ESCITALOPRAM ALTERS BDNF, CREB AND CaRF GENE EXPRESSION IN DISCRETE RAT BRAIN AREAS

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Escitalopram is the S(+) enantiomer of citalopram, one of the most widely prescribed serotonin selective reuptake inhibitor (SSRIs) antidepressants. In the chronic mild stress model of depression sucrose intake was already normalized after one week of treatment.
Consequently, considering the fast onset of action of this drug, the first aim of this study was to evaluate the effect of 7 days of treatment (subchronic) with escitalopram (10 mg/kg die i.p) on expression levels of possible targets of antidepressant drugs such as the neurotrophin *Brain Derived Neurotrophic Factor* (BDNF), the transcription factors *cAMP Response Element Binding* (CREB) *Protein* and *Calcium Responsive Factor* (CaRF).
Secondly, we tested the hypothesis that a chronic treatment (21 days) with escitalopram could be able to alter gene expression of BDNF, CREB and CaRF.
BDNF, CREB and CaRF mRNAs were evaluated using RNAse Protection Assay in the following limbic areas: hippocampus, frontal cortex and prefrontal cortex.
No difference was observed on BDNF, CREB and CaRF expression in hippocampus and frontal cortex of animals treated subchronically with escitalopram with respect to the group treated with saline. In contrast a significant induction of BDNF mRNA was observed in prefrontal cortex of escitalopram-treated rats with respect to saline treated ones. CaRF expression patterns were similar. Exposure to Escitalopram for 7 days caused a significant induction of CaRF mRNA with respect to the group treated with saline, while CREB mRNA remained unaffected.
Following a chronic treatment with Escitalopram, BDNF, CREB and CaRF mRNA levels were significantly decreased with respect to the group treated with saline in hippocampus, whereas a 21 day treatment with escitalopram failed to produce changes in gene expression in frontal and prefrontal cortex.
Taken together our results show that escitalopram differentially affects BDNF, CREB and CaRF expression with respect to treatment duration and that the observed effects are area-specific. Moreover BDNF and CaRF expression displayed similar expression patterns following Escitalopram administration. This suggests their involvement in mediating the rapid antidepressant action of this drug as well as possible long term modifications induced by a chronic treatment.