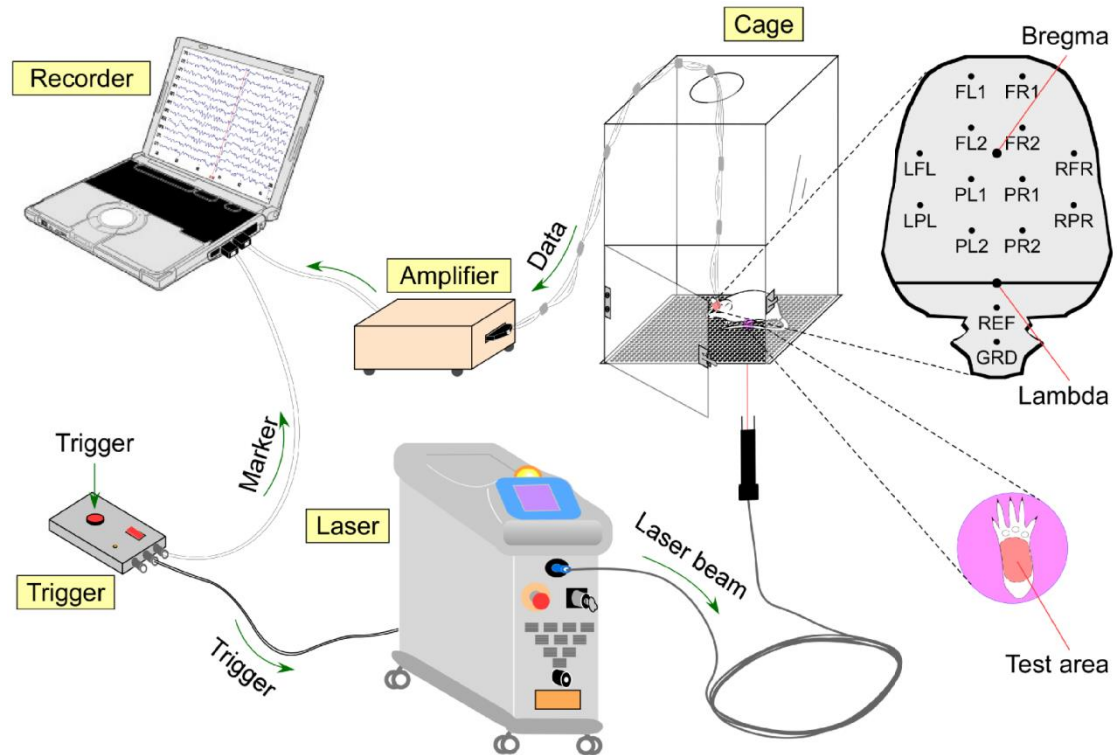
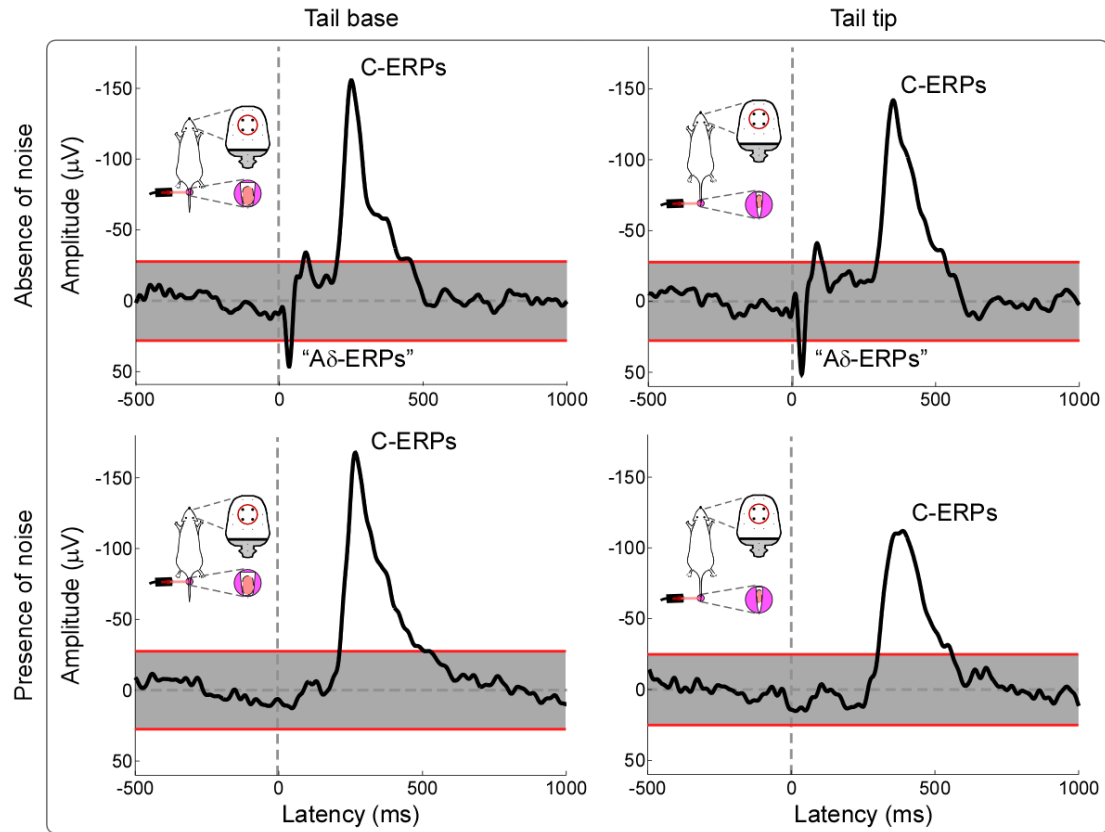




