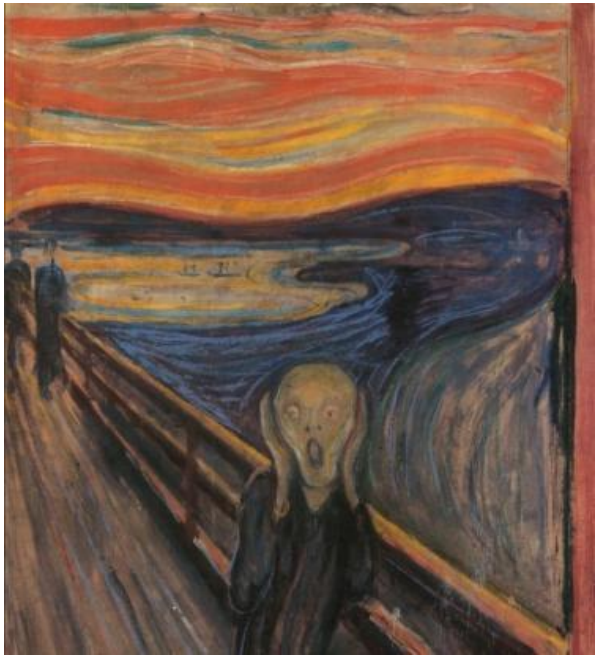
C82NAB Neuroscience and Behaviour

Emotion I:

General concepts, fear and anxiety

Tobias Bast, School of Psychology, University of Nottingham



The University of Nottingham

UNITED KINGDOM · CHINA · MALAYSIA

Outline

Emotion I (first part)

- Studying brain substrates of emotions in animals and humans – general considerations and concepts
- Fear and anxiety and relevant brain substrates

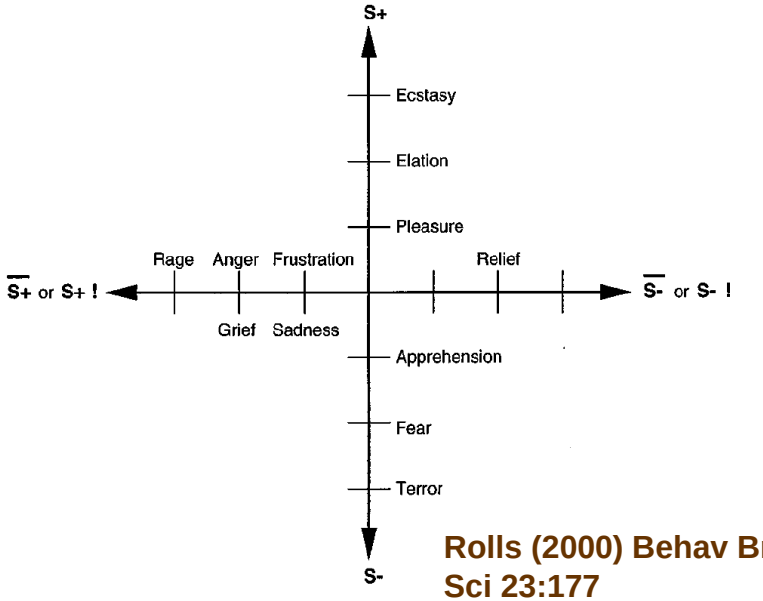
Emotion II (second part)

- Reward, pleasure, and desire, and relevant brain substrates
- Overlap between brain substrates of positive and negative emotions
- Recapitulation

"You always complain that I don't know how to show my emotions, so I made these signs."

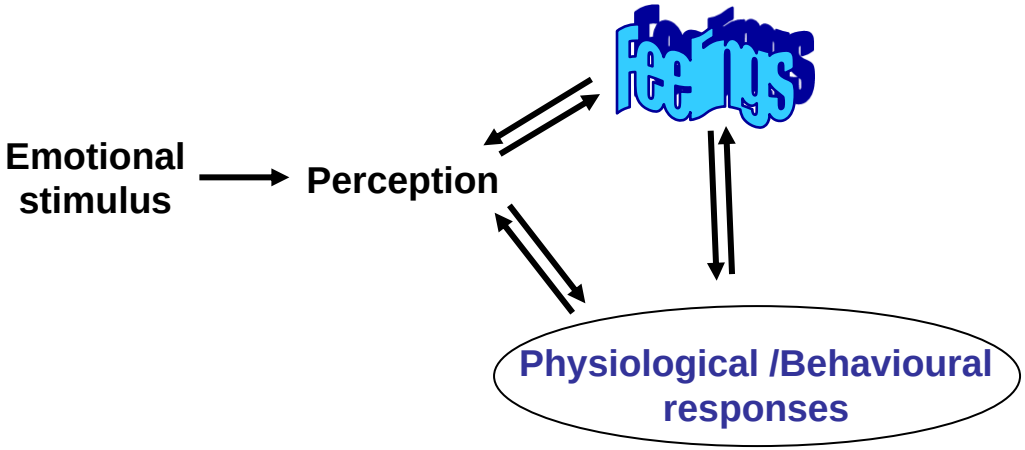
Emotional states and associated responses in humans and non-human animals

Emotions are states elicited by rewarding or aversive stimuli (S+ or S-) and their omission (–) or termination (!).



Rolls (2000) Behav Brain Sci 23:177

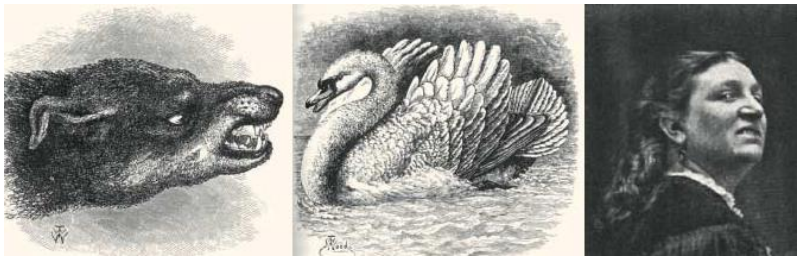
These states comprise thoughts ("feelings") and physiological/behavioural responses to emotional (i.e., rewarding or aversive) stimuli.



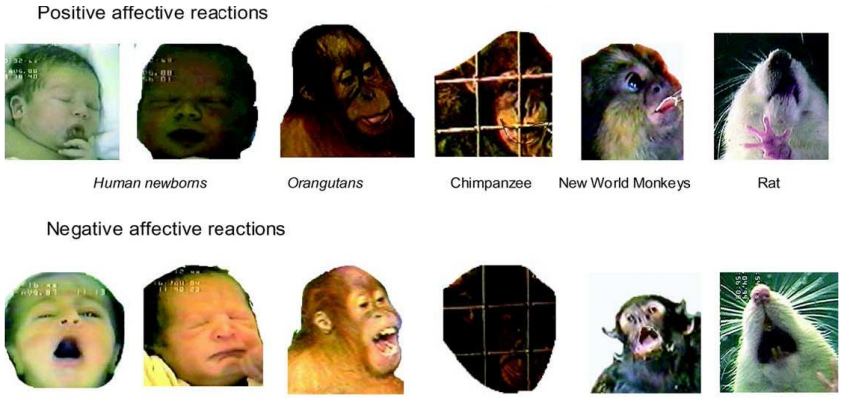
Physiological/behavioural responses to emotional stimuli can unambiguously be measured in humans and nonhuman animals.

