

**How Neuroscience Can Inform
Prevention:**
Development and Anxiety

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NIMH
National Institute
of Mental Health

Outline

- **Selecting targets for prevention science**
- **Neuroscience and anxiety**
 - *The fear-circuit, conditioning-extinction, & development*
 - *Fear conditioning and extinction in humans*
 - *Clinical implications of reframing conceptualizations of anxiety*
- **Neuroscience & prevention**
 - *Anxiety as a “learning” disorder*
 - *Importance of early intervention/prevention*
 - *Stress inoculation*

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Selecting Targets

- Potentially reasonable targets?
 - Post-Traumatic Stress Disorder (PTSD)
 - Major Depressive Disorder (MDD)
 - Schizophrenia
 - Conduct Disorder/Violence/Aggression
 - Substance Abuse
 - Anxiety Disorders
- How to select from among possible targets?
 - Developmentally relevant and clinically important
 - Specific clinical target measured easily & reliably with high sensitivity
 - Specific behavioral manifestation amenable to experimental approaches
 - Behavioral manifestation suitable for cross-species investigation
 - Neuroscience-informed intervention feasible in at-risk children

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Any Adolescent Anxiety Disorder & Any Adult Mood/Anxiety Disorder

	Disorder as Adults?		
Disorder as Adolescents?	No	Yes	
No	390	36	426
Yes	191	62	253
	581	98	679

Pine et al. 1998, 2001, 2002

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VISUAL
CORTEX

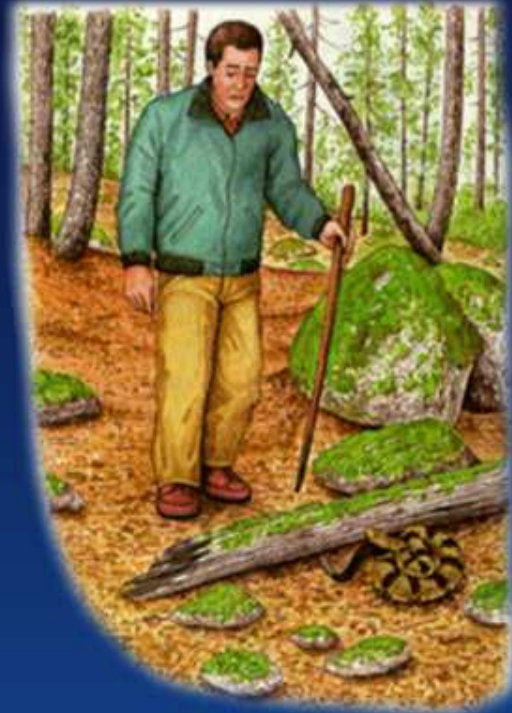
VISUAL THALAMUS

AMYGDALA



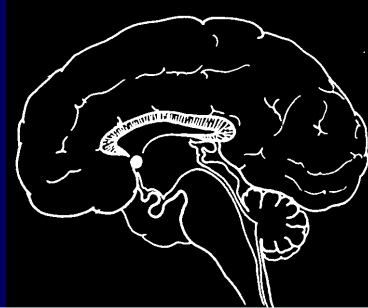
BLOOD PRESSURE

MUSCLE



LeDoux. *Sci Am.* 1994;270:50.

Timeline of Brain Development



Anxiety

Underlying circuitry is known

Early life experiences shape its function

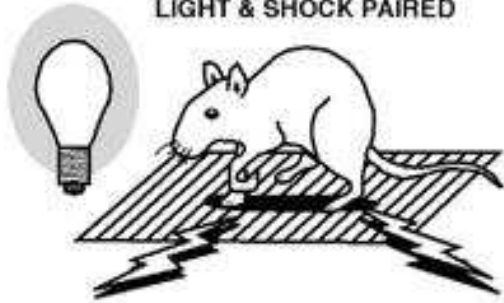
Genes operate on development

Stress-inoculation is preventative

Andersen (2003) Neuroscience and Biobehavioral Reviews 27, 3-18.

