Supplementary Table 1. Skilled reaching ability (mean ± SD)

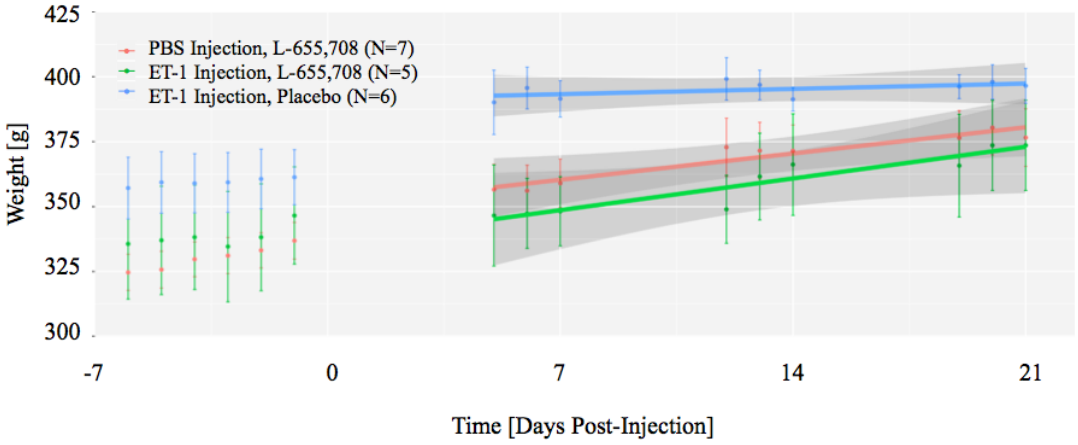
Injection	Treatment	N	Baseline	7 days	14 days	21 days
PBS	L-655,708	7	100 ± 10	101 ± 13	105 ± 10	107 ± 11
ET-1	L-655,708	11	100 ± 15	37 ± 27	51 ± 32	62 ± 31
ET-1	Placebo	9	100 ± 13	31 ± 24	28 ± 25	37 ± 25

Supplementary Table 2. Animal body weight

Group			Starting weight (on day -6)			Growth after injection (day 0-21)	
Injection	Treatment	N	Mean	SEM	SD	[g /week]	p-value
PBS	L-655,708	7	325	7	18	9.8 ± 0.2	< 0.0001
ET-1	L-655,708	5	336	21	47	11.8 ± 0.2	< 0.0001
ET-1	Placebo	6	357	12	29	2.8 ± 0.2	0.1

The mean animal weights at the start of baseline skilled reaching ability evaluation (6 days before ET-1 or PBS injection) are listed in columns 4-7. Post-surgery rate of change (mean ± SEM) in animal weight from day 0 to day 21 is shown in column 7, with the p-value on this slope quoted in column 8.

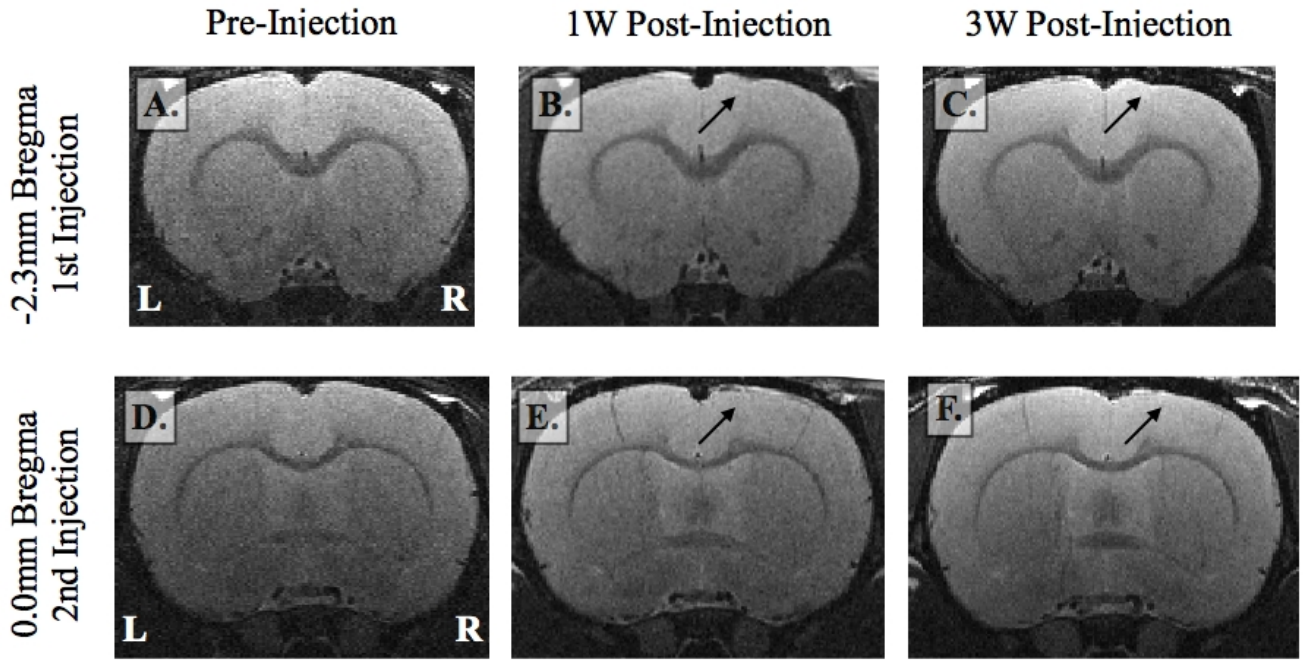
Supplementary Figure 1. Animal body weight



