Effects of maternal separation on apoptosis related gene expression and neurogenesis

Oosting RS, Bultje R, Verdouw M, Olivier B
Department of Psychopharmacology, University of Utrecht, Utrecht

Adverse experiences as a child are a major risk factor for the development of anxiety disorders. To model this, we separated newborn rats from their mother for 3 h a day during the first 14 days of life. From literature, we know that this treatment leads to an increased anxiety-like behavior in adult animals as measured, for instance, in the elevated plus-maze and the social interaction test.
Here we studied mRNA expression of a large number of genes in amygdala, hippocampus, hypothalamus, striatum, septum, and prefrontal cortex of maternally separated and normally reared Wistar rats via real-time quantitative RT-PCR. Brains of ~100 days old animals were collected and transferred into RNA-later to preserve mRNA's. Brains were cut in 1 mm thick slices and selected brain areas were dissected and used for RNA isolation.
First we measured mRNA levels of various $GABA_A$ receptor subunits. $GABA_A$ receptors are the targets for the anxiolytic benzodiazepines. Significant decreases in mRNA levels of $GABA_A$ receptor subunits in separated rats vs non-separated rats were observed in prefrontal cortex ($\gamma3$), septum ($\gamma3$), hippocampus ($\gamma3$), amygdala ($\alpha2$, $\alpha4$) and the hypothalamus ($\alpha1$, $\alpha2$, $\alpha4$, $\beta2$, $\gamma1$, $\gamma2$, $\gamma3$).
In the next set of experiments we measured mRNAs of Bcl-2, a suppressor of apoptosis, and of the pro-apoptotic regulator Bax. Only in the hypothalamus of maternally deprived rats, we found indications for increased apoptosis, measured as a significant 70% increase in Bax mRNA combined with a decrease (although not-significant) in Bcl-2 mRN. In addition to the mRNA measurements we also injected BRDU to measure neurogenesis. Results of these experiments will be presented.
In conclusion, our data indicate that early maternal separation leads to long-lasting changes in mRNA expression. Whether these changes translate into changes in behavior and cell number/turnover will be subject to future research.

Ronald Oosting, Department of Psychopharmacology, Faculty of Pharmaceutical Sciences, Utrecht University, Sorbonnelaan 16, 3584 CA Utrecht, t 030-2533730, e-mail r.s.oosting@pharm.uu.nl

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