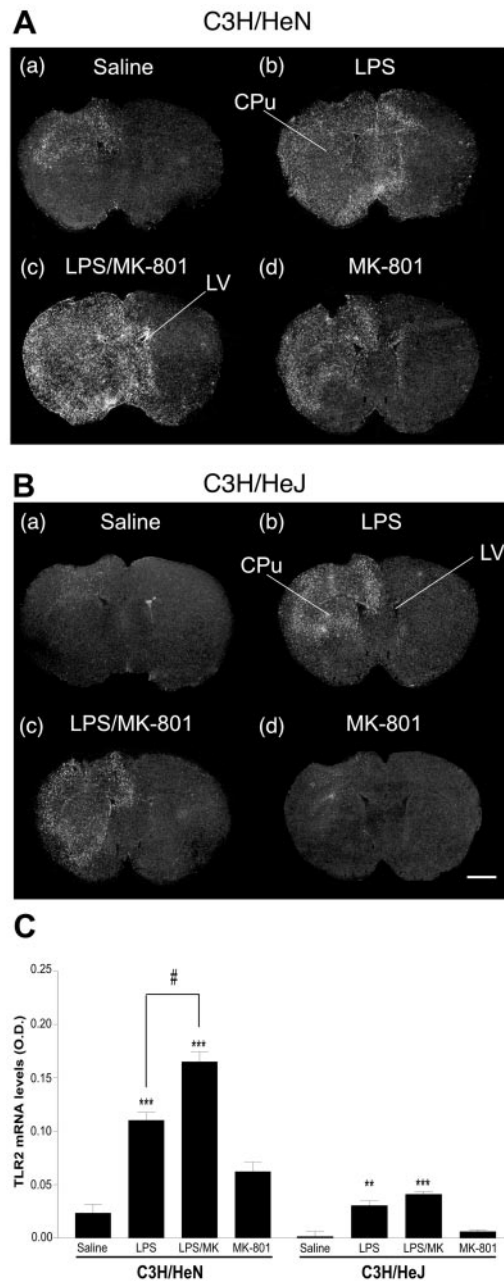


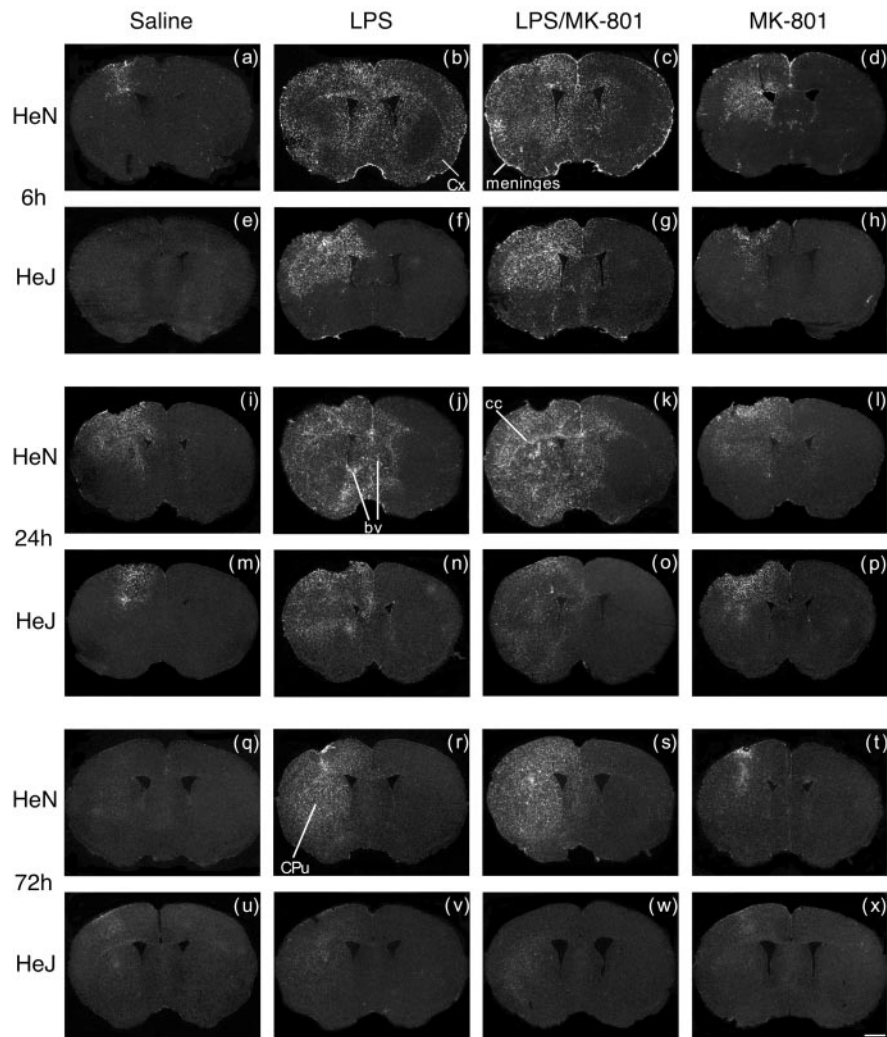
## Erratum

In the article “Modulation of the Innate Immune Response by NMDA Receptors Has Neuropathological Consequences,” by Isaias Glezer, Hakima Zekki, Cristoforo Scavone, and Serge Rivest, which appeared on pages 11094–11103 of the December 3, 2003 issue, a printer’s error resulted in poor-quality reproductions of Figures 1–7. Correct versions of the figures, as well as each corresponding legend, are printed here.



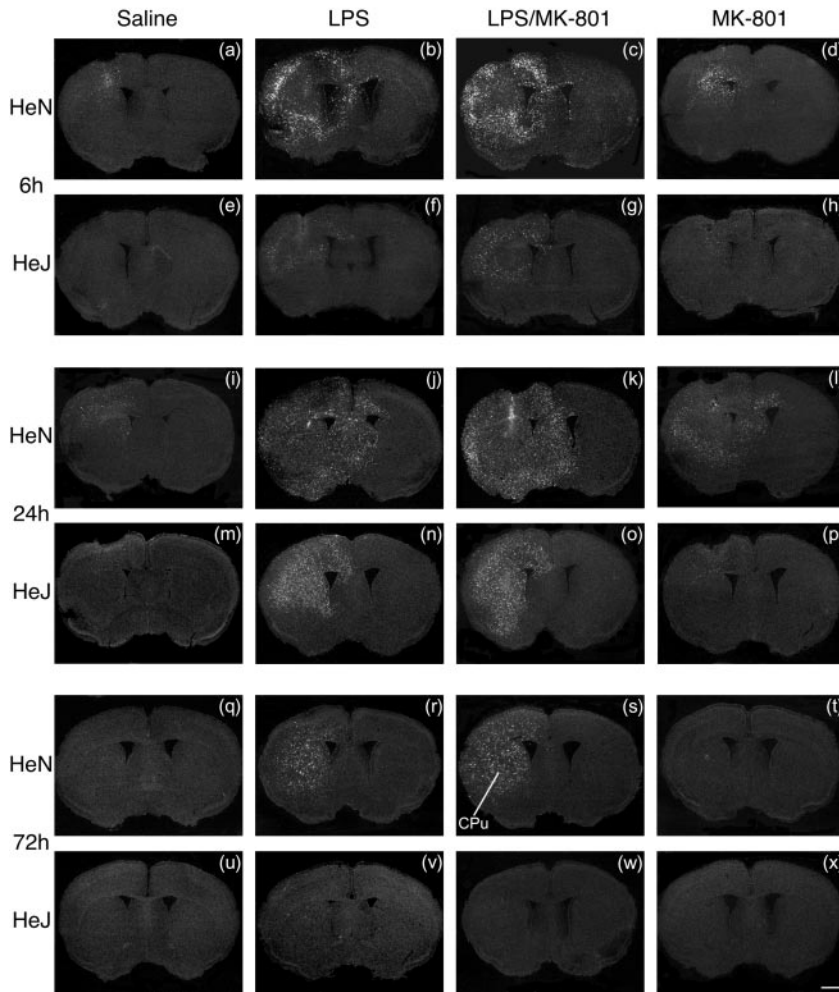
**Figure 1.** TLR2 mRNA expression in the brain of C3H/HeN and C3H/HeJ mice after an intraparenchymal bolus of saline, LPS, or the antagonist of the NMDAR MK-801. *A*, Representative hybridization signals in emulsion-dipped coronal sections (20  $\mu$ m) taken from C3H/HeN mice that received only saline solution (*a*), LPS (*b*; 0.5  $\mu$ g), a mixture containing LPS (0.5  $\mu$ g) and MK-801 (*c*; 1  $\mu$ g, LPS/MK-801), or MK-801 (*d*; 1  $\mu$ g) in the dorsal basal ganglia. *B*, Emulsion-dipped coronal sections of C3H/HeJ mice, which bear a loss of function in the TLR4, killed 24 hr after a single bolus of saline solution (*a*), LPS (*b*), LPS combined with MK-801 (*c*), and MK-801 (*d*). *C*, Semiquantitative analysis of TLR2 mRNA levels (OD) in the ipsilateral side of C3H/HeN and C3H/HeJ mice 24 hr after the intracerebral insults. Please note the robust hybridization signal across the ipsilateral side of mice that received LPS combined with the antagonist of the NMDARs. Results represent means  $\pm$  SEM of three to four mice per group. Statistical analysis was performed by using a two-way ANOVA, followed by a Bonferroni’s multiple comparison test. \*\*Significantly different ( $p < 0.01$ ) from saline-injected group; \*\*\*significantly different ( $p < 0.001$ ) from saline-injected group; #significantly different ( $p < 0.05$ ). For more details, see Materials and Methods. CPU, Caudate putamen; LV, lateral ventricle. Scale bar, 1250  $\mu$ m.

