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Who will guard; the guards themselves?

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Background: Astrocytes have long been established as sentinels for infection. Glial activation has downstream effects on the blood-brain barrier and neurons. However, for many years, astrocyte activation following host infection was essentially limited to “astrogliosis”, with the occasional addition of hypertrophy or atrophy. More recently, it has become possible to quantify the degree to which astrocytes are activated, and to discern which parameters are important for astrocyte function.

Methods: To determine how infectious agents alter astrocyte activation, we “mined” the archives at Tulane National Primate Research Center to find matched tissues from macaques infected with SIV (the parental virus of HIV), Chikungunya, Dengue and *Brucella*. Paraffin embedded cortical tissues were cut at 6 μ m thickness and stained for GFAP and Toll-like receptor 2 for morphometric analyses and innate immune activation, respectively. Morphometric analyses were performed using NeuroLucida software. Routine measures included cell body area, total arbor, arbor volume, number of dendrites, bifurcations, process endings and modified Sholl analyses.

Results: Bacterial infection (with *Brucella melitensis*) induced increases in all the parameters indicated above. In contrast, lentiviral infection induced decreases in the measured parameters, with the exception of cell body area in white matter, although that only occurred in animals with active encephalitis. Two closely associated flaviviruses, Chikungunya and Dengue, produced very different effects on the astrocytes. Whereas Dengue infection induced increases in all the parameters in white matter, Chikungunya induced decreases in bifurcations and tips, with increases in process volume in grey matter. Only cell body area was increased in white matter.

Discussion: Astrocytes respond rapidly to host infection. While it is not hugely surprising that glia respond differently to bacteria and viruses, what was surprising was that even very closely associated viruses induce different responses in astrocytes. We are currently generating software to differentiate astrocytes based on morphometric data.

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