Sex and Hemisphere Influences on Emotional Memory

The burden of proof has shifted

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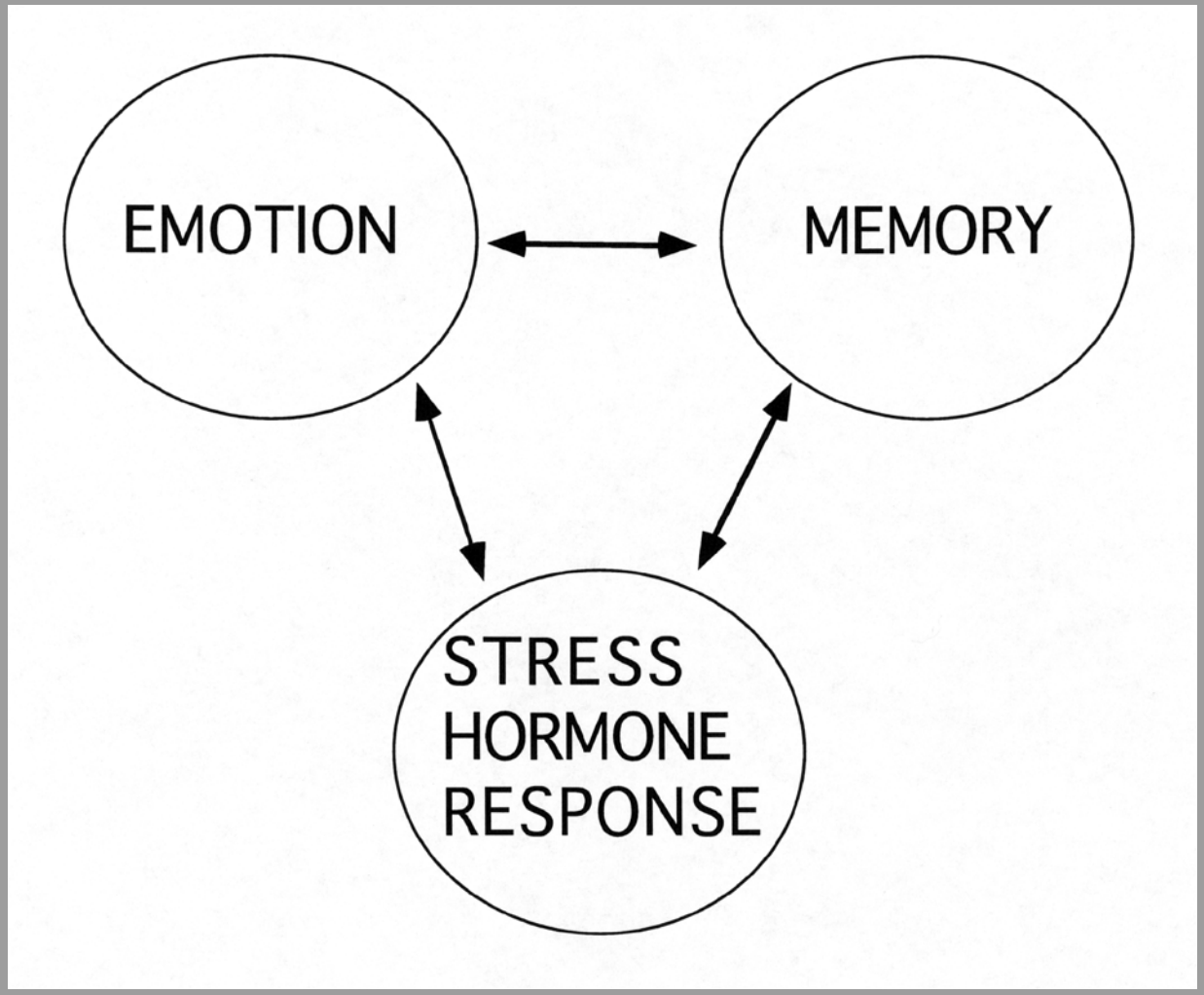
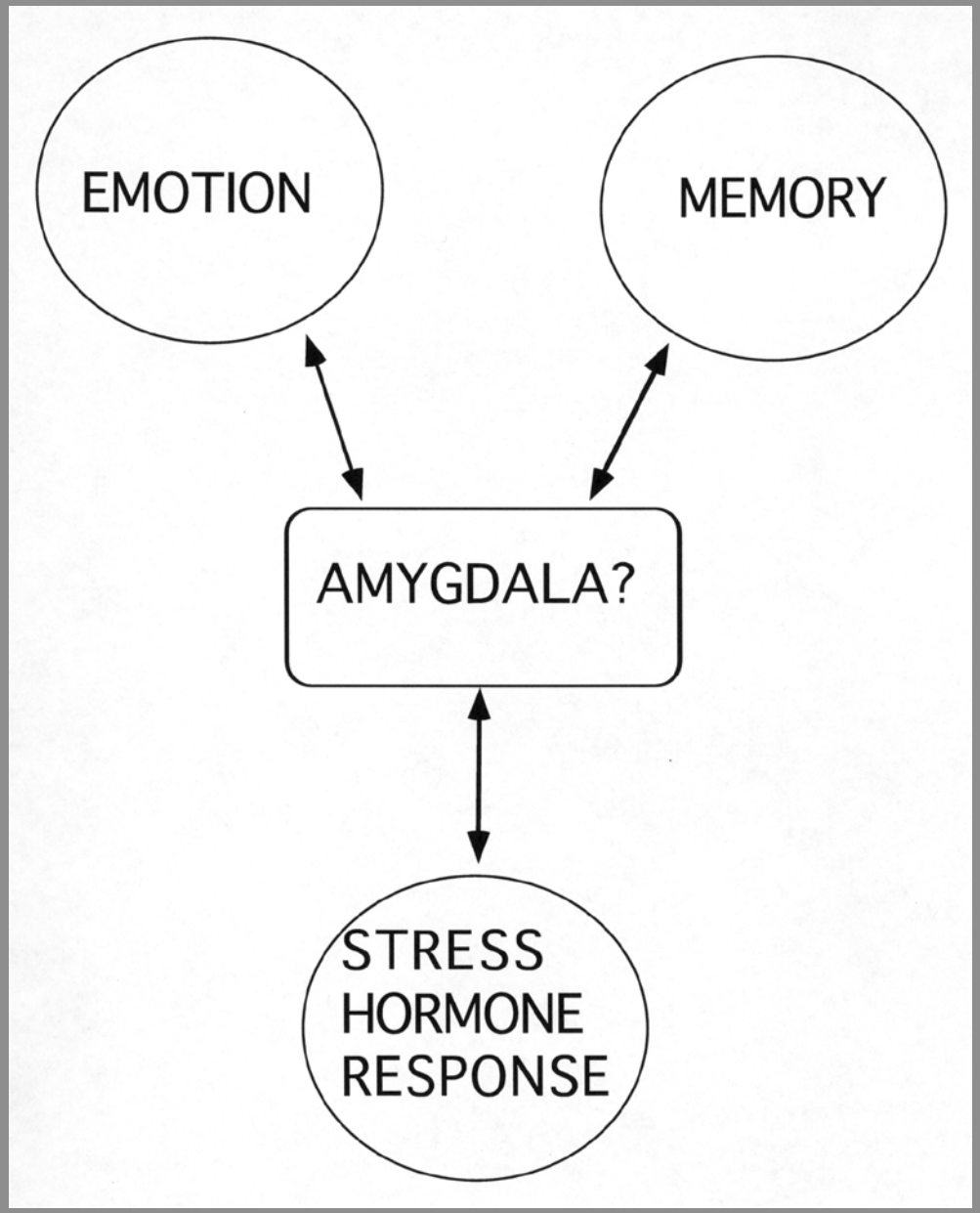
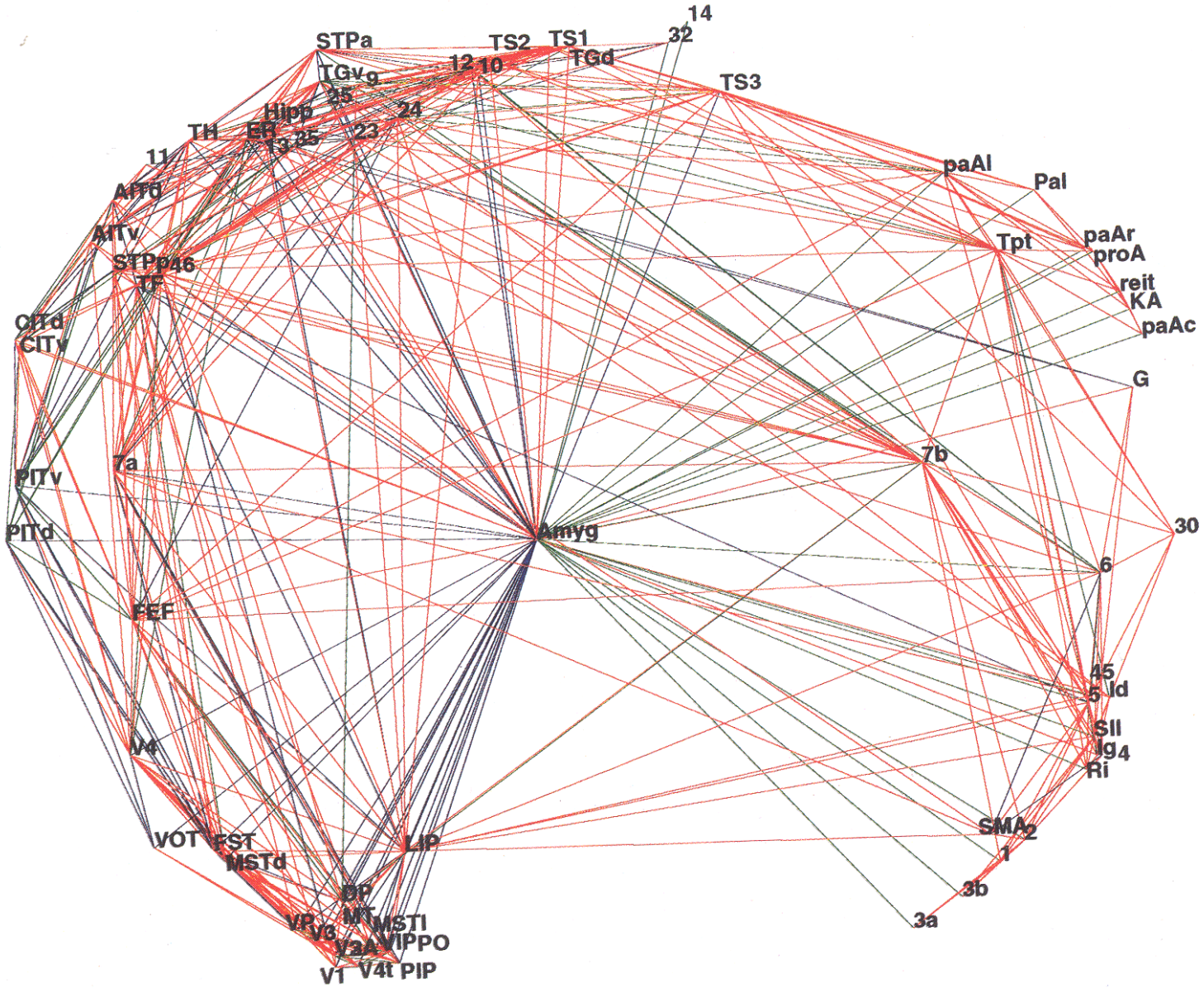
3 Parts

- Background- Brain Mechanism of Emotional Memory
- Sex Influences on Brain
- The blinders come off: Sex influences on brain mechanisms of emotional memory

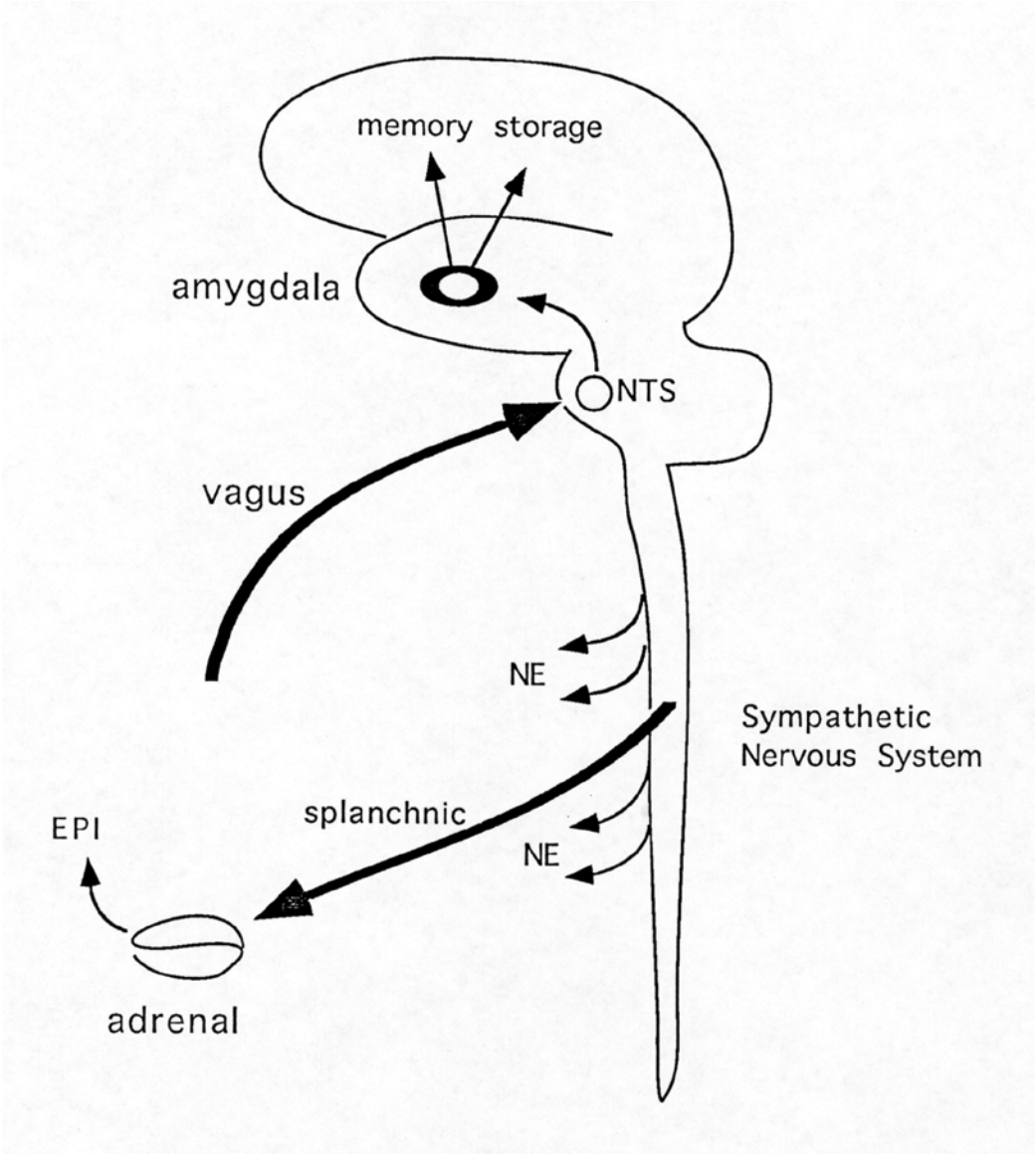

EMOTION
MEMORY
STRESS
HORMONE
RESPONSE

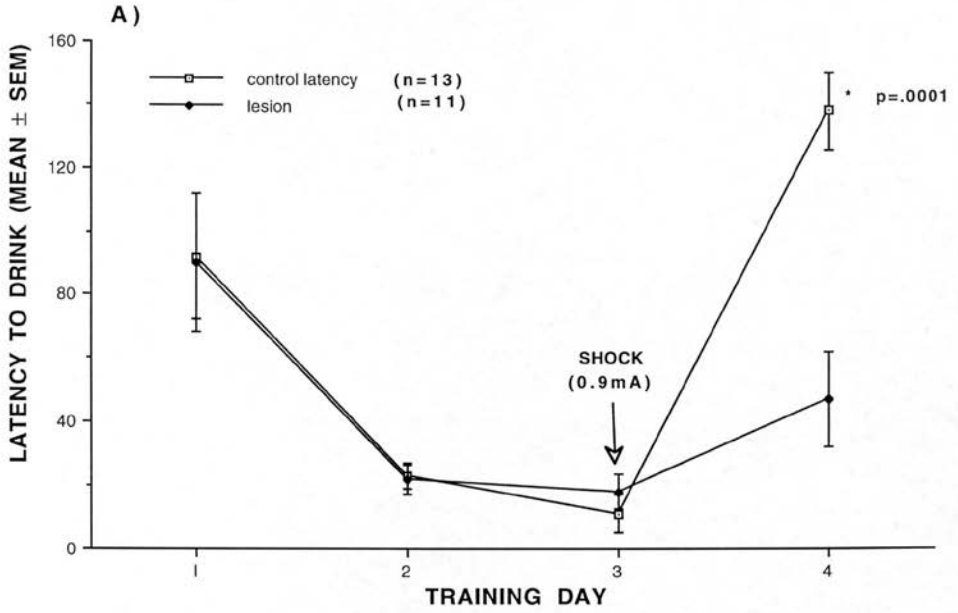

EMOTION
MEMORY
AMYGDALA?
STRESS
HORMONE
RESPONSE

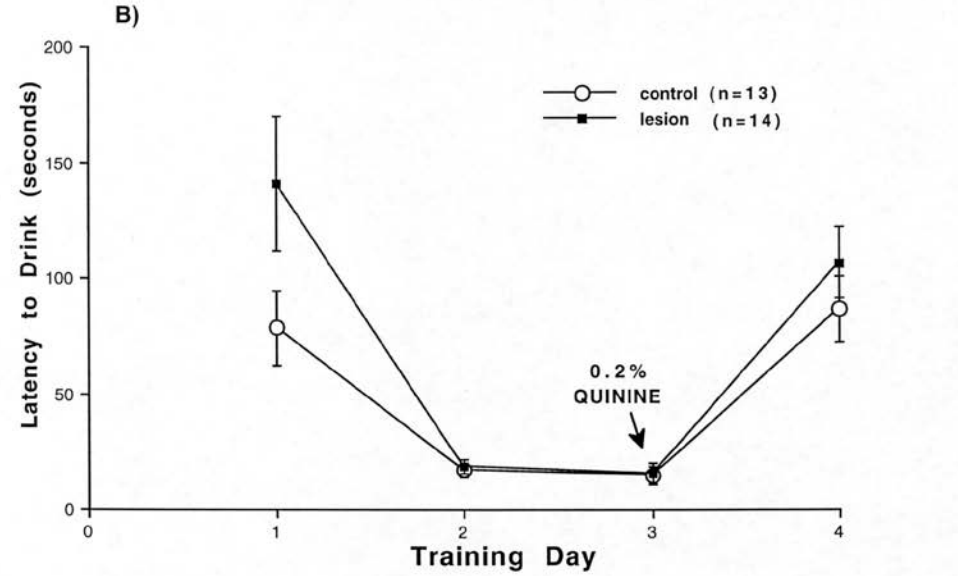
Cortex Wiring Diagram

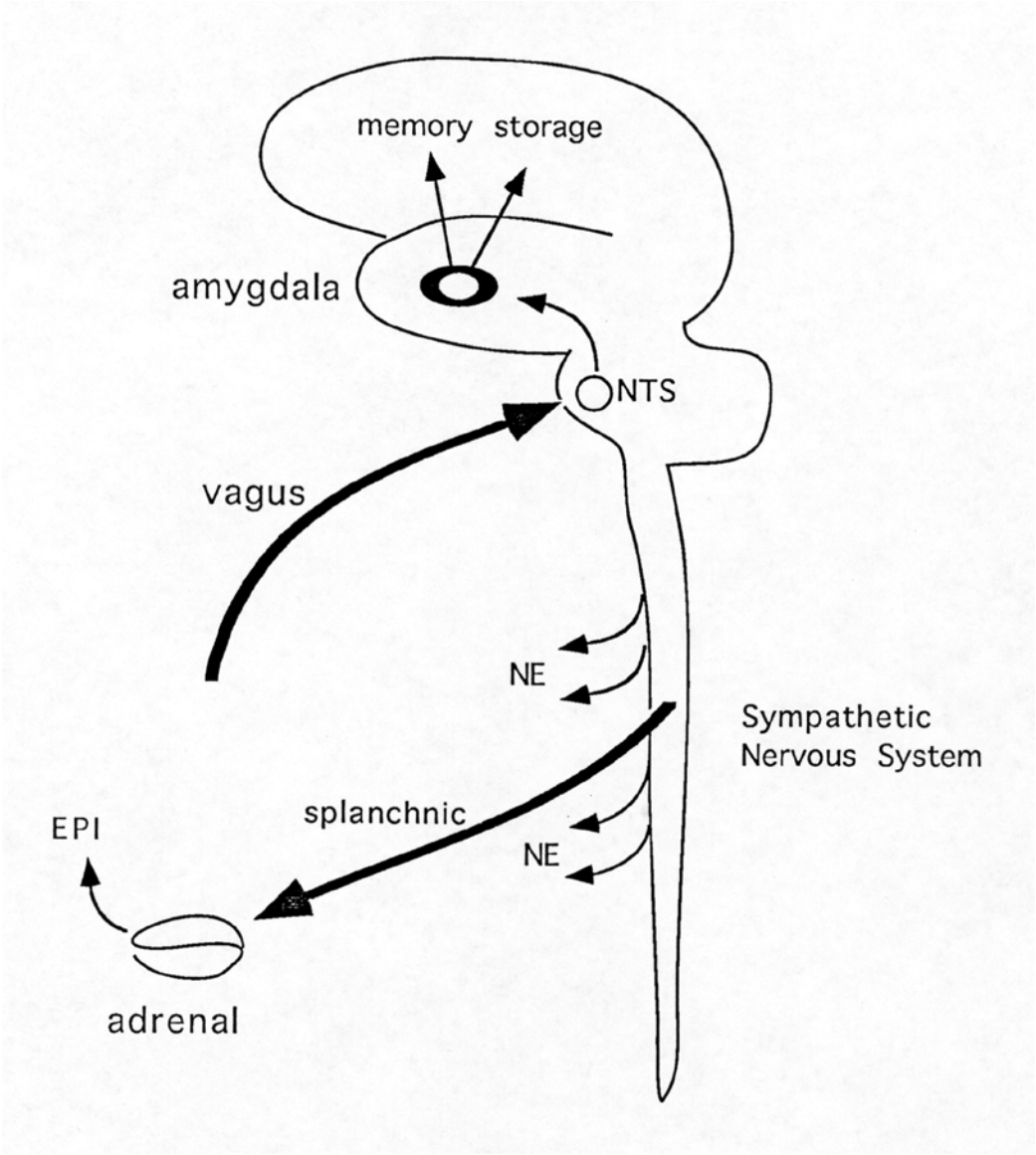


Young and Scannell,1994


memory storage
amygdala
NTS
vagus
NE
Sympathetic
Nervous System
splanchnic
EPI
NE
adrenal


A)
LATENCY TO DRINK (MEAN ± SEM)
160
120
80
40
0
control latency (n=13)
lesion (n=11)
* p=.0001
SHOCK
(0.9mA)
1
2
3
4
TRAINING DAY


B)
Latency to Drink (seconds)
200
150
100
50
0
control (n=13)
lesion (n=14)
0.2%
QUININE
0
1
2
3
4
Training Day


memory storage
amygdala
NTS
vagus
NE
Sympathetic
Nervous System
splanchnic
EPI
NE
adrenal

"...the degree of arousal produced by the unconditioned stimulus, and not the aversive nature per se, determines the level of amygdala involvement...The AC appears to participate in learning especially when the reinforcement is of a highly arousing nature."

