

immunoreactivity (see inset). Representative images of tissue immunostained for GFAP taken at 20x magnification from the central striatum at Bregma  $0.3 \pm 0.2$ mm.

**Figure 7.** Binge MA dosing activates striatal microglia. (A) MA treatment increased the area occupied by Iba-1 immunoreactivity compared to saline one day after treatment, though only the highest dose group achieved statistical significance. This increase in area occupied did not persist. Data are presented as mean + SEM (n = 3 per dose group per day). \*\*  $p < 0.01$ . (B) All doses of MA induced pronounced microglial activation one day after MA treatment, as evidenced by larger cell bodies, thicker processes, and intense Iba-1 immunoreactivity. This activation diminished over the following days, leaving clusters of activated cells scattered throughout the striatum on day 7. By day 14, the microglial activation had subsided. Representative images of tissue immunostained for Iba-1 taken at 20x magnification from the central striatum at Bregma  $0.3 \pm 0.2$ mm.

**Table 1.** A summary of the changes seen in markers of neurotoxicity and neuroinflammation for each dose and time point. Up and down arrows indicate statistically significant changes, compared with the saline-treated group of the same time point. Arrows in parentheses indicate changes of two-fold or greater for which a significant main effect of MA was revealed by two-way ANOVA, but that did not reach statistical significance in pairwise comparisons with the saline-treated group of the same time point. NC indicates no change.

**Supplementary Table 1.** Summary data tables indicating the number of animals in each group and mean body mass (g,  $\pm$  SEM) at sacrifice in the behavioral, HPLC, and IHC cohorts.

**Supplementary Figure 1.** Binge MA dosing does not significantly alter cortical monoamines or their metabolites. Although a few pairwise comparisons reached statistical significance, there were no clear effects of MA treatment on cortical DA (A), DOPAC (B), HVA (C), DA turnover rates (D), 5-HT (E), HIAA (F), or NE levels (G). Data are presented as mean fold change from respective saline + SEM (n = 4-8 per dose group per day). \*  $p < 0.05$ , \*\*  $p < 0.01$  compared with saline group of the same time point.