## CD14 mRNA



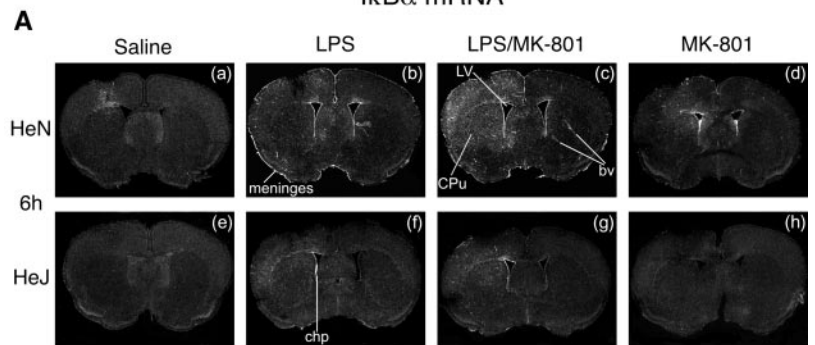
**Figure 2.** Time-related expression of CD14 mRNA in the brain of C3H/HeN and C3H/HeJ mice after a single intraparenchymal bolus of LPS and MK-801. These dark-field photomicrographs were taken from coronal sections hybridized with radioactive CD14 cRNA probe and dipped into nuclear emulsion milk. These images are representative examples of the expression pattern of CD14 transcript 6 hr (*a–h*), 24 hr (*i–p*), and 72 hr (*q–x*) after the infusion with saline, LPS, LPS plus MK-801, or MK-801 alone. Please note the robust signal in the area ipsilateral to the injection site of C3H/HeN mice challenged with LPS and MK-801. Although this effect was impaired in HeJ mice, the endotoxin was still capable of causing a significant increase in CD14 transcription in the brain of this strain (*f, g*). *bv*, Blood vessels; *cc*, corpus callosum; *CPu*, caudate putamen; *Cx*, cortex. Scale bar, 1000  $\mu\text{m}$ .

