Maternal nematode infection induces transcription of Long-term potentiation in the postnatal brain via Wnt signaling

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Background: Development of the mammalian brain initiates at early pregnancy and continues postpartum through neural differentiation, migration and synaptogenesis until early adulthood. Maternal intestinal nematode infection has been shown to alter fetal brain gene expression in mice and here we used next generation RNA sequencing to determine whether this maternal influence continues postpartum.

Methods: Timed-pregnant CD1 mice were either infected with four doses of 100± 3 *Heligmosomoides bakeri* larvae (gestation day [GD] 7, 12, 17, postpartum day [PPD] 3) or intubated four times with distilled water (n = 5 / group). On PPD 7, six pups were randomly selected from each litter, livers and brains were collected, and pup sex was determined by PCR. Brain RNA was extracted and sequenced in the illumina Hi-seq sequencer from one male pup per litter. HTSeq was used to count expressed transcripts and differential expression of genes was determined by edgeR. The Protein-protein interaction networks of the differentially expressed genes were generated by functional exploration against KEGG pathway database.

Results: Using a P value cut-off of 0.05 and log2 fold-change cut-off of 1, a total of 5736 differentially expressed genes were recorded. Among them, 2751 were up-regulated and 2985 were down-regulated. Pathway analysis revealed upregulation of a number of favorable pathways. Long-term potentiation (LTP) was of particular interest as synaptogenesis is one of the main events in postnatal brain development. Our data showed up-regulation of all five sequential pathways and receptors required for synaptic plasticity and LTP: Wnt signaling, N-methyl D-aspartate receptors (NMDARs), Ca+ signaling, ras-MAPK signaling, and α-amino-3-hydrozy-5-methylisoxazole-4-propionic acid receptors (AMPARs). On the other hand, several pathways that respond to stress and inflammation were down-regulated including p53 signaling and cytokine-cytokine

receptor interaction, suggesting that maternal nematode infection might provide a less stressful inflammatory milieu during postnatal brain development.

Conclusion: Exposure to maternal nematode infection altered the postnatal brain gene expression which may have a positive impact on postnatal brain development, synaptic plasticity and LTP.

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