Low G preconditioning reduces liver injury induced by high +Gz exposure in rats

Bin Shi, Zhi-Qiang Feng, Wen-Bing Li, Hong-Yi Zhang

AIM: To investigate the effect of repeated lower +Gz exposure on liver injury induced by high +Gz exposure in rats.

METHODS: Sixty male Wister rats were randomly divided into a blank control group, a low G preconditioning group (LG) (exposed to +4 Gz/5 min per day for 3 d before +10 Gz/5 min exposure), and a +10 Gz/5 min group (10G) (n = 20 in each group). Blood specimens and liver tissue were harvested at 0 h and 6 h after +10 Gz/5 min exposure. Liver function was analyzed by measuring serum alanine transaminase (ALT) and aspartate aminotransferase (AST) levels, and liver injury was further assessed by histopathological observation. Malondialdehyde (MDA), superoxide dismutase (SOD) and Na\(^+\)-K\(^+\)-ATPase were determined in hepatic tissue.

RESULTS: The group LG had lower ALT, AST, and MDA values at 0 h after exposure than those in group 10G. SOD values and Na\(^+\)-K\(^+\)-ATPase activity in the LG group were higher than in group 10G 0 h post-exposure. Hepatocyte injury was significantly less in group LG than in group 10G on histopathological evaluation.

CONCLUSION: It is suggested that repeated low +Gz exposure shows a protective effect on liver injury induced by high +Gz exposure in rats. Key words: Positive acceleration (+Gz); Liver injury; Preconditioning; Animal centrifuge; Rat

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.
Shi B, Feng ZQ, Li WB, Zhang HY. Low G preconditioning reduces liver injury induced by high +Gz exposure in rats. World J Gastroenterol 2015; 21(21): 6543-6549. Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i21/6543.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i21.6543

INTRODUCTION

Ischemic preconditioning (IPC) refers to a phenomenon in which the tissue can not only increase resistance to further ischemic injury but also reduce the degree of organ dysfunction or subsequent damage following ischemia reperfusion[1,2]. To some extent, ischemia of a brief period initiates an endogenous protection for the following sustained ischemic period[3]. At first, the protective effect of IPC was verified in the heart[4]. Although the potential mechanism is not fully understood, the protective effect of IPC in delaying cell injury of skeletal muscle[5], brain[6], kidney[7], liver[8] and small intestine[9] is generally accepted. More and more studies have demonstrated that many different stimuli can induce preconditioned status of the liver. Ren et al[10] reported that liver IPC played a beneficial role in hepatic graft function and intestinal barrier function, contributing to stabilization of intestinal microbiota in liver transplantation. Currin et al[11] found that IPC markedly reduced hepatocellular injury after aortic clamping and ameliorated the survival rate. Lee et al[12] showed that hepatic IPC directly reduced distant renal ischemia and reperfusion injury in animal experiments. Figueira et al[13] demonstrated that hepatic IPC could not only recover portal vein flow, but also relieve hepatocellular injury. During a flight, pilots may experience high sustained +Gz acceleration that results in gravity load and hemodynamic changes. Repeated +Gz exposure can cause accumulative stress damage in the body[14], inducing organ dysfunction and triggering pathologic changes. For a long time, many researchers were interested in the problem and tried to figure out some useful safeguard measures[15]. Cao et al[16] found that repeated low +Gz preconditioning could obviously ameliorate memory and balance changes induced by high +Gz exposure in rats. It was also found that lower gravity preconditioning was able to dramatically improve rat learning and memory impairment induced by high gravity exposure[17]. Li et al[18]'s study showed that brain injury induced by high +Gz exposure could be remarkably alleviated by low +Gz exposures in rats. It was also found that the left ventricular contractility and secretions of vascular endothelioctyes in the heart of rats following high +Gz exposure were significantly improved by low G preconditioning[19]. Moreover, it was discovered that low G preconditioning was protective for several enzyme activities in myocardial tissue after high +Gz stress in rats[20]. The liver is the largest internal organ, and an important metabolic organ[21,22]. Without timely and effective preventive measures, the natural protective mechanism of the liver may be overpowered by continuous and repeated exposures to +Gz acceleration. In experimental studies, repeated +Gz exposure can transiently cause liver dysfunction and trigger pathologic changes. We are interested in whether low G preconditioning has a similar protective effect on liver injury and dysfunction induced by high +Gz stress. The aim of this study is to investigate the possible protective effect of repeated low +Gz exposure on liver injury induced by high +Gz exposure in rats.

