NEURAMINIDASE-ACTIVATED MICROGLIA COMPROMISE THE VIABILITY OF EPENDYMOCYTES

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Neuraminidase (NA) is a sialidase present in the envelope/wall of some virus/bacteria responsible for brain infections, such as flu, mumps or meningitis. The intracerebroventricular injection of NA in the rat brain provokes ependymal detachment and death, and an acute inflammatory process. Although inflammation reverses, ependymal lining is not regenerated.

Complement system activation within the CSF contributes to ependymal damage, but is not the only cause (Granados-Duran et al, 2016). Here we aimed to investigate if microglial activation might also play a role. For this purpose we used pure isolated ependymocytes (Grondona et al, 2013) and ventricular wall explants, which were co-cultured with microglial cells, both in basal conditions and with agents that induce microglial activation: NA, LPS, or Pam3CSK4 (synthetic lipopeptide). The viability of the ependymal cells was assessed by trypan blue exclusion.

The viability of isolated ependymocytes was reduced when NA or LPS were added to the culture, compared to controls without additives. In the absence of microglia, NA or LPS did not compromise viability significantly, indicating that microglia was involved in ependymocytes death.

The addition of NA to cultured explants reduced ependymocytes viability only when microglial cells were present in the culture; a similar reduction was observed when LPS or Pam3CSK4 were added. Conversely, explants cultured in the absence of microglia did not suffer a significant decrease in ependymocytes viability upon NA addition to the medium.

We hypothesized that cytokines released by activated microglia, such as IL1β or TNFα, could mediate ependymocytes death. RT-PCR performed in RNA obtained from pure ependymocytes confirmed the presence of IL1β and TNFα receptors in ependymal cells. Nevertheless further experiments are required to confirm this hypothesis.

We conclude that microglia activated by NA mediates, at least in part, ependymal cell death, what might be relevant for neuroinflammatory diseases mediated by NA bearing virus/bacteria.