Supplementary Figure Legends

Supplementary Figure 1

Effect of pancuronium and physiological saline (NaCl) on cerebral metabolite concentrations (normalized to baseline, mean ± standard error) as a function of time under constant isoflurane. In comparison to untreated controls (n = 5, open symbols) injection of either pancuronium (n = 2) or NaCl (n = 6) revealed no significant changes. Cho = choline-containing compounds, GABA = γ-aminobutyric acid.

Supplementary Figure 2

Metabolite concentrations (normalized to baseline, mean ± standard error) as a function of time for mice with constant supply of 1.75% isoflurane (n = 11, open symbols) and mice subjected to a protocol with an intermediate 35 min period at 0% isoflurane (n = 22, solid symbols). Withdrawal of isoflurane led to a mild reduction of total creatine (tCr) and *N*-acetylaspartate (NAA) most likely due to a MRS signal loss by motion-induced phase incoherence. The NAA/tCr ratio was not significantly affected by isoflurane.

Supplementary Figure 3

Glutamine concentration (normalized to baseline, mean ± standard error) as a function of time for mice with constant supply of 1.75% isoflurane (n = 11, open symbols) and mice subjected to a protocol with an intermediate 35 min period at 0% isoflurane (n = 22, solid symbols). Withdrawal of isoflurane did not significantly change the glutamine concentration.

Supplementary Figure 4

Metabolite concentrations (mean ± standard error) in cerebral cortex (n = 12), hippocampus (n = 9), striatum (n = 8), a volume with at least 50% being CSF (n = 6), and cerebrum (n = 7) under 1.75% isoflurane. Ala = alanine, Cho = choline-containing compounds, Cr = creatine, GABA = γ-aminobutyric acid, Glc = glucose, Glu = glutamate, Gln = glutamine, Ins = *myo*-inositol, NAA: *N*-acetylaspartate, PCr = phosphocreatine. *p < 0.05, (ANOVA, Bonferroni *post hoc* test)

Supplementary Figure 5

Effect of blood glucose on cerebral concentrations of lactate and glucose. Concentrations of lactate and glucose before (25 min), during (125 min) and after (120 min) intravenous glucose infusion during constant isoflurane (1.75%). While brain glucose reflected the intravenous supply, lactate remained essentially unchanged.

Supplementary Figure 6

Effect of oxygen supply on cerebral lactate under isoflurane. Cerebral lactate at ambient air and ambient air plus 50% oxygen within the same animals (n = 6). The absence of a significant difference suggests that 1.75% isoflurane anesthesia in ambient air does not correspond to a condition of inadequate oxygen supply that leads to elevated lactate.

Supplementary Figure 7

Cerebral lactate concentration in response to non-volatile anesthetics. Thirtyfive minutes after withdrawal of isoflurane, mice received either ketamine/medetomidine (n = 2), medetomidine (n = 3), pentobarbital (n = 2), diazepam (n = 1), fentanyl (n =

1), or no further medication (n = 2). None of these narcotics caused a relevant increase of brain lactate (normalized to baseline, mean ± standard error). Only pentobarbital resulted in a minor and transient elevation of brain lactate.

Supplementary Figure 8

Effect of medetomidine on cerebral metabolites. Thirtyfive minutes after withdrawal of isoflurane, mice received medetomidine (n = 3, soild symbols, normalized to baseline and total creatine, mean ± standard error). No changes in glutamate, GABA, choline-containing compounds (Cho), and *myo*-inositol were observed relative to controls (n = 3) receiving no further medications (open symbols, mean ± standard error).

