# Isoflurane preconditioning enhances repair of damaged striatum in post-stroke adult mice

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## INTRODUCTION

- Neurogenesis in the intact adult brain is found in two germinal areas: the dentate gyrus (DG) and the subventricular zone (SVZ). In the SVZ, situated alongside the lateral ventricles, newborn neurons develop and – under physiologic conditions - track along the rostral migratory tract towards the olfactory bulb and integrate accordingly.
- After cerebral ischemia, neuronal stem cell proliferation is stimulated and some newborn cells appear in damaged brain areas striatum and are believed to play an important role in post-ischemic functional recovery.
- Exposure to isoflurane prior to brain ischemia ("anesthetic preconditioning") was shown to reduce stroke volume and improve functional outcome, which has been attributed to neuroprotective effects of the volatile anesthetic.

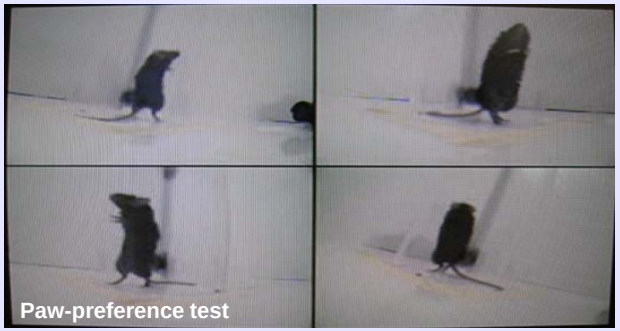
## HYPOTHESIS

- Improved post-stroke outcome following isoflurane preconditioning (IsoPC) is associated with improved repair of damaged neuropil: more newborn neurons and more new dendrites are present in the injured striatum 6 weeks after reversible middle cerebral artery occlusion in adult mice.

## METHODS

- Animals: male C57BL/6 mice
- Mice were exposed to 1 Vol% isoflurane for 4hr (IsoPC) or sham preconditioning (sham PC)
- 24hr after preconditioning, mice underwent 60min of right-sided middle cerebral artery occlusion (MCAO) via the intraluminal filament technique
- Subsequently, animals received intra-peritoneal injections of 5-bromo-2 -deoxyuridine-5 monophosphate(BrdU, 50 mg/kg, twice daily) for 4 days, and were then survived for 6 weeks
- Assessment of motor deficit 6 weeks after MCAO: the mice were placed in a cylinder (height 15 cm; diameter 9 cm) and 4 cameras registered the sequence of the two paw touches per one rearing. A total of 20 rearing were recorded (10min) and *right side* vs. *total* paw touches was calculated

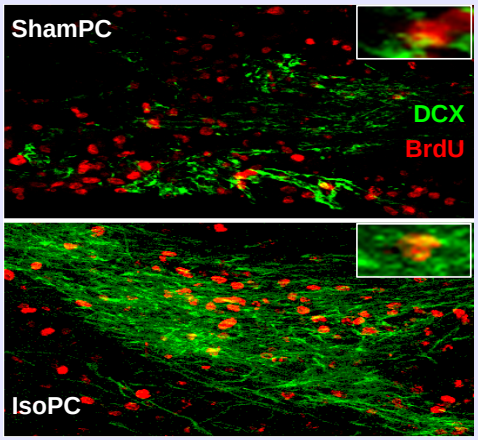
## METHODS (cont'd)




- Assessment of new neurons/dendrides 6 weeks after MCAO: brains were processed (intravital perfusion-fixation, 4% PFA, free-floating 40µm cryosections) and stained for BrdU (proliferating cells) and doublecortin (DCX, stains young newborn neuronal cells). Unbiased stereology was used to quantify DCX positive, double-labeled cells (BrdU/DXC) and DCX positive dendrites in damaged striatum

## RESULTS

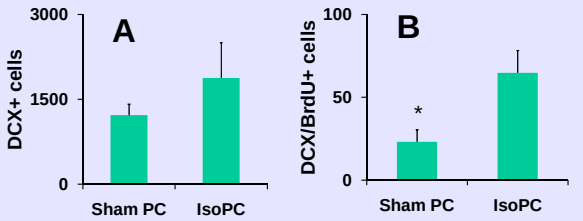
**1. Newborn neuronal cells /dendrites in injured striatum**




**Six weeks after MCAO more new neuronal cells and dendrites are present in damaged striatum following IsoPC vs.ShamPC**

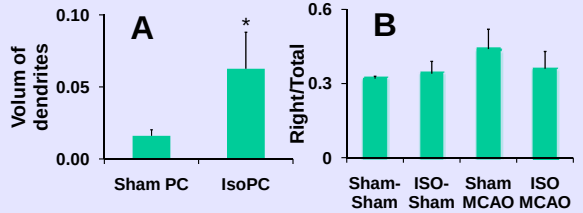
## RESULTS (cont'd)

**2. More new neurons in injured striatum with IsoPC**




**More new young neurons (A, DCX+), and more neurons born in the 4 days after the insult (B, BrdU/DCX+), are present in injured striatum of IsoPC vs. ShamPC mice 6 weeks after MCAO (n=5, each, *p<0.01)**

**3. More new dendrites, and reduced deficit with IsoPC.**




**Volume ($mm^3$) of new dendrites in injured striatum was increased in IsoPC vs. ShamPC mice 6 w after MCAO (A; n=5 each; *p<0.01). *Paw Preference Test* revealed increased right paw preference after ShamPC+MCAO (L sided weakness), while motor performance with IsoPC+MCAO was similar to that in Sham+Sham animals [no insult] (B; n=5 each).**

## CONCLUSIONS

- Anesthetic preconditioning using isoflurane prior to MCAO increases the number of new neurons and dendrites in damaged striatum 6 weeks after the insult, which is paralleled by improved motor performance. Additional experiments are necessary to determine the underlying mechanisms.

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