Cahill and McGaugh, 1990, Behavioral Neuroscience

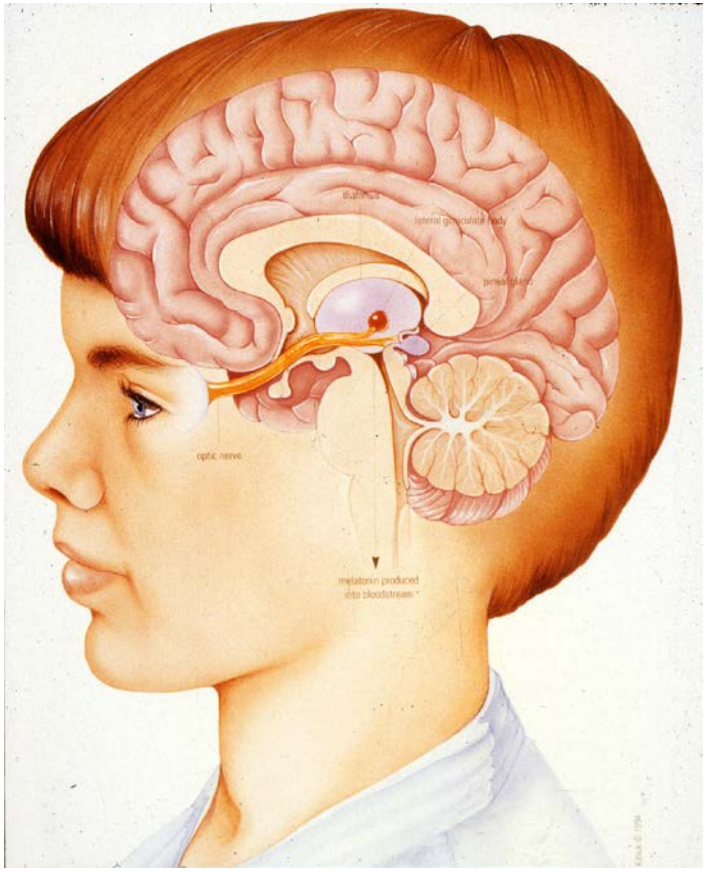
"…the degree of arousal produced by the unconditioned stimulus, and not the aversive nature per se, determines the level of amygdala involvement…The AC appears to participate in learning especially when the reinforcement is of a highly arousing nature."

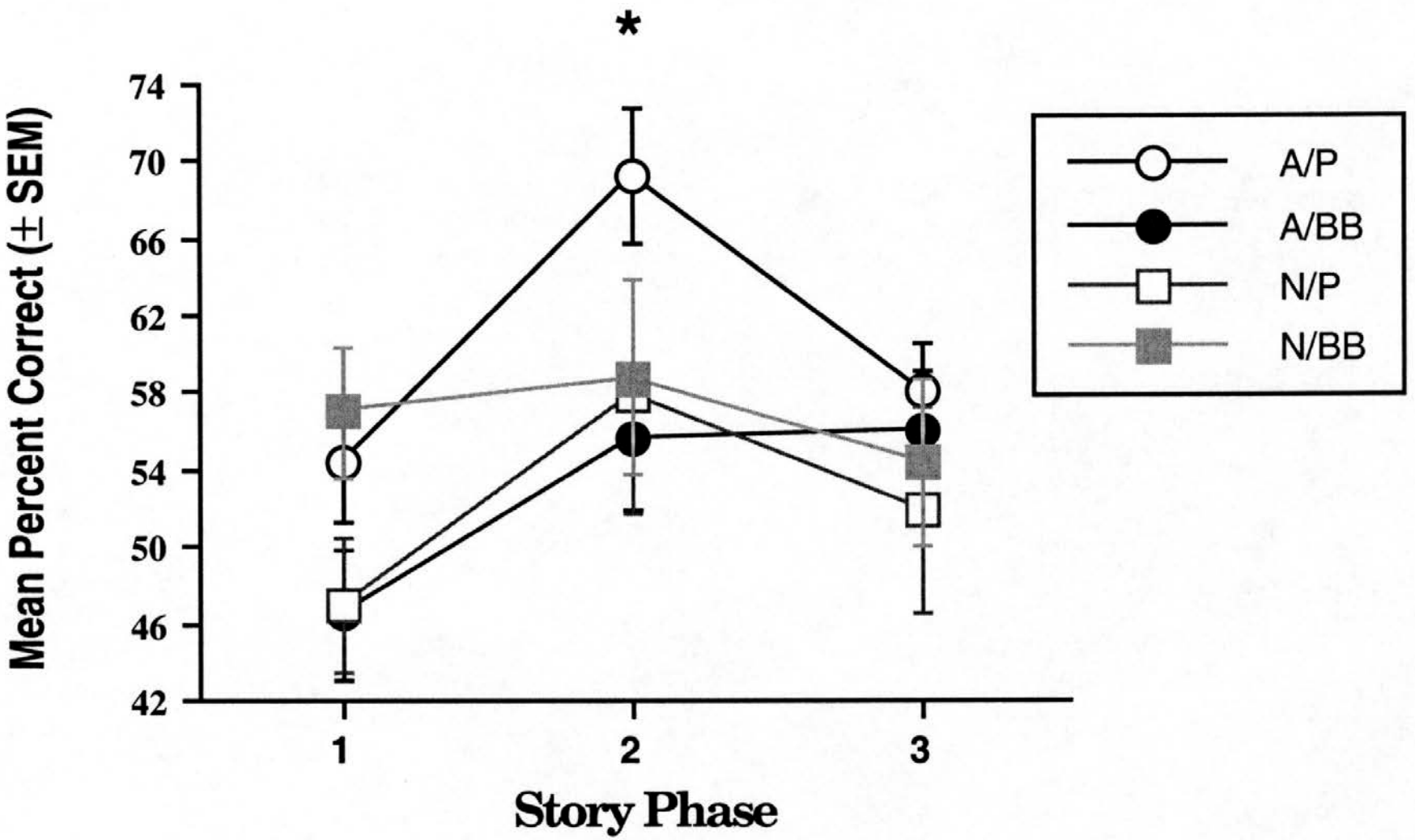
Cahill and McGaugh, 1990, Behavioral Neuroscience

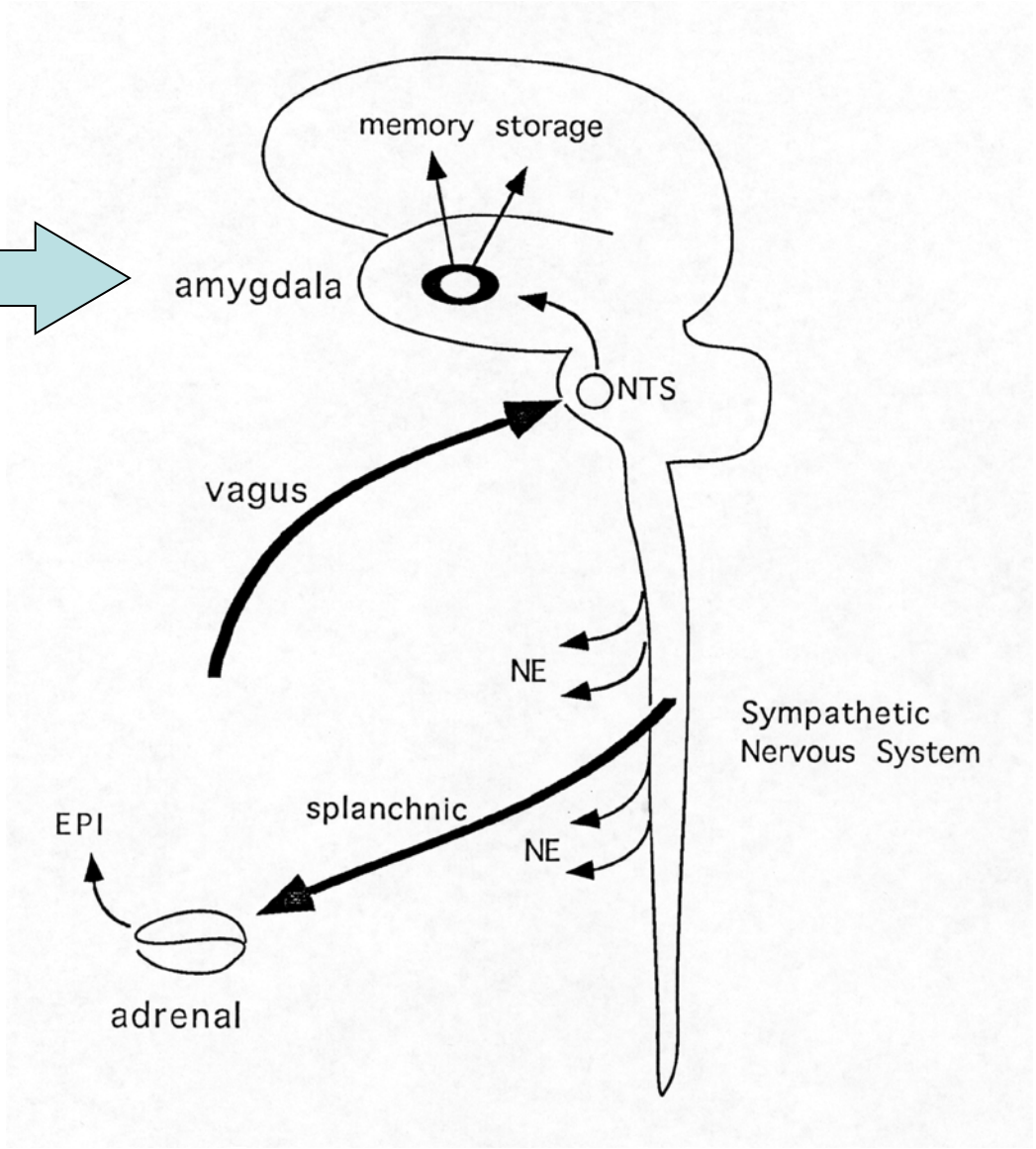
4 Human Imaging Studies contrasting valence and arousal vis-à-vis amygdala:

Small et al 2003, Neuron 2003	Arousal
Anderson et al, Nat Neurosci 2003	Arousal
Kensinger and Corkin, PNAS 2004	Arousal
Lewis et al, Cerebral Cortex, 2006	Arousal

ANIMAL ⟷ **HUMAN**




*
74
70
66
62
58
54
50
46
42
Mean Percent Correct (± SEM)
1
2
3
Story Phase
A/P
A/BB
N/P
N/BB


memory storage
amygdala
NTS
vagus
NE
Sympathetic
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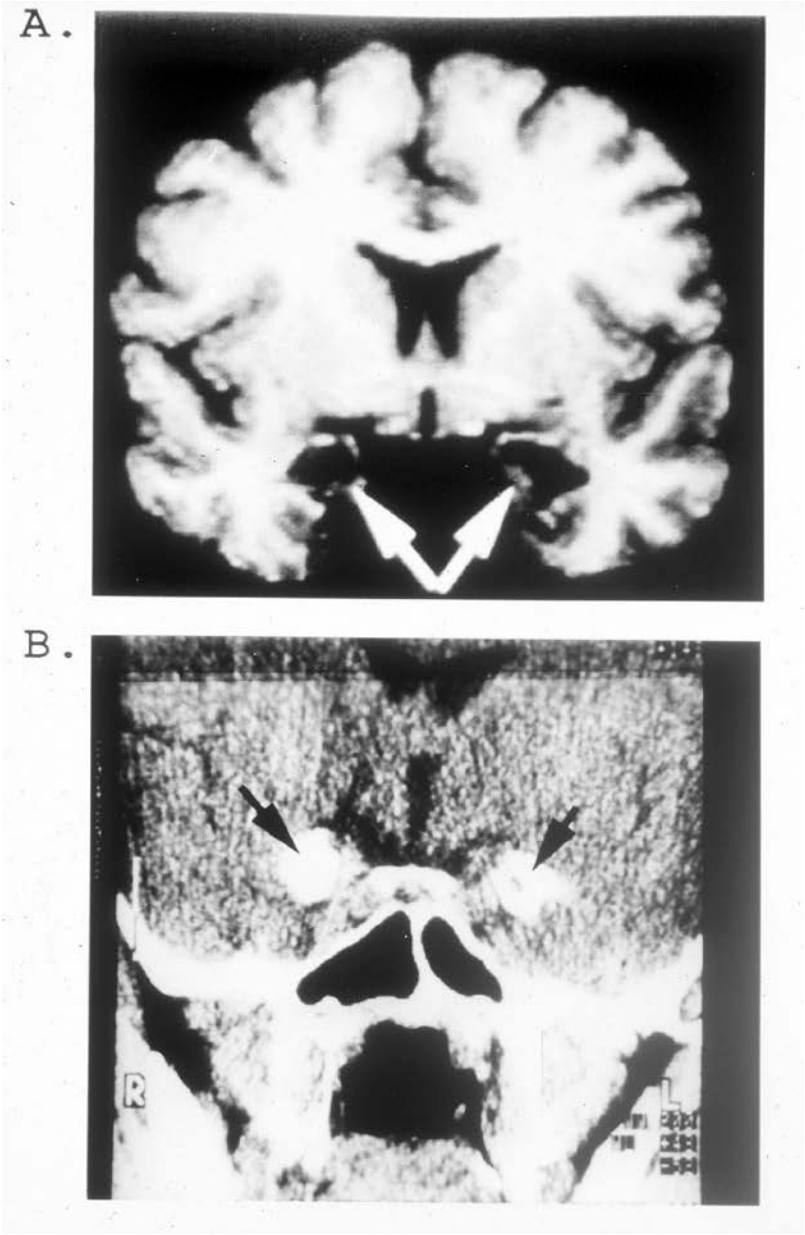
adrenal



Ralph Babinsky, Ralph Adolphs

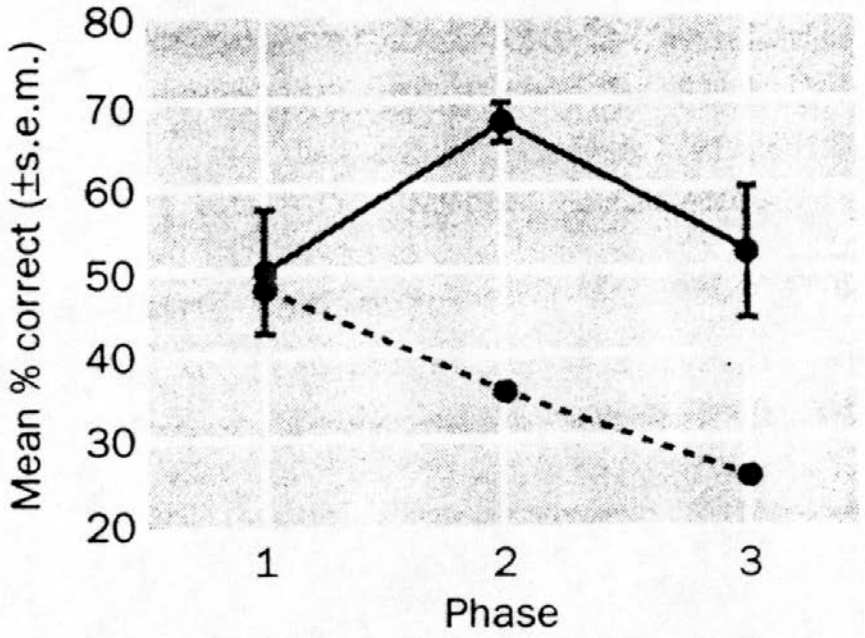
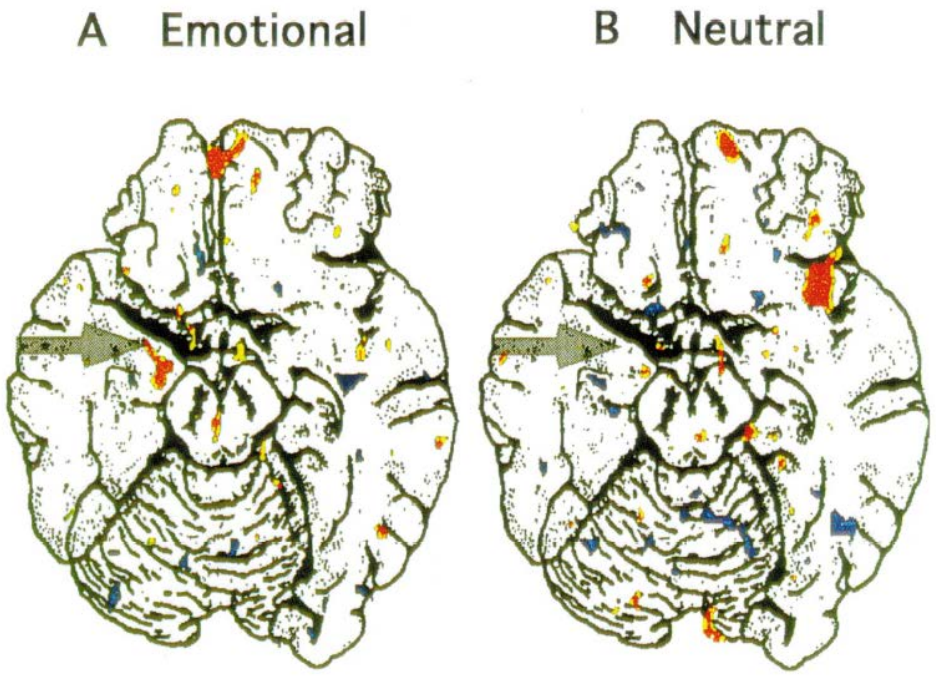
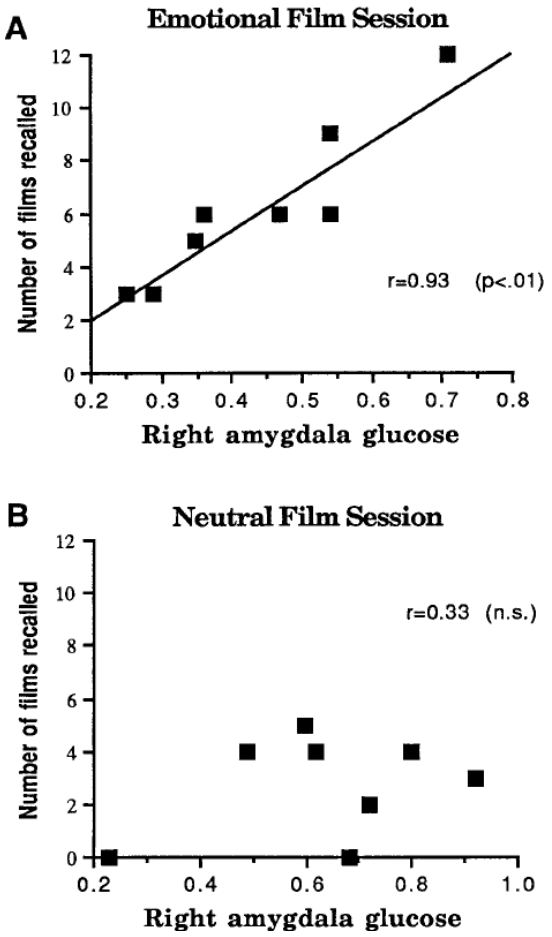


FIG. 2 Memory test performance for controls (solid line; n=6) and patient B.P (dotted line). Controls were matched to B.P. for age (mean age, 34.8±1.5 yr; B.P. age, 37 yr) and for education (mean number of school years, 10.5±0.67; B.P., 10 yr). Controls show the expected increase in memory for phase 2 of the story, in which the strong emotional elements were introduced (phase 3 is the final phase of the story).

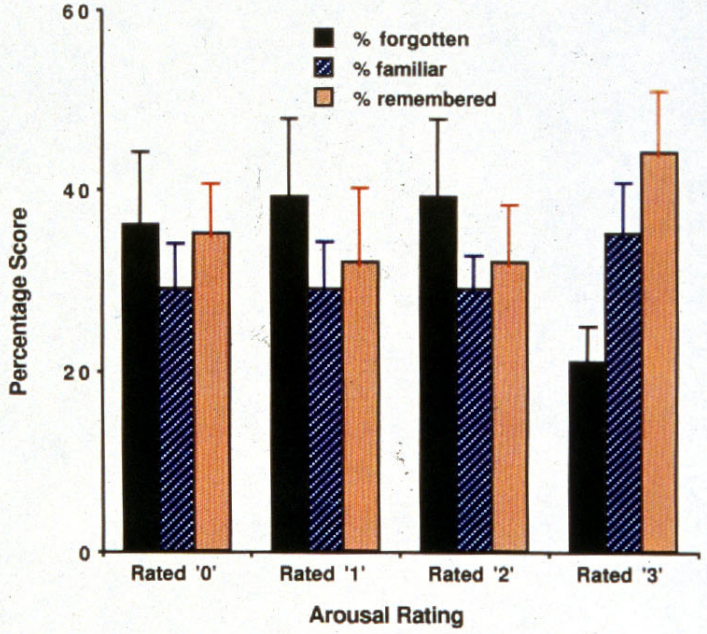




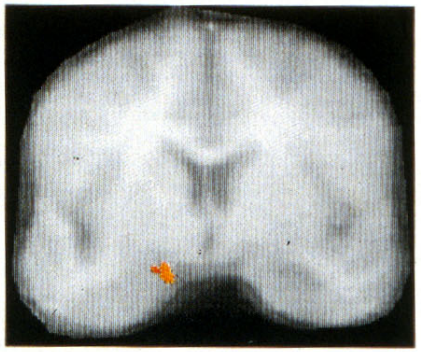
Cahill et al., 1996, Mike Alkire

Enhanced Emotional Memory Correlates With Amygdala Activation to Highly Arousing Stimuli

