TITLE: EFFECTS OF ISOFLURANE ANESTHESIA ON THE BLOOD-BRAIN BARRIER TRANSPORT

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The purpose of our study was to determine the effect of isoflurane on the transport of small molecules across the blood-brain barrier (BBB). Isoflurane may effect the capillary permeability(P) or the perfused capillary surface area (Sv). In our study, the regional blood-brain transfer coefficient (Ki) was measured in rats using C^{14}-alpha aminoisobutyric acid (C^{14}-AIB) which is a small neutral amino acid. Ki depends on P and Sv.

In the experimental group, 6 rats (368±40 g) were anesthetized with 2% isoflurane in air through a tracheal tube and were mechanically ventilated. The femoral artery and vein were cannulated. After one hour of the anesthesia, Ki was measured by injecting 20 µCi of C^{14}-AIB through the venous cannula while multiple arterial samples were obtained during a 10 min period. Five minutes after the injection of C^{14}-AIB, 10 µCi of H^3-dextran was injected through the venous cannula. The brain was removed after the last blood sample was collected. The C^{14} and H^3 radioactivity of different brain regions and the plasma samples were determined with color and quench correction. Ki was obtained from the equation described by Blasberg et al. and others (1,2). In the control group, 7 rats (380±36 g) were cannulated in the femoral artery and vein under isoflurane anesthesia. Then, the anesthesia was discontinued and they were allowed to remain awake for 2 hrs before Ki measurement. Blood gases and rectal temperature were maintained within normal ranges. The mean arterial pressures were 118±12 mmHg and 86±13 mmHg for the control and for the isoflurane group respectively.

The Table below shows Ki values (µl/g/min, mean±SD) obtained from various regions of the brain. Ki was significantly decreased in the isoflurane group in almost all the brain regions studied.

Brain region	Control N=7	Isoflurane N=6	Brain region	Control N=7	Isoflurane N=6
Me	9.94±2.57	6.73±2.19*	Ol	14.47±3.66	9.59±4.20
Po	7.71±1.47	4.15±0.88*	Su	8.17±1.89	4.37±1.38*
Ce	11.23±3.82	5.40±1.82*	In	5.86±0.84	4.23±1.41
Hy	23.00±4.16	13.15±4.22*	Ac	6.84±1.93	4.53±1.11*
W	7.08±3.86	2.55±1.03*	Lc	8.64±1.27	4.33±0.91*
Ba	5.53±1.06	2.25±0.58*	Pc	13.56±2.26	4.87±1.32*
Hi	6.07±1.68	2.38±1.33*			

Me:Medulla Po:Pons Ce:Cerebellum Hy:Hypothalamus W:White matter Ba:Basal ganglia Hi:Hippocampus Ol:Olfactory bulb Su:Superior colliculus In:Inferior colliculus Ac:Anterior cortex Lc:Lateral cortex Pc:Posterior cortex

*Statistically different from the control. ($p<0.05$ by two-tailed unpaired t-test.)

The reduction of the blood-brain transfer coefficient (Ki) in our study could be a result of decreased capillary permeability or decreased surface area of the perfused capillaries by isoflurane. The amount that each of these two factors contributed in reducing Ki is unknown. Decreased Ki may potentially help to preserve the internal milieu of the brain during isoflurane anesthesia.

REFERENCES: 1.J Cereb Blood Flow Metab 3:8-32,1983
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THE EFFECT OF CHRONIC MORPINE ADMINISTRATION ON SPINAL ß-ENDORPHIN LEVELS

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Investigators have wondered if the tolerance and/or dependence induced by chronic opiate administration is related to alterations in endogenous opioid systems. Previous studies showed that chronic morphine administration had an inhibitory effect on rostral ß-endorphinergic (ßE) systems.[1] The present study was undertaken to see if spinal cord ßE systems were regulated similarly.

60 male Sprague-Dawley rats anesthetized with ether were implanted with a single morphine (75 mg) or placebo pellet on day 1, and 3 additional pellets of the same type on day 4. On day 7, animals were injected i.p. with either naloxone (2.5 mg/kg) or saline and sacrificed 1 hour later. Spinal cords were immediately dissected and frozen on dry ice. ßE immunoreactivity (ßEIR) was determined for different spinal cord regions of each animal by radioimmunoassay. Data were analyzed using 2 factor ANOVA, with $p<0.05$ considered significant.

Animals implanted with morphine showed a significant increase in ßEIR in cervical and thoracic regions compared with controls (See figure). In the lumbosacral region this trend did not reach statistical significance. Acute injection of naloxone had no significant effect on ßEIR in either placebo or morphine implanted animals.

Our results showing an increase in spinal ßEIR with chronic morphine administration appear to differ from what was observed in more rostral CNS systems. Spinal ßE mainly projects from the nucleus tractus solitarius, while brain ßE mainly arises form the arcuate nucleus.[2] This suggests that these two discrete endorphinergic systems may be regulated differently. Preliminary studies in our lab examining ßE forms present after these treatments show no difference in the peptide forms, suggesting that post-translational processing is similar among the treatment groups. Another mechanism, such as increased biosynthesis or decreased release, may be responsible for the increase in ßE observed in morphine treated animals. These findings may have important implications for understanding the intrinsic mechanisms resulting in narcotic tolerance and dependence.

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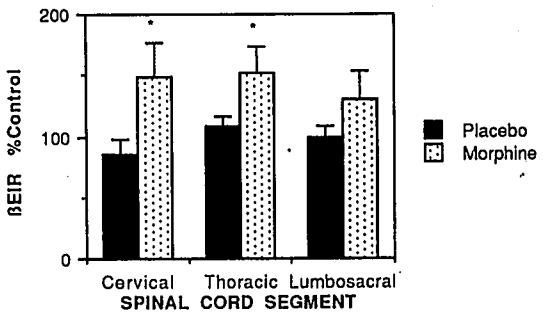

Naloxone and saline acute treatment groups pooled for each segment.
* $p<0.05$