MATERIALS AND METHODS

Experimental animals

Sixty male Wister rats (provided by the Experimental Animal Center of the Academy of Military Medical Science, Beijing, China), weighing between 250 and 300 g, were randomly divided into three groups: blank control group (group BC, n = 20), low G preconditioning group (group LG, n = 20) (exposed to +4 Gz/5 min per day for 3 d before +10 Gz/5 min exposure) and +10 Gz/5 min group (group 10G, n = 20). All rats were housed under standard experimental conditions: 12:12-h light-dark cycle, humidity 70%-80%, and room temperature 23-26 ℃. Standard laboratory chow and water were provided and rats were allowed to aclimatize for 7 d. The rats were fasting but had access to water for 12 h before the experiment to reduce experimental errors. All experiments were conducted between 8:00 am and 12:00 am. The experimental schemes were approved by the Animal Care and Use Committee of China PLA Air Force General Hospital and carried out according to the Guide for the Care and Use of Laboratory Animals.

Exposure of animals to acceleration and specimen collection

The animal centrifuge had an arm length of 2 m and was provided by the Air Force Aeromedicine Institute (Beijing, China), with an onset rate of 0.1-6 Gz/s, and acceleration range of 1-15 G. Each rat was placed inside a 15 cm × 5 cm × 3 cm cylindrical plastic restraint device which was mounted in the centrifuge arm with the head of the rat facing the axis of the centrifuge for +Gz orientation. In the +10 Gz/5min group, the rats were exposed to +10 Gz lasting for 5 min as reported elsewhere[23]. For the low G preconditioning group, the rats were exposed to +4 Gz/5 min every day for 3 d before +10 Gz/5 min exposure. The onset/offset rate of +Gz was set at +1 G/s. The rats in the blank control group were mounted on the arms of centrifuge, but were free from acceleration. After exposure to acceleration for 0 h and 6 h, general anesthesia, routine disinfection, and laparotomy were...
performed for specimen collection. A blood sample of about 2 mL was drawn from the inferior vena cava to measure serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Liver tissue was quickly removed and weighed. One part of the tissue was fixed in 4% formaldehyde for the histopathological examination, and the other part was immediately frozen in liquid nitrogen and stored under -80°C for determination of malondialdehyde (MDA), superoxide dismutase (SOD) and Na⁺-K⁺-ATPase.

Blood sampling and analysis
Blood samples were obtained and separated by centrifugation (1500 rpm, 20 min). Activity changes of serum ALT and AST were measured using a serum analyzer (Cobas-Mira Plus; Roche Manheim, Germany).

Determination of oxidative stress markers
MDA level and SOD activity were measured spectrophotometrically using the corresponding kits (Nanjing Jiancheng Biotechnology Institute, Nanjing, China), respectively. Liver specimens were homogenized and treated in accordance with the manufacturer’s recommendations. The results were expressed as nmol/mg protein for MDA, and U/mg protein for SOD.

Measurement of Na⁺-K⁺-ATPase activity levels
Na⁺-K⁺-ATPase activity in liver specimens was measured using an ATPase Assay Kit (Nanjing Jiancheng Biotechnology Institute, Nanjing, China) according to the manufacture’s protocol. Na⁺-K⁺-ATPase activity was measured based upon the principle of inorganic phosphate measurement that was decomposed by adenosine triphosphate [24]. Changes of enzymatic activity indirectly indicated membrane damage or not. Na⁺-K⁺-ATPase activity was expressed as μmolPi/mg protein/h.