A

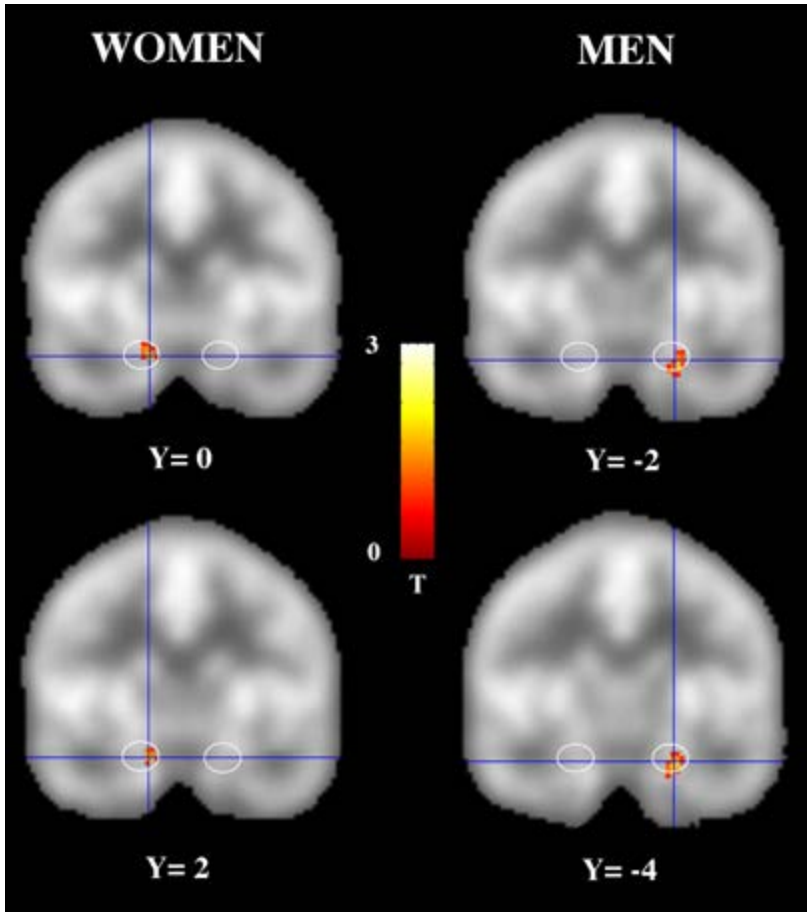


B

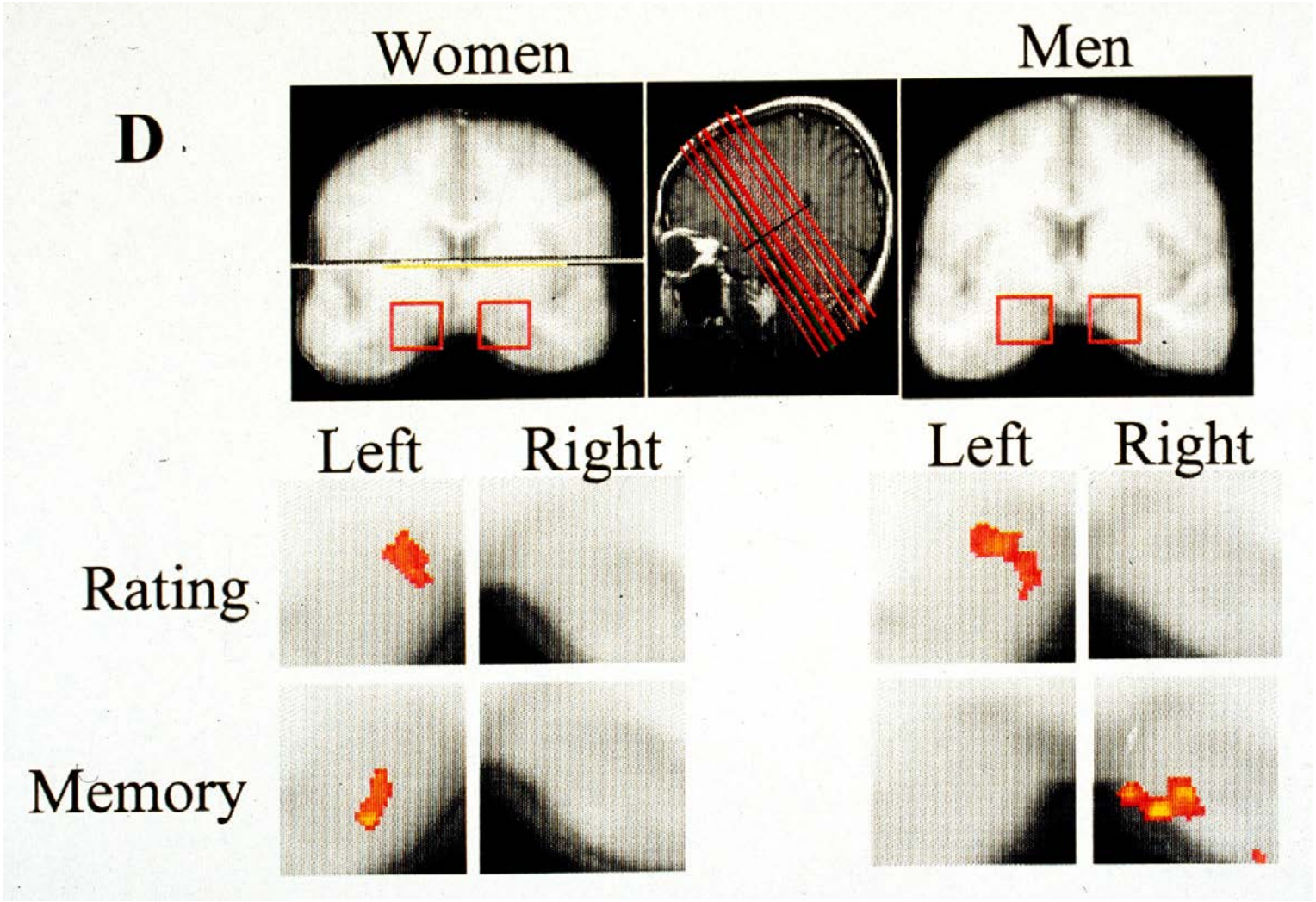


Turhan Canli
John Gabrieli

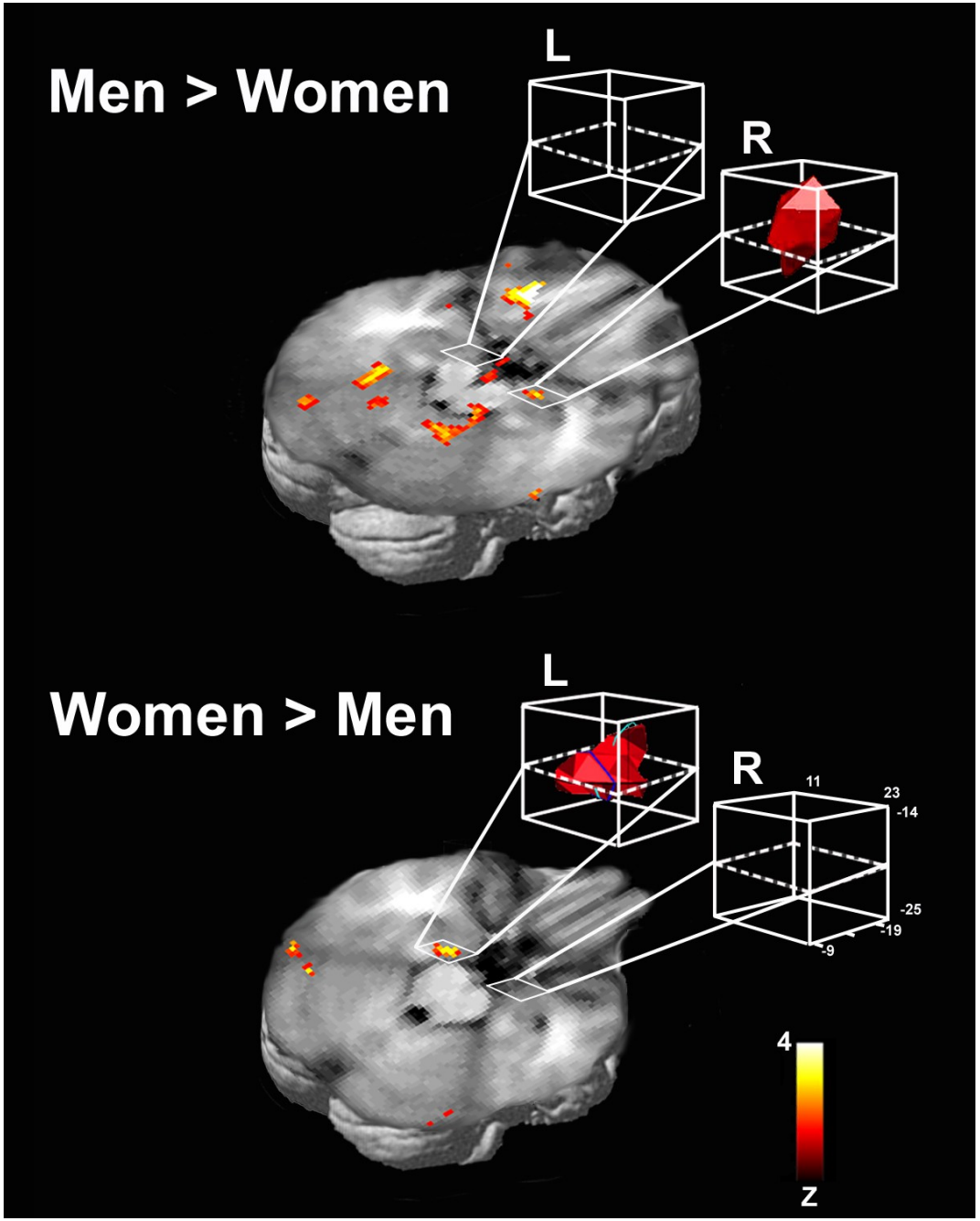
(Glucose PET)



Cahill et al., 2001



Canli et al., PNAS, 2002



Jessica Turner
Lisa Kilpatrick

Melina Uncapher

Cahill et al., 2004

Studies Relating Amygdala Activity at Encoding to Long-Term Memory for Emotionally Arousing Material

Reference	Method	Sex (M,F)	Hemisphere (R,L)
Canli et al., 1999	fMRI	F	L>R
Canli et al., 2000	fMRI	F	L
Dolcos et al., 2003	fMRI	F	L
Cahill et al. 1996	glucose PET	M	R
Hamann et al., 1999	O-15 PET	M	R>L
Kensinger et al, 2004	fMRI	F and M	L
Cahill et al., 2001 *****	glucose PET	F and M	F-L, M-R
Canli et al., 2002 *****	fMRI	F and M	F-L, M-R
Cahill et al, 2004 *****	fMRI	F and M	F-L, M-R
Mackiewicz et al 2006*****	fMRI	F and M	F-L, M-R

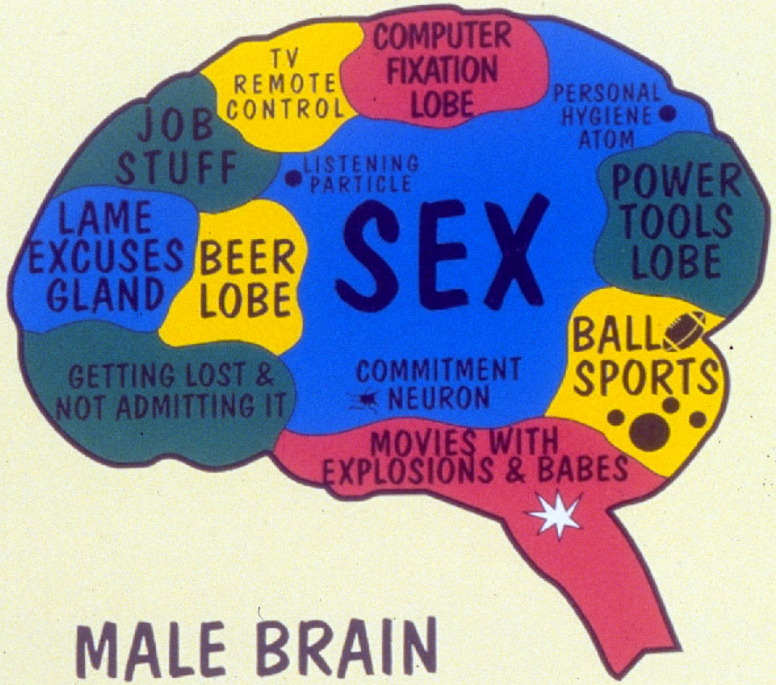
****** directly compared women and men*

WHAT DOES IT MEAN?

Sex-Related Differences in Brain and Cognition

"Why Sex Matters for Neuroscience"
Nature Neuroscience Reviews, June 2006

FEMALE BRAIN



MALE BRAIN


Man
ON
OFF
Woman
ON
OFF

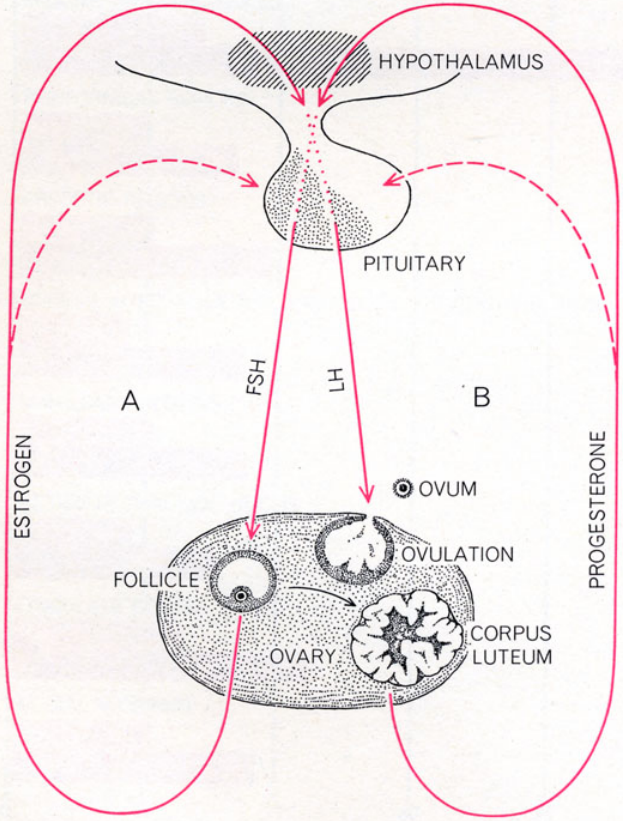

Difference between
men and women

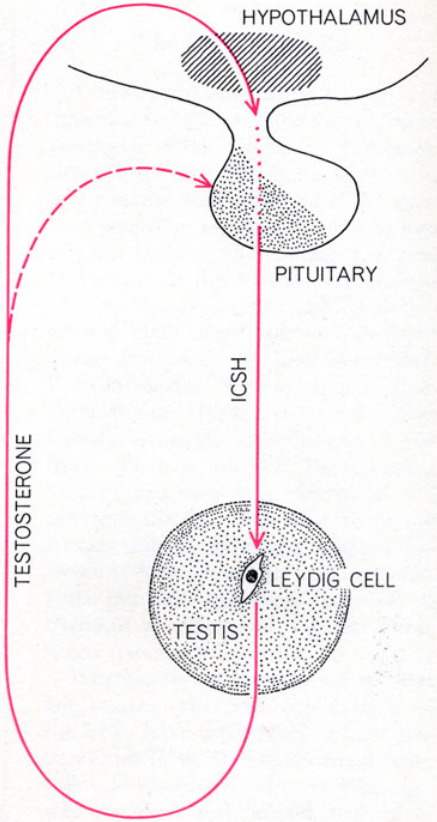
SEX DIFFERENCES IN THE BRAIN

SEYMOUR LEVINE

April 1966

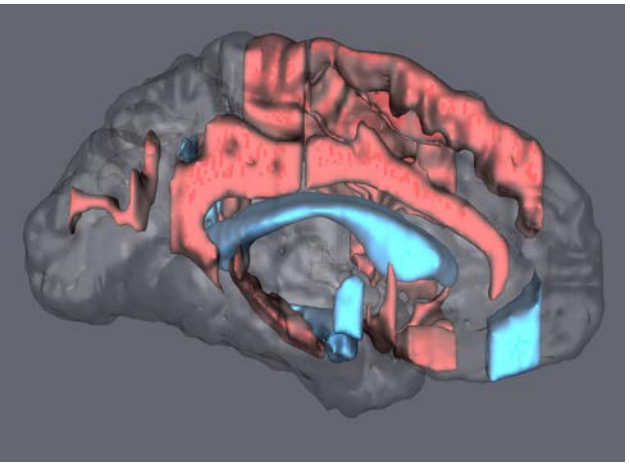
What makes a male mammal male and a female mammal female? We might sum up the answer in the word heredity, but this would evade the question. How is the genetic information translated into the differentiation of the sexes, as expressed in their physiology and behavior? Again we might summarize the answer in a single word: hormones. Recent investigations have revealed, however, that sexual differentiation in mammals cannot be explained solely in terms of hormones. There is now considerable evidence that the brain is also involved. According to this evidence there are distinct differences between the male brain and the female brain in a mammal, differences that determine not only sexual activity but also certain other forms of behavior.



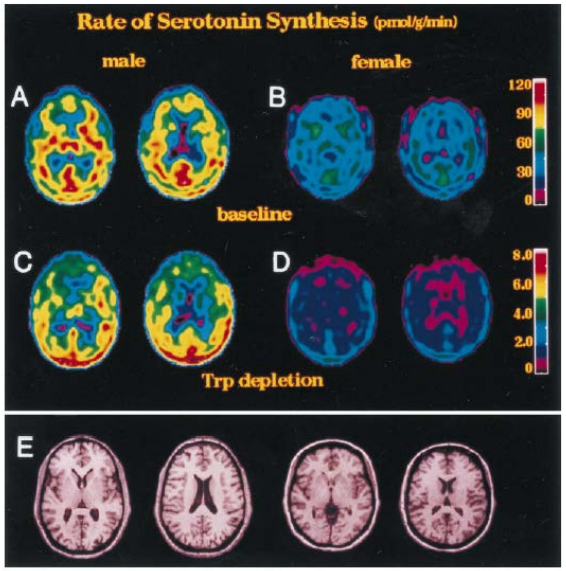


SEX DIFFERENCES AT ALL LEVELS OF NEUROSCIENCE

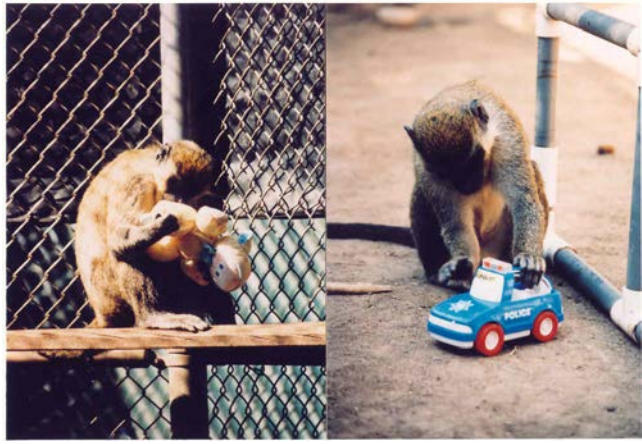
Human Anatomy



Human Neurochemistry

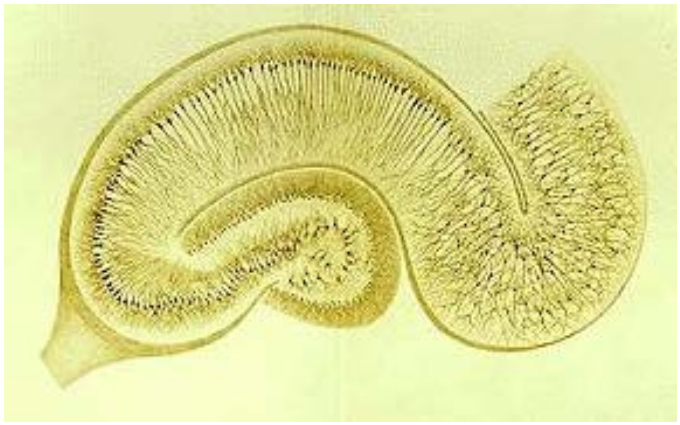


Primate Play Behavior

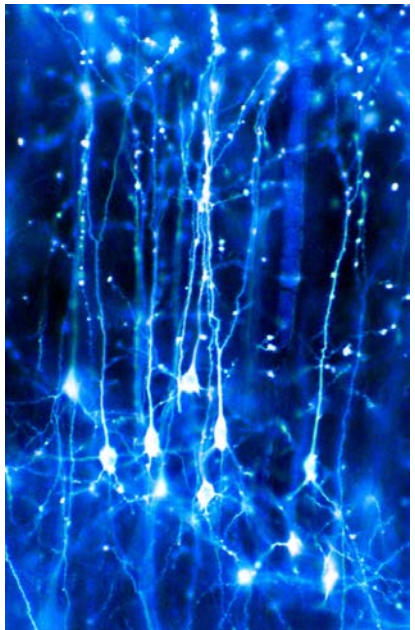


Transgenic Mice

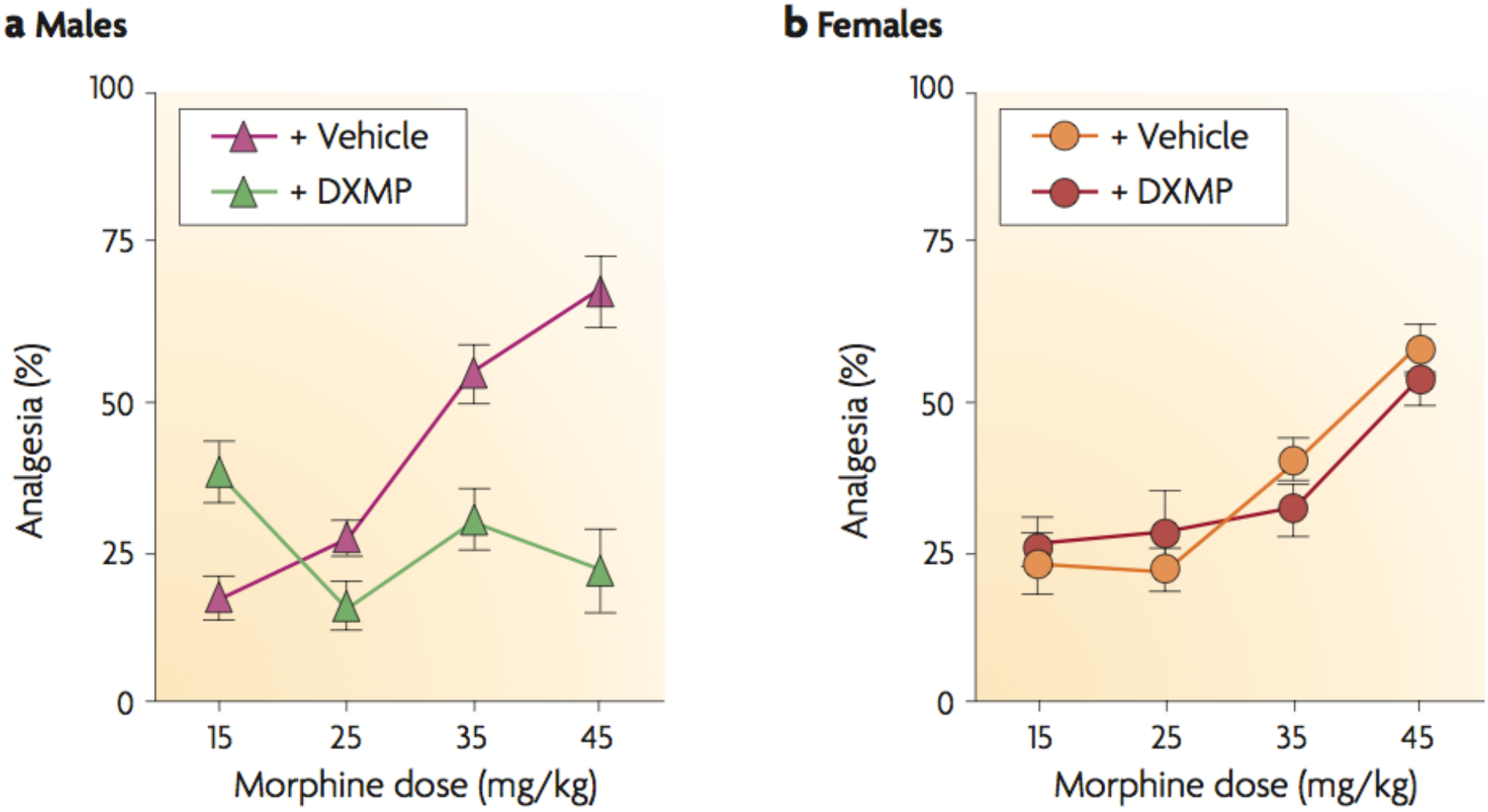
Hippocampus



Cell Culture!



