Neonatal bacterial endotoxin exposure exacerbates stress-induced changes of NMDA and AMPA receptor expression in the rat brain

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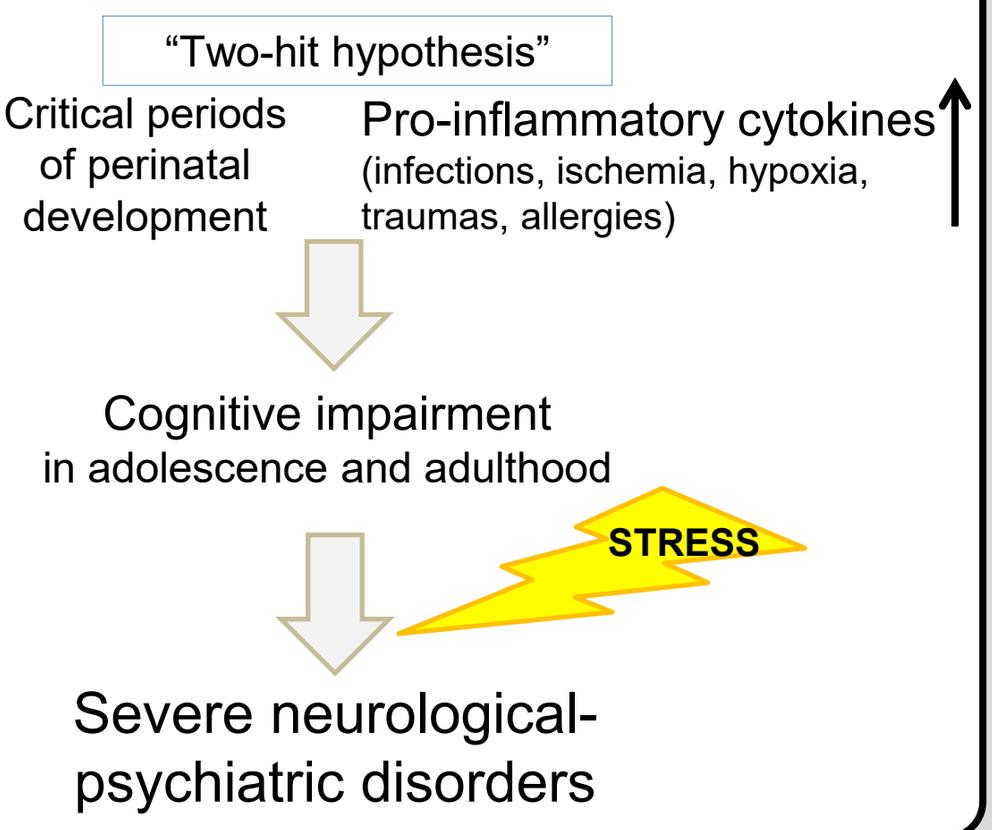
INTRODUCTION

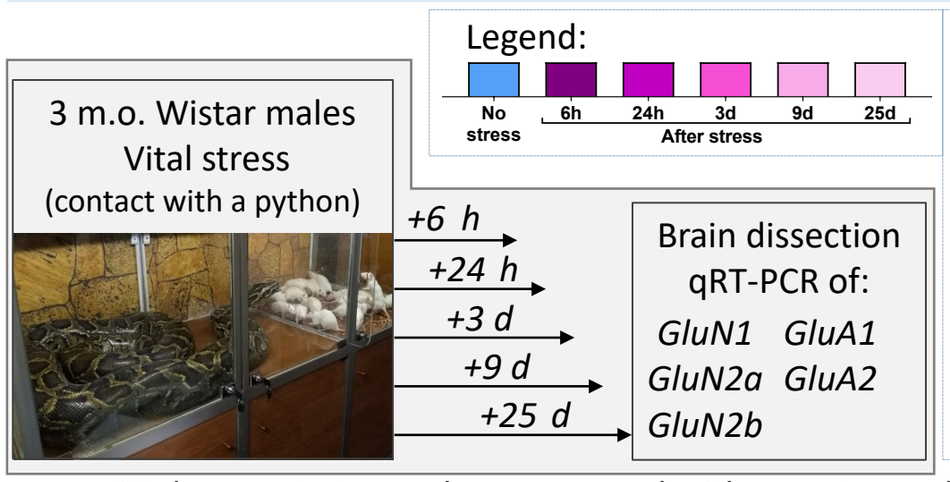
- Deregulated glutamatergic transmission may be implicated in neurological disorders.
- Structural changes of glutamate receptors alter the parameters of glutamatergic transmission: in the developing neonatal brain, the number of NMDA receptors increases (expression of obligatory ***GluN1*** **subunit gradually rises)**, GluN2a/2b ratio of NMDA subunits increases (these NMDARs have higher probability of opening).
- Long-term changes of gene expression of NMDA receptor subunits (*GluN1, GluN2a, GluN2b*) and AMPA **receptor subunits (*GluA1, GluA2*)** after vital stress are not well studied, while it seems important for understanding the mechanisms of stress-evoked neurological-psychiatric disorders.
- Neonatal pro-inflammatory activation can affect brain maturation by making it more vulnerable to stressful events later in life and increasing the risk of various psychopathologies.