Evolutionary considerations

Physiological/behavioural responses to aversive and positive stimuli have fundamental survival value and, therefore, have been relatively preserved throughout evolution and are often very similar in different animals incl. humans.

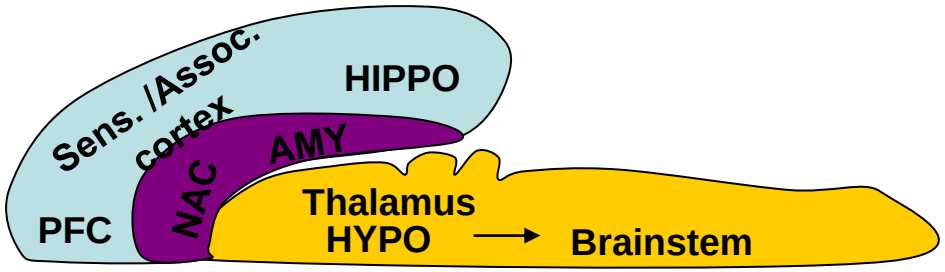


Darwin (1872) *The Expression of the Emotions in Man and Animals*



Berridge (2003) *Brain Cogn* 493:122

The principal organization of the brain is very similar among all mammalian species.



After Swanson (2005)
J Comp Neurol 493:122

Rat as a model system

ADVANTAGES

Easy to breed and keep

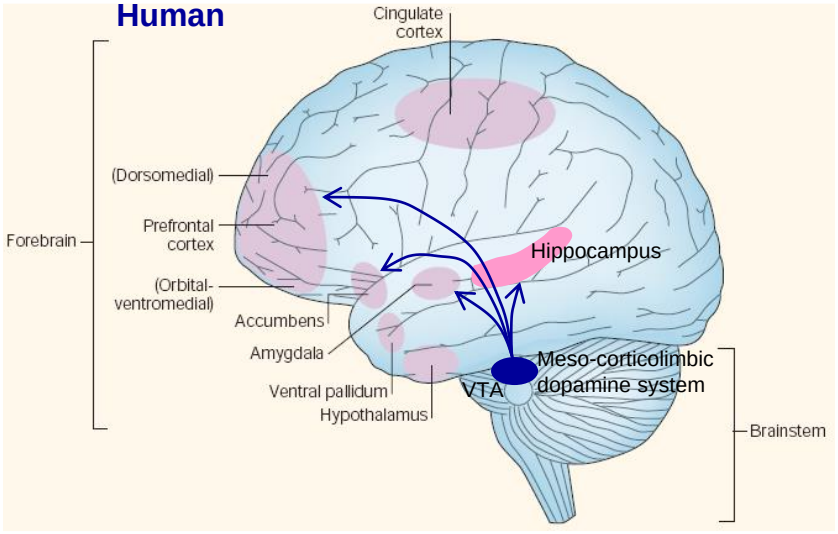
Well-established behavioural tests

Brain large enough to apply selective manipulations to distinct brain structures and brain anatomy very well characterized

DISADVANTAGE

Genetic manipulations difficult (alternative: mouse)

The emotional brain – an overview and short list of classic milestones



Hippocampus, amygdala, and hypothalamus:

Papez theory of emotion (1937)

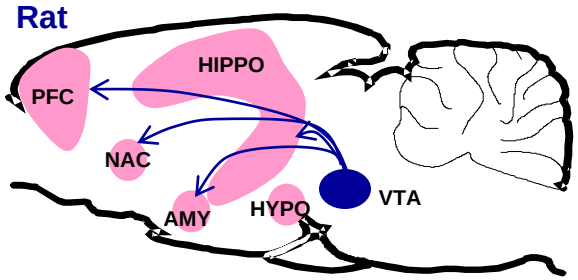
Klüver and Bucy‘s description of temporal lobe lesion effects in monkeys (1939)

MacLean‘s limbic system theory (1949)

Prefrontal cortex:

Case of Phineas Gage described by Harlow (1868)

Nauta (1971): Frontal lobes and interoception



Meso-corticolimbic dopamine system :

Olds and Milner (1954): Brain-stimulation induced reward

Wise et al. (1978): Neuroleptic-induced anhedonia

How could ANXIETY and FEAR be characterised without reference to subjective feelings?

a) A state caused by presence of a positive reinforcer.

b) A state caused by presence of aversive stimulus.

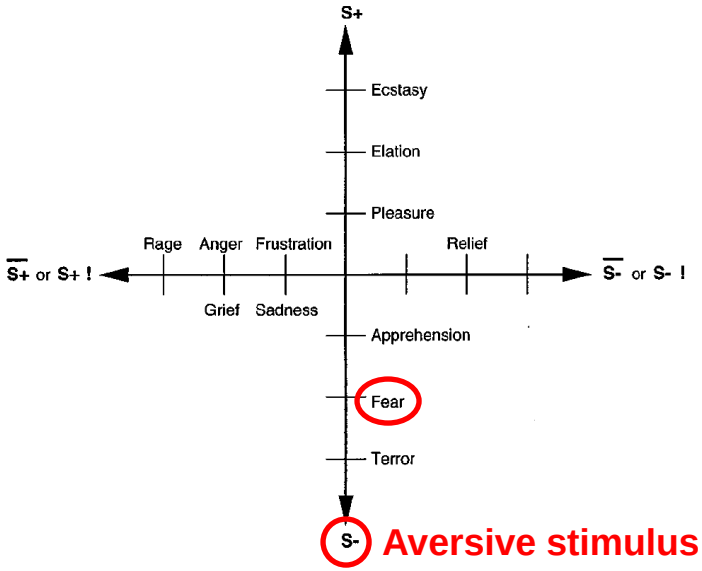
c) A state caused by absence of positive reinforcer.

d) A state caused by omission or termination of aversive stimulus.

Fear and anxiety 1

Much animal research on brain substrates of emotion over the last 30 years has focused on fear and anxiety (Caroline and Robert Blanchard, Jeffrey Gray, Michael Davis, Michael Fanselow, Joseph LeDoux, and colleagues).

Fear and anxiety comprise protective/defensive responses normally elicited by aversive stimuli.



Aversive stimulus

Fear and anxiety 2

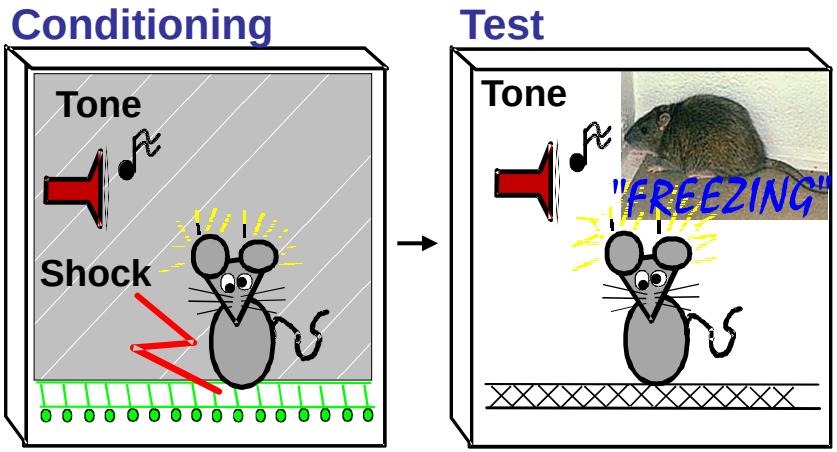
Fear rather refers to phasic escape or avoidance responses to distinct aversive stimuli. Anxiety rather refers to a tonic response to diffuse aversive situations and is associated with conflict and uncertainity (comapre Davis et al., 2010, *Neuropsychopharmacology* 35: 105–135).

