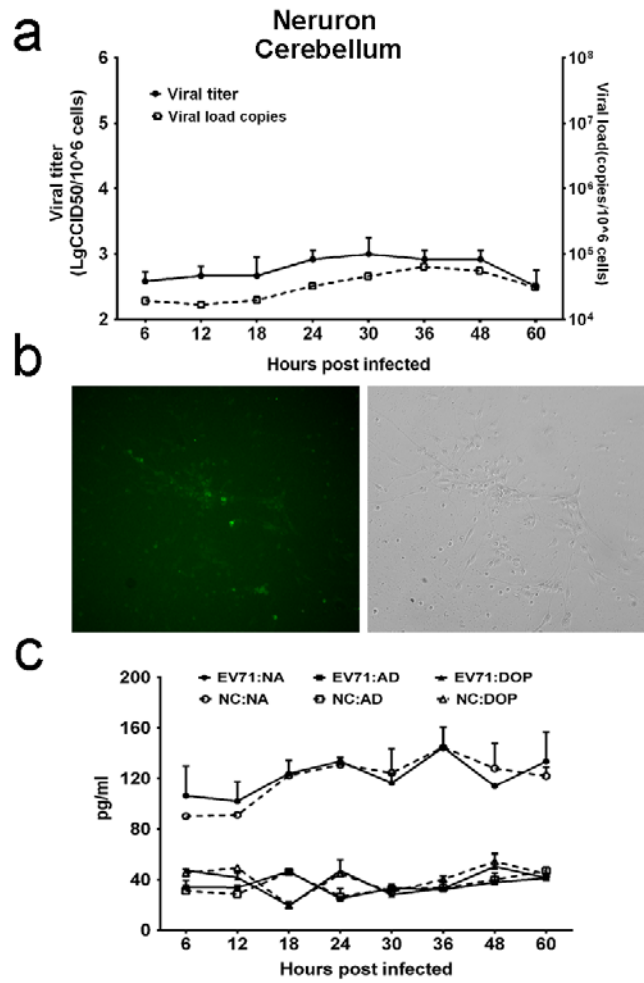
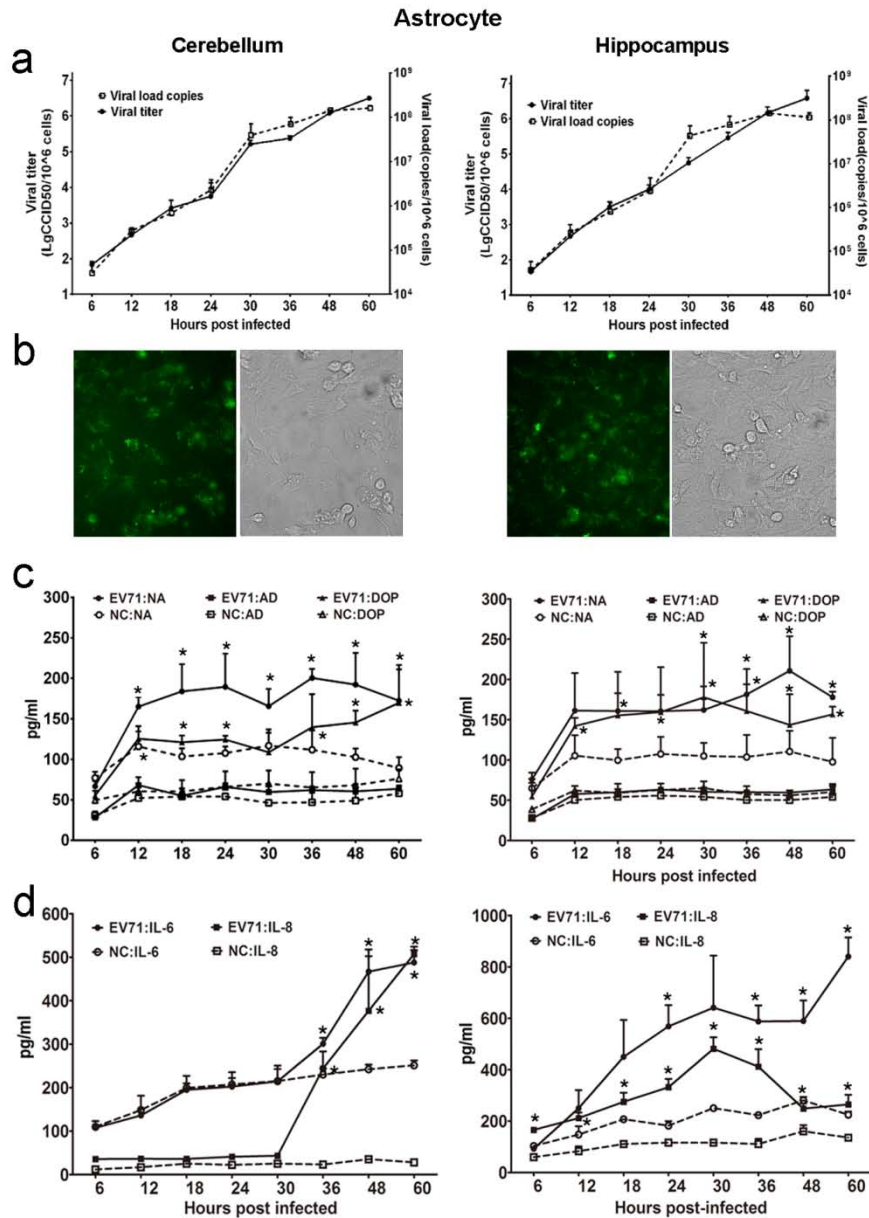