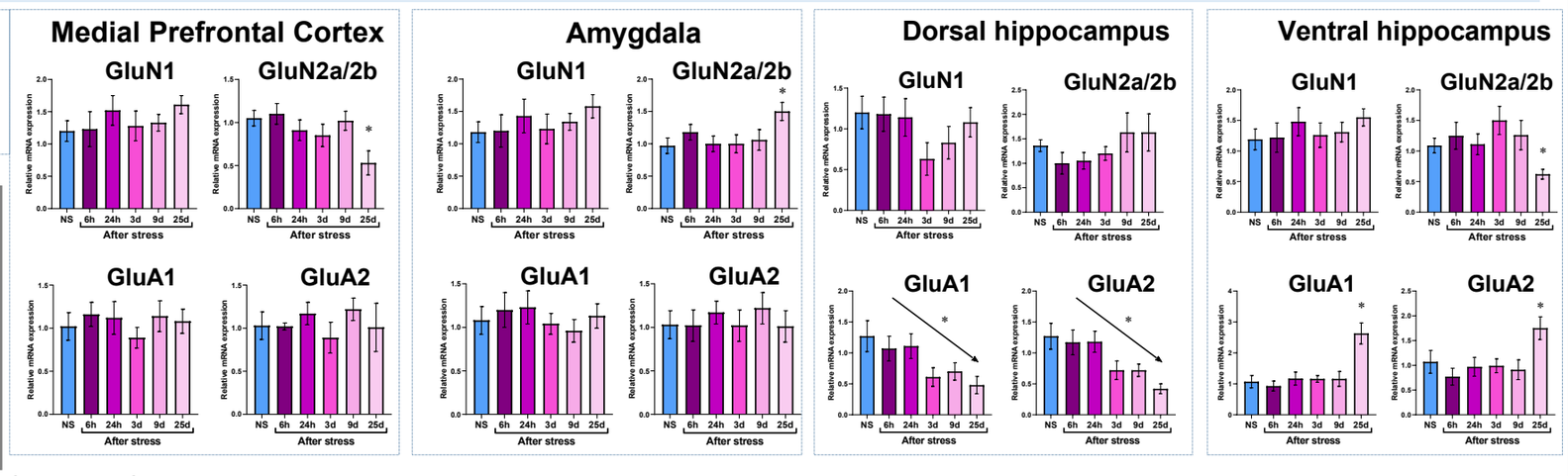
We aimed to investigate NMDA-R and AMPA-R subunit gene expression in the rat brain in a model of vital stress alone or combined with neonatal LPS exposure



STUDY DESIGN and RESULTS

Study I. ***Effects of vital stress on NMDA-R and AMPA-R subunit mRNA expression in the brain areas of adult rats***