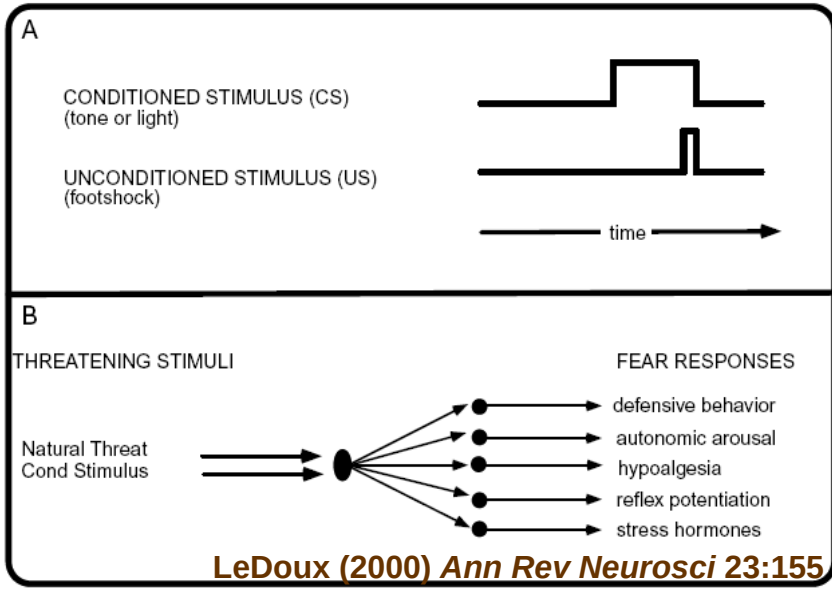
There are many different types of fear and anxiety responses, and the brain substrates of these different responses may differ.

Fear- and anxiety-related disorders in humans include generalized anxiety disorder, obsessive compulsive disorder (OCD), panic disorder, phobias, and post-traumatic stress disorder (PTSD).

Conditioned fear and the amygdala

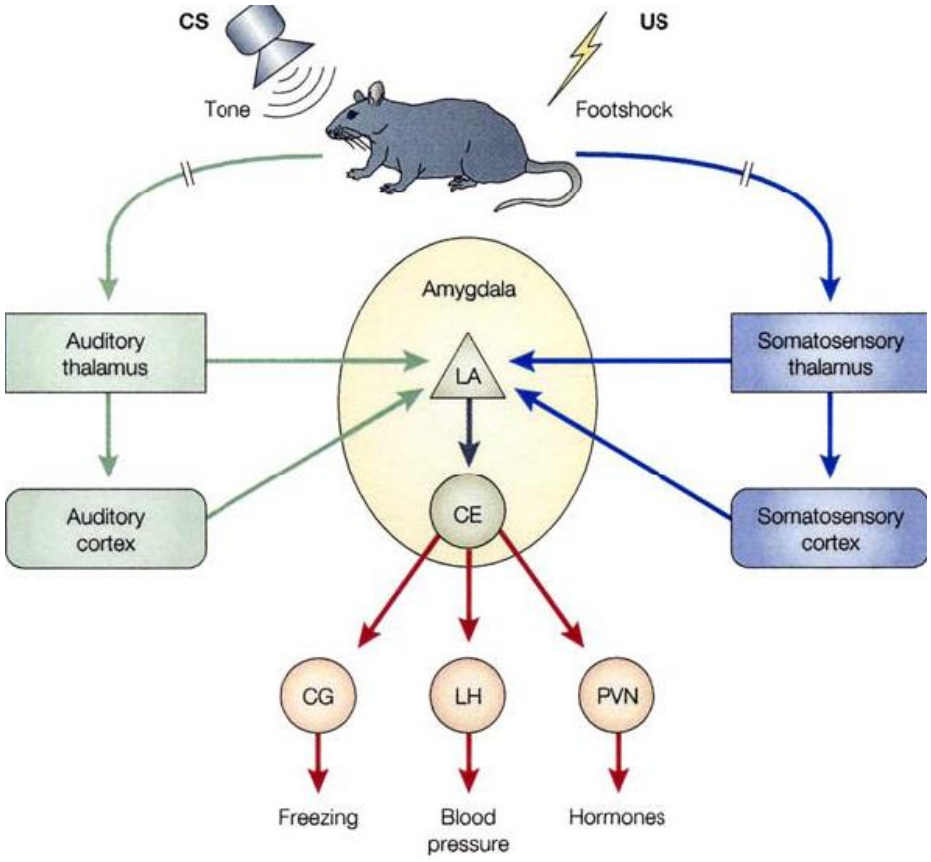
Classical fear conditioning





LeDoux (2000) *Ann Rev Neurosci* 23:155

Functional-anatomical model of conditioned fear: central role for the amygdala



Phelps & LeDoux (2005) *Neuron* 48 :175

Trends in Cognitive Sciences April 2013, Vol. 17, No. 4

The slippery slope of fear

Joseph E. LeDoux

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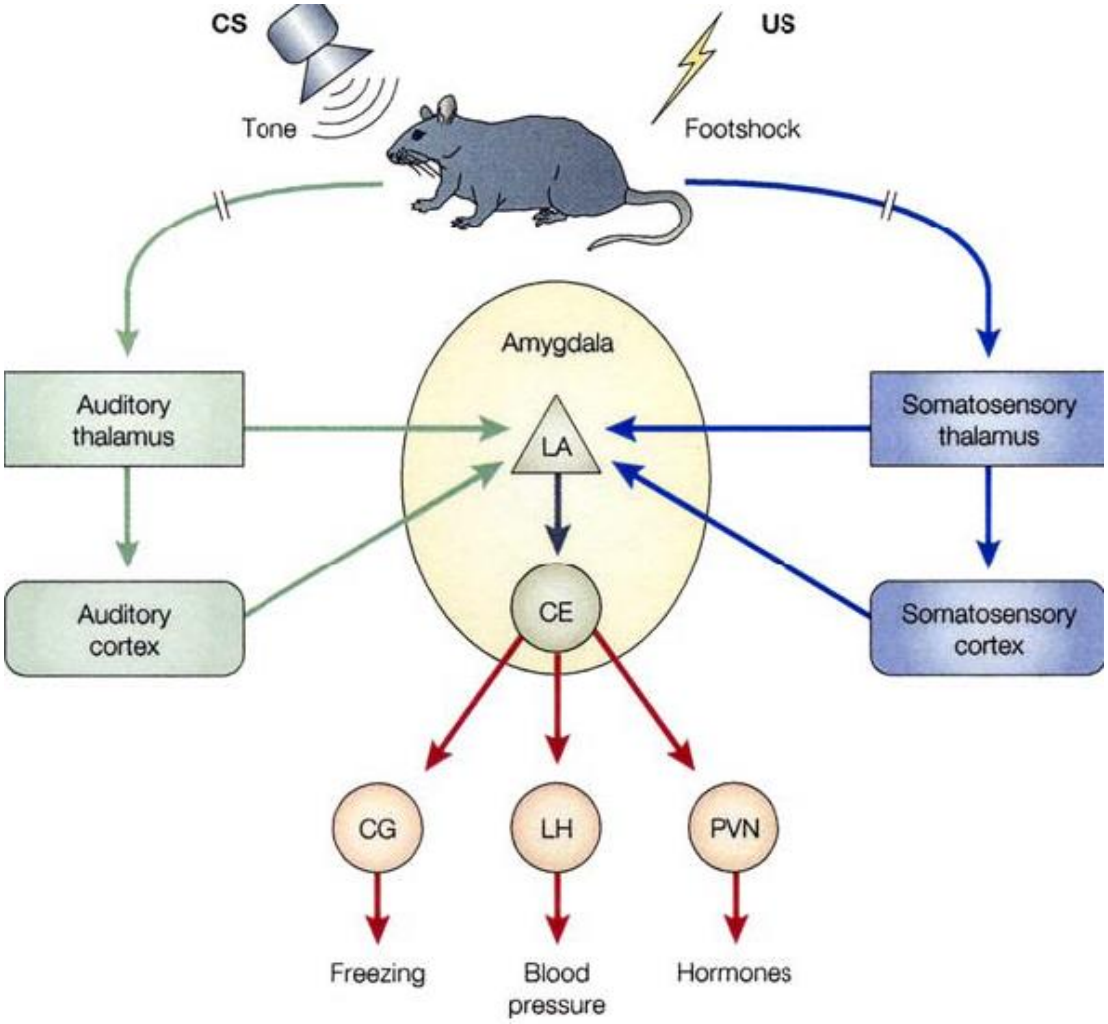
'Fear' is used scientifically in two ways, which causes confusion: it refers to conscious feelings and to behavioral and physiological responses. Restricting the use of 'fear' to denote feelings and using 'threat-induced defensive reactions' for the responses would help avoid misunderstandings about the brain mechanisms involved.

