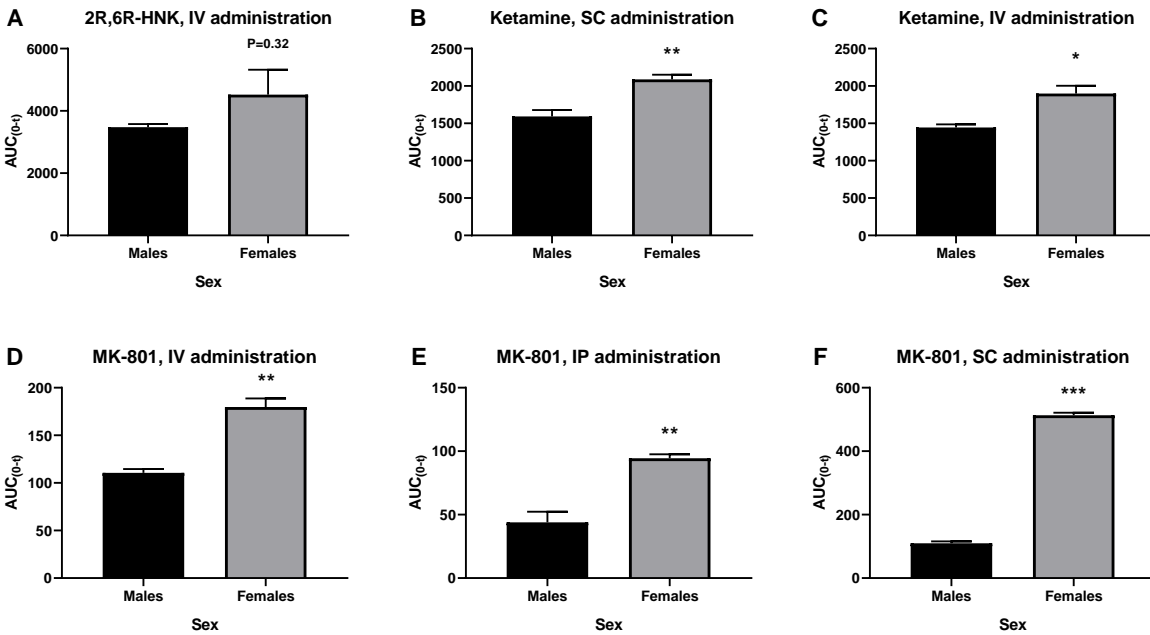


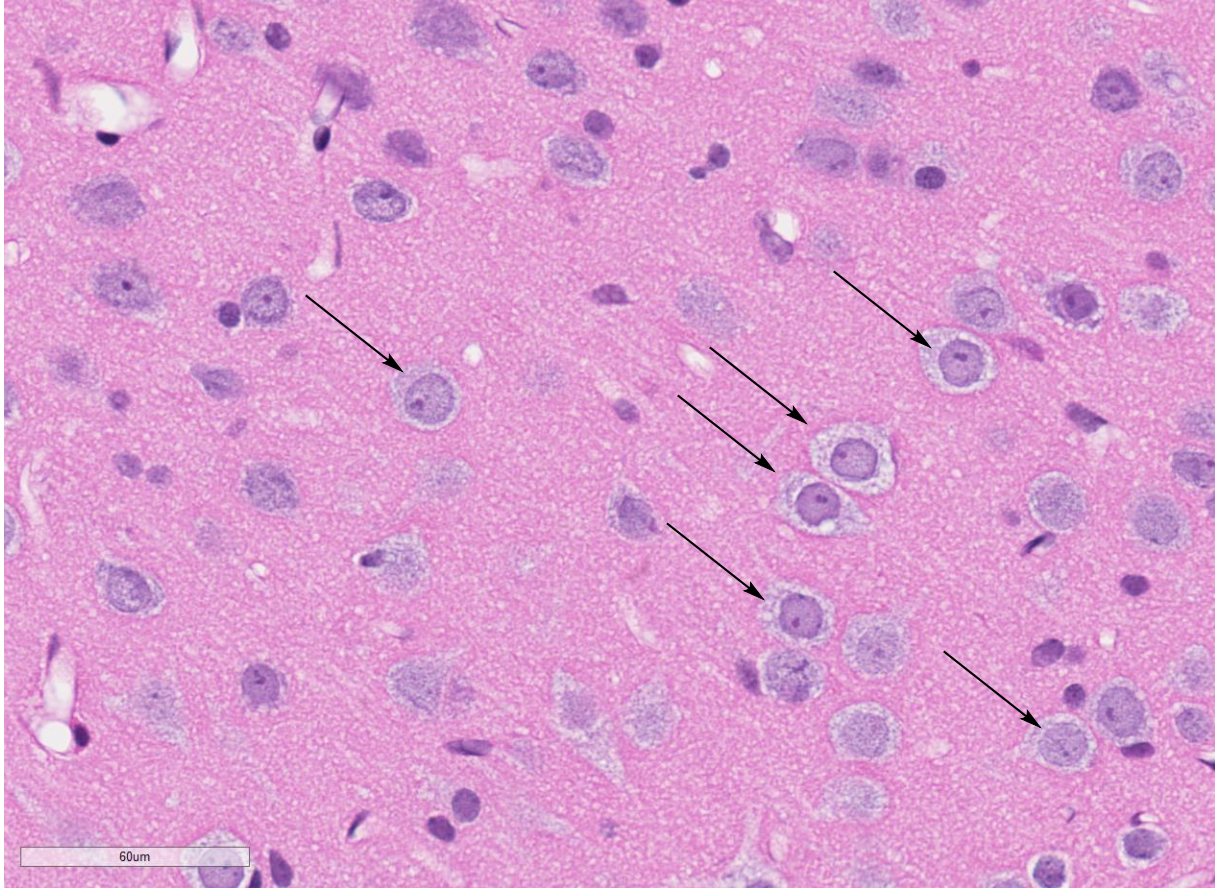
1 Supplemental Information



2

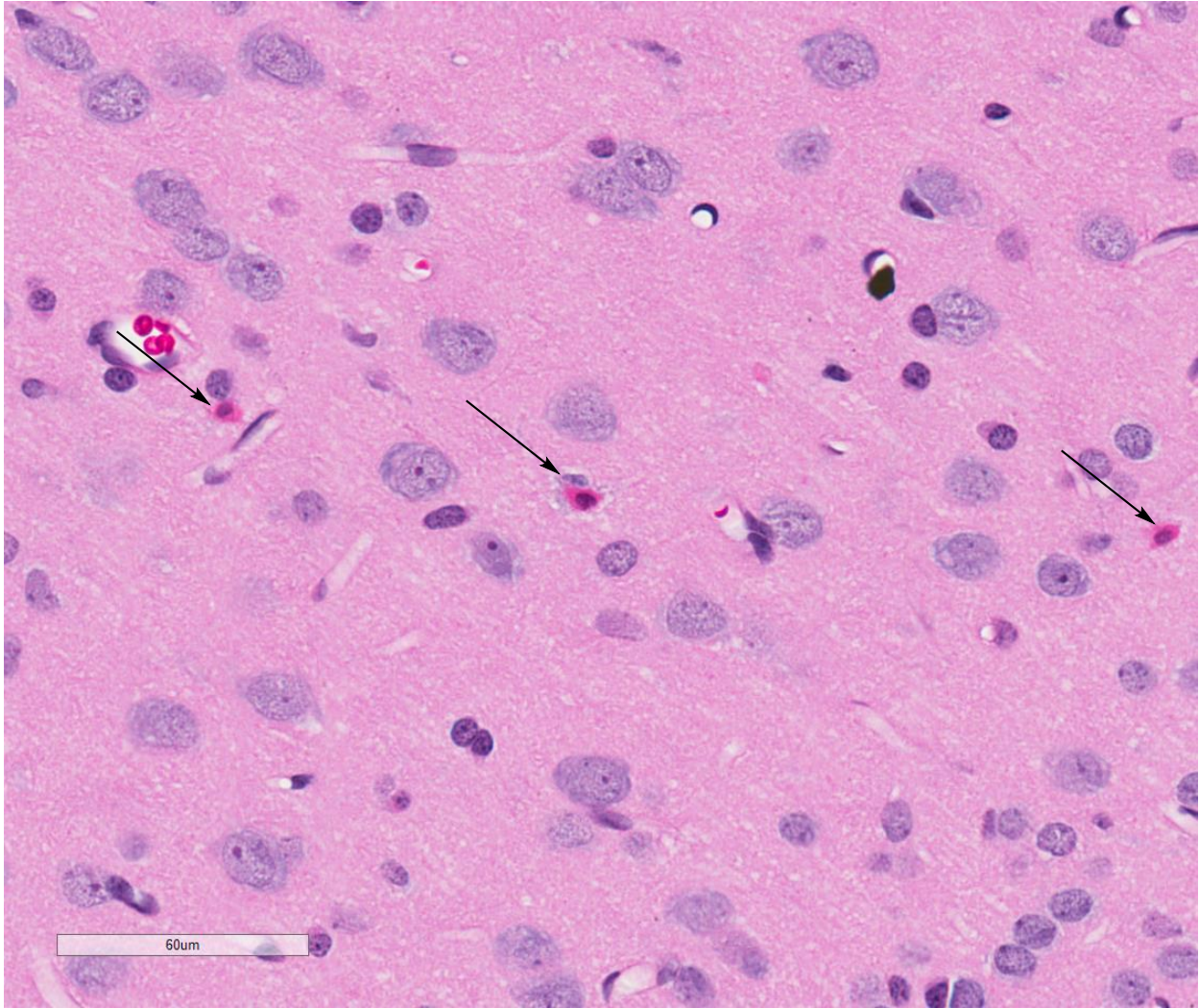
3

4 **Figure S1:** Comparison of male versus female area under the curve (AUC) for administration of 2R,6R-HNK,
5 ketamine, and MK-801 administration, including different routes of administration A) 2R,6R-HNK, IV
6 administration. B) Ketamine, SC administration. C) Ketamine, IV administration. D) MK-801, IV administration. E)
7 MK-801, IP administration. F) MK-801, SC administration. Dosing is as per Table 1. AUC_(0-t) is in nanogram hours
8 per milliliter (ng * h / mL). * indicates $p < 0.05$, ** indicates $p < 0.01$, *** indicates $p < 0.001$. Statistical
9 comparison is by unpaired t-test. Error bars are standard deviation.



10

11 **Figure S2:** Example of vacuolization in the neurons after dosing with MK-801 in the single dose experiment at 0.8
12 mg/kg. 3 hours time point, H&E staining. Bar is 0.06 mm. Note arrows highlight select cells with prominent
13 cytoplasmic vacuolization.