Supplementary Figure 9

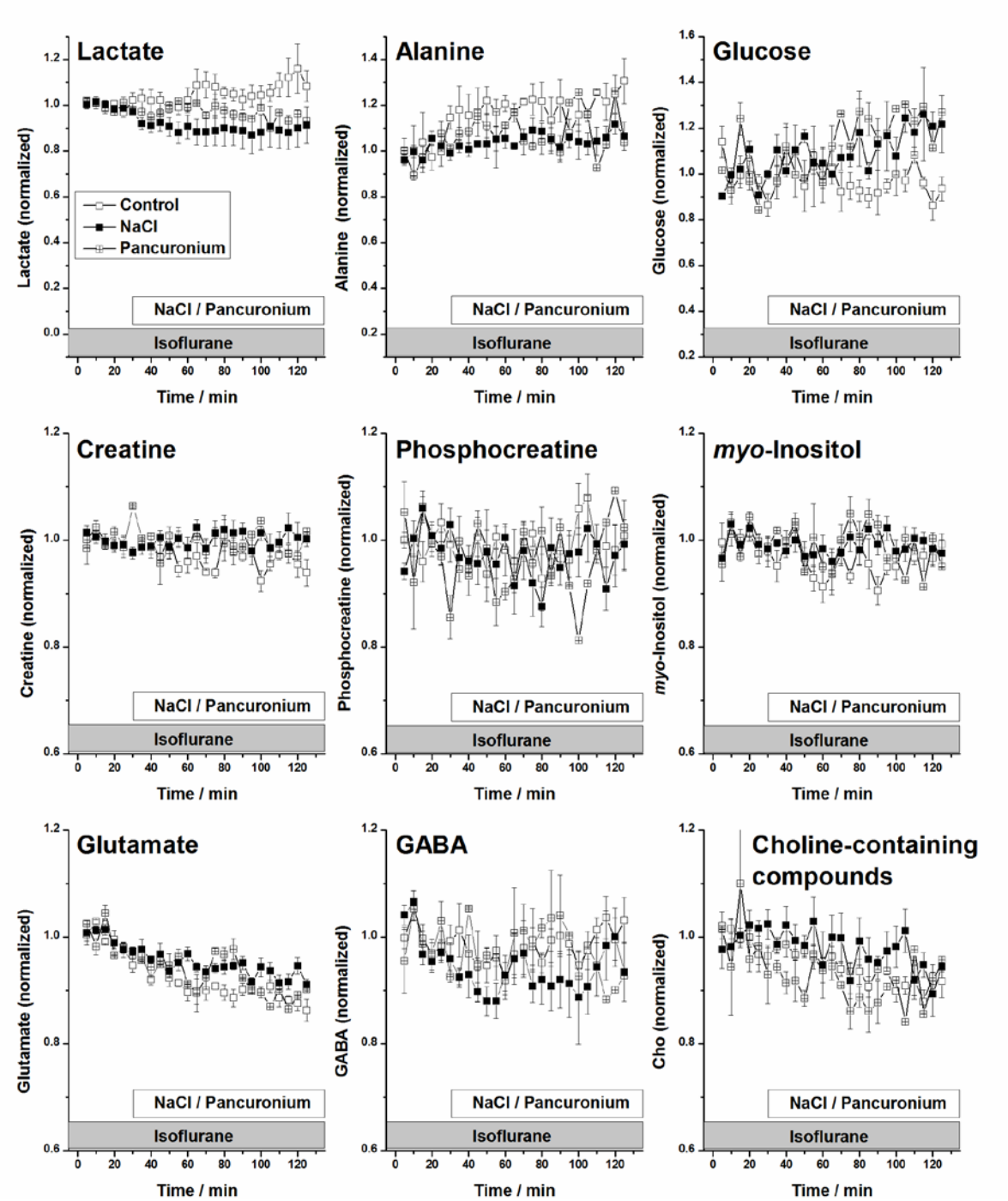
Modulation of brain lactate under isoflurane by clonidine. Administration of clonidine (n = 3) caused a significant reduction of lactate (solid symbols, normalized to baseline, mean ± standard error).Open symbols refer to lactate under constant isoflurane without further medication (n = 11).

Supplementary Figure 10

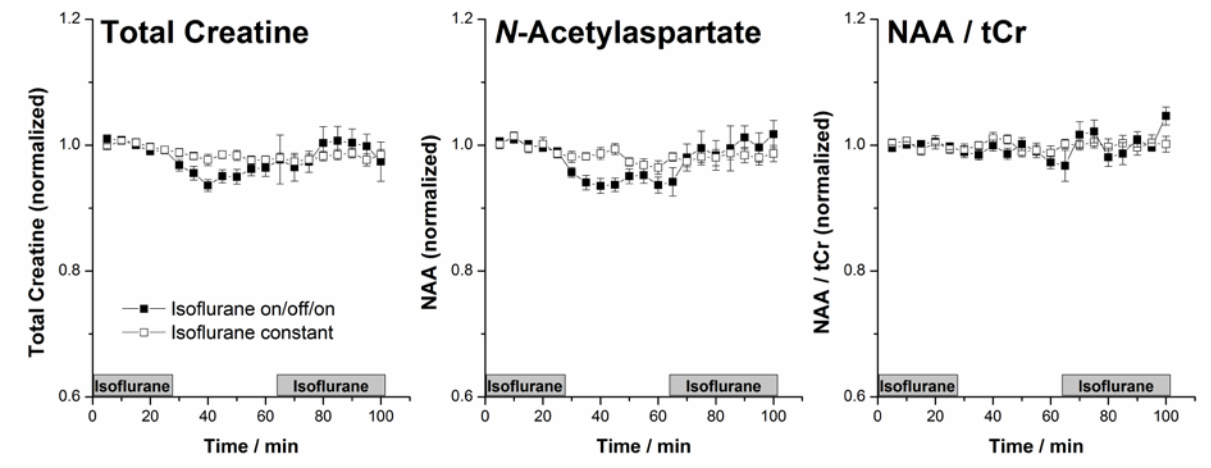
Cerebral glucose concentration. After withdrawal of isoflurane (left) glucose increased over time in awake, paralyzed mice. Subsequent sedation by medetomidine (n = 3, solid symbols, normalized to baseline, mean ± standard error) did not reduce the increase of glucose in comparison to untreated mice (n = 2, open symbols). Administration of medetomidine in addition to isoflurane (right, n = 3, solid symbols) showed only minimally increased glucose compared to untreated controls (n = 3, open symbols).

