Supplementary Figures

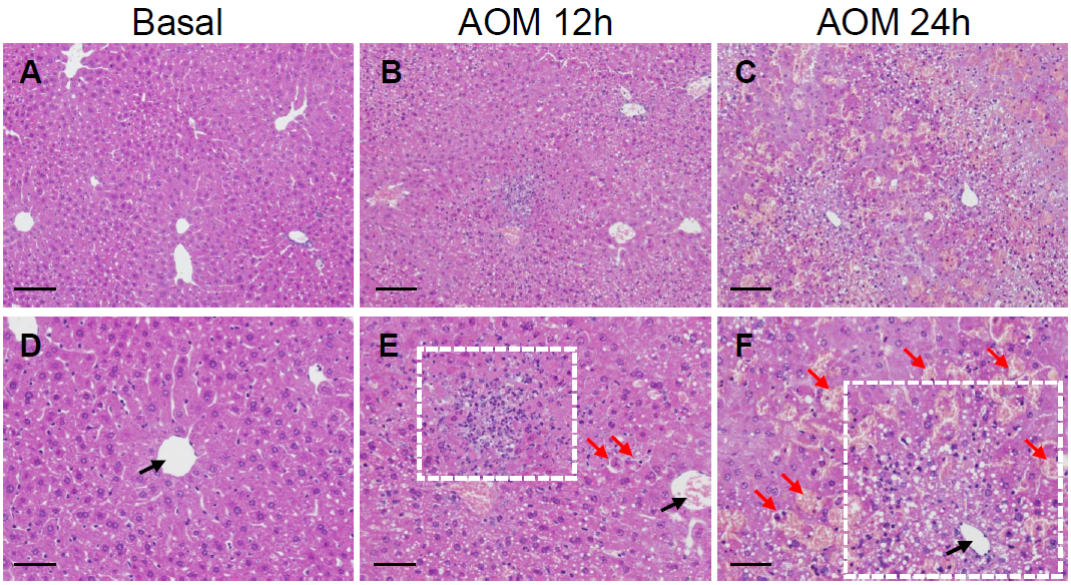

Figure S1. Histopathology of the liver in the HE model. Low-power (**A-C**) or high-power (**D-F**) photomicrographs showing typical histological changes in the liver stained with hematoxylin and eosin 12 and 24 h after mice received azoxymethane (AOM) administration. Note in (**E,F**) progressive increase in necrotic cells (red arrows) and neutrophil infiltration (white box). Black arrows denote centrilobular vein. Scale bars, 100 µm in (**A-C**), and 50 µm in (**D-F**).