Histopathological analysis
After being fixed in 4% formaldehyde solution, the tissue samples were embedded in paraffin, cut into 5-μm-thick sections, and stained with hematoxylin-eosin (HE). The histological changes after repeated +Gz exposure were graded using Suzuki’s criteria [25]. There were three features to assess the morphometric parameters: sinusoidal congestion, hepatocyte necrosis, and ballooning degeneration, graded from 0 to 4. A specific grading method was introduced: 0, none; 1, minimal congestion and ballooning degeneration as well as single cell necrosis; 2, minor congestion and ballooning degeneration as well as <30% lobular necrosis; 3, moderate congestion and ballooning degeneration as well as 30%-60% lobular necrosis; 4, severe congestion and ballooning degeneration as well as >60% lobular necrosis. The pathological changes were observed under microscope by an experienced blinded histologist.

Statistical analysis
The data was expressed as the mean ± SD. The unpaired t-test was used to compare low G preconditioning group and +10 Gz/5 min group. SPSS 13.0 software (SPSS, Chicago, IL, United States) was involved for data analysis, and P < 0.05 indicated significant difference.

RESULTS
Low G preconditioning reduced hepatocellular damage
Plasma ALT and AST levels were measured to assess liver damage at 0 and 6 h after exposure. ALT and AST values in the BC group were 46.7 ± 4.6 IU/L and 110.6 ± 7.4 IU/L, respectively. In group LG or group 10G, ALT and AST levels were higher than those in BC group (P < 0.05 BC vs 10G) at 0 h after exposure, respectively. The rats in LG group showed lower ALT and AST levels than those in 10G group at 0 h after exposure (P < 0.05, LG vs 10G). BC: Blank control.
structure in the LG group (Figure 2C; Suzuki’s score = 2.28 ± 0.16). At 6 h after exposure, hepatocyte edema became lighter, and liver lobule structure was arranged in a more orderly manner in the 10GS group (Figure 2E; Suzuki’s score = 2.53 ± 0.25; \( P < 0.01 \)).

There was no significant difference between 0 and 6 h after exposure in the LG group (Figure 2B and D; Suzuki’s score = 2.28 ± 0.16 vs 2.31 ± 0.14; \( P < 0.01 \)). BC: Blank control.

To analyze the extent of hepatocyte injury induced by high +Gz acceleration, liver sections were stained with HE at 0 and 6 h after exposure (Figure 2). No significant injury was found in the blank control group (Figure 2A; Suzuki’s score = 2.12 ± 0.13). At 0 h after exposure, there was a disorderly hepatic sinus cord-like structure associated with hepatocyte edema in the +10 Gz/5 min (10G) group (Figure 2B; Suzuki’s score = 3.23 ± 0.37). In sharp contrast, there was regular liver lobule structure in the low G preconditioning (LG) group (Figure 2C; Suzuki’s score = 2.28 ± 0.16). At 6 h after exposure, hepatocyte edema became lighter, and liver lobule structure had orderly arrangement in the 10G group (Figure 2E; Suzuki’s score = 2.53 ± 0.25; \( P < 0.01 \)). There was no significant difference between 0 and 6 h after exposure in the LG group (Figure 2C and D; Suzuki’s score = 2.28 ± 0.16 vs 2.31 ± 0.14; \( P < 0.01 \)). BC: Blank control.

**Low G preconditioning protected hepatocytes from damage of oxidative stress**

To assess oxidative stress effect on hepatocytes induced by +Gz exposure, MDA and SOD were measured at 0 and 6 h after exposure. The MDA level in the BC group was 1.14 ± 0.25 nmol/mgprot. At 0 and AST levels than those in the 10G group at 0 h after exposure (\( P < 0.05 \)). Group LG displayed normal ALT and AST levels at 6 h after exposure (Figure 1). These results demonstrate that low G preconditioning had a protective effect on liver function in rats after high G stress.