### TNF $\alpha$ mRNA

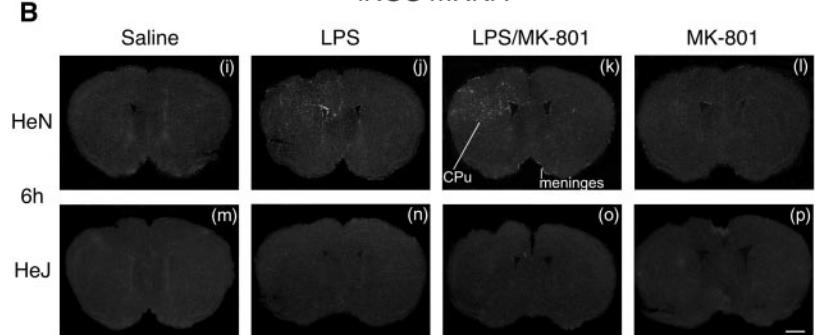


**Figure 3.** Expression wave of the proinflammatory cytokine TNF- $\alpha$  in response to intrastriatal infusion of LPS and MK-801. Representative nuclear emulsion dipped coronal sections depicting the effects of LPS and MK-801 on TNF- $\alpha$  gene expression in C3H/HeN and C3H/HeJ mouse brains at 6 hr (a–h), 24 hr (i–p), and 72 hr (q–x) after injections. Please note the rapid expression of the gene encoding the cytokine in the brain of C3H/HeN mice after coadministration of LPS and MK-801. The endotoxin also stimulated TNF- $\alpha$  gene expression in the CNS of C3H/HeJ mice, especially at 24 hr (n, o). CPu, Caudate putamen. Scale bar, 1000  $\mu$ m.

