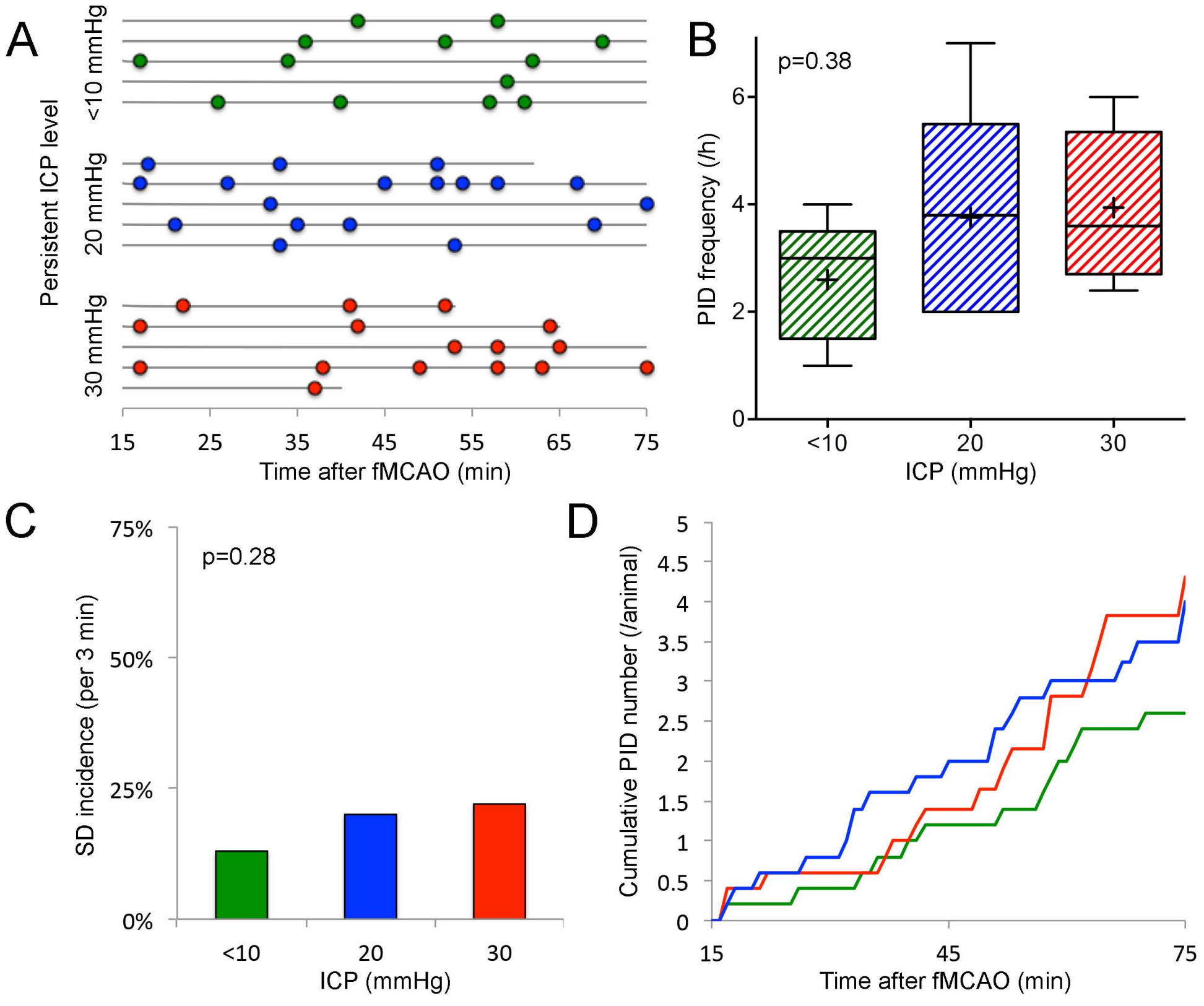
Supplementary Figure 1. Persistent ICP elevation does not increase PID occurrence

(A) Timeline shows the timing of occurrence of SDs at ICP levels of <10 (normal, green symbols), 20 (blue symbols) or 30 mmHg (red symbols). Each horizontal line is one animal (n=5/group).