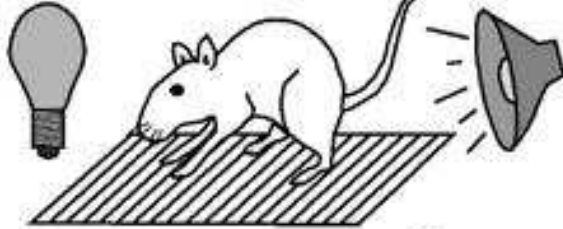
A

**CONDITIONING:
LIGHT & SHOCK PAIRED**



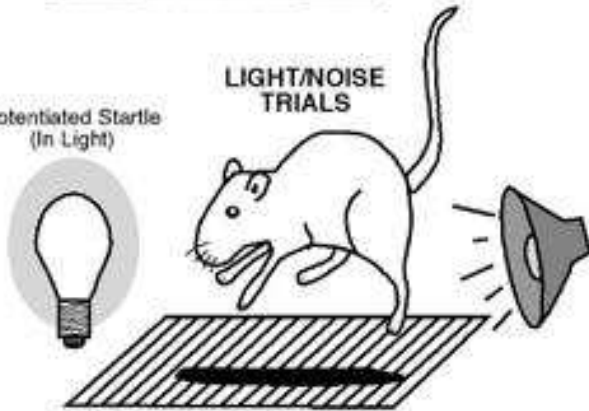
**TESTING:
NOISE-ALONE
TRIALS**

Normal Startle
(In Dark)

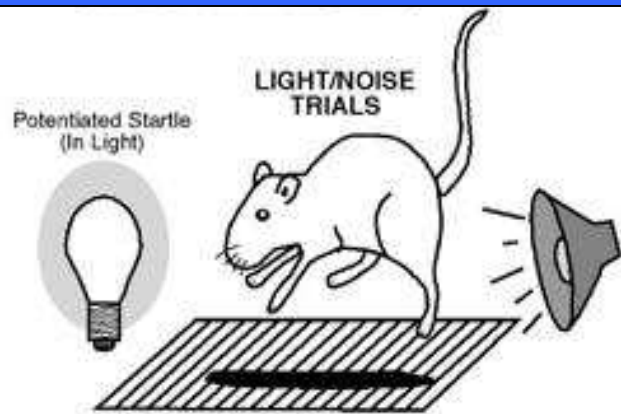


**LIGHT/NOISE
TRIALS**

Potentiated Startle
(In Light)



Ressler & Davis 2003



Extinction:

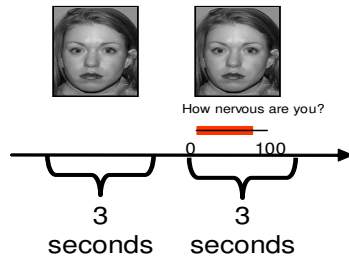
Not forgetting but new learning

Anxiety disorders as problems in new learning

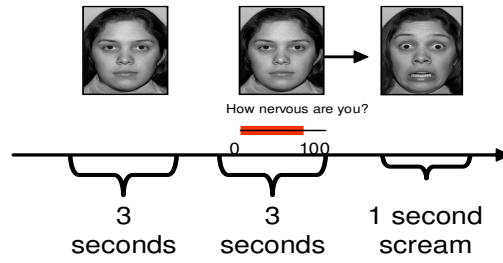
Ressler & Davis 2003

Acquisition (60 trials)

