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Early antibiotic administration prevents cognitive damage induced by *pneumococcal meningitis* in Wistar rats

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Bacterial meningitis is an infection of the central nervous system characterized by a strong inflammation of the meninges and the subarachnoid space. Pneumococcal meningitis in humans is associated with long-term sequelae including sensory-motor deficits, seizures, and impairments of learning and memory. In order to evaluate this in an animal model, *Streptococcus pneumoniae* was cultured overnight in Todd Hewitt broth, diluted in fresh medium and grown to logarithmic phase, washed and resuspended in sterile normal saline 5×10^9 cfu/ml. Meningitis was induced by inoculating 10 μL of the *S. pneumoniae* suspension into the cisterna magna of the animals (rats, 60 days old, weighing 250–300 g) after removal of 10 μL of cerebrospinal fluid (CSF). All surgical procedures and bacteria administrations were performed under anesthesia. Meningitis was documented by a quantitative culture of 5 μl of CSF obtained by puncture of the cisterna magna at 8 h and 16 h after infection followed by the initiation of the antibiotic treatment (ceftriaxone 100 mg/kg bid). On day 10, rats were submitted to a behavioural task. Habituation to an open field was carried out in an open arena divided into 9 equal rectangles by black lines. Animals were gently placed on the left quadrant, and was allowed to explore the arena for 5 min (training session) and 24 hrs later submitted again to a similar session (test session). Crossing of the black lines and rearing performed in both sessions were counted. All data are presented as mean ± SD. Data were analyzed by Student's T test, considered $p < 0.05$ to be significant. In the rats that were treated with antibiotic beginning at both 8 h and 16 h after infection no differences in the number of crossings and rearings were observed between groups in the habituation to the open-field training session ($p > 0,05$). In the test session, in animals that antibiotic starts 8 h after infection, we did not observe reduction in both crossings and rearings in meningitis survivors rats compared with sham ($p > 0.05$). However, in rats that antibiotic starts 16 h after infection, we observed a significant reduction in both crossings and rearings in meningitis survivors rats compared with sham ($p < 0.05$). In conclusion, early antibiotic administration (8 h after infection) prevents cognitive damage induced by *pneumococcal meningitis* in Wistar rats.

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