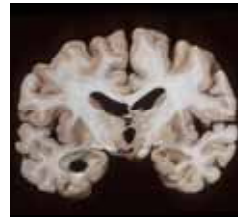
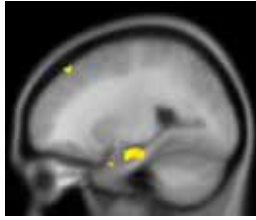


Genetik emotionaler Erinnerungen



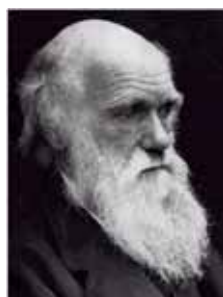
Prof. Andreas Papassotiropoulos, M.D.
Division of Molecular Psychology, Faculty of Psychology
Life Sciences Training Facility, Biozentrum
University of Basel

Zitate

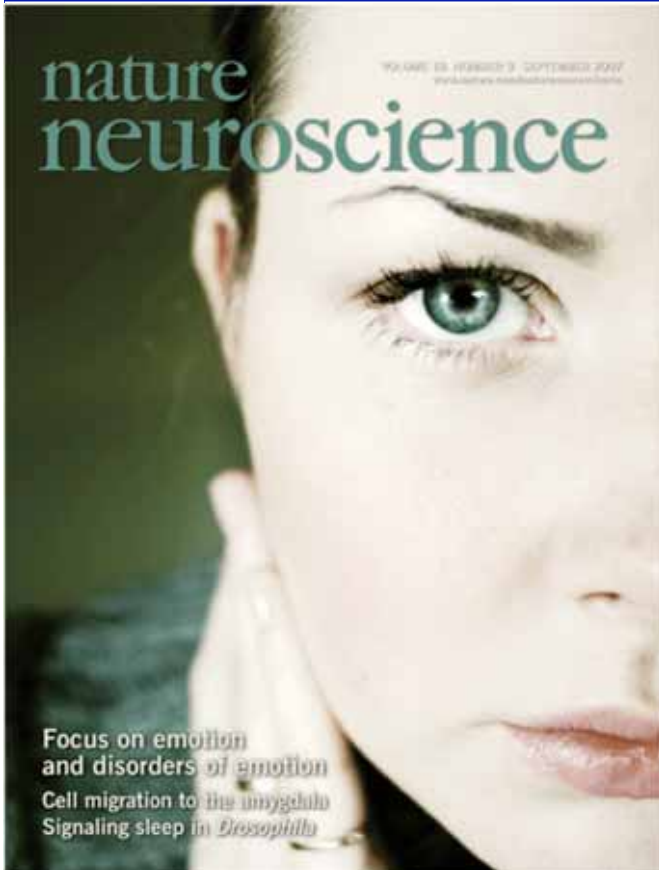
“In the distant future I see open fields for far more important researches. Psychology will be based on a new foundation, that of the necessary acquirement of each mental power and capacity by gradation.”

“There is grandeur in this view of life, with its several powers, having been originally breathed into a few forms or into one; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved.”

1859



Charles Darwin
On the origin of the species



“...how the brain regulates emotions, how this regulation becomes impaired by disorders of emotion and which therapies may be effective in treating these disorders.”

Five important points

- Genetics of complex human phenotypes: A tool to understand biology
- Genome-wide association studies revolutionize our knowledge on complex traits relevant to neuropsychiatric diseases
- Genetic clusters rather than single genes are potential biomarkers
- The use of human genetic information will lead to improved characterization of human complex traits
- The combination of genetics with other relevant sources of information (e.g. fMRI, PET) will contribute to better predictions

Importance of the phenotype

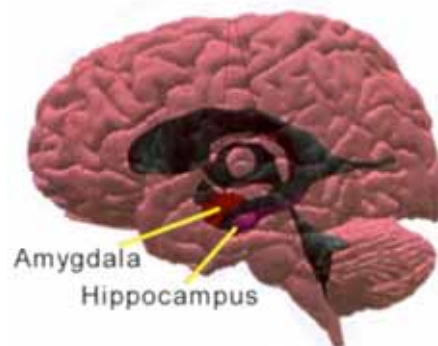
- heritable
- reliable assessment
- biological correlate

