Microglial activation and alteration of mitochondrial and peroxisomal dynamics in neurons after Influenza virus pulmonary infection

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INTRODUCTION

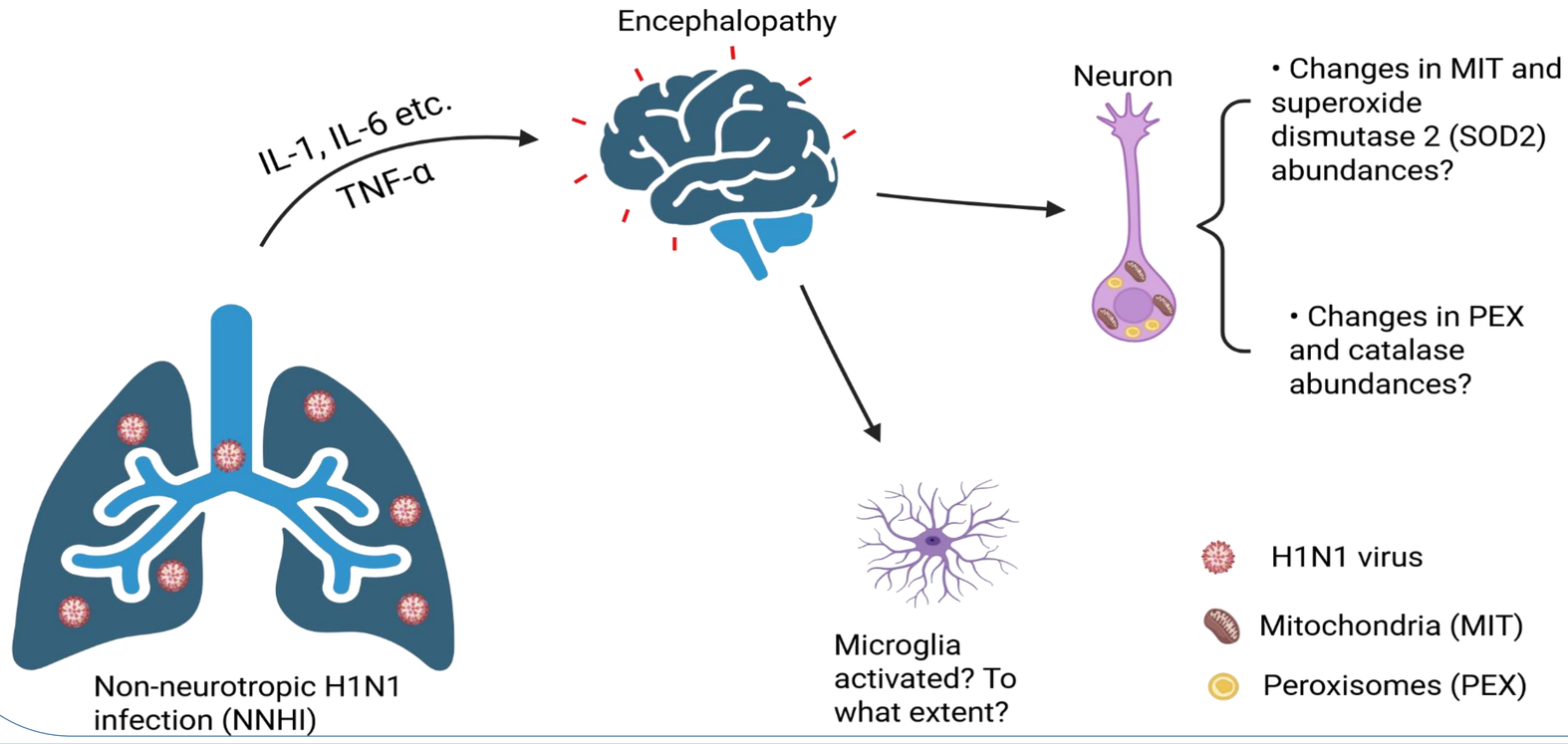


Figure 1. Non-neurotropic influenza A viruses like H1N1 can cause pulmonary disease and indirectly activate microglia and neuronal cells of the central nervous system (**1**). CNS activation may lead to neurological syndromes including seizures, Guillain-Barré syndrome, and Reye's syndrome. Mitochondria and peroxisomes influence intracellular redox homeostasis by producing and detoxifying reactive oxygen species(**1**, **2**). Within their matrices, mitochondria and peroxisomes harbor superoxide dismutase 2 (SOD2) and catalase, respectively, as their main antioxidant enzymes (**3**). Nonetheless, the collateral effects of H1N1 pulmonary infections on brain cells, specifically on mitochondrial and peroxisomal numerical abundances as well as their antioxidant capacities in distinct neuronal cell types of different parts of the brain remain unexplored.

