

Implication of the Gabaergic System in Altered Responses to Stress Associated to Maternal Separation

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This diploma thesis studied whether the GABA system alters responses to stress induced by maternal separation in rats.

The aim was to examine the influence of maternal separation on GABA neurotransmission, in particular, the biochemical markers of the system (levels of the neurotransmitter GABA, GABA A receptor expression), and to study of gender-related differences in behavioral and neurochemical processes in rats induced by maternal separation.

In order to pursue the objectives, it was necessary to develop a model of maternal separation in rats. Rat pups were separated from their mother for three hours a day from postnatal day 2 to postnatal day 21 (in the postnatal period, when the reduced ability to respond to stressful stimuli). At postnatal day 23 pups were removed from mothers, divided into groups of the same sex. Then pups were without significant manipulation left to grow into adulthood. After reaching adulthood (> 60 days) rats were divided into two groups. The first group was killed by decapitation and different brain regions (anterior and temporal cortex, corpus striatum and hippocampus) were used to determine the levels of GABA using high performance liquid chromatography and the expression of GABA A receptor was examined employing Western blot technique. The second group was subjected to Porsolt forced swimming test. 14 days after the experiment these animals were also killed by decapitation. Maternal separation was used to simulate changes in behavior related to exposure to stress early in life and to alter HPA response.

We found that both maternally separated male and female rats show signs of depression in adult behavior in the Porsolt forced swimming test, which reflects a significant increase in immobility in this laboratory animal experiment. We also observed increased levels of GABA in the front, accompanied by reduced cerebral cortex GABAA receptor expression. In the temporal cortex, there were no differences between maternally separated rats and control groups or between sexes. Significant gender differences were found in the corpus striatum and hippocampus regarding changes in the GABA system attributed to maternal separation. In the corpus striatum maternally separated males had significantly elevated expression of GABA receptor that they could compensate for decreased levels of GABA in this region. In the hippocampus, maternally separated females had significant increase in expression of GABAA receptor, although no differences in the levels of GABA in combination with maternal separation were measured.

The results support the idea that GABA system plays a role in the depressive syndrome, and that the system could contribute to altered responses to stress stimuli-induced maternal separation process. The results to date thus represent a challenge for future research of the system GABA neurotransmission in etiology of depression.