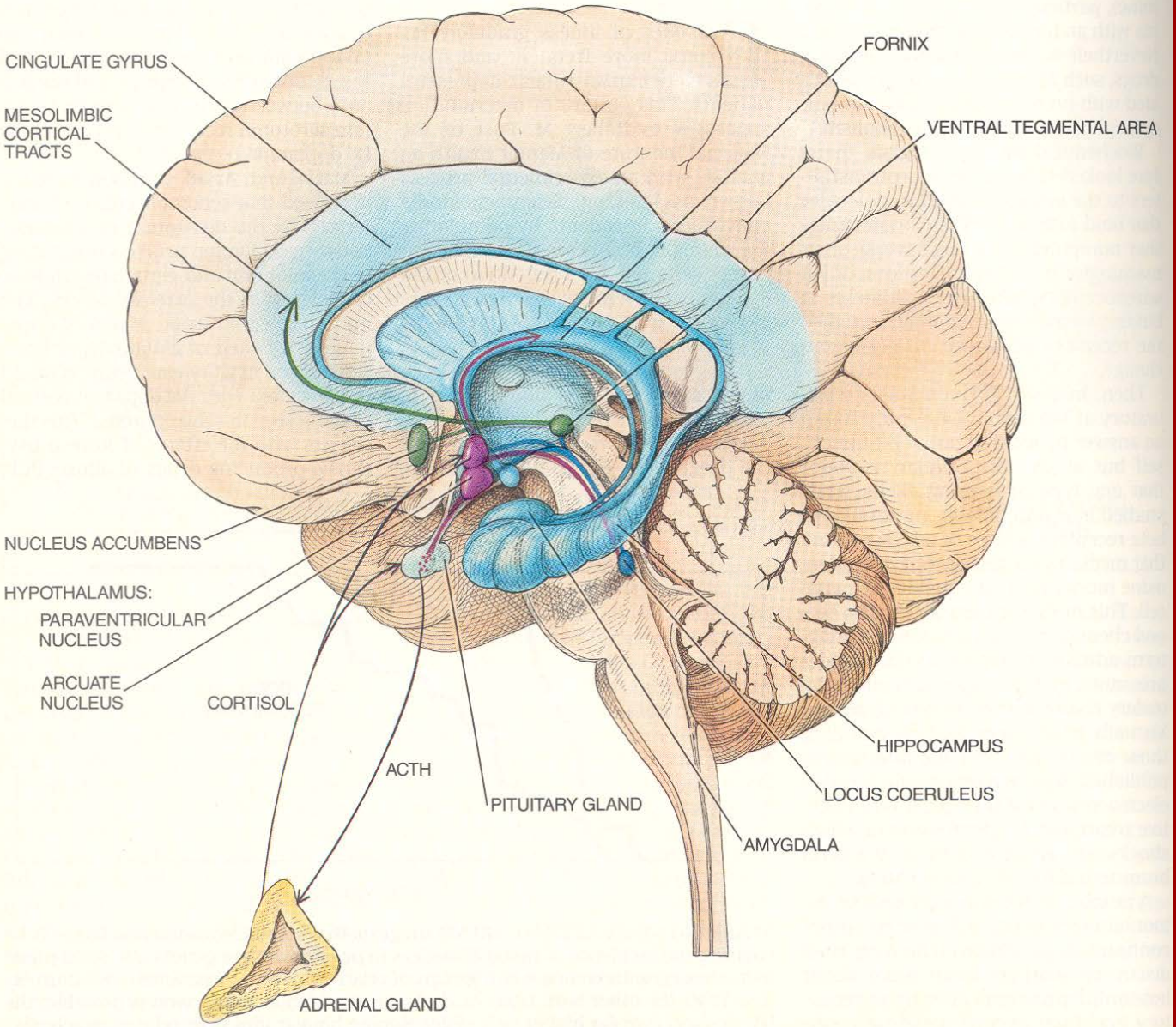