Body weights (N=18) of PBS injected and treated with L-655,708 (red); ET-1 injected and treated with L-655,708 (green); ET-1 injected and given a placebo (blue). Weight was measured daily during the behavioural training and testing periods, namely: prior to stroke induction (training) on days -6 through -1; prior to treatment on days 4-6 after surgery; after one week of L-655,708 treatment or placebo administration on days 11-13; and after two weeks of L-655,708 treatment or placebo administration on days 18-20. Body weight in grams is shown as mean ± SEM. There was no dependence of starting weight (Supplementary Table 2.) on group (p=0.2). Comparing starting weight between groups: there was neither a difference between L-655,708 treated groups nor between ET-1 injected groups (p=0.6 and 0.4 respectively), however, there was a difference between the placebo and PBS injected groups (p=0.03), with the mean weight of the former being greater. The slope of weight after ET-1 or PBS injection, was positive in L-655,708 treated groups (ET-1: 11.8 ± 0.2 g/week, and PBS: 9.8 ± 0.2 g/week, p-values <0.00001), while the placebo group showed a trend (2.8 ± 0.2 g/week, p=0.1). The rate of increase in weight of the placebo group was different from both L-655,708 treated groups after injection (p-values < 0.00001), while there was no difference between L-655,708 treated groups (p=0.2). After ET-1 or PBS injection (but before treatment) there was a difference in weight between the placebo group and both L-655,708 treated groups (p-values=0.02), but no difference between L-