Figure 2 Pathological changes in the liver tissue at 0 and 6 h after +Gz exposures in the blank control group, low G preconditioning group and +10 Gz/5 min group. No significant injury was found in blank control group (A; Suzuki’s score = 2.12 ± 0.13). At 0 h after exposure, there was disorderly hepatic sinus cord-like structure associated with hepatocyte edema in +10 Gz/5 min (10G) group (B; Suzuki’s score = 3.23 ± 0.37). In sharp contrast, there was regular liver lobule structure in low G preconditioning (LG) group (C; Suzuki’s score = 2.28 ± 0.16). At 6 h after exposure, hepatocyte edema became lighter, and liver lobule structure had orderly arrangement in 10G group (E; Suzuki’s score = 2.53 ± 0.25; \( P < 0.01 \)). There was no significant difference between 0 and 6 h after exposure in LG group (C and D; Suzuki’s score = 2.28 ± 0.16 vs 2.31 ± 0.14; \( P < 0.01 \)). BC: Blank control.
h after exposure, levels of MDA activity in the LG and 10G groups were 1.56 ± 0.05, 1.99 ± 0.14 nmol/mgprot, respectively, which were higher than that of the blank control group (P < 0.05). However, MDA level in liver tissue in the LG group was lower than that in the 10G group at 0 h after exposure (P < 0.05, LG vs 10G). MDA level in liver tissue in LG group was lower than that in 10G group at 0 h after exposure. There was no significant difference between MDA level in liver tissue of LG and 10G groups at 6 h after exposure (P > 0.05, Figure 3A). Compared with blank control group, liver tissue superoxide dismutase (SOD) level in LG or 10G group reduced significantly at 0 h after exposure (P < 0.05, vs BC). Compared to 10G group, SOD level was higher in LG group at 0 h after exposure (P < 0.05, LG vs 10G); C: The Na⁺-K⁺-ATPase activity in LG group was higher than that in 10G group at 0 h after exposure (P < 0.05, LG vs 10G). BC: Blank control.

**DISCUSSION**

With the progress of aviation science and technology, maneuverability of the fighter plane has been improved to a large extent. Modern aircrafts are capable of generating positive acceleration of +9 Gz range and +6 Gz/s rapid onset rate which is sustained for 15–45 s, which may exceed the human body’s physical capabilities [26,27]. More attention should be paid to pilots’ health and flight safety.

In clinical practice, IPC is a surgical tactic to increase tissue tolerance and reduce ischemia-reperfusion injury (I/R) [4,28]. Several studies support the safety and efficacy of IPC against liver IR [29,30]. During flight, direct action and stress response caused by repeated +Gz exposure may cause liver I/R injury. Several anti-G measures have been adopted
to reduce organism damage and build G tolerance, such as anti-G suit\textsuperscript{31}, anti-G straining maneuvers and positive pressure breathing\textsuperscript{32}, tilt-back seat\textsuperscript{33}, and comprehensive protection measures\textsuperscript{34}. It is worth mentioning that centrifuge training is an important way of improving the strength and stamina of pilots\textsuperscript{35}. Low G training might be a better way to help build endurance. In the field of gravitation physiology, other studies have shown that low G training could increase reserves of circulatory system and elevate the G tolerance of pilots\textsuperscript{36}. In the preliminary experiments, it has been demonstrated that long-term exposure to the +4 G environment shows no harmful effects on liver morphology, which is the basis of selecting +4 G as the preconditioning condition in this study (data is not shown). The liver is a vital organ in the body. Liver injury after high +Gz exposure may be life threatening. Hence, we carried out the study to ascertain whether low G training could reduce liver injury induced by high +Gz exposure.

Both ALT and AST are markers of hepatic damage after +Gz exposure. Our results indicated that the rats in the LG group had lower serum ALT and AST level than those in the 10G group. Thereby, low G preconditioning was able to reduce liver injury induced by high +Gz exposure.

MDA is used widely as a sensitive marker of oxidative stress\textsuperscript{37}. In our study, hepatic MDA in the LG group was lower compared to the 10G group. Furthermore, SOD activity was significantly decreased after +10 Gz/5 min exposure, indicating that liver tissue was vulnerable to oxidative damage. Our results showed that low G preconditioning may reduce the oxidative stress caused by high +Gz exposure and attenuate subsequent tissue damage. Na\textsuperscript{+}-K\textsuperscript{+}-ATPase activity decreased significantly in liver tissue after +Gz exposures compared to the blank control group. Nevertheless, Na\textsuperscript{+}-K\textsuperscript{+}-ATPase activity in the LG group was significantly higher than that in the 10G group at 0 h after exposure, further supporting that low G preconditioning improved hepatic energy metabolism. Morphologically, our study of rat liver in the +Gz exposure model demonstrated that low +Gz preconditioning could reduce hepatocyte injury.

