Supplemental Digital Content 1 – Characteristics of Included Studies [i]

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
Adembri C. Anesthesiology 2006;104:80	Rats, Sprague Dawley (S-D), adult male, permanent middle cerebral artery occlusion (MCAO)	Propofol 100 $mg.kg^{-1}$ intraperitoneal (i.p.) Treatment during/after ischemia	Lipid emulsion	Neurological deficit score (NDS), Infarct volume (IV) 24 h post-ischemia/reperfusion (I/R)	Treatment decreased IV and NDS	Decrease in mitochondrial swelling
Bhardwaj A. Stroke 2001;32:1920	Rats, Wistar, adult male. 2 h MCAO	Exposure to halothane (1-2%, 1 or 8 h) exposure 24 h pre-I/R. Treatment before ischemia	Propofol (30 $mg.kg^{-1}.h^{-1}$, 1 or 8 h)	IV: 22 h post-I/R	Treatment with halothane reduced IV	Short exposure halothane better than propofol, independent of blood flow effects
Bleilevens C. Exp Brain Res 2013;224:155	Rats, Wistar, adult male. 1 h MCAO	Isoflurane 1.5-2% during surgery and ischemia. Treatment during/after ischemia	Anesthesia for ischemia ketamine (100 $mg.kg^{-1)}$/xylazine (10 $mg.kg^{-1}$) i.p.	NDS, IV 24 h post-I/R	IV, NDS reduced and survival improved by isoflurane	Isoflurane decreased edema and inflammatory responses
Chang ML. Neurosc Lett 2002;322:137	Rats, Wistar, adult male. 90 min MCAO	Ketamine 200 $mg.kg^{-1}$ i.p. ± nicotinamide 500 $mg.kg^{-1}$. Treatment during/after ischemia	Isoflurane, 5% in 70% nitrous oxide (N_2O), 30% oxygen (O_2)	IV 6h or 24 h post I/R	IV reduced with combination of ketamine and nicotinamide	Nicotinamide may prevent energy depletion.

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Chaparro E. Journal of Enzyme Inhib Med Chem 2013;28:1324	Rats, S-D, adult male, permanent MCAO	Isoflurane, propofol ± intraperitoneal caspase inhibitor days 0, 1,7 post-I/R. Treatment during/after ischemia	No injections, isoflurane anesthesia for surgery	NDS, IV 14 d post I/R	Caspase inhibition reduced injury, anesthetics did not	Reduction of caspase-mediated apoptosis
Chen L. Acta Anaesthesiol Scand 2008;52:413	Rats, S-D, adult male. permanent MCAO	Propofol , 80 $mg.kg^{-1}$, i.p. added to isoflurane maintenance. Treatment during/after ischemia	Anesthesia for ischemia: Isoflurane 1.5-2%	NDS, IV: 3, 6, and 24 h post-I/R	Propofol reduced NDS, infarct volume and apoptosis	Time-response experiment. Enhanced expression of anti-apoptotic B-cell lymphoma-2 (Bcl-2)
Chen Y. Br J Anaesth 2015;114:327	Rats, S-D, adult male. 1 h MCAO	Sevoflurane 2.7/97% O_2 vols% for 45 min 1h before I/R. Treatment before ischemia	97% O_2 vols%. Anesthesia for MCAO – 3% Sevoflurane	NDS, IV 1, 7 d post-I/R	Treatment reduced NDS, IV at 1, 1 and 7 d post-I/R respectively,	Protein kinase B (Akt) activation
Codaccione J-L. Anesthesiology 2009;110:1271	Rats, S-D, adult male. 1 h MCAO	Sevoflurane 2.7% in 30% O_2/ 70%N_2 before I/R, ischemia awake. Treatment before ischemia	Anesthesia: Sevoflurane (3%), removed during ischemia	NDS, IV: 3, 7, 14 d post-I/R	Sevoflurane reduced NDS and IV at 3 d but not 7 or 14 d post I/R	Sevoflurane decreased ischemia-induced apoptosis for

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						recovery times up to 7 d post-I/R
David HN. J Cereb Blood Flow Metabol 2003;23:1168	Rats, S-D, adult male. 90 min MCAO	Xenon 50%, 75%, N_2O 75%. Treatment during/after ischemia	N_2O 75%, Air	IV 24 h after I/R	Both Xenon and N_2O reduced IV	
Dong, P. Neuroscience 2014;275:2	Rats, Fisher 344, adult male - young (4 months), old (24 months), 2 h MCAO	Sevoflurane 2.6% for 15 min at the start of reperfusion. Treatment during/after ischemia	Anesthetic for ischemia: Chloral hydrate (300 $mg.kg^{-1}$)i.p.	NDS,IV 24 h after I/R	Sevoflurane improved NDS, IV, edema formation and apoptosis in young but not aged subjects	Aging-associated decreases in expression of anti-apoptotic molecules may explain lack of neuroprotection.
Haelewyn B. Br J Anaesth 2003;91:390	Rats, S-D, adult male. 2 h MCAO	Halothane or desflurane during ischemia, Treatment during/after ischemia	Awake during ischemia	IV 24 h after I/R	Both desflurane and halothane reduced IV	
Homi HM. Anesthesiology 2003;99:876	Mice C57BL/6, adult male, 1 h MCAO	70% Xenon. Treatment during/after ischemia	70% N_2O	NDS, IV 24 h after I/R	70% Xenon reduced NDS, IV	