that, because amygdala det
havior in mice, patients wit
some healthy people, shoul
CO_2. As a result, the author
amygdala-damaged patients
ditions. The study makes ir
tions, but also contributes to

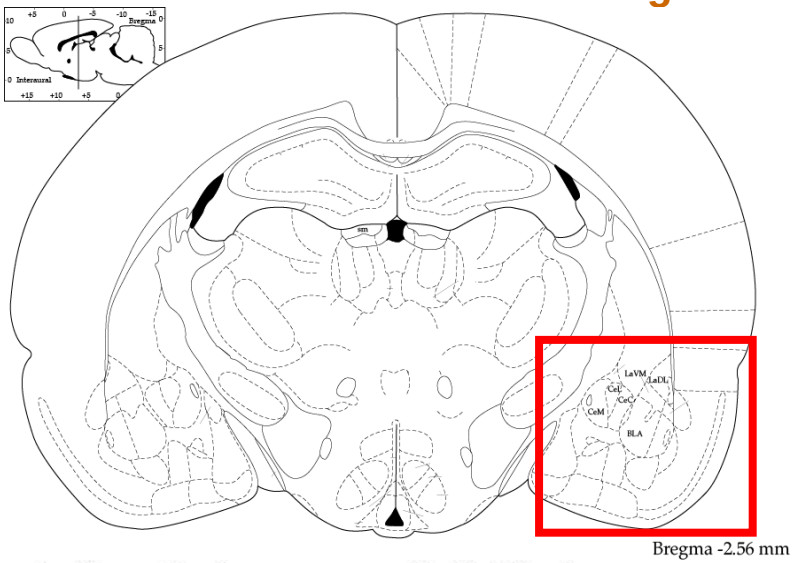
Functional anatomical model of conditioned fear (aka threat-induced defensive reactions): a central role for the amygdala



