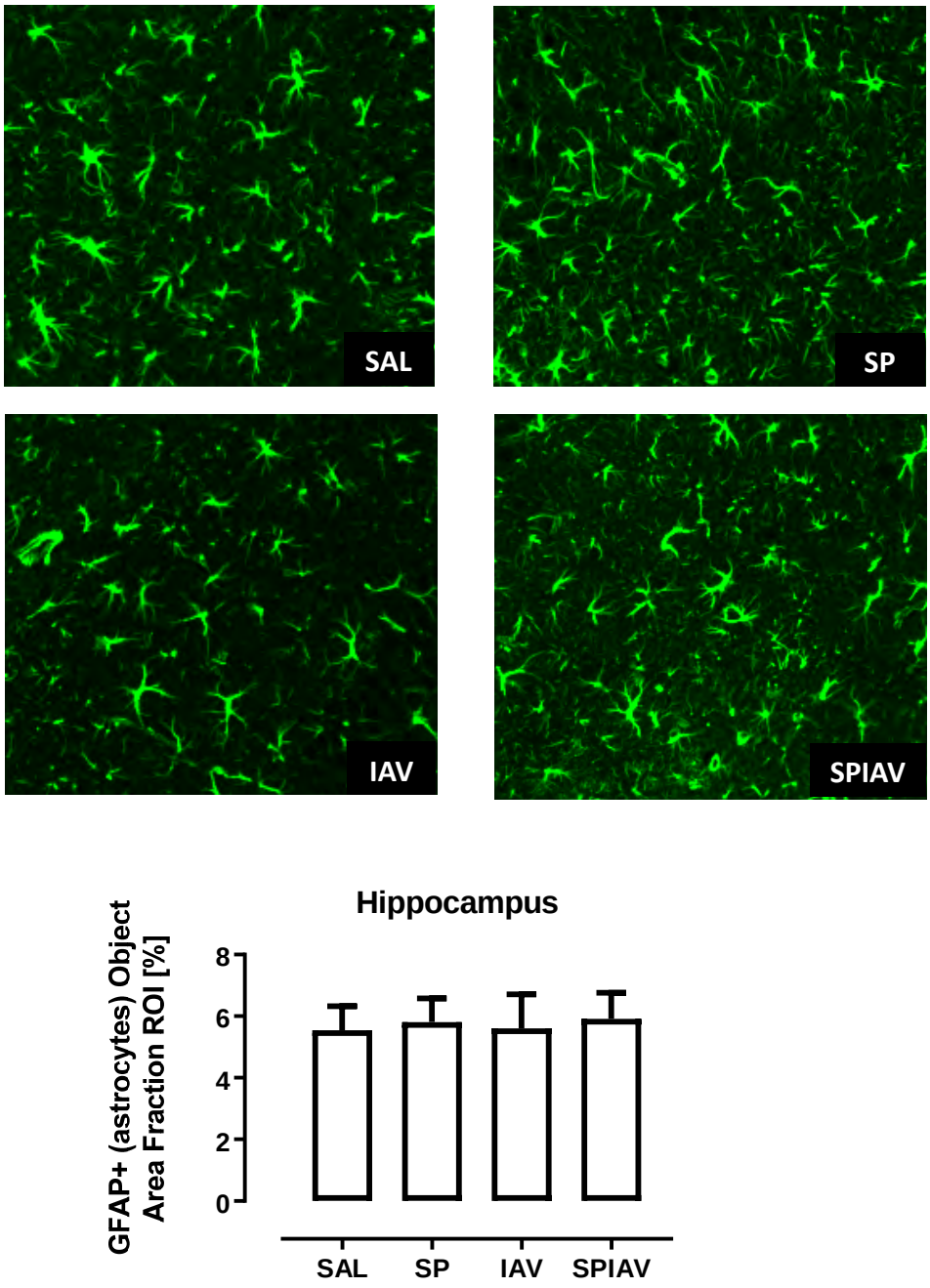
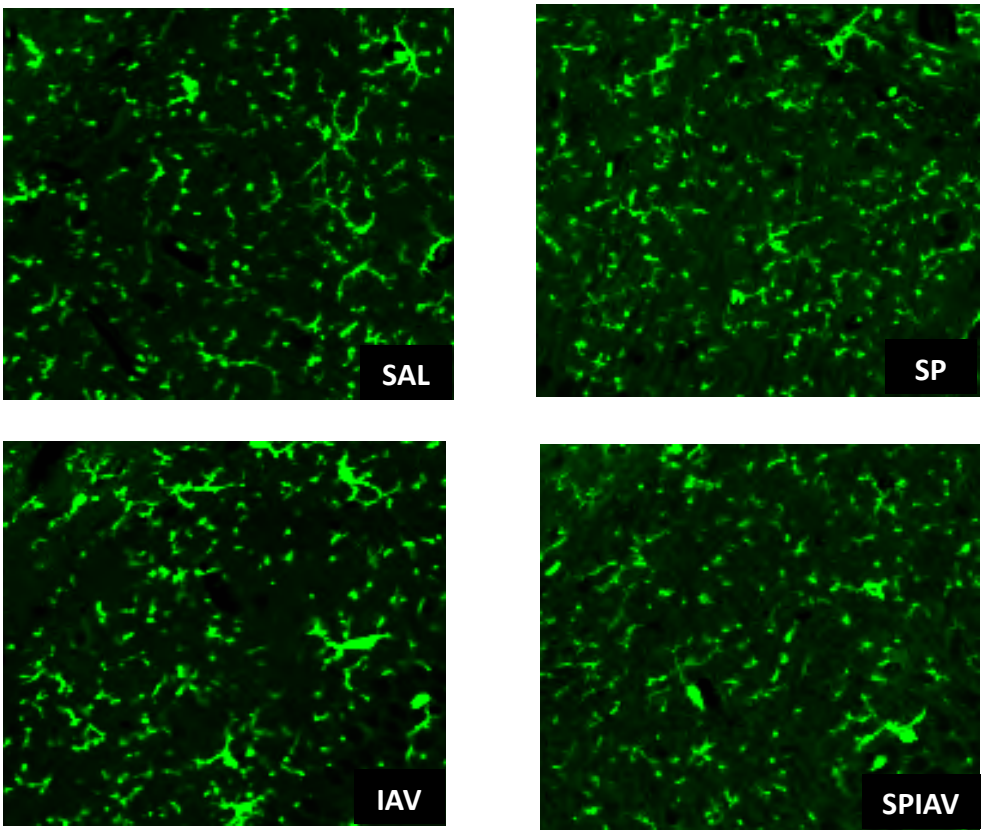