Memory / Memory-related disorders

Post-traumatische Belastungsstörung

Alpträume
Schlafstörungen
Flashbacks (Intrusionen)
Konzentrationsstörungen
Depressionen
Dissoziative Störungen
Persönlichkeitsveränderungen
Interessensverlust
Emotionale Störungen
Vermeidungsverhalten
Selbstverletzendes Verhalten
Angzustände und Panikattacken
Suizidalität

Hippocampale Atrophie



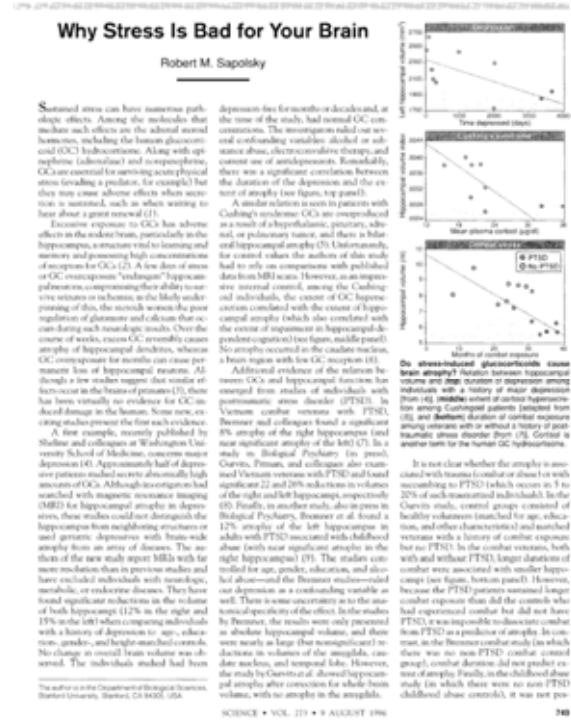
Cortisol

Folge oder Ursache?

Beispiel: Post-traumatische Belastungsstörung



stanford.edu



Beispiel: Post-traumatische Belastungsstörung

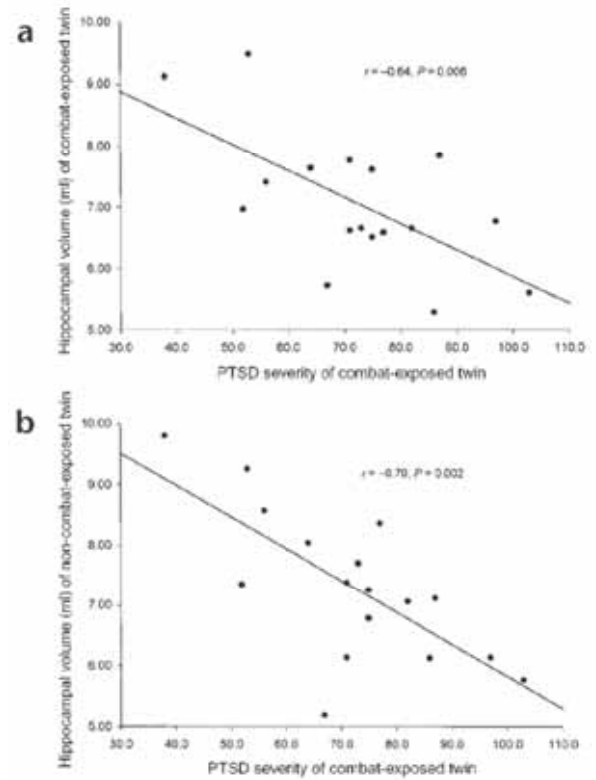
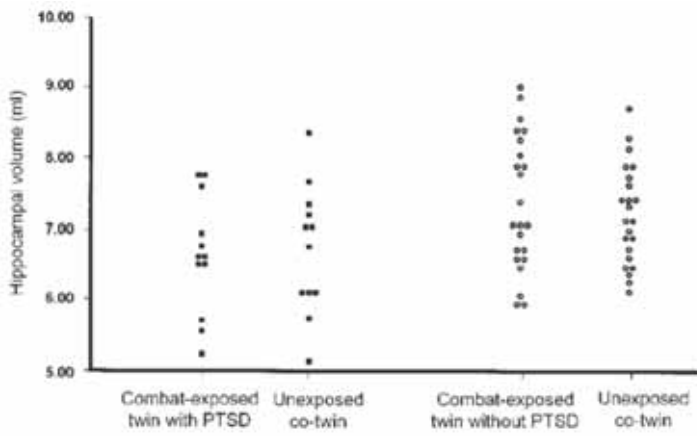