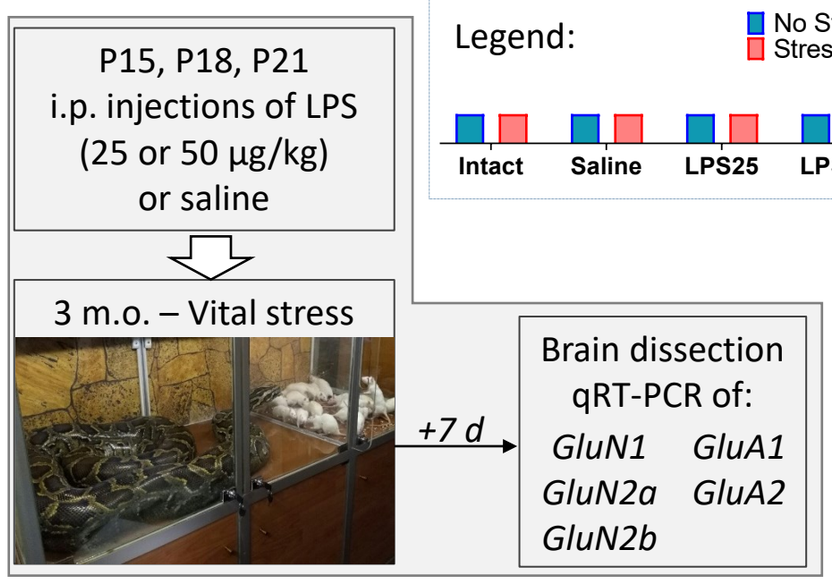


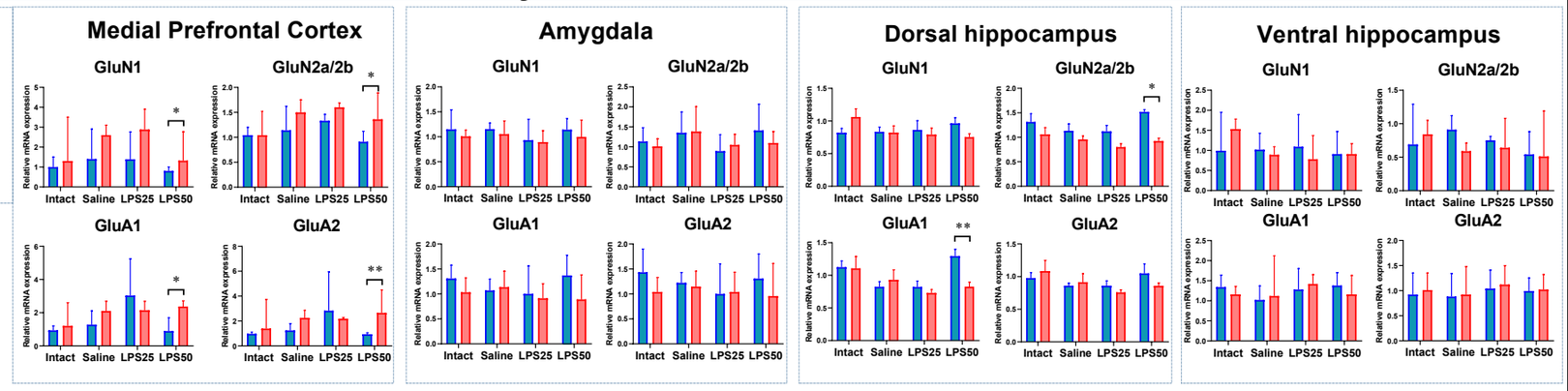


25 days post-stress when compared with non-stressed control:

- no alterations of GluN1 subunit mRNA expression were seen in either of the studied brain structures;
- ratio of GluN2a/GluN2b mRNA was found to be decreased in medial prefrontal cortex and ventral hippocampus and upregulated in amygdala;
- expression of GluA1 and GluA2 decreased in dorsal hippocampus and increased in ventral hippocampus after stress.

Study II. ***Effects of early life LPS treatment on stress-induced alterations of NMDA-R and AMPA-R subunit mRNA expression in the brain areas of adult rats***





- in medial prefrontal cortex of stressed LPS-treated rats (50 µg/kg), when compared with non-stressed group, the levels of GluN1, GluA1, GluA2 mRNA, as well as GluN2a/GluN2b ratio were increased;
- in dorsal hippocampus of stressed LPS-treated rats (50 µg/kg), in comparison with non-stressed group, GluN2a and GluA1 subunit mRNA levels were downregulated, and GluN2a/GluN2b ratio decreased;
- no differences have been found in ventral hippocampus and amygdala.

CONCLUSIONS

- After stress alone, the most pronounced alterations of gene expression were revealed **25 days after stress**.
- When combined with early life inflammation, stress-induced changes of gene expression (7 days post-stress) were more prominent in animals injected with **50 µg/kg LPS** during early-life development.
- Early-life LPS treatment aggravates stress-induced disturbances of NMDA-R and AMPA-R subunit expression in the brain, which may contribute to severe mental illnesses.

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