



Wellman Center
for Photomedicine

Pre-conditioning with low level light therapy: Light before the storm

Michael R Hamblin PhD



Mechanisms of LLLT

Mechanisms of Low Level Light Therapy.

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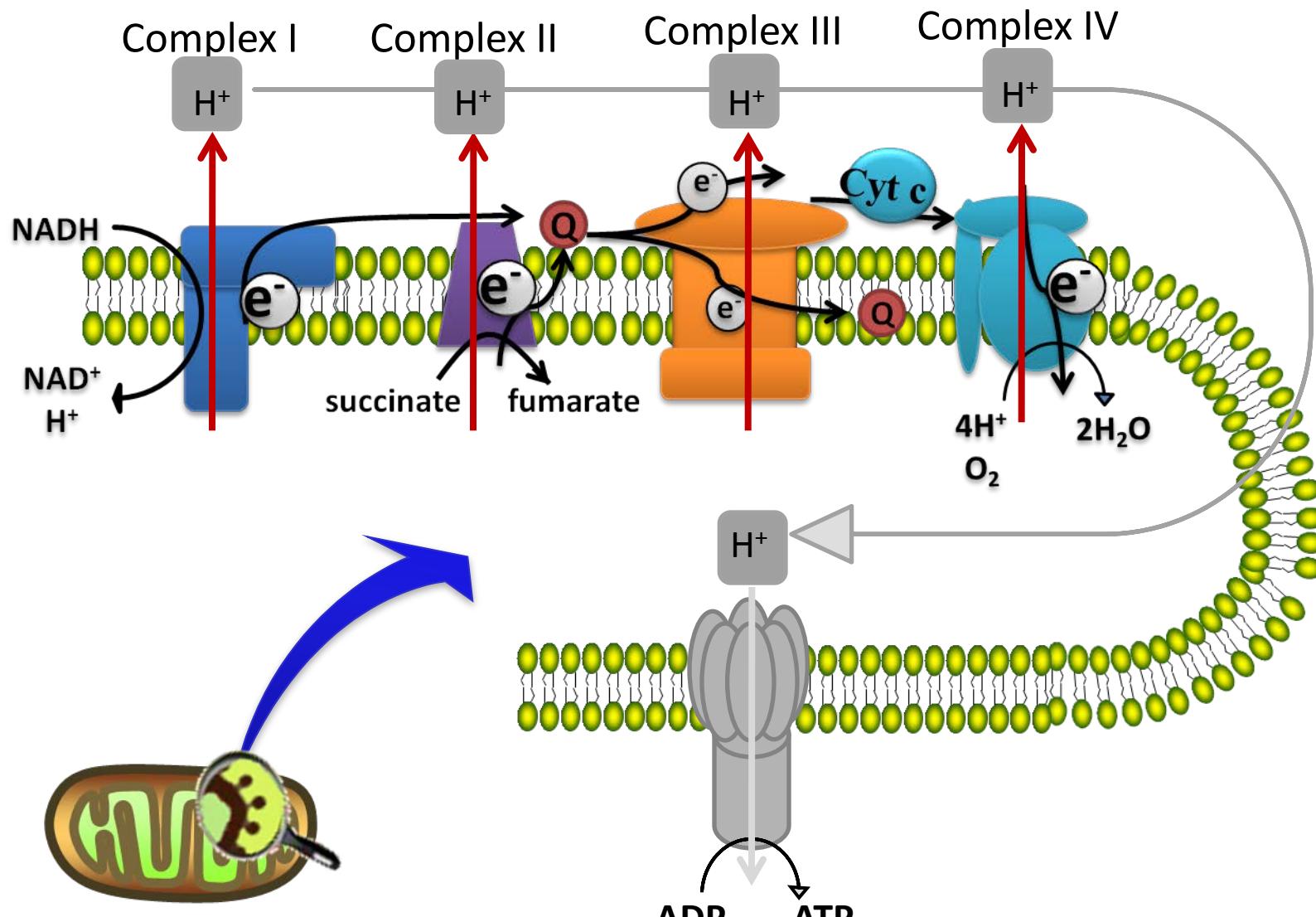
Proc. of SPIE Vol. 6140 614001-1

DOI: 10.1007/s10439-011-0454-7

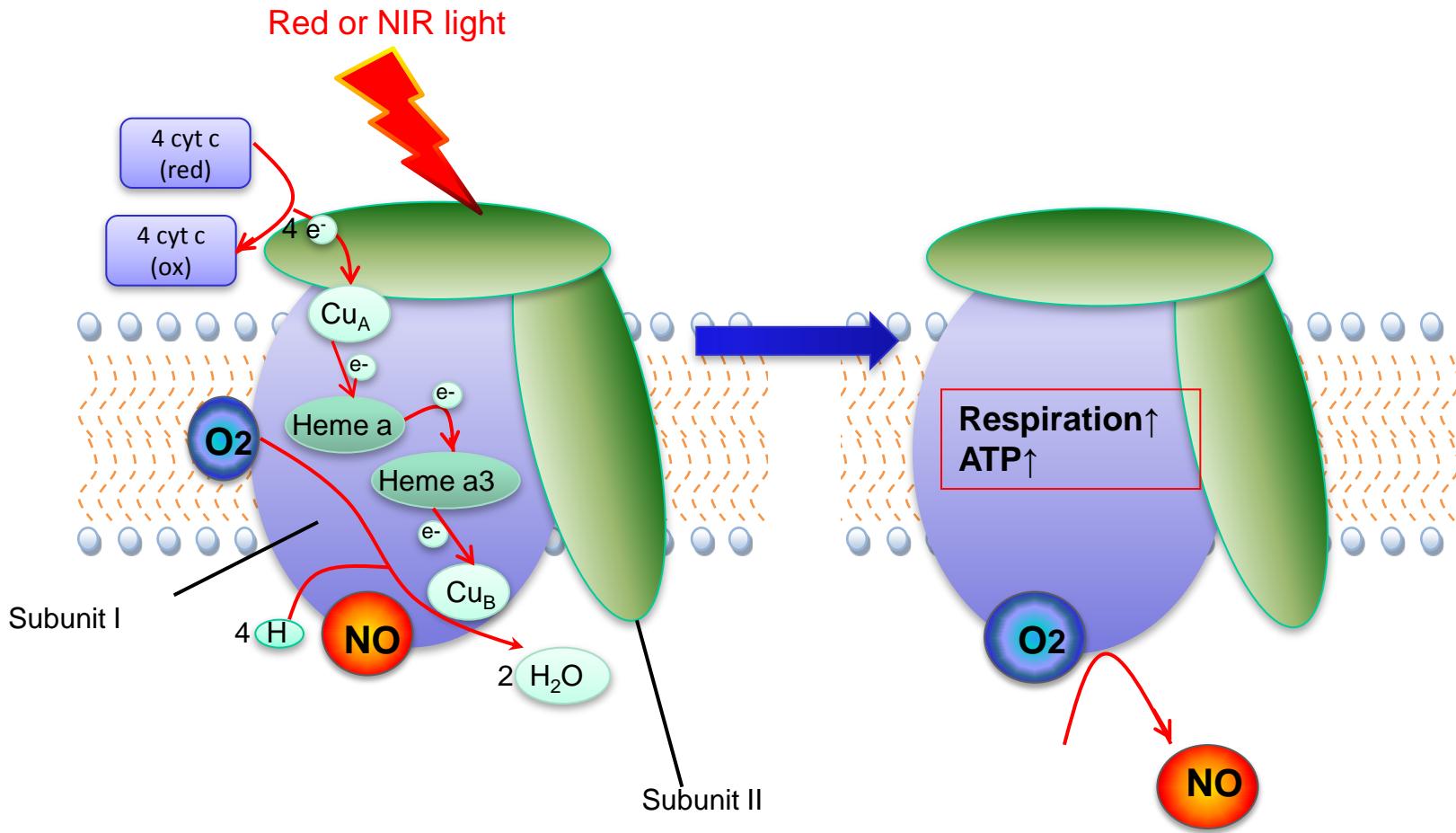
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The Nuts and Bolts of Low-level Laser (Light) Therapy

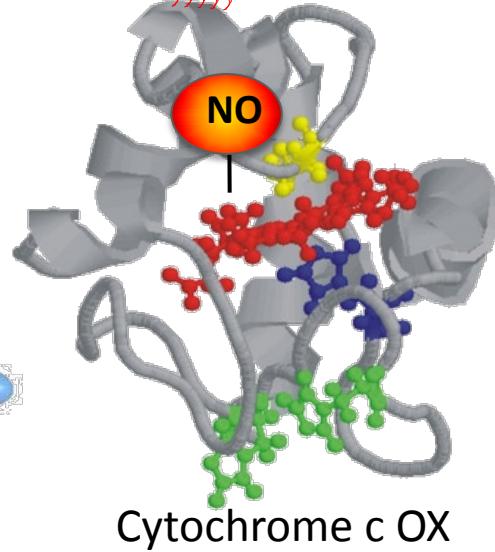
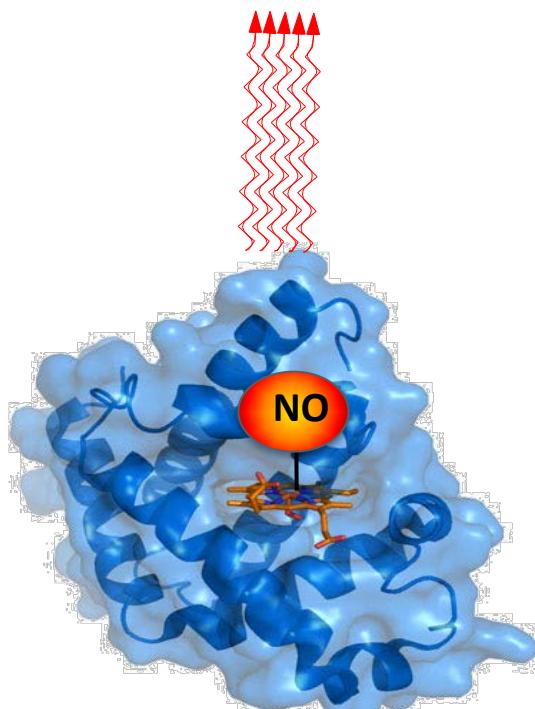
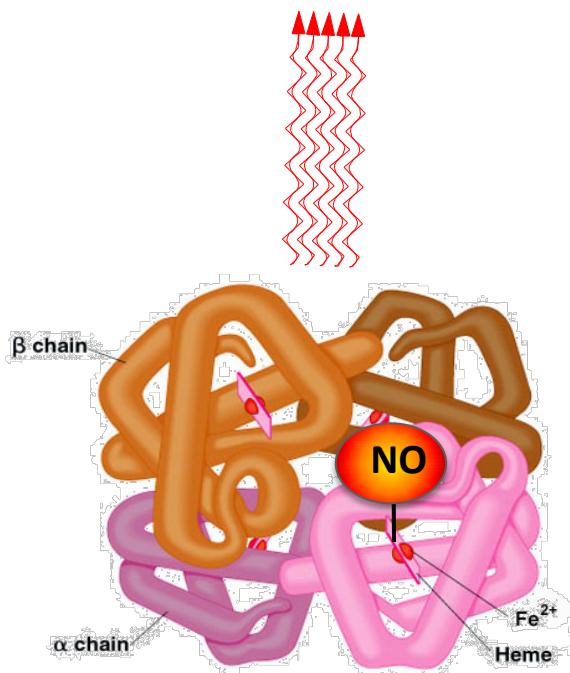
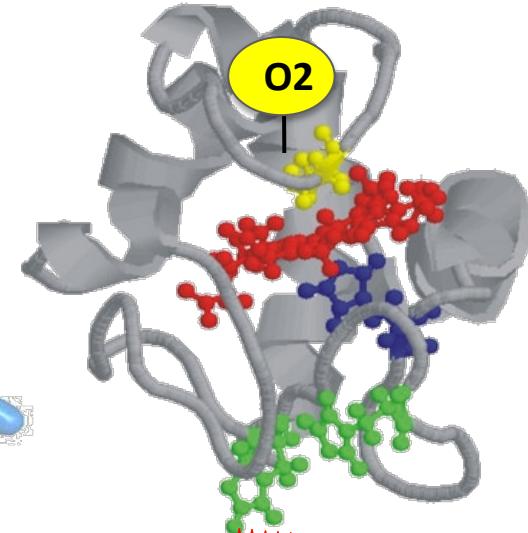
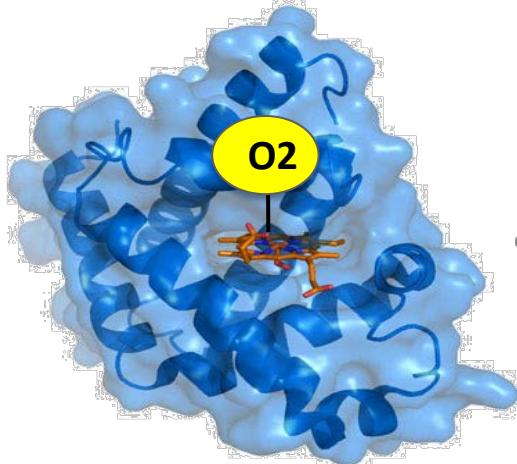
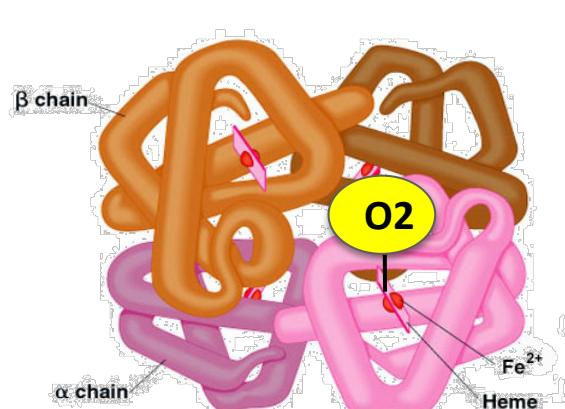
HOON CHUNG,^{1,2} TIANHONG DAI,^{1,2} SULBHA K. SHARMA,¹ YING-YING HUANG,^{1,2,3} JAMES D. CARROLL,⁴ and MICHAEL R. HAMBLIN^{1,2,5}



Mitochondrial
Respiratory chain



Oxygen consumption ↑
 Mitochondrial membrane potential ↑
 ATP ↑ cAMP ↑
 NO released
 Brief burst of ROS
 Calcium modulation



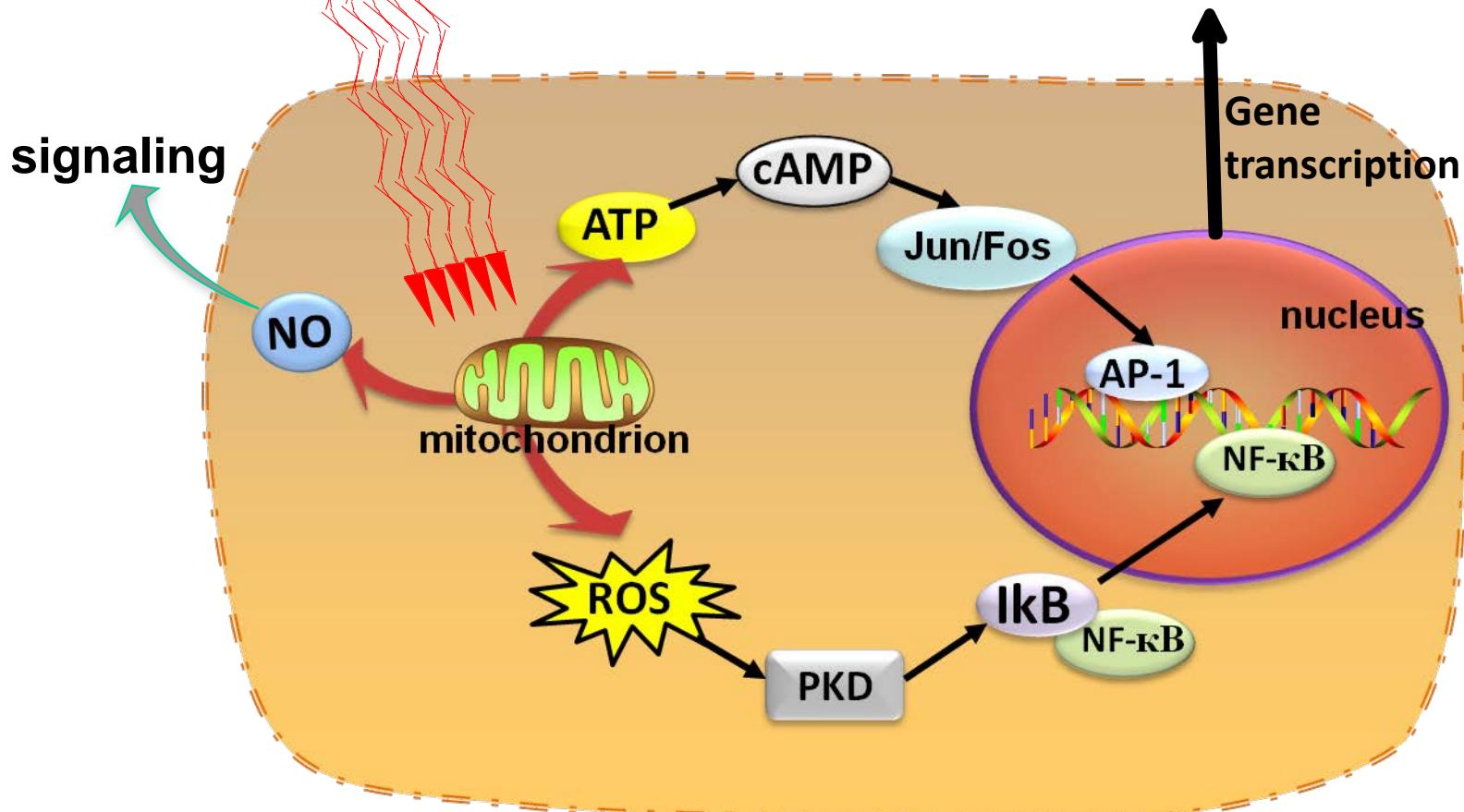
Hemoglobin

Myoglobin

Cytochrome c OX

near infrared light

growth factor production
extracellular matrix deposition
cell proliferation & motility
anti-apoptosis and pro-survival



Main effects of LLLT on tissues

Vasodilation

Lymphatic drainage

Less pro-inflammatory cytokines

More anti-inflammatory cytokines

Less iNOS

More antioxidants

Less oxidative damage

Increased activation of stem/progenitor cells

Which tissues respond to light?

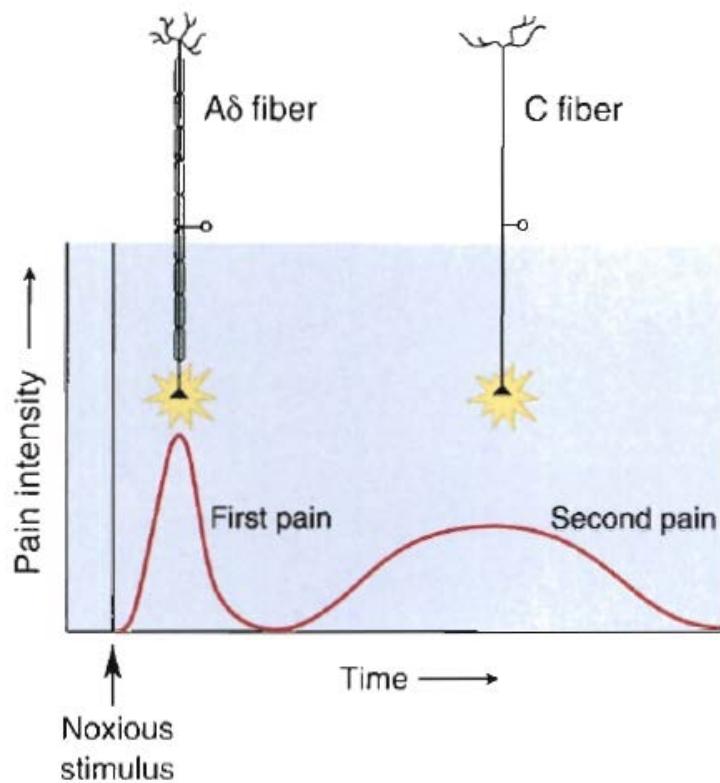
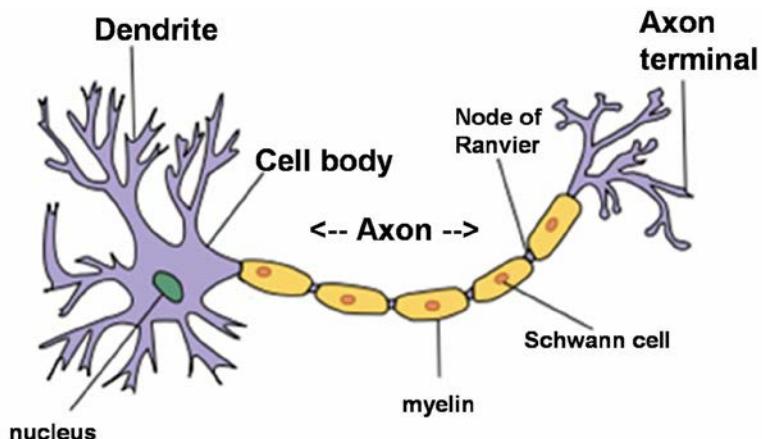
Tissues with high mitochondrial content respond well to light