PTSD

keine PTSD

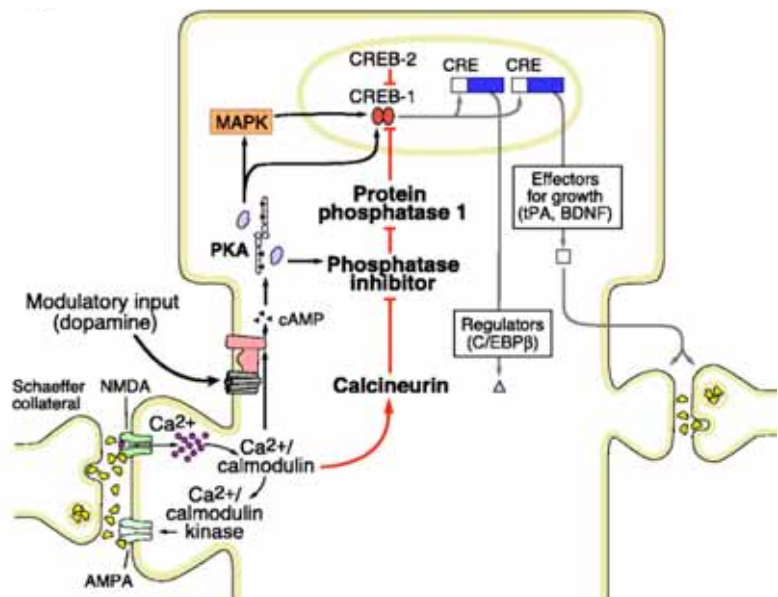
keine PTSD

Post-traumatische Belastungsstörung



Gilbertson et al., Nature Neuroscience 2002

Signaling cascade involved in animal memory

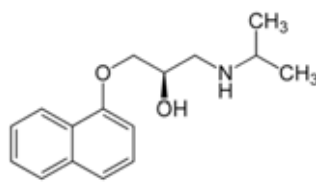
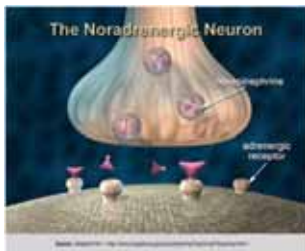


Kandel, Science, 2001

Signaling cascade in humans?

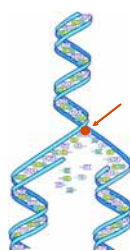


Two possibilities



However:

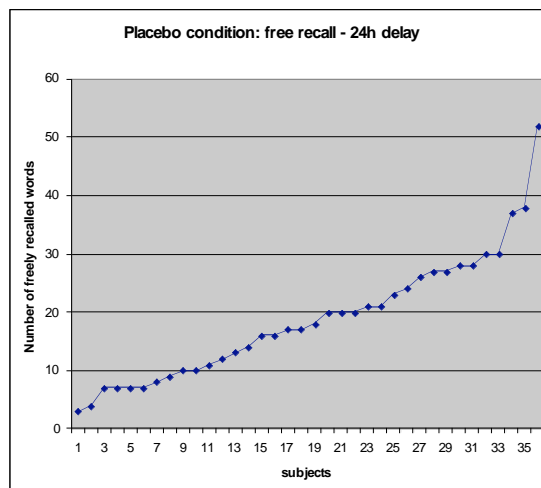
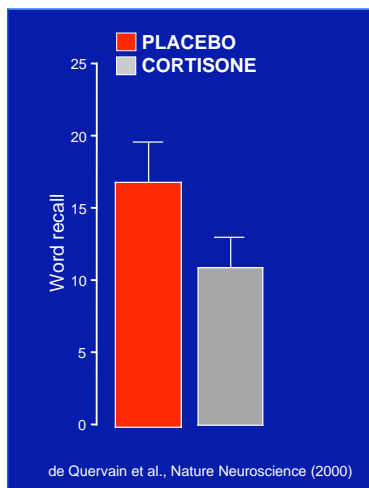
Availability
Safety
Specificity



However:

All issues related to human genetics studies

Background: variability of human memory



- ▶ Studies in twins indicate that inherited factors account for about 50% of this variability.
- ▶ Which genes are involved herein?