(B) Whisker-bar plots show the average SD frequency per hour at three ICP levels throughout the 60-minute recordings (one-way ANOVA).

(C) Bar graphs show the 3-minute SD incidence at three persistent ICP levels (χ^2), as shown in Figure 2B for ICP spikes.

(D) Cumulative SD occurrence rate per animal at ICP levels of <10 (normal, green), 20 (blue) or 30 mmHg (red) during 60 minutes of recording.

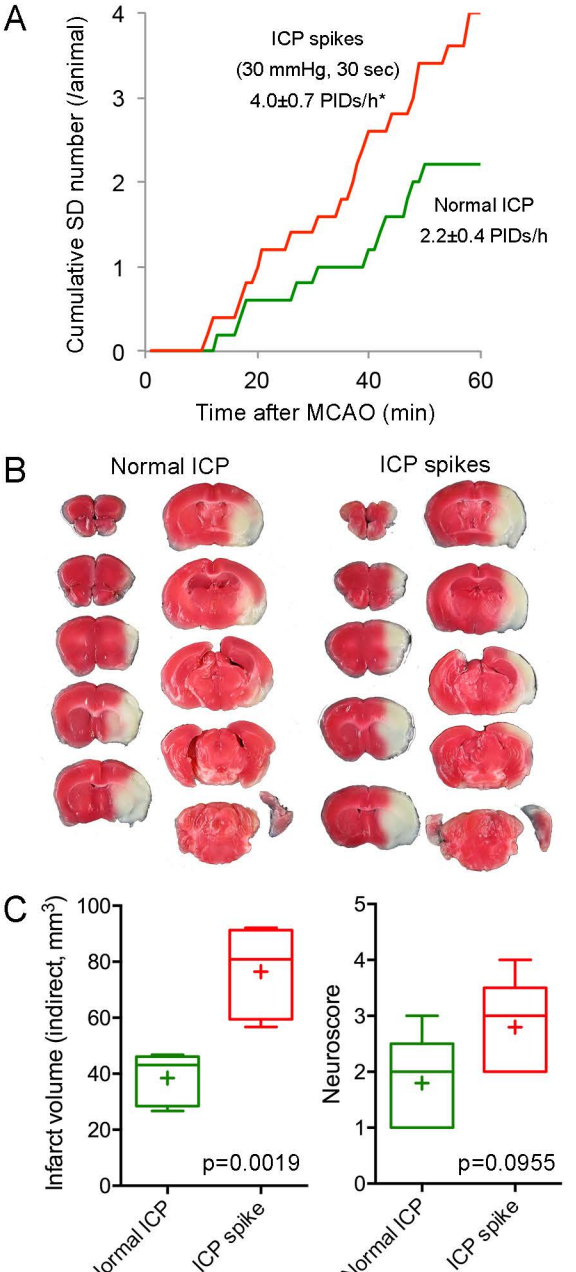

A
Persistent ICP level
<10 mmHg
20 mmHg
30 mmHg
15
25
35
45
55
65
75
Time after fMCAO (min)
B
p=0.38
PID frequency (/h)
0
2
4
6
<10
20
30
ICP (mmHg)
C
p=0.28
SD incidence (per 3 min)
0%
25%
50%
75%
<10
20
30
ICP (mmHg)
D
Cumulative PID number (/animal)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
15
45
75
Time after fMCAO (min)

Supplementary Figure 2. Mild and brief ICP spikes worsen stroke outcome

(A) Cumulative SD occurrence per animal in the normal ICP group (<10 mmHg, green) or with five ICP spikes (30 mmHg for 30 seconds) is shown during 60 minutes fMCAO (n=5 each). *p<0.05 vs. normal ICP.

(B) Representative TTC-stained 1 mm-thick coronal slices show ischemic infarct in MCA territory (white tissue) in two animals with normal ICP or with ICP spikes.

