The effects of glucocorticoids on cognitive function in humans

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We all know intuitively that stress can impair our memory. For the last two decades, science has managed to delineate the mechanisms by which stress hormones [particularly glucocorticoid secretion through activation of the hypothalamic-pituitary-axis] can impact on memory function in humans. Receptors for glucocorticoids are found in the human hippocampus and frontal lobes, two brain regions involved in memory processing. Studies have shown that acute increases of glucocorticoids through exposure to stress and/or pharmacological administration of synthetic glucocorticoids impair the type of memory processes sustained by these two brain regions. These studies will be reviewed.
However, in the past 5 years, animal studies have shown that the actions of glucocorticoids on the brain are relative, i.e., they depend on the activation of two glucocorticoid receptor types [mineralocorticoid (MR) and glucocorticoid (GR)]. MRs and GRs differ in two important ways. First, MRs present a higher affnity for glucocorticoids then GRs, which suggests that the ratio of MR/GR occupancy as a function of glucocorticoid levels should be a strong predictor of memory performance in humans. Second, in primates and humans, MRs and GRs have been shown to be present in the hippocampus, while the frontal lobes contain mostly GRs. This suggests that an acute increase of glucocorticoids should have a differential impact on the hippocampus and frontal lobes. In the second part of this presentation, we will present data obtained in humans that confirm this model. A first study will be presented in which human memory was acutely modulated by pharmacological manipulations of glucocorticoid levels. A second study will be presented in which the *in vivo* modulation of memory function by pharmacological manipulations of glucocorticoids has been observed through a pharmacological functional brain imaging (fMRI) protocol. The implication of these findings for the study of human stress-related disorders will be discussed.

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