Supplementary Figure 11

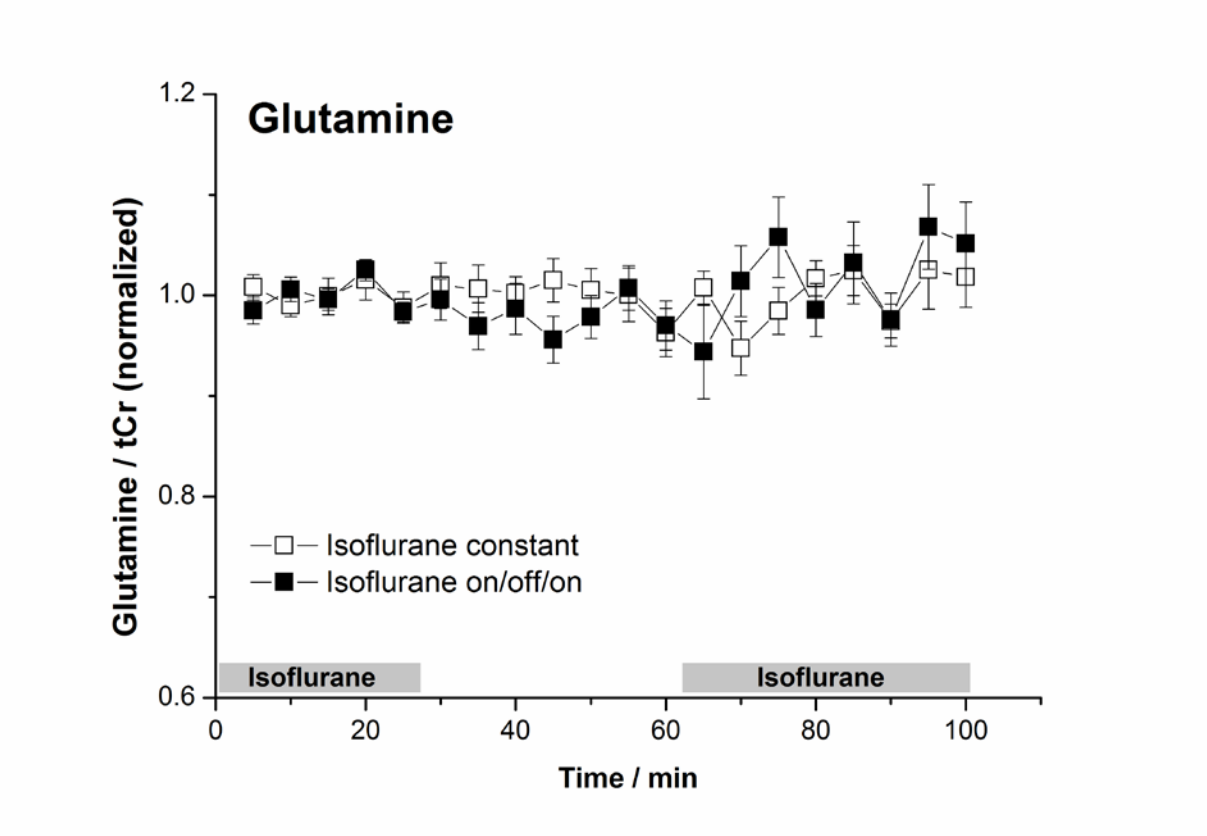
Influence of hypercapnia on cerebral lactate under isoflurane. Isoflurane at 1.75% in ambient air was complemented by 30% CO_2 (25 min), 20% CO_2 (25 min), and 10% CO_2 (25 min), while keeping the total gas flow constant. CO_2 reduced the isoflurane-induced increase of cerebral lactate in a dose-dependent manner.