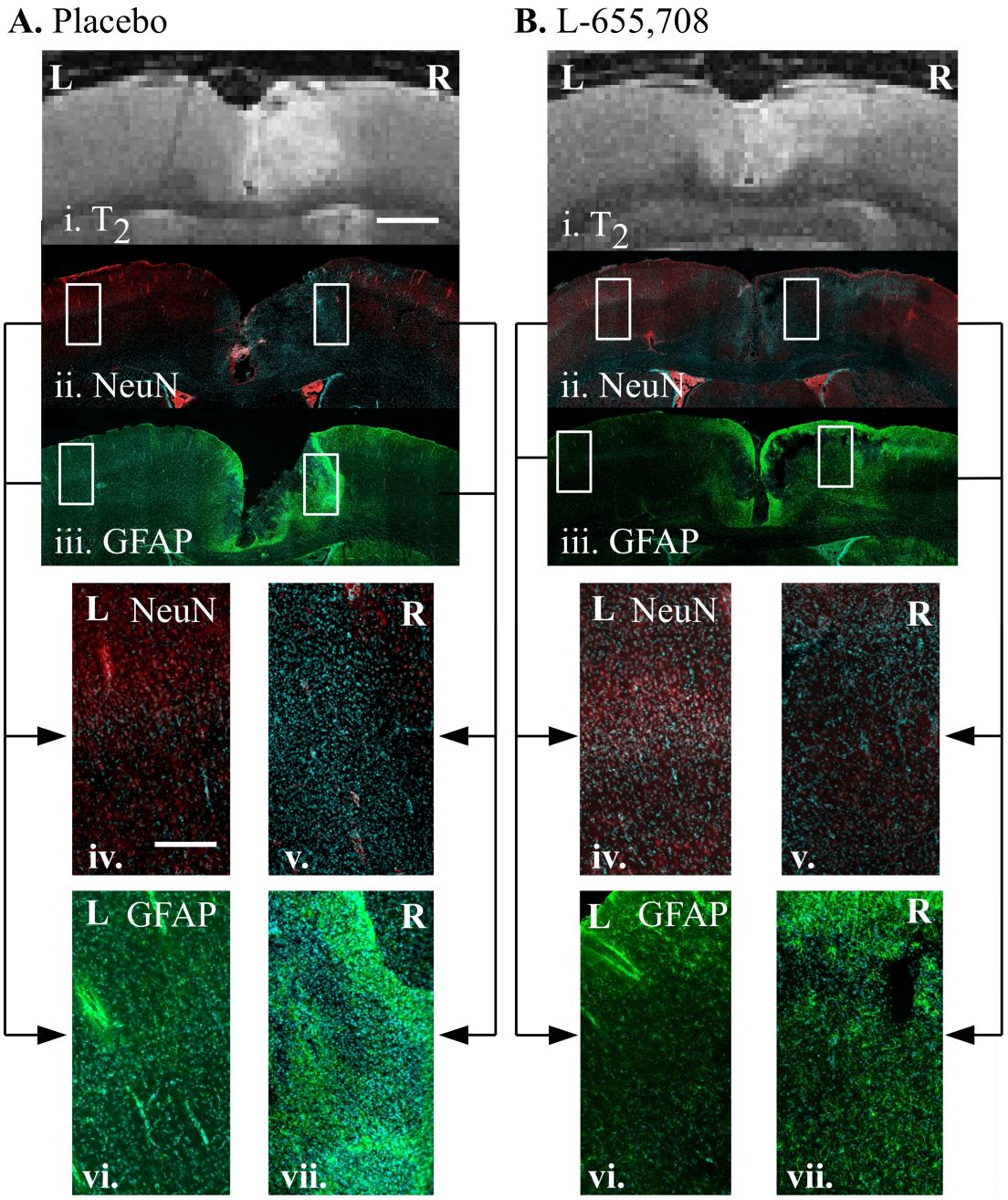
655,708 treated groups (p=0.6). After the first week of treatment, the weight of the placebo group was different from the ET-1 injected L-655,708 treated group (p=0.05), and showed a trend towards being different from the placebo group (p=0.09), with still no difference between L-655,708 treated groups (p=0.5). At the final time point (after two weeks of treatment), there were no differences in weight between groups (p-values > 0.2).

Supplementary Figure 2. T_2-weighted MRI in sham stroke with L-655,708 treatment



Six images collected from a representative animal prior to (**A** and **D**), 7 days (**B** and **E**), and 21 days (**C** and **F**) after sham stroke induction (intra-cortical injection of PBS). Seven days after sham surgery this animal was treated with L-655,708 for 14 days (i.e. until the study end point 21 days after sham stroke induction). The first row of images (**A**, **B**, and **C**) were collected at the level of the anterior injection site (-2.3mm Bregma), and the second row of images (**D**, **E**, and **F**) were collected at the level of the posterior injection site (0.0mm Bregma). The black arrows (in **B**, **C**, **E**, and **F**) indicate the site of PBS injection. Minimal signal contrast along the needle tract was observed following PBS injection (in **B**, **C**, **E**, and **F**). No change in image contrast was observed between 7 and 21 days (before and after L-655,708 treatment).

Supplementary Figure 3. GFAP and NeuN Immunohistochemistry



Immunohistochemical results for the regions of interest in two animals with ET-1 induced injury and corresponding T_2-weighted MR images (**Ai** and **Bi**). (**A**) was administered a placebo and (**B**) was treated with L-655,708; both were sacrificed three weeks after stroke (i.e. after two weeks of treatment). In **A/Bi** the T_2-weighted cortical regions of interest (~0.0 Bregma) are shown for both

animals (scale bar 1mm). The immunohistological sections corresponding to the same ROI as **A/Bi** are shown in **A/Bii** (NeuN - red, DAPI - blue) and **A/Biii** (GFAP - green, DAPI - blue) [scale same as **A/Bi**]. Surrounding the necrotic core, devoid of NeuN or GFAP positive cells, is the peri-lesional zone characterized by low neuronal density (NeuN, red), and astrogliosis (GFAP, green). Within **A/Bii** and **A/Biii** six smaller regions of interest are indicated corresponding to images **A/Biv** (NeuN - left hemisphere), **A/Bv** (NeuN - right hemisphere), **A/Bvi** (GFAP - left hemisphere), and **A/Bvii** (GFAP - right hemisphere) [scale shown in **Aiv** 300μm, equivalent for **A/Biv-vii**] .