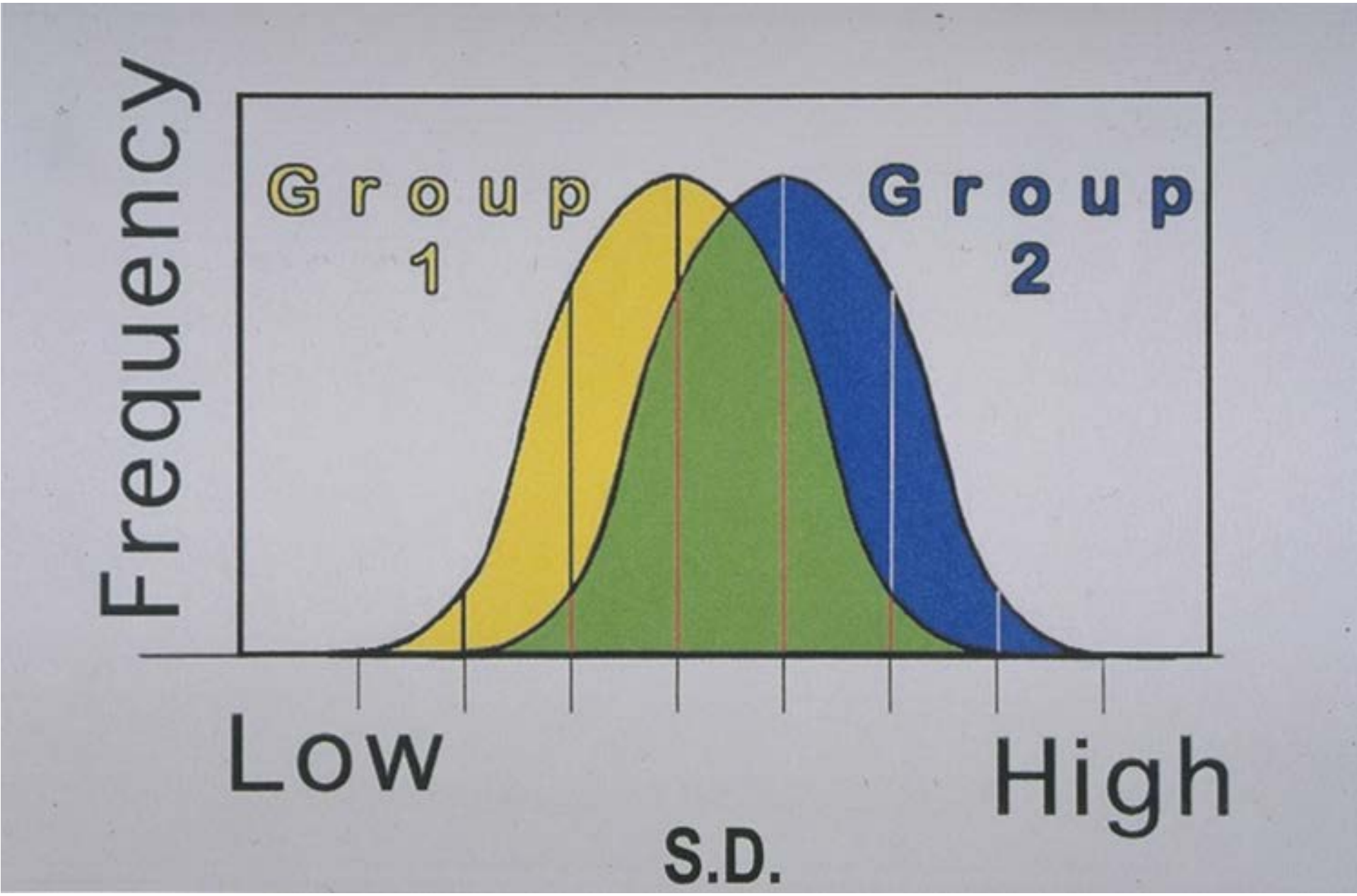
Are sex influences on brain function “fundamental?”



Jeffrey Mogil, McGill University

Given these facts, one might argue that basic scientists are shirking their responsibilities to half of the human population by avoiding the use of direct animal models of them. We simply do not see any valid excuses remaining for the continued exclusion of female rodents from basic science studies of pain.

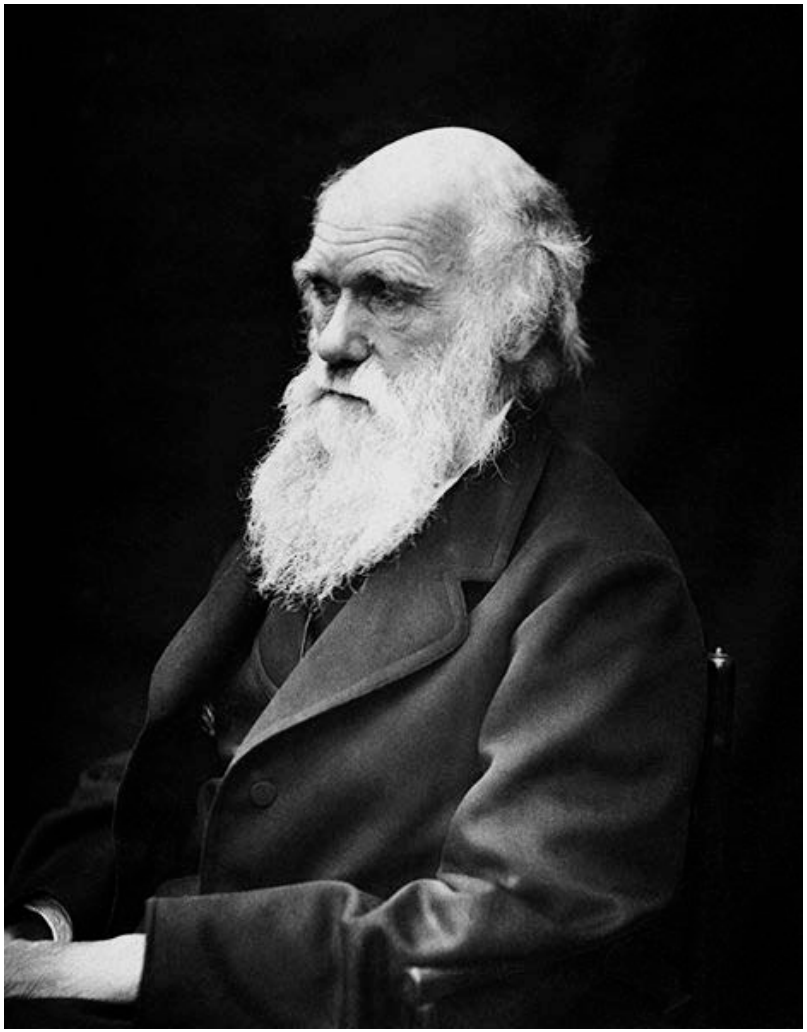
Mogil et al., 2005


Frequency
Group 1
Group 2
Low
High
S.D.

Natural Selection

Did NOT

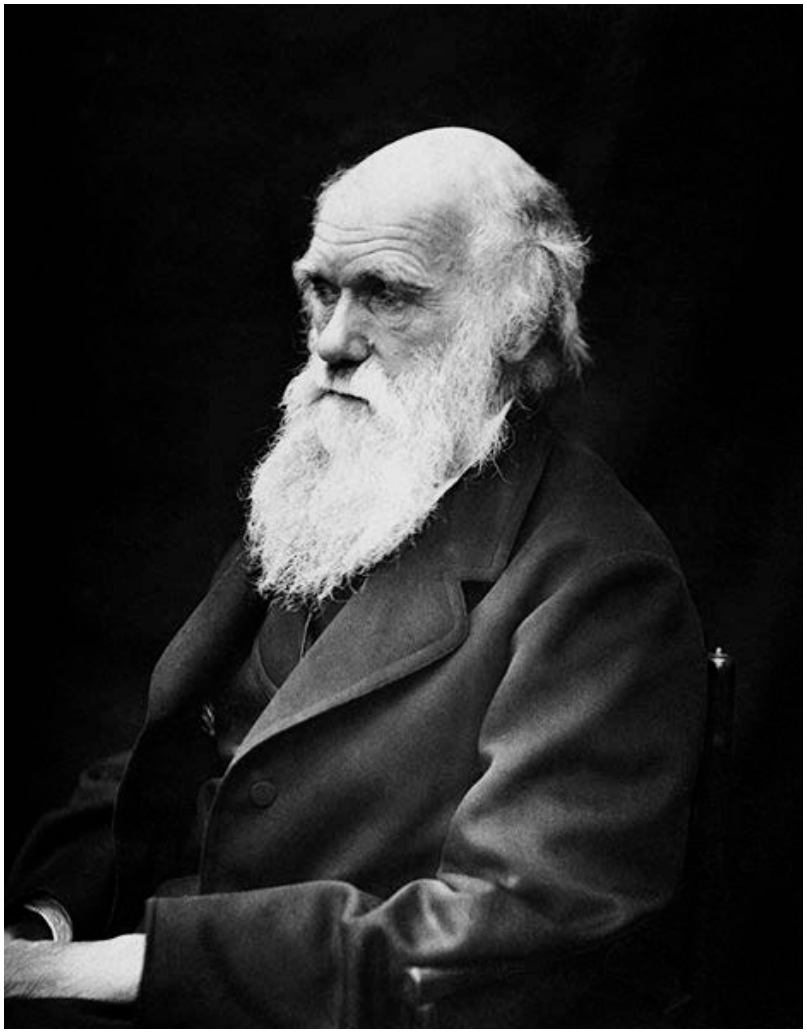
Drive Evolution

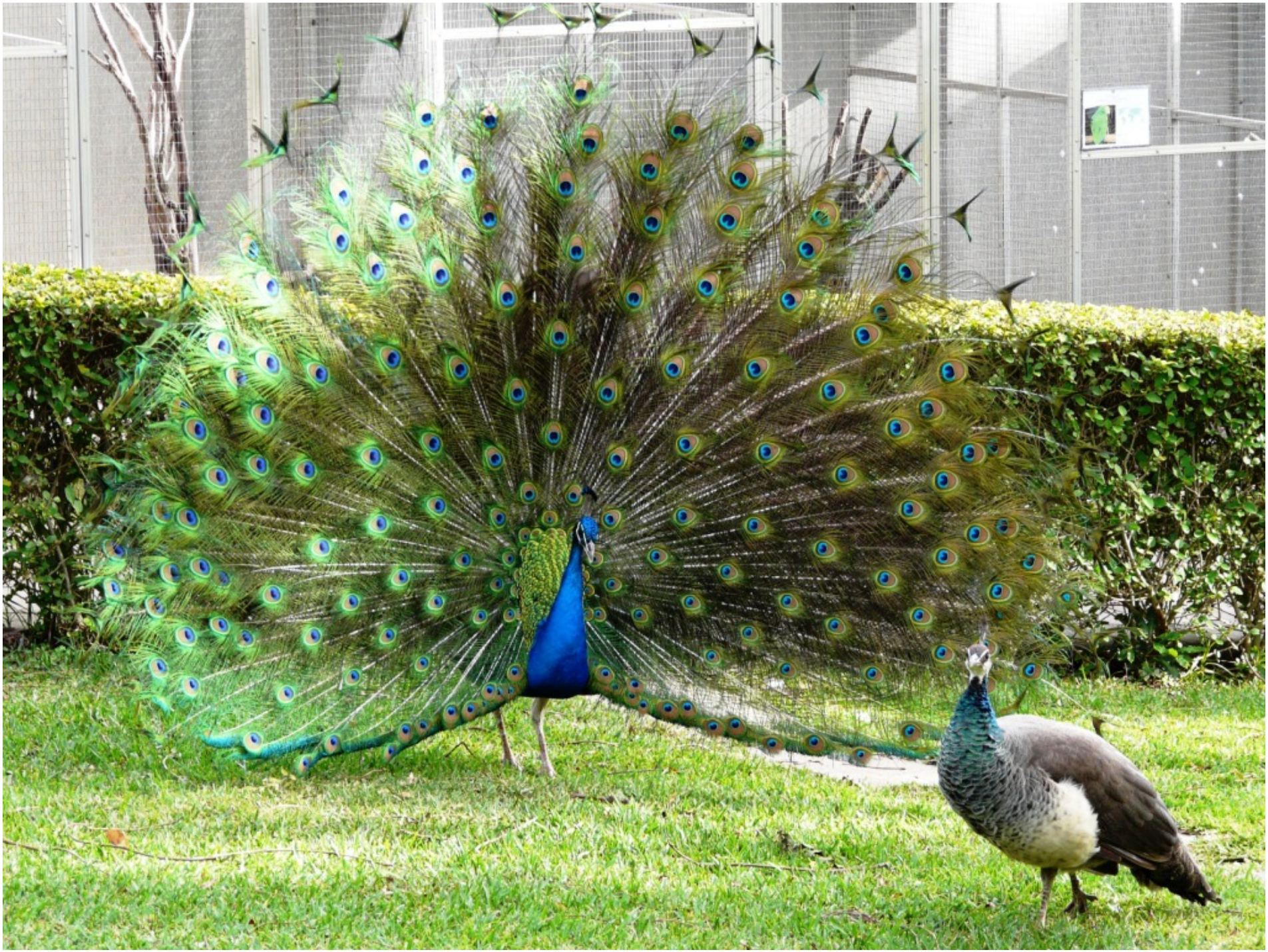


Natural Selection

And Sexual Selection

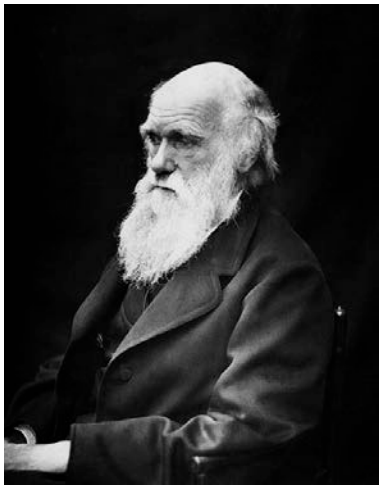
Drove Evolution





Pyranga aestiva
“Coopers Tanager”

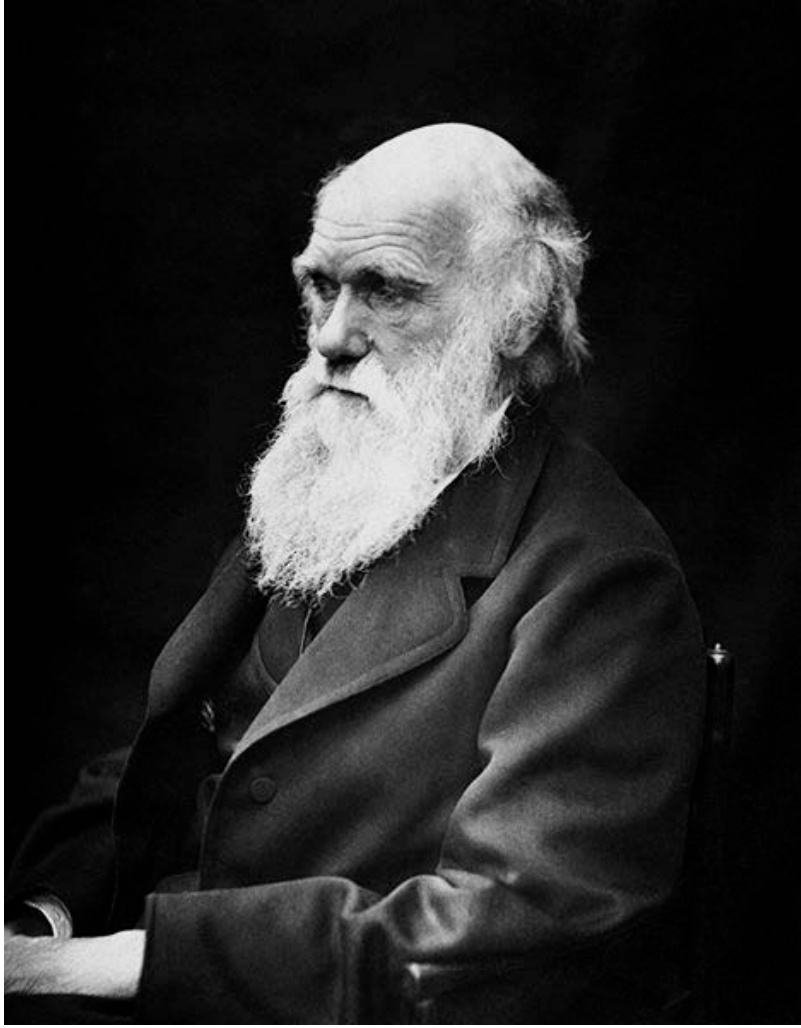
(Summer Tanager,
pyranga rubra)



“…one of the most splendid birds of the United States… now if brilliant colors had been extremely dangerous to the birds whilst sitting in their open nests, the males in these cases could have suffered greatly. It might, however, be of such paramount importance to the male to be brilliantly colored, in order to beat his rivals, that this may have more than compensated for some additional danger.”

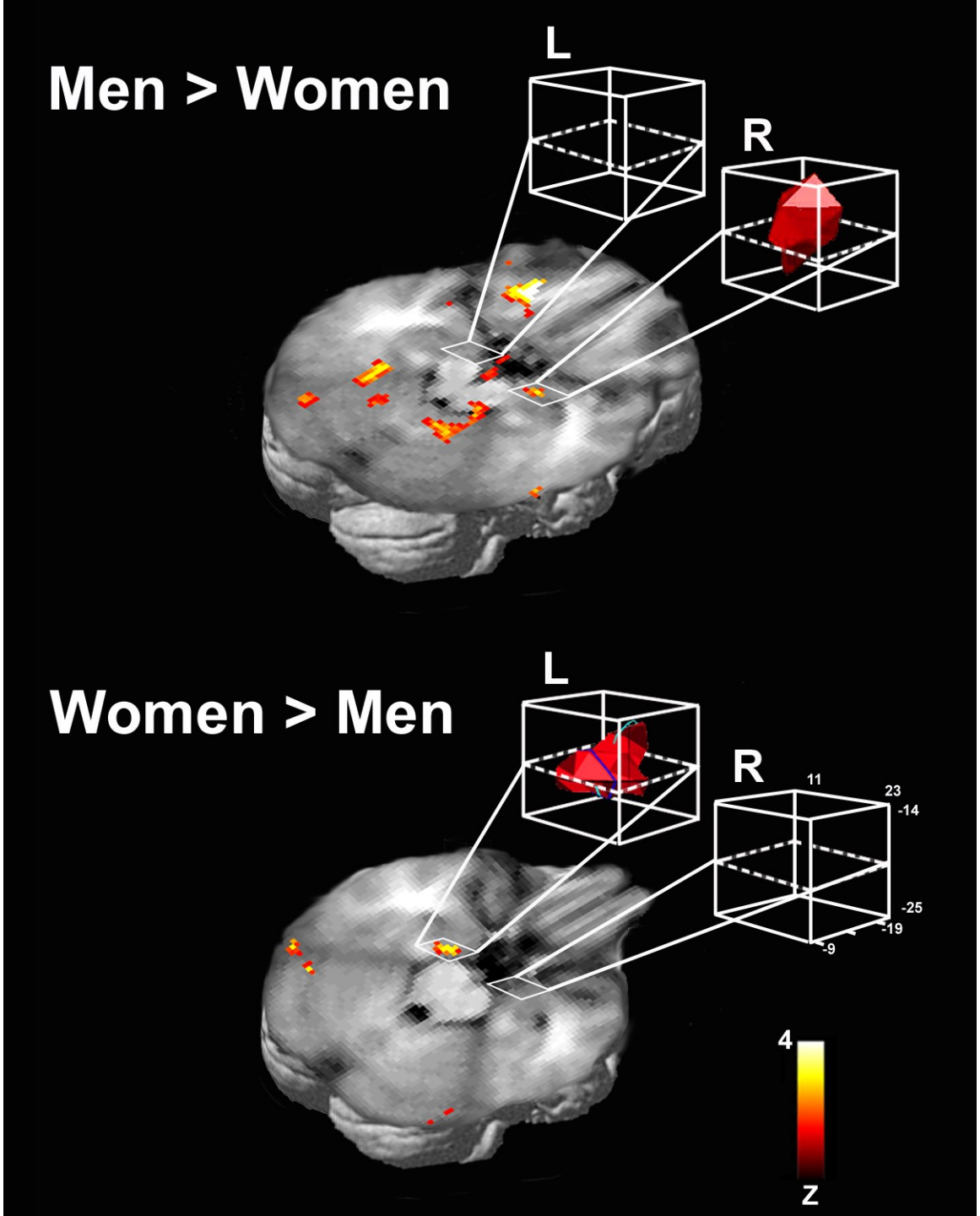
“Descent of Man and Selection in Relation to Sex”, 2nd Ed, 1875, page 453

“It has been said by several critics that when I found that many details of the structure of man could not be explained by natural selection, I invented sexual selection; I gave, however, a tolerably clear sketch of this principle in the first edition of “Origin of Species,” and there I stated it was applicable to man…I have been struck with the likeness of many of the half-favourable criticisms on sexual selection, with those which appeared at first on natural selection; such as, that it would explain some few details, but certainly was not applicable to the extent to which I have employed it. My conviction in the power of sexual selection remains unshaken.”

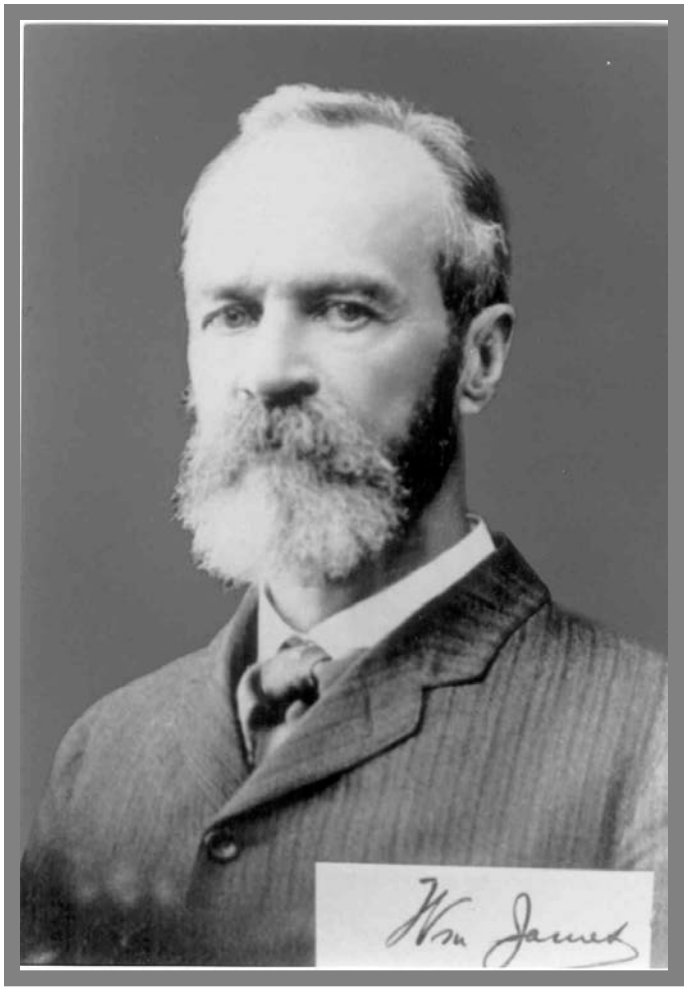


“Descent of Man and Selection in Relation to Sex”, 2nd Ed, 1875, Preface to the Second Edition, page vi.

