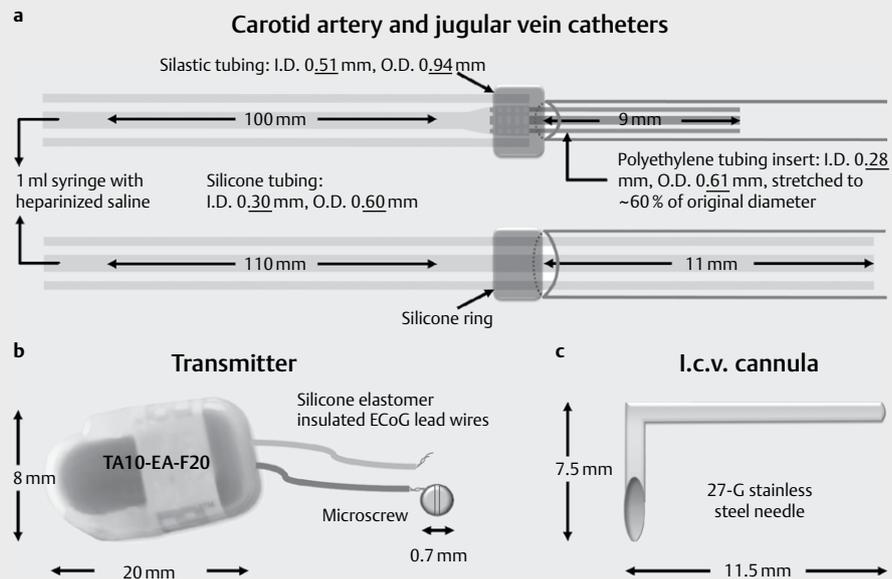


Supplementary Material

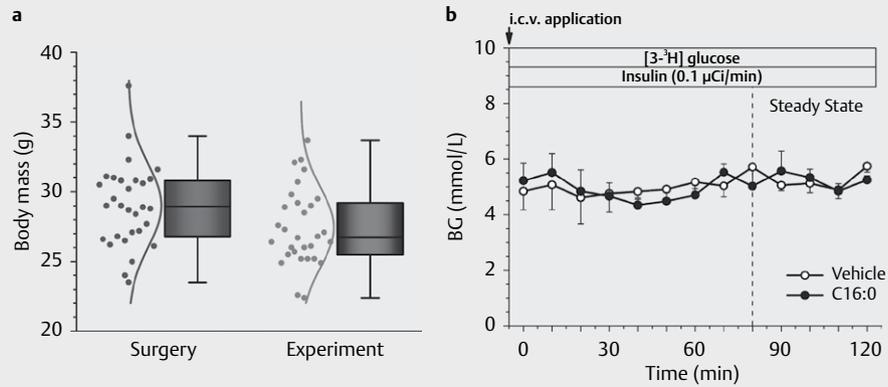


► **Fig. 1S** Carotid artery and jugular vein catheters, transmitter, and intracerebroventricular cannula. **a** For preparation of the carotid artery catheter (upper) PE10 polyethylene tubing is slightly stretched and then inserted into a silicone tubing piece with an ~5 mm overlap. By stretching with sharp forceps a piece of silicone tubing is mounted in the region where the tubing overlaps for a more even surface area. The jugular catheter is prepared from a single silicone tubing piece. A liquid silicone (aquarium grade) is applied in a ring around the jugular catheter and once it is dry, tips are cut blunt to introduction-length with a scalpel. Before insertion into the blood vessels, catheters are prefilled with a sterile 0.6% saline solution containing heparin (10 U/mL) in an air bubble-free manner. **b** Subcutaneously implanted telemetry ECoG transmitter (TA10-EA-F20, Data Sciences International, USA) with two silicone elastomer insulated ECoG lead wires connected to epidurally placed microscrews. **c** I.c.v. cannula implanted in the left ventricle to directly inject substances in the cerebrospinal fluid of mice.