Supplementary Fig. 1. Schematic of the setup to record laser-evoked ERPs in rats.

Infrared neodymium yttrium aluminum perovskite (Nd:YAP) laser pulses activate selectively nociceptive terminals in the superficial skin layers. Laser pulses are delivered through an optic fibre to the freely moving rat. EEG signals are transmitted through flexible wires to the EEG amplifier and recording system. EEG data are recorded from 14 electrodes placed according to stereotaxic coordinates. The coordinates of 12 active electrodes are as follows (positions are expressed in respect to the Bregma, in mm; positive X and Y axis values indicate right and anterior locations, respectively). FL1: X=-1.5, Y=4.5; FR1: X=1.5, Y=4.5; FL2: X=-1.5, Y=1.5; FR2: X=1.5, Y=1.5; LFL: X=-4.5, Y=0; RFR: X=4.5, Y=0; PL1: X=-1.5, Y=-1.5; PR1: X=1.5, Y=-1.5; LPL: X=-4.5, Y=-3; RPR: X=4.5, Y=-3; PL2: X=-1.5, Y=-4.5; PR2: X=1.5, Y=-4.5. Reference (REF) and ground (GRD) electrodes are respectively placed at 2 mm and 4 mm caudally to the Lambda, on the midline.



Supplementary Fig. 2. Statistical assessment of the significance of the laser-evoked brain responses (Experiment 2).

Without ongoing white noise, both early “Aδ-ERP” and late “C-ERP” responses were significantly different from the pre-stimulus variability (top panels). With ongoing white noise, only the late “C-ERP” responses were significantly different from the pre-stimulus variability, whereas the early “Aδ-ERP” responses were not (bottom panels). The red lines indicate the $p=0.05$ threshold (corresponding to 1.96 times the averaged variability – estimated as SD – of the pre-stimulus fluctuations across subjects).

Supplementary Table 1. Latency and amplitude of ERPs elicited by laser stimulation at different sites (tail base and tip) and energies (E1-E5) (Experiment 1).

	Tail base					Tail tip				
	E1 (1.5 J)	E2 (2 J)	E3 (2.5 J)	E4 (3 J)	E5 (3.5 J)	E1 (1.5 J)	E2 (2 J)	E3 (2.5 J)	E4 (3 J)	E5 (3.5 J)
P1 latency (ms)	33±5	36±6	37±6	34±4	35±6	35±9	35±6	35±4	34±4	35±5
P1 amplitude (μV)	12.5±12.6	29.5±20.1	38.3±27.5	48.8±31.7	53.2±30.5	10.3±15.8	28.9±20.5	34.8±29.7	49.6±30.3	51.2±32.1
N1 latency (ms)	90±10	87±7	90±12	89±9	88±6	89±11	86±9	89±11	88±7	90±7
N1 amplitude (μV)	-9.3±9.4	-4.8±18.4	-17.0±22.2	-20.7±36.8	-29.6±33.5	-9.0±7.8	-2.9±18.1	-17.3±21.6	-14.3±34.2	-30.3±36.0
N2 latency (ms)	284±39	290±27	272±22	257±10	255±16	507±35	423±28	398±31	367±18	353±32
N2 amplitude (μV)	-48.9±29.2	-122.7±61.7	-159.1±74.5	-186.7±60	-167.8±42.7	-37.6±22.9	-113.5±58.7	-137.4±60.3	-152.5±66.0	-147.6±54.8

Supplementary Table 2. Two-way repeated-measures analysis of variance (ANOVA) exploring the effect of stimulation site (tail base vs. tip) and stimulus energy (E1-E5) on laser ERPs (Experiment 1).