**Figure S1. Co-infection in the lung does not activate astrocytes in the hippocampus.** Brain sections containing hippocampus from saline (SAL), *S. pneumoniae* (SP), influenza A virus (IAV) or co-infection (SPIAV)-treated mice were immunolabelled for astrocytic marker GFAP (upper panel) and GFAP-positive area were quantified (lower panel). n = 5 – 6 with 3 – 4 sections from each brain.



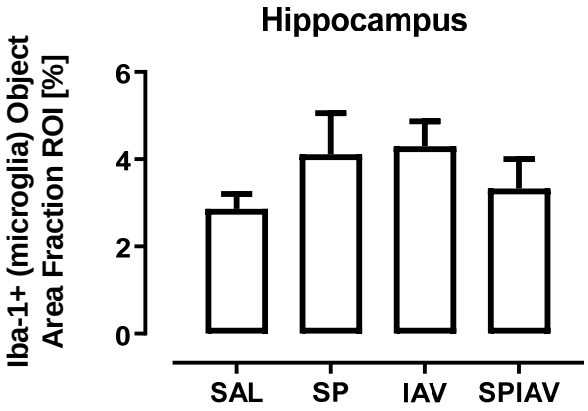




**Figure S2. Co-infection in the lung does not activate microglia in the hippocampus.** Brain sections containing hippocampus from saline (SAL), *S. pneumoniae* (SP), influenza A virus (IAV) or co-infection (SPIAV)-treated mice were immunolabelled for astrocytic marker GFAP (upper panel) and GFAP-positive area were quantified (lower panel). n = 5 – 6 with 3 – 4 sections from each brain.