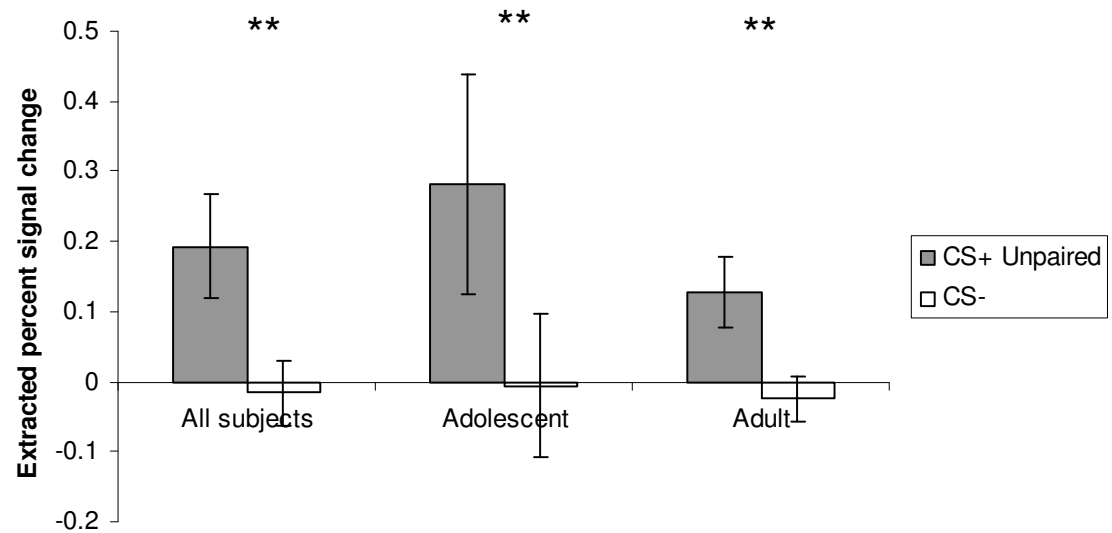
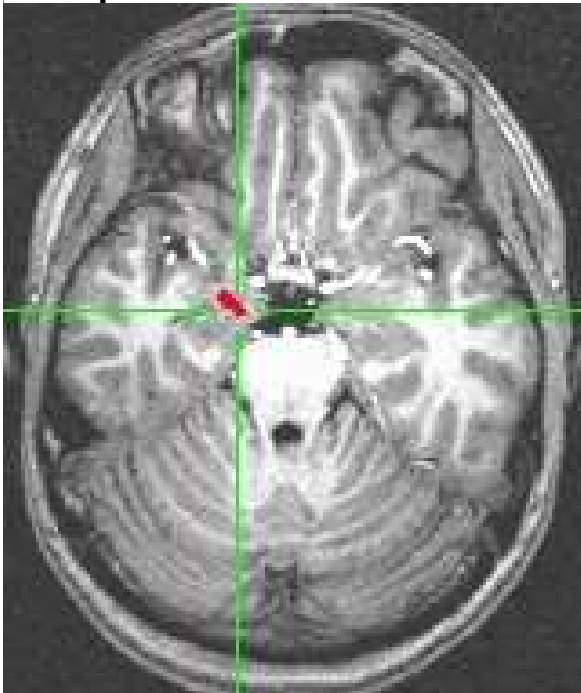
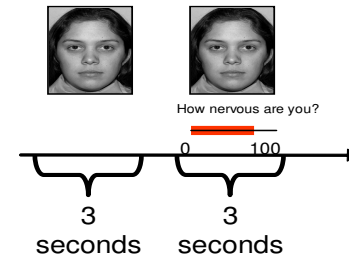
30 CS- trials