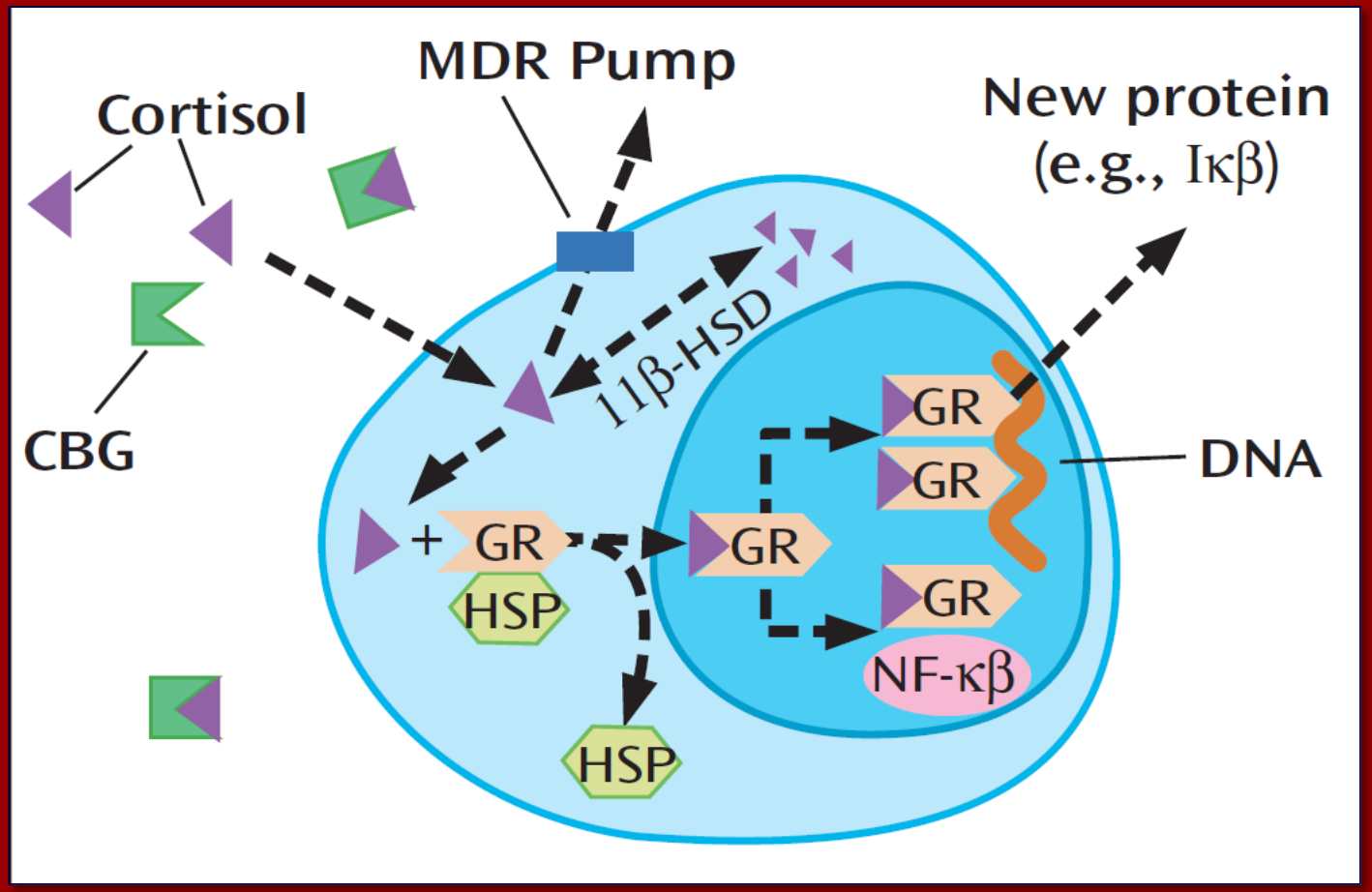
Experience can get under the skin