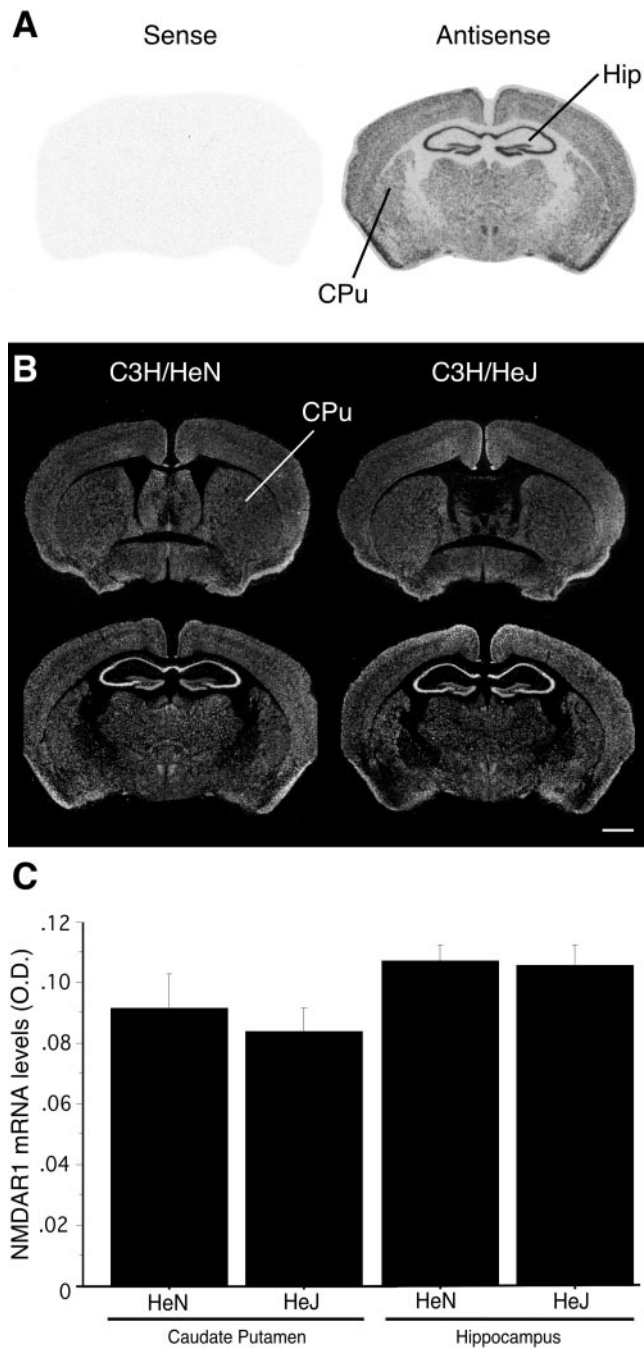
### I $\kappa$ B $\alpha$ mRNA



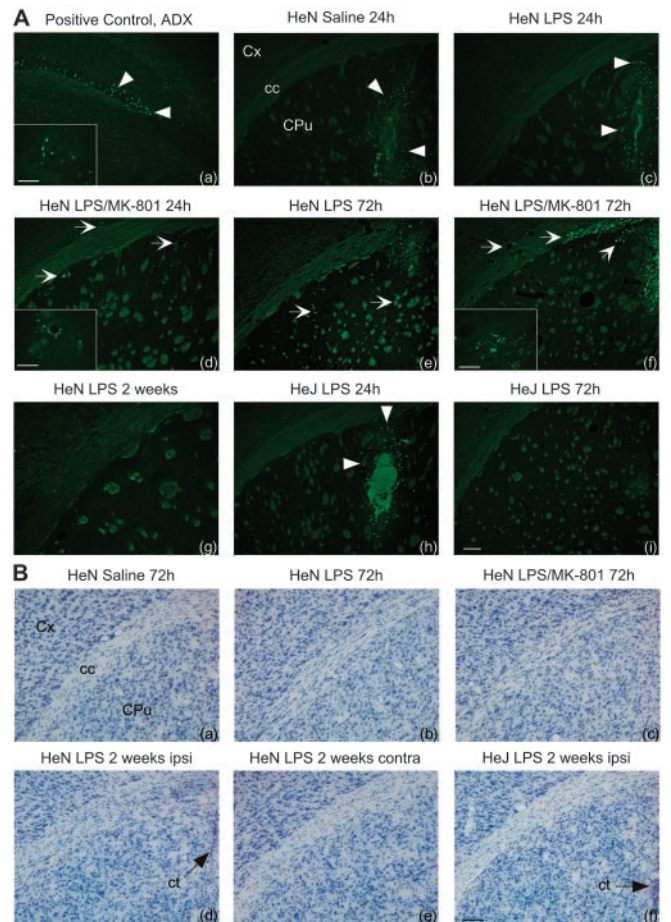
### iNOS mRNA



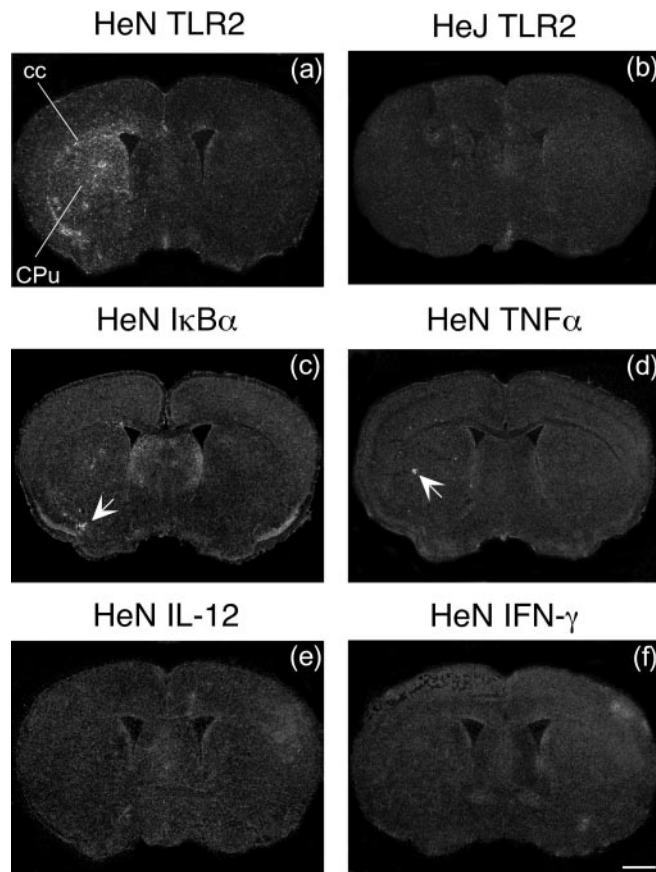
**Figure 4.** TLR4-dependent effects of MK-801 on LPS-induced I $\kappa$ B $\alpha$  and iNOS gene expression. *A*, Dark-field photomicrographs taken from coronal sections hybridized with radioactive I $\kappa$ B $\alpha$  cRNA probe and dipped into nuclear emulsion milk. These images are representative examples of the expression pattern of I $\kappa$ B $\alpha$  transcript (used here as an index of NF- $\kappa$ B activity) (a–h) 6 hr after the infusion with saline, LPS, LPS plus MK-801, or MK-801 alone. *B*, Positive signals for iNOS mRNA were only detected in C3H/HeN mice treated with LPS or LPS plus MK-801 (j and k, respectively) 6 hr after the infusion. The cerebral tissues of C3H/HeJ mice failed to show any positive signal for the mRNA encoding iNOS. bv, Blood vessels; cc, corpus callosum; chp, choroid plexus; CPu, caudate putamen; LV, lateral ventricle. Scale bar, 1000  $\mu$ m.