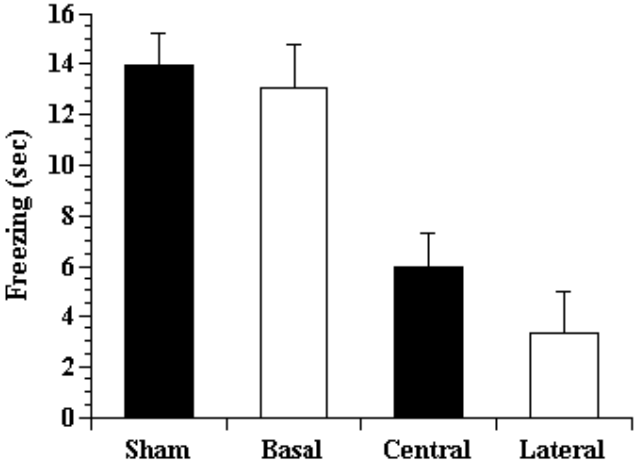
Phelps & LeDoux (2005) *Neuron* 48 :175

Requirement of lateral and central amygdala in conditioned fear

Lesions of different amygdala nuclei before fear conditioning

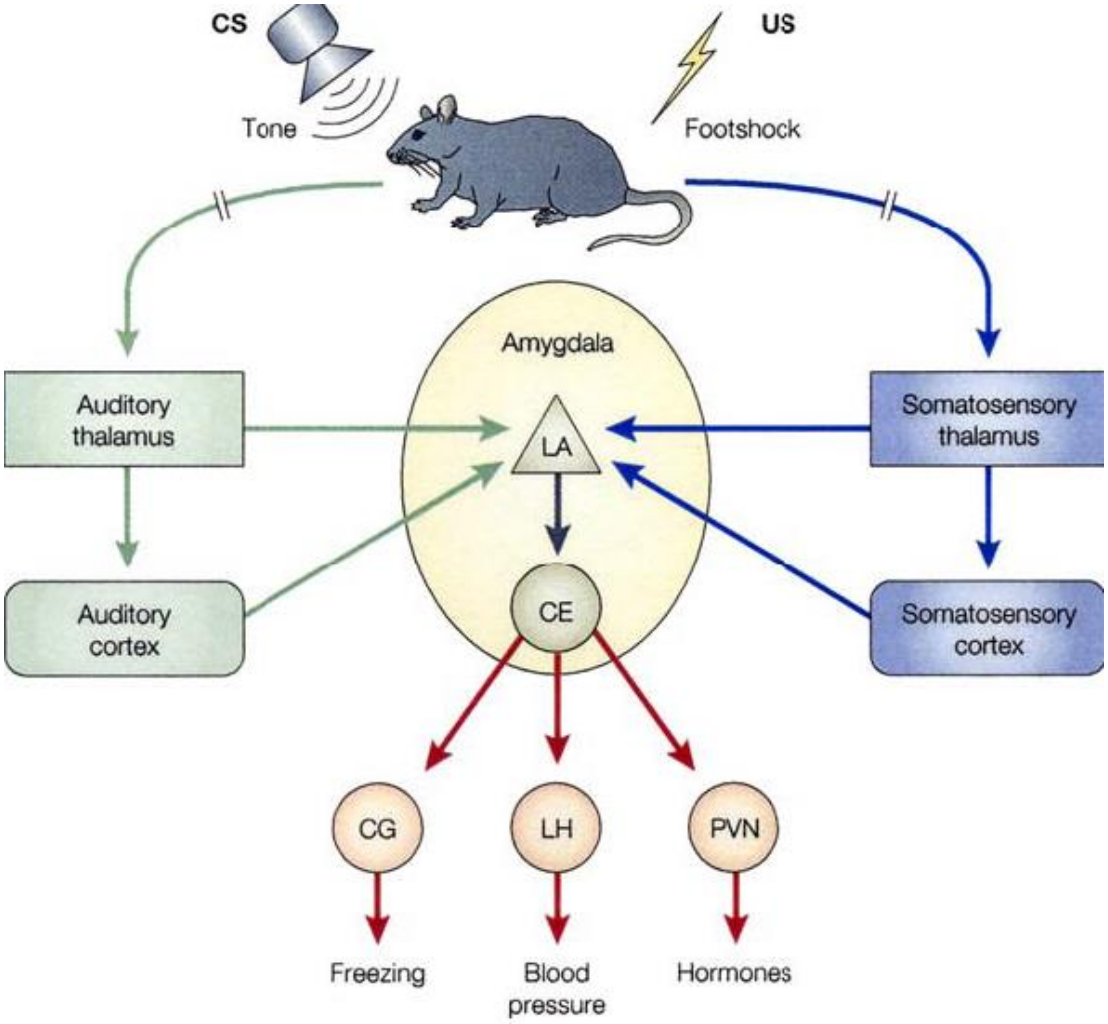


Lesion effects on conditioned freezing



Amorapanth et al. (2000) *Nature Neurosci* 3 :74

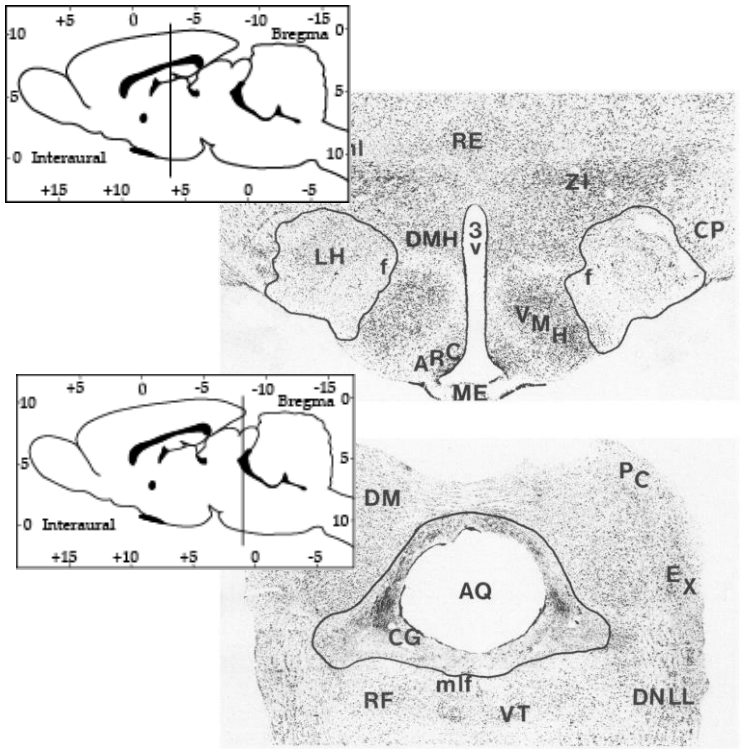
Different CE outputs mediate different conditioned fear responses