- Example: Adverse early experiences cause lifelong alterations in cellular signaling of glucocorticoids
- Relevance for psychiatric treatment


CINGULATE GYRUS
MESOLIMBIC CORTICAL TRACTS
FORNIX
VENTRAL TEGMENTAL AREA
NUCLEUS ACCUMBENS
HYPOTHALAMUS:
PARAVENTRICULAR NUCLEUS
ARCUATE NUCLEUS
CORTISOL
ACTH
PITUITARY GLAND
HIPPOCAMPUS
LOCUS COERULEUS
AMYGDALA
ADRENAL GLAND

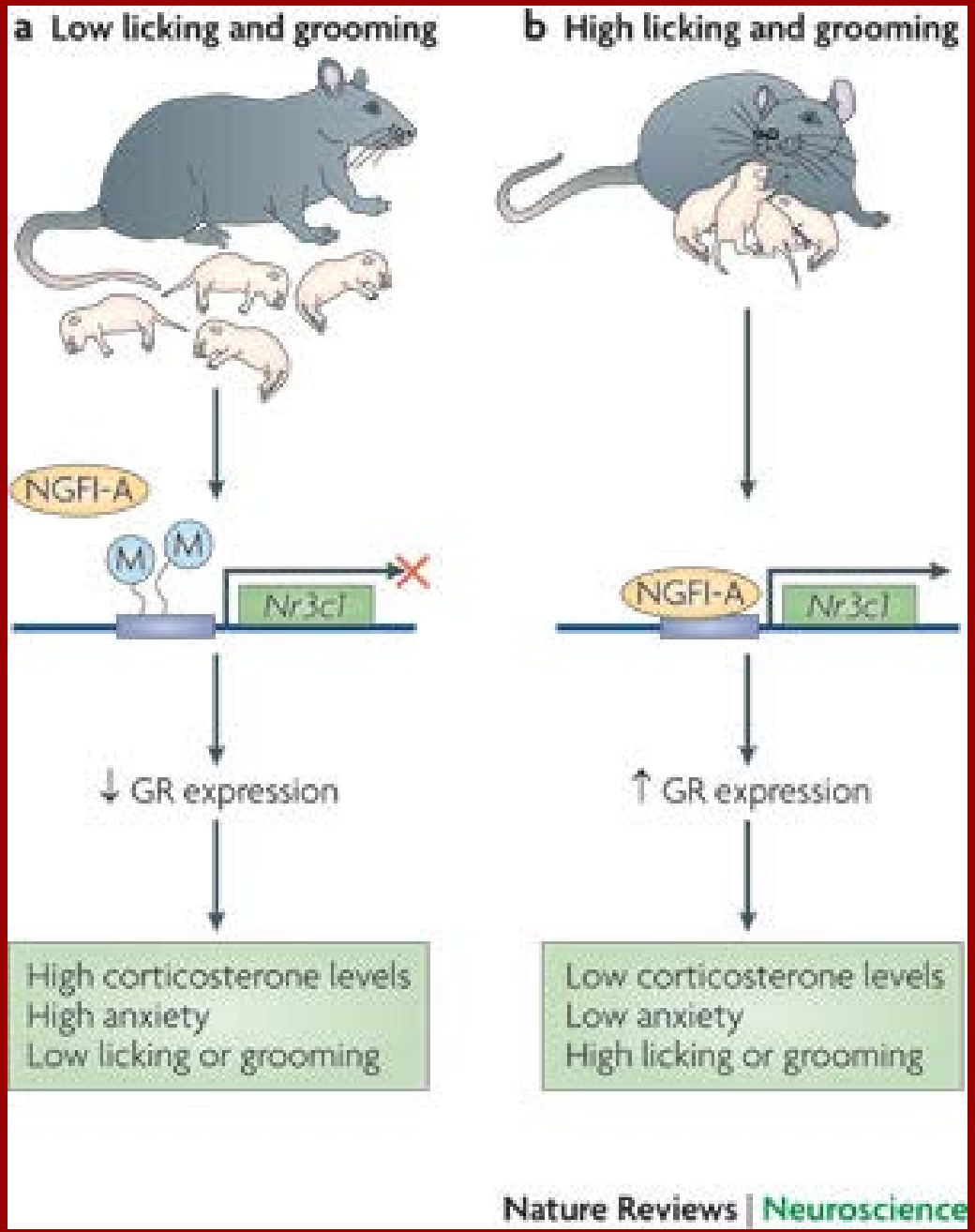
Many potential cellular mechanisms for under-signaling of cortisol in target tissues