**Figure 5.** Expression of NMDAR1 subunit mRNA in the brain of C3H/HeN and C3H/HeJ mice. *A*, Representative signals in coronal sections hybridized with sense or antisense riboprobe and exposed to x-ray films (Biomax; Kodak). *B*, Dark-field photomicrographs taken from coronal sections hybridized with radioactive NMDAR1 cRNA probe and dipped into nuclear emulsion milk. Intensity and pattern of the hybridization signal were similar across the brains of C3H/HeN and C3H/HeJ mice. *C*, Semiquantitative analysis of relative NMDAR1 mRNA levels (OD) in the caudate putamen (CPu) and hippocampus (Hip) of C3H/HeN and C3H/HeJ mice. Scale bar, 1000  $\mu$ m.



**Figure 6.** Neuronal integrity in the brain of C3H/HeN and C3H/HeJ mice after intrastriatal infusion of LPS and the antagonist of NMDARs. *A*, The fluorochrome FJB was used as a marker for histochemical localization of degenerative neurons. Degenerating neurons (positive control) were found in hippocampus of a rat killed 6 d after being adrenalectomized (*a*, inset). Such positive neurons were never observed in regions depicting the robust expression of the different transcripts, except along the needle track because of the mechanical injury (white arrowheads). Small non-neuronal cells (probably infiltrating cells) were also found in the CNS of C3H/HeN mice treated with LPS alone or combined with MK-801 (white arrows). *B*, Nissl-stained sections at the level of dorsal basal ganglia. Neuronal density and morphology were similar among all the groups included in this study. Black arrows point to the cannula track. Cx, Cortex; cc, corpus callosum; contra, contralateral side; CPu, caudate putamen; ipsi, ipsilateral side; ct, cannula track. Scale bars, 100  $\mu$ m; insets, 50  $\mu$ m.



**Figure 7.** The innate immune response is not associated with a transfer to the adaptive immunity. Representative examples of nuclear emulsion-dipped coronal sections depicting expression of genes involved in the transfer from the innate to adaptive immune response 2 weeks after LPS injection in the dorsal striatum. TLR2 mRNA was still expressed in the ipsilateral side of C3H/HeN mice 14 d after a single bolus of LPS (*a*), whereas such signal was not present in the infused regions of C3H/HeJ mice (*b*). Few I $\kappa$ B $\alpha$ - and TNF- $\alpha$ -expressing cells were also found in the brain of C3H/HeN mice (*c*, *d*, white arrows). *In situ* hybridization failed to detect any positive signal for IL-12 and IFN- $\gamma$  across the cerebral tissue of C3H/HeN mice (*e* and *f*, respectively). cc, Corpus callosum; CPu, caudate putamen. Scale bar, 1000  $\mu$ m.