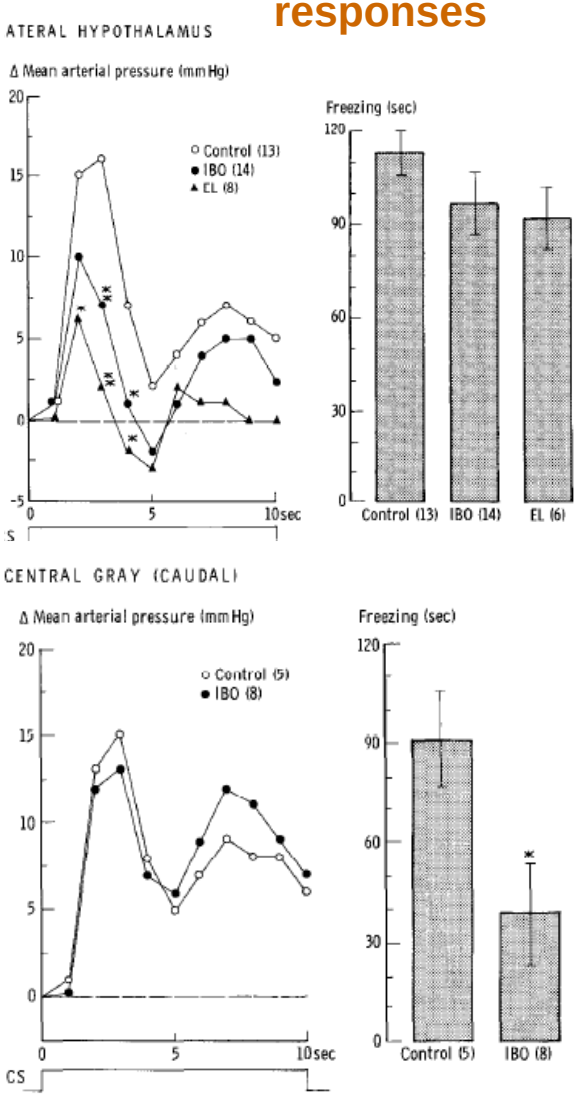
Phelps & LeDoux (2005) *Neuron* 48 :175

Different CE outputs mediate different conditioned fear responses

Lesions of lateral hypothalamus and caudal central gray before fear conditioning

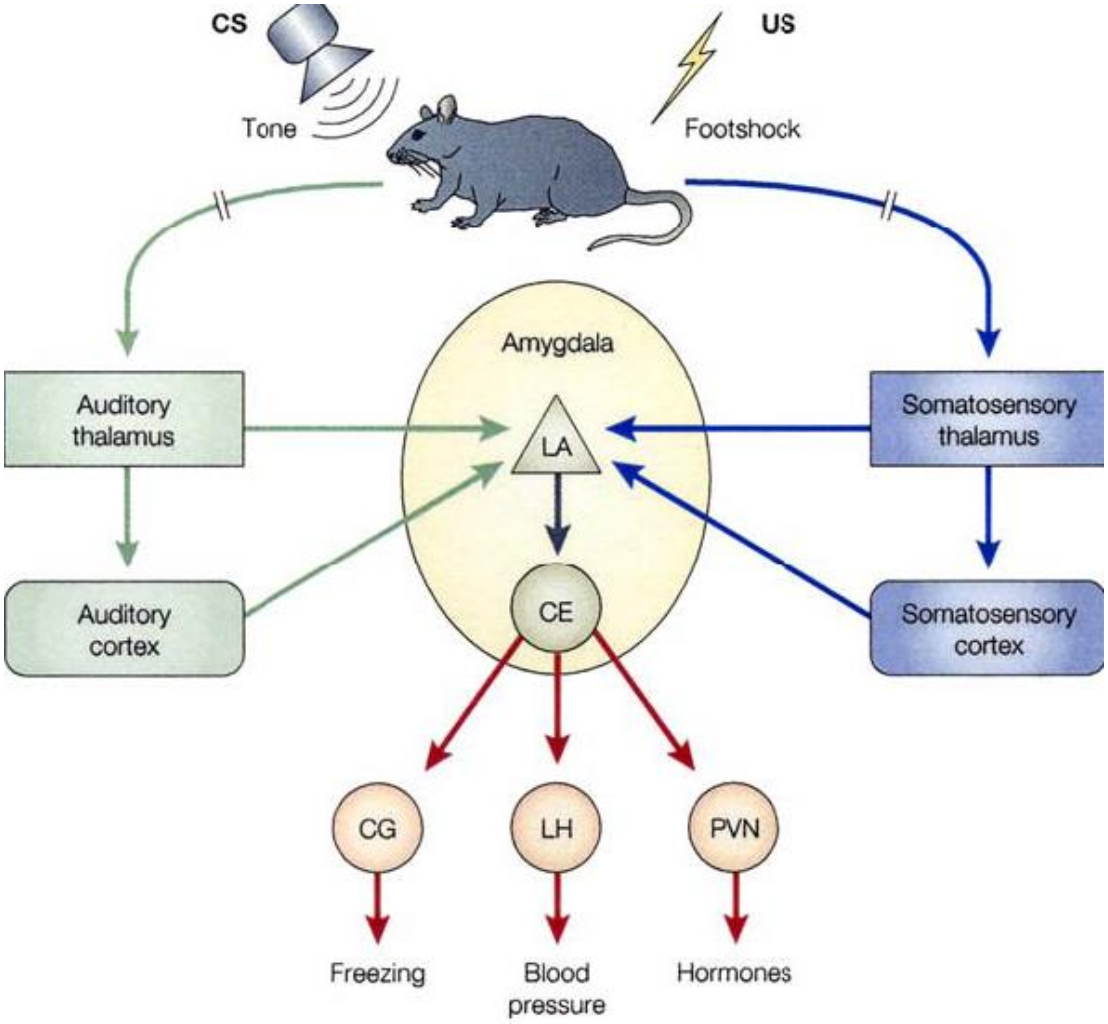


Lesion effects on conditioned fear responses



LeDoux et al. (1988) *J Neurosci* 8 :2521

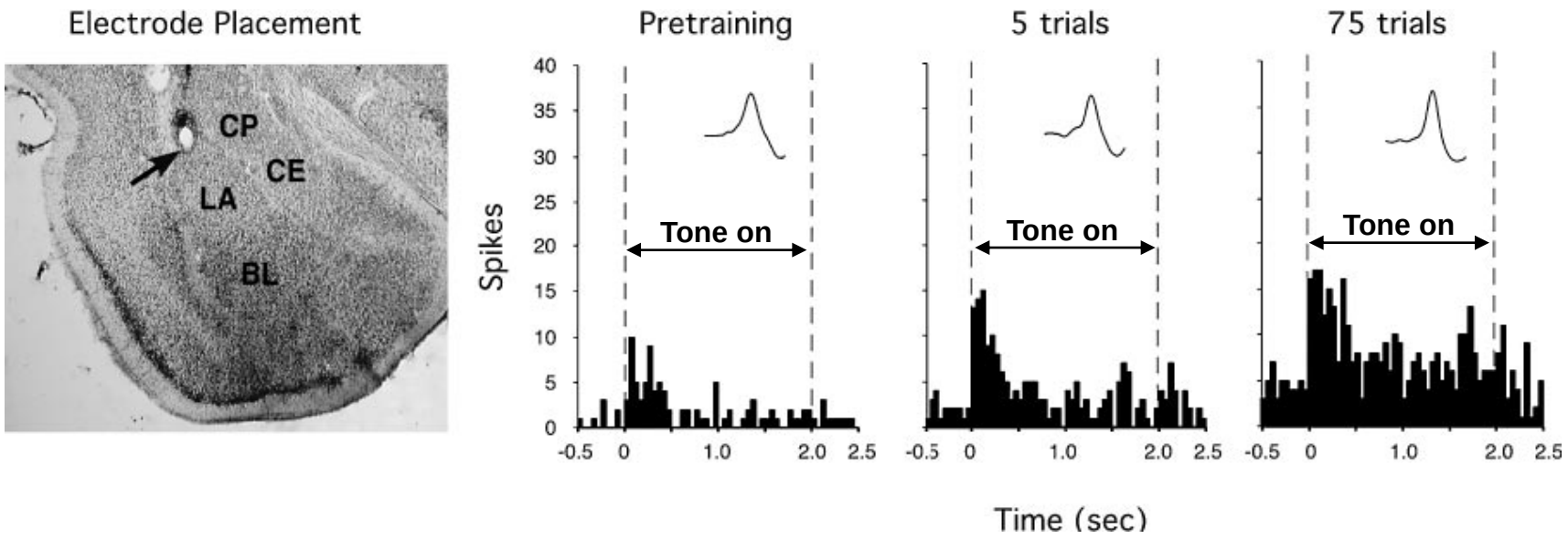
Fear-conditioning-related plasticity in LA neurons



Phelps & LeDoux (2005) *Neuron* 48 :175

Fear-conditioning-related plasticity in LA neurons

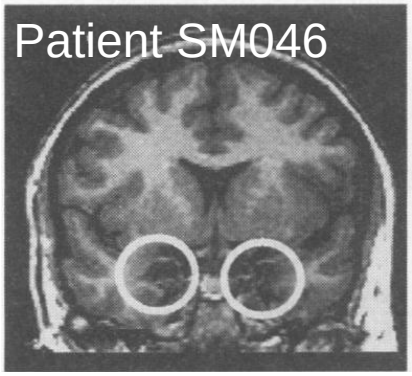
LA neurons come to fire in response to a tone when the tone is paired with a foot shock

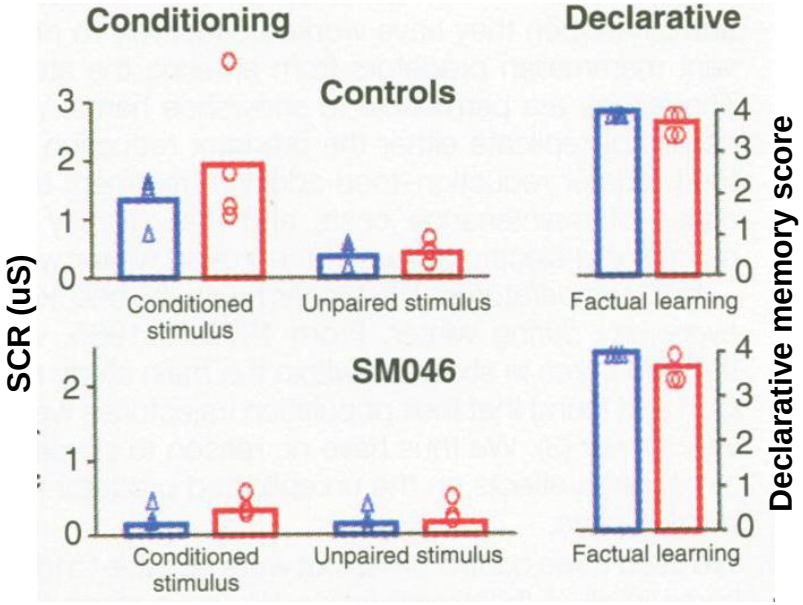


Maren (2001) *Ann Rev Neurosci* 24 :897

And the human amygdala?

