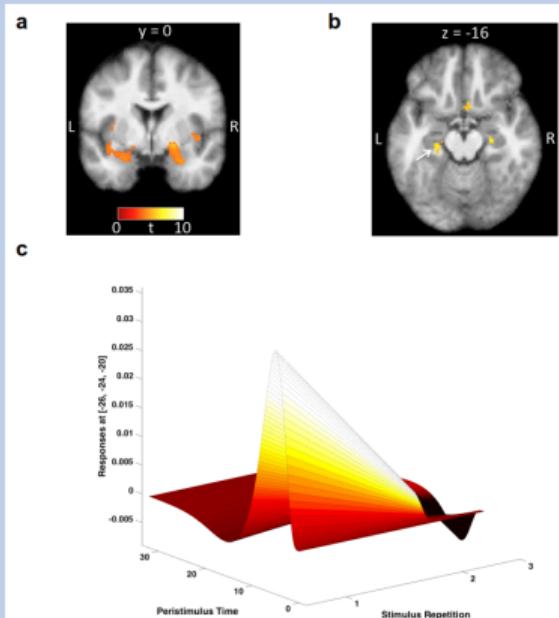


Duits et al. 2015, *Depress Anxiety*



Ektin and Wager 2007, *Am J Psychiatry*

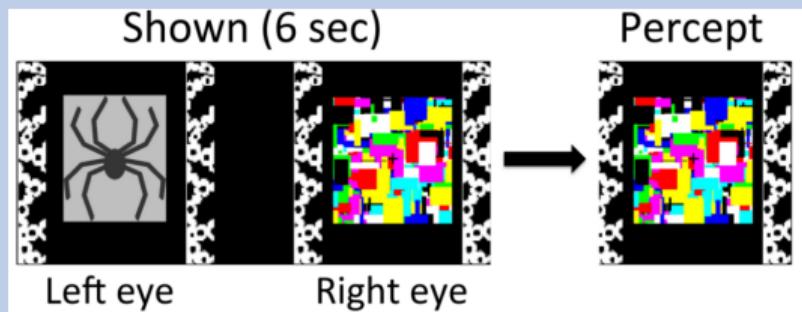
# A central role for the amygdala



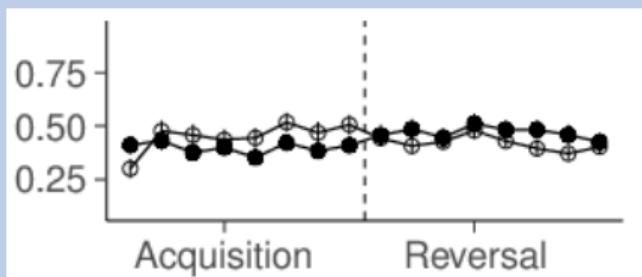
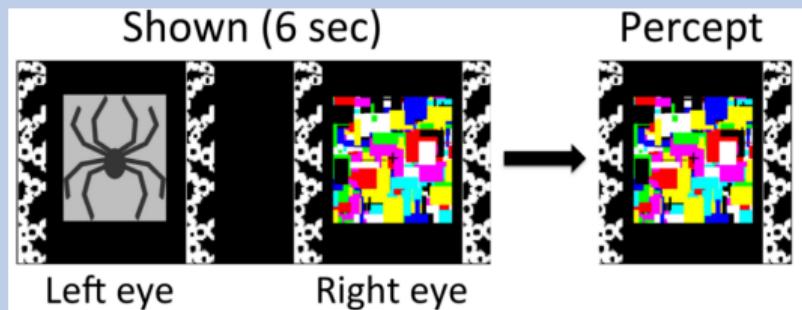
- Activates in response to aversive stimuli
- Is the neural correlate of the conditioned response
- Activates even without conscious awareness of the stimulus