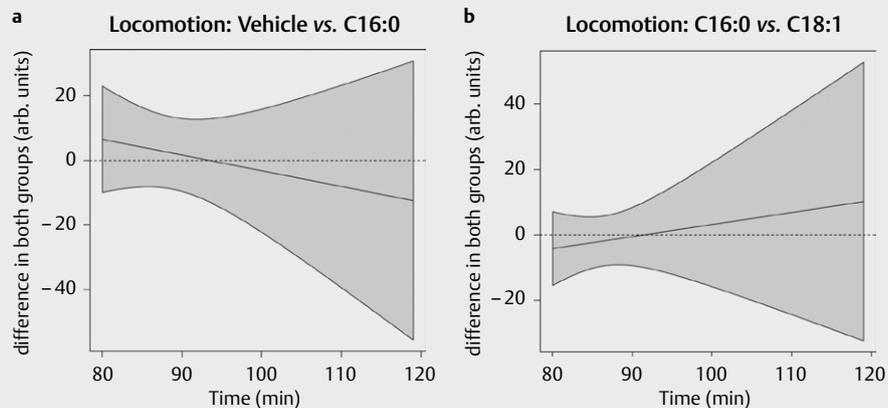
► Table 15 Scoring Sheet for extensive daily monitoring during post-surgical period.

Parameter	Mouse ID:		Score	Date/ Time	
Appearance	Normal grooming status, no discharges, no piloerection, etc.		0		
	Lack of grooming		1		
	Ocular and nasal discharges		2		
	Piloerection, hunched back		3		
Food/Water Intake	Normal consumption of water/food, feces in cage		0		
	No food/water consumed, no feces for 1 day		1		
	No food/water consumed, no feces for 2 days		2		
	No food/water consumed, no feces for 3 days		3		
BM Regulation	Normal, no decrease in BM equal to or higher 10%		0		
	BM stagnation		1		
	Moderate BM decrease (<10%)		2		
	Marked BM decrease (>15%)		3		
Natural Behavior	Normal mobility, alertness, no vocalization		0		
	Minor changes		1		
	Less mobile, more alert		2		
	Vocalization, restlessness, immobility		3		
Clinical Signs (post-surgery)	Normal, no signs of inflammation or local sensitivity to touch		0		
	Signs of beginning local inflammation (wound areas), irregular ECoG patterns		1		
	Local inflammation (reddening of skin, swelling, sensitive to touch), alteration BCT (± 2 to 4°C)		2		
	Extreme sensitive/aggressiveness, unresponsiveness to touch, BCT changes $>4^{\circ}\text{C}$, persistent CA changes		3		
	Torticollis		15		
	Score	If score of 3 more than once, then score an extra point per 3 points		2–5	
	Total				
	<4	normal			
Total Scoring:	5–9	monitor carefully, consider additional analgetic treatment			
	10–14	Suffering, provide relief, observe regularly, seek second opinion from vet or animal care officer			
	>15	severe pain, sacrifice (consider experimental adjustments)			

BG blood glucose (random fed) BM body mass BCT resting body core temperature CA cortical activity; List of parameters with different scoring classifications (0–3) and total scoring conditions scaled from <4 to >15. BG: blood glucose (random fed), BM: body mass, BCT: resting body core temperature, CA: cortical activity.



► **Fig. 2S** Individual net body mass change between surgery and in vivo experiment and blood glucose levels during glucose clamp conditions. **a** Body mass was determined in 30 random-fed animals prior to the first surgery conducted between 7 a.m. and 4 p.m.. After surgery mice were single housed. The second measurement was performed following a recovery period of 7 ± 1 days at 6 a.m. in random-fed mice prior to diet removal for the in vivo experiment. The average body mass \pm SEM at surgery was 29.1 ± 0.5 g and prior to the in vivo experiment 27.3 ± 0.5 g. **b** Blood glucose (BG) levels during the euglycemic-hyperinsulinemic clamp. Solutions of palmitic acid (C16:0) or vehicle were i.c.v. injected at $t = -120$ min prior to insulin infusion. Data are mean \pm SEM of $n = 8$ /group.



► **Fig. 3S** Univariate analysis of time-resolved differences between groups. Result of functional test for detecting differences in time courses at 95% confidence level. The test computes a confidence band (grey shaded area) around the functional mean difference (solid line) for each parameter between two groups: Parameter locomotion **a**, **b**, comparison between vehicle and C16:0 **a** and between C16:0 and C18:1 **b**. In case the confidence band does not cover the zero line in some time interval, a significant difference can be assumed there. This case did not occur for the parameter locomotion or group comparison here.