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Inoue S. Anesthesiology 2004;101:75	Rats, Wistar, adult male 1 h MCAO	Isoflurane 1.8% maintained during ischemia. Treatment during/after ischemia	Isoflurane discontinued during ischemia "Awake controls"	NDS, IV evaluated 14 d after I/R	Isoflurane did not reduce NDS or IV.	Caspase inhibition reduced IV, NDS in both awake and isoflurane-treated subjects
Inoue S. Anesth Analg 2006;102:1548	Rats, Wistar, adult male 1 h MCAO	Isoflurane 1.8% maintained during ischemia. Treatment during/after ischemia	Isoflurane discontinued during ischemia "Awake controls"	Neurologic scores, i IV evaluated 14 d after I/R	Isoflurane decreased NDS and IV.	Intraventricular a caspase 8 inhibitor enhanced neuroprotection
Jeong S. J Neurosurg Anesthesiol 2012;24:51	Rats, S-D, adult male. 90 min MCAO	Remifentanil, 5 $\mu g.kg^{-1}.min^{-1}$ ± opioid receptor antagonists. Treatment during/after ischemia	Sevoflurane ± opioid receptor antagonists	NDS, IV 1d post-I/R	Remifentanil decreased both NDS and IV	Remifentanil reduced overexpression of inflammatory mediators: tumor necrosis factor (TNF-α)
Ji F-T. Mol Med Reports 2015;12:2049	Rats, Wistar, adult male. 2 h MCAO	Propofol, 20 or 40 $mg.kg^{-1}.hr^{-1}$, Treatment during/after ischemia	Anesthesia for surgery – halothane 1.3%/70% N_2O	NDS, Evan's blue extravasation, brain water content	Propofol decreased NDS, brain water and Evan's blue extravasation	Metalloproteinase (MMP) activity and aquaporin (AQP) expression attenuated by propofol

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Kapinya KJ. NeuroReport 2002;13:1431	Mice, C57BL/6, adult male 1 h MCAO	Exposure to 0.8-1.4% isoflurane . Treatment before ischemia	Preconditioned with air.	IV 48 h after I/R	IV reduced by isoflurane	Neuroprotection abolished with mild hypoxia or iron chelator. Dose-response relationship.
Kawaguchi M. Anesthesiology 2000;92:1335	Rats, Kyoto Wistar, adult male, 1 h MCAO	Isoflurane 1.8% maintained during ischemia. Treatment during/after ischemia	Isoflurane for procedure, I/R awake	Neurologic scores, infarct volume; 2, 14 d after I/R	Isoflurane reduced IV at 2 but not 14 days after I/R	Concern that effects of isoflurane may be transient.
Kawaguchi M. Anesth Analg 2004;98:798	Rats, Wistar-Kyoto, adult male. 70 min MCAO	Isoflurane 1.8% maintained during ischemia. Treatment during/after ischemia	Isoflurane for procedure, I/R awake.	IV, # of apoptotic neurons 7 h, 1,4 or 7days post-I/R	Isoflurane reduced IV in the acute but not the delayed stage after I/R	Isoflurane decreased apoptotic neuron count in the acute but not the delayed stage after I/R
Kitano H. J Cereb Blood Flow Metabol 2007;27:1377	Mice, young & middle aged male and female, protein kinase B (Akt) + and Akt –	Exposure (4h) to isoflurane 1% in O_2-enriched air 24 h before I/R. Treatment before ischemia	Exposure (4h) to O_2-enriched air 24 h before I/R. Isoflurane for surgery, awake during ischemia	NDS, IV 22 h post I/R	Treatment decreased injury in young, middle-aged males, increased injury in young females, no	Neuroprotection not observed in Akt- male mice.