Muscles, heart

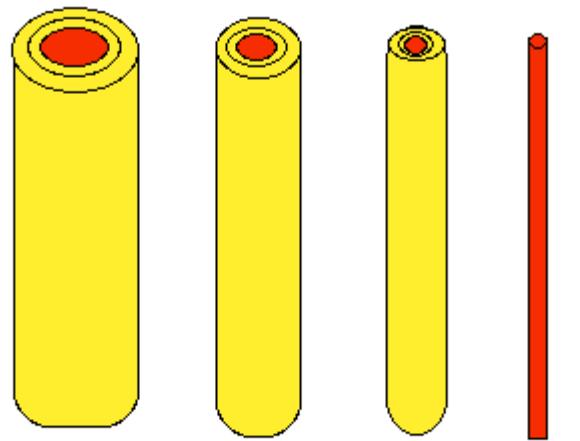
Neurons, brain

Liver, kidney

Neurons

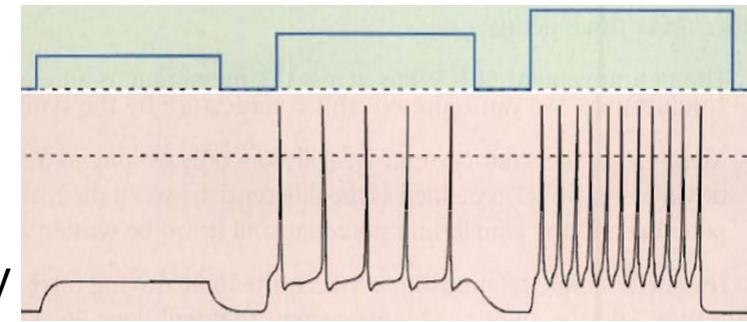
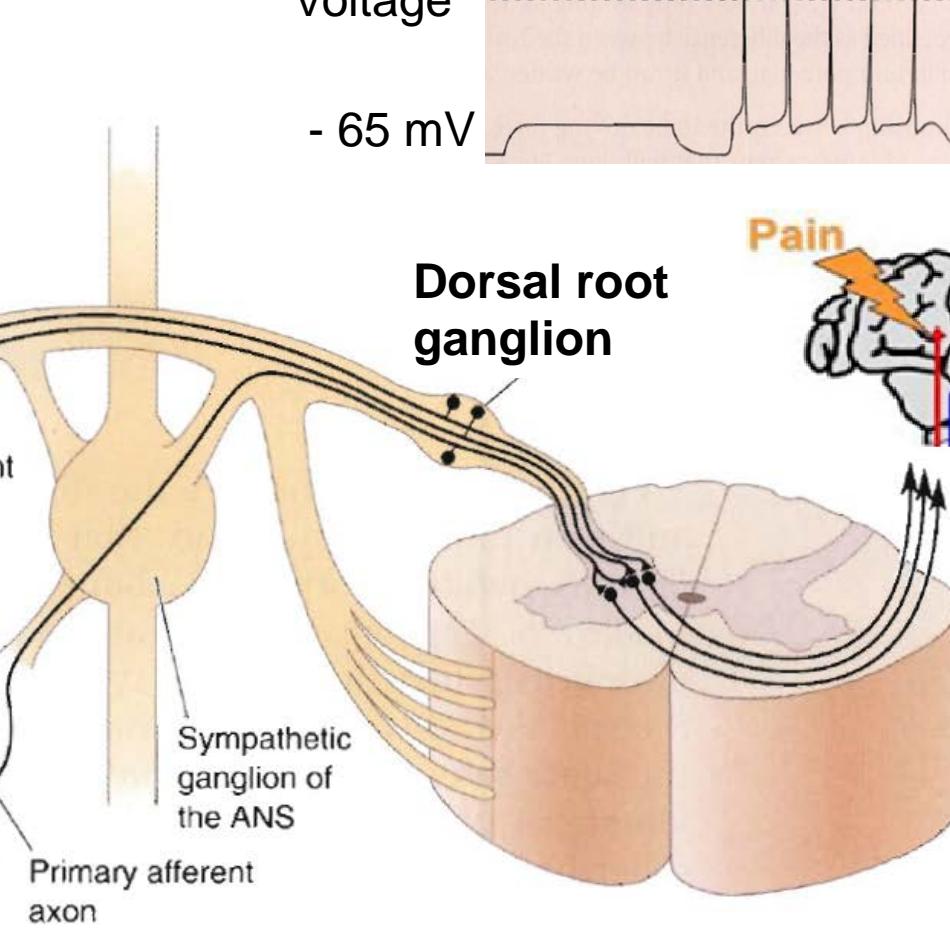
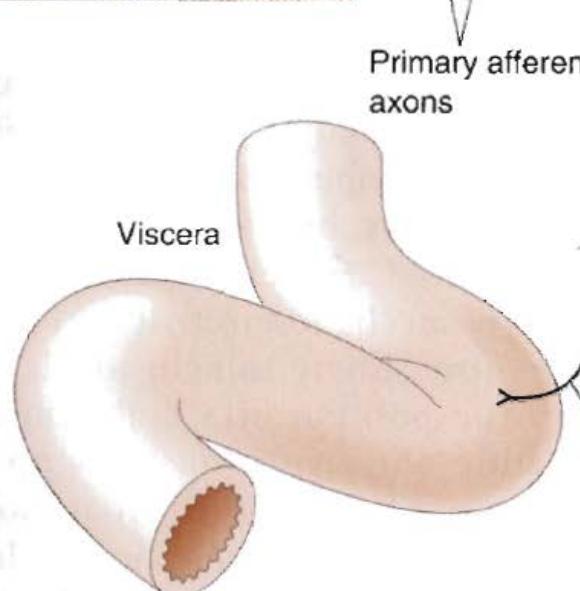
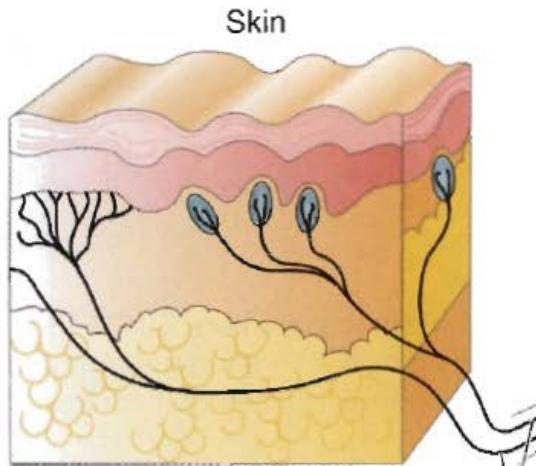


Primary Afferent Axons

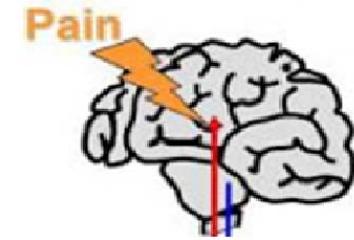


Axon Type	A α	A β	A δ	C
Diameter (μm)	13-20	6-12	1-5	.2-1.5
Speed (m/s)	80-120	35-75	5-35	.5-2.0

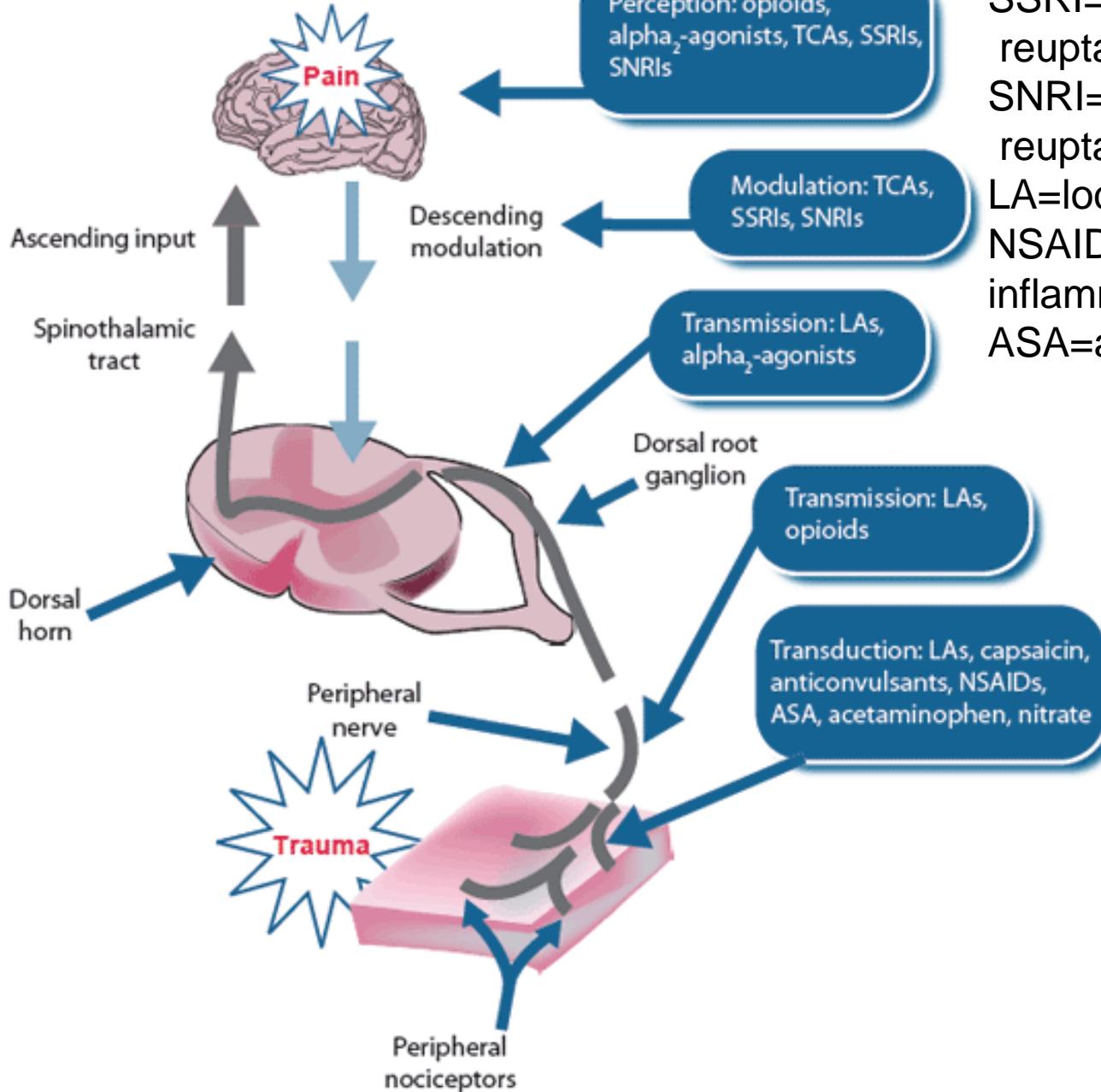
Pain Pathways



Dorsal root ganglion

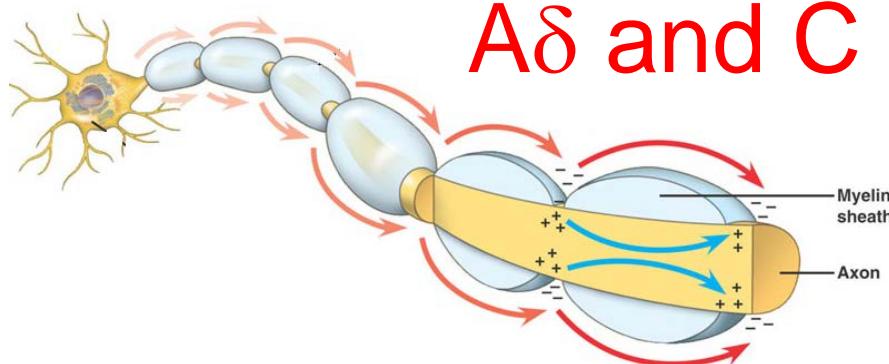


Analgesics



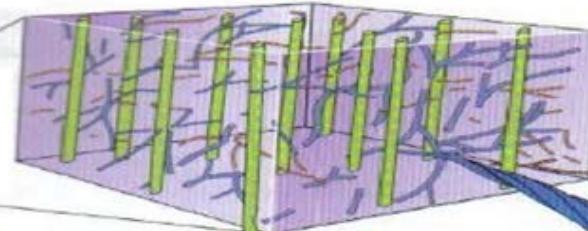
TCA=tricyclic antidepressants
SSRI=selective serotonin reuptake inhibitors
SNRI=serotonin-norepinephrine reuptake inhibitors
LA=local anesthetics
NSAIDS=nonsteroidal anti-inflammatory drugs
ASA=aspirin

Mechanism of analgesic effect



A δ and C

AP frequency



Disarray of
cytoskeleton

Tubulin

20 nm

Microtubule

10 nm

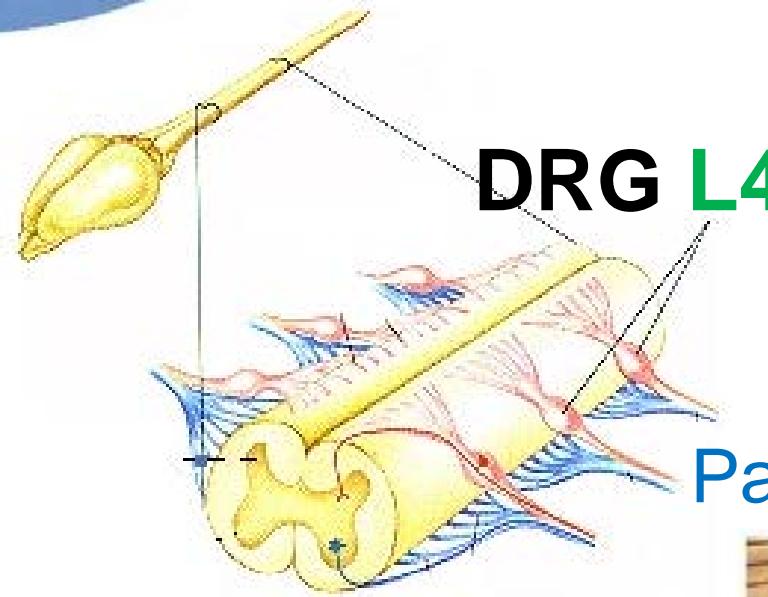
Neurofilament

5 nm

Microfilament



1st Objective



DRG L4 / L5

Pain threshold alteration



Laser irradiation and pain evaluation

$\lambda = 808 \text{ nm}$

$P = 300 \text{ mW}$; $A = 6 \text{ cm}^2$; $PD = 50 \text{ mW/cm}^2$

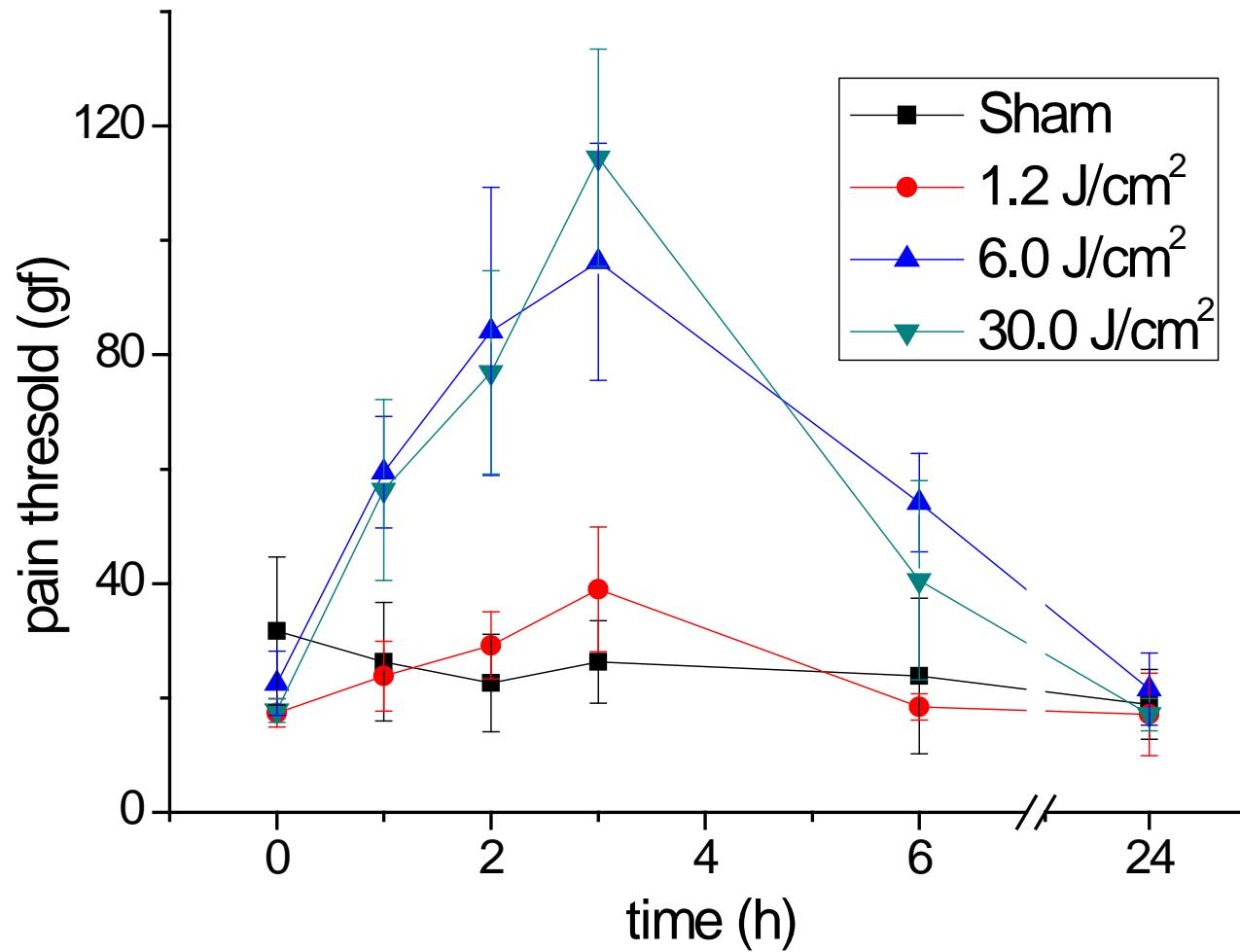
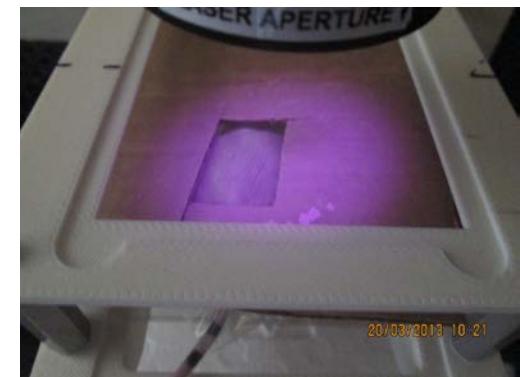


Irradiation time (s)	0	24	120	600
Energy density (J/cm ²)	0	1.2	6.0	30.0

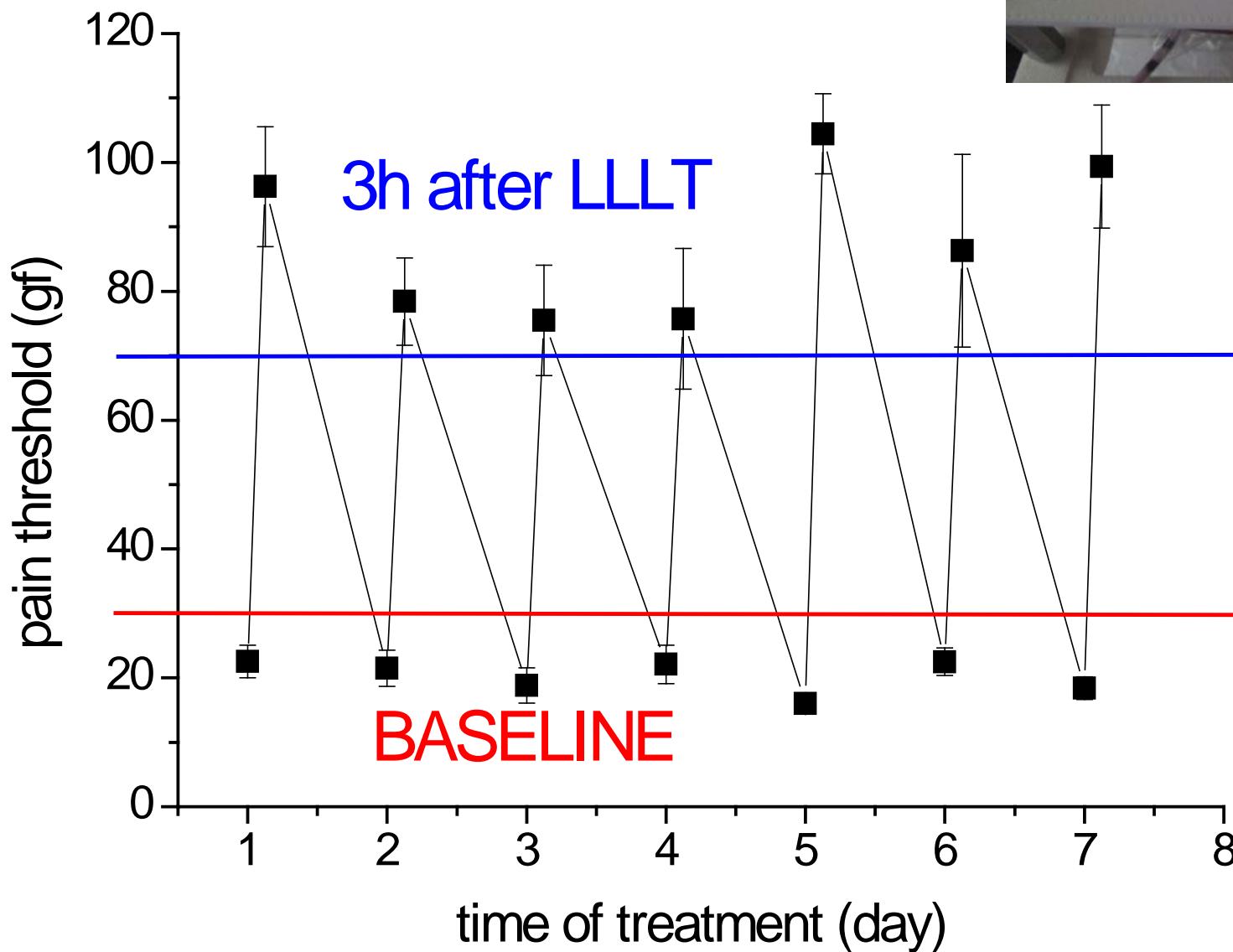
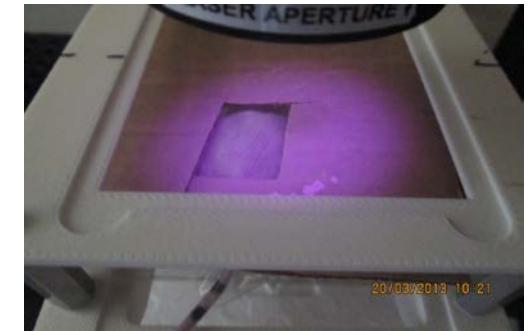




Pain evaluation (24 hours)



1 LLLT/day during 7 days



What markers for analgesia?