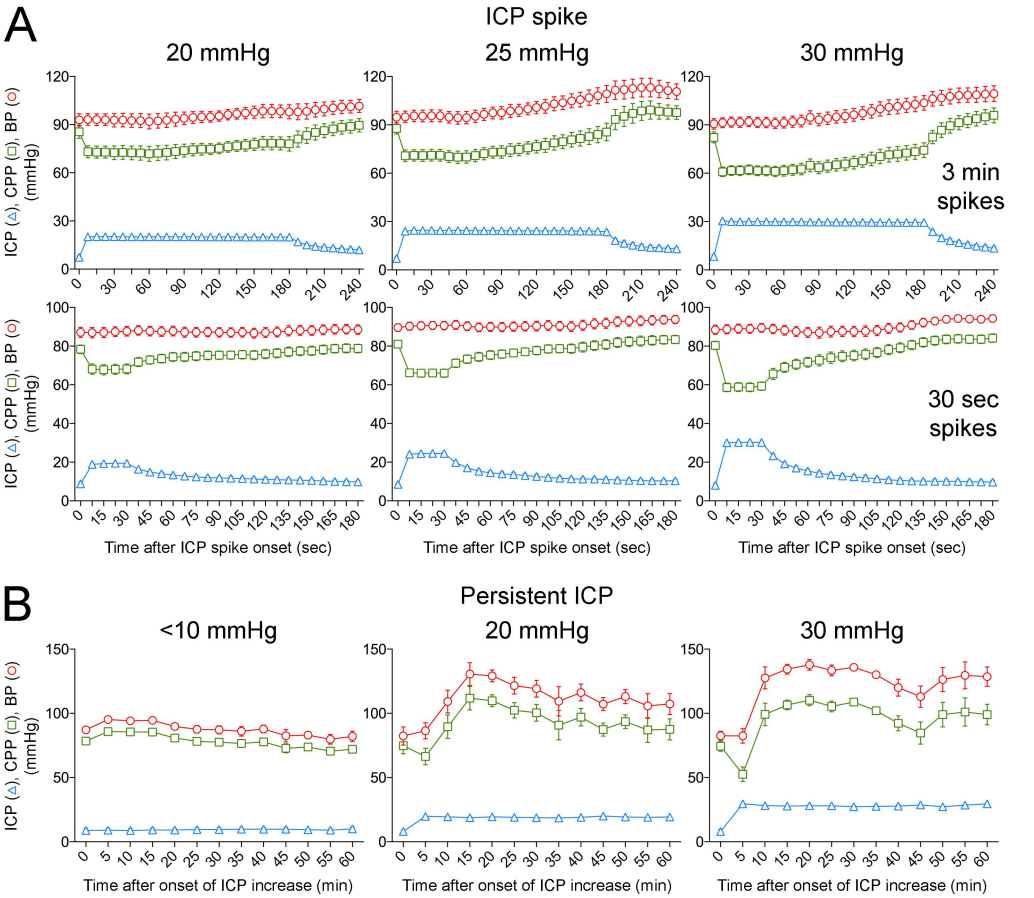
(C) Whisker-box plots show indirect infarct volume (left) and neurological deficit score (right) in normal ICP (green) and ICP spike (red) groups (n=5 each; Student's t-test).


A
Cumulative SD number (/animal)
ICP spikes
(30 mmHg, 30 sec)
4.0±0.7 PIDs/h*
Normal ICP
2.2±0.4 PIDs/h
Time after MCAO (min)
B
Normal ICP
ICP spikes
C
Infarct volume (indirect, mm3)
p=0.0019
Neuroscore
p=0.0955
Normal ICP
ICP spike
Normal ICP
ICP spike

Supplementary Figure 3. Effects of ICP elevations on systemic blood pressure and cerebral perfusion pressure after fMCAO

(A) Transient ICP elevations for 3 minutes (upper row) or 30 seconds (lower row) caused an acute reduction in cerebral perfusion pressure (CPP) and a slower rise in systemic blood pressure (BP), in proportion to the ICP level (n=5 each).

