

Legends:

Figure E1: Methods used for measurement of the genioglossus negative pressure reflex.

Negative pressure was delivered to the rats isolated upper airway. For this purpose, the rats' nares were occluded by a plastic cap placed over their muzzle, sealed with epoxy glue, and connected to a vacuum source. The magnitude of the applied pressure was measured by a pressure-sensitive catheter inserted by the tracheostomy into the rostral trachea. For evaluation of the negative pressure reflex, the change in genioglossus electromyography amplitude in response to a negative pressure stimulus was measured. The degree of the supramaximal stimulus was individually determined to produce consistently a maximum change in genioglossus activity.

Figure E2: End-tidal carbon dioxide concentration standardized experiments.

Repetitive measurements at isoflurane 1.0%, 1.5%, and 2% (protocol 1).

- A. Effects of isoflurane on end-tidal carbon dioxide concentration. End-tidal carbon dioxide concentration increased significantly with isoflurane dose.
- B. Phasic genioglossus electromyography during carbon dioxide insufflation to the inspiration gas (end-tidal carbon dioxide concentration: 50 mmHg, which was the average concentration observed at isoflurane 2%). Phasic genioglossus electromyography increased with increasing isoflurane dose, and the increase did not differ from conditions observed when end-tidal carbon dioxide was not standardized (see figure 3A of the main manuscript for comparison). * $p < 0.05$ for dose effect (linear mixed model).

Figure E3: Mean arterial blood pressure standardized experiments.

Repetitive measurements at isoflurane 1.0%, 1.5%, and 2% (protocol 1).

A. Mean arterial blood pressure (MAP) at different isoflurane concentrations.

Repetitive measurements at isoflurane 1.0%, 1.5%, and 2%. MAP decreases in a dose-dependent fashion.

B. Phasic genioglossus electromyography at different isoflurane concentrations with

and phasic arterial blood pressure standardized to 115 mm Hg with vasopressin

(n=11) or phenylepinephrine (n=6). Phasic genioglossus activity increased dose-

dependently, and the increase did not differ from conditions observed when MAP was

not standardized (see figure 3A for comparison). * $p < 0.05$ for dose-effect (linear mixed model).

Figure E4:

Photomicrograph showing KF lesions. Coronal section through the rostral pons at the level of the KF nucleus. Note the bilateral area of neuron loss and gliosis (arrows).

Figure E5: Typical response to administration of isoflurane.

A. Chronically instrumented rat. Genioglossus (GG) electromyogram

(electromyography, raw signal and moving time average [MTA]). Left: Rat not

anesthetized (quiet wakefulness and/or sleep). Tonic genioglossus activity was

strong, whereas phasic (respiratory) activity was relatively low, and was even not

measurable in some other rats. Right: Rat under light anesthesia (end-tidal

isoflurane concentration of 1 vol%). Tonic genioglossus activity decreased

compared with the non-anesthetized condition, whereas a robust phasic activity was always present during light anesthesia.

- B. Acute experiment. GG electromyography, respiratory flow, and mean arterial blood pressure (MAP, from top to bottom) during increasing concentrations of isoflurane. With increasing isoflurane concentrations, phasic genioglossus activity increased whereas tonic genioglossus activity, respiratory rate, and MAP decreased.