(fMRI)

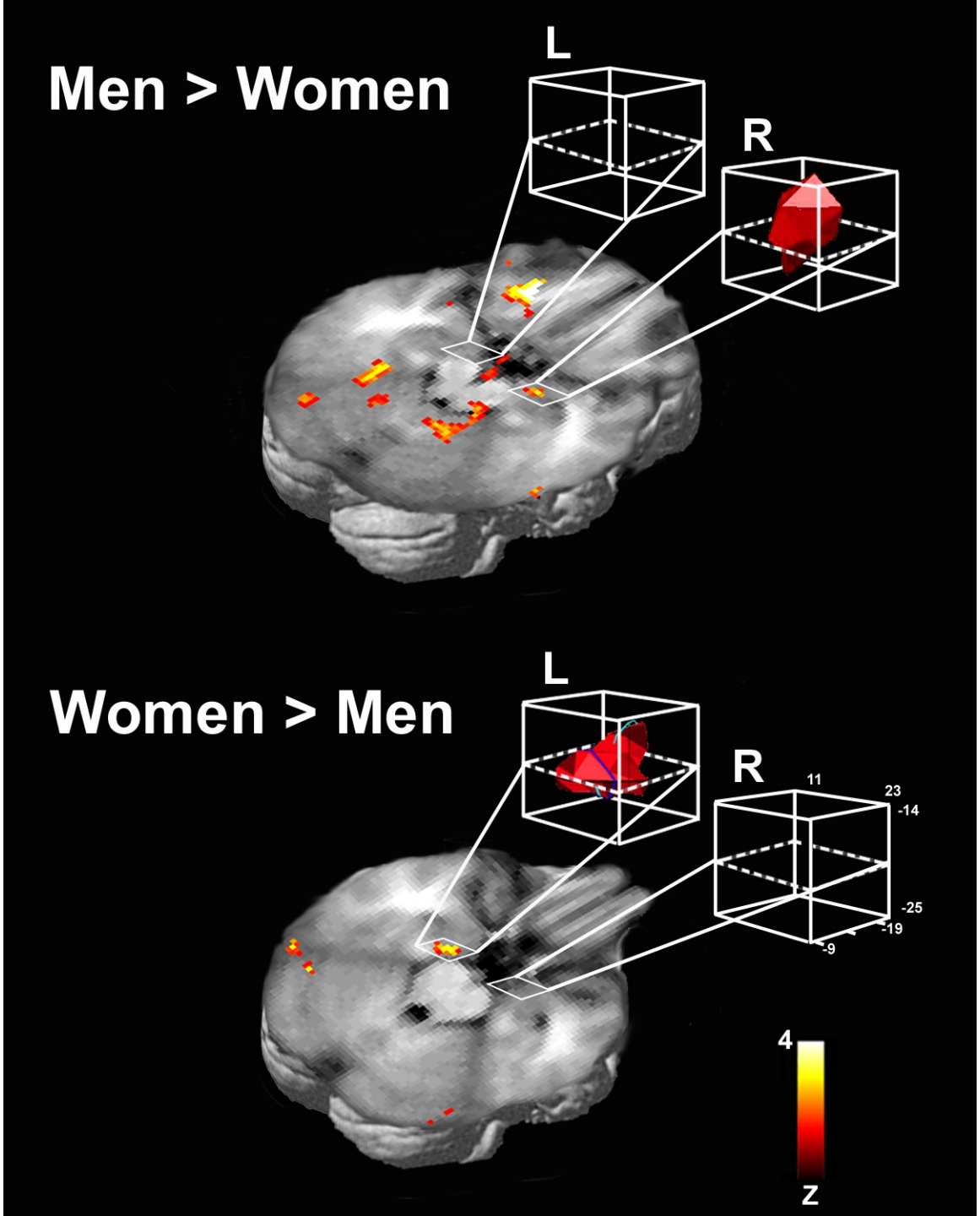


“The great field for new discoveries...is always the unclassified residuum. Round about the accredited and orderly facts of every science there ever floats a sort of dust-cloud of exceptional observations, of occurrences minute and irregular and seldom met with, which it always proves more easy to ignore than to attend to. The ideal of every science is that of a closed and complete system of truth... Phenomena unclassifiable within the system are paradoxical absurdities, and must be held untrue...--- one neglects or denies them with the best of scientific consciences... Any one will renovate his science who will steadily look after the irregular phenomena. And when the science is renewed, its new formulas often have more of the voice of the exception in them than of what were supposed to be the rules.”

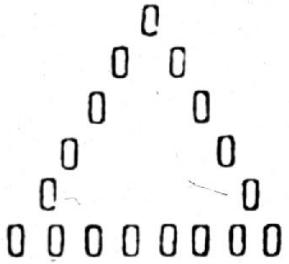


William James, *The Will to Believe*

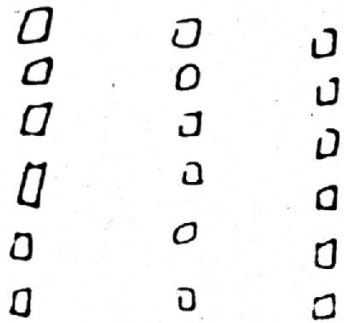
(fMRI)



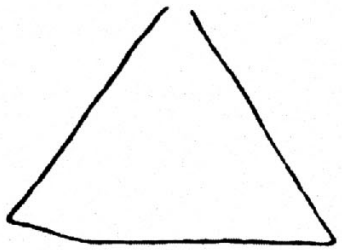
Target stimulus

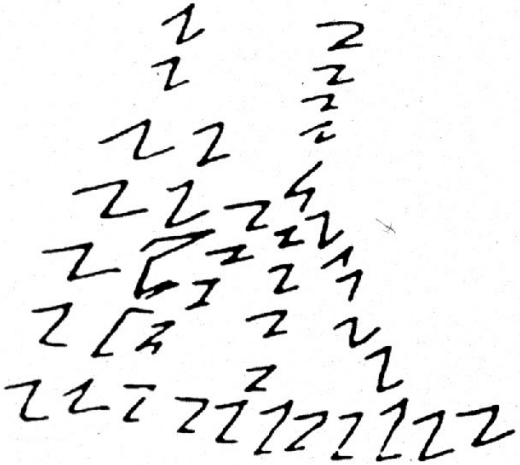


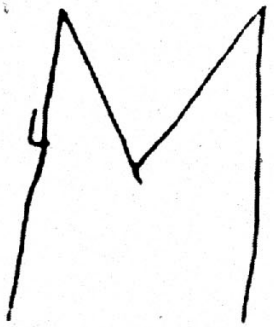
Right hemisphere lesion

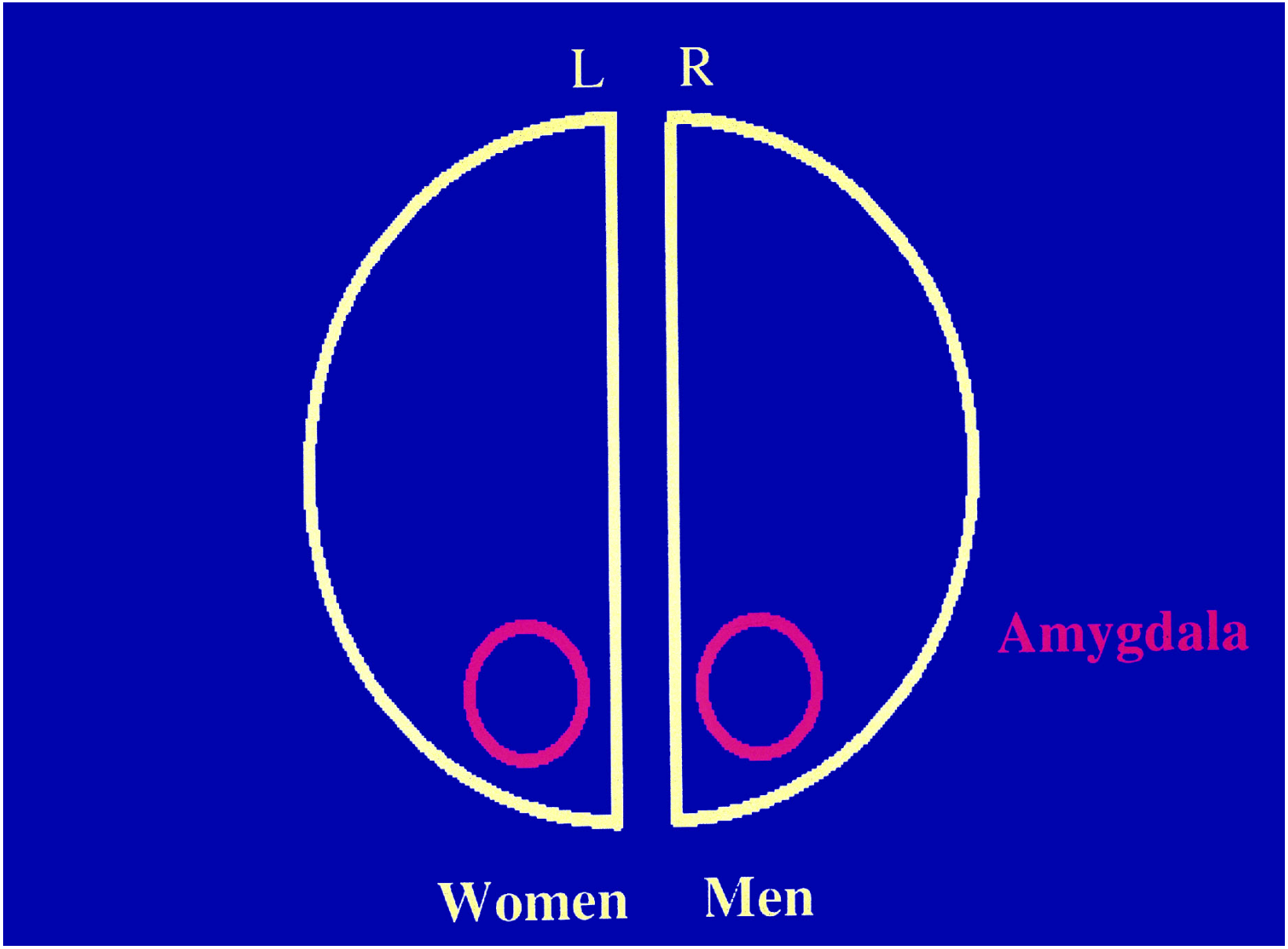


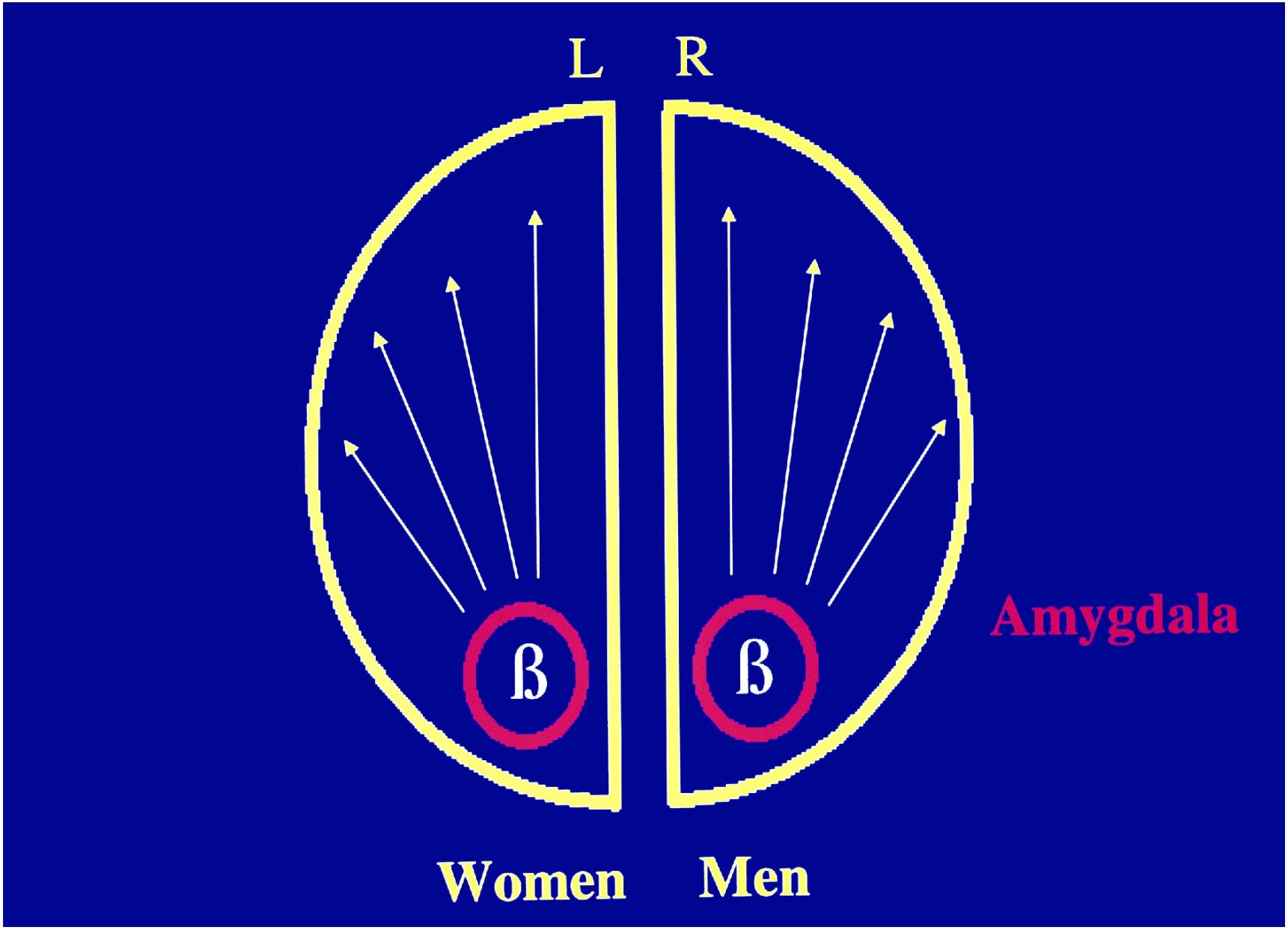
Left hemisphere lesion

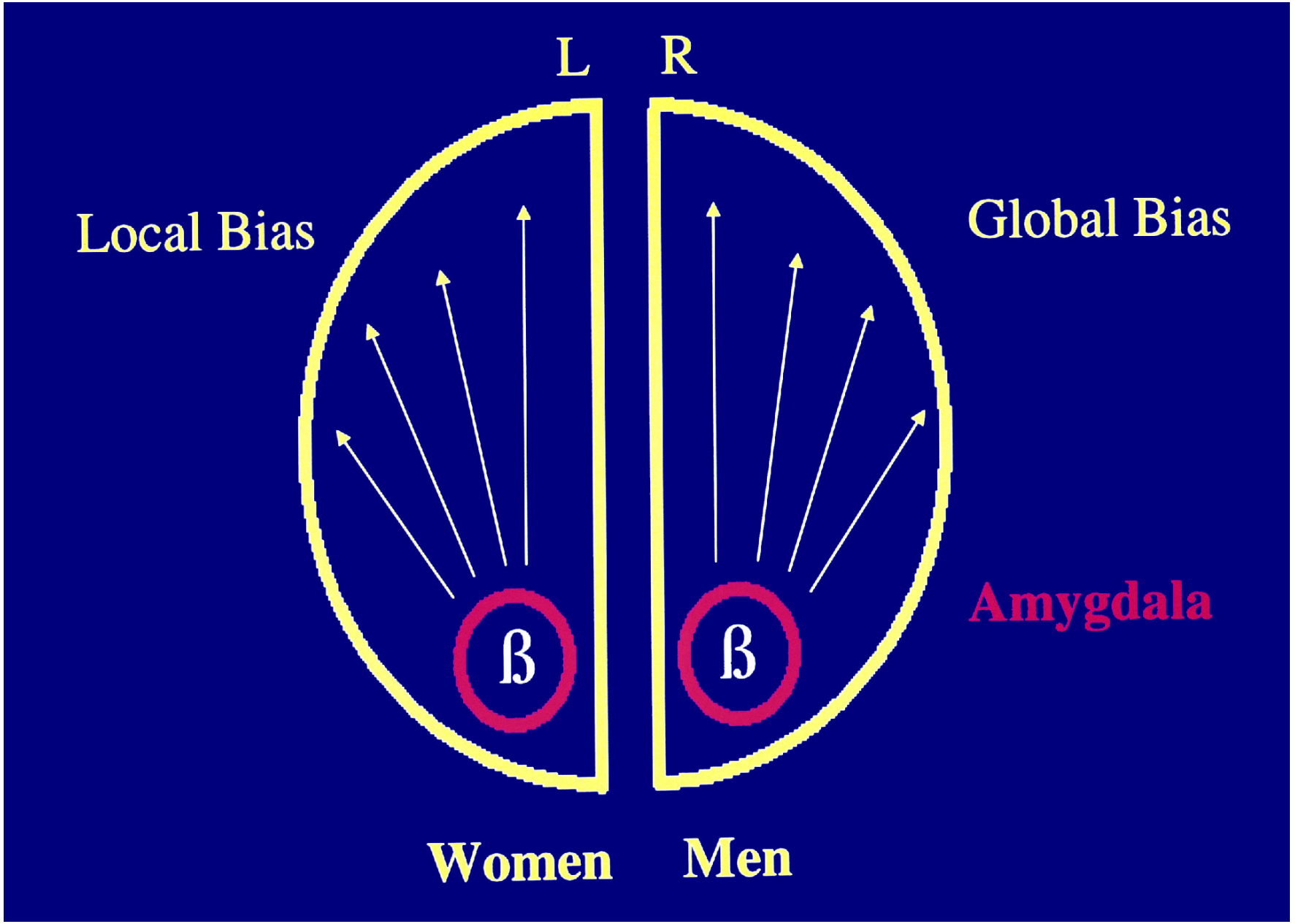




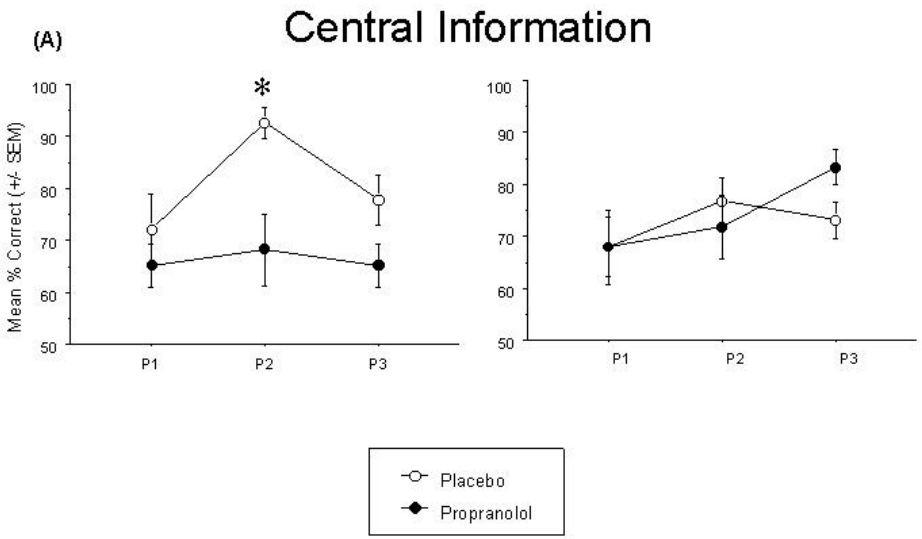


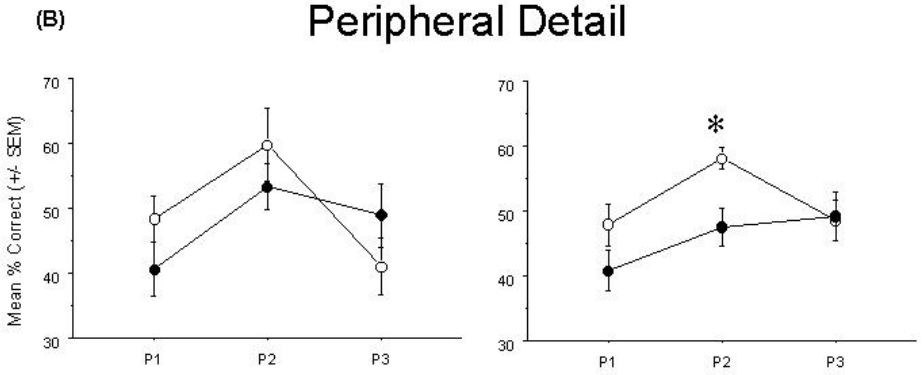

L
R
Amygdala
Women
Men


L
R
ß
ß
Amygdala
Women
Men


L
R
Local Bias
Global Bias
ß
ß
Amygdala
Women
Men

Men Women





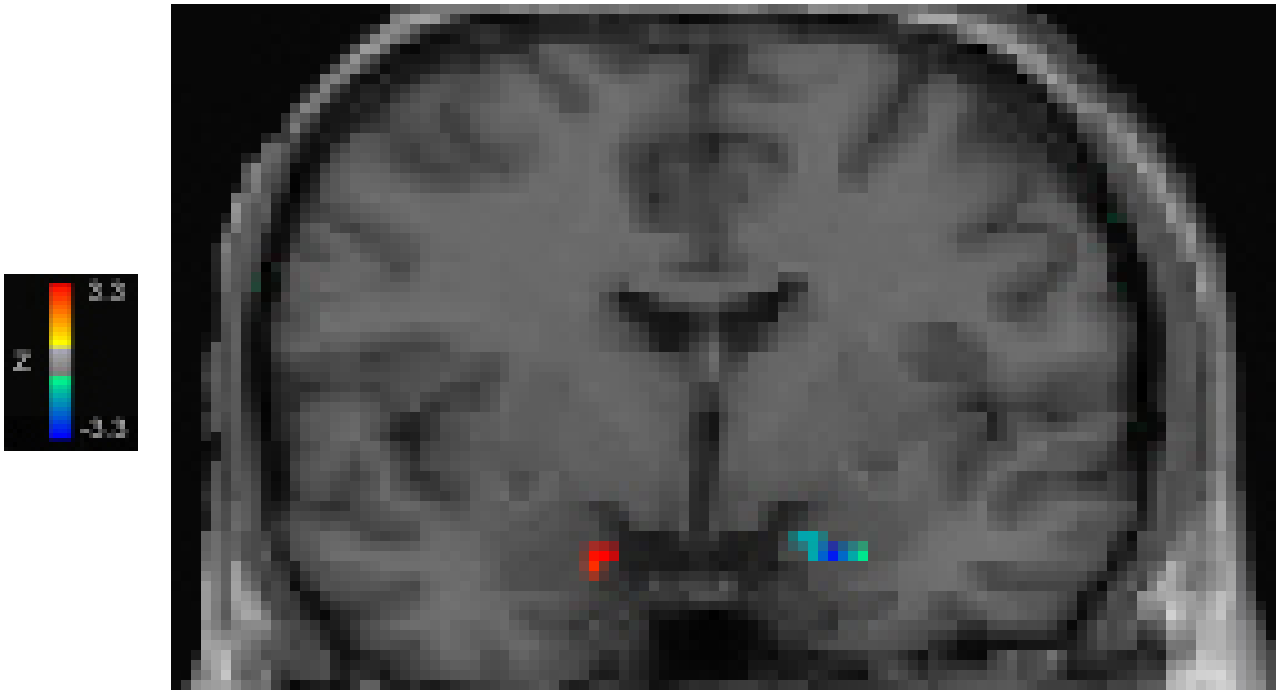
Cahill and van Stegeren, 2003

Are there sex-related differences in the functional connectivity of the left and right hemisphere amygdalae at rest?