Supplementary



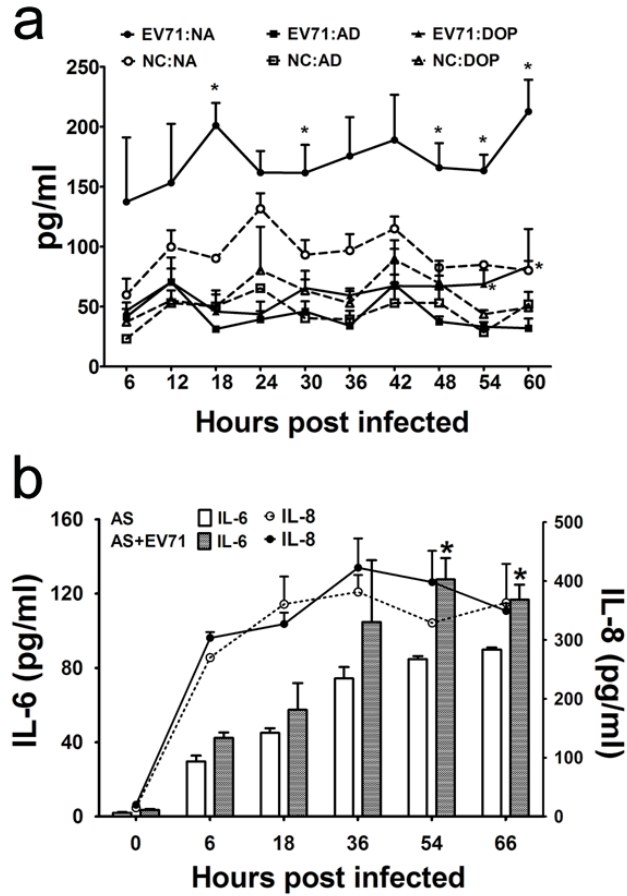
**S1. Detection of EV71 replication in cultured neurons from the cerebellum *in vitro*.**

Proliferation of the virus in cultured human neurons (a) was measured based on virus titration and the viral load from 6 to 60 hours post infection. Immunofluorescence microscopy observations of the EV71 antigen in cultured EV71-infected neurons (b, images are shown at 100 × magnification). Monoamine release by neurons (c) from 6 to 60 hours post EV71 infection. NA: noradrenaline; AD: adrenaline; DOP: dopamine.