- Prostatic acid phosphatase (PAP)
- Tubulin & cytoskeleton
- Glutamate receptor

PAP

- 1: Chen L, Zhu L, Wang K, Wang W, Mei XP, Liu T, Zhang FX, Wang W, Chen T, Li YQ. Antinociceptive effect of prostatic acid phosphatase in a rat model of cancer-induced bone pain. *Pain Physician*. 2013 Nov-Dec;16(6):533-46
- 2: Hurt JK, Coleman JL, Fitzpatrick BJ, Taylor-Blake B, Bridges AS, Vihko P, Zylka MJ. Prostatic acid phosphatase is required for the antinociceptive effects of thiamine and benfotiamine. *PLoS One*. 2012;7(10):e48562. doi: 10.1371/journal.pone.0048562. Epub 2012 Oct 31
- 3: Hurt JK, Zylka MJ. PAPupuncture has localized and long-lasting antinociceptive effects in mouse models of acute and chronic pain. *Mol Pain*. 2012 Apr 23;8:28.doi: 10.1186/1744-8069-8-28.
- 4: Hurt JK, Fitzpatrick BJ, Norris-Drouin J, Zylka MJ. Secretion and N-linked glycosylation are required for prostatic acid phosphatase catalytic and antinociceptive activity. *PLoS One*. 2012;7(2):e32741. doi:10.1371/journal.pone.0032741. Epub 2012 Feb 28.
- 5: Sowa NA, Street SE, Vihko P, Zylka MJ. Prostatic acid phosphatase reduces thermal sensitivity and chronic pain sensitization by depleting phosphatidylinositol 4,5-bisphosphate. *J Neurosci*. 2010 Aug 4;30(31):10282-93.doi: 10.1523/JNEUROSCI.2162-10.2010.
- 6: Zylka MJ, Sowa NA, Taylor-Blake B, Twomey MA, Herrala A, Voikar V, Vihko P. Prostatic acid phosphatase is an ectonucleotidase and suppresses pain by generating adenosine. *Neuron*. 2008 Oct 9;60(1):111-22. doi: 10.1016/j.neuron.2008.08.024.

Tubulin & cytoskeleton

- 1: Culley DJ, Cotran EK, Karlsson E, Palanisamy A, Boyd JD, Xie Z, Crosby G. Isoflurane affects the cytoskeleton but not survival, proliferation, or synaptogenic properties of rat astrocytes in vitro. *Br J Anaesth.* 2013 Jun;110 Suppl 1:i19-28. doi: 10.1093/bja/aet169.
- 2: Wei H, Zhang Y, Fan ZZ, Ge HY, Arendt-Nielsen L, Jiang H, Yao W, Yue SW. Effects of colchicine-induced microtubule depolymerization on TRPV4 in rats with chronic compression of the dorsal root ganglion. *Neurosci Lett.* 2013 Feb 8;534:344-50. doi: 10.1016/j.neulet.2012.12.003. Epub 2012 Dec 20
- 3: Storti B, Bizzarri R, Cardarelli F, Beltram F. Intact microtubules preserve transient receptor potential vanilloid 1 (TRPV1) functionality through receptor binding. *J Biol Chem.* 2012 Mar 2;287(10):7803-11. doi: 10.1074/jbc.M111.332296. Epub 2012 Jan 17.
- 4: Goswami C, Goswami L. Filamentous microtubules in the neuronal spinous process and the role of microtubule regulatory drugs in neuropathic pain. *Neurochem Int.* 2010 Nov;57(5):497-503. doi: 10.1016/j.neuint.2010.06.022
- 5: Lee JJ, Swain SM. Peripheral neuropathy induced by microtubule-stabilizing agents. *J Clin Oncol.* 2006 Apr 1;24(10):1633-42. Review. PubMed PMID: 16575015.
- 6: Liu YH, Ho CC, Cheng CC, Hsu YH, Lai YS. Photoradiation could influence the cytoskeleton organization and inhibit the survival of human hepatoma cells in vitro. *Lasers Med Sci.* 2006 Apr;21(1):42-8. Epub 2006 Mar 29. PubMed.
- 7: Goswami C, Dreger M, Otto H, Schwappach B, Hucho F. Rapid disassembly of dynamic microtubules upon activation of the capsaicin receptor TRPV1. *J Neurochem.* 2006 Jan;96(1):254-66. Epub 2005 Dec 5.
- 8: Goswami C, Dreger M, Jahnel R, Bogen O, Gillen C, Hucho F. Identification and characterization of a Ca²⁺ -sensitive interaction of the vanilloid receptor TRPV1 with tubulin. *J Neurochem.* 2004 Dec;91(5):1092-103. PubMed PMID: 15569253.

Glutamate receptor

1. Bardoni R. Role of presynaptic glutamate receptors in pain transmission at the spinal cord level. *Curr Neuropharmacol.* 2013 Sep;11(5):477-83. doi: 10.2174/1570159X11311050002
2. Zugaib J, Coutinho MR, Ferreira MD, Menescal-de-Oliveira L. Glutamate/GABA balance in ACC modulates the nociceptive responses of vocalization: An expression of affective-motivational component of pain in guinea pigs. *Physiol Behav.* 2013 Dec 29;126C:8-14. doi: 10.1016/j.physbeh.2013.12.004. [Epub ahead of print]
3. de Andrade DC, Mhalla A, Adam F, Texeira MJ, Bouhassira D. Repetitive transcranial magnetic stimulation induced analgesia depends on N-methyl-d-aspartate glutamate receptors. *Pain.* 2013 Dec 14. pii:S0304-3959(13)00670-2. doi: 10.1016/j.pain.2013.12.022. [Epub ahead of print]
4. Walker AK, Kavelaars A, Heijnen CJ, Dantzer R. Neuroinflammation and comorbidity of pain and depression. *Pharmacol Rev.* 2013 Dec 11;66(1):80-101. doi: 10.1124/pr.113.008144. Print 2014 Jan;
5. Chen NF, Huang SY, Chen WF, Chen CH, Lu CH, Chen CL, Yang SN, Wang HM, Wen ZH. TGF- β 1 attenuates spinal neuroinflammation and the excitatory amino acid system in rats with neuropathic pain. *J Pain.* 2013 Dec;14(12):1671-85. doi: 10.1016/j.jpain.2013.08.010.
6. Vilar B, Busserolles J, Ling B, Laffray S, Ulmann L, Malhaire F, Chapuy E, Aissouni Y, Etienne M, Bourinet E, Acher F, Pin JP, Eschalier A, Goudet C. Alleviating pain hypersensitivity through activation of type 4 metabotropic glutamate receptor. *J Neurosci.* 2013 Nov 27;33(48):18951-65. doi: 10.1523/JNEUROSCI.1221-13.2013. PubMed PMID: 24285900.
7. Youn DH, Gerber G, Sather WA. Ionotropic glutamate receptors and voltage-gated Ca- $\leq\sqrt{\text{Å}}$ channels in long-term potentiation of spinal dorsal horn synapses and pain hypersensitivity. *Neural Plast.* 2013;2013:654257. doi: 10.1155/2013/654257. Epub 2013 Oct 2. Review.
8. Hung KL, Wang SJ, Wang YC, Chiang TR, Wang CC. Upregulation of presynaptic proteins and protein kinases associated with enhanced glutamate release from axonal terminals (synaptosomes) of the medial prefrontal cortex in rats with neuropathic pain. *Pain.* 2014 Feb;155(2):377-87. doi: 10.1016/j.pain.2013.10.026. Epub 2013 Nov 8
9. Bonnet CS, Williams AS, Gilbert SJ, Harvey AK, Evans BA, Mason DJ. AMPA/kainate glutamate receptors contribute to inflammation, degeneration and pain related behaviour in inflammatory stages of arthritis. *Ann Rheum Dis.* 2013 Oct 15. doi: 10.1136/annrheumdis-2013-203670. [Epub ahead of print]

Immunofluorescence

Ganglion
extracted 3h
after LLLT

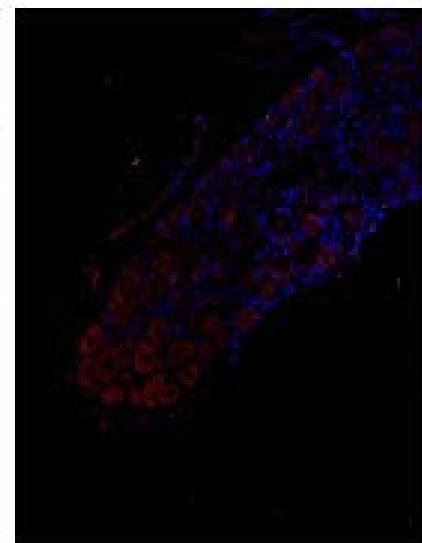
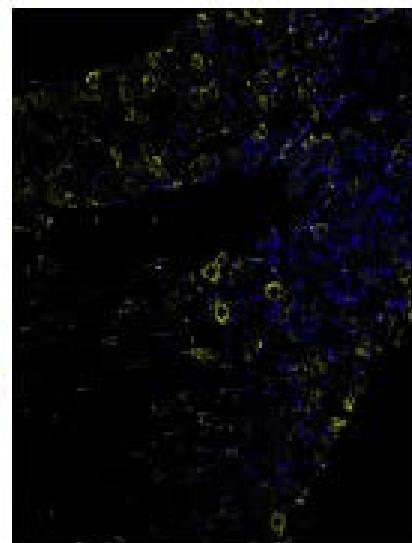
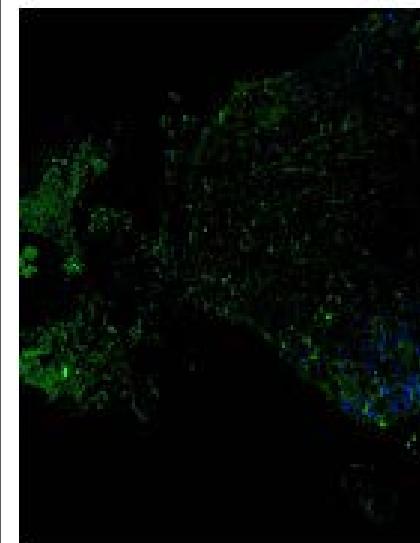
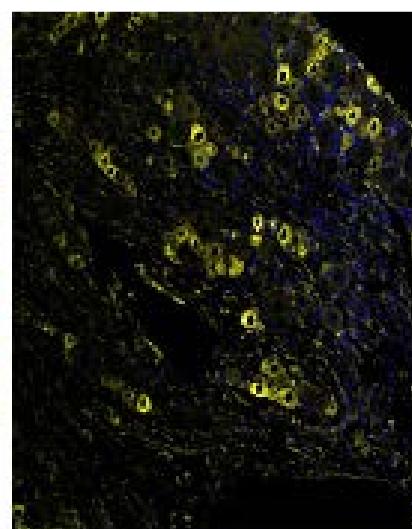
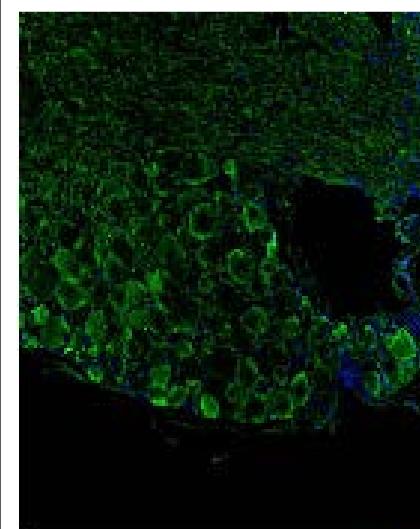
2 min LLLT

Sham

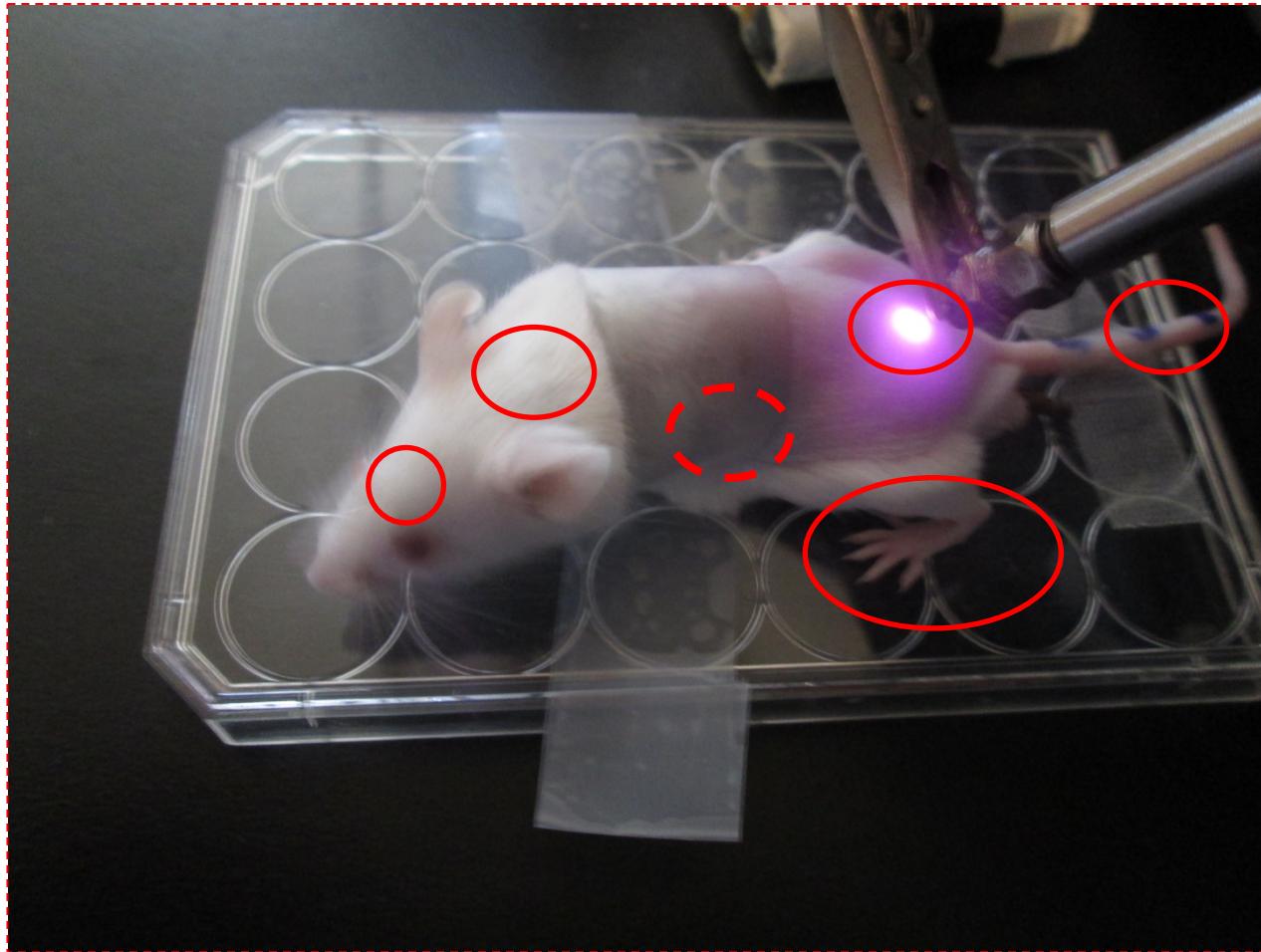
Tubulin

PAP

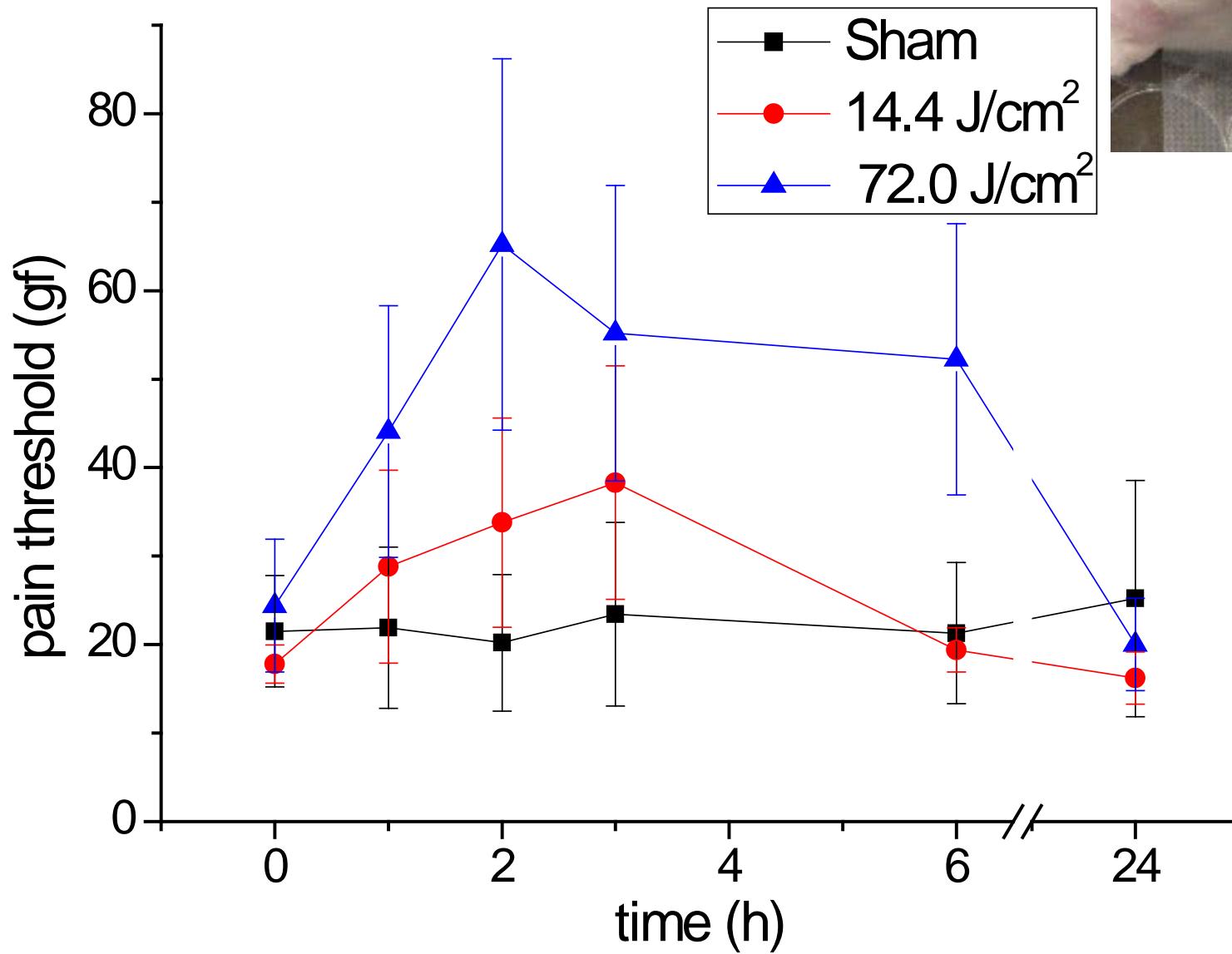
Glutamate



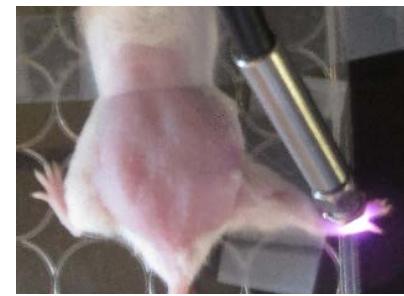
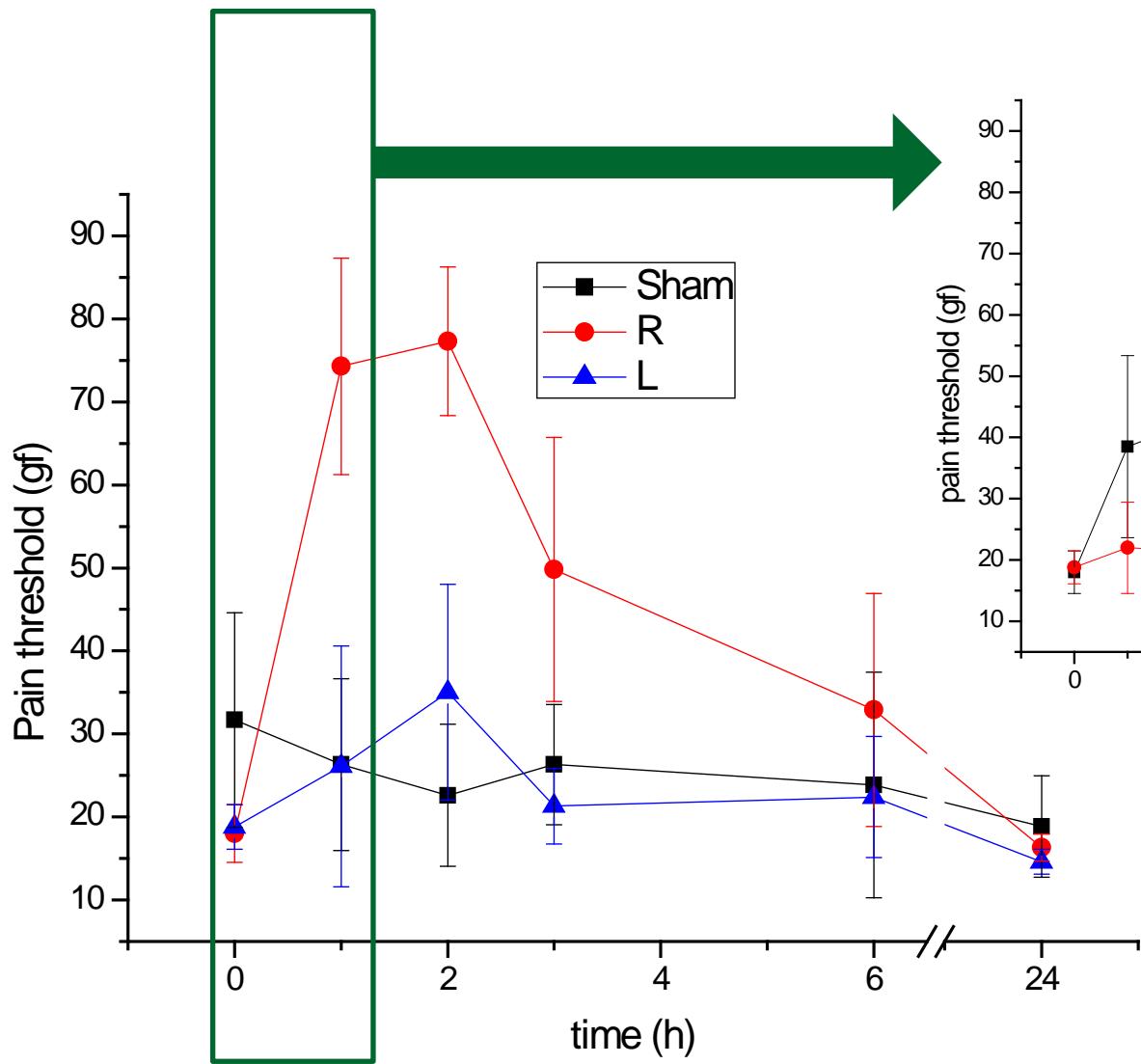
Searching for new points of LLLT