	Stimulation site		Stimulus energy		Interaction	
	F value	p value	F value	p value	F value	p value
P1 latency	0.02	0.89	0.68	0.61	1.13	0.41
P1 amplitude	1.48	0.25	11.56	<0.001***	0.83	0.55
N1 latency	0.33	0.58	0.24	0.92	0.53	0.72
N1 amplitude	0.93	0.36	2.83	<0.05*	0.59	0.68
N2 latency	438.07	<0.001***	66.58	<0.001***	9.91	<0.01**
N2 amplitude	7.64	<0.05*	19.87	<0.001***	0.99	0.43

*p<0.05; **p<0.01; ***p<0.001.

Supplementary Table 3. Latency and amplitude of ERPs elicited by laser stimulation at different tail sites (base and tip) and noise conditions (presence and absence of ongoing white noise) (Experiment 2).

	Tail base		Tail tip	
	Absence of noise	Presence of noise	Absence of noise	Presence of noise
P1 latency (ms)	34±7	—	32±8	—
P1 amplitude (μV)	52.6±30.2	—	54.2±36.7	—
N1 latency (ms)	90±8	—	88±6	—
N1 amplitude (μV)	-26.8±38.7	—	-34.3±39.9	—
N2 latency (ms)	254±15	262±19	352±33	366±28
N2 amplitude (μV)	-175.0±42.0	-194.1±78.3	-155.7±53.0	-156.4±66.9

Supplementary Table 4. Paired sample t-test exploring the effect of stimulation site (tail base vs. tip) on “Aδ-ERPs” (Experiment 2).

Paired sample t-test (stimulation site)		
	t value	p value
P1 latency	1.21	0.25
P1 amplitude	0.24	0.81
N1 latency	1.21	0.25
N1 amplitude	0.86	0.41

Supplementary Table 5. Two-way repeated-measures ANOVA exploring the effect of stimulation site (tail base vs. tip) and noise condition (presence vs. absence of ongoing white noise) on “C-ERPs” (Experiment 2).

Two way repeated-measures ANOVA						
	Stimulation site		Noise condition		Interaction	
	F value	p value	F value	p value	F value	p value
N2 latency	361.70	<0.001***	3.87	0.08	0.35	0.57
N2 amplitude	9.38	<0.05*	0.43	0.53	1.93	0.19

*p<0.05; ***p<0.001.

Supplementary Table 6. Latency and amplitude of “Aδ-ERPs” elicited when laser stimuli are not delivered on the skin, at different noise conditions (presence and absence of ongoing white noise) (Experiment 3).

	Absence of noise	Presence of noise
P1 latency (ms)	34±3	—
P1 amplitude (μV)	39.6±27.5	—
N1 latency (ms)	86±3	—
N1 amplitude (μV)	-48.1±45.0	—

Supplementary Table 7. Latency and amplitude of ERPs elicited by laser stimulation of hairy and glabrous skin, at different noise conditions (presence and absence of ongoing white noise) (Experiment 4).

	Hairy		Glabrous	
	Absence of noise	Presence of noise	Absence of noise	Presence of noise
P1 latency (ms)	30±4	—	31±3	—
P1 amplitude (μV)	42.6±35.0	—	37.2±25.3	—
N1 latency (ms)	84±5	—	84±7	—
N1 amplitude (μV)	-77.1±58.5	—	-68.8±39.8	—
N2 latency (ms)	137±13	143±14	145±9	147±12
N2 amplitude (μV)	-139.0±43.0	-146.4±64.3	-165.2±52.8	-151.4±67.9

Supplementary Table 8. Paired sample t-test exploring the effect of skin type (hair vs. glabrous) on “Aδ-ERPs” (Experiment 4).

	t value	p value
P1 latency	0.80	0.44
P1 amplitude	0.70	0.50
N1 latency	0.45	0.67
N1 amplitude	0.57	0.58

Supplementary Table 9. Two-way repeated-measures ANOVA exploring the effect of skin type (hair vs. glabrous) and noise condition (presence vs. absence of white noise) on “C-ERPs” (Experiment 4).

