Neonatal motor damage presented after gestational sepsis is mediated by inflammatory response and synaptic changes


Objectives
The aim of this study was to evaluate the involvement of pro-inflammatory cytokines, synaptic proteins and motor damage in neonatal mice offsprings submitted to gestational sepsis.

Material and methods
Pregnant mice at 14th day of gestation were intratracheally instilled with saline 0,9% solution (saline group) or Klebsiella spp. (3X10^6 UFC) (sepsis group) and treated with meropenem after 5h. The offsprings were sacrificed 2 days after birth and samples of brain tissue were collected for measuring TNF-α, IL-1β and IL-6 by ELISA. Furthermore, we also analyzed synaptic proteins (synaptophysin) from cortex and hippocampus using Western Blot. The motor outcomes were evaluated by cliff aversion, negative geotaxis, and hindlimb suspension.

Results
Our study shows that the concentration of TNF-α was higher in sepsis group (50,8 pg/mL; e=6,78) than in saline group (25,7 pg/mL; e=2,59). Likewise, levels of IL-1β were higher in sepsis group (34,1 pg/mL; e=4,7) in comparison with saline group (27,7 pg/mL; e=0,59). IL-6 showed a lower concentration in sepsis group (30,4 pg/mL; e=2,46) than saline group (32,9 pg/mL; e=4,28). Analyzing the synaptic marker in both groups, the synaptophysin expression in cortex was higher in saline group (98,87; e=1,48) than in sepsis group (87,75; e=1,77). Moreover, the synaptophysin expression in hippocampus showed even greater decrease in sepsis group (63,93; e=12,16) comparing with saline group (103,3; e=5,52). Motor tests showed that, in cliff aversion the sepsis group spent more time at the edge of platform than saline group. In negative geotaxis test, both groups had similar performances. The hindlimb suspension showed that saline group moved more and had an escape behavior from an adverse situation, while sepsis group had lower attempt to escape and moved less.

Conclusions
These data indicate that gestational sepsis induces an inflammatory response in neonatal mice, decrease the synaptic activity and generates delayed motor response. Based on these observations, it is suggested that gestational sepsis may cause neurological consequences even after birth.