Haut

Haut

Lawine

Geschenk

Schleim

Kategorie

Wahnsinn

Täuschung

Duft

Erdgeschoss

Entspannung

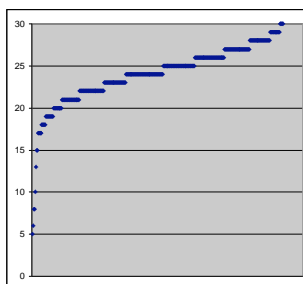
Bitte aufschreiben

Design

- 349 young healthy human subjects (mean age 22 years ranging from 18 to 35)
- Presentation of 30 words (6 series of 5 words)

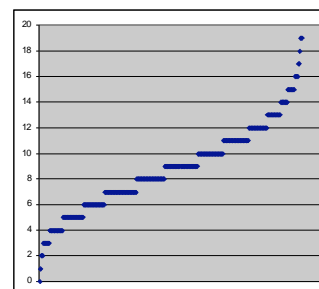
Working memory

Immediate free recall



Short-term memory

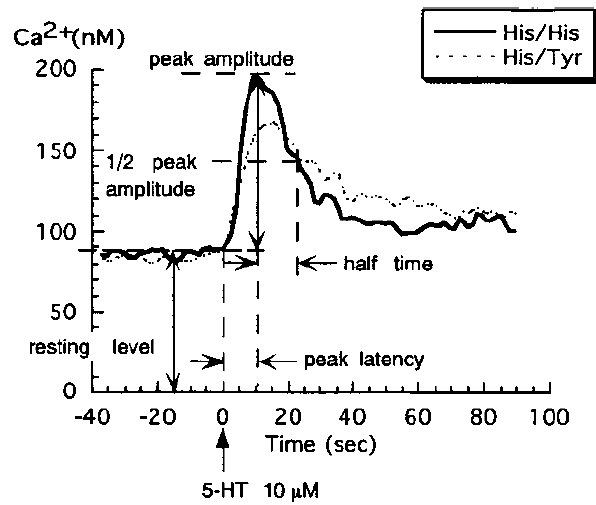
Free recall 5-min delay



5-HT2a receptor gene

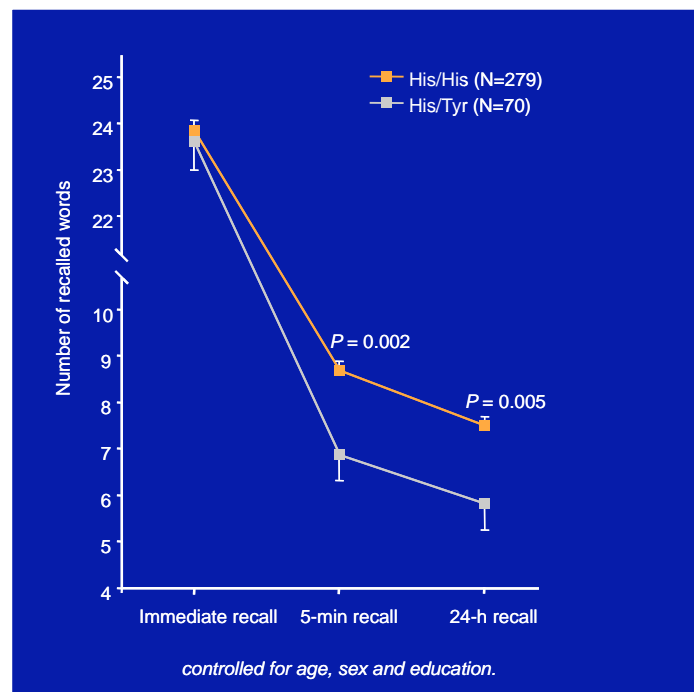
- 5-HT2a receptor involved in memory formation in rats (Meneses et al., 1997, 2002).
- Well characterized functional polymorphism (His452Tyr)

As compared with His/His carriers, heterozygous His/Tyr carriers show a blunted receptor response, as measured by amplitude and timing of intracellular calcium mobilization upon 5-HT stimulation.



Ozaki et al., *Journal of Neurochemistry* (1997)

5-HT2a receptor gene



controlled for age, sex and education.

de Quervain, Henke, Aerni, Coluccia, Wollmer, Hock, Nitsch, Papassotiropoulos
Nature Neuroscience (2003)

Emotional Memory



- ▶ How variable is emotional memory?
- ▶ Which genes are involved?

Background

- ▶ This phenomenon has adaptive value in evolutionary terms, as it is vital to remember both dangerous and favorable situations.

“The usefulness of all of the passions consists in their strengthening and prolonging in the soul thoughts which are good for it to conserve.”