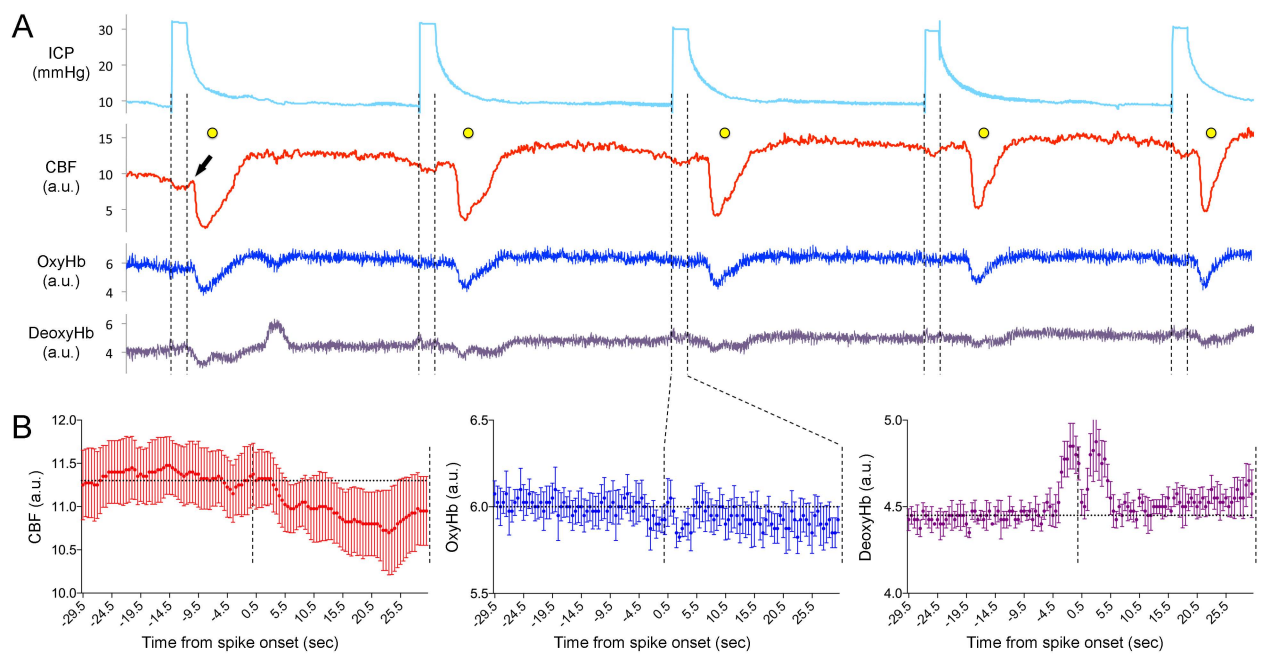
(B) Persistent ICP elevation caused an initial drop in CPP, as observed with ICP spikes, followed by a sustained BP rise (Cushing response), which offset this initial CPP drop and elevated the CPP. In normal ICP group (<10 mmHg), BP and CPP were stable over the duration of recordings (n=5 each).


A
ICP spike
20 mmHg
25 mmHg
30 mmHg
ICP (△), CPP (□), BP (○) (mmHg)
3 min spikes
30 sec spikes
Time after ICP spike onset (sec)
B
Persistent ICP
<10 mmHg
20 mmHg
30 mmHg
Time after onset of ICP increase (min)

Supplementary Figure 4. Effects of ICP elevations on cortical oxyhemoglobin and deoxyhemoglobin concentrations