Homan et al. 2017, Neurobiol Learn Mem

# Fear conditioning without conscious awareness

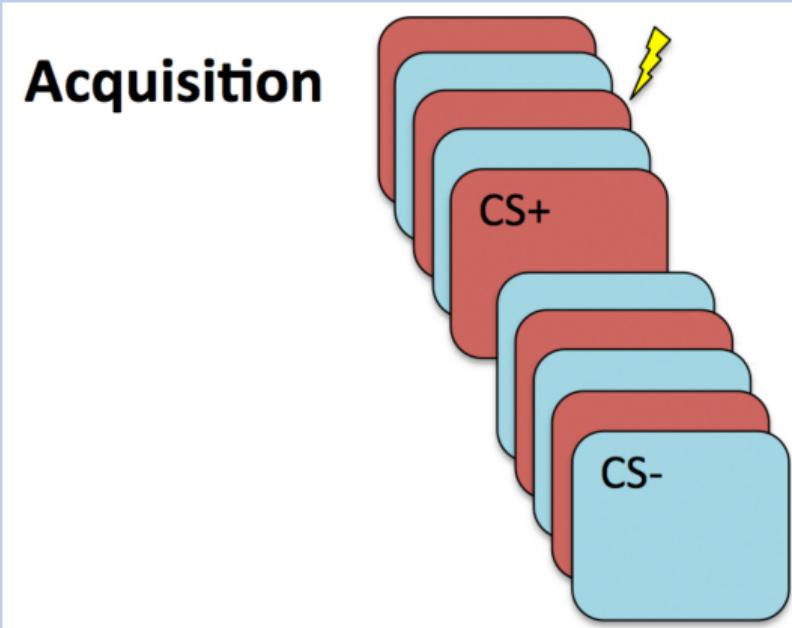


# Fear conditioning without conscious awareness



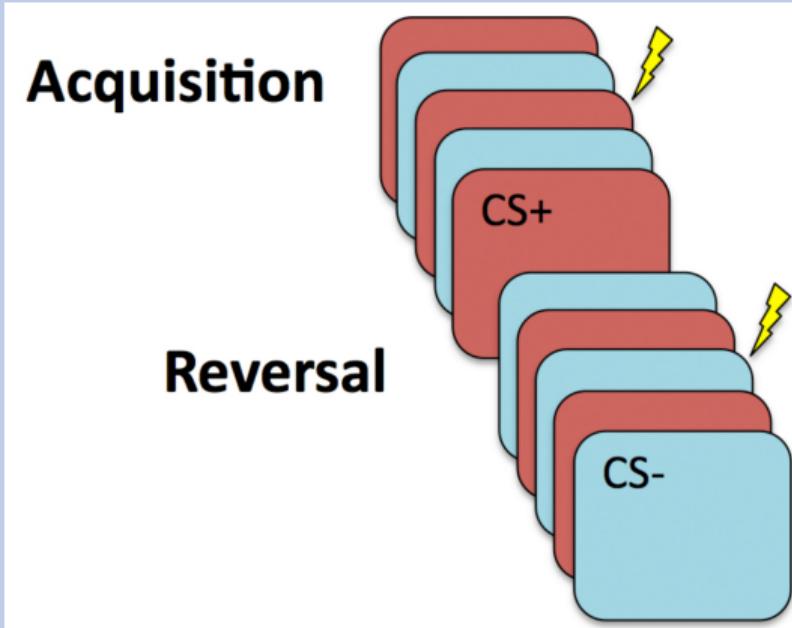
Homan et al. 2018, bioRxiv

# Beyond fear conditioning: reversal learning



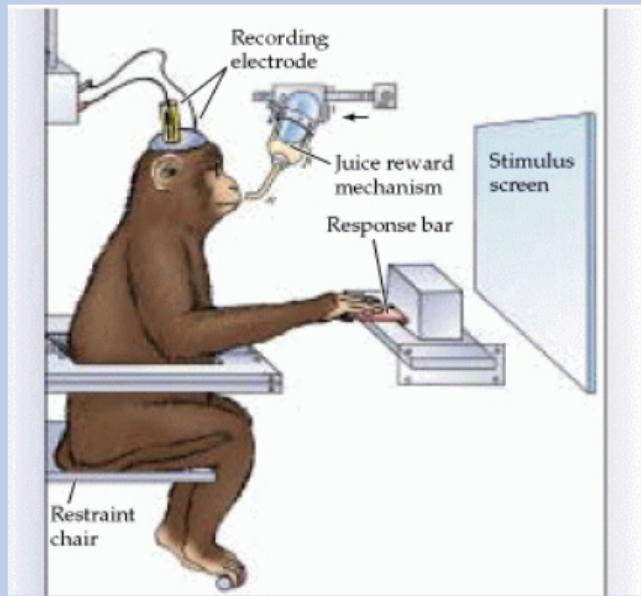
Homan et al. 2019, Nat Neurosci