René Descartes (1596 - 1650)

Emotional Memory

- 435 participants
- Emotional and neutral photographs

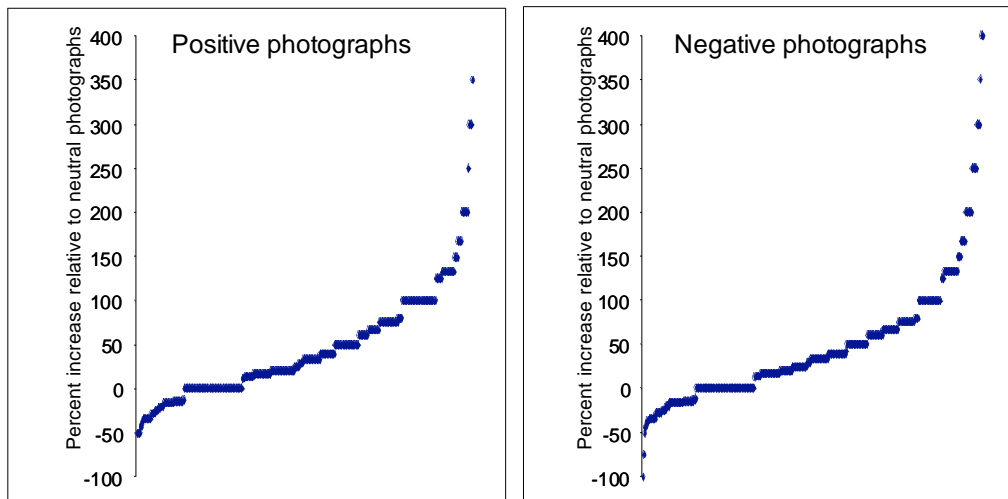


de Quervain, Kolassa, Ertl, Lamaro Onyut, Neuner, Elbert & Papassotiropoulos
Nature Neuroscience, 2007

Example: Pictures

Emotional Memory

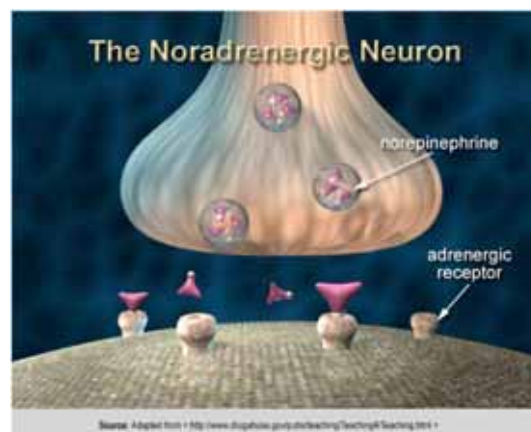
- 435 participants
- Emotional and neutral photographs



de Quervain, Kolassa, Ertl, Lamm, Onyut, Neuner, Elbert & Papassotiropoulos
Nature Neuroscience, 2007

Background

- ▶ The memory-enhancing effect of emotional arousal depends on the activation of noradrenergic transmission within the brain.
 - McGaugh, J.L. et al. The Making of Lasting Memory. in Memory and Emotion: (2003)
 - Cahill, L. & McGaugh, J.L. Trends Neurosci. 21, 294-299 (1998)
- ▶ In humans, a pharmacological stimulation of noradrenergic transmission with the alpha-2-adrenergic receptor antagonist yohimbine potentiates the memory-enhancing effect of emotional arousal.
 - O'Carroll, R.E. et al. Psychol.Med. 29, 1083-1088 (1999)

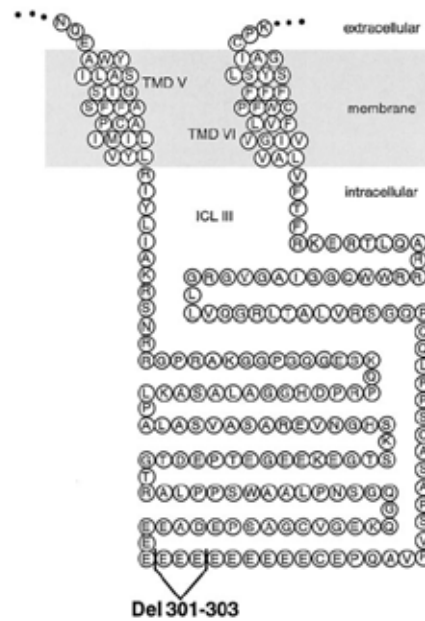


Background

- ▶ Human alpha(2b)-adrenergic receptor (ADRA2B)