-- Partial Least Squares Analysis of Functional Connectivity
-- O-15 scans, 36 men, 36 women
-- At rest, eyes closed

Lisa Kilpatrick

NeuroImage 2006

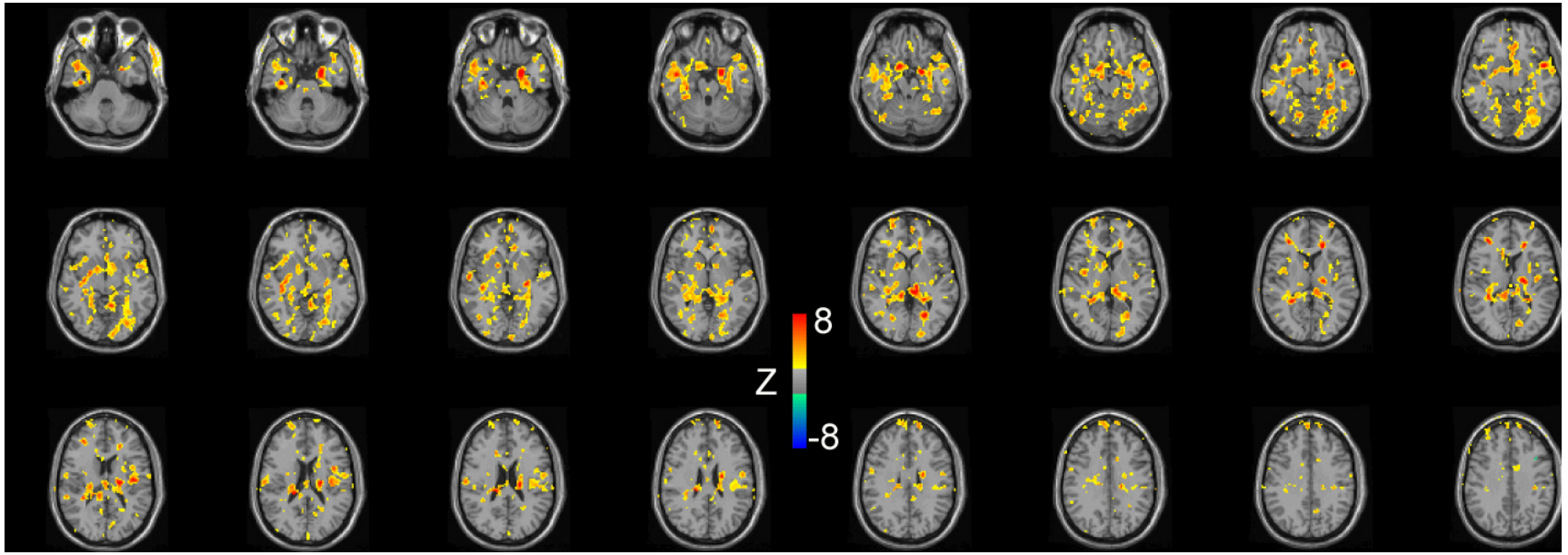


Location of Amygdala Seed Voxels Displaying Significant Sex-related Differences in Amygdala Functional Connectivity during Resting Conditions

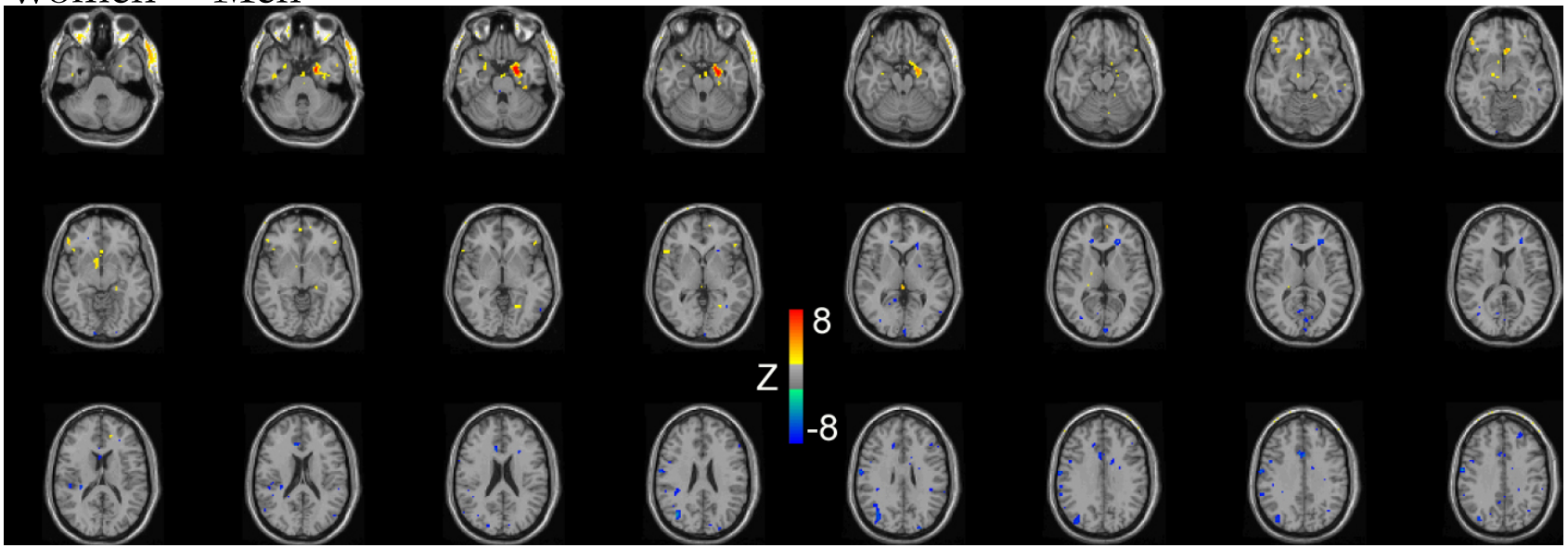
Red areas are associated with greater functional connectivity in women than in men. Blue areas are associated with greater functional connectivity in men than in women.

Sex-related differences in right amygdala functional connectivity

Men > Women

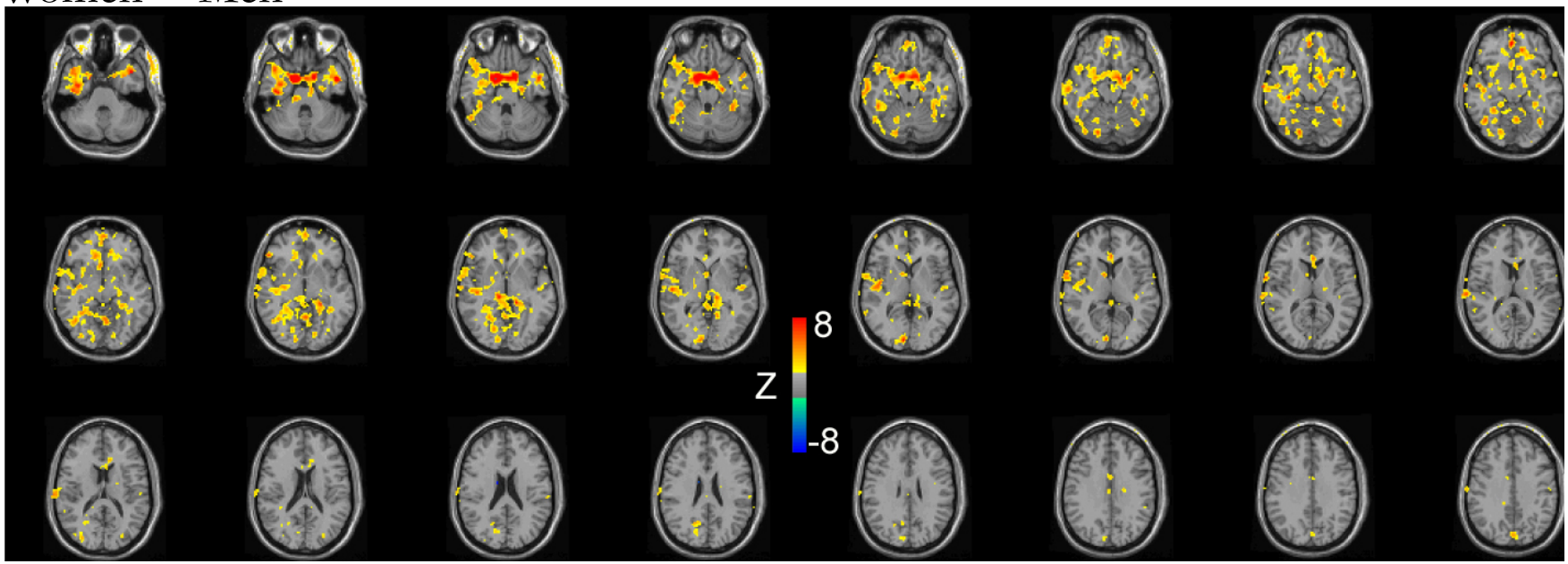


Women > Men

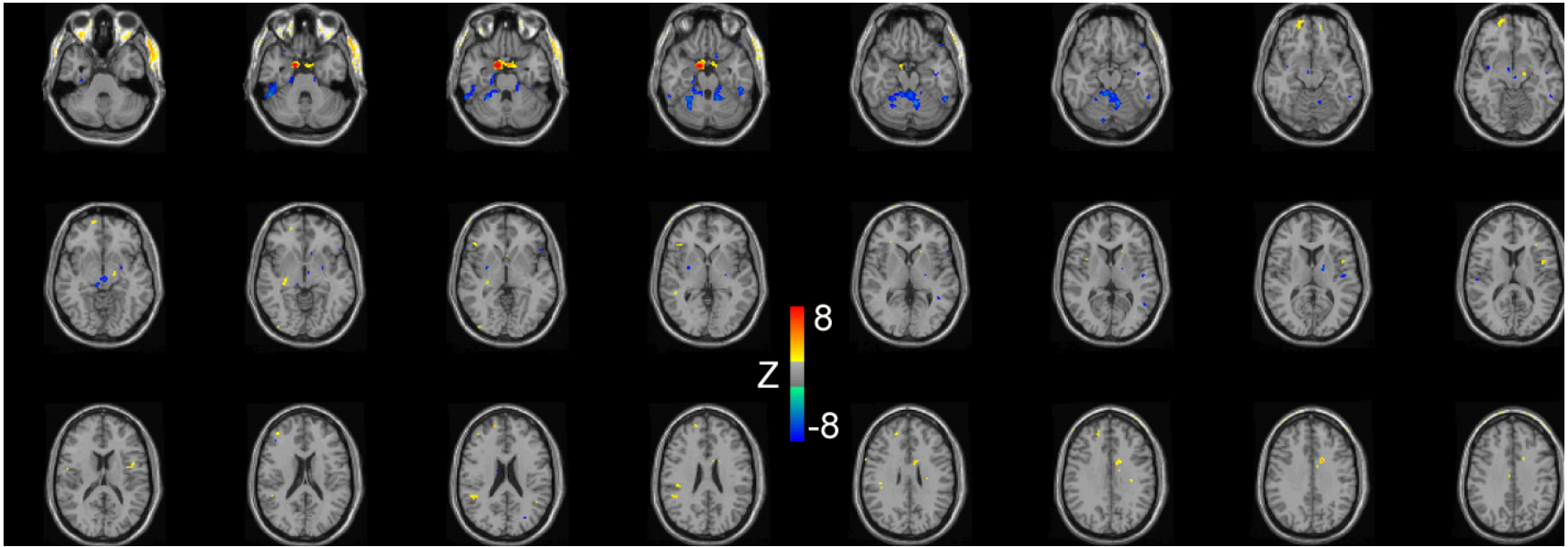


Sex-related differences in left amygdala functional connectivity

Women > Men

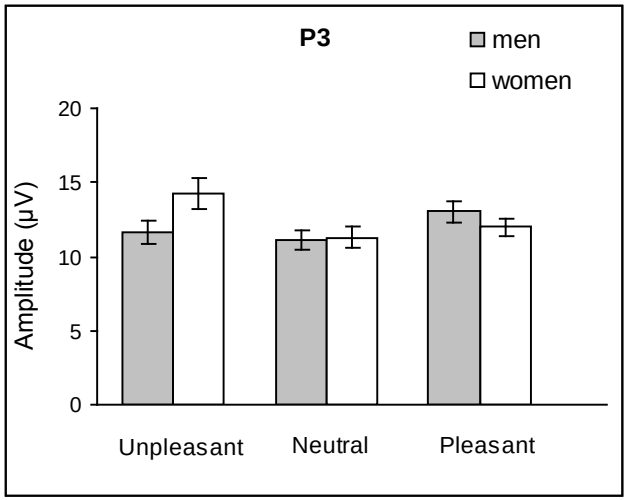


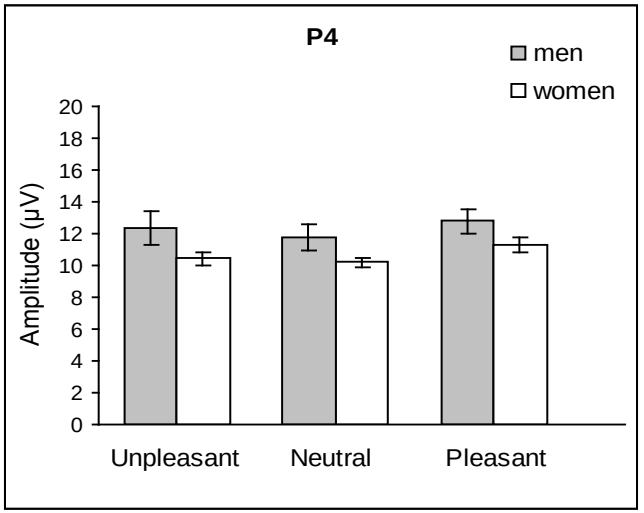
Men > Women



SEX DIFFERENCES in EEG RESPONSE to EMOTIONAL SLIDES

P300 Amplitude



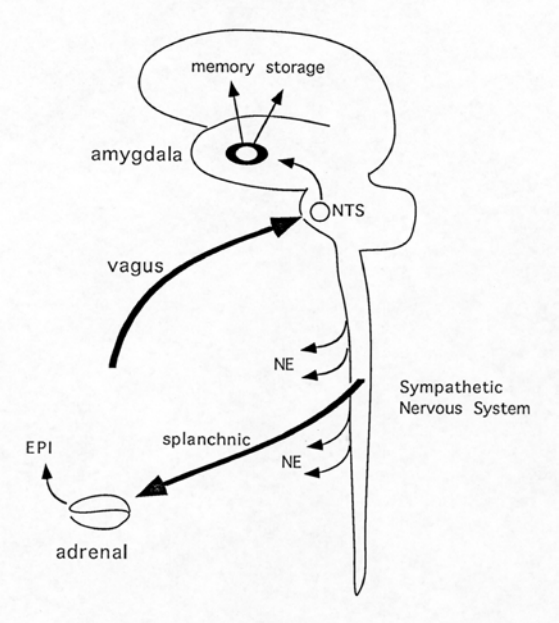


Antonella Gasbarri

Post-Learning Cold Pressor Stress Enhancing Memory Consolidation

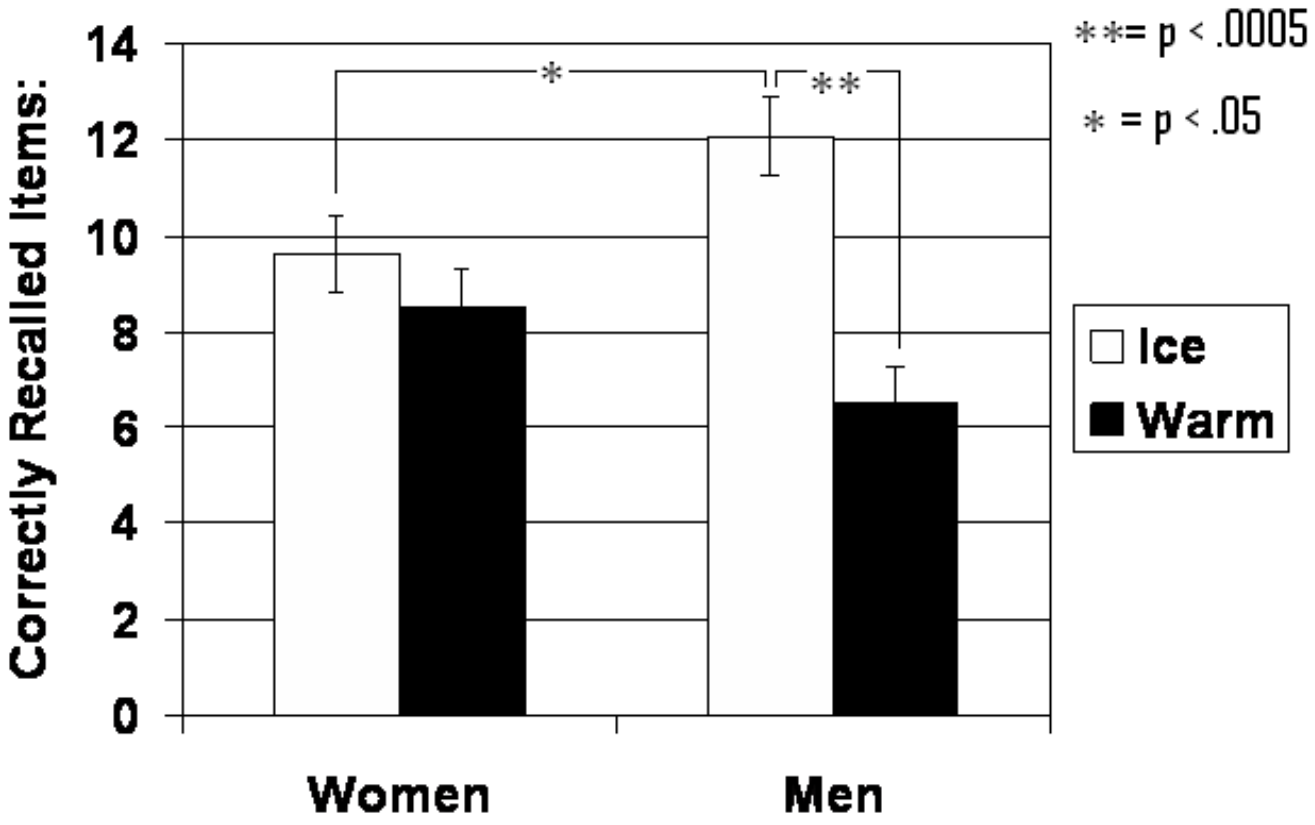
Procedure:

War of the Ghosts-- Cold Pressor Stress-- 1 Week-- Memory Test

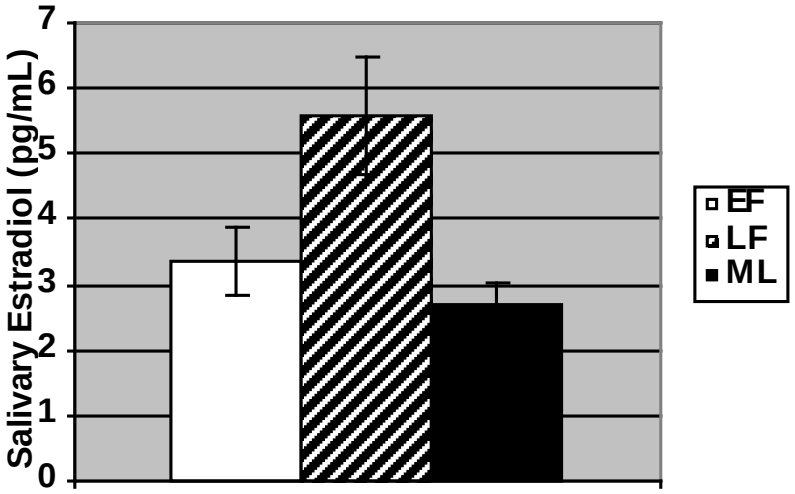


Joe Andreano

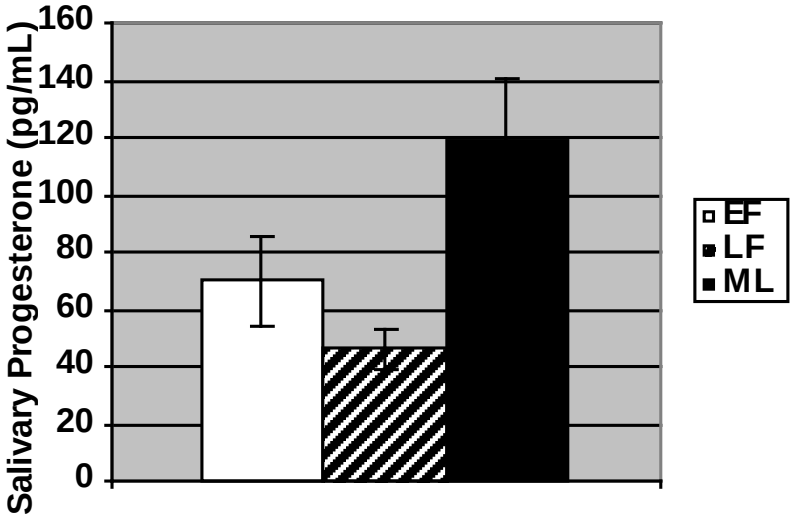
Memory Enhanced in Men but not Women



Menstrual Hormone Effect?