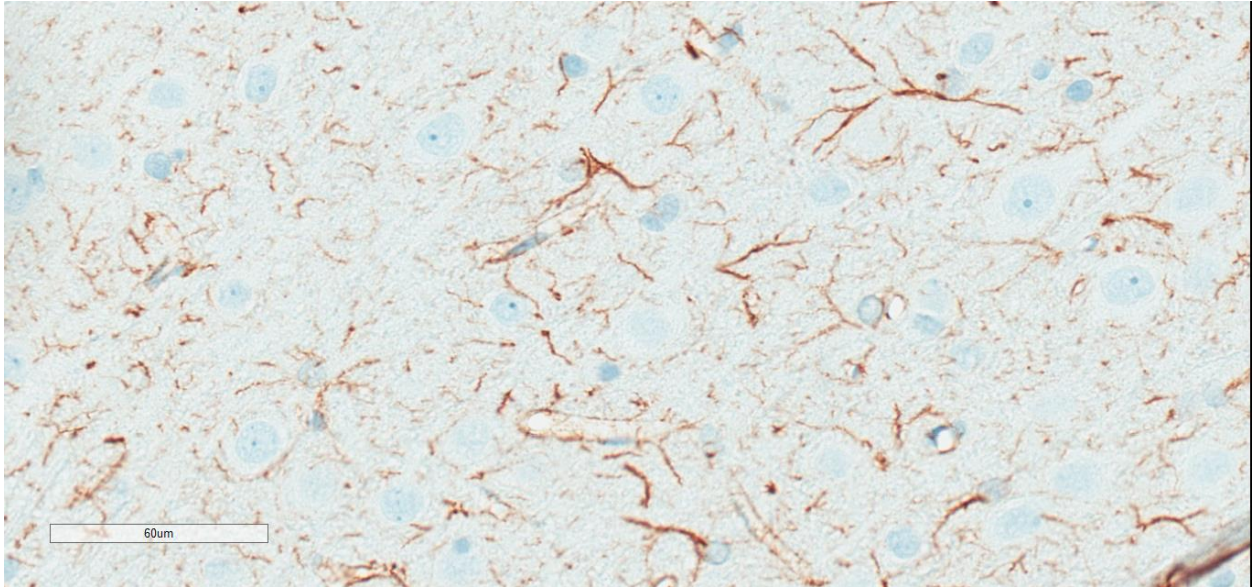
14

15 **Figure S3:** Example of necrosis in the neurons after dosing with MK-801 at 0.8 mg/kg in the single dose experiment.
16 72 hour time point, H&E staining. Bar is 0.06 mm. Note necrosis in cells that have the arrow pointing at them.

17

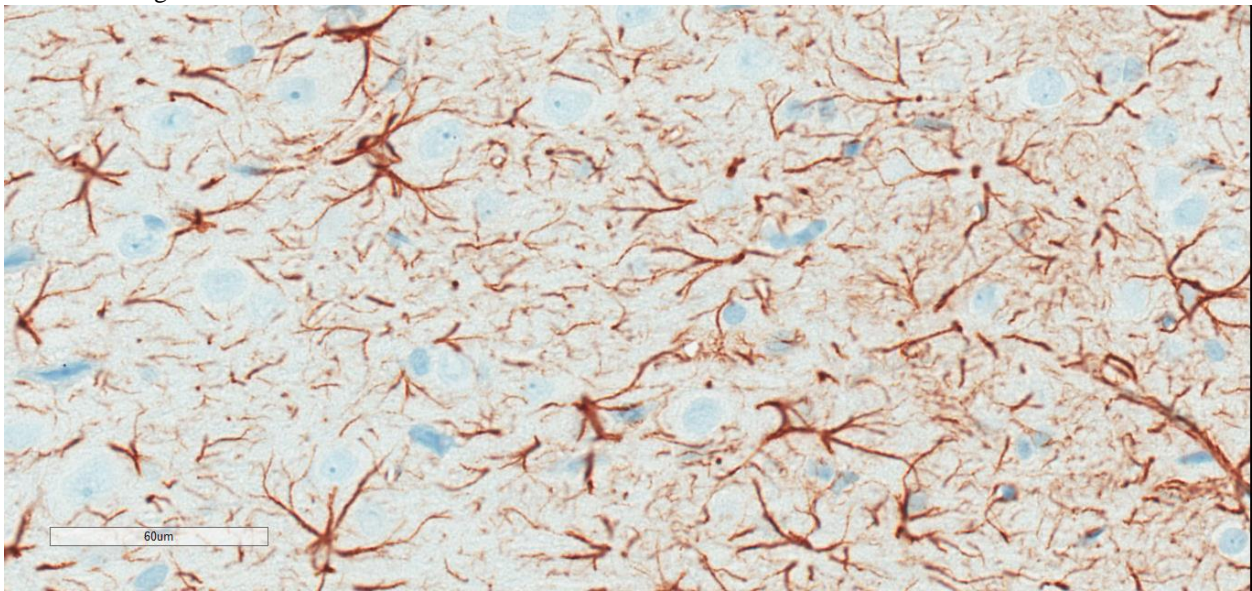
18

19



20

21 **Figure S4:** Example of the GFAP staining for the negative control in the multiple dose experiment at 15 days + 72
22 hours. Bar length = 0.06 mm



23

24 **Figure S5:** Example of the increased GFAP staining in the 0.8 mg/kg MK-801 dosing level in the multiple dose
25 experiment at 15 days + 72 hours. Bar length = 0.06 mm

26