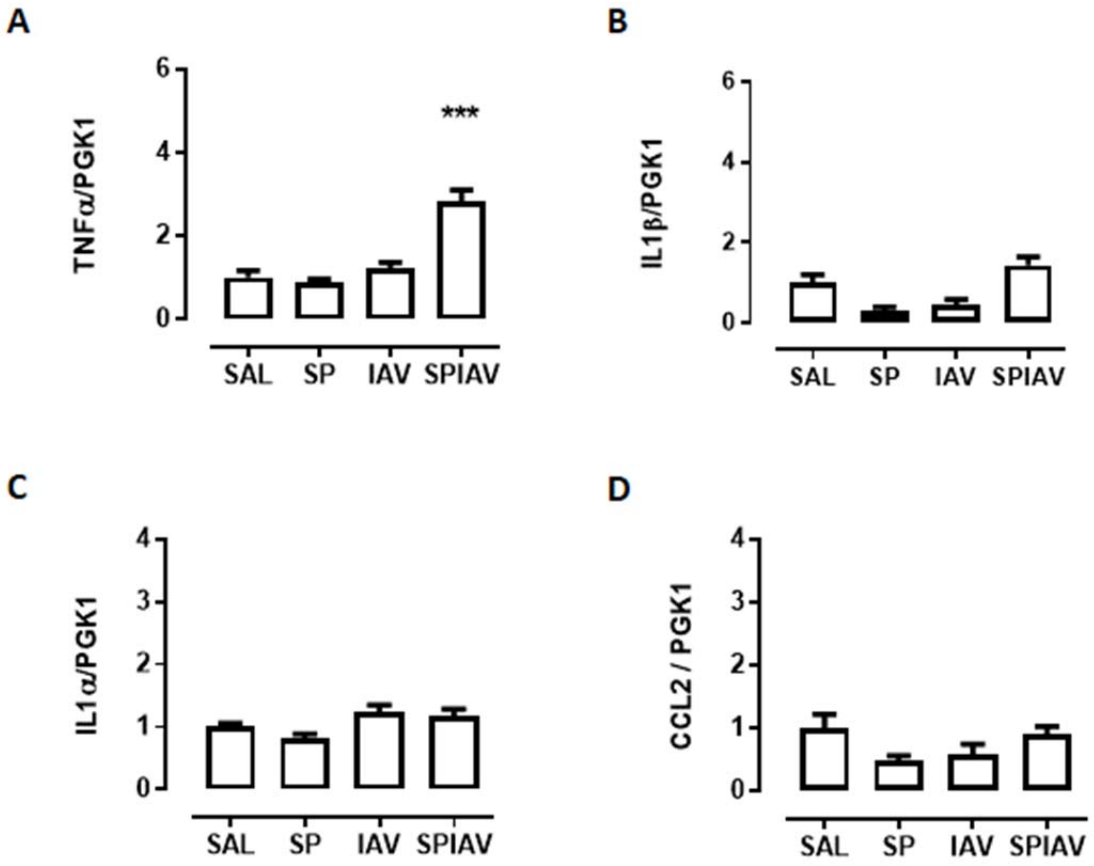



**Figure S3. Co-infection selectively increases TNFα gene expression in the hippocampus.**

The hippocampal region of the brains were dissected from mice treated with saline (SAL), *S. pneumoniae* (SP), influenza A virus (IAV) or co-infection (SPIAV). Gene expression of (**A**) TNFα, (**B**) IL-1β, (**C**) IL-6 and (**D**) CCL-2 was measured. n = 6 – 8; *$p<0.05$, one-way ANOVA compared to SAL.

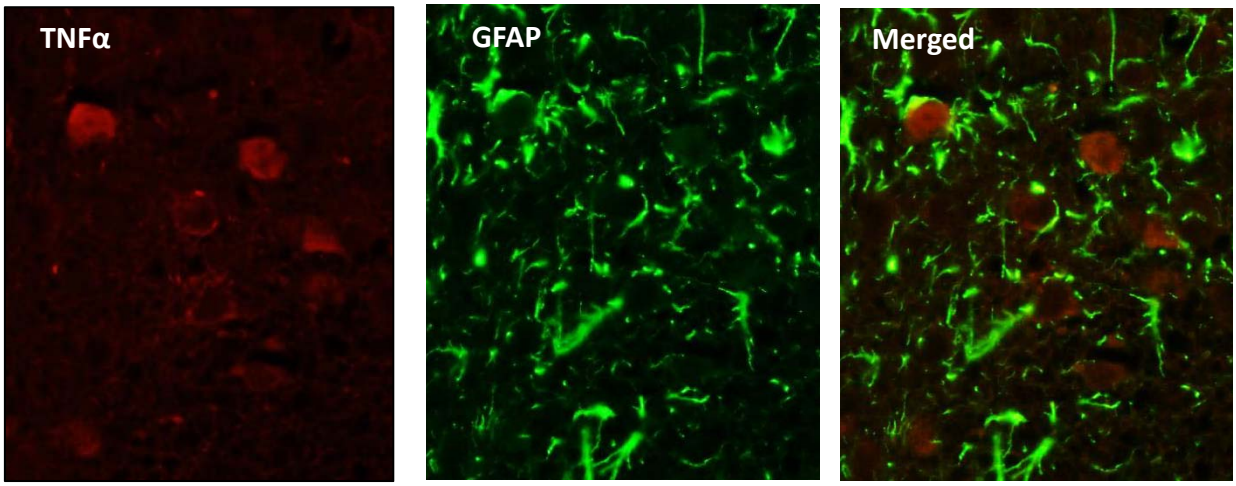



**Figure S4. TNFα does not co-localise with GFAP in the hypothalamus of co-infected mice.** Brain sections containing hypothalamus from co-infected mice (SPIAV) were double-stained for TNFα (red) and astrocytic marker GFAP (green) and images were merged for co-localisation.