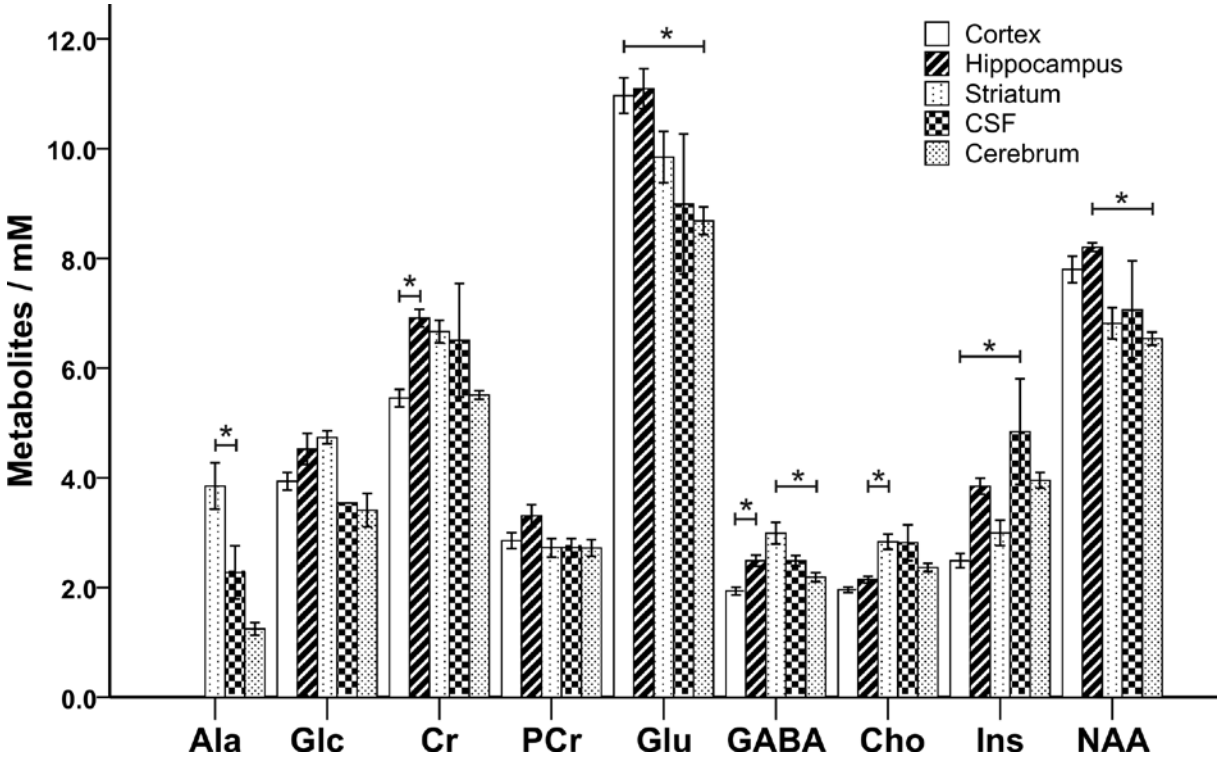
Supplementary Figure 1



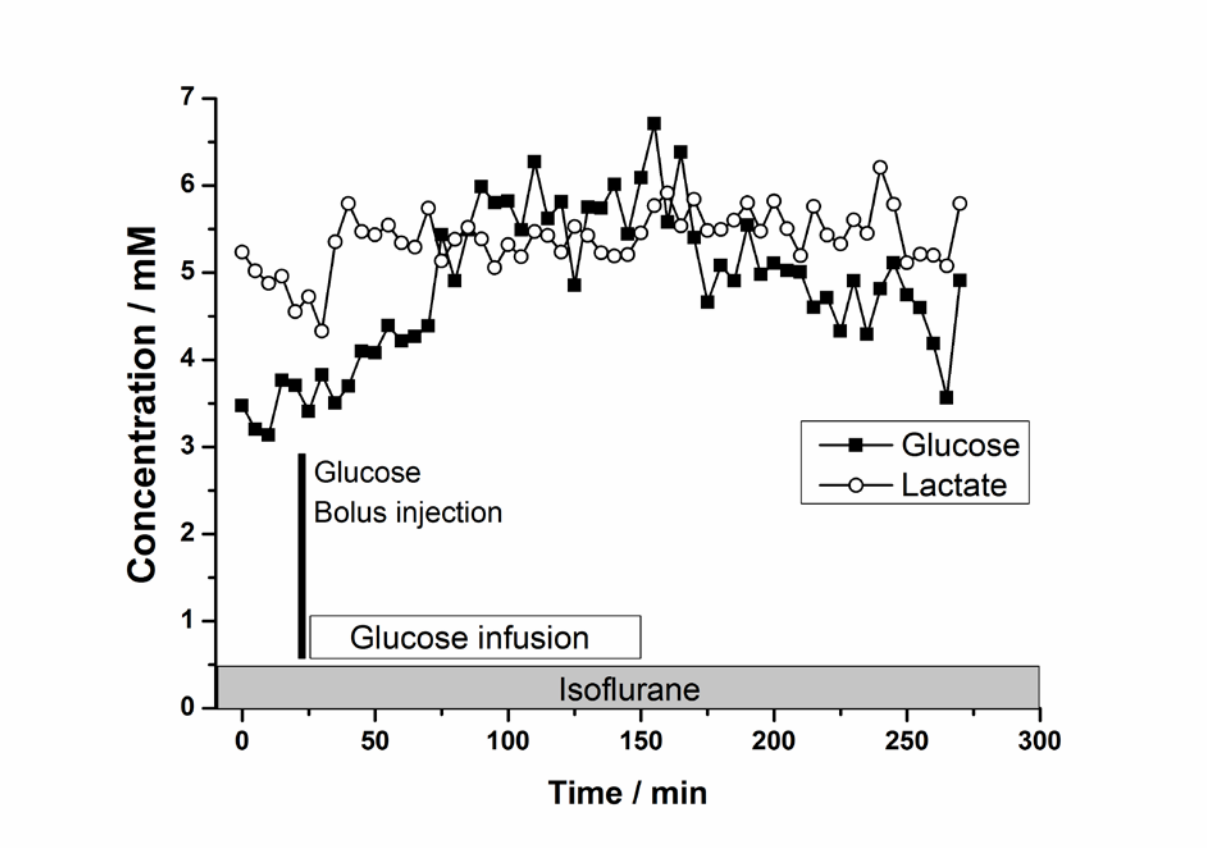
Supplementary Figure 2