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	strains, 2 h MCAO				effect in middle-aged females.	
Kotani Y. J Cereb Blood Flow Metabol 2008;28:354	Mice, ddY, adult male	Propofol 1, 5 or 10 $mg.kg^{-1}$ i.p. ± disodium edetate (EDTA), Treatment before ischemia	1-1.5% Isoflurane in 60% nitrous oxide	NDS, IV 24 h or 7 d after I/R	Propofol decreased IV but not NDS	Addition of EDTA increased neuroprotection possibly by zinc chelation
Lee J. Anesthesiology 2008; 108:1055	Rats, S-D, adult male 90 min MCAO	Exposure to isoflurane 2% for 1 h at the start of reperfusion. Treatment during/after ischemia	No exposure to isoflurane during reperfusion – awake ischemia and awake reperfusion	NDS, IV 24 h after I/R	Treatment during/after ischemia improved both outcomes.	Block of mitochondrial ATP-sensitive K^+ channels ($mitoK_{ATP}$) abolished neuroprotection.
Lee J. Neurochem Res 2013;38:2276	Rats, S-D, adult male, 1 h MCAO	Propofol 0.1 $ml.kg^{-1}.min^{-1}$ for 1 h from the start of reperfusion Treatment during/after ischemia	Anesthesia for surgery was zoletil (30 $mg.kg^{-1}$)/xylazine (10 $mg.kg^{-1}$) i.p. Controls received saline infusion	NDS, IV, blood brain barrier (BBB) integrity, cerebral edema 24h after I/R.	Treatment decreased IV and NDS, cerebral edema and improved BBB integrity	Treatment decreased the expression of AQP, MMP, and hypoxia-inducible factor(HIF) -1α
Li B. Int J Devl Neuroscience 2014;38:79	Rats, S-D, adult male 1 h MCAO	Exposure to 2.6% sevoflurane for 1 hour at onset of reperfusion.	Surgery, Ischemia under pentobarbital	Infarct volume, neurobehavioral scores 72 h after I/R	Treatment reduced NDS and infarct size	Effect may involve Akt

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
		Treatment during/after ischemia	anesthesia (35 mg.kg^{-1} i.p.)			
Li D. PLoS ONE 2013; 8:e73334	Rats, S-D, adult male 2h MCAO	Normal and diabetic animals exposed to 2.6% sevoflurane for 15 min at the start of reperfusion. Treatment during/after ischemia	Ischemia performed under chloral hydrate anesthesia (300 mg.kg^{-1})	IV NDS, 24 h after I/R	Treatment reduced NDS and IV in normal but not diabetic Rats.	Decreased mitoK_{ATP} channel in diabetic rats interferes with neuroprotection.
Li H. Neurobiol Dis 2013;54:216	Rats, S-D, adult male 90 min MCAO	Exposure to isoflurane (2 %) for 60 minutes immediately after MCAO. Treatment during/after ischemia	Anesthetized for MCAO with isoflurane, but awake during I/R	NDS and IV determined 1,2 and 4 weeks after I/R	Improved outcomes in isoflurane-treated persisted for 4 weeks	Treatment during/after ischemia reduced nuclear transcription factor (NF-KB) activation and interleukin 1β (IL-1β) and interleukin-6 (IL-6) production in the penumbra
Li L. Eur J Pharmacol 2008;586:106	Rats, S-D, adult male permanent MCAO	Exposure to isoflurane 2% for 30 min, 24 h before I/R. Treatment before ischemia	Anesthetized for MCAO with isoflurane, but awake during I/R	NDS, IV determined 24 h after I/R	Treatment decreased IV, NDS	Treatment increased Bcl-2 expression, and reduced mitochondrial

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						cytochrome c release
Li L. Neuroscience 2009;164:497	Rats, S-D, adult male 90 min MCAO	Exposure to isoflurane (1.1,2.2%) or desflurane (6,12%) for 30 min immediately before MCAO. Treatment before ischemia	Anesthetized for MCAO with isoflurane or desflurane	NDS, IV volumes determined 24 h and 4 weeks after I/R	Isoflurane decreased NDS, IV at both assessment times. Desflurane did not.	Dose-response relationship. Increased Bcl-2 expression associated with neuroprotection
Li L. Brain Res Bull 2013;98:23	Mice, wild-type and excitatory amino acid receptor-deficient ($EAAT_3$) adult male, 60 or 90 min MCAO	Exposed to 1.5% isoflurane for 30 minutes, with a 30 min washout period before the onset of surgery. Treatment before ischemia	Surgery performed under isoflurane anesthesia, for ischemia/reperfusion animals were awake	NDS, IV 24 h after I/R.	Treatment decreased NDS and IV in wild-type mice but not in $EAAT_3$ mice	$EAAT_3$ deficient mice did not show neuroprotection at either 60 or 90 min ischemia time. Downstream event includes Akt activation
Li Q. Brain Res 2012;1451:1	Rats, S-D, adult male 90 min MCAO	Exposure to isoflurane (1.4 %) for 30 minutes immediately after MCAO. Treatment during/after ischemia	Anesthetized for MCAO with isoflurane	NDS, IV 24 h after I/R	Isoflurane Treatment during/after ischemia reduced IV and NDS	Possible involvement of HIF-1α and nitric oxide synthase (NOS) in neuroprotection