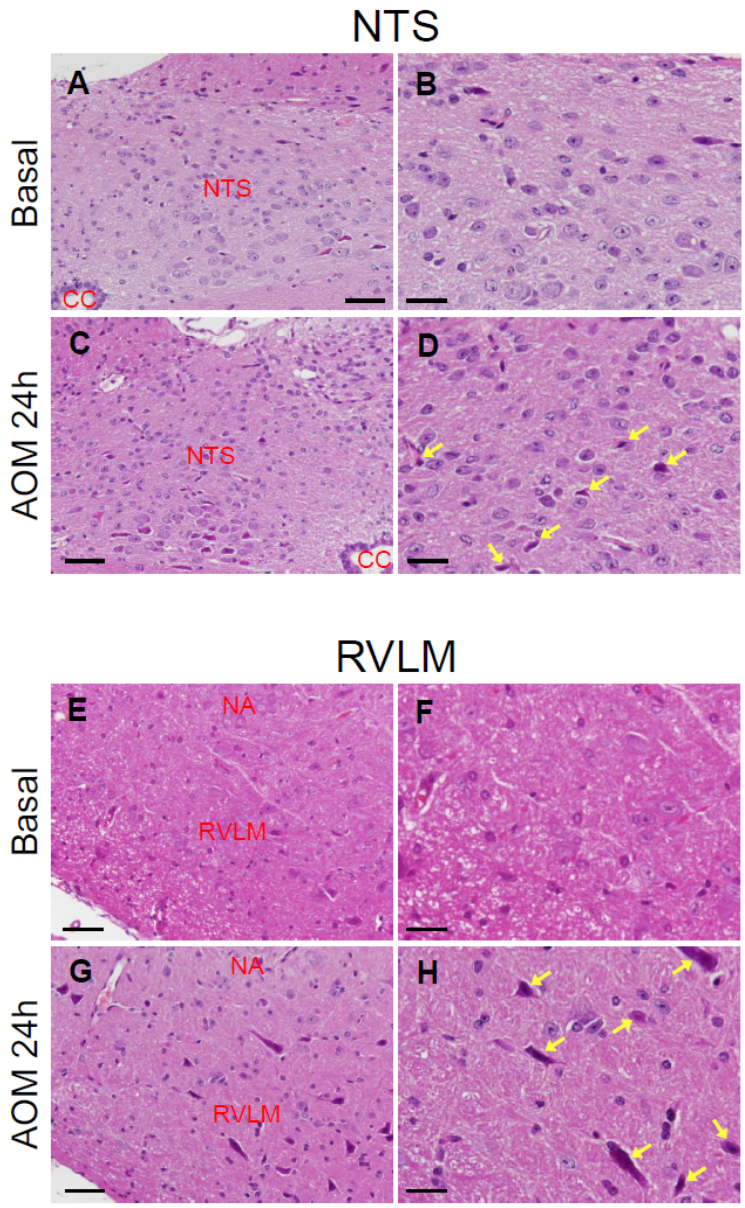

Figure S2. Histopathology of the NTS and RVLM in the HE model. Low-power **(A,C, E,G)** or high-power **(B,D,F,H)** photomicrographs showing typical histological changes in the NTS and RVLM stained with hematoxylin and eosin 24 h after mice received azoxymethane (AOM) administration. Note in **(B,D,F,H)** damaged neurons (yellow arrows) characterized by shrunken cell body, intensive eosinophilic cytoplasm, and pycotic nucleus that lacks discernible nucleolus. CC = central canal; NA = nucleus ambiguus; NTS = nucleus tractus solitarii; RVLM = rostral ventrolateral medulla. Scale bars, 100 μm in **(A,C,E,G)**, and 50 μm in **(B,D,F,H)**.

Supplementary Tables

Supplementary Table 1. Optimal parameters for high resolution T_2-weighted sagittal anatomical reference imaging of the brain of the mouse, using multislice turbo rapid acquisition with refocusing echoes (Turbo-RARE) sequence.

Parameter	
Field of view	18.0 mm × 15.0 mm
Matrix dimension	384 × 320 pixels
Spatial resolution	47 µm × 47 µm
Slice thickness	200 µm
Interslice distance	200 µm
Echo time	12.6 ms
Effective echo time	25.3 ms
Repetition time	3000 ms
Rare factor	4
Number of averages	3
Total acquisition time	12 min

Supplementary Table 2. Optimal parameters for high resolution T_2-weighted sagittal anatomical imaging of a restricted area of the brain stem that covered the medullary portion of the nucleus tractus solitarii (NTS), nucleus ambiguus (NA) and rostral and caudal ventrolateral medulla (RVLM, CVLM) of the mouse, using multislice turbo rapid acquisition with refocusing echoes (Turbo-RARE) sequence.

Parameter	
Field of view	12.0 mm × 12.0 mm
Matrix dimension	192 × 192 pixels
Spatial resolution	62 μm × 62 μm
Slice thickness	200 μm
Interslice distance	200 μm
Echo time	12.5 ms
Effective echo time	25 ms
Repetition time	3000 ms
Rare factor	4
Number of averages	5
Total acquisition time	12 min

Supplementary Table 3. Optimal parameters for imaging the connectivity between the NTS and NA, RVLM of CVLM of the mouse, using spin echo-planar imaging-DTI sequence in the coronal plane covering the same ten 200-μm slices in the T_2-weighted coronal reference images without gap.

Parameter	
Field of view	12.0 mm × 12.0 mm
Matrix dimension	128 × 128 pixels
Spatial resolution	94 μm × 94 μm
Slice thickness	200 μm
Interslice distance	200 μm
Echo time	24 ms
Repetition time	2500 ms
Number of diffusion directions	46
Optimized b value/direction	1500 s/mm^2
Gradient duration	4.1 ms
Gradient separation	10.3 ms
Number of averages	15
Acquisition time	33 min 45 s

Supplementary Table 4. Blood chemistry in animals after administration of azoxymethane (AOM; 100 μg/g, i.p.).

	AST (U/l)	ALT (U/l)	T-Bilirubin (mg/dl)	Albumin (g/dl)
Basal	68 ± 15	17 ± 2	0.50 ± 0.15	2.60 ± 0.10
AOM 12h	934 ± 217*	358 ± 114*	0.80 ± 0.13	2.00 ± 0.07*
AOM 24h	2153 ± 179*	3070 ± 680*	1.27 ± 0.19*	1.70 ± 0.12*

Values are mean ± SEM of 3-4 animals per group. *P < 0.05 versus corresponding basal group in the post hoc Scheffé multiple-range analysis. AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-Bilirubin, total-bilirubin.