OBJECTIVES OF THE STUDY

- To examine the level of microglial activation in different brain regions after NNHI pulmonary infection.
- To understand the effect of NNHI pulmonary infection on mitochondrial and peroxisomal abundances in distinct neuronal cell types of mice.
- To investigate the potential changes in antioxidant capacities of peroxisomes and mitochondria in distinct neuronal cell types after NNHI pulmonary infection, with peculiar focus on catalase and superoxide dismutase 2 (SOD2).

METHODOLOGY

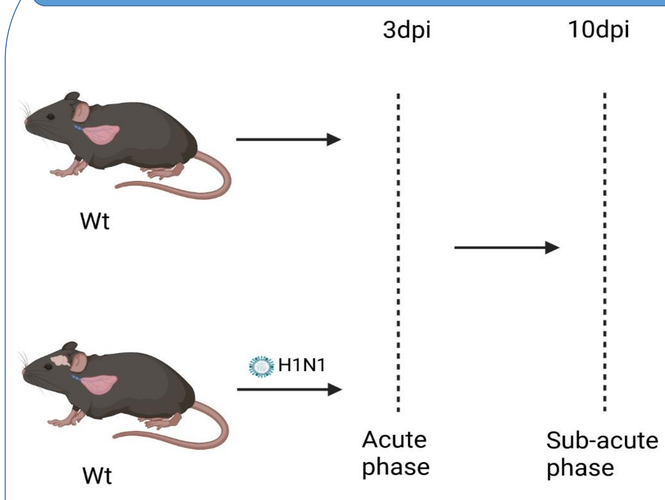


Figure 2. Two groups of 3-month-old Wt mice (non-infected and H1N1-infected cohorts) were set up and euthanized 3dpi and 10 dpi to mimic the acute and sub-acute phases of H1N1 infection

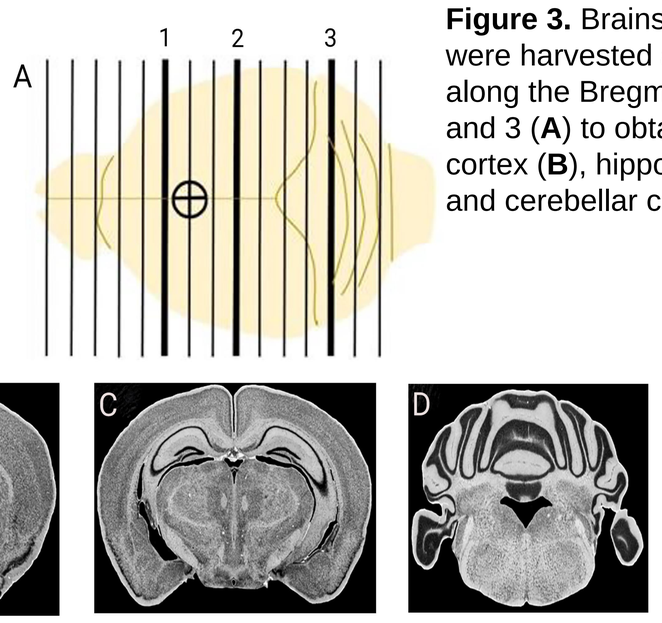


Figure 3. Brains of all mice were harvested and sectioned along the Bregma points 1, 2, and 3 (**A**) to obtain the cerebral cortex (**B**), hippocampus (**C**) and cerebellar cortex (**D**)