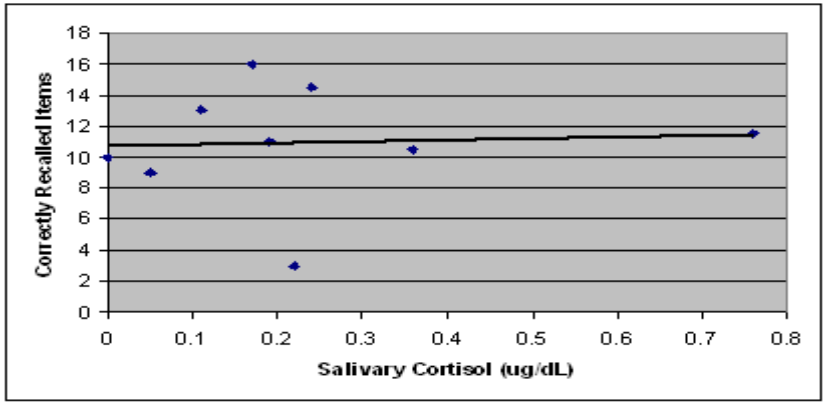


Estradiol

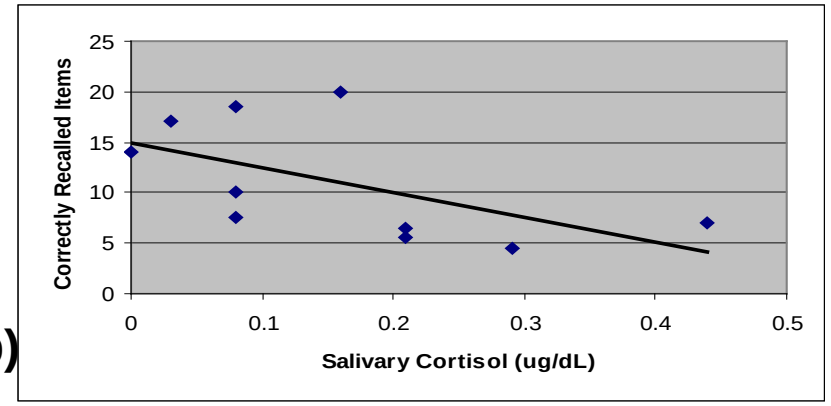


Progesterone

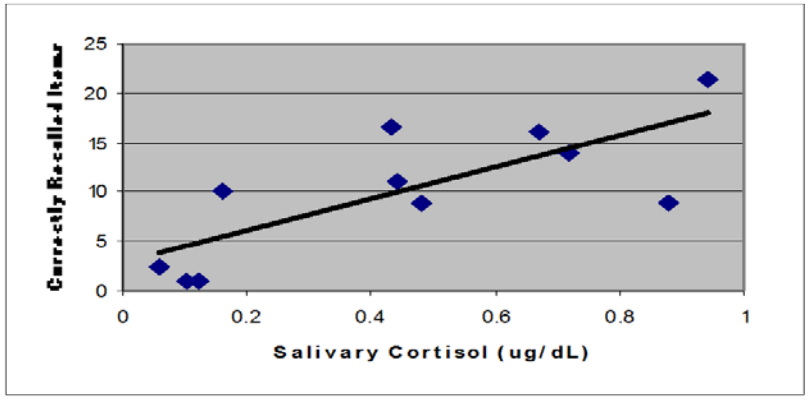
a)



b)

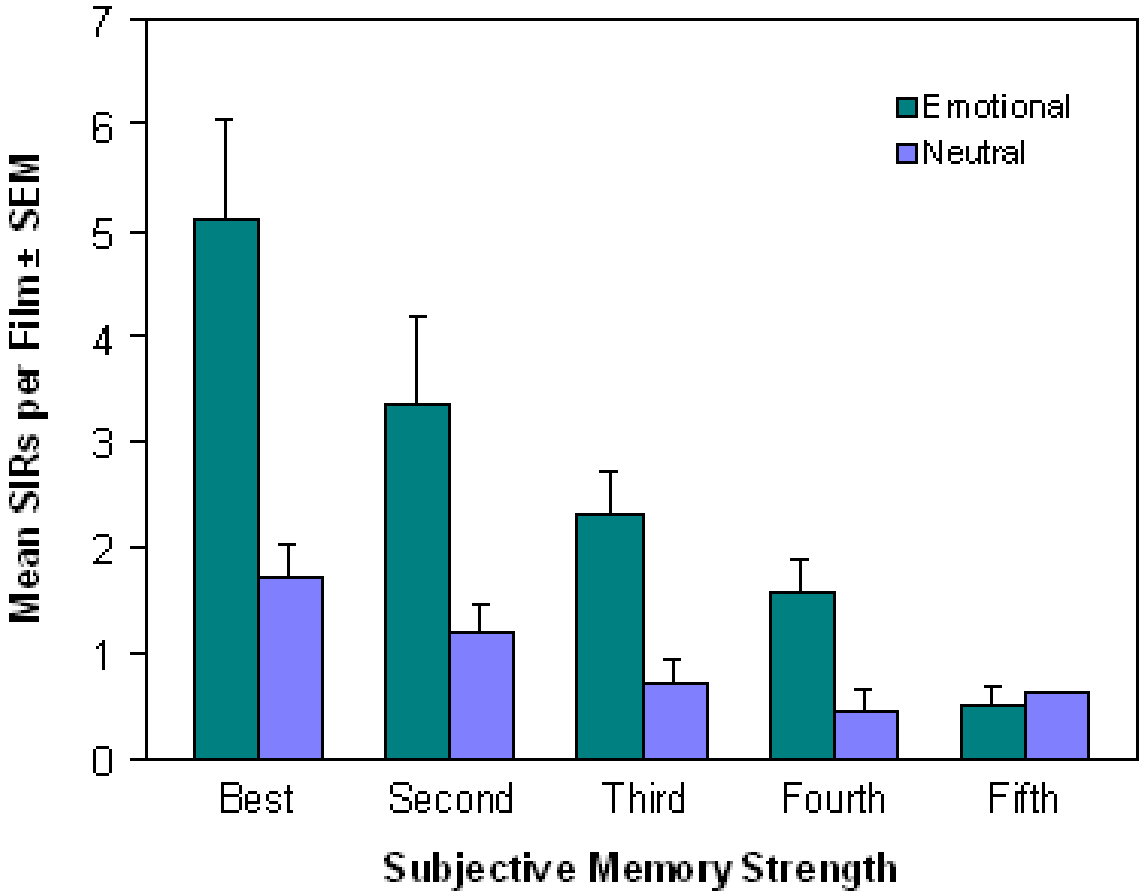


c)



Relationship between salivary cortisol and recall performance CPS subjects only in the a) early follicular b) late follicular and c) mid-luteal phases

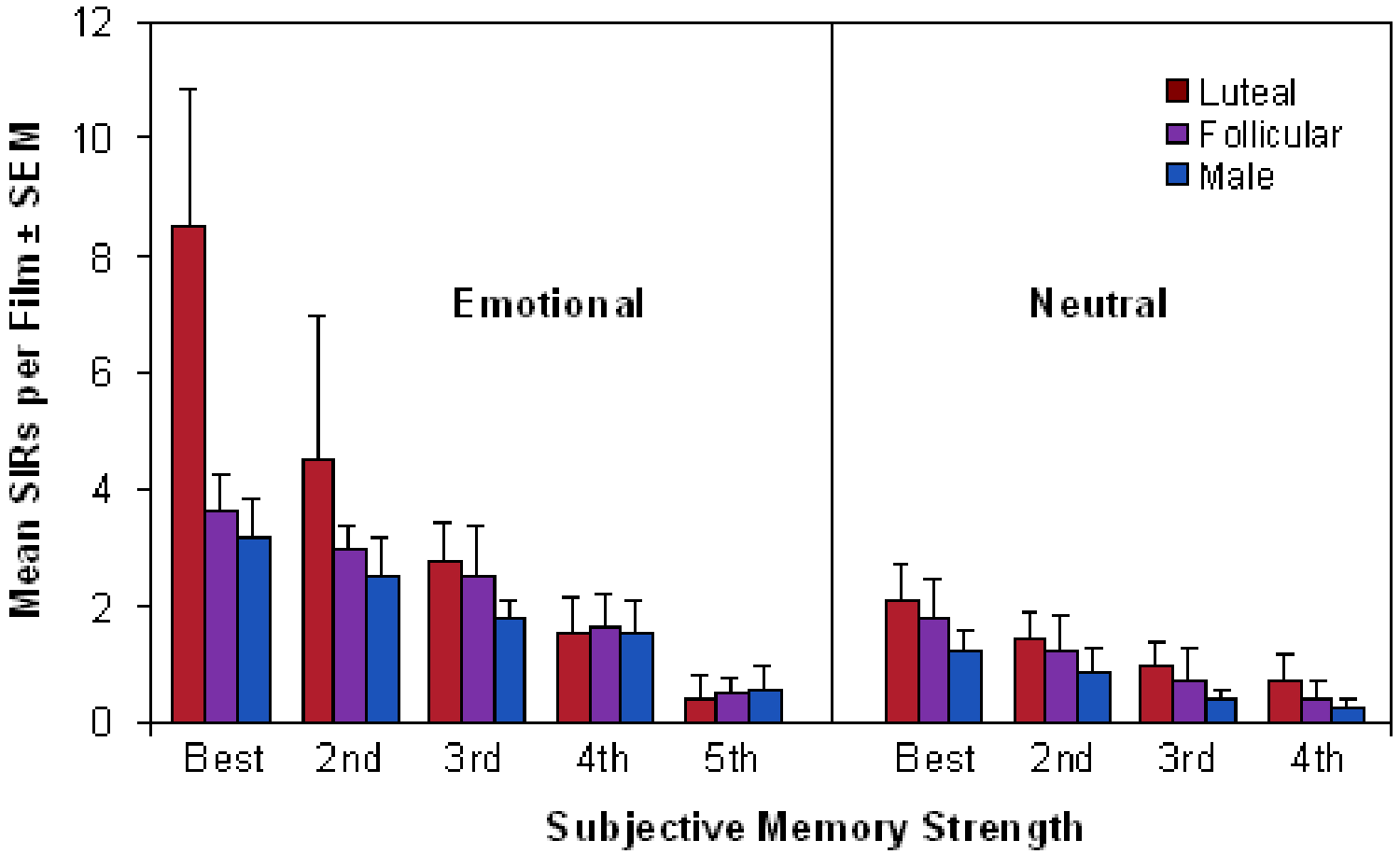
Rumination and Emotional Memory



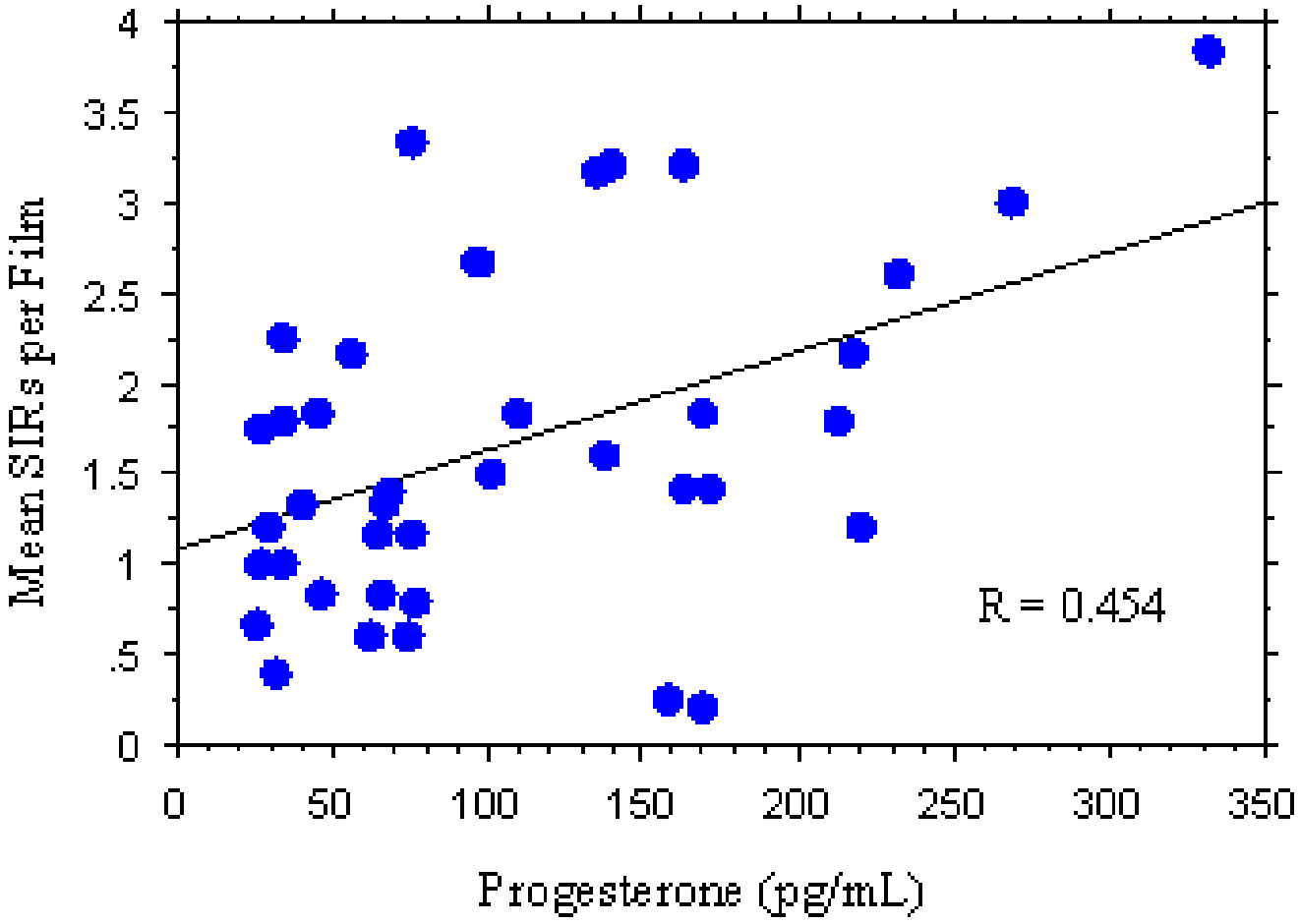
Nikole Ferree

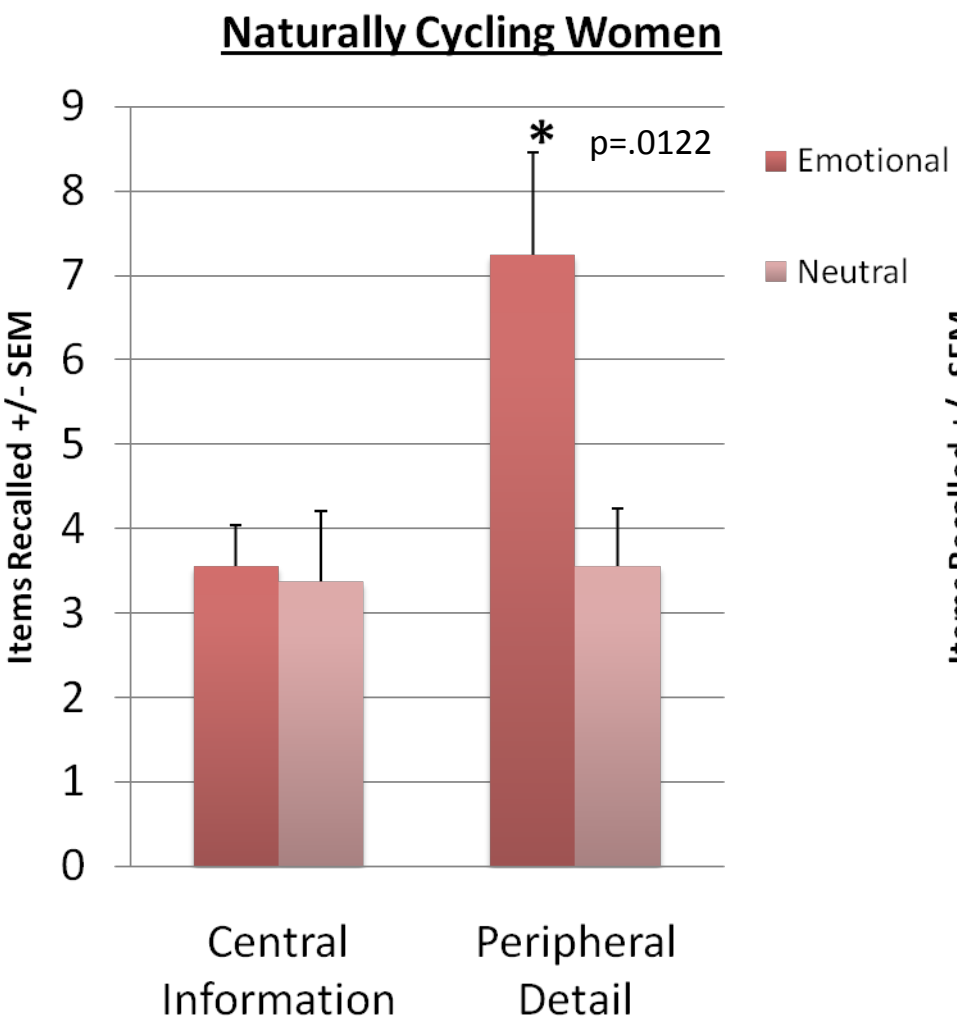
Rumination and Emotional Memory-

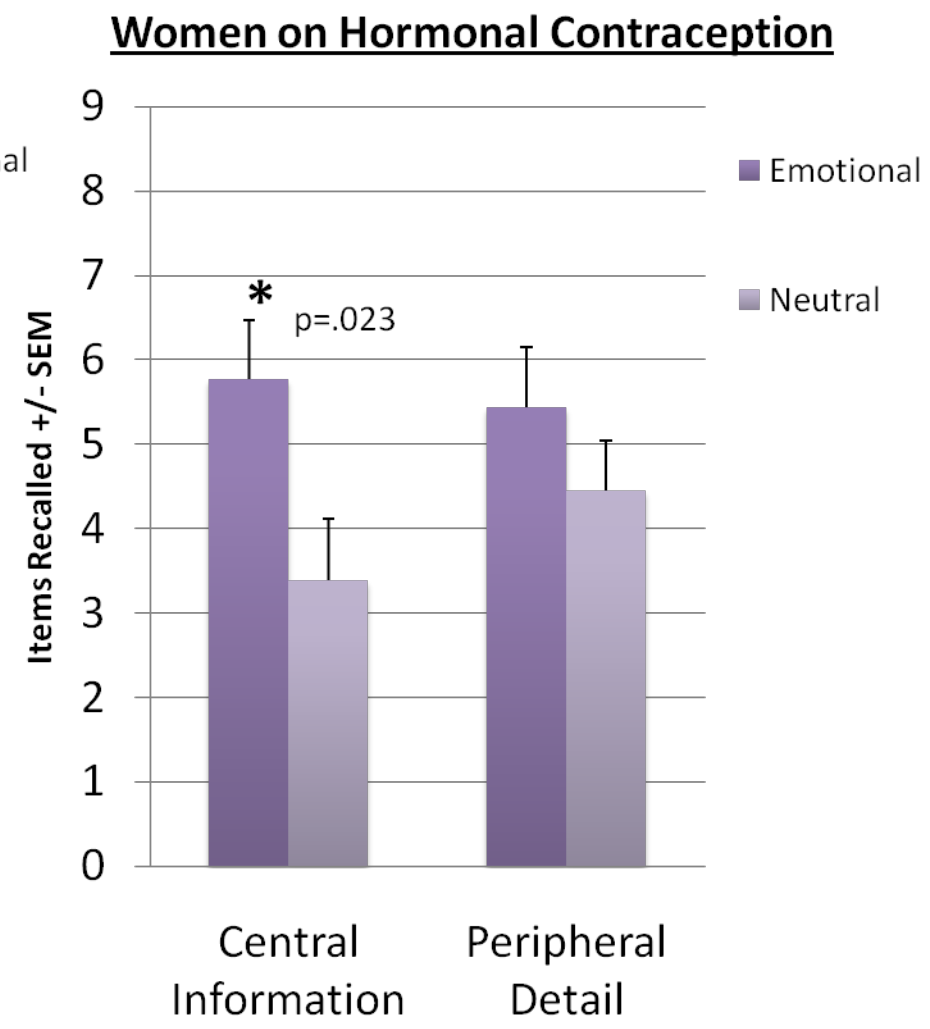
Effect of Menstrual Cycle



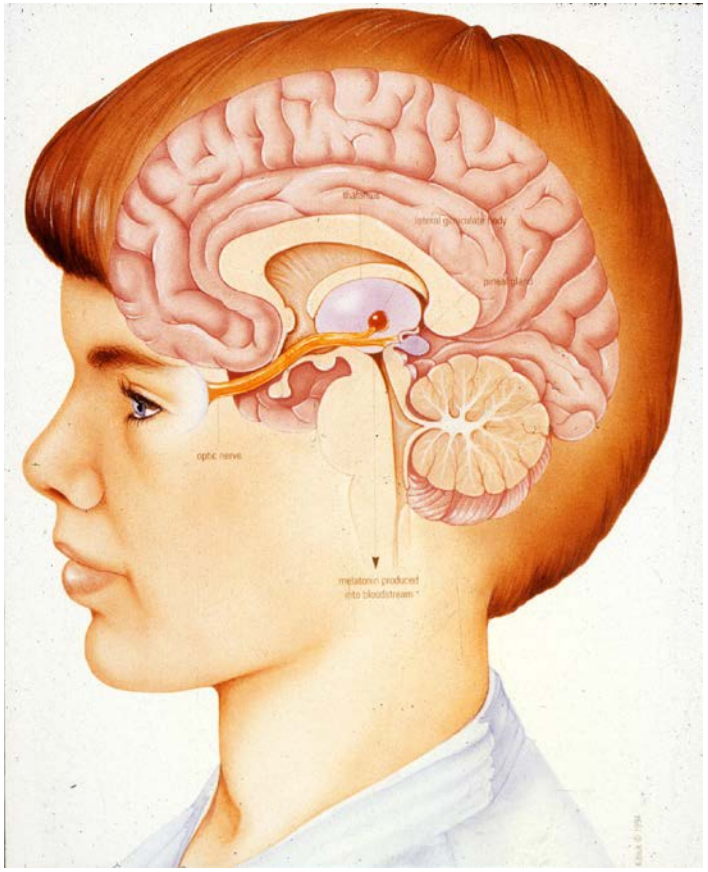
Progesterone Predicts Intrusive Recollections



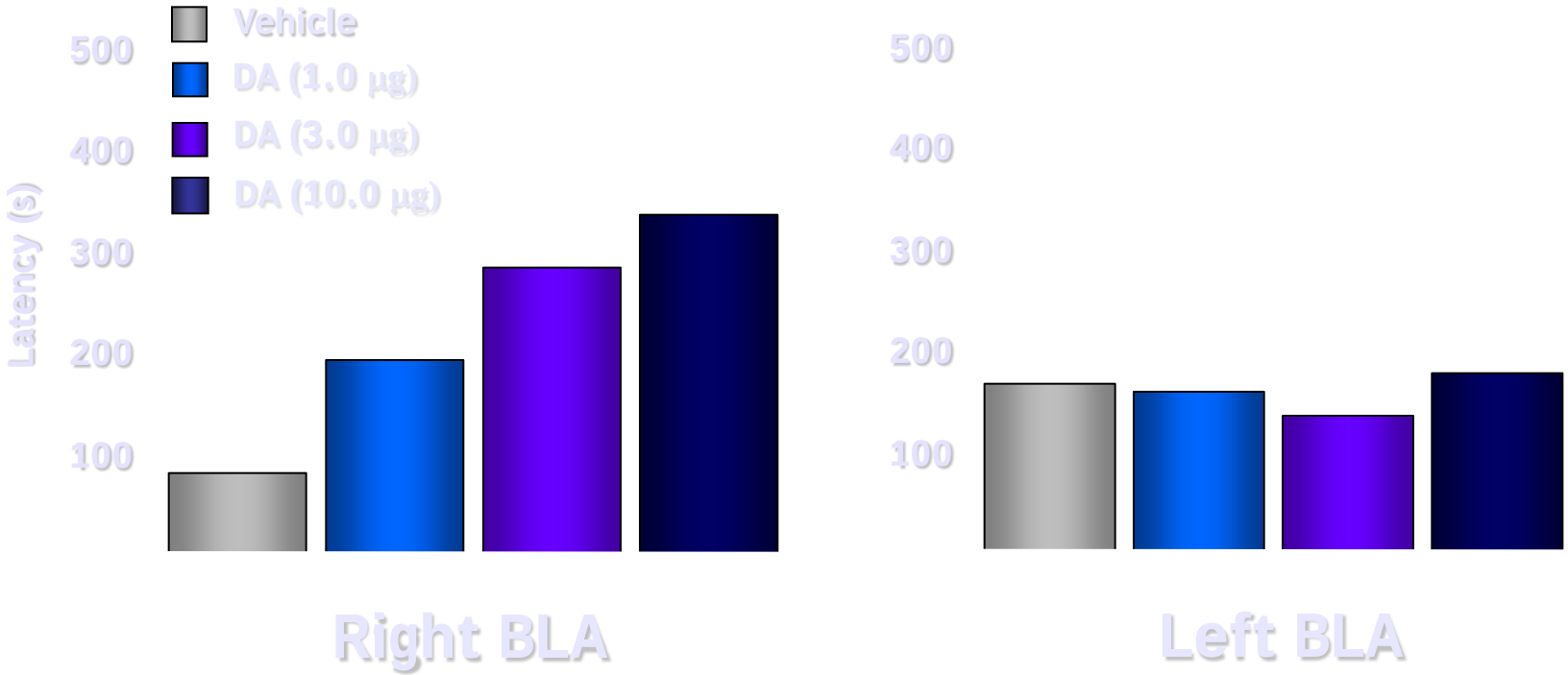

Naturally Cycling Women
Items Recalled +/- SEM
0
1
2
3
4
5
6
7
8
9
*
p=.0122
Emotional
Neutral
Central Information
Peripheral Detail