In summary, low G preconditioning is protective for liver injury induced by high +Gz exposure in rats, and the precise mechanism includes decrease of oxidative stress, preservation of hepatic energy metabolism and improvement of cellular morphology.

**REFERENCES**

1. Ishida T, Yarimizu K, Gute DC, Korthuis RJ. Mechanisms of ischemic preconditioning. Shock 1997; 8: 86-94 [PMID: 9261897 DOI: 10.1097/00000658-199708000-00003]
2. Kharbanda RK, Peters M, Walton B, Kattenhorn M, Mullen M, Klein N, Vallance P, Deanfield J, MacAllister R. Ischemic preconditioning prevents endothelial injury and systemic neutrophil activation during ischemia-reperfusion in humans in vivo. Circulation 2001; 103: 1624-1630 [PMID: 11273988 DOI: 10.1161/01.CIR.103.12.1624]
3. de Groot PC, Thijsen DH, Sanchez M, Ellenkamp R, Hopman MT. Ischemic preconditioning improves maximal performance in humans. Eur J Appl Physiol 2010; 108: 141-146 [PMID: 19760432 DOI: 10.1007/s00421-009-1195-2]
4. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. Circulation 1986; 74: 1124-1136 [PMID: 3769170 DOI: 10.1161/01.CIR.74.5.1124]
5. Gürke L, Marx A, Sutter PM, Frentzel A, Salm T, Harder F, Seelig J, Heberer M. Ischemic preconditioning improves post-ischemic skeletal muscle function. Am Surg 1996; 62: 391-394 [PMID: 8651570]
6. Sang H, Li J, Liu J, Wang Z, Hao T, Sun J, Xiong L. Preconditioning with +Gz acceleration (head-to-foot inertial load) produces neuroprotection against transient focal cerebral ischemia in rats. Neurosci Lett 2008; 445: 78-82 [PMID: 18778750 DOI: 10.1016/j.neulet.2008.08.067]
7. Cochran J, Williams BT, Banerjee A, Harken AH, Burke TJ, Cairns CB, Shapiro JL. Ischemic preconditioning attenuates functional, metabolic, and morphologic injury from ischemic acute renal failure in the rat. Ren Fail 1999; 21: 135-145 [PMID: 10088174 DOI: 10.3109/0886022990966978]
8. Clavien PA, Yadav S, Sindram D, Bentley RC. Protective effects of ischemic preconditioning for liver resection performed under inflow occlusion in humans. Ann Surg 2000; 232: 155-162 [PMID: 10903590 DOI: 10.1097/00000658-200000800-00001]
9. McCallion K, Wattanarisachigoon S, Gardiner KR, Fink MP. Ischemic preconditioning ameliorates ischemia- and reperfusion-induced intestinal epithelial hyperpermeability in rats. Shock 2000; 14: 429-434 [PMID: 11049105 DOI: 10.1097/0000024382-200001404-00002]
10. Ren Z, Cui G, Lu H, Chen X, Jiang J, Liu H, He Y, Ding S, Hu Z, Wang W, Zheng S. Liver ischemic preconditioning (IPC) improves intestinal microbiota following liver transplantation in rats through 16s rDNA-based analysis of microbial structure shift. PLoS One 2013; 8: e75950 [PMID: 24098410 DOI: 10.1371/journal.pone.0075950]
11. Curtin RT, Peng XX, Lemasters JJ. Ischemic preconditioning of rat livers from non-heart-beating donors decreases parenchymal cell killing and increases graft survival after transplantation. HPB Surg
Shi B et al. Low G preconditioning reduces liver injury in rats

J Exp Physiol Cogn Med Sci 2012; 65: 105-116 [PMID: 6251506]

Lee JA, Choi JW, In JH, Jung HS, Kim YS, Jeon YS, Kang YJ, Kim DW, Lim YG, Park JH, Joo JD. Hepatic