INCREASE OF MICROGLIA MORPHOLOGICAL COMPLEXITY AT EARLY STAGE OF HOST INFLAMMATORY RESPONSE IS ASSOCIATED WITH ACUTE COGNITIVE DECLINE AFTER LIPOPOLYSACCHARIDE

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The morphological changes of microglia has been directly related to its activation. However little is known about microglia morphometric detailed changes in association with cognitive decline after acute infections. Here we tested the hypothesis that an increase in the morphological complexity of microglia observed in the initial stage of activation, may be associated with spatial learning and memory decline. Thus, in this study, we aimed to investigate whether LPS induced morphological complexity increasing at early stage of host response, is associated with the spatial learning and memory impairments following acute infections (figure 03).

Adult female mice (BALB/c) were used to investigate spatial learning and memory before and after saline or LPS (3.3 mg/kg) injections using the Morris-Water-Maze (MWM) task (figure 01). All procedures were approved by the Ethics Committee on Animal Use of the Federal University of Pará (CEUA/UFPA), protocol number: 7135101017. During 5 days, animals (N=10) were trained and then subjected to LPS injection. 1h and 24h after the injection all animals were tested again. Labeled microglia were 3D microscopically reconstructed and classified using hierarchical cluster analysis.

Figure 01. Morris Water Maze (MWM) test apparatus with quadrant division (east, west, north and south) and video capture system for further behavioral analysis.

Before LPS injection significant decrease in escape latency was detected from 2nd training day onwards. At 5th day all animals received intraperitoneally equal volumes of saline or LPS. After inoculation (6th and 7th days) significant increase in escape latency was observed in the LPS but not saline group (figure 02).

Figure 02. Morris Water Maze (MWM) task comparing the escape latency of the animals before and after LPS inoculation.

3D microglia reconstruction of saline and LPS groups confirmed that LPS induced robust microglial activation which was associated with significant impairment in water-maze performances of LPS injected mice. We suggest that cognitive decline and increase of microglia morphological complexity at early stage of host response might be associated.

Figure 03. Morphological changes of microglia regarding the absence of infection (control) in figures A, B and C. Or presence (infected) of LPS, figures D, E and F. Scale bars: A: 250µm, B: 125µm and C 25µm.