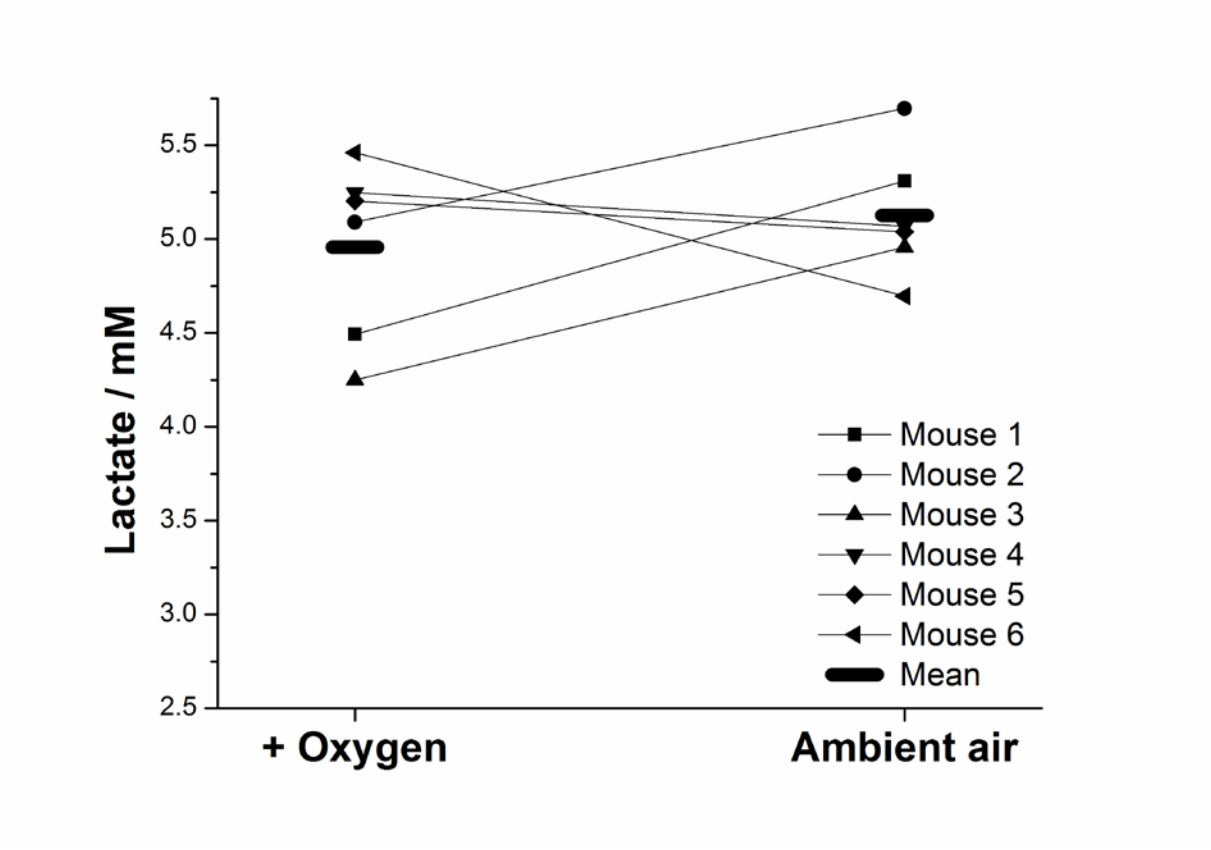
Supplementary Figure 3



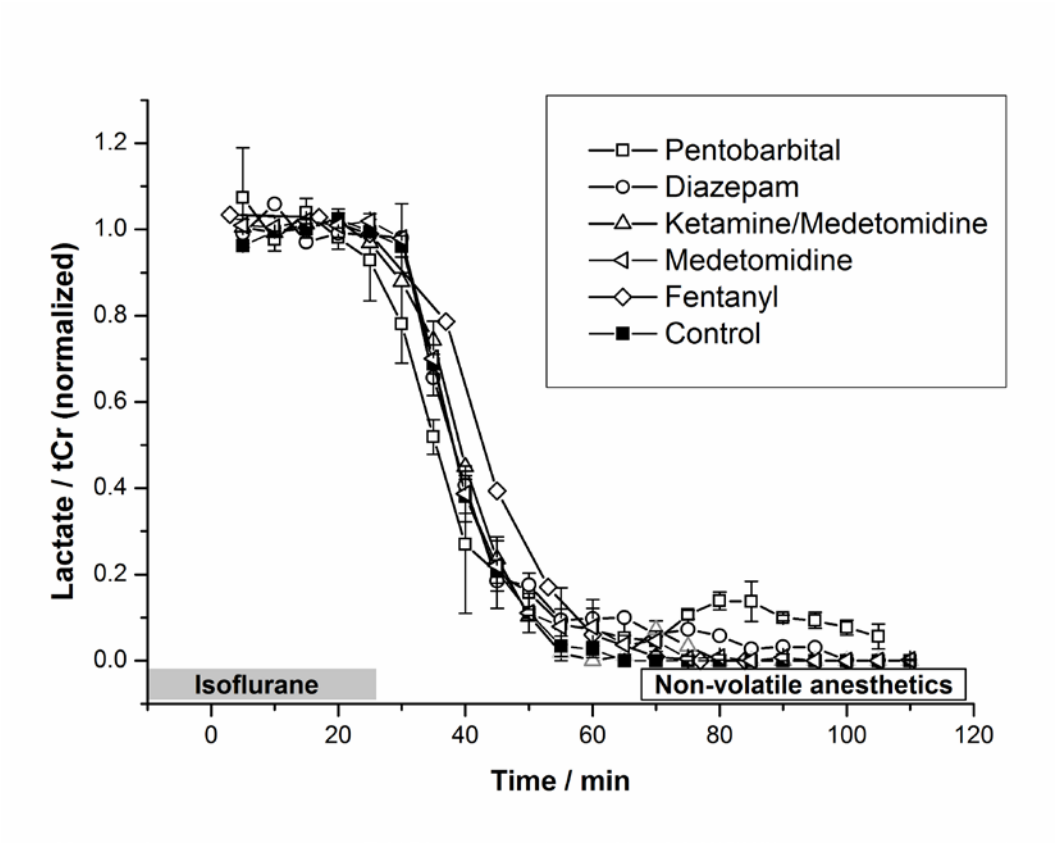