# Beyond fear conditioning: reversal learning

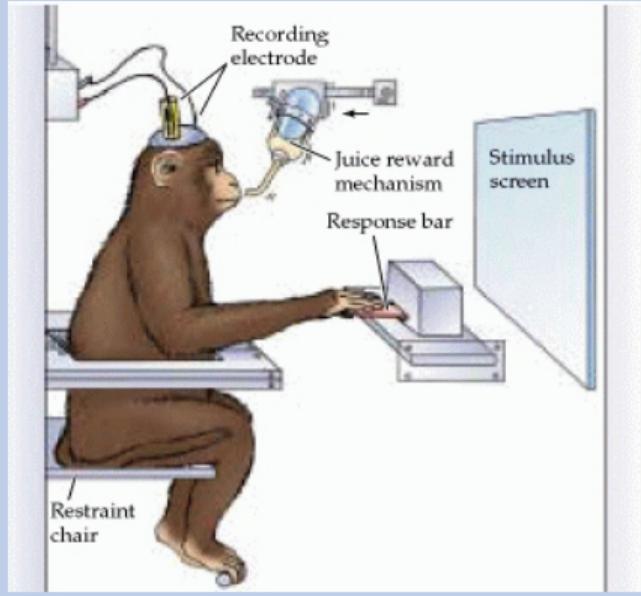


Homan et al. 2019, Nat Neurosci

# Dopamine and prediction error



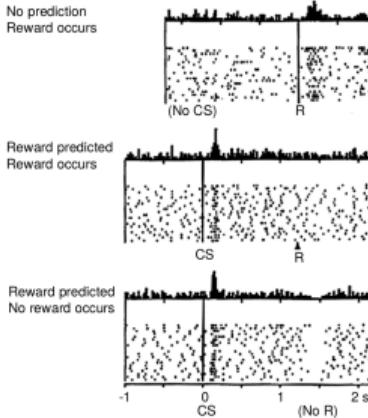
# Dopamine and prediction error



## A Neural Substrate of Prediction and Reward

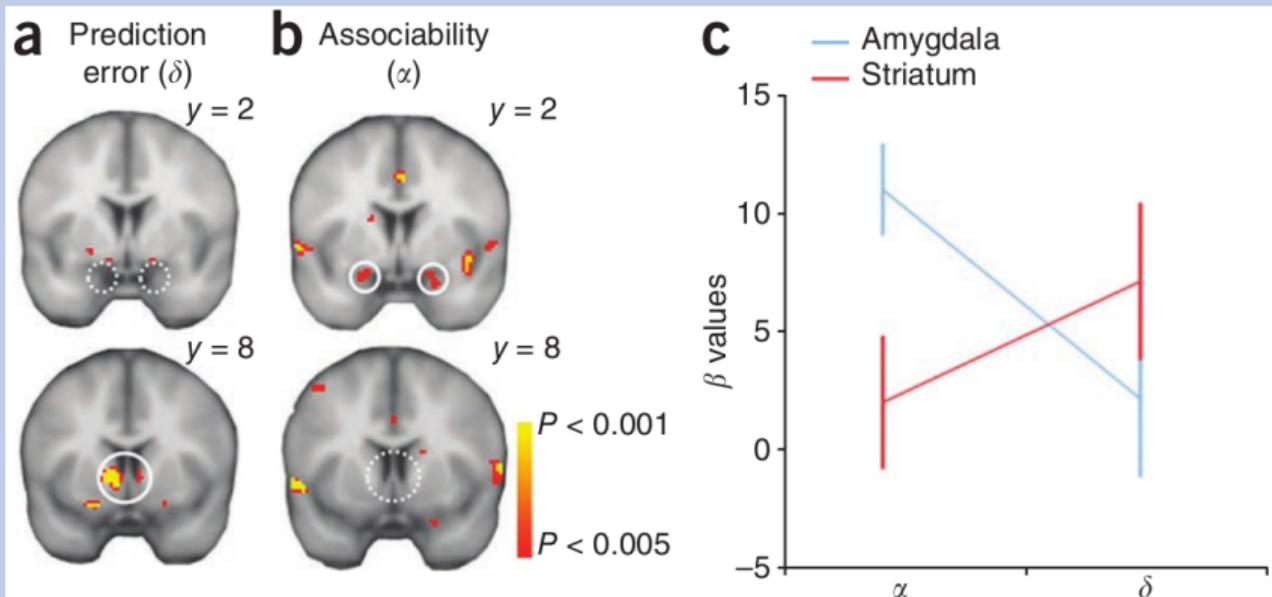
Wolfram Schultz, Peter Dayan, P. Read Montague\*

Do dopamine neurons report an error  
in the prediction of reward?