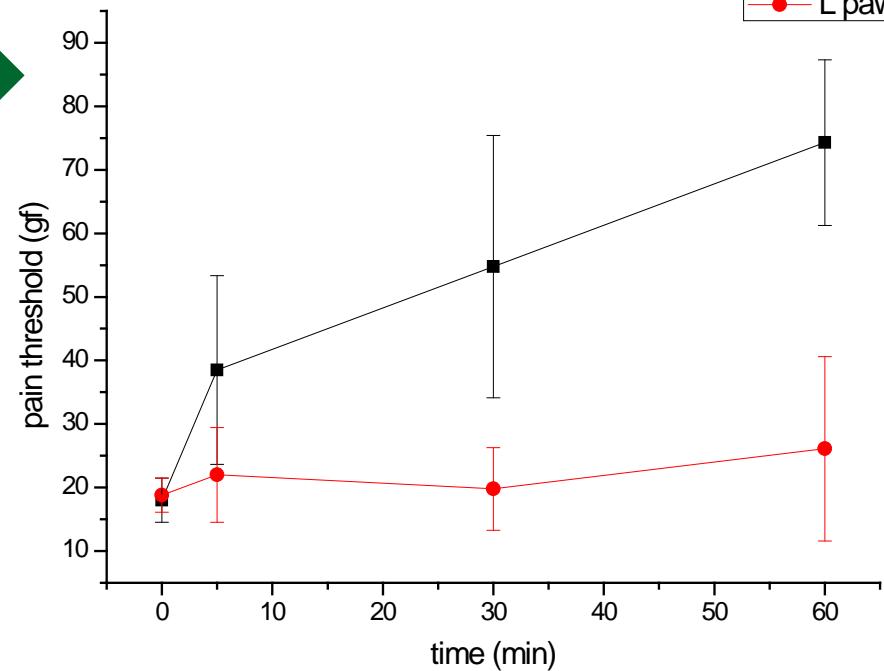
Transcranial LLLT for pain



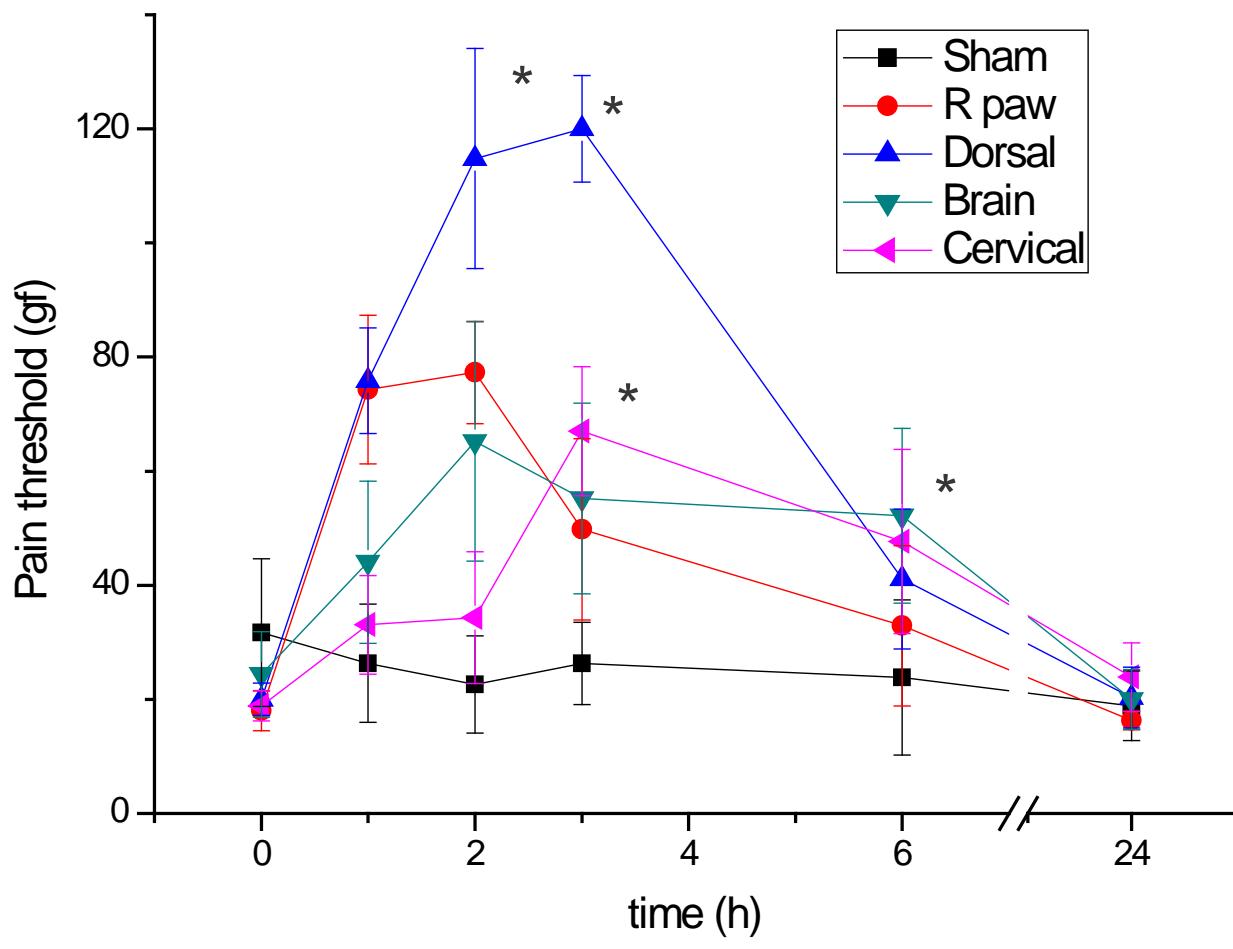
LLLT on the right (R) paw



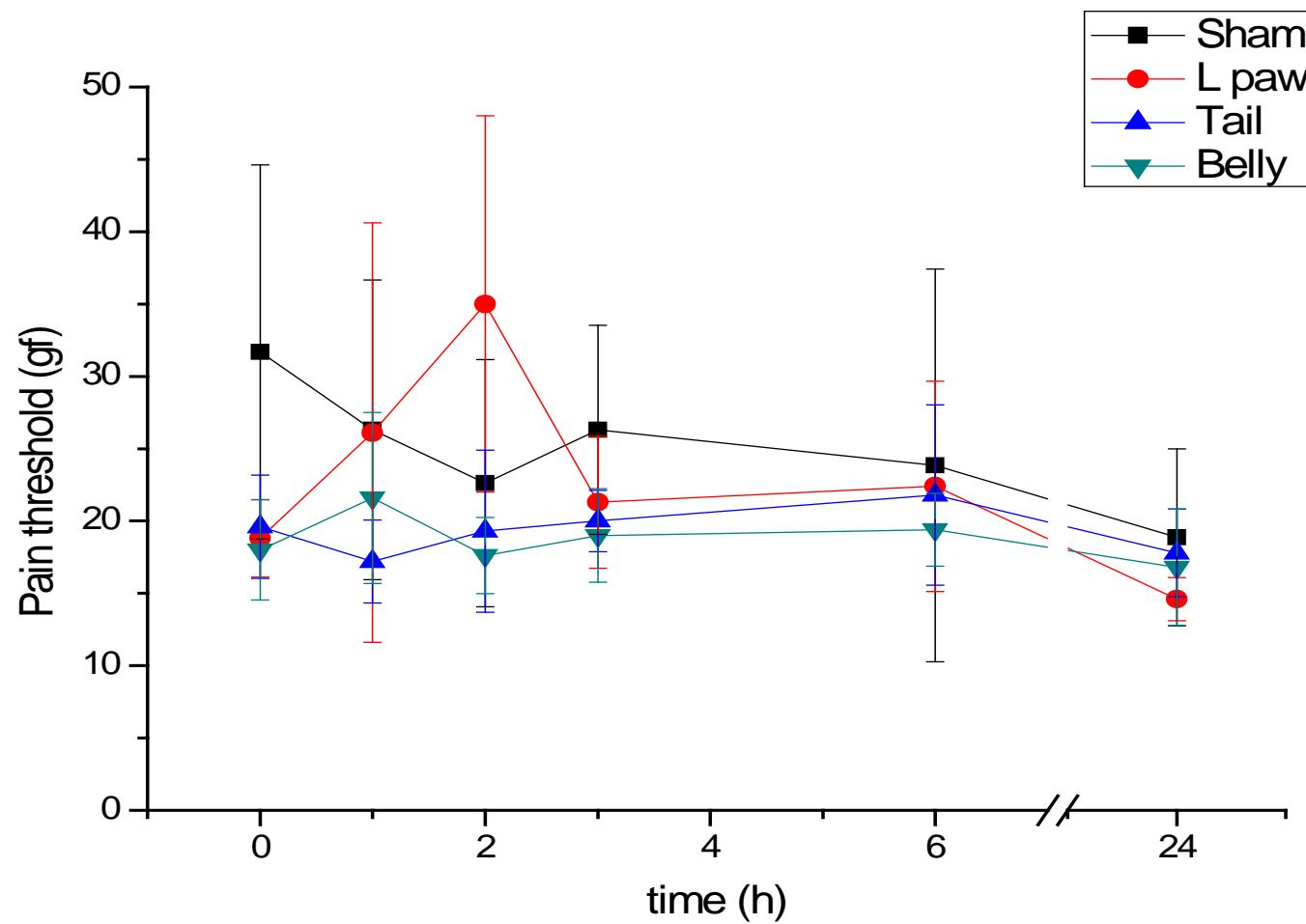
■ R paw
● L paw



Pain evaluation in several points



Pain evaluation in several points



$p > 0.05$ compared
Sham group

Comparison with acupuncture

Progress in Neurobiology 85 (2008) 355–375



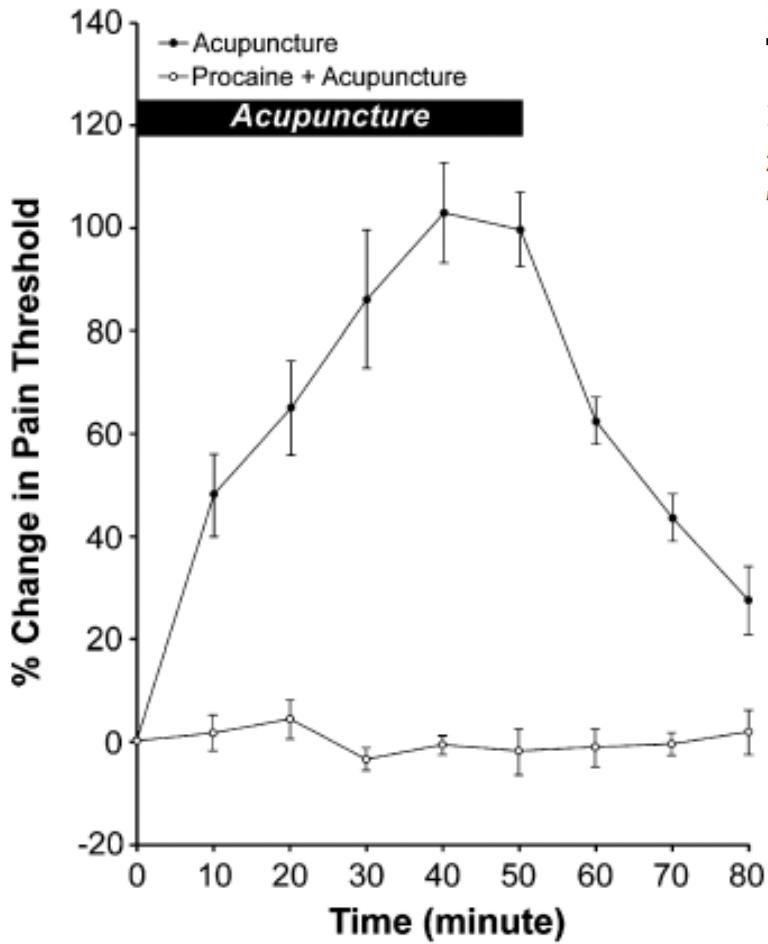
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Progress in Neurobiology



journal homepage: www.elsevier.com/locate/pneurobio



Neural mechanism underlying acupuncture analgesia

Zhi-Qi Zhao *

Institute of Neurobiology, Institutes of Brain Science and State Key Laboratory of Medical Neurobiology, Fudan University, Shanghai 200032, China

Therapeutic approaches for stroke/TBI

Antioxidants

Ebselen
NXY-059 a nitrone spin-trap agent
Tirilazad
Edaravone
Iron chelator
Traditional Chinese medicine

Anti-inflammatory

Anti-neutrophil adhesion molecule
Nitric oxide signal transduction
down-regulator:lubeluzole
Corticosteroid
Interleukin-1 receptor antagonist

Circulation

Volume expansion
Flow enhancer
Vasodilator
Hemodilution
Blood pressure-related strategy

Neurochemical

Serotonin antagonist
Serotonin receptor agonist
Serotonin uptake inhibitor

STROKE
TBI

Oxygen

Hyperbaric oxygen
Oxygenated fluorocarbon
Oxygen supplementation

Metabolism

Ganglioside, Astrocyte modulator
Beta blocker,CNS stimulant
Phosphatidylcholine precursor
Fibroblast growth factor
Opioid antagonist
Prostanoid, Statin

Excitotoxicity

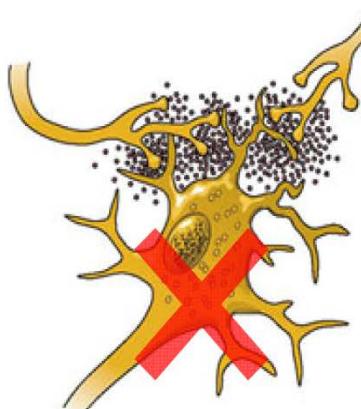
Potassium channel opener
Sodium channel blocker
Calcium chelator
Magnesium
GABA agonist
Glutamate/AMPA antagonist
NMDA receptor/polyamine blocker

Physical intervention

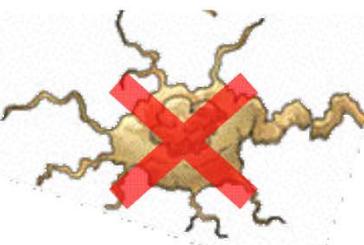
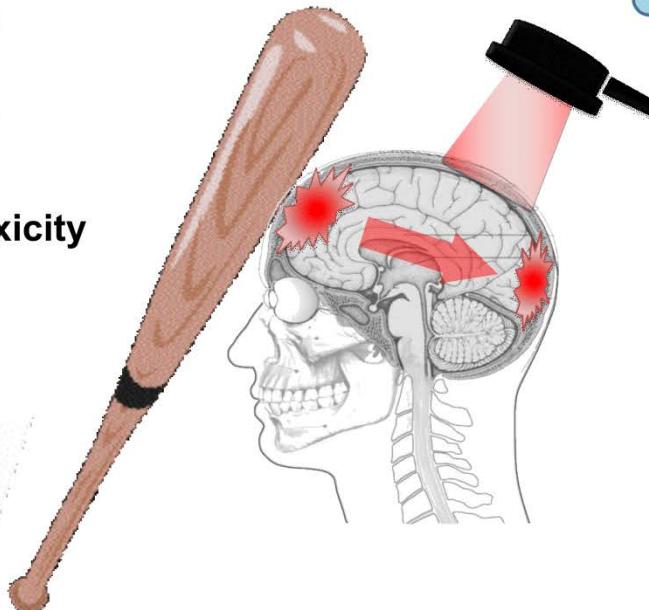
Hypothermia (brain cooling)
Hemicraniectomy
Osmotic agent

Clinical trials of pharmacological and physical therapies for stroke/TBI

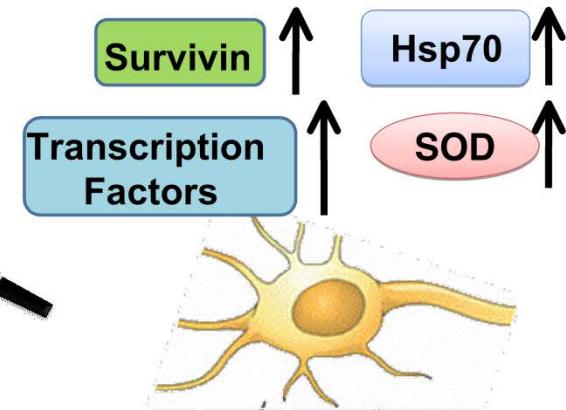
Transcranial Laser may improve TBI



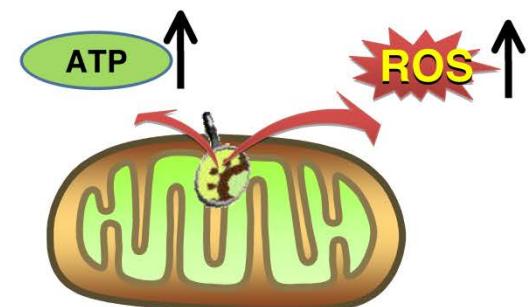
Neuron excitotoxicity



Neuron apoptosis



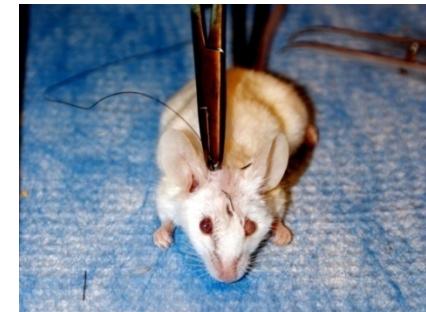
Neuron prosurvival



Mitochondrial function

Transcranial LLLT for TBI in mouse model (IACUC approved)

closed head weight drop method based on Marmarou (1994)



Michael R Hamblin PhD

WALT 2010 Bergen
Norway

Neurological performance testing

Neurological Severity Score(NSS) for Brain-Injured Mice	
Presence of mono- or hemiparesis	1
Inability to walk on a 3-cm-wide beam	1
Inability to walk on a 2-cm-wide beam	1
Inability to walk on a 1-cm-wide beam	1
Inability to balance on a 1-cm-wide beam	1
Inability to balance on a round stick (0.5 cm wide)	1
Failure to exit a 30-cm-diameter circle (for 2 min)	1
Inability to walk straight	1
Loss of startle behavior	1
Loss of seeking behavior	1
Maximum total	10

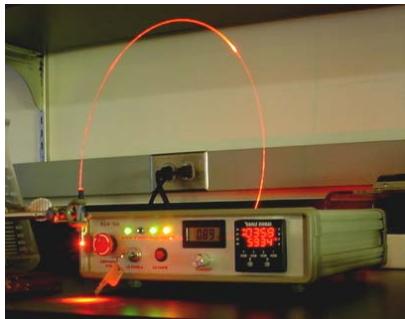
One point is awarded for failure to perform a task.



Michael R Hamblin PhD

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Four different wavelength lasers



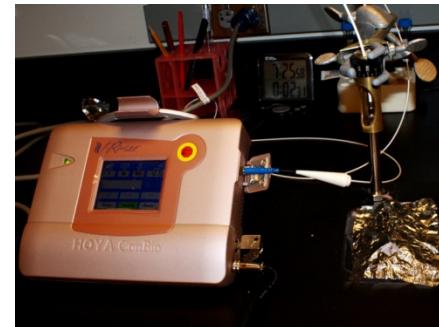
665-nm laser



732nm Laser



810-nm laser



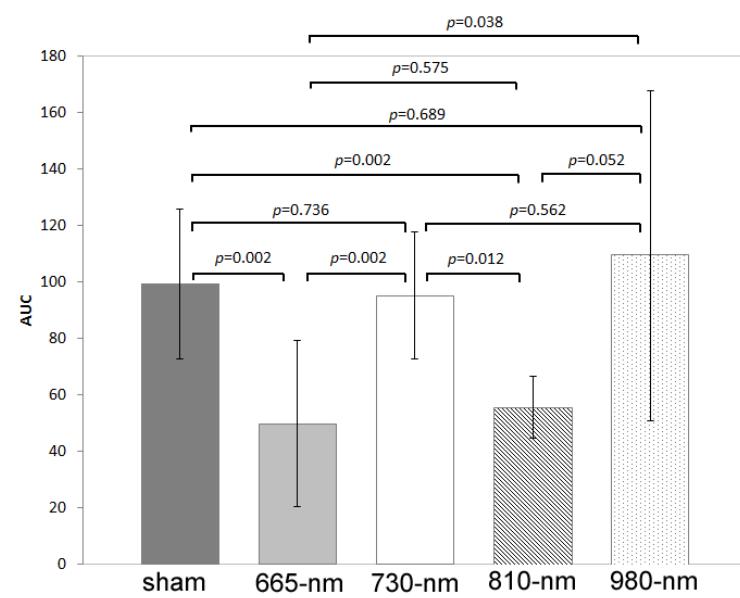
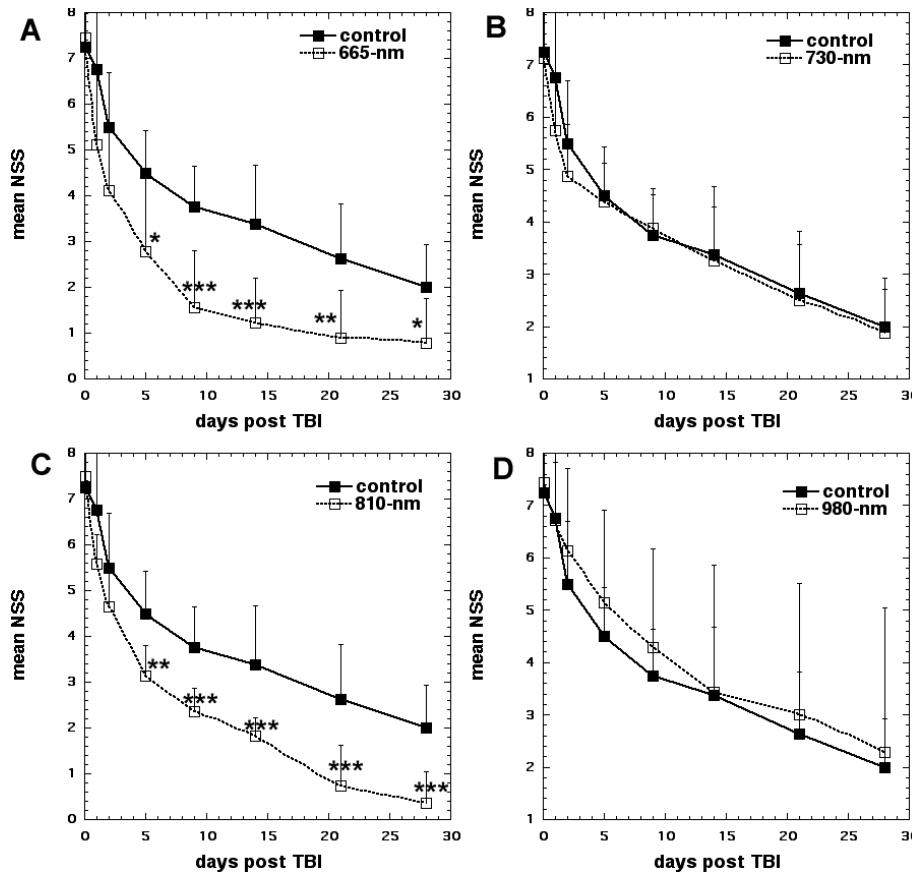
980-nm laser

