

# SPATIAL MEMORY, EXPRESSION LEVELS OF BDNF AND STEROID HORMONE RECEPTORS IN THE HIPPOCAMPUS OF SOCIAL ISOLATED OFFSPRING

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## Introduction

Rats deprived of social contact with other rats at a young age experience a form of prolonged stress that leads to long-lasting alteration in their behavior profile. Such isolation is thought to be anxiogenic for these normally gregarious animals, and the abnormal reactivity of isolated rats to environmental stimuli is thought to be a product of prolonged stress. Since this chronic stress results in changes of emotional state, hormonal secretion, abnormal reactivity to environmental, pharmacological stimuli and changes in GABA<sub>A</sub> receptor plasticity and function [1,2], social isolation can be used as a valid experimental model of chronic stress where rats were isolated for 30 days in single cages after weaning.

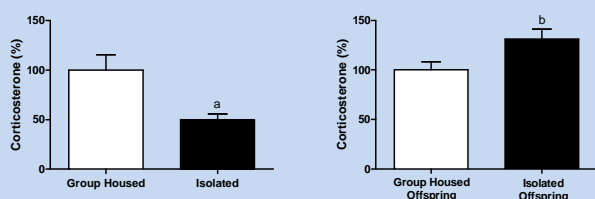
## Aims

To examine a possible trans-generational effects on social isolated offspring we have investigated: 1) basal plasma levels of corticosterone 2) spatial memory performance in the Morris Water Maze 3) hippocampal expression levels of brain-derived neurotrophic factor (BDNF) in basal conditions and at the 5th day of Morris Water Maze 4) expression levels of glucocorticoid (GR) and mineralocorticoid (MR) receptors. These data were compared with previous studies done on isolated rats [3].

## Methods

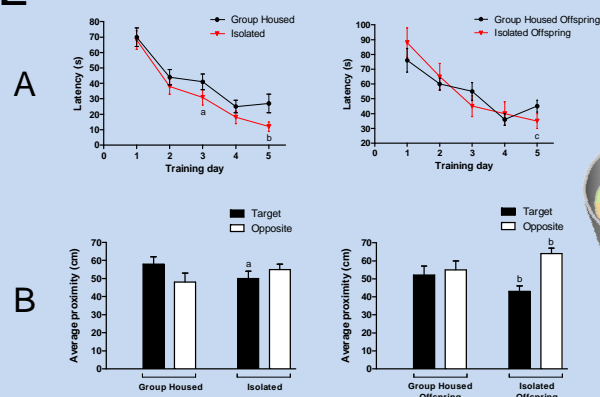
Male Sprague-Dawley rats were used. Corticosterone was extracted from plasma with ethyl acetate and quantified by radioimmunoassay. The levels of BDNF, GR and MR peptides were determined by Western Blot analysis. The measurement of spatial memory was performed through the Morris Water Maze. Data were analyzed by one-way, two-way or repeated-measures ANOVA followed by Newman-Keuls post-hoc test.

## 1 BASAL PLASMA LEVELS OF CORTICOSTERONE



Animals were housed in single cages (isolated) or in groups of 5 per cage (group-housed) for 30 days. The day of the experiment rats were killed by guillotine for plasma steroid measurement. Data are expressed as percentage and are means  $\pm$  SEM. <sup>a</sup> $p < 0.05$  vs group housed animals; <sup>b</sup> $p < 0.05$  vs group housed offspring.