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Li X. Anesthesiology 2014;121:549	Rats, S-D adult male 120 min MCAO	Exposure to 2% sevoflurane for 2 h, 2 hour washout before I/R Treatment before ischemia	Surgery, I/R under pentobarbital anesthesia (40 $mg.kg^{-1}$ i.p.)	NDS, IV 24 h after I/R	Treatment decreased NDS and IV.	Treatment decreased the ischemia-induced upregulation of astrocyte apoptotic signalling pathways
Liang C. J Neurosurg Anesthesiol 2013; 25:311	Rats, S-D adult male, 90 min MCAO	Propofol infusion (10,20,50 $mg.kg^{-1}$) for 30 min at start of reperfusion. Treatment during/after ischemia	Ischemia/reperfusion done under pentobarbital anesthesia (50 $mg.kg^{-1}$, i.p.)	NDS, IV 24 h after I/R	Treatment decreased NDS, IV and apopotosis.	Treatment upregulated expression of the antioxidant heme oxygenase-1
Liu Y. Can J Anesth 2006;53:194	Rats, S-D adult male, 120 min MCAO	Exposure to 1.5% isoflurane for 1 h before I/R. Treatment before ischemia	Ischemia/reperfusion under isoflurane anesthesia	NDS, IV 24 h after I/R	Treatment decreased NDS and IV	Ischemic tolerance attenuated by adenosine A_1 receptor antagonist
Lückl J. Brain Res 2008;1191:157	Rats, S-D adult male 90 min MCAO	Isoflurane (1%)/nitrous oxide during I/R. Treatment during/after ischemia	α-chloralose	NDS at 24, 72 h post-I/R; IV at 72 h post-I/R	Isoflurane decreased IV, NDS similar	

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Lückl J. Neuroscience 2012;226:197	Rats, S-D adult male 90 min MCAO	Post-hoc comparison of isoflurane/nitrous oxide Treatment during/after ischemia	Halothane/N_2O	IV 72 h post-I/R	No difference in IV between anesthetics	Post-hoc collection of data from pilot studies. Anesthetic comparison accidental
Maud P. Biomed Res Int 2014; ID 802539	Rats, Wistar adult male 60 min MCAO	Isoflurane (2%) for ischemia. Treatment during/after ischemia	Chloral hydrate (300 $mg.kg^{-1}$) for ischemia	IV 24 h post-I/R	No difference in IV between anesthetics	
Mayanagi K. Brain Res 2007;1168:106	Rats, Wistar adult male 90 min MCAO	Isoflurane 1.7% for ischemia. Treatment during/after ischemia	Halothane 1.2% for ischemia.	IV determined immediately	No difference in IV between anesthetics	Manipulation of mitoK_{ATP} channel opening alters neuroprotection
Pittman JE. Anesthesiology 1997;87:1139	Rats, Wistar, adult male 75 min MCAO	Propofol (total dose: 291±45 $mg.kg^{-1)}$). Treatment during/after ischemia	Pentobarbital (total dose:135±12 $mg.kg^{-1}$	NDS, IV 7 d post-I/R	No difference in IV or NDS between anesthetics	Equal metabolic suppression by EEG criteria
Qiu C. Neural Regen Res 2013;8:2126	Rats, S-D adult male, permanent MCAO	Sevoflurane 2.4% for 15,30,60 or 120 min 50 min before I/R. Treatment before ischemia	Air	IV, NDS 24 h after I/R	Treatment for 15, 30, and 60 min reduced IV but not NDS	Time-dose study

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Ritz M-F. Intern J Neurosci 2006;116:191	Rats, Wistar, adult male 90 min MCAO	Isoflurane 1.5% during I/R.Treatment during/after ischemia	Pentobarbital 50 $mg.kg^{-1}$ during I/R	IV 24 h post-I/R, glutamate and taurine (EAA) concentrations	No difference in IV between anesthetics	Isoflurane prevented the ischemia-induced increase in EAA's
Sakai H. Anesthesiology 2007;106:92	Rats, Wistar adult male 50 or 80 min MCAO	Exposure to isoflurane 1.5% during ischemia. Treatment during/after ischemia	Anesthetic removed – 'awake' controls	NDS, IV 2 weeks and 8 weeks post-I/R	Treatment reduced NDS and V persisting to 8 weeks post-I/R	Block of mitoK_{ATP} did not alter outcomes in any group
Sarraf-Yazdi S. Anesth Analg 1998;87:72	Rats, Wistar adult male, 75 min MCAO	Exposure to low-dose isoflurane (0.7%) during ischemia ± dizocilpine (1 $mg.kg^{-1}$) i.p. 30 min before MCAO.	Anesthetic removed – 'awake controls	NDS, IV 1 week post-I/R	Isoflurane did not reduce NDS or IV compared to awake or to dizocilpine-treated subjects	Comparison with glutamate receptor blocker
Schmid-Elaesser R. J Neurol Sci 1999;162:14	Rats, S-D, adult, 120 min MCAO	Low-and high-dose pentobarbital by EEG criteria Treatment during/after ischemia	Halothane	IV immediately after ischemia	Pentobarbital reduced IV	No difference between doses