Adapted from Raison & Miller (2003) *Am J Psychiatry.*

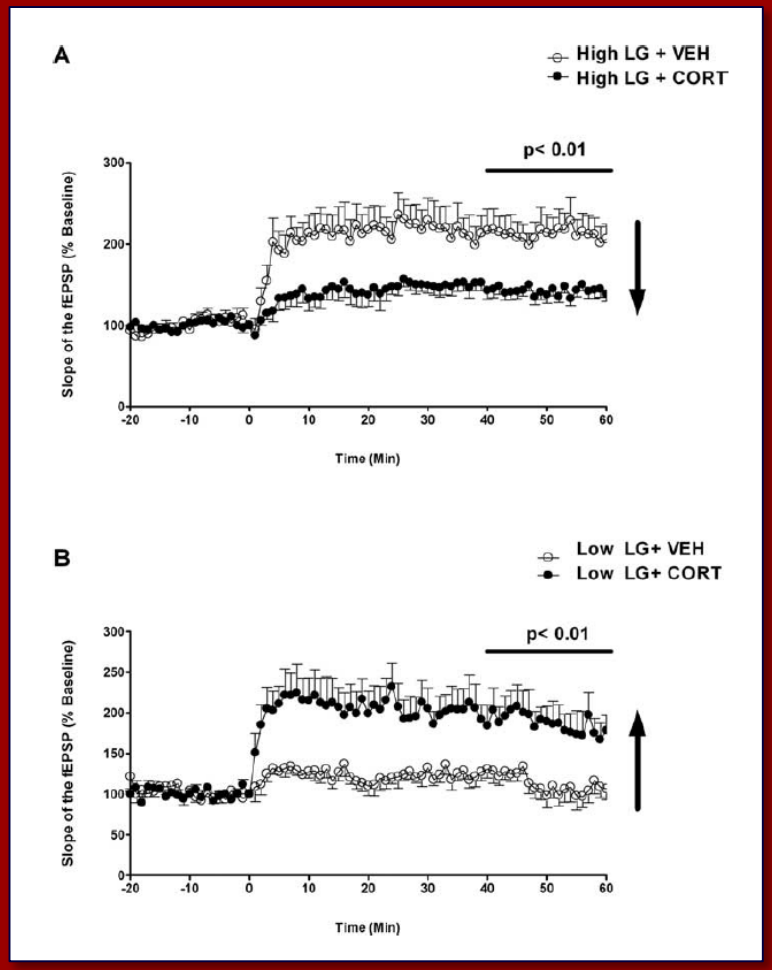
High levels of maternal care

Low levels of maternal care



Hackman, Farah, & Meaney.
Nat Rev Neurosci. 2010

CORT effects on synaptic plasticity in hippocampal slices depend on the early environment



History of *high* maternal care:
CORT *decreases* synaptic strength

History of *low* maternal care:
CORT *increases* synaptic strength

Champagne et al. (2008) *J Neuroscience*.

Lasting effects of early experience on biobehavioral functioning – "nurture" becomes "nature"

- Proof of concept – Rodent research shows that aversive caregiving causes:
  - Alteration in regulation & cellular signaling of stress hormones into adulthood
  - Lasting effects are due to epigenetic modifications
  - Altered effects of stress hormones on synaptic neuroplasticity

Translation to humans

- Psychoneuroendocrine research in Psychiatry:
  - Early experience of aversive caregiving is associated with glucocorticoid insensitivity in adulthood
  - Increasing cortisol signaling may be neurocognitively beneficial
  - Biobehavioral alterations related to stress may operate in many forms of mental illness

- Relevance for psychiatric treatment:
  - Cellular signaling of stress hormones as a psychiatric treatment target
  - Many effective treatments restore cellular sensitivity to glucocorticoids