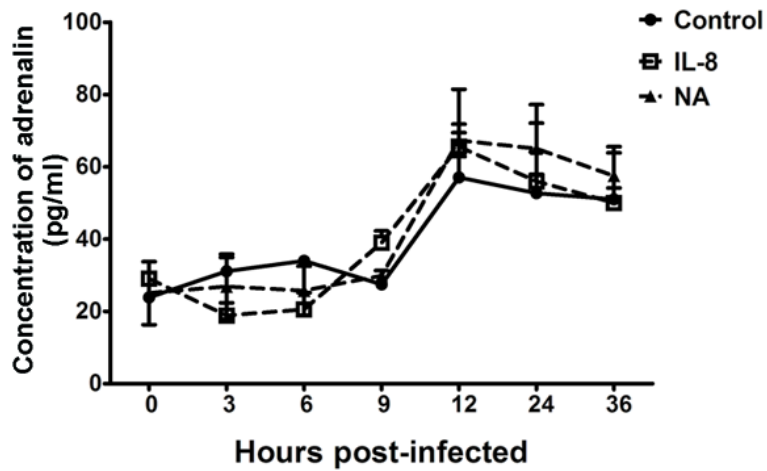


## S2. Detection of EV71 replication in cultured astrocytes from the cerebellum and hippocampus *in vitro*.

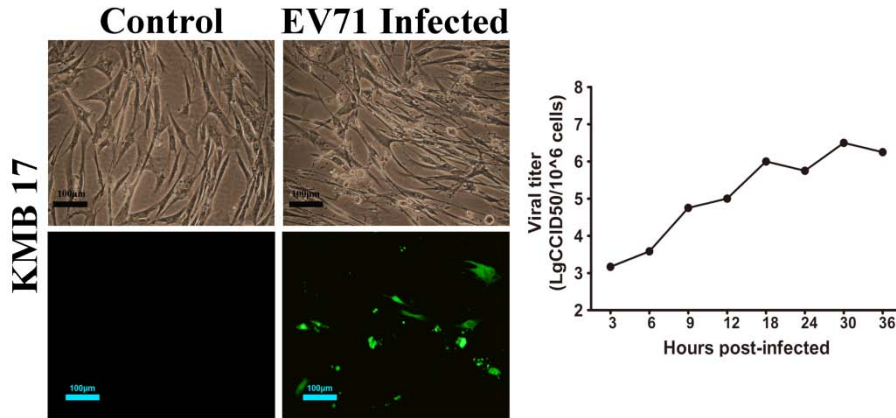
Proliferation of the virus in cultured human astrocytes (a) was measured based on virus titration and the viral load from 6 to 60 hours post infection. Immunofluorescence microscopy observations of the EV71 antigen in cultured EV71-infected astrocytes (b, images are shown at 400 × magnification). Monoamine (c) and cytokines (d) release by astrocytes from 6 to 60 hours post EV71 infection. NA: noradrenaline; AD: adrenaline; DOP: dopamine. \* $p \leq 0.05$ , compared with the corresponding control group.



**S3.** Monoamine (a) and cytokines (b) detected in rhesus macaque astrocytes with EV71 infection. NA: noradrenaline; AD: adrenaline; DOP: dopamine; NC: negative control. \* $p \leq 0.05$  compared to the corresponding control group.



**S4.** Adrenaline released by neurons from brain stem treated with IL-8 and noradrenalin. NA: noradrenaline



**S5.** EV71 infected human fibroblasts in vitro. (a) The cytopathic effect of KMB 17 cells 24 hours post EV71 infection, as observed by microscopy. Immunofluorescence confocal microscopy observations of KMB 17 infected with EV71 using fluorescent anti-EV71 antibodies. (b) The proliferation of virus in KMB 17 cells, and measured by virus titration from 3-36 hours p.i. (MOI=0.05).