Supplementary Figure 4



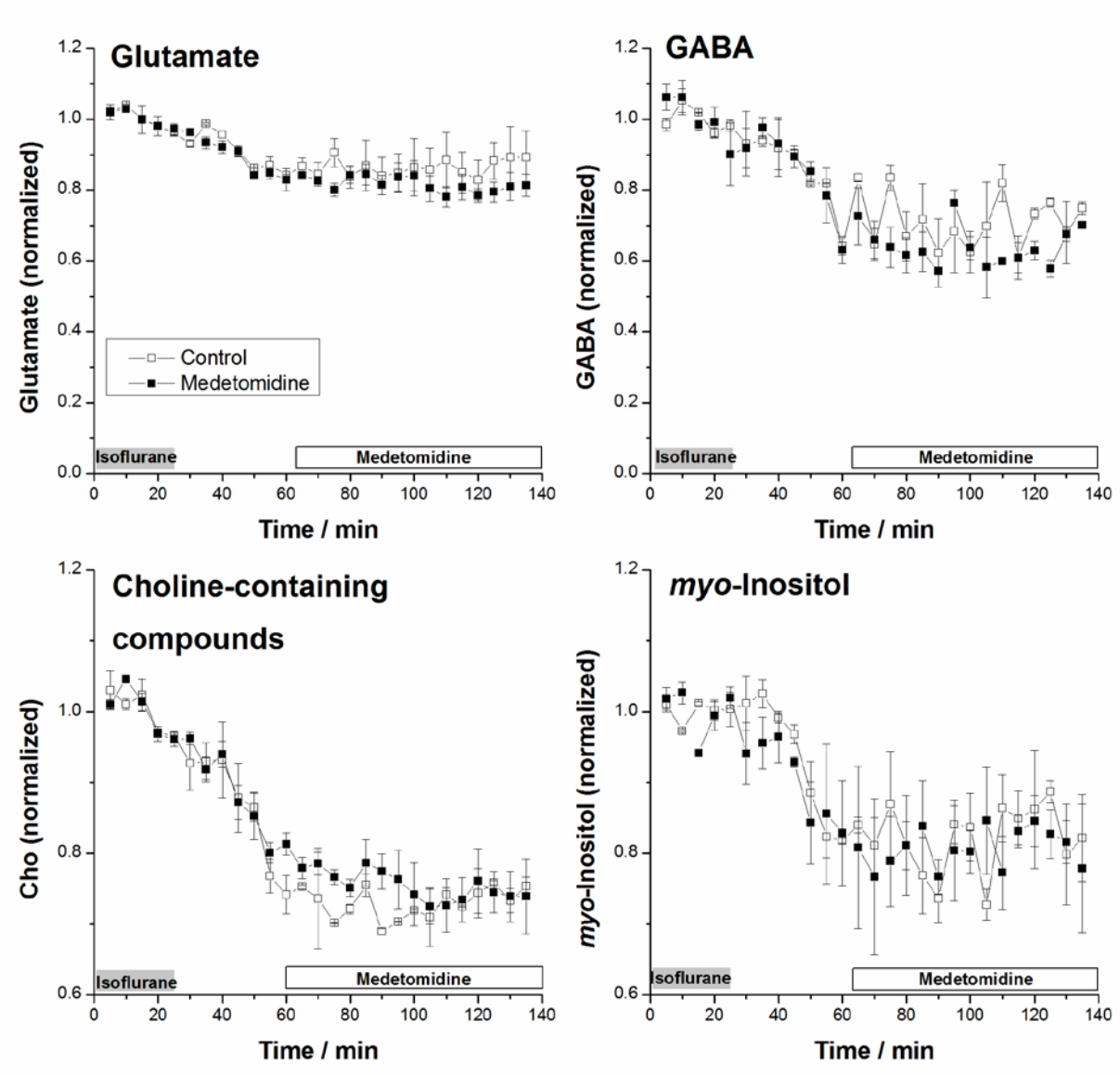
Supplementary Figure 5



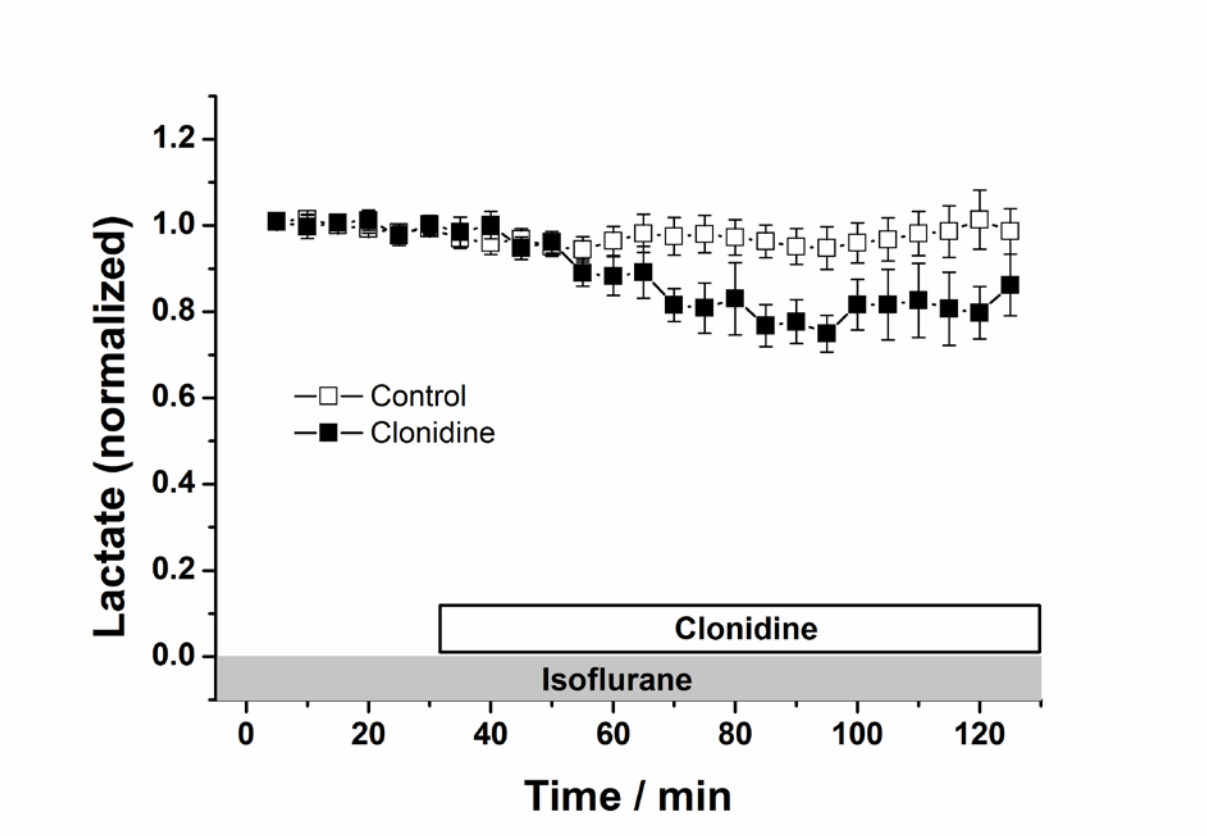