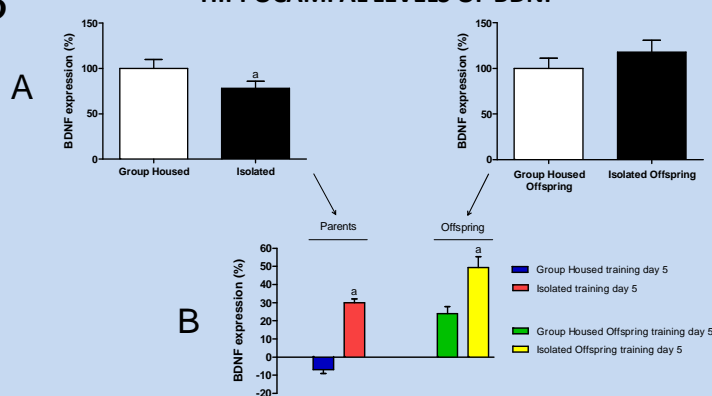
## 2 SPATIAL LEARNING AND MEMORY IN THE MORRIS WATER MAZE



Animals were housed in single cages (isolated) or in groups of 5 per cage (group-housed) for 30 days before the test. (A) Latency for each animal to reach the hidden platform during 4 consecutive trials on each of 5 consecutive days was determined. Data are expressed as means  $\pm$  SEM for 30 animals per condition. <sup>a</sup> $p < 0.05$ , <sup>b</sup> $p < 0.01$  vs group housed rats; <sup>c</sup> $p < 0.05$  vs group housed offspring. (B) Distance from target refers to the average distance from the target location during the probe trial. Distance from opposite refers to the average distance from a comparable location in the opposite quadrant of the maze, that is 180° from the target, during the probe trial. Data are expressed as means  $\pm$  SEM for 30 animals per condition. <sup>a</sup> $p < 0.05$  vs group housed rats; <sup>b</sup> $p < 0.05$  vs group housed offspring.

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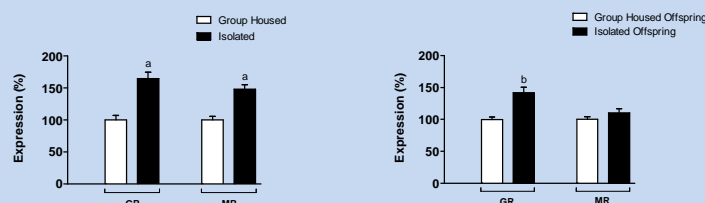
## HIPPOCAMPAL LEVELS OF BDNF



Animals were housed in single cages (isolated) or in groups of 5 per cage (group-housed) for 30 days. Hippocampal homogenates were prepared and subjected to immunoblot analysis with antibodies to BDNF as well as with those to GAPDH. The immunoblots were subjected to densitometric analysis, and the abundance of mature BDNF was normalized by the corresponding amount of GAPDH. (A) Basal expression levels of BDNF. Data are expressed as percentage and are means  $\pm$  SEM. <sup>a</sup> $p < 0.05$  vs group housed rats. (B) Effects of Morris water maze on BDNF expression levels. The expression of BDNF in the hippocampus were measured 90 min after the last training trial on day 5 of training in the Morris water maze. Data are expressed as percentage and are means  $\pm$  SEM. <sup>a</sup> $p < 0.05$  vs corresponding value for controls not subjected to training.

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## HIPPOCAMPAL LEVELS OF GLUCOCORTICOID AND MINERALCORTICOID RECEPTORS



Animals were housed in single cages (isolated) or in groups of 5 per cage (group-housed) for 30 days, after which hippocampal homogenates were prepared and subjected to immunoblot analysis with antibodies to GR or MR as well as with those to GAPDH. The immunoblots were subjected to densitometric analysis, and the abundance of mature BDNF was normalized by the corresponding amount of GAPDH. Data are expressed as percentage and are means  $\pm$  SEM. <sup>a</sup> $p < 0.05$  vs group housed rats; <sup>b</sup> $p < 0.05$  vs group housed offspring.

## Conclusions

- High circulating levels of corticosterone with high levels of GR expression in the hippocampus may play an important role in improving the cognitive performance of these animals.
- Isolated offspring showed an improvement in learning and spatial memory in MWM vs the control offspring.
- These data are in agreement with the increased expression of BDNF since it is involved in various forms of hippocampal learning.
- These results suggest that a stressful condition that have been experienced by the parents in early life time influence hormonal secretion, neuronal plasticity and cognitive performances in the offspring.

## References

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