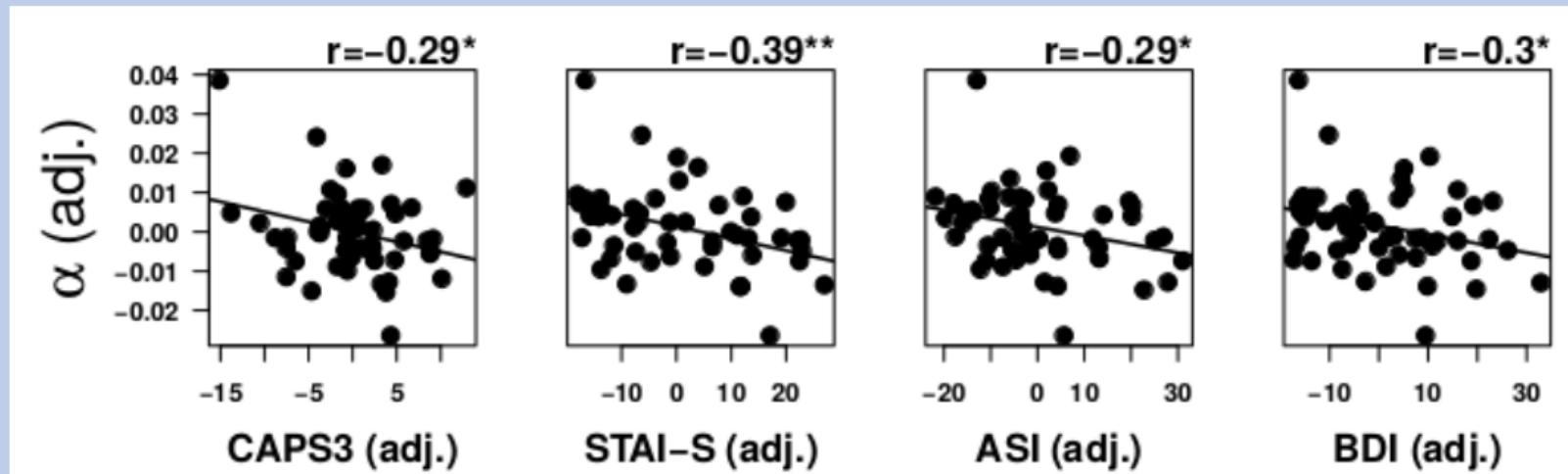
Schultz, Dayan, Montague 1997, Science

# A computational approach to fear reversal learning



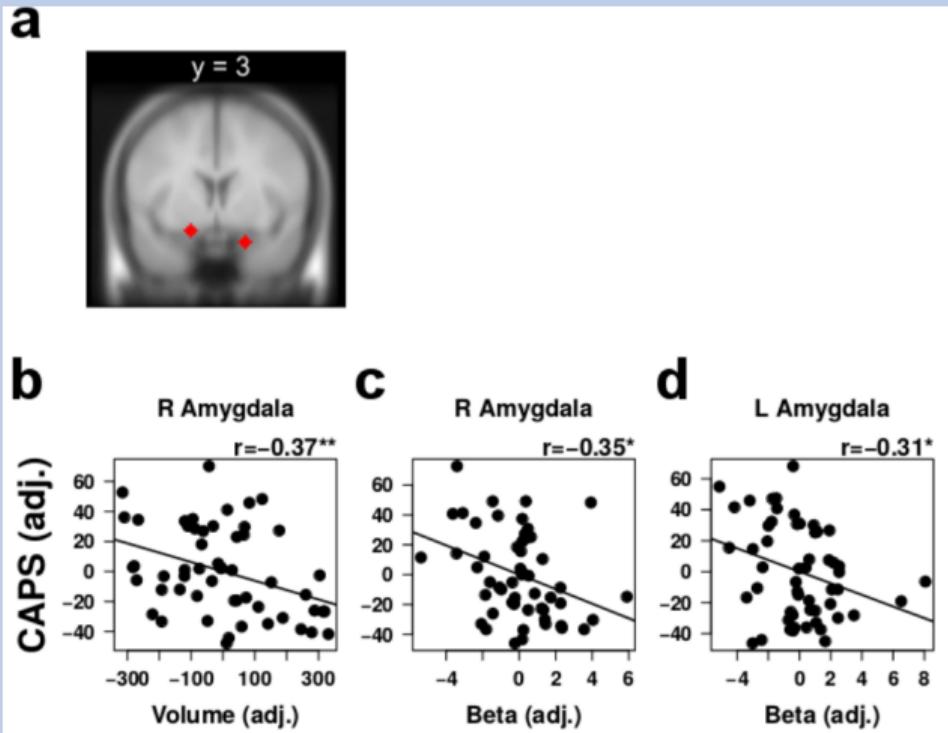
Li et al. 2011, Nat Neurosci

# Model predictions correlate with PTSD symptoms



Homan et al. 2019, Nat Neurosci

# Amygdala computations contribute to PTSD symptoms



Homan et al. 2019, Nat Neurosci



# Summary

- Fear conditioning as a crucial mechanism for anxiety disorders
- Informs treatment: exposure therapy
- Central role of amygdala: encodes expected aversive value
- Prediction error as a teaching signal computed in striatal neurons

# What does that all mean for our patient?



Credit: <http://www.x-rayscreener.co.uk>

- USA combat veteran with PTSD
- Injured by explosion while on street patrol in Iraq
- Acquired fear reaction to a trash pile used to hide an improvised explosive device
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Lissek and Van Meurs 2015



# Conclusion

- Clinical implications:
  1. Lower learning rates predicted higher numbing/depression symptoms
  2. May suggest that depression should be treated before extinction therapy

# Acknowledgments

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