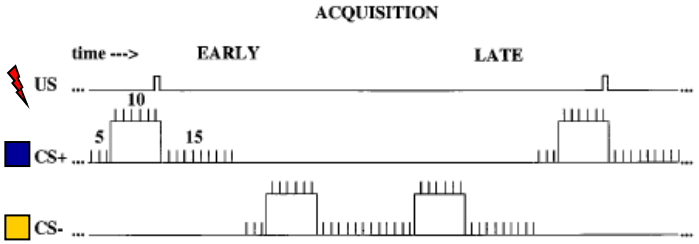
Amygdala damage impairs conditioned fear





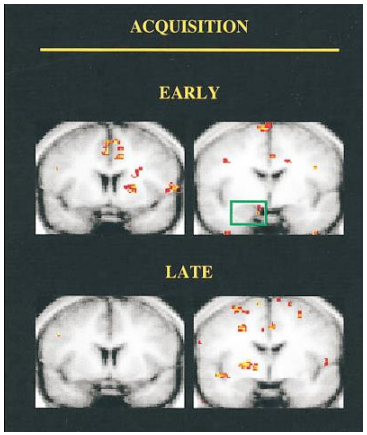
Bechara et al. (1995) *Science* 269:1115

Amygdala fMRI signals in a conditioned fear paradigm



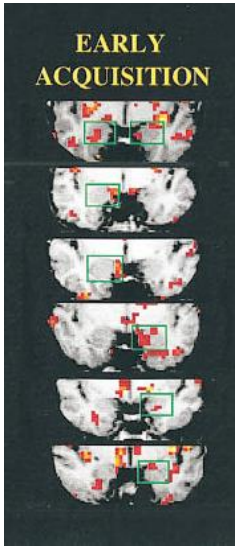
Vertical lines indicate MRI scans

Average

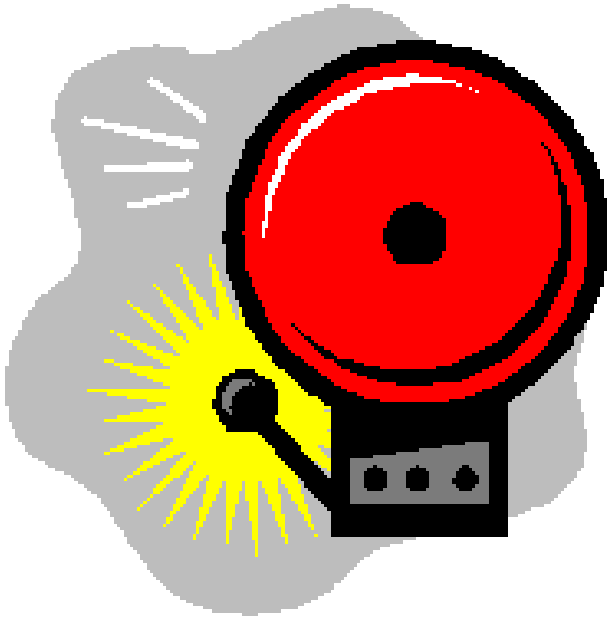


Amyg.

Individuals



LaBar et al. (1998) *Neuron* 20 :937



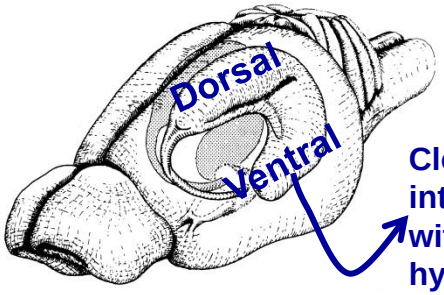
IMPORTANT NOTES:

The role of the amygdala in conditioned fear has been very well characterised, nevertheless:

-Other brain structures (e.g., hippocampus, prefrontal cortex) may also make important contributions to fear and anxiety, and the substrates of conditioned fear may differ from those of other fear/anxiety-related behaviours.

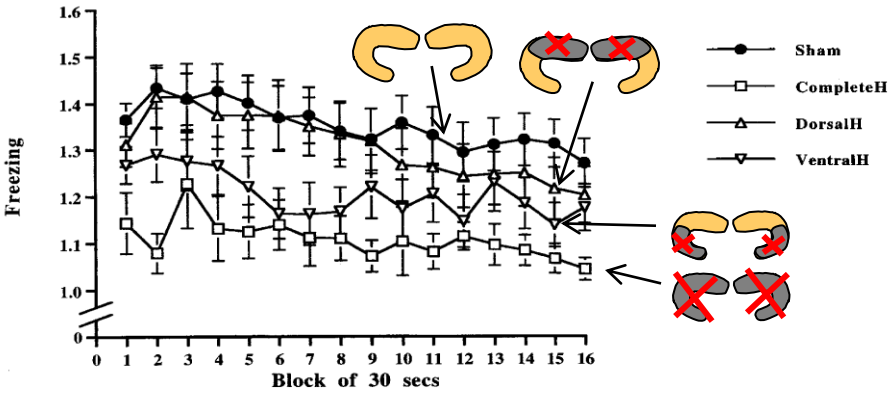
-Amygdala is involved in other emotional and behavioural processes as well.

Hippocampus in fear and anxiety



Close interconnections with amygdala and hypothalamus

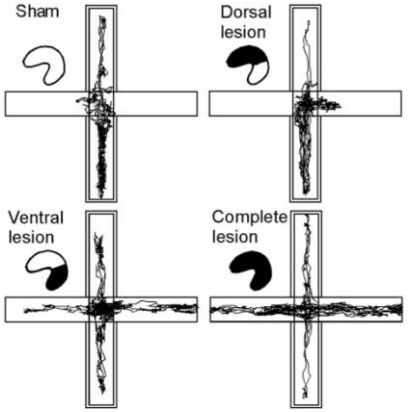
Ventral hippocampus and conditioned freezing

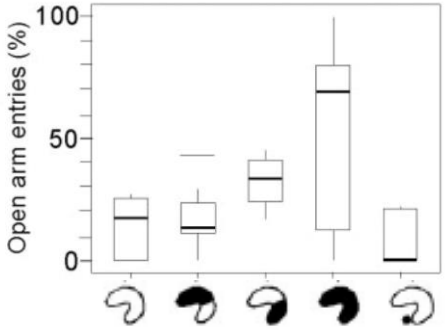


Richmond et al. (1999) *Behav Neurosci* 113:1189

Ventral hippocampus and innate/unconditioned anxiety responses

Elevated plus maze





Kjelstrup et al. (2002) *Proc Nat Acad Sci 99*:10825

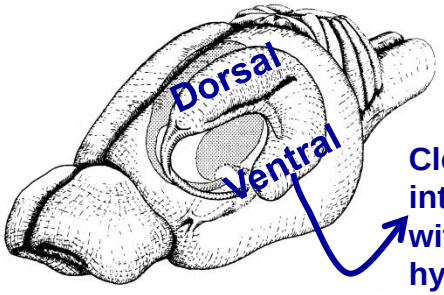
Hippocampal lesions increase the time rats spent in the open arms of the elevated plus maze. What does this finding indicate?

a) Hippocampal lesions cause anxiety.

b) Hippocampal lesions reduce anxiety.

c) Hippocampus does not play a role in anxiety.