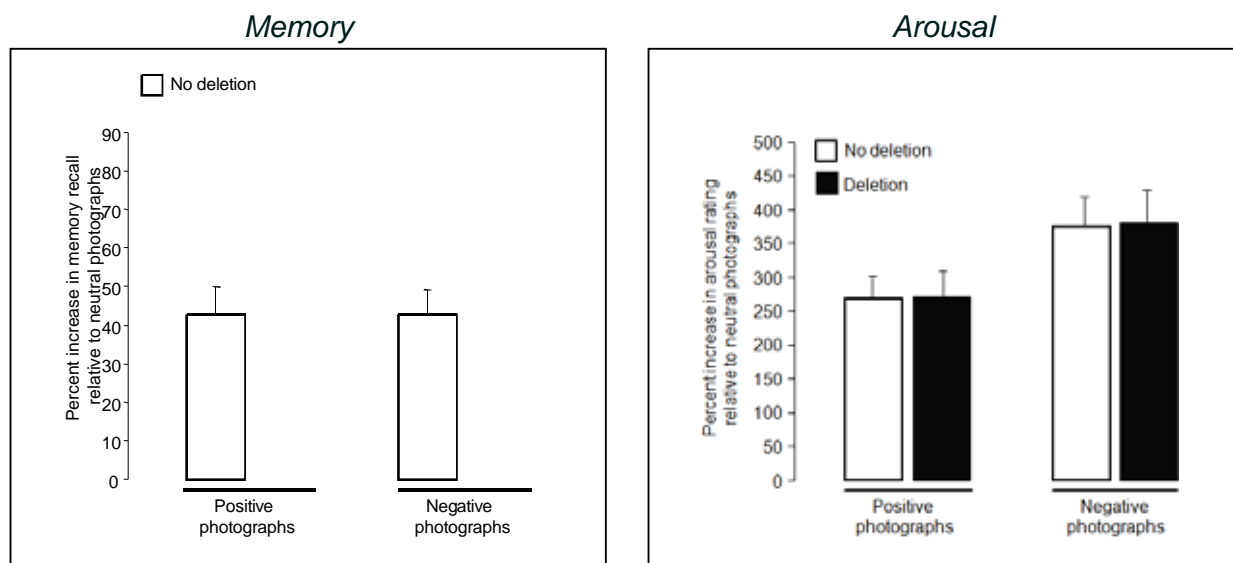
Functional variant which consists of a deletion of three glutamic acids (Small et al., 2001).

The variant is found in 30% of Caucasians and in 12% of African-Americans.



- ▶ The deletion variant may be related to emotional memory

Results



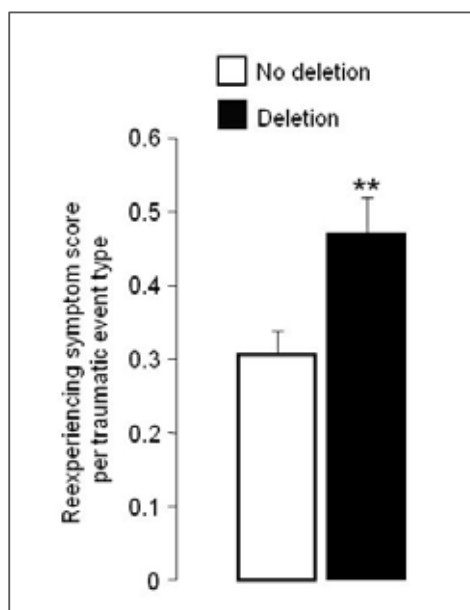
Attention and concentration were not affected by the genotype

Emotional memory and traumatic memories



Results

Traumatic Memory



- Effect was independent of the presence of the diagnosis PTSD

- Avoidance and hyperarousal symptoms were not affected by the genotype

▶ Consistent with the findings that a genetically anchored alteration in the noradrenergic system is related to traumatic memory, recent studies have indicated that the noradrenergic system is a promising pharmacological target to reduce traumatic memory (Pitman et al., 2002).

Summary and Conclusion

“The usefulness of all of the passions consists in their strengthening and prolonging in the soul thoughts which are good for it to conserve. And all the harm they (passions) can do consists in their strengthening and conserving others (thoughts) which ought not to be fixed there”

René Descartes (1596 - 1650)

Contributors / Collaborators

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