Hypothalamic Expressions of Apelin, Apelin Receptor and Neuritin in the First Generation Rat Pups: A Maternal Depression Model

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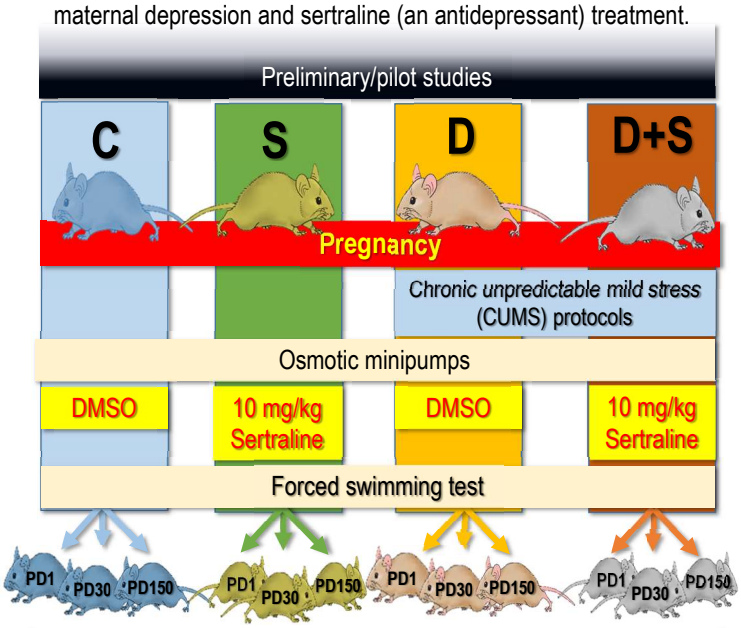
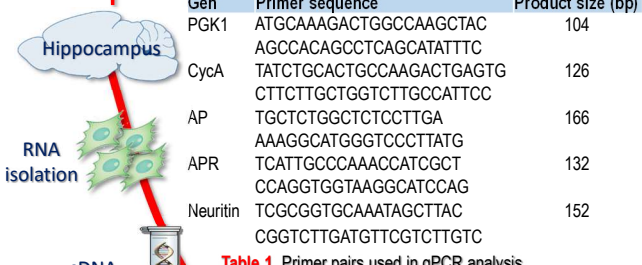
Introduction

- Major depression is one of the most common psychiatric illness; and, women are twice as likely to have depression compared to man.
- Maternal depression may cause some fetal and neonatal effects related to feeding. Hypothalamus has a critical role in food intake and metabolism.
- Apelin (AP) and its receptor (APR) are expressed in different tissues including hippocampus and play important physiological functions.
- Neuritin has also critical physiological functions including dendritic outgrowth, maturation and axonal regeneration, and it is a critical downstream mediator of antidepressant mediated plasticity.

Objective

- Objective of this study was to investigate hypothalamic expression levels of AP, APR and neuritin in the first generation pups of rat exposed to maternal depression and sertraline (an antidepressant) treatment.





Gen	Primer sequence	Product size (bp)
PGK1	ATGCAAAGACTGGCCAAGCTAC	104
	AGCCACAGCCTCAGCATATTTC	
CycA	TATCTGCACTGCCAAGACTGAGTG	126
	CTTCTTGCTGGTCTTGCCATTCC	
AP	TGCTCTGGCTCTCCTTGA	166
	AAAGGCATGGGTCCCTTATG	
APR	TCATTGCCCAAACCATCGCT	132
	CCAGGTGGTAAGGCATCCAG	
Neuritin	TCGCGGTGCAAATAGCTTAC	152
	CGGTCTTGATGTTCGTCTTGTC	

Table 1. Primer pairs used in qPCR analysis

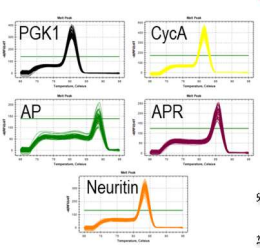


Figure 1. Melting curve analysis

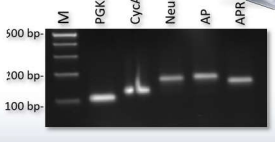


Figure 2. Agarose gel electrophoresis

Materials & Method

- Adult female Wistar albino rats weighing 250-280g and aging 10-11 months of were used in this study.
- Chronic unpredictable mild stress (CUMS) protocol was applied to assess experimental depression model during gestation period.
- Pregnant rats were divided to control (C), depression (D), 10 mg/kg sertraline (S), depression + 10 mg/kg sertraline (D+S) groups.
- Drug infusions were subcutaneously performed for 14 days using osmotic minipumps.
- Hypothalamus tissues were dissected from the first generation pups at postnatal day (PD) 1, 30 and 150.
- Hippocampal tissues were used for total RNA isolation and cDNA synthesis.
- mRNA level expressions of AP, APR, neuritin and reference genes (PGK1 and CycA) were evaluated using qRT-PCR (Table 1) .
- Quality of resulting PCR products were visualized by melting curve analysis (Figure 1) and agarose gel electrophoresis (Figure 2).
- Our previous study (Kurar et al. 2019) indicated that PGK1 and CycA were the most stable reference genes for normalization of qRT-PZR data in rat chronic stress model.
- qRT-PCR data were normalized with housekeeping genes and *ΔCt* values were used for analysis of variance.

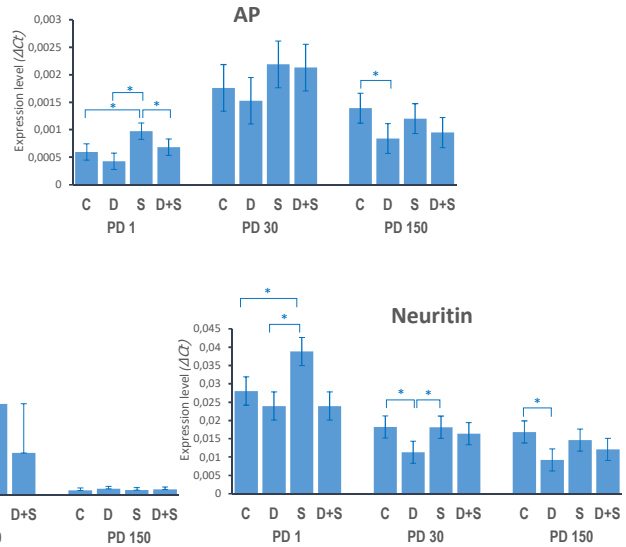


Figure 3. mRNA level expressions of AP, APR and Neuritin

Results and Conclusion

- Hypothalamic neuritin expressions were decreased with age when PD 1 were compared with PD 30 and PD 150. However, AP expression was upregulated in the same days.
- Depression tends to downregulate but sertraline treatment increased expressions of AP and neuritin (Figure 3).
- When compared to the control and depression groups in PD 1, both AP and neuritin expression were upregulated in sertraline group ($p<0.05$). Depression downregulated AP and neuritin expressions in PD 150 ($p<0.05$).
- Our results suggest an evidence that maternal depression and sertraline administration may affect expressions of AP and neuritin and thereby hypothalamic neurogenesis in the first generation pups.
- There is a need for further studies to investigate epigenetics mechanisms to understand pathophysiology of maternal depression.

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