Hippocampus in fear and anxiety



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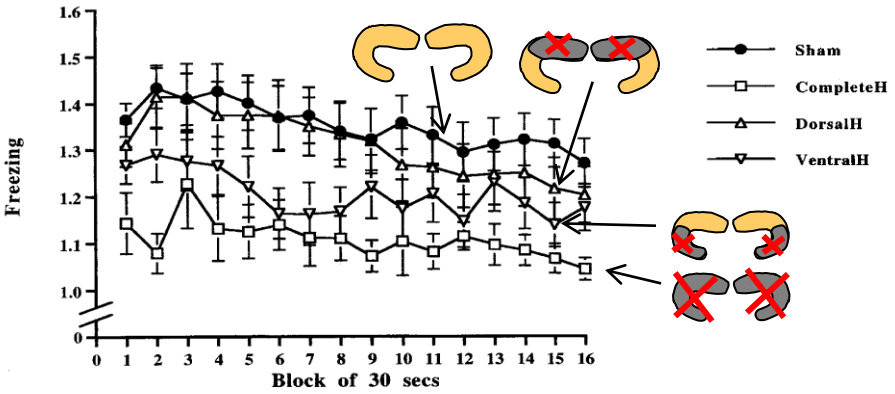
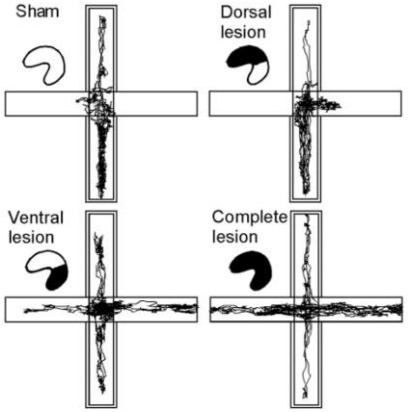
Ventral hippocampus and conditioned freezing

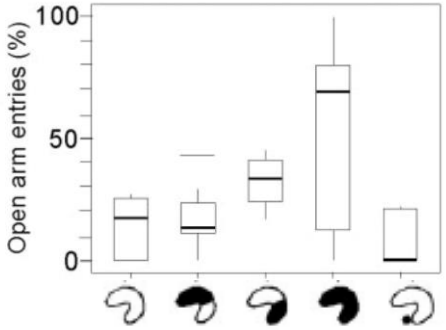


Richmond et al. (1999) *Behav Neurosci* 113:1189

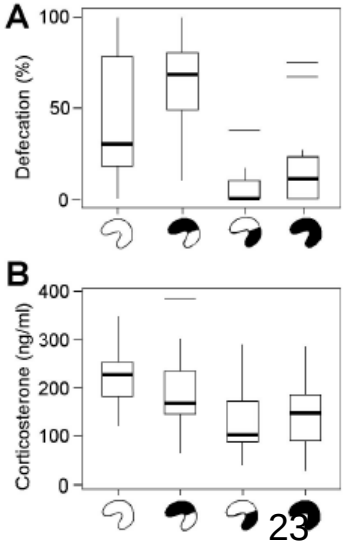
Ventral hippocampus and innate/unconditioned anxiety responses

Elevated plus maze





Brightly lit test chamber



Kjelstrup et al. (2002) *Proc Nat Acad Sci 99*:10825

Hippocampus and anxiety disorders

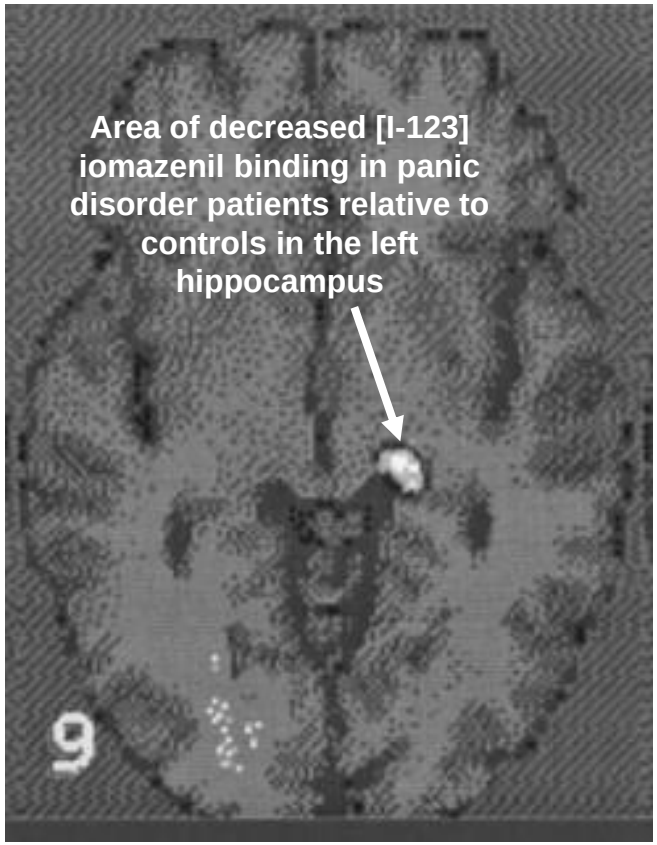
Similarity between effects of hippocampal lesions and anxiolytics

Task	HIP	ANX
Rewarded Bar Pressing, CRF	0	[0]
Rewarded Running, CRF	0	0
Simultaneous Discrimination	0	0
Shock, Skilled Escape, Active Avoidance	0	0
Resistance to Extinction	+	+
Two Way Active Avoidance	+	+
Non-spatial Active Avoidance	+	[+]
Rewarded Bar Pressing, Intermittent Reinforcement	+	+
Successive Discrimination	-	[-]
Spontaneous Alternation	-	-
Rearing	-	[-]
Mazes (not Radial Arm)	-	[-]
Passive Avoidance	-	[-]
Differential Reinforcement of Low Rates	-	[-]
Spatial Discrimination Reversal	-	[-]
Water Maze	-	[-]

[ ] = *Tested with Buspirone*

McNaughton & Gray (2000) *J Affect Dis* 61:161

Decreased hippocampal benzodiazepine receptor binding in panic disorder



Bremner et al. (2000) *Biol Psychiatry* 47:96

Emotion I: General concepts, fear and anxiety – Selected Reading

***Textbook chapter*:**

Carlson NR (any edition) The physiology of behavior. Chapter 11.

***Book*:**

Le Doux J (1996) The emotional brain – the mysterious underpinnings of emotional life.

***Review articles*:**

General

Dalgleish T (2004) The emotional brain. *Nature Rev Neurosci* 5:582-589.

Rolls ET (2000) Précis of The brain and emotion. *Behav Brain Sci* 23:177-234.

Fear and anxiety:

Le Doux J (2000) Emotion circuits in the brain. *Annu Rev Neurosci* 23:155-184.

Phelps EA & Le Doux JE (2005) Contributions of the amygdala to emotion processing: from animal models to human behavior. *Neuron* 48:175-187.

Ross DA, Arbuckle MR, Travis MJ, Dwyer JB, van Schalkwyk GI, Ressler KJ (2017) An Integrated Neuroscience Perspective on Formulation and Treatment Planning for Posttraumatic Stress Disorder: An Educational Review. *JAMA Psychiatry*: Published online March 8, 2017. doi:10.1001/jamapsychiatry.2016.3325

Emotion I: General concepts, fear and anxiety

– Some questions for revision

• Is it necessary to refer to subjective feelings if we want to study brain substrates of emotions?

• What advantages and disadvantages does it have to study neural mechanisms of emotion without reference to subjective feelings?

•How can we study brain substrates relevant to fear/anxiety in rat models?

•How can we confirm that similar brain substrates are also important for human fear/anxiety?