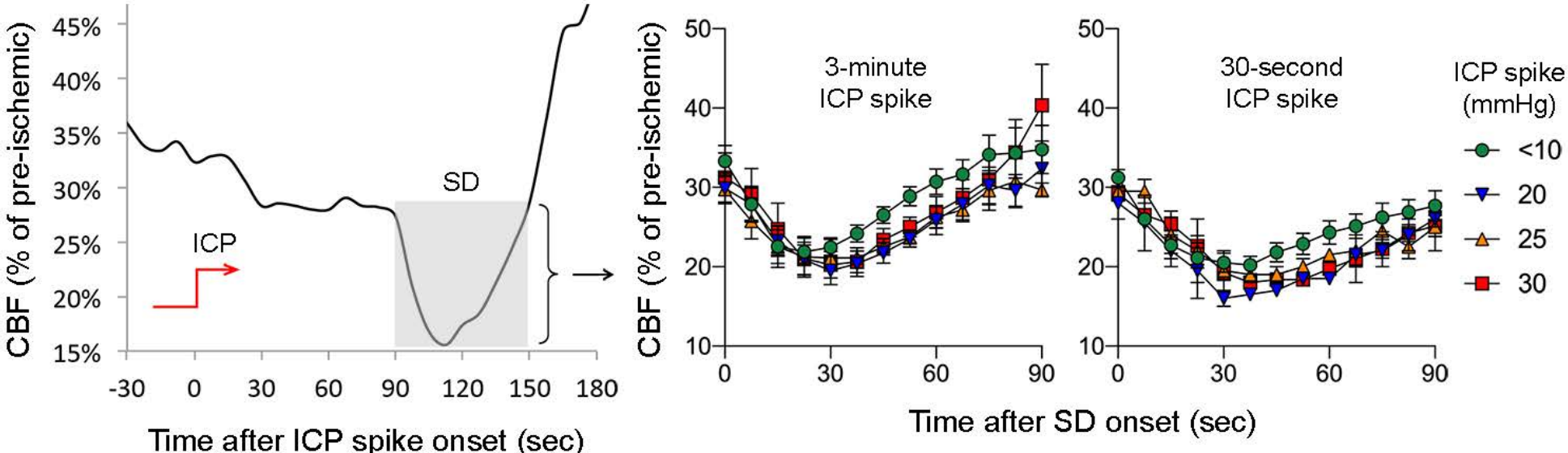
(A) Tracing from a representative experiment showing the effect of 30 second, 30 mmHg ICP spikes on CBF, oxyhemoglobin and deoxyhemoglobin concentrations at the SD origin. All 5 ICP spikes triggered a SD (yellow circles) in this experiment, which caused a precipitous drop in CBF and oxyhemoglobin. During the ICP spike, there as a small CBF drop and minimal change in oxyhemoglobin and deoxyhemoglobin concentrations. Dashed lines indicate the period of ICP elevation.

(B) Summary data showing CBF, oxyhemoglobin and deoxyhemoglobin concentrations within a region of interest placed in penumbra 30 seconds before and during 30 second, 30 mmHg ICP spikes ($n=4$; $p>0.05$, one-way ANOVA for repeated measures).


A
ICP (mmHg)
30
20
10
CBF (a.u.)
15
10
5
OxyHb (a.u.)
6
4
DeoxyHb (a.u.)
6
4
B
CBF (a.u.)
12.0
11.5
11.0
10.5
10.0
OxyHb (a.u.)
6.5
6.0
5.5
DeoxyHb (a.u.)
5.0
4.5
4.0
-29.5
-24.5
-19.5
-14.5
-9.5
-4.5
0.5
5.5
10.5
15.5
20.5
25.5
Time from spike onset (sec)

Supplementary Figure 5. Effects of ICP elevation on the hypoperfusion response to SDs

CBF changes during SD in ischemic penumbra (residual CBF ~30%) were calculated by measuring the hypoperfusion response to an SD (left panel, gray shaded area) that occurred spontaneously (circles) or triggered by a 3-minute or 30-second ICP spike at different ICP levels (middle and right panels). There was a slight but statistically insignificant worsening of hypoperfusion during SDs triggered by ICP spikes (regardless of the ICP level) compared with spontaneous SDs that occurred under normal ICP (two-way ANOVA for repeated measures).


CBF (% of pre-ischemic)
45%
40%
35%
30%
25%
20%
15%
SD
ICP
-30
0
30
60
90
120
150
180
Time after ICP spike onset (sec)
CBF (% of pre-ischemic)
50
40
30
20
10
3-minute
ICP spike
30-second
ICP spike
ICP spike
(mmHg)
<10
20
25
30
0
30
60
90
Time after SD onset (sec)

Supplementary Table 1. Arterial blood gas values.

	pH	**pCO_2**	**pO_2**
Normal (ICP<10 mmHg)	7.34 ± 0.01	39 ± 3	114 ± 2
Persistent ICP=20 mmHg	7.37 ± 0.02	30 ± 1	114 ± 4
Persistent ICP=30 mmHg	7.37 ± 0.02	28 ± 2	109 ± 7
3 min ICP spikes	7.36 ± 0.01	32 ± 1	123 ± 7
30 sec ICP spikes	7.40 ± 0.01	31 ± 1	125 ± 9

Blood gas values are in mmHg.