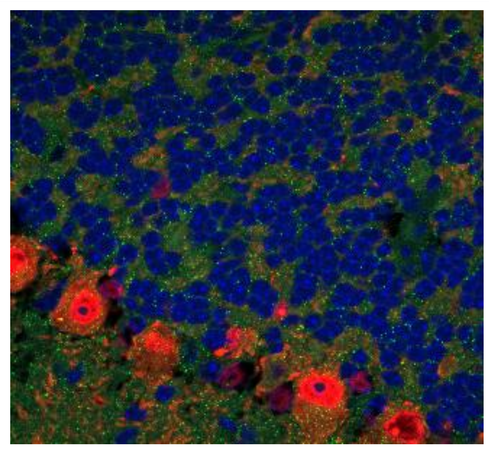
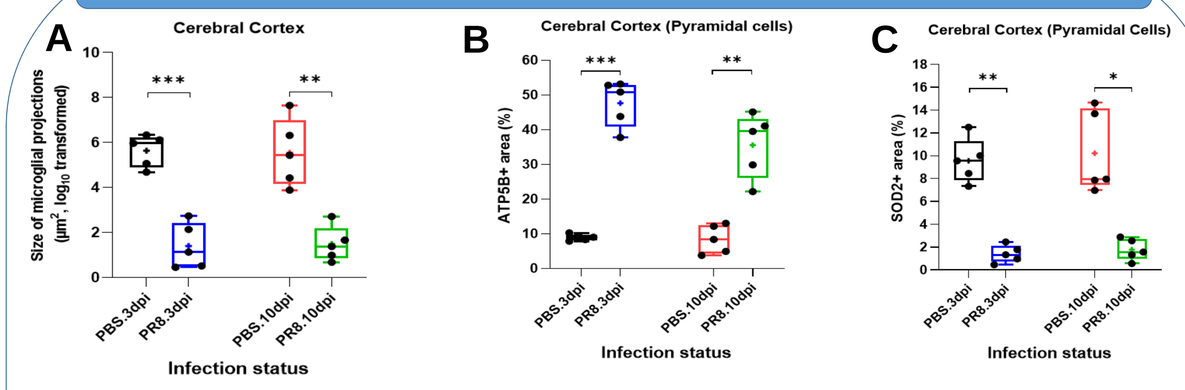


Figure 4. Sample micrograph. Indirect immunofluorescence (IF) staining was performed to identify Iba1, ATP5B, PEX14, SOD2, and catalase in the brains regions shown in Figure 3**B** - **D**. IF micrographs were used as the basis for the morphometric analyses.

RESULTS



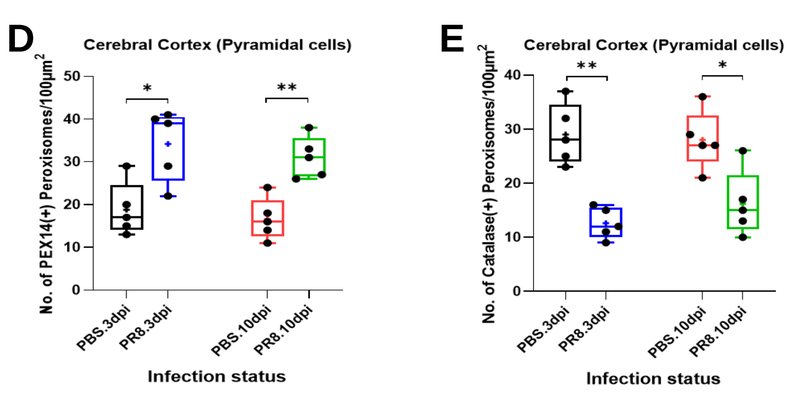


Figure 5. NNHI activated microglia in all brain regions 3 dpi and 10 dpi (**A**). Mitochondrial abundances increased but their antioxidant capacities (i.e. SOD2 abundances) decreased 3 dpi and 10 dpi (**B**, **C**). Peroxisomal abundances increased 3 dpi but decreased 10 dpi (**D**), whereas catalase decreased 3 dpi and increased 10 dpi (**E**). PR8 = strain of H1N1 virus used for this study.

CONCLUSION

NNHI pulmonary infection of Wt mice:

(i) activated microglial in the brain during the acute and subacute phases of infection.

(ii) increased mitochondrial abundances but decreased their antioxidant capacity (SOD2) in the brain during the acute and subacute phases of infection.

(iii) increased peroxisomal abundances during acute phase of infection but reduced during the subacute phase.

(iv) decreased the antioxidant capacity (catalase) of peroxisomes during the acute phase of infection but increased during the subacute phase.

Thus, NNHI of the lung can increase the densities of mitochondria and peroxisomes without concomitant increases in their main antioxidant enzymes, and thus, may cause subsequent oxidative brain damage.

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