Supplementary Figure 6



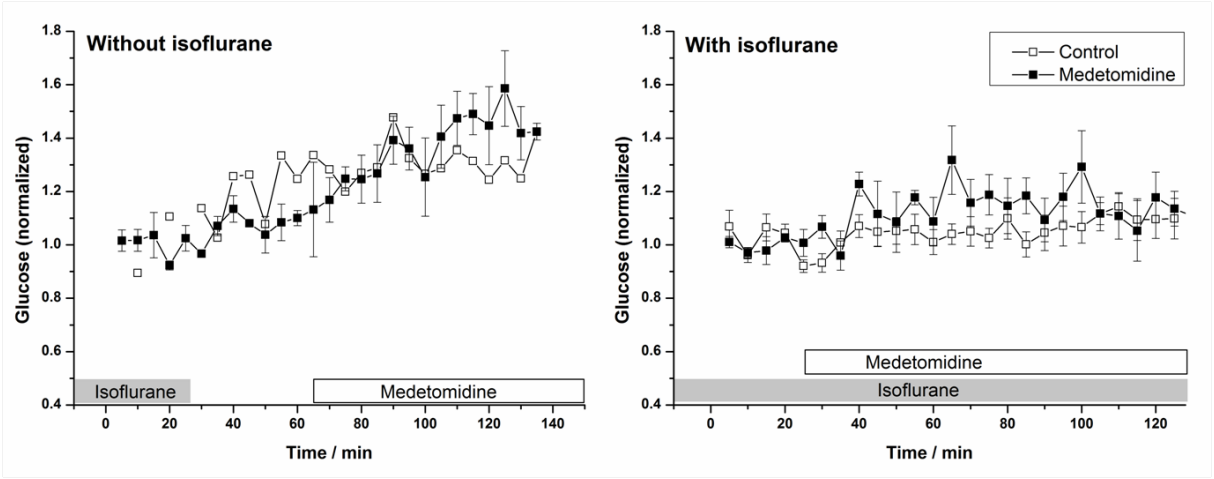
Supplementary Figure 7



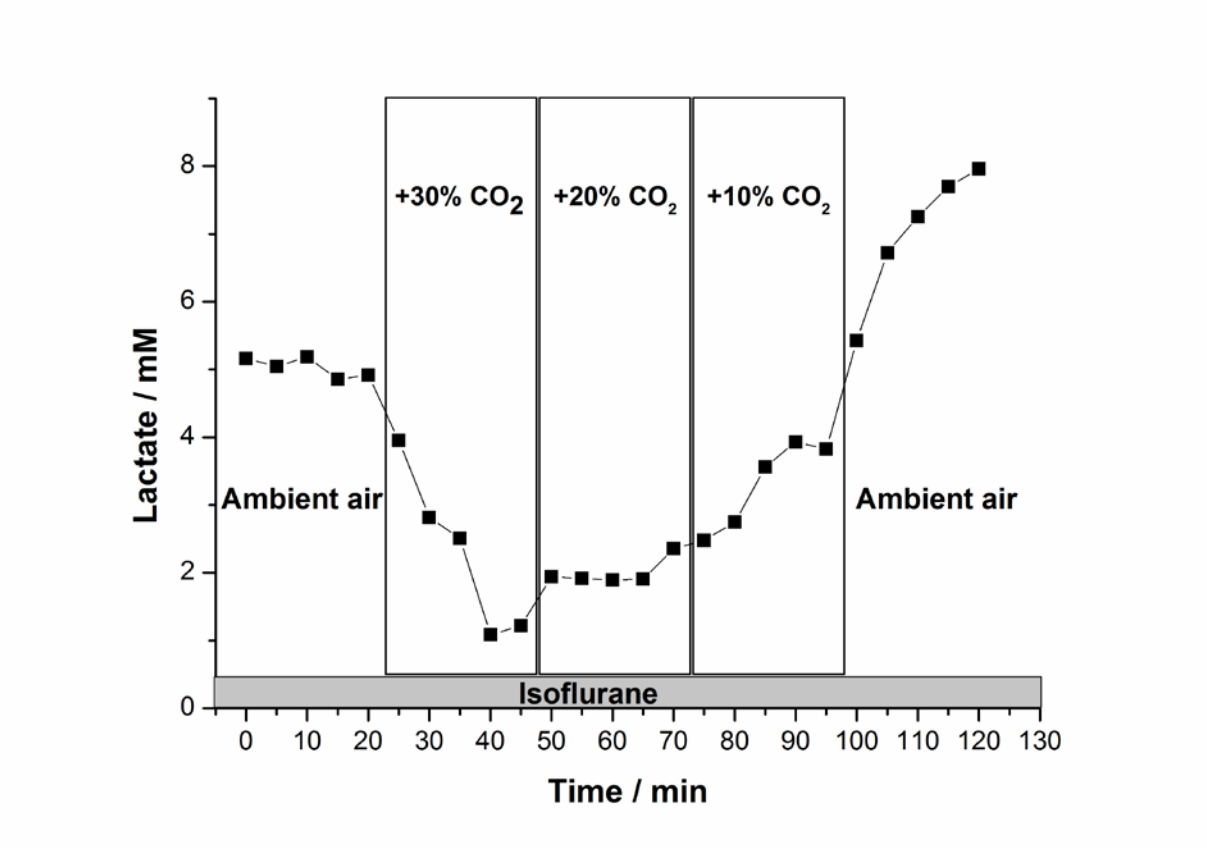
Supplementary Figure 8



Supplementary Figure 9



Supplementary Figure 10



Supplementary Figure 11