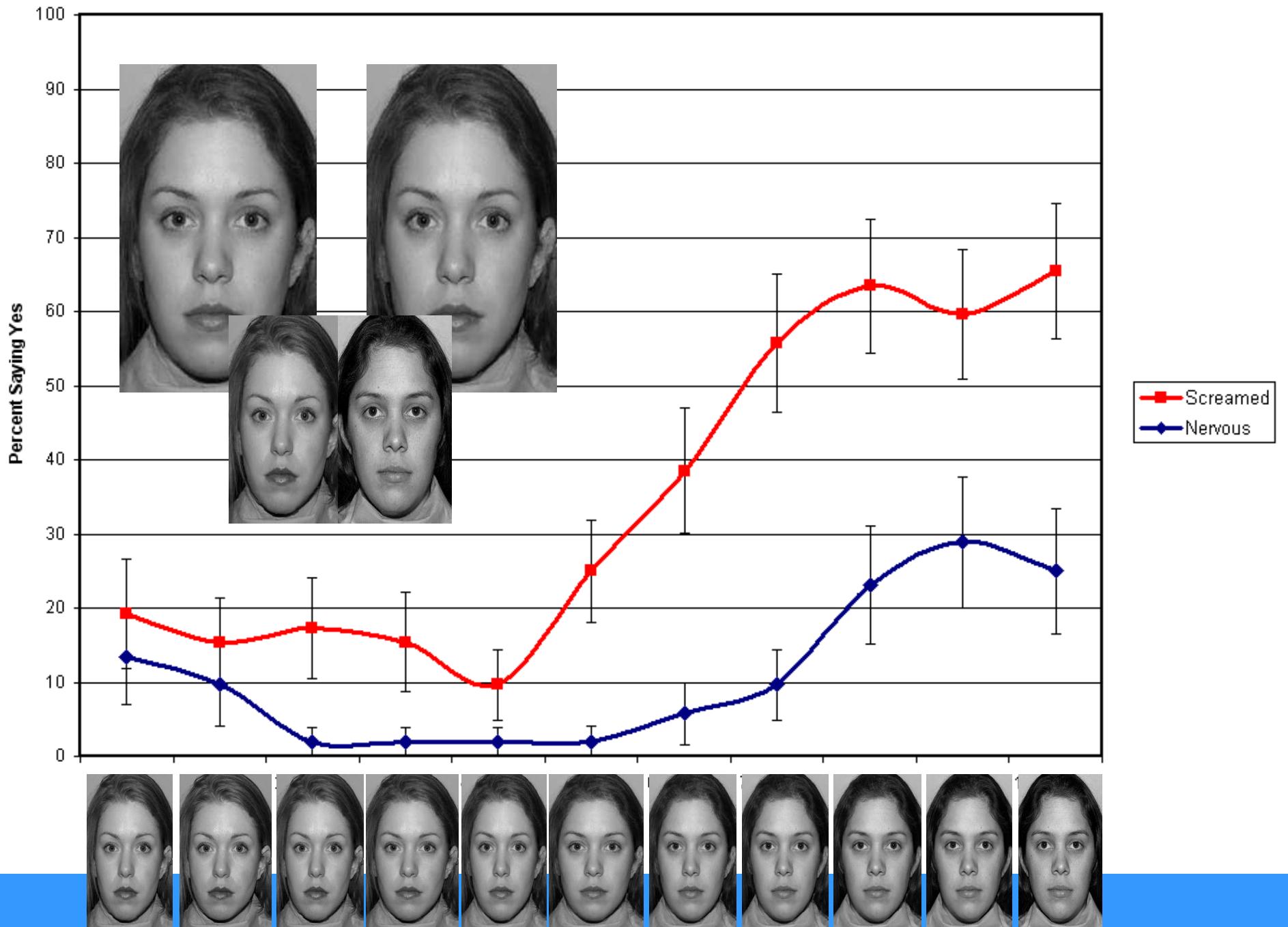


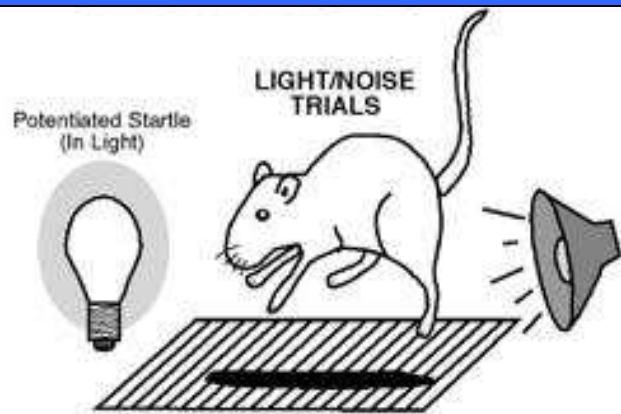
15 Paired CS+ trials



15 Unpaired CS+ trials







Extinction:

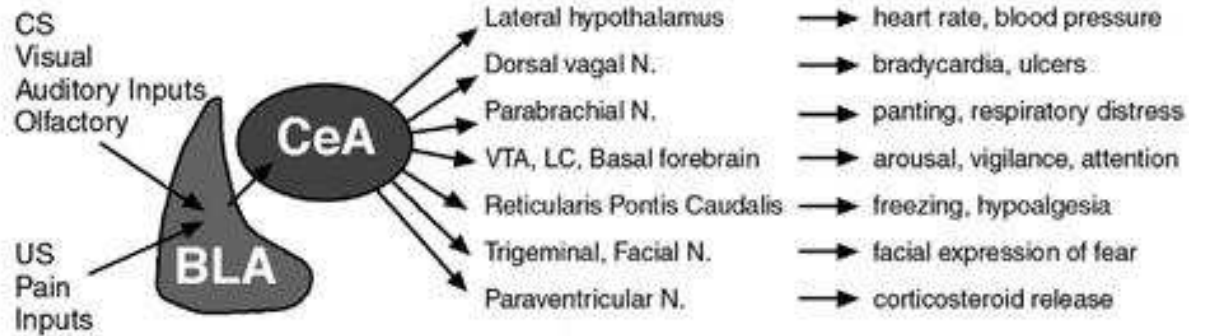
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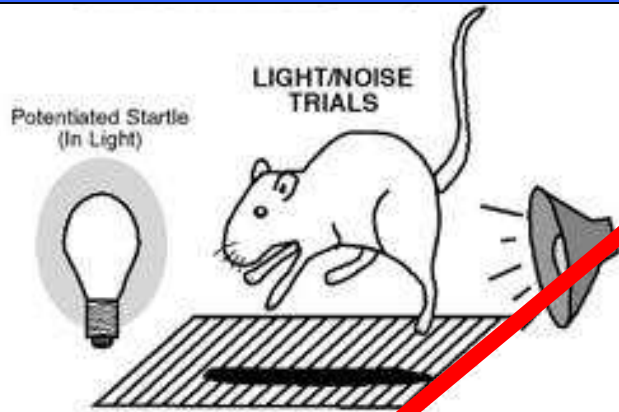
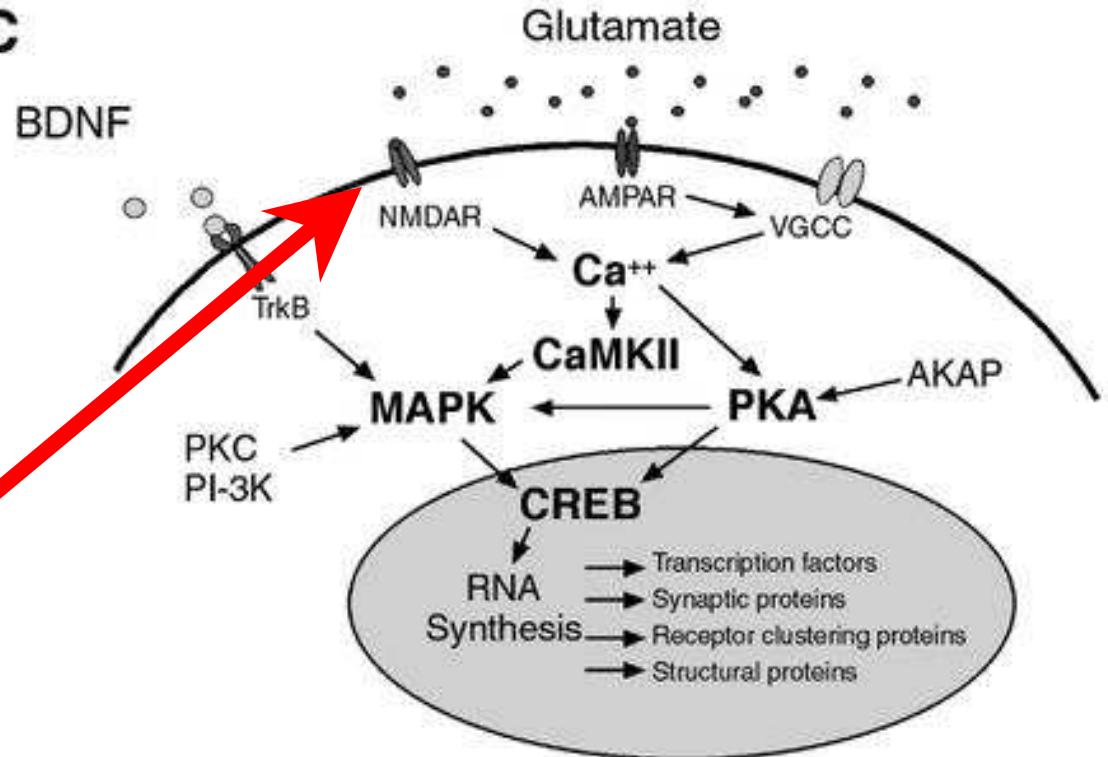
Ressler & Davis 2003



B



C



NMDA manipulation

Ressler & Davis 2003

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Conclusions

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