Women on Hormonal Contraception
Items Recalled +/- SEM
0
1
2
3
4
5
6
7
8
9
*
p=.023
Emotional
Neutral
Central Information
Peripheral Detail

ANIMAL ⟷ **HUMAN**

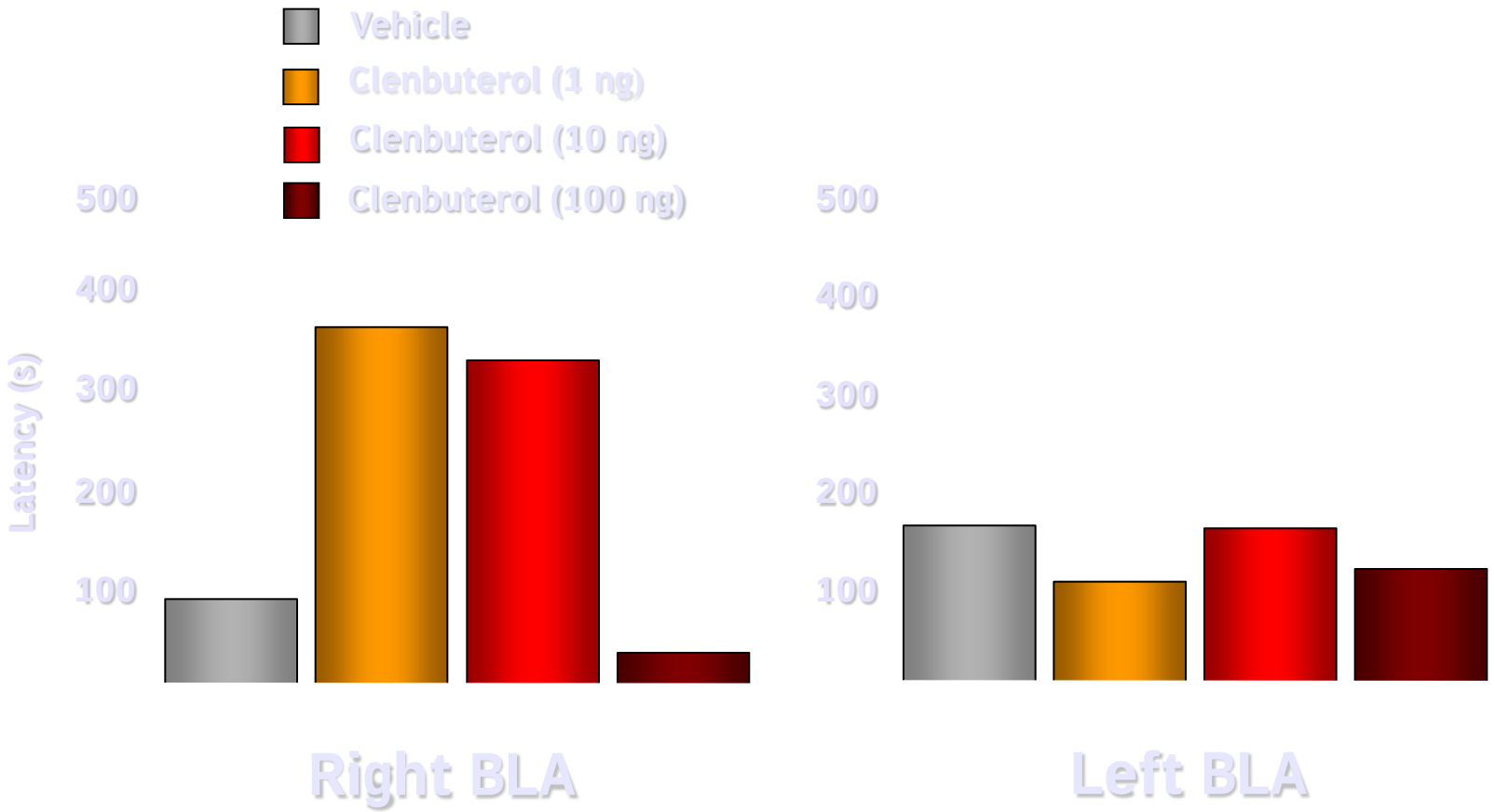


Effects of DA in right vs. left BLA



Is the noradrenergic system lateralized?

Clenbuterol: β-adrenergic agonist



Diseases with Sex Differences in Incidence and/or Nature

Alzheimer's Disease

Schizophrenia

PTSD

Anxiety Disorders

Stroke

Epilepsy

Depression

Autism

Eating Disorders

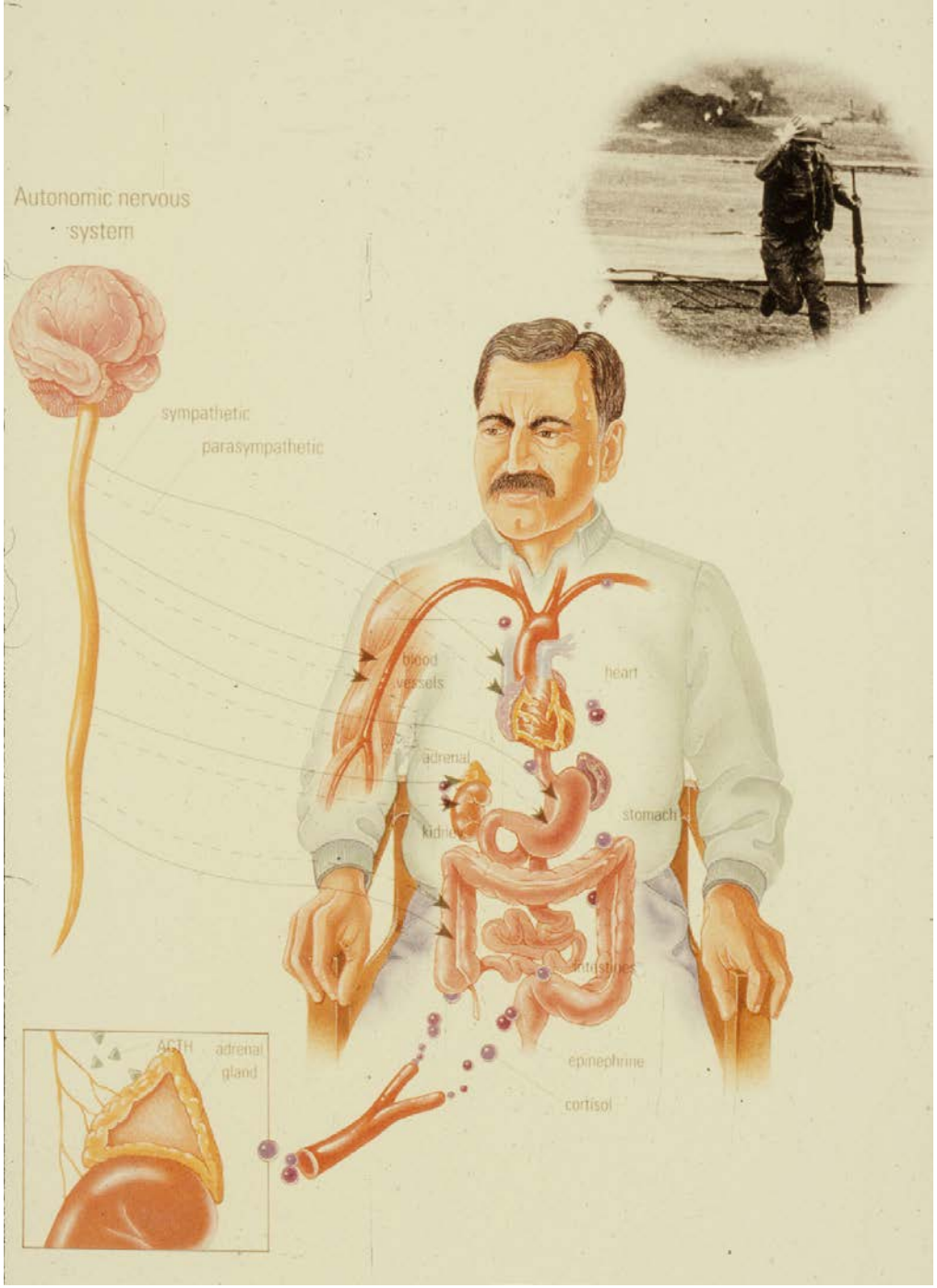
Autoimmune Disorders

Addiction

Irritable Bowel Syndrome

Pain

Tourette's Syndrome


Autonomic nervous system
sympathetic
parasympathetic
blood vessels
heart
adrenal
stomach
kidney
epinephrine
cortisol
ACTH
adrenal gland

Clinical Case Conference

Individual Differences in a Husband and Wife Who Developed PTSD After a Motor Vehicle Accident: A Functional MRI Case Study

Ruth A. Lanius, M.D., Ph.D.

James W. Hopper, Ph.D.

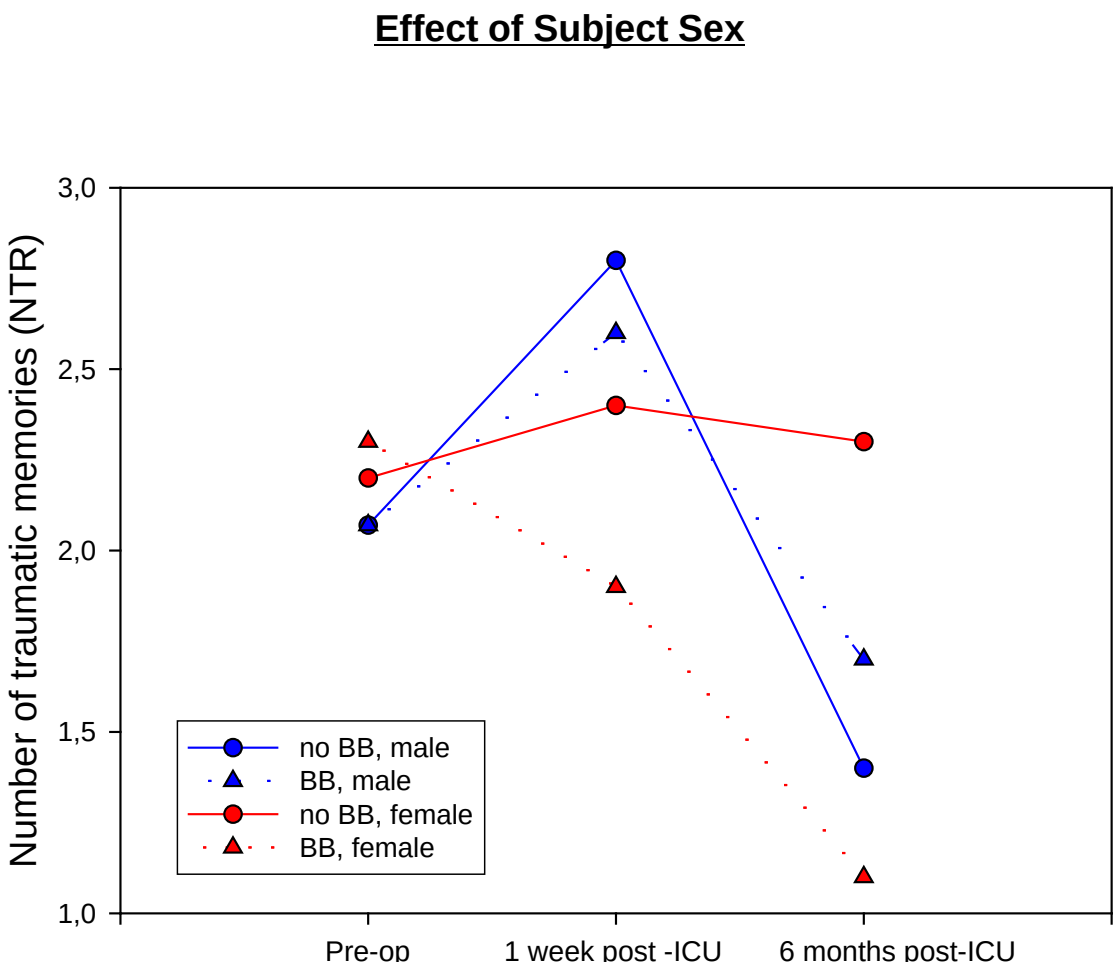
Ravi S. Menon, Ph.D.

This report describes a husband and wife with acute posttraumatic stress disorder (PTSD) who exhibited differ-

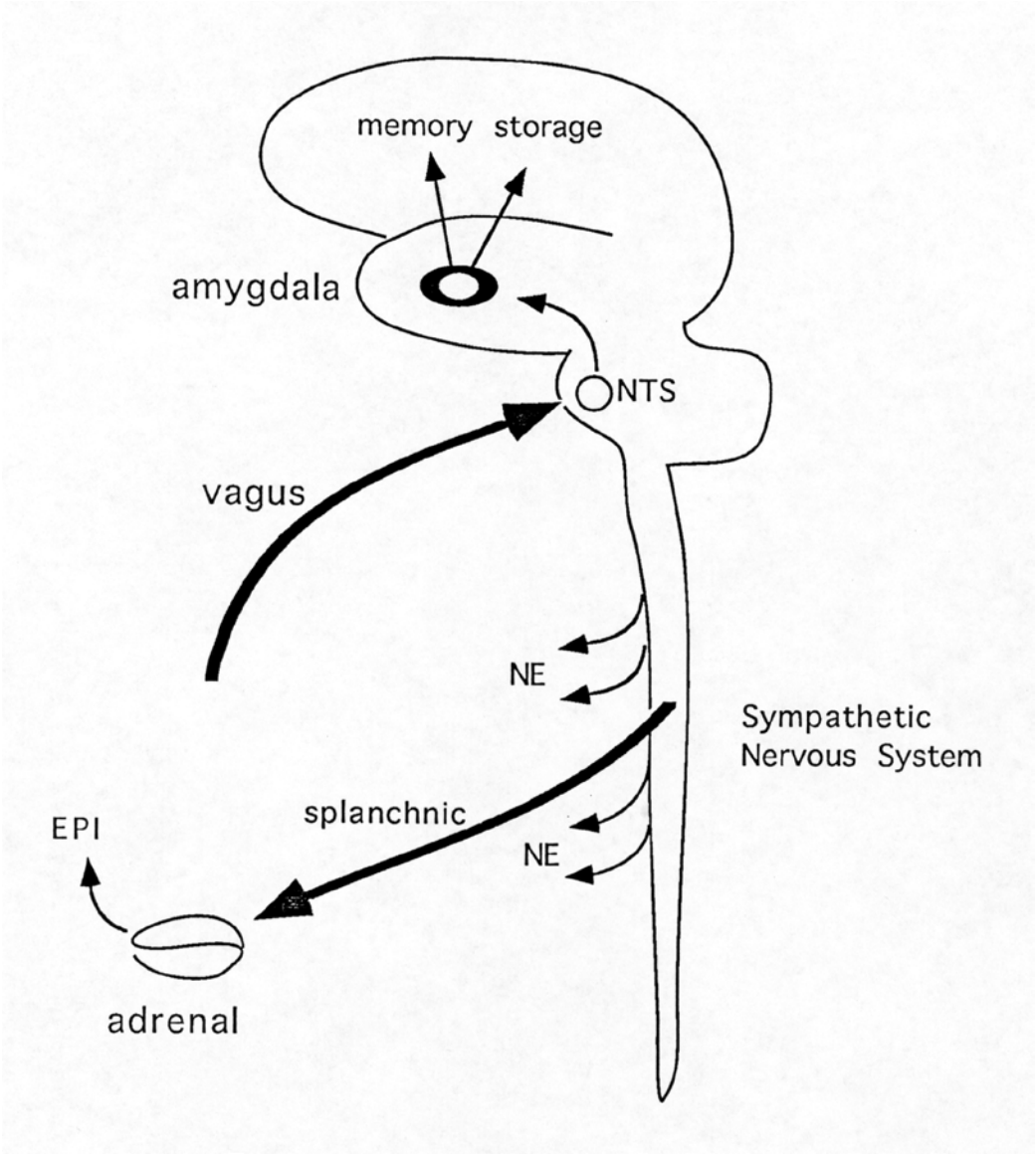
The wife experienced much greater peritraumatic dissociation and had a score on the Peritraumatic Dissociative Experiences Scale of 22 versus her husband's score of 1; however, both had low trait dissociation, with scores on the Dissociative Experiences Scale of less than 3. Responses to script-driven traumatic imagery were measured with 4-T fMRI, a heart rate monitor, and self-report measures (for detailed methods, see references 5–8).

Case Presentations

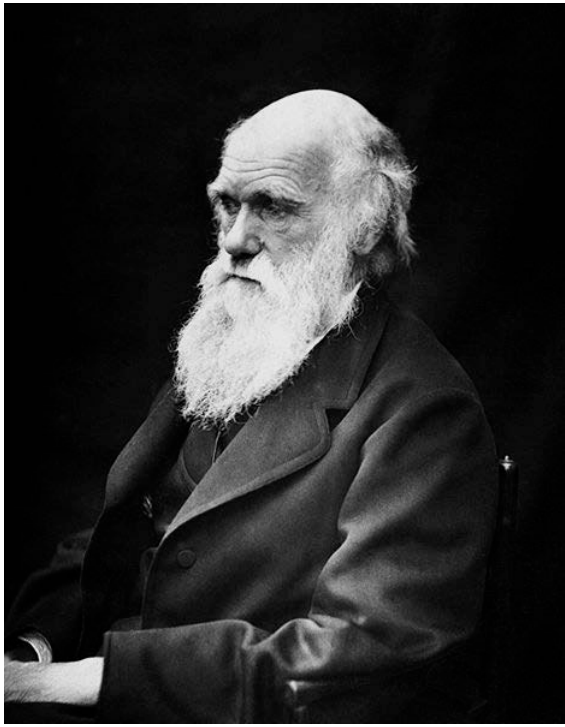
β-Adrenoceptor Antagonists Block Traumatic Memories from the ICU*



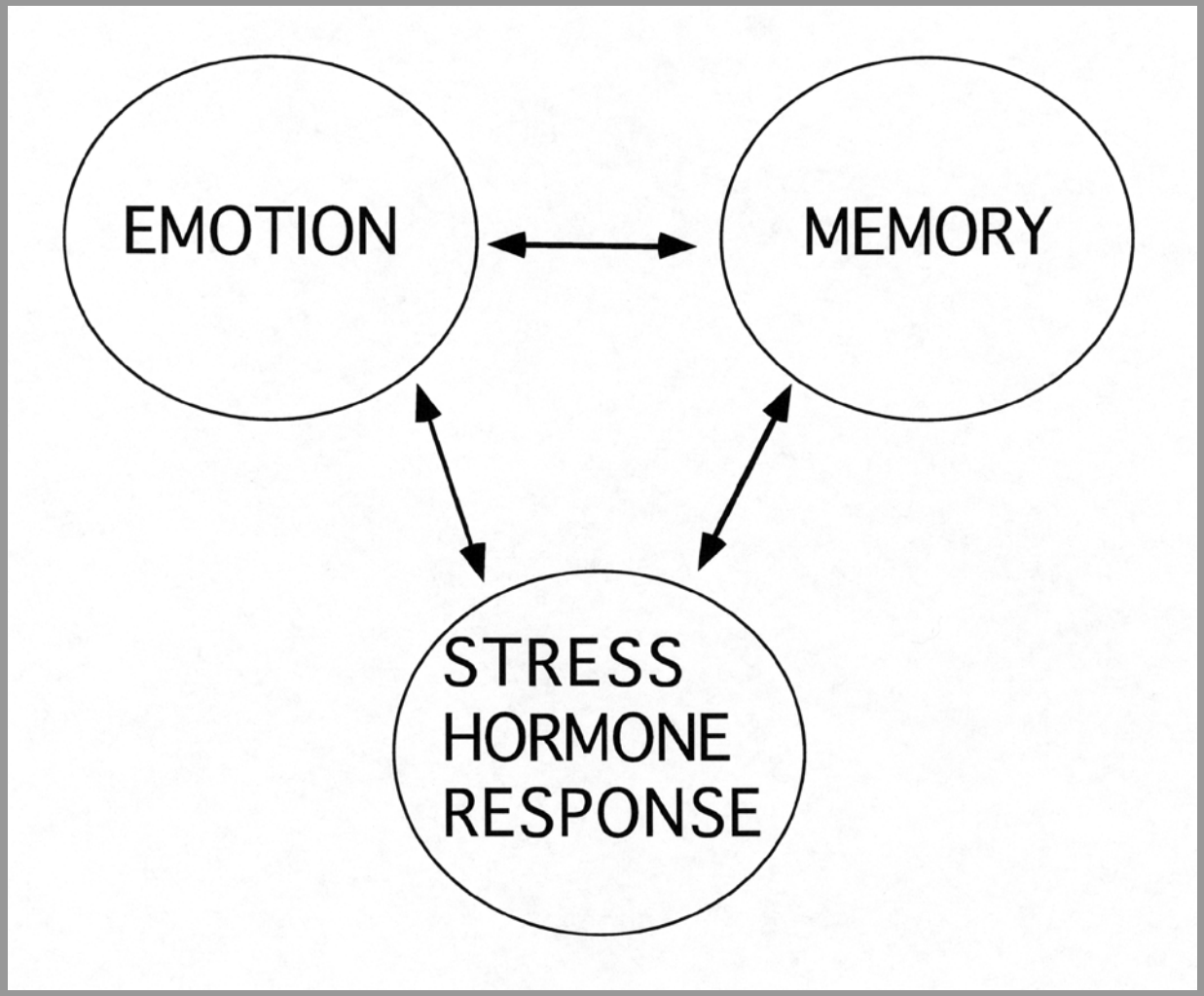
*Schelling, G., Rothenhausler, H., Krauseneck, T., Nollert, G., Kapfhammer, H. (2003): Sex-Related Effects of Beta-Adrenergic Blockade on Memory for Traumatic Events from the Perioperative Period of Cardiac Surgery. Anesthesiology 99: A310.


memory storage
amygdala
NTS
vagus
NE
Sympathetic
Nervous System
splanchnic
EPI
NE
adrenal

“To kill an error is as good a service as, and sometimes even better than, the establishing of a new truth or fact”



LEFT RIGHT



WOMAN MAN

What Does It Mean?

The Burden of Proof has Shifted

Sex Matters