Two way repeated-measures ANOVA						
	Stimulation site		Noise condition		Interaction	
	F value	p value	F value	p value	F value	p value
N2 latency	3.62	0.08	13.38	<0.01**	0.81	0.39
N2 amplitude	1.96	0.19	0.03	0.86	2.97	0.11

**p<0.01.

Supplementary Table 10. Behavioral scores at different stimulus intensities (E1'-E5') and stimulation sites (left forepaw, right forepaw, left hindpaw, and right hindpaw) (Experiment 5).

	E1' (1 J)	E2' (1.75 J)	E3' (2.5 J)	E4' (3.25 J)	E5' (4 J)
Left forepaw	0.03±0.06	1.83±0.93	3.09±0.25	3.29±0.15	3.51±0.11
Right forepaw	0.09±0.15	2.01±0.82	2.96±0.35	3.37±0.15	3.52±0.18
Left hindpaw	0.04±0.08	1.65±0.98	2.91±0.48	3.35±0.17	3.53±0.17
Right hindpaw	0.01±0.04	1.58±0.85	2.89±0.50	3.37±0.23	3.59±0.18

Supplementary Table 11. Two-way repeated-measures ANOVA exploring the effect of stimulation site (left forepaw, right forepaw, left hindpaw, right hindpaw) and stimulus energy (E1'-E5') on behavioural scores obtained after laser stimulation (Experiment 5).

Two way repeated-measures ANOVA						
	Stimulation site		Stimulus energy		Interaction	
	F value	p value	F value	p value	F value	p value
Behavioural score	1.94	0.14	161.20	<0.001***	2.56	0.06

***p<0.001.

Supplementary Table 12. Latency and amplitude of ERPs elicited by laser stimulation at different stimulation sites (left hand and foot) and noise conditions (presence and absence of ongoing white noise) (Experiment 6).

	Left hand		Left foot	
	Absence of noise	Presence of noise	Absence of noise	Presence of noise
A δ -N2 latency (ms)	209 $\pm$ 18	216 $\pm$ 19	264 $\pm$ 33	264 $\pm$ 44
A δ -N2 amplitude (μ V)	-12.1 $\pm$ 5.4	-15.4 $\pm$ 8.6	-6.98 $\pm$ 4.60	-7.68 $\pm$ 4.26
A δ -P2 latency (ms)	356 $\pm$ 29	350 $\pm$ 33	415 $\pm$ 41	422 $\pm$ 33
A δ -P2 amplitude (μ V)	11.8 $\pm$ 6.0	15.3 $\pm$ 10.4	8.63 $\pm$ 3.61	10.20 $\pm$ 5.32
C-N2 latency (ms)	780 $\pm$ 82	783 $\pm$ 80	1070 $\pm$ 103	1059 $\pm$ 127
C-N2 amplitude (μ V)	-5.96 $\pm$ 4.45	-5.09 $\pm$ 3.53	-6.16 $\pm$ 2.96	-7.01 $\pm$ 3.53
C-P2 latency (ms)	915 $\pm$ 93	918 $\pm$ 110	1212 $\pm$ 107	1219 $\pm$ 122
C-P2 amplitude (μ V)	7.63 $\pm$ 3.24	6.59 $\pm$ 3.23	4.94 $\pm$ 2.44	6.26 $\pm$ 2.75

Supplementary Table 13. Two-way repeated-measures ANOVA exploring the effect of stimulation site (left hand vs. foot) and noise condition (presence vs. absence of ongoing white noise) on “A δ -ERPs” and “C-ERPs” in humans (Experiment 6).

Two way repeated-measures ANOVA						
	Stimulation site		Noise condition		Interaction	
	F value	p value	F value	p value	F value	p value
A δ -N2 latency	33.25	<0.001***	0.30	0.60	0.33	0.58
A δ -N2 amplitude	16.07	<0.01**	5.24	<0.05*	1.63	0.22
A δ -P2 latency	46.89	<0.001***	0.01	0.92	0.57	0.46
A δ -P2 amplitude	4.44	0.05	4.54	0.05	1.14	0.30
C-N2 latency	251.6	<0.001***	0.34	0.57	1.28	0.28
C-N2 amplitude	3.37	0.09	0.00	0.97	3.02	0.10
C-P2 latency	359.4	<0.001***	0.31	0.59	0.03	0.87
C-P2 amplitude	6.87	<0.05*	0.10	0.76	9.66	<0.01**

*p<0.05; **p<0.01; ***p<0.001.