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Shi H. CNS Neurol Disord Drug Targets 2013;12:381	Rats, S-D, adult male, 120 min MCAO	Exposure to 1 MAC (2.4%) sevoflurane in air for 30 min per day on 4 consecutive days. Treatment before ischemia	Air Isoflurane (1-2%) to both groups during ischemia.	NDS, IV 24 and 48 hrs after I/R	Treatment decreased NDS and IV	Treatment reverses suppression of anti-apoptotic Bcl-2 pathways; microRNA's involved
Shi S-s. Neurochem Res 2014;39:793	Rats, S-D, adult male, permanent MCAO	Propofol 10 or 50 $mg.kg^{-1}$; Treatment during/after ischemia	Chloral hydrate (300 $mg.kg^{-1}$ i.p.)in all groups	NDS, IV 24 h after ischemia	NDS and IV reduced by propofol	Attenuation of overexpression of inflammatory mediators: TNF-α, NF-κB, cyclooxygenase-2 (COX-2)
Shu L. Neurochem Res 2012;37:49	Mice, BABL/c, adult male, Permanent MCAO	Propofol or ketamine 25, 50, 100 $mg.kg^{-1}$, Treatment during/after ischemia	Pentobarbital (60 $mg.kg^{-1}$ i.p.)	NDS, IV 6 h after MCAO	NDS, IV decreased by both propofol and ketamine	Inhibition of cAMP response element-binding protein (CREB) by both drugs. Dose response study
Soonthon-Brant V. Anesth Analg 1998;88:49	Rats, Wistar-Kyoto adult male, 90 min MCAO	Isoflurane 1 MAC (1.1%) or	Anesthetic removed – 'awake' controls	IV 1 week after I/R	Isoflurane, but not fentanyl decreased IV	High dose fentanyl, no detrimental effect

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		Fentanyl 50 µg.kg^{-2}.hr^{-1} Treatment during/after ischemia				
Sun H. Brain Res 2008;1194:73	Rats, S-D, adult male, 120 min MCAO	Ischemia/reperfusion under isoflurane 2%/30% air Treatment during/after ischemia	Ketamine/xylazine (100/15 mg.kg^{-1} i.p.)	NDS,IV 24 hrs after I/R	No difference between anesthetics	IV, NDS greater in alcohol-fed animals
Sun M. Scientific Reports 2015;5:11445	Rats, S-D, adult male, 90 min MCAO	Thirty min exposure to isoflurane 2%, 24 hours before I/R Treatment before ischemia	Chloral hydrate	NDS, IV 24 hr after I/R	Treatment decreased IV and NDS	Decreased activation of NF-κB pathway, Toll-like receptor-4 (TLR-4); decreased microglial inflammation
Taheri S. Brain Res 2014;1586:173	Rats, Wistar, adult male, 90 min MCAO	Ischemia/reperfusion under 2% isoflurane. Treatment during/after ischemia	Anesthetic removed – 'awake controls	IV measured with magnetic resonance imaging 0-12d after I/R	IV peaked from 24-72 h post-I/R, defining the acute phase	Treatment enhanced expression of HIF-α and vascular endothelial growth factor (VEGF)

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Tong L. Br J Anaesth 2014;113:157	Rats, S-D, adult male, 120 min MCAO	Sevoflurane 2.7% in oxygen for 1 h, with 1 h washout before MCAO. Treatment before ischemia	97 % oxygen	NDS 24,48, 72 h after I/R, IV 72 h and 1 week after I/R	Treatment decreased NDS and IV	Neuroprotection attenuated by knockdown of a two-pore domain K+ channel (K_2P TREK-1)
Tong L. Mol Neurobiol 2015;51:1221	Rats, S-D, adult male, 120 min MCAO	Isoflurane 2% 1h.d^{-1} x 5 d before I/R; Treatment before ischemia ± small interfering RNA (siRNA) for ubiquitin (Ubc9) conjugase . Treatment before ischemia	98% O_2	NDS at 1, 2, 3,7, and 14 d post I/R; IV at 3,7, 14 d	Treatment reduced NDS at all times, IV at 3d and 7 d	Ubc9 expression increased by Treatment, neuroprotection abolished by siRNA knockdown of Ubc9
Wang H. Front Biosci 2011; E3:604	Rats, S-D, adult male, 60 min MCAO	Exposure to sevoflurane (1.2% or 2.4%)in air for 30 min on 4 consecutive days , ending 1 d before MCAO Treatment before ischemia	Ambient air	NDS, IV 72 h after I/R	Both doses of sevoflurane decreased NDS and IV	Neuroprotection associated with suppression of NF-KB, P38 mitogen-activated kinase (MAPK)

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Wang H. J Neurochem 2011;119:210	Rats, S-D, adult male, 60 min MCAO	Thiobutabarbital 100 $mg.kg^{-1}$ i.p. Propofol, 20 $mg.kg^{-1}.h^{-1}$, for 4 h beginning at the onset of reperfusion. Treatment during/after ischemia	Thiobutabarbital 100 $mg.kg^{-1}$ i.p. Intralipid® infusion	Morris water maze test at 14, 28 d post-I/R, infarct size 1, 14 and 28 d after I/R. NDS only used to exclude uninjured animals, not reported	Propofol improved maze performance and decreased IV at all times	Neuroprotection associated with glutamate receptor dynamics
Wang H. Brain Res 2015;1597:210	Rats, S-D adult male, 60 min MCAO	Propofol 20 $mg.kg^{-1}.hr^{-1}$ during ischemia and 1 h of reperfusion. Treatment during/after ischemia	Thiobutabarbital 100 $mg.kg^{-1}$ i.p. Saline infusion	NDS 24 h post-I/R	Treatment decreased NDS.	Treatment during/after ischemia enhanced the expression of K^+ - Cl^- co-transporter 2 (KCC2)
Wang H-y. Brain Res 2009;1297:177	Rats, S-D adult male, 120 min MCAO	Thiobutabarbital + Propofol (10,20,35 $mg.kg^{-1}.hr.^{-1}$) Treatment during/after ischemia	Thiobutabarbital 100 $mg.kg^{-1}$ i.p.	NDS, IV 22 h after I/R	Treatment with 10 and 20 $mg.kg^{-1}.h^{-1}$ but not 35 $mg.kg^{-1}.h^{-1}$ decreased IV and NDS	Dose-response relationship, Phosphoinositide-3-kinase (PI3K) – Akt pathway inhibition attenuated neuroprotection

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
Wang J-K. Brain Res 2010; 1357:142	Rats, S-D adult male, 90 min MCAO	Exposure to sevoflurane 0.5, 1 and 1.5 MAC in O_2 for 30 min starting 90 min after MCAO. Treatment during/after ischemia	Chloral hydrate 350 $mg.kg^{-1}$ i.p.; O_2 for 30 min starting 90 min after MCAO	Neurologic outcome, Infarct volume 22 h after I/R	Treatment with 1 and 1.5 MAC isoflurane decreased IV and NDS	Dose-response relationship, PI3K inhibition attenuated neuroprotection.
Wang J-K. Neurol Res 2015;37:77	Rats, S-D adult male, 90 min MCAO	Exposure to sevoflurane 1 MAC in O_2 for 30 min starting 90 min after MCAO. Treatment during/after ischemia	Chloral hydrate 350 $mg.kg^{-1}$ i.p.; O_2 for 30 min starting 90 min after MCAO	Neurologic outcome, Infarct volume 24 h after I/R	Treatment reduced IV and NDS	Block of mitoK_{ATP} channel and mitochondrial permeability pore attenuated neuroprotection.
Wang L. J Cereb Blood Flow Metabol 2008;28:1824	Mice, C57BL/6 young adult female, 120 min MCAO	Exposure to 1 % isoflurane/O_2-enriched air for 4 h, 1 d before I/R Treatment before ischemia.	No exposure	NDS, IV 22 h after I/R	Treatment reduced IV volume in ovariectomized mice	Role of estrogen, including estrogen receptor deficient subjects
Wang Z. NeuroRehabilitation 2014;35:825	Rats, S-D, adult male, 120 min MCAO Treatment	Propofol (10 $mg.kg^{-1}.h^{-1}$), dexmedetomidine (4 $\mu g.kg^{-1}.h^{-1}$) intravenously alone	All groups received chloral hydrate (350 $mg.kg^{-1}$)	NDS, Morris water maze test	Both drugs reduced NDS and the combination had additive effects	Neuroprotection was associated with decrease in TNFα and IL-1β expression; increae

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		or in combination 20 min before and during I/R Treatment during/after ischemia				in expression of Akt
Warner DS. Anesthesiology 1996;84:1475	Rats, Wistar, adult male, 90 min MCAO	Pentobarbital low or high dose measured by EEG. Treatment during/after ischemia	Pentobarbital 40 $mg.kg^{-1}$ i.p. Ischemia/reperfusion awake	NDS, IV 7d post I/R	No difference in outcome measures between anesthetics; 'awake' controls worse	Greater metabolic suppression with high dose not associated with improved outcome
Xiao Z. Mol Med Rep 2015;12:675	Rats, S-D, adult male, 120 min MCAO	Isoflurane 2%/Nitrogen(N_2) 40%, O_2 60% for 1 h, 1 day before I/R, Treatment before ischemia.	N_2 40%, O_2 60% for 1 h, 1d before I/R	NDS, IV 1d post I/R	Treatment before ischemia decreased NDS and IV	Decreased levels of inflammatory mediators: TLR4,Nf-κB, TNF-α
Xiong L. Chinese Med J 2003; 116:108	Rats, S-D, adult male, 120 min MCAO	Isoflurane 1.5 % for 30 min/day for 5 days Electroacupuncture (EA) under 1.5% isoflurane for 5 days	No treatment	Neurological deficit score and infarct volume 24 h after I/R	Outcomes were similar in isoflurane-treated and control groups. IV and NDS were decreased with EA.	EA effective

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
		Treatment before ischemia.				
Xiong L. Anesth Analg 2003; 96:233	Rats, S-D, adult male, 120 ;min MCAO	Isoflurane (0.75, 1.5 and 2.25%) in oxygen, for 1 hour for 4 days before I/R Treatment before ischemia.	O_2	NDS, IV volume 24 h after I/R	1.5%, 2.25% isoflurane Treatment decreased NDS and IV	Neuroprotection abolished by glibenclamide, a mitoK_{ATP} channel blocker. Dose response relationship
Yang Q. Anesth Analg 2011;112:931	Rats, S-D, adult male, 120 min MCAO	Sevoflurane (1, 2, 4%) in O_2 for 1 hour for 5 consecutive d before I/R. Treatment before ischemia.	O_2	NDS, IV evaluated at 24, 48 and 72 h after I/R	NDS, IV decreased by Treatment with 2,4% sevoflurane	Neuroprotection abolished by antioxidant or free radical scavenger
Yang Q. Anesthesiology 2012;117:996	Mice, C57BL/6; Conditional Notch-RBP-J knockout, adult male, 60 min MCAO	Sevoflurane (2.5%) in oxygen for 1 hour for 5 consecutive days before ischemia reperfusion. Treatment before ischemia.	air, O_2	NDS, IV determined 72 h after I/R	NDS and IV decreased by Treatment with sevoflurane	Treatment activated the Notch signalling pathway. Neuroprotection was attenuated by pathway inhibition and in Notch pathway- deficient mice

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
Yang Z. Mol Med Rep 2014;9:843	Rats, S-D, adult male, high- and low-fat diets, 60 min MCAO	Sevoflurane 2.6% for 15 min at the onset of reperfusion . Treatment during/after ischemia	Chloral hydrate (300 $mg.kg^{-1}$)	NDS, IV 24 h after I/R	Treatment improved outcome in low fat but not high fat diet animals	Obesity associated with an impaired mitoK_{ATP} channel
Ye R. Crit Care Med 2012;40:2685	Rats, S-D, adult male 120 min MCAO	Exposure to 2.3% sevoflurane in oxygen for 1 h, 24 h before ischemia. Treatment before ischemia.	Exposure to O_2 for 1 h, 24 h before ischemia	NDS determined 1,3,7,14,28,42 d post-I/R. IV 3 d post-I/R	Treatment decreased IV and NDS day 7-42	Treatment associated with reduced opening of mPTP
Ye Z. Neurol Sci 2012;33:239	Rats, S-D adult male 60 min MCAO	Exposure to 2.4% sevoflurane in oxygen for 1h, 24 h before ischemia. Treatment before ischemia.	Exposure to oxygen for 1 h, 24 h before ischemia	NDS, IV evaluated 24 and 72 h after I/R	Treatment decreased IV and NDS.	Neuroprotection was attenuated by mitoK_{ATP} channel block.
Ye Z. Mol Biol Rep 2012;39:5049	Rats, S-D adult male 120 min MCAO	Exposure to 2.4% sevoflurane in O_2 for 1h, 24 h before I/R Treatment before ischemia.	Exposure to O_2 for 1 h, 24 h before ischemia	NDS and IV evaluated 6 and 24 h after I/R	Treatment decreased NDS and IV.	Neuroprotection attenuated by mitoK_{ATP} channel block.

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
Ye Z. Brain Res 2012;1463:63	Rats, S-D adult male permanent min MCAO	Sevoflurane 2.5% for 60 min after reperfusion . Treatment during/after ischemia	Chloral hydrate (350 $mg.kg^{-1}$)	IV 24 h after I/R	Treatment decreased IV	Treatment increased brain levels of Akt and HIF-1α
Yu H. Obesity 2014;22:2396	Mice, CD-1, adult male, 90 min MCAO Regular diet and high fat diet animals	Exposure to 1 or 2% isoflurane in O_2 for 30 min at the start of reperfusion. Treatment during/after ischemia	Exposure to O_2 for 30 min at the start of reperfusion	NDS, IV determined 24 h after I/R	Treatment decreased IV and NDS in regular diet but not high-fat diet mice	Impaired Akt signalling in high fat diet animals
Yung LM. Stroke 2012;43:199	Mice, C57BL/J; sphingosine kinase (SPK) knockouts: $SPK1^{-/-}$, $SPK2^{-/-}$ adult males, 90 min MCAO	Exposure to 1% isoflurane/ 30% O_2 for 3 h, 1 day before MCAO Treatment before ischemia.	Exposure to air for 4 hours	NDS, IV determined 24 h after I/R	Treatment decreased NDS and IV in wild-type and $SPK1^{-/-}$ but not $SPK2^{-/-}$ mice	Neuroprotection abolished with a SPK inhibitors. SPK2may be a mediator isoflurane Treatment.
Zhang Y. Molecules 2012;17:341	Rats, Wistar adult male 90 min MCAO	Sevoflurane 0.5, 1.0 or 1.5 MAC / O_2 for 30 min at the onset of reperfusion	Chloral hydrate (350 $mg.kg^{-1}$ i.p.) to all groups. Exposure to	IV 24 h after I/R	IV decreased at all doses of sevoflurane	Treatment dose-dependently decreased serum

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
		Treatment during/after ischemia	O_2 for 30 min at the onset of reperfusion.			levels of TNF-α and IL-1β
Zhao H. Brain Res 2008; 1246:158	Rats, S-D, adult male, 120 min MCAO	Isoflurane 2% in 30% O_2 during ischemia. Treatment during/after ischemia	Ketamine/xylazine, 80/40 $mg.kg^{-1}$i.p.	NDS, IV determined 24 h after I/R	NDS, IV decreased in isoflurane group	
Zhao X-C. Neurochem Res 2013;38:530	Rats, S-D adult male, 120 min MCAO	Propofol 20 mg/kg/hr for 4 hrs beginning at reperfusion, Treatment during/after ischemia	Chloral hydrate (350 $mg.kg^{-1}$ i.p.)	NDS determined at 1, 3, 7d post-I/R; IV at 6h, 1,3 7 d post I/R	Treatment improved NDS and IV at all times	Expression of basic fibroblast growth factor increased by propofol
Zheng Y-Y. Anesth Analg 2008;107:2009	Rats, S-D adult male, 120 min MCAO	Propofol infusion for 15 min before I/R, .Treatment before ischemia.	Chloral hydrate (300 $mg.kg^{-1}$ i.p.) to all groups	NDS, IV determined 24 h after I/R	No difference in IV, NDS	Brain water and AQP overexpression reduced by Treatment
Zheng S. Mol Pharmacol 2004;65:1172	Rats, S-D adult male, permanent MCAO	Isoflurane 2% for 30 min 1 d before I/R. Treatment before ischemia.	Air	NDS measured 6 h, 1,3 and 14 d post-I/R, IV measured 6 h, 1 and 3 d post I/R	Treatment reduced NDS 1d and 3 d after I/R and IV at all times post-I/R	Isoflurane induced an increase of phosphorylated p38 MAPK

First Author, Source	Species, Strain, Sex, Occlusion time	Treatment Group	Control Group	Outcome Measures	Results	Comments
Zhou R. PLoS ONE 2013;8:e82729	Rats, S-D adult male, 120 min MCAO,	Propofol 50 $mg.kg^{-1}.h^{-1}$ for 30 min at onset of reperfusion. Treatment during/after ischemia	Pentobarbital 50 $mg.kg^{-1}$ to all groups	NDS, IV measured 24 h after I/R	Treatment decrease NDS and IV	Decreased microglial activation in propofol group.
Zhu W. Neuroscience 2010;169:758	C57BL/6 mice, adult male, 120 min MCAO	Exposure to 1.0% Isoflurane for 4 h 24 h prior to I/R. Treatment before ischemia.	Oxygen-enriched air	IV 24 h after I/R	Treatment decreased IV.	Protective effect was androgen-dependent. Multiple groups with hormone manipulation.

[i]Abbreviations: AKT, protein kinase B; Bax, Bcl-2-like protein 4; Bcl-2, B-cell lymphoma 2; cJNK, c-Jun-N-terminal kinase; COX, cyclooxygenase; CTMP, carboxy-terminal protein; EEAT3, excitatory amino acid transporter 3; ERK, extracellular signal-related kinases; GSK-3β, glycogen synthase kinase 3-β, HES, hairy and enhancer of split; HIF, hypoxia-inducible factor, Hsp, heat shock protein; H_2O_2, hydrogen peroxide; ICAM, intercellular adhesion molecule; IL, interleukin; MAPK, Mitogen-activated protein kinase; miRNA, micro RNA; MMP, matrix metalloproteinases; mPTP, mitochondrial permeability transition pore; MyD88, myeloid differentiation primary response gene 88; NDRG2, n-myc downstream regulated gene 2; NF, nuclear factor; NICD, Notch intracellular domain; NO, nitric oxide; NOS, nitric oxide synthase; Nrf2, nuclear factor erythroid 2-related factor, NQ01, quinidine oxidoreductase 1; PI3K, phosphatidylinositol 3-kinase; PKC, protein kinase C; Prok2, prokineticin 2; SPK2, sphingosine kinase 2; TIMP, tissue inhibitor of metalloproteinase; TNFα, tumor necrosis factor alpha; TREK, TWIK-related (2-pore domain) K+ channel,

Ubc9, ubiquitin conjugase 9; 3’UTR, three prime untranslated region;VCAM, vascular cell adhesion protein; VEGF, Vascular endothelial growth factor.