Michael R Hamblin PhD

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Norway

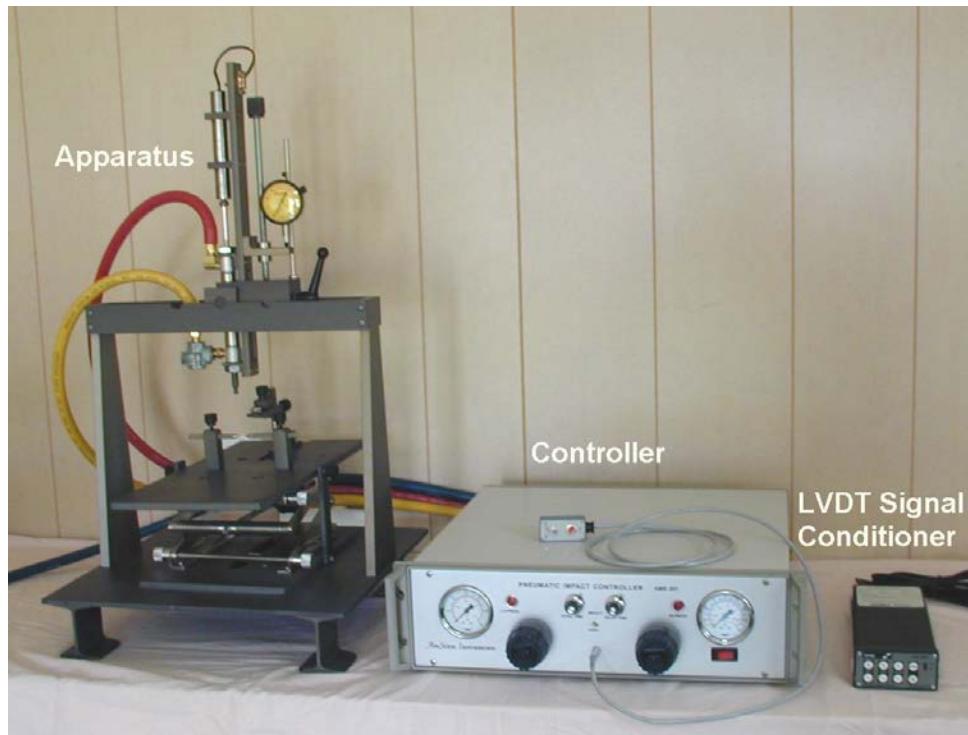
Low-Level Laser Therapy for Closed-Head Traumatic Brain Injury in Mice: Effect of Different Wavelengths

Qiuhe Wu, MD, PhD,^{1,2,3} Weijun Xuan, MD, PhD,^{1,2,4} Takahiro Ando, MS,^{1,5} Tao Xu, MD, PhD,^{1,2,6} Liyi Huang, MD, PhD,^{1,2,7} Ying-Ying Huang, MD,^{1,2,8} Tianghong Dai, PhD,^{1,2} Saphala Dhital, PhD,^{1,9} Sulbha K. Sharma, PhD,¹ Michael J. Whalen, MD,¹⁰ and Michael R. Hamblin, PhD^{1,2,11*}

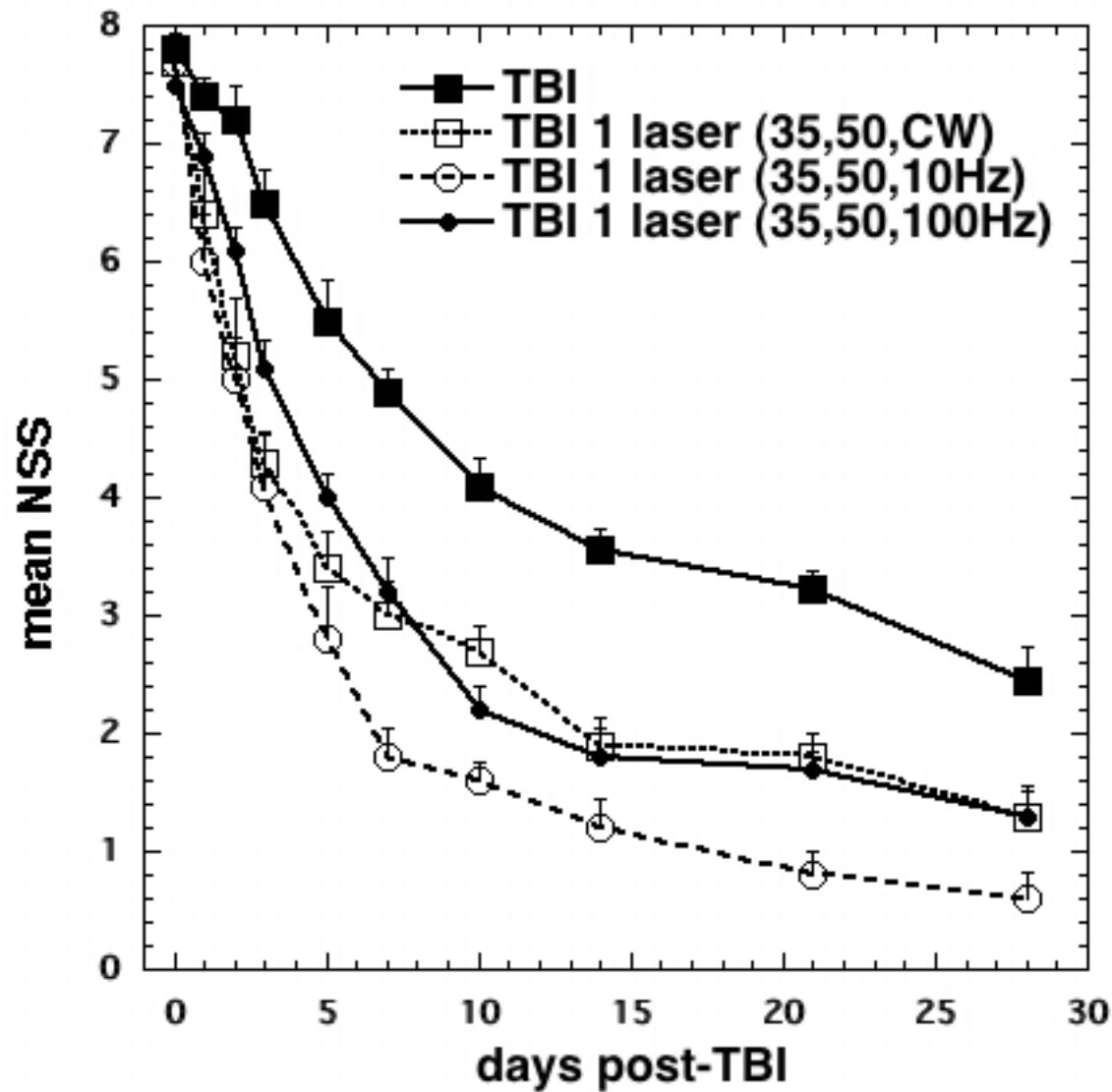


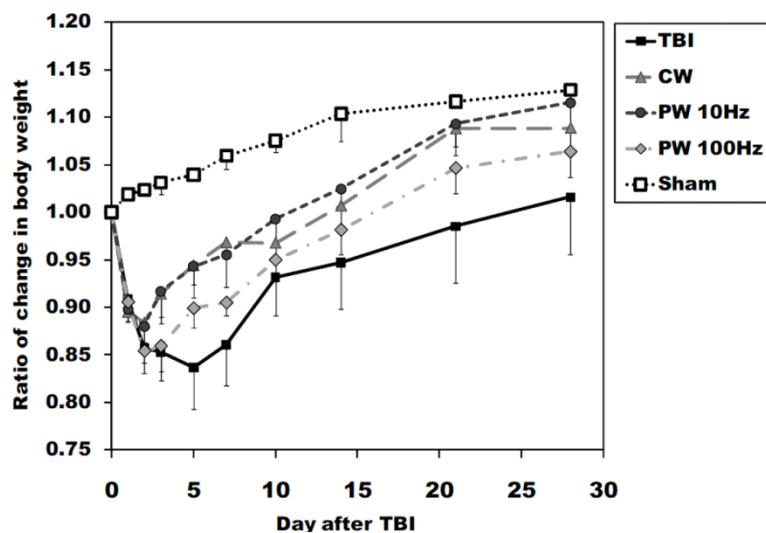
Comparison of Therapeutic Effects between Pulsed and Continuous Wave 810-nm Wavelength Laser Irradiation for Traumatic Brain Injury in Mice

Takahiro Ando^{1,2}, Weijun Xuan^{1,3,4}, Tao Xu^{1,3,5}, Tianhong Dai^{1,3}, Sulbha K. Sharma¹, Gitika B. Kharkwal^{1,3}, Ying-Ying Huang^{1,3,6}, Qiuhe Wu^{1,3,7}, Michael J. Whalen⁸, Shunichi Sato⁹, Minoru Obara², Michael R. Hamblin^{1,3,10*}

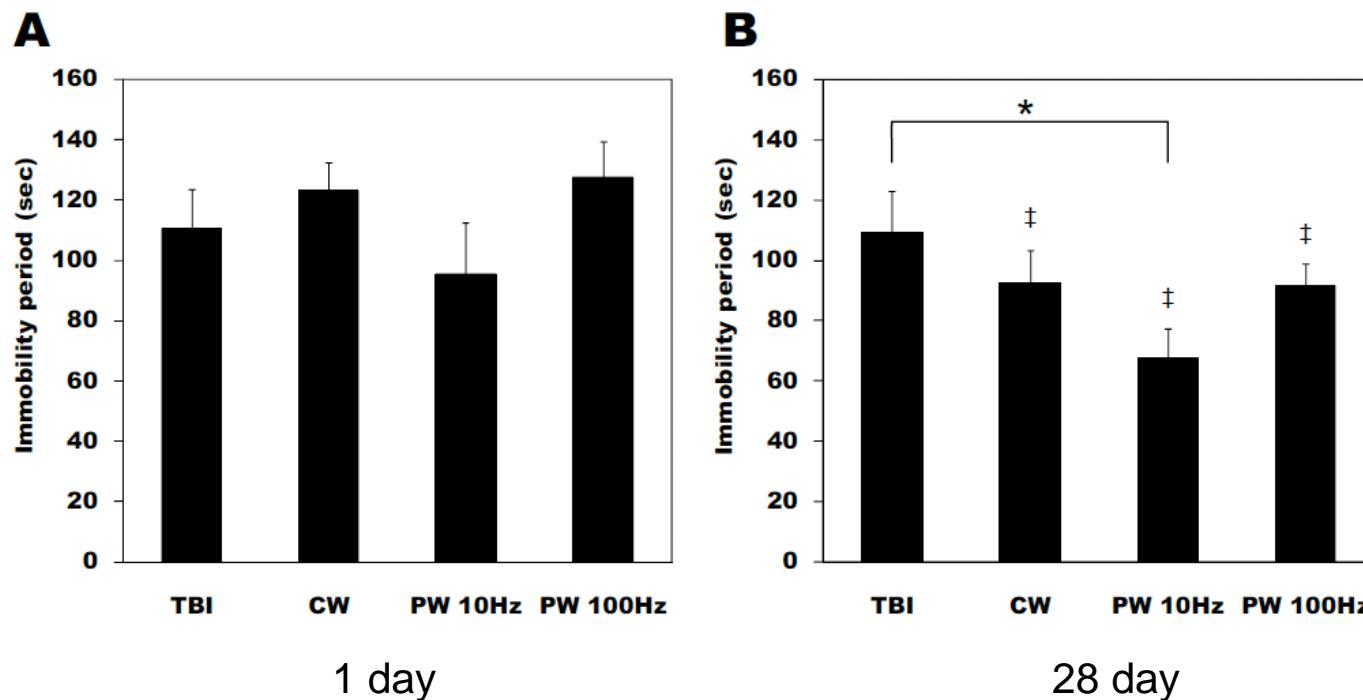


A single laser Tx of 36 J/cm² at 50 mW/cm² pulsed at 10 Hz is better than CW or 100 Hz

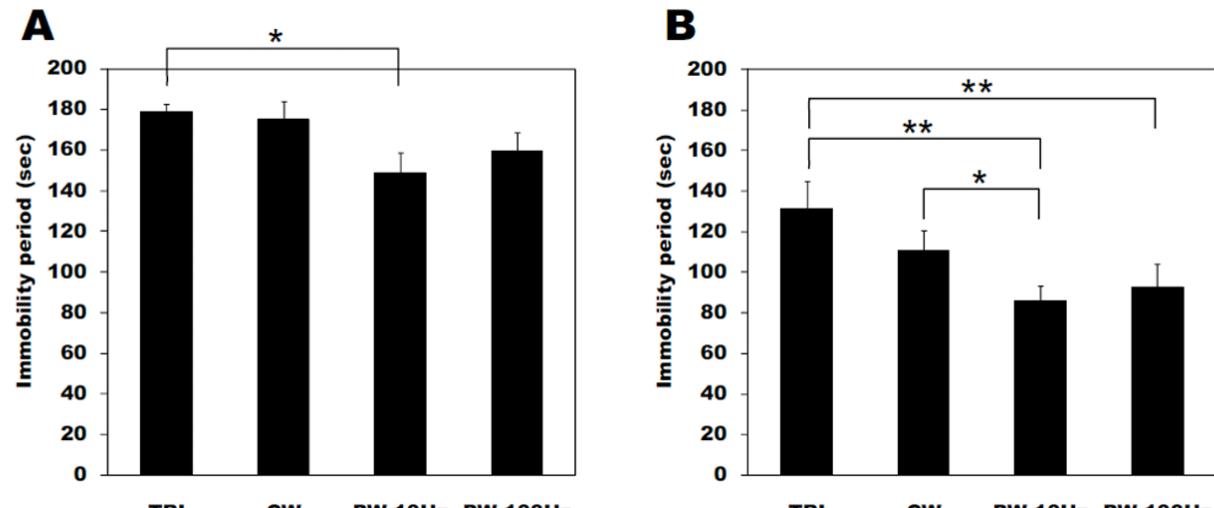




Body weight (overall health)



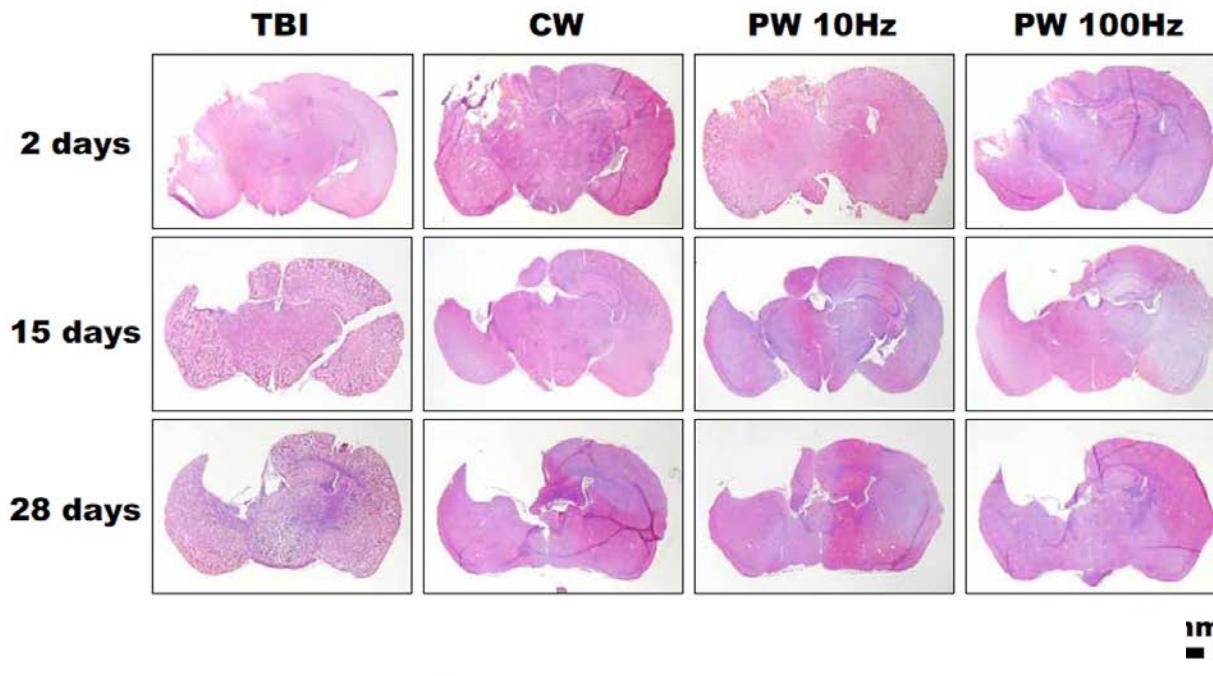
Forced swim test (depression)



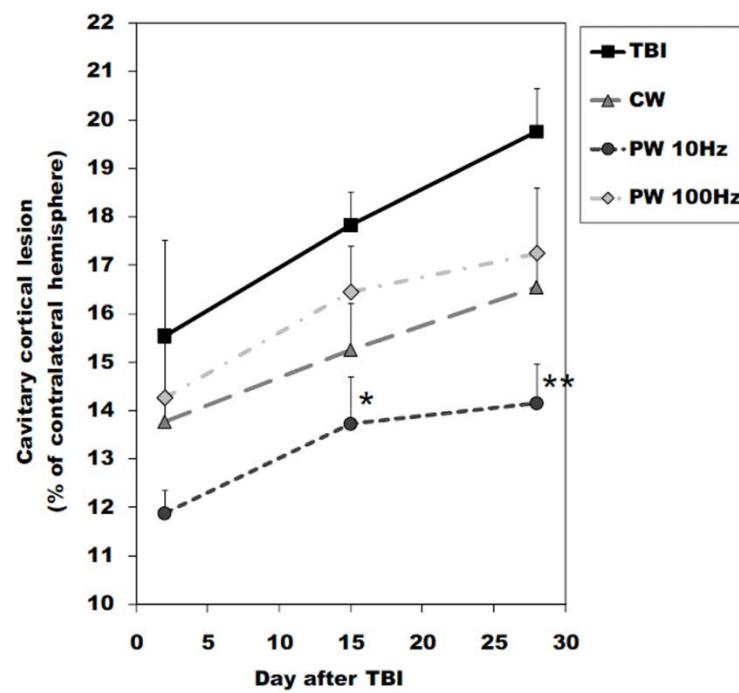
1 day

28 day

Tail suspension test (depression and anxiety)



1m



Transcranial Low-Level Laser Therapy Improves Neurological Performance in Traumatic Brain Injury in Mice: Effect of Treatment Repetition Regimen

Weijun Xuan^{1,2,3*}, Fatma Vatansever^{1,2*}, Liyi Huang^{1,2,4}, Qiuhe Wu^{1,2,5}, Yi Xuan^{1,6}, Tianhong Dai^{1,2}, Takahiro Ando^{1,7}, Tao Xu^{1,2,8}, Ying-Ying Huang^{1,2,9}, Michael R. Hamblin^{1,2,10*}

1 Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, Massachusetts, United States of America, **2** Department of Dermatology, Harvard Medical School, Boston, Massachusetts, United States of America, **3** Department of Otolaryngology, Traditional Chinese Medical University of Guangxi, Nanning, China, **4** Department of Infectious Diseases, First Affiliated College & Hospital, Guangxi Medical University, Nanning, China, **5** Department of Burn, Jinan Center Hospital, Jinan, China, **6** School of Engineering, Tufts University, Medford, Massachusetts, United States of America, **7** Department of Electronics and Electrical Engineering, Keio University, Kohoku-ku, Yokohama, Japan, **8** Laboratory of Anesthesiology, Shanghai Jiaotong University, Shanghai, China, **9** Aesthetic and Plastic Center of Guangxi Medical University, Nanning, China, **10** Harvard-MIT Division of Health Sciences and Technology, Cambridge, Massachusetts, United States of America

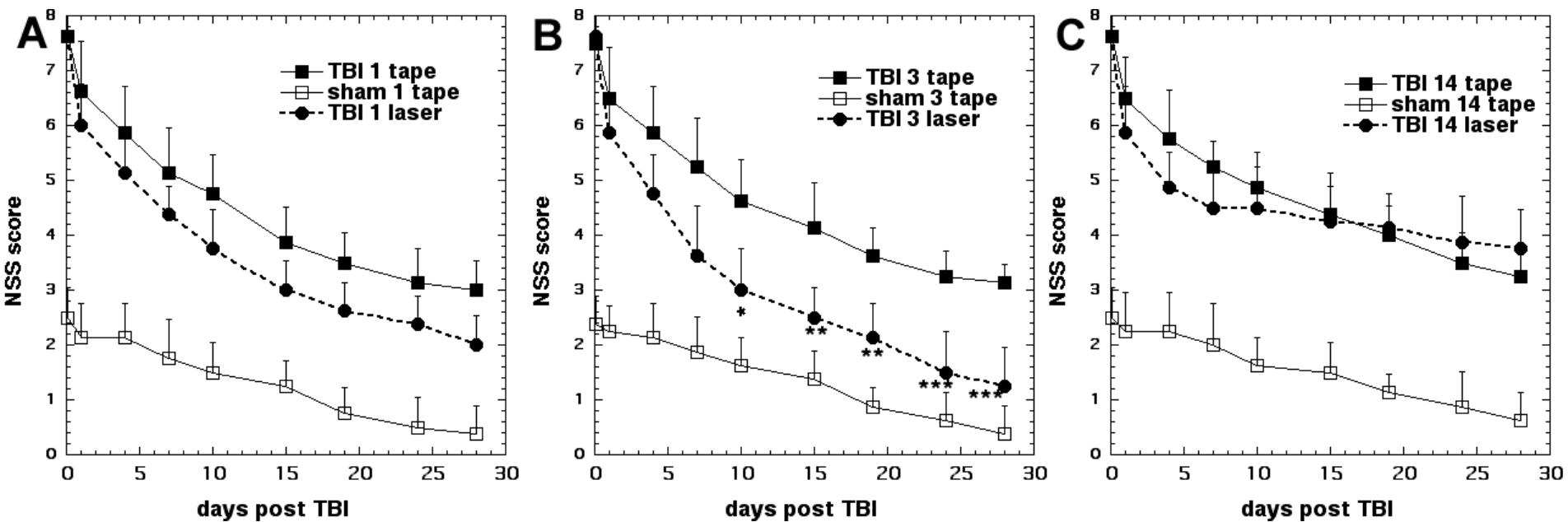
Treated mice - 1X (4 h post TBI)

- 3X (1 per day for 3 days)
- 14X (1 per day for 2 weeks)

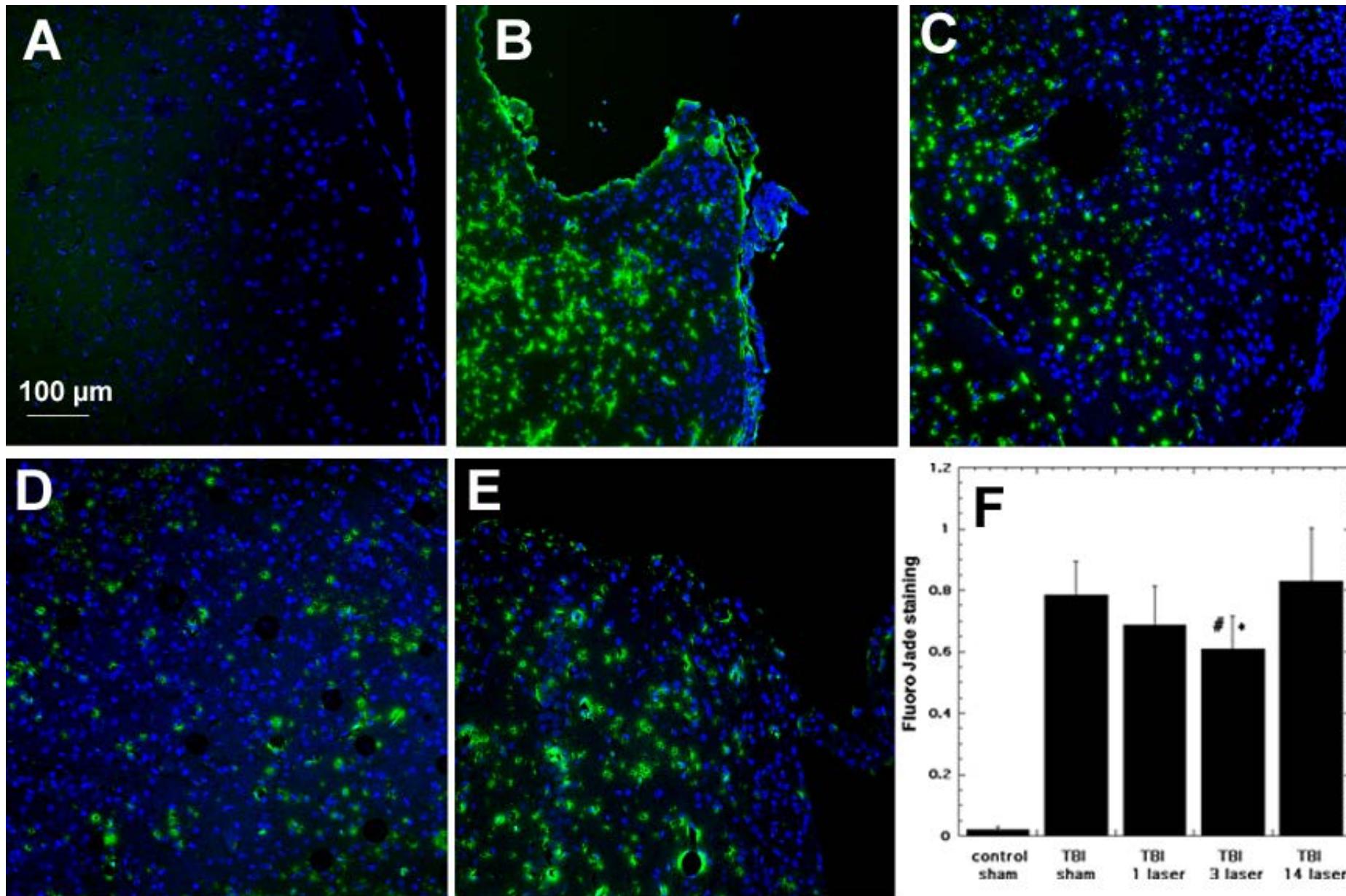
mice were sacrificed after 7 and 28 days

14X laser after 7 days = 7X laser

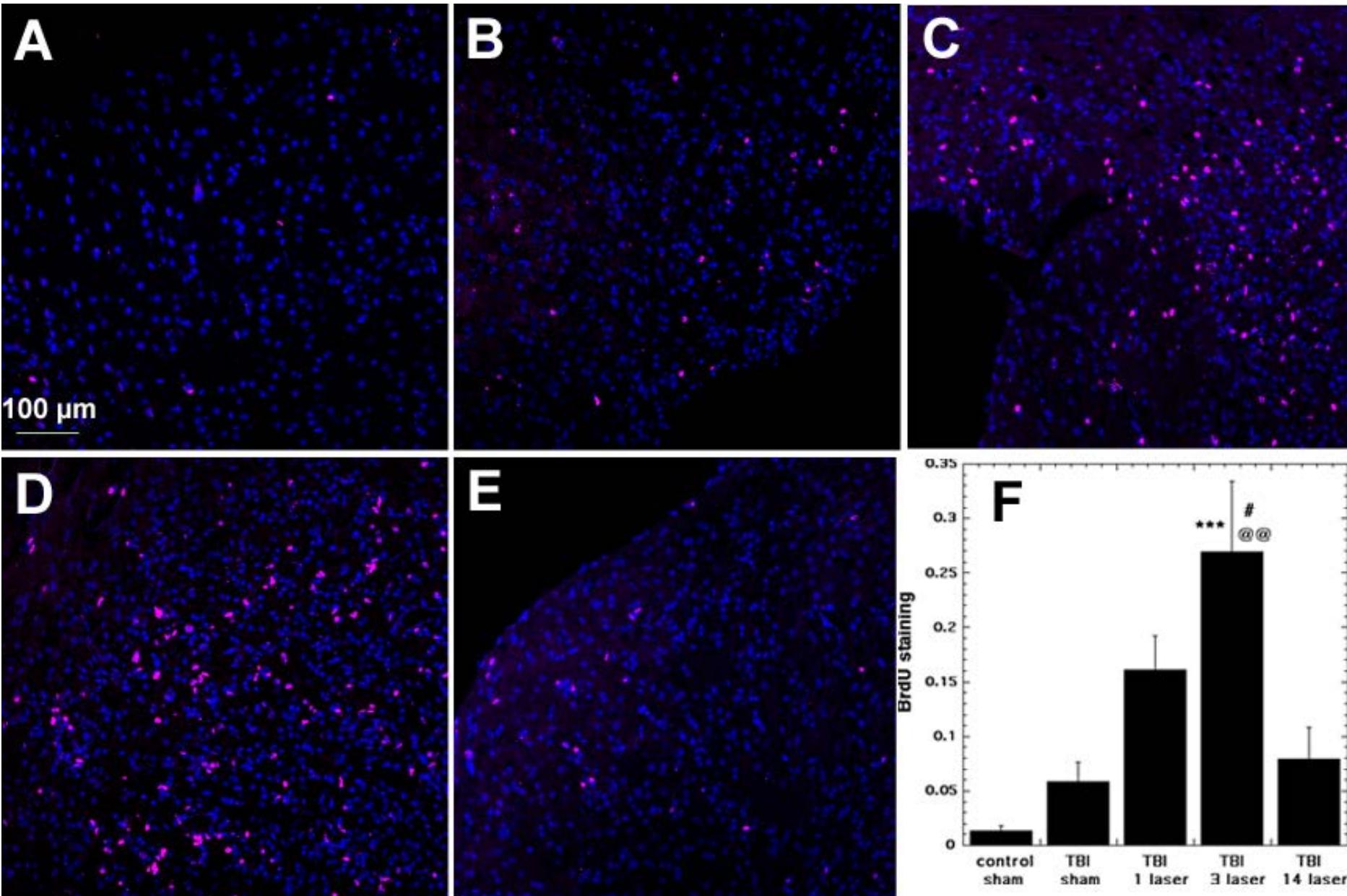
Different numbers of daily 810-nm laser Tx (18 J/cm² at 25 mW/cm²) in CCI TBI



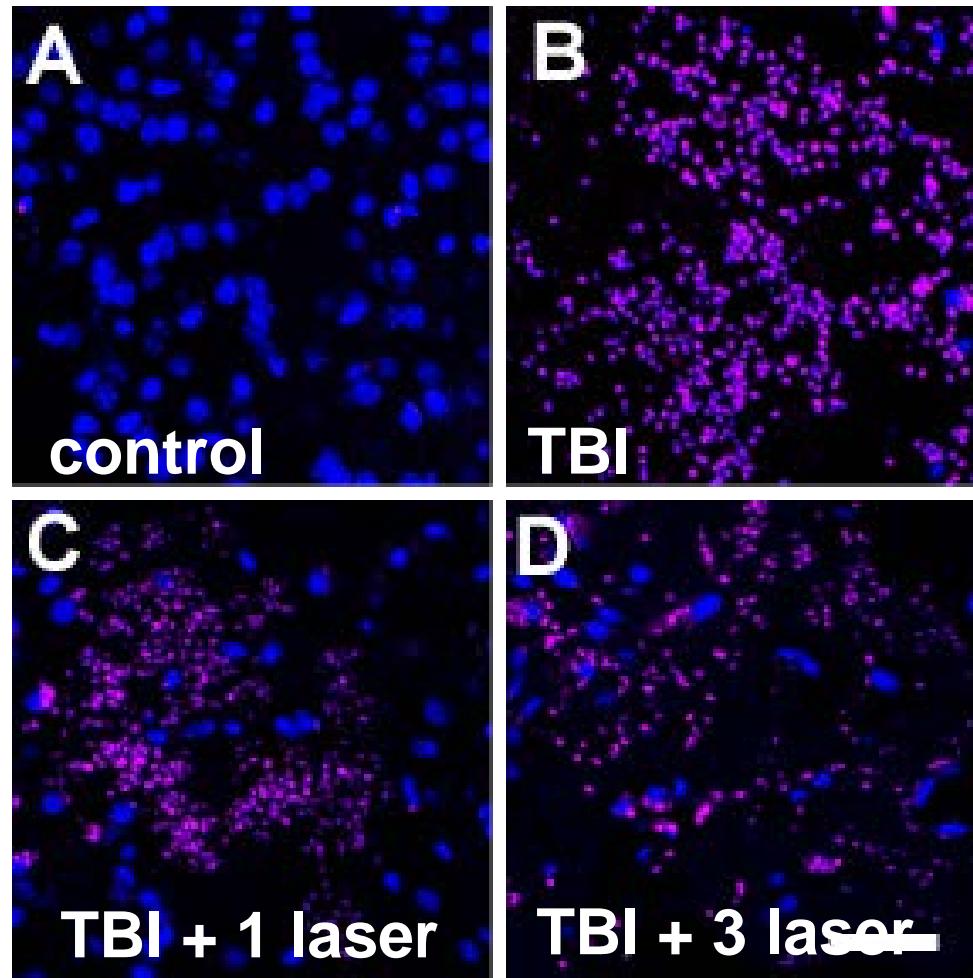
Fluoro Jade C for neurodegeneration (lesion) 14 days

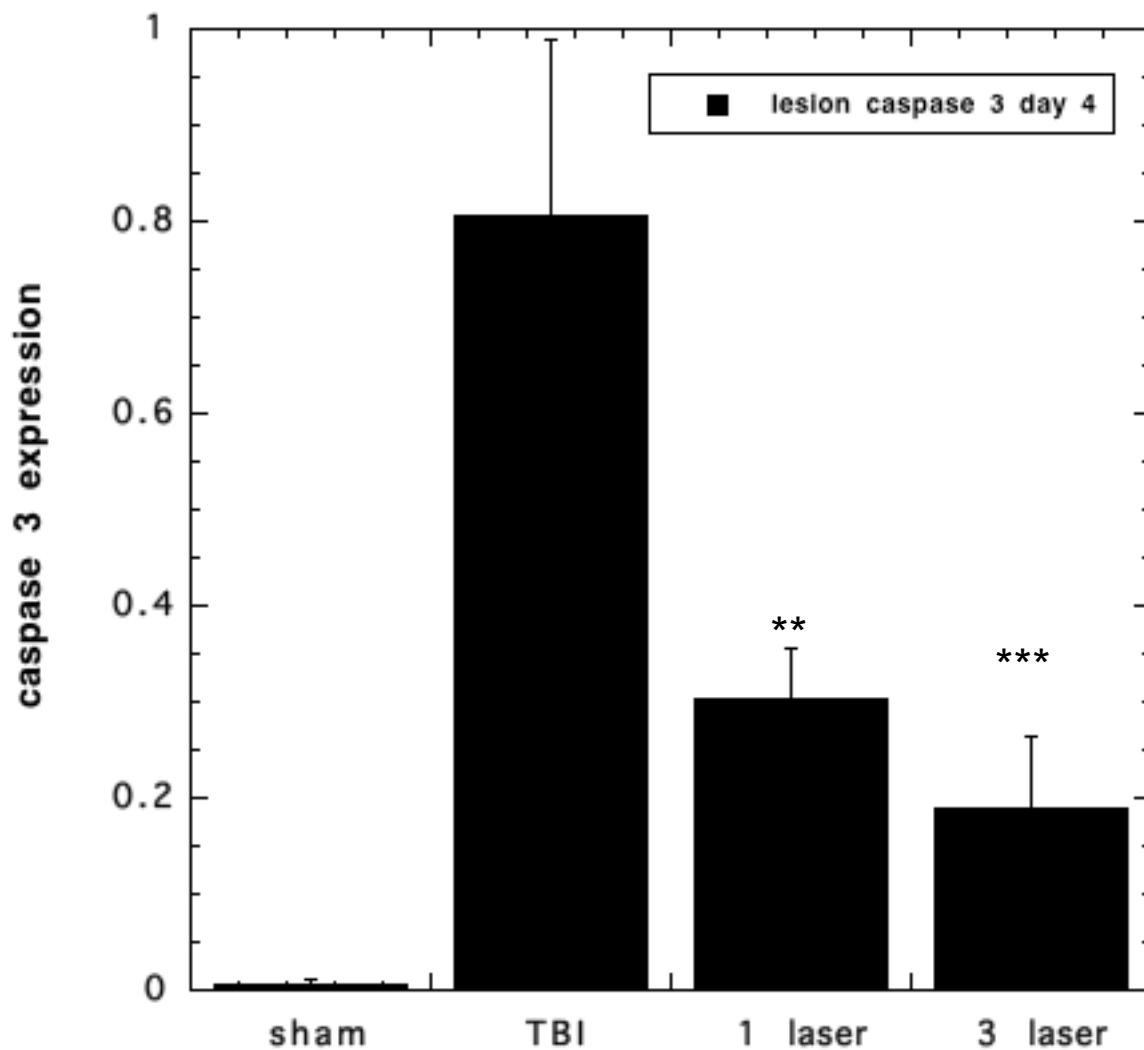


BrdU+ cells for neurogenesis (lesion) 28 days

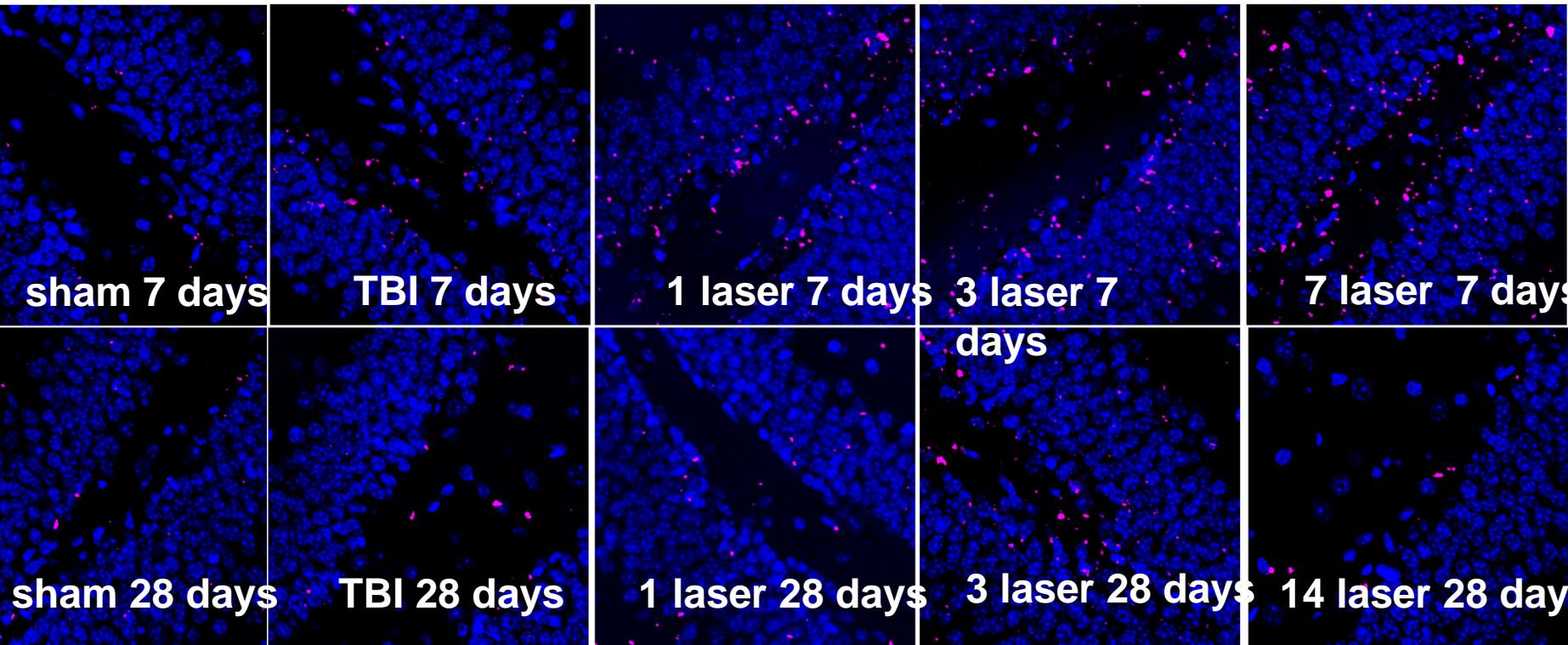


Caspase 3 in lesion area measured at 4 days post-TBI

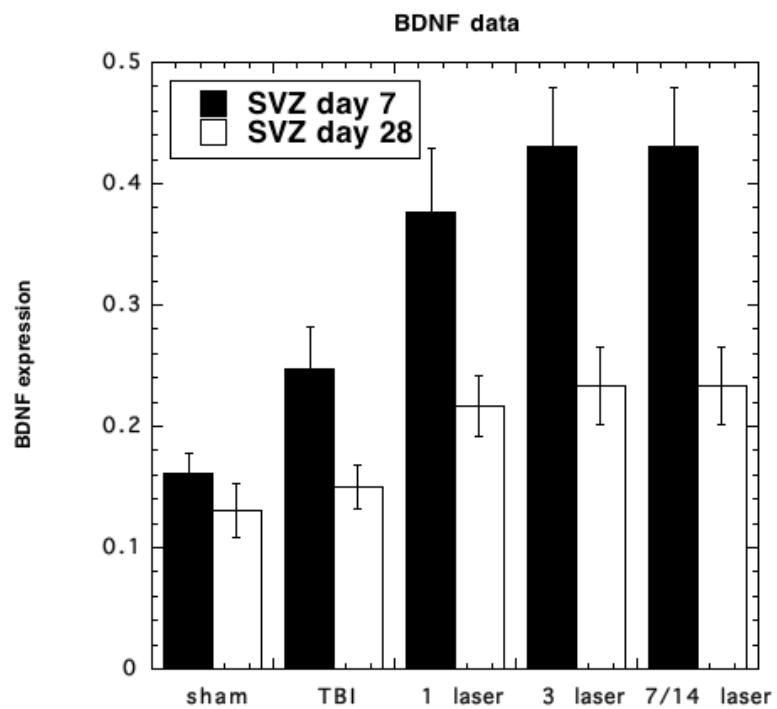
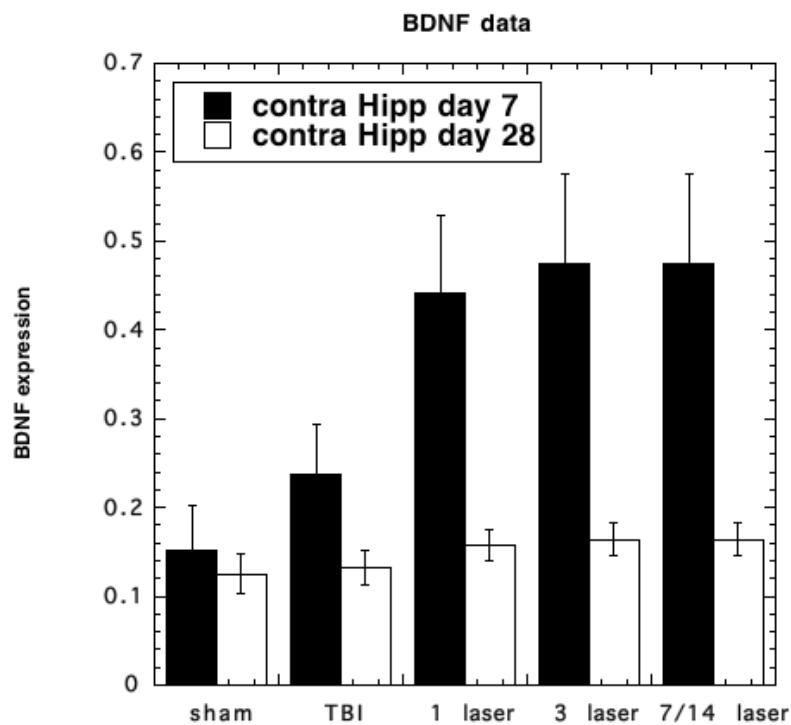




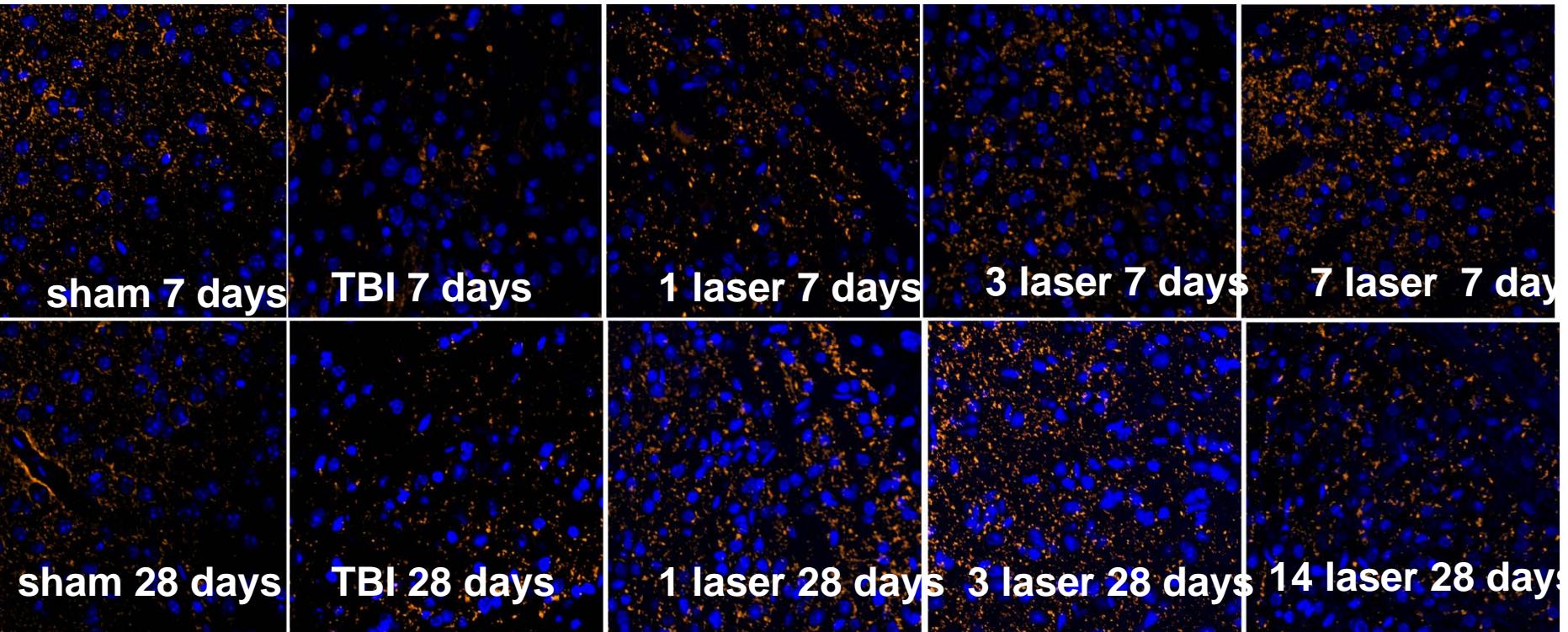
BDNF in hippocampus at days 7 & 28



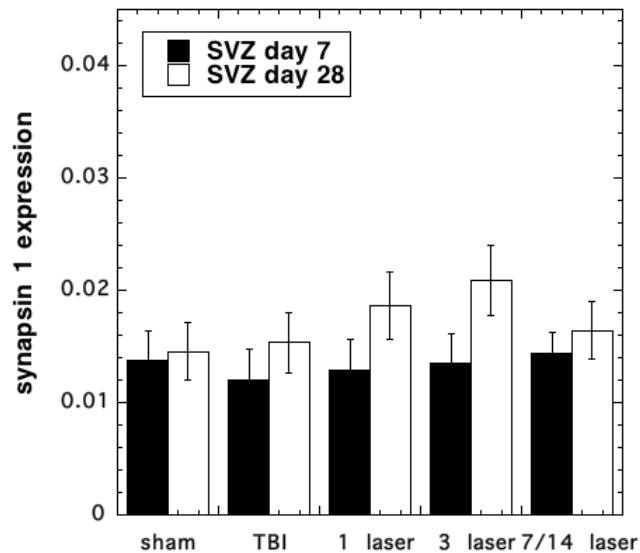
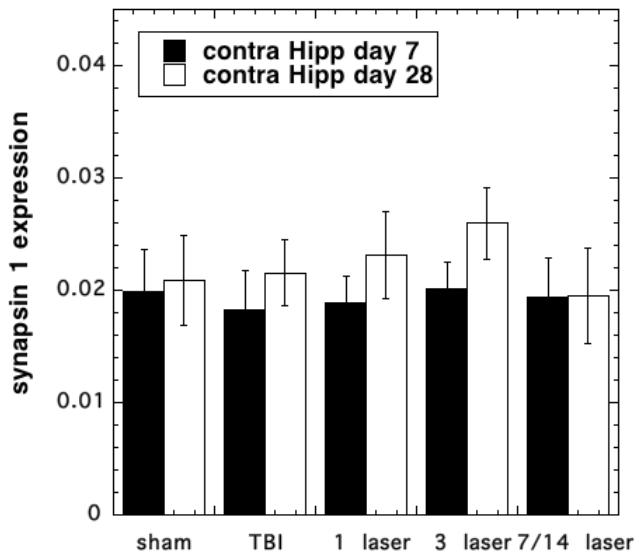
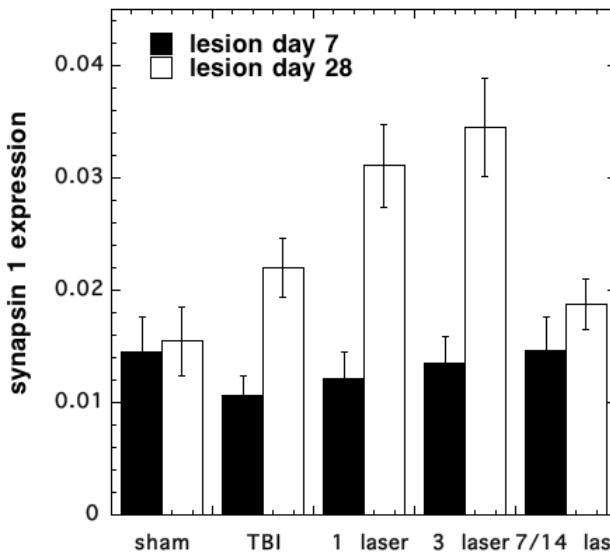
BDNF in hipp & SVZ at days 7 & 28



Synapsin-1 in lesion at days 7 & 28



Synapsin-1 in lesion, hipp & SVZ at days 7 & 28

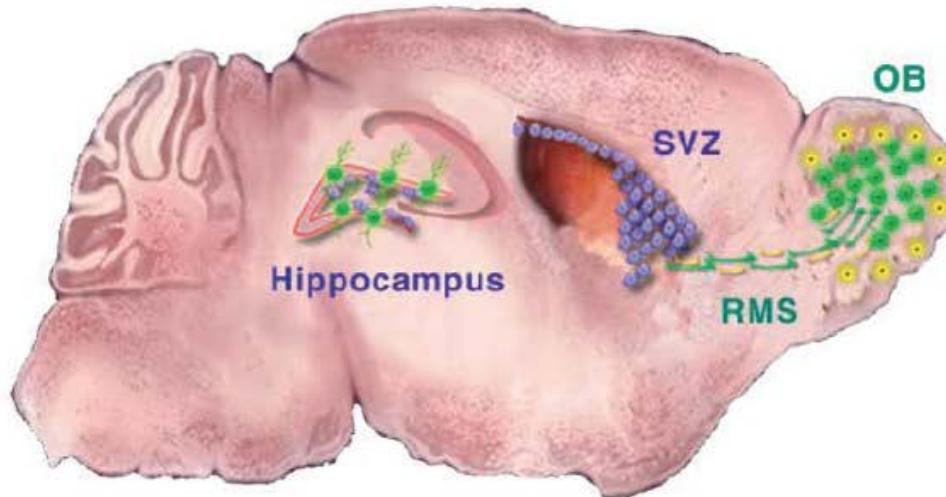


Injury-Induced Neurogenesis in the Adult Mammalian Brain

JACK M. PARENT

The persistence of neurogenesis in the adult mammalian forebrain suggests that endogenous precursors may be a potential source for neuronal replacement after injury or neurodegeneration. Limited knowledge exists, however, regarding the normal function of neurogenesis in the adult and its alteration by brain injury. Neural precursors generate neurons throughout life in the mammalian forebrain subventricular zone (SVZ)-olfactory bulb pathway and hippocampal dentate gyrus. Accumulating evidence indicates that various brain insults increase neurogenesis in these persistent germinative zones. Two brain injury models in particular, experimental epilepsy and stroke in the adult rodent, have provided significant insight into the consequences of injury-induced neurogenesis. Studies of dentate gyrus neurogenesis in adult rodent epilepsy models suggest that seizure-induced neurogenesis involves aberrant neuroblast migration and integration that may contribute to persistent hippocampal hyperexcitability. In contrast, adult rat forebrain SVZ neurogenesis induced by stroke may have reparative effects. SVZ neural precursors migrate to regions of focal or global ischemic injury and appear to form appropriate neuronal subtypes to replace damaged neurons. These findings underscore the need for a better understanding of injury-induced neurogenesis in the adult and suggest that the manipulation of endogenous neural precursors is a potential strategy for brain reparative therapies. NEUROSCIENTIST 9(4):261–272, 2003. DOI: 10.1177/1073858403252680

KEY WORDS Stem cell, Neural regeneration, Neurogenesis, Epilepsy, Stroke



Medline citations

Adult neurogenesis = 4,580

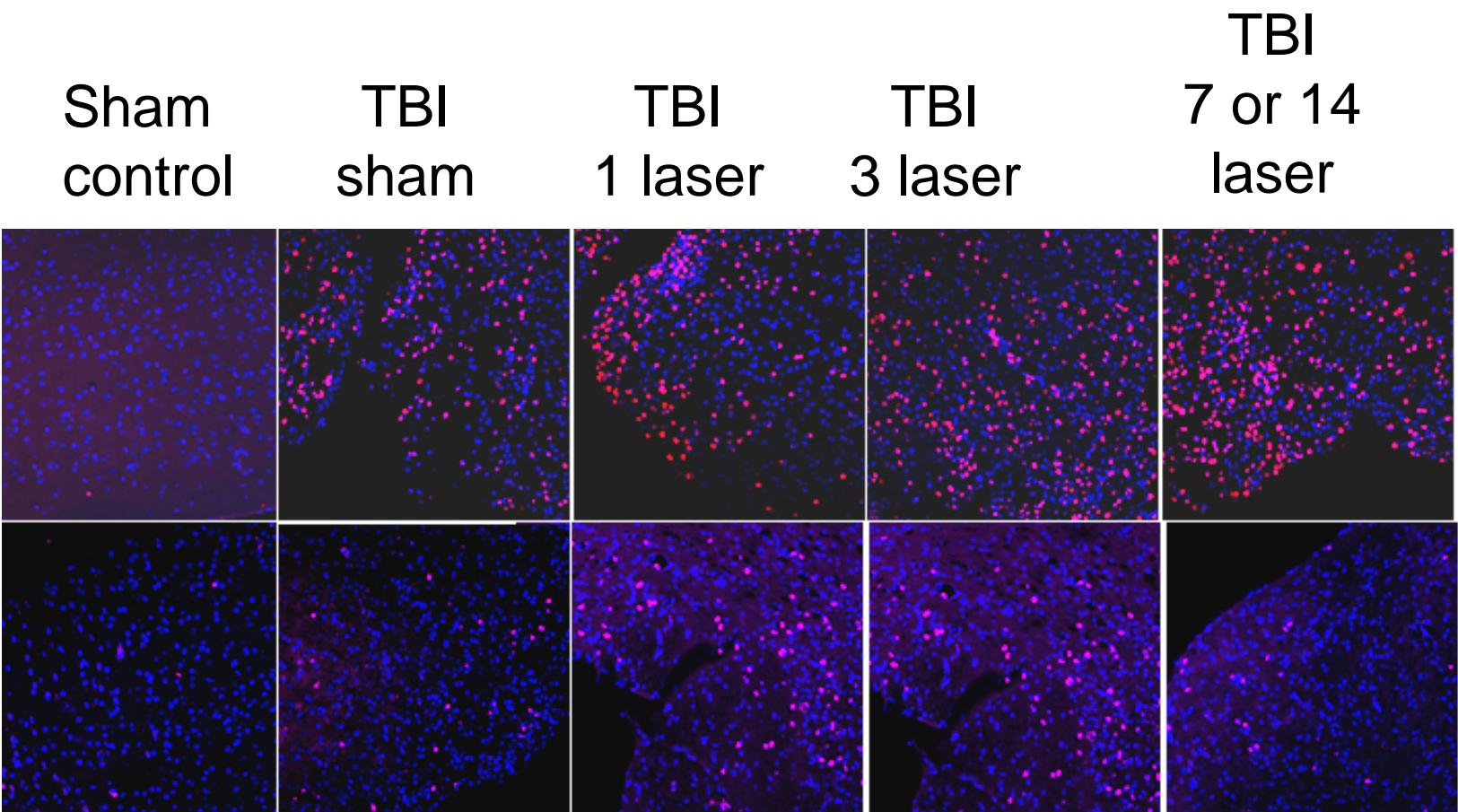
Synaptic plasticity = 17,841

BDNF = 10,522

Hippocampus = 104,022

Fig. 1. Schematic sagittal view of the adult rat brain showing the two regions of persistent neurogenesis. Neural precursor cells in the subventricular zone (SVZ; purple) undergo a long-distance, tangential migration in the rostral migratory stream (RMS) to reach the olfactory bulb (OB), where they differentiate into granule (green) and periglomerular (yellow) neurons. Precursors (purple) in the hippocampal dentate gyrus migrate a short distance into the dentate granule cell layer (outlined in red) and give rise to dentate granule neurons (green).

BrdU+ cells in lesion area



BrdU+ cells in SVZ

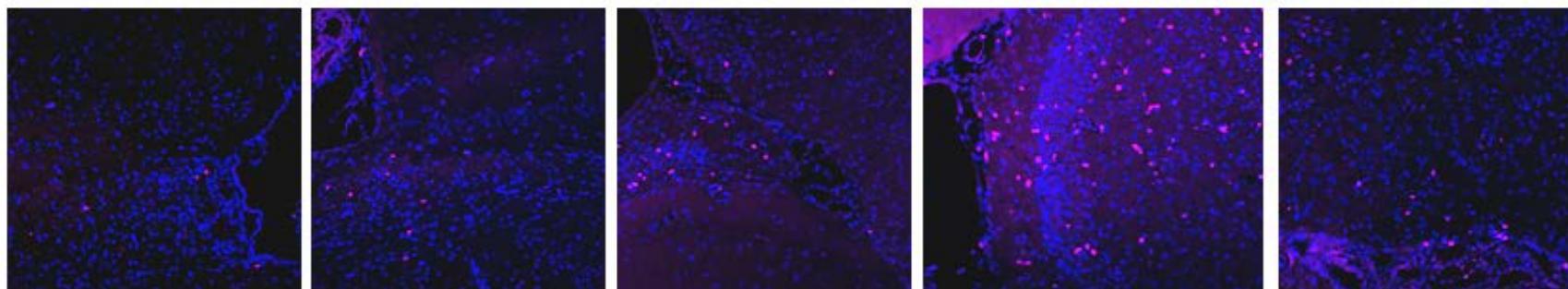
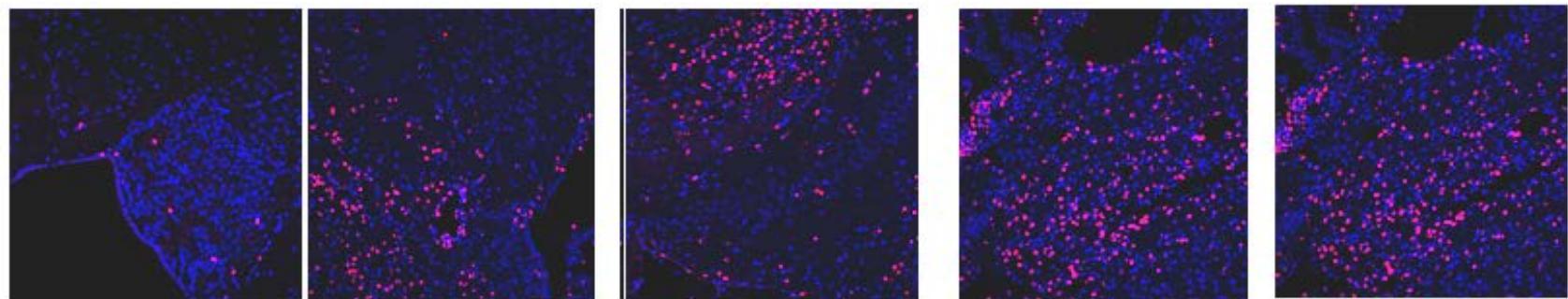
Sham
control

TBI
sham

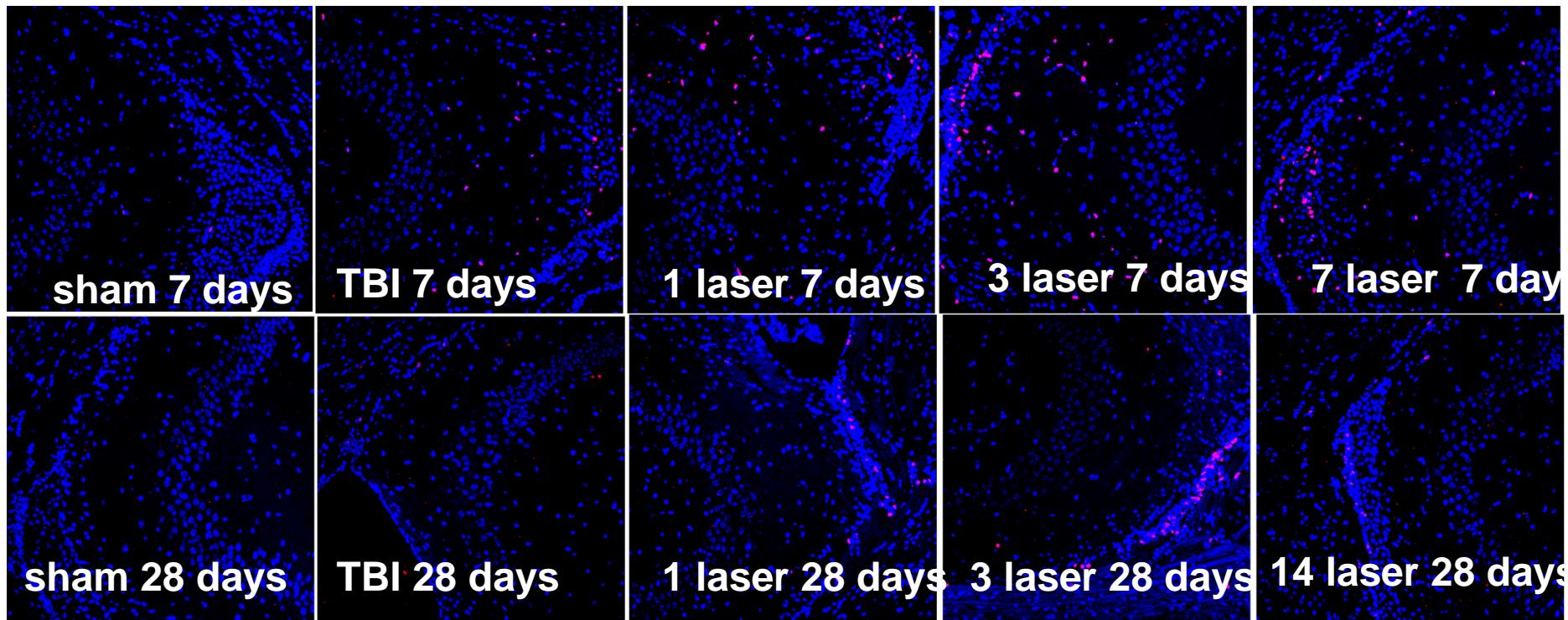
TBI
1 laser

TBI
3 laser

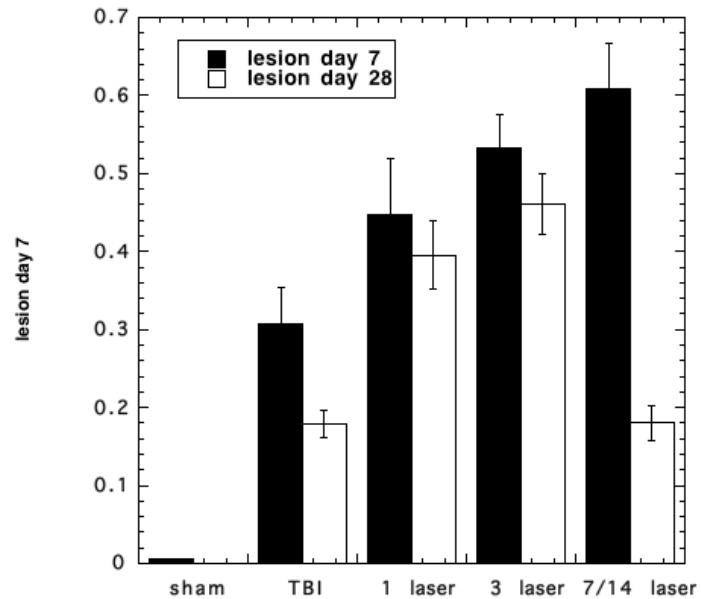
TBI
7 or 14
laser



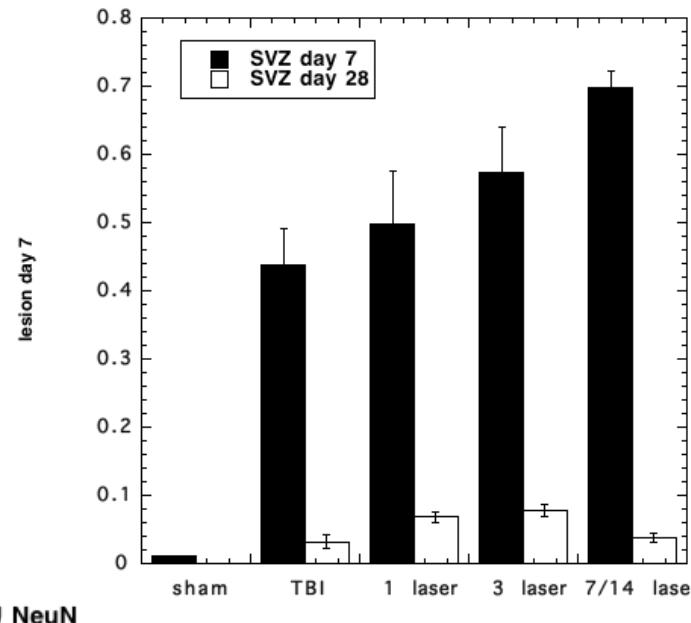
BrdU in hipp at days 7 & 28



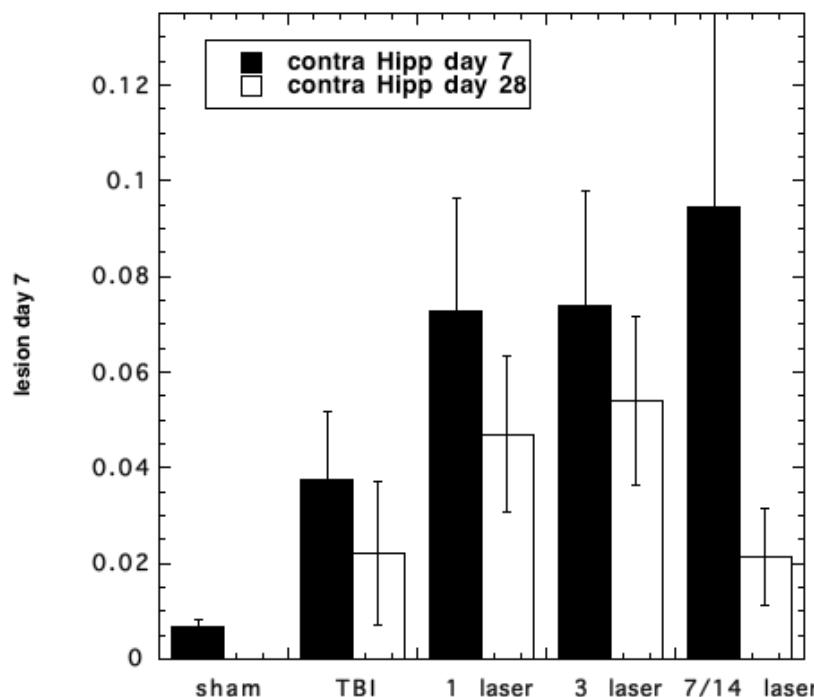
BrdU-Neu-N



BrdU-NeuN



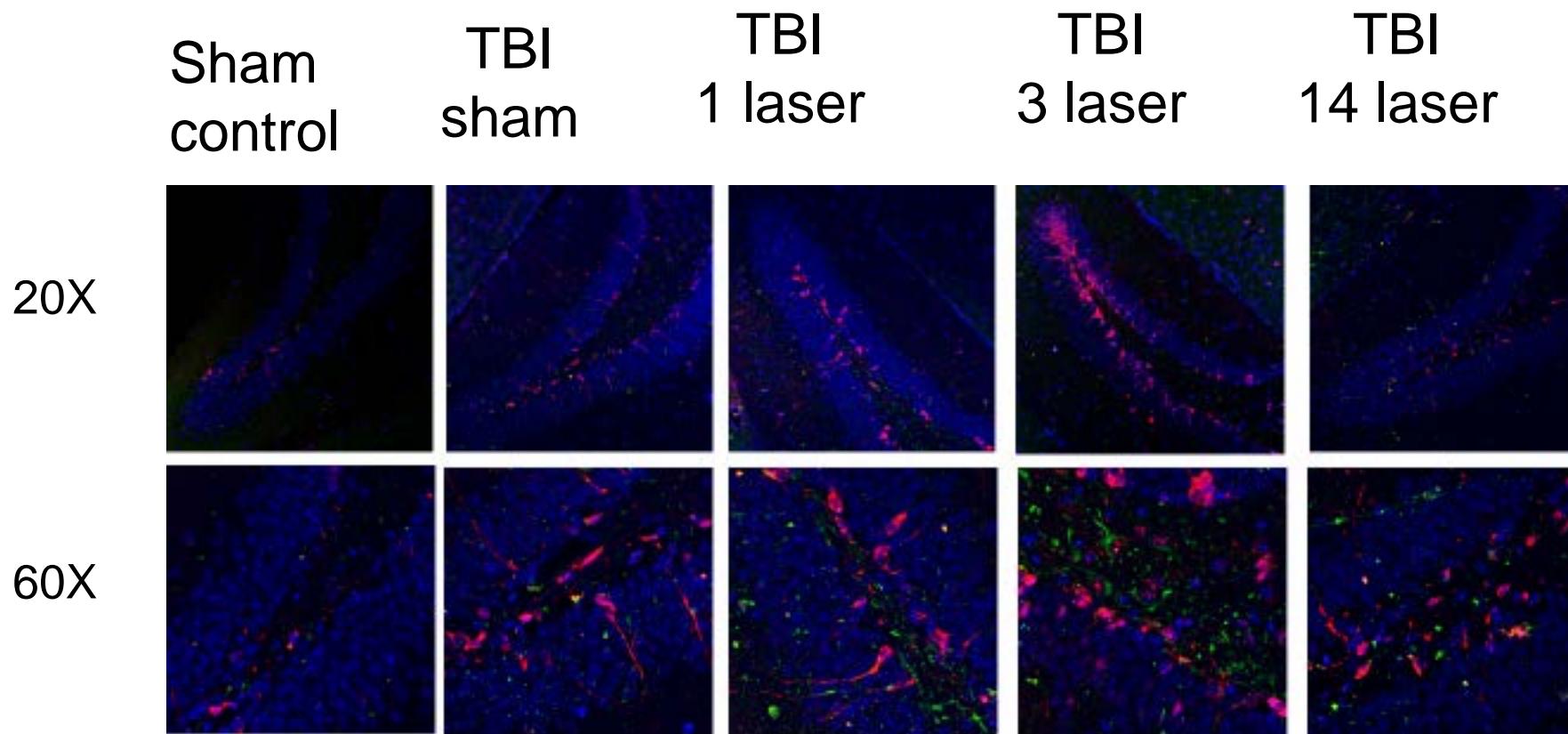
BrdU NeuN

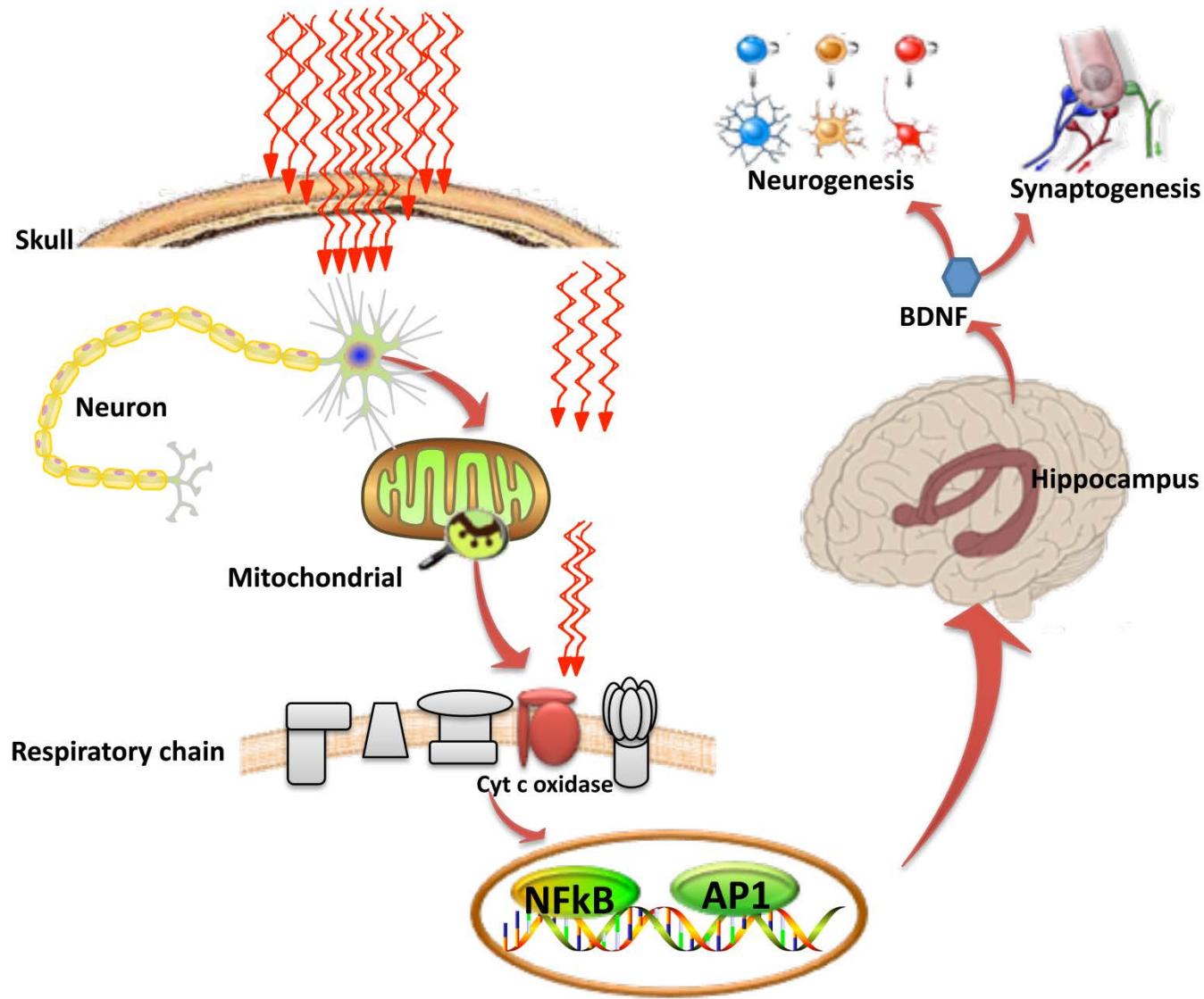


DCX and Tuj1 cells in DG (day28)

Double cordin (DCX) red

Tuj1 – green (Neuron-specific class III beta-tubulin is an excellent Neural Stem Cell Marker)





Mechanisms of Transcranial Light Therapy

Traumatic	Degenerative	Psychiatric	Mitochondrial
Acute stroke	Alzheimer's	Depression	MELAS
Acute TBI	Parkinson's	Anxiety	Fibromyalgia
Chronic stroke	Huntington's	Schizophrenia	Gulf War Syndrome
Chronic TBI	Amyotrophic lateral sclerosis	Addiction	Tinnitus
Global ischemia	Primary Aphasia	Bipolar disorder	Attention deficit hyper activity disorder
		Autism spectrum disorders	

Common pathways in neurodegenerative and psychiatric disease

Neuroinflammation

Low BDNF

Alzheimer's

Oxidative Stress

Impaired Neurogenesis

Parkinson's

Excitotoxicity

Hippocampal Shrinkage

Depression

Mitochondrial Dysfunction

Impaired Synaptogenesis

Schizophrenia

Neuronal Apoptosis

Cortical Shrinkage

Bipolar Disorder

LLLT for Depression and PTSD

Behavioral and Brain Functions

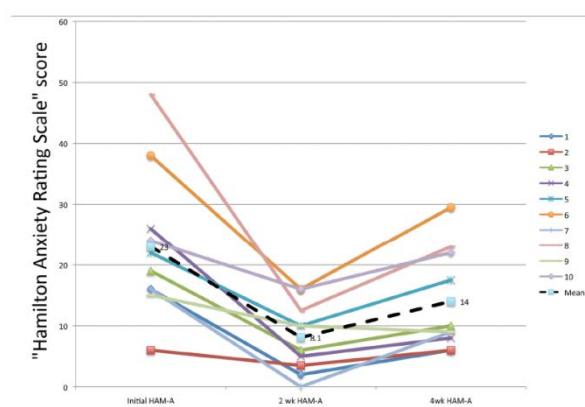
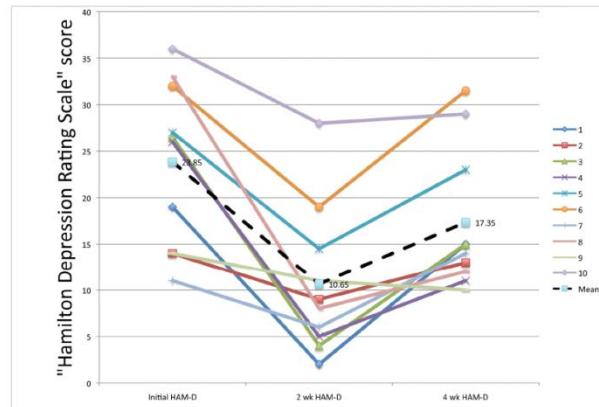
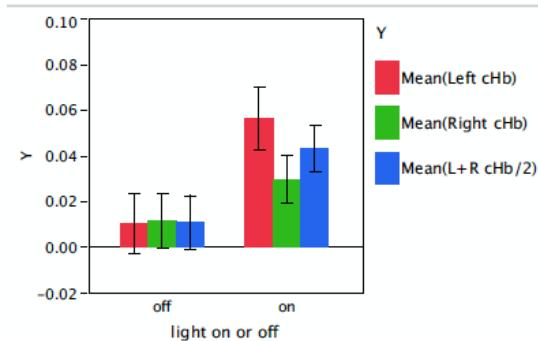


Research

Open Access

Psychological benefits 2 and 4 weeks after a single treatment with near infrared light to the forehead: a pilot study of 10 patients with major depression and anxiety

Fredric Schiffer^{*1}, Andrea L Johnston³, Caitlin Ravichandran², Ann Polcari¹, Martin H Teicher¹, Robert H Webb^{3,4} and Michael R Hamblin^{3,4,5}



Transcranial LED therapy for cognitive dysfunction in chronic, mild traumatic brain injury: Two case reports

Margaret A. Naeser^{*a,b}, Anita Saltmarche^c, Maxine H. Krengel^{a,b}, Michael R. Hamblin^{d,e,f}, Jeffrey A. Knight^{a,b,g}

^aVA Boston Healthcare System (12-A), 150 So. Huntington Ave., Boston, MA, USA 02130

^bDept. of Neurology, Boston Univ. School of Medicine, 85 E. Concord St., Boston, MA, USA 02118

^cMedX Health Inc., 220 Superior Blvd., Mississauga, ON L5L 2L2, Canada

^dWellman Center for Photomedicine, Massachusetts General Hospital, Boston MA 02114

^eDept of Dermatology, Harvard Medical School, Boston MA 02115

^fHarvard-MIT Division of Health Sciences and Technology, Cambridge, MA

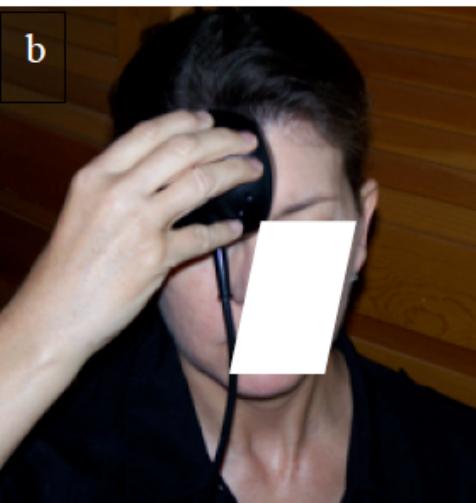
^gNational Center for PTSD - Behavioral Sciences Division, VA Boston Healthcare System



MedX LED cluster
870-nm & 633-nm

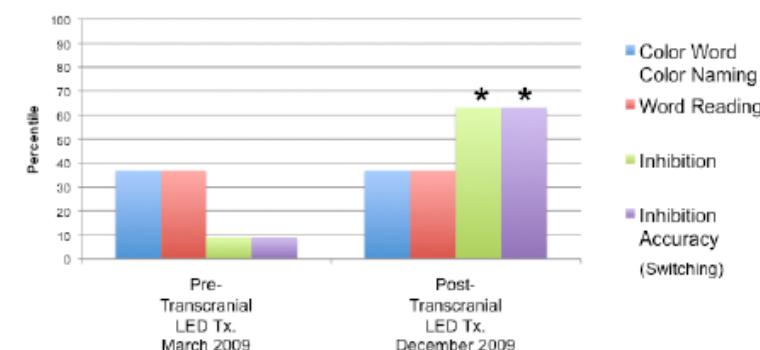
Case 1. 59 yo F, 7 yr. post-MVA after 8 weekly Tx.'s, ability to do computer work had improved 10-fold, obtained home unit and has used daily for 5 years.

Case 2. 52 yo F, multiple concussions and PTSD, Tx.'d daily with home unit, memory and "executive function" tests improved >2 SD, after 9 months. Off "Medical Disability" status after 4 months of home treatments; returned to full-time work.



Color-Word Interference Test

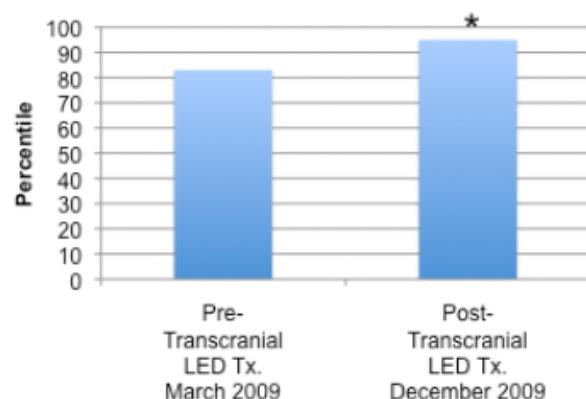
Stroop ("Executive Function Test")



* +2 SD Improvement, inhibition, inhibition accuracy

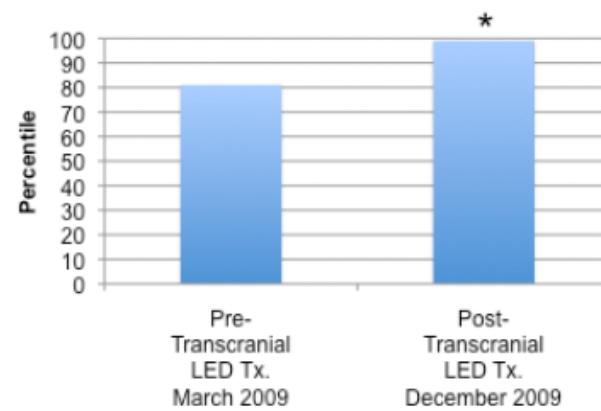
P2, Pre- and Post- LED Tx., *Neuropsychological Test Results* P2, Pre- and Post- LED Tx., *Neuropsychological Test Results*
Post- LED Testing, Post- 9 months, nightly, transcranial LED Tx. Post- LED Test, Post- 9 months, nightly, transcranial LED Tx.

c **2 Stories, Immediate Recall**
Wechsler Memory Scale-R



* Significant Improvement, +1 SD: Memory

c **2 Stories, Delayed Recall (30 minutes)**
Wechsler Memory Scale-R



* Significant Improvement, +2 SD: Memory

Michael R Hamblin PhD

WALT 2010 Bergen
Norway

Forthcoming Clinical Trial, at VA Boston Healthcare System (VABHS), Jamaica Plain

“Transcranial, Light-emitting Diode (LED) Therapy to Improve Cognition in Gulf War Veterans’ Illnesses”

PI: Margaret Naeser, PhD

VABHS and Department of Neurology, Boston University School of Medicine (BUSM)

Co-Investigators and Consultants:

Maxine Krengel, PhD, Neuropsychologist, VABHS, and Neurology, BUSM

Jeffrey Knight, PhD, Neuropsychologist, National Center for PTSD, VABHS

Michael R. Hamblin, PhD, Wellman Center for Photomedicine, Massachusetts General Hospital,

Beatrice Golomb, MD, PhD, Univ. of Calif., San Diego; and VA San Diego Healthcare System

Marc S. Goldstein, MD, Primary Care, Worcester VA Outpatient Clinic

Manisha Thakore-James, MD, Neurology VABHS and Neurology, BUSM

Carlos Tun, MD, Rehabilitation Medicine VABHS and Harvard Medical School



VA-funded, 4-Yr. - blinded, randomized, sham-controlled, cross-over study.

◆ 160 GWI Veterans with cognitive problems; recruited through Ft. Devens, MA Cohort Previously participated in GWI surveys, under direction of Maxine Krengel, PhD

2 Groups: A) Sham LED helmet 1st series; Real, 2nd series. B) Real LED helmet 1st series; Sham 2nd.

15 Tx.’s per series; 2x/Wk for 7.5 Wks. Tested at 1 Week and 2 Mo. post- Tx.

Each red/NIR LED pod inside helmet: 692.5mW; 36.5mW/cm²; CW, 13 J/cm², 10 min per LED pod locus.

Primary Outcome Measures: Attention/Executive Function; Learning & Memory; Psychomotor/Visuospatial

Secondary Measures: Pain, Fatigue, Mood, Blood Tests: mitochondrial function; inflammation; coagulation; general health

Forthcoming Clinical Trial at MGH

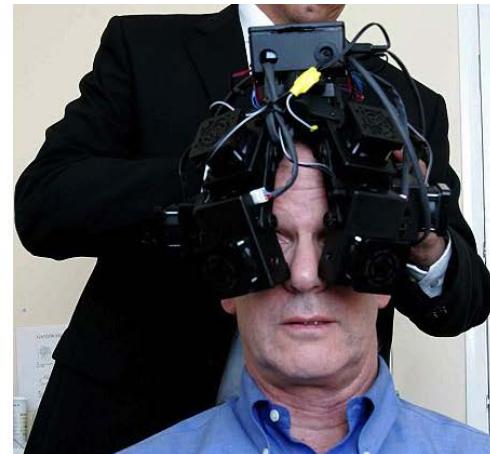
Acute Low-Level Laser Therapy for the Treatment of Moderate Traumatic Brain Injury

PI: Benjamin Vakoc, PhD

Double-blinded, randomized, and placebo-controlled. 82 moderate TBI patients admitted to Massachusetts General Hospital will be randomly assigned into equal treatment and control (sham therapy) groups. LLLT or sham treatment will be given daily for 1 week after injury

Endpoints: Neuroimaging data (MRI-BOLD, ASL, DTI) ; clinical evaluation, neurofunctional tests at 3 and 6-month follow ups

Previous transcranial helmet devices





“Brain Cap”
PhotoTherapeutics



PhotoMedex®
Dermatology • Surgical



Conclusions

Mechanisms of LLLT are becoming understood

Pre-conditioning nerves with LLLT reduces pain

Transcranial LLLT improves acute TBI

Transcranial LLLT may be applicable for large range of brain disorders

Acknowledgments



Qiuhe Wu, MD, PhD



Weijun Xuan MD, PhD



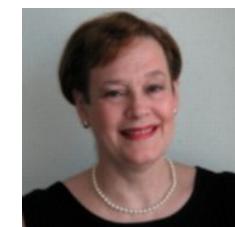
Ben Vakoc PhD



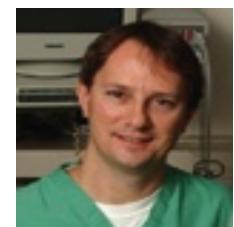
Mei X Wu MD, PhD



Frederic Schiffer MD



Margaret Naeser PhD Michael J Whalen MD



Pinar Avci MD



Ying-Ying Huang MD



Tianhong Dai,
PhD



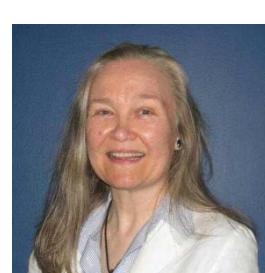
Takahiro Ando
MS



Tao Xu PhD



Liyi Huang MD, PhD



Fatma Vatansever
MD, PhD



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health



THOR
THE FUTURE OF MEDICINE

CIMIT
Center for Integration of Medicine & Innovative Technology

Air Force Office of Scientific Research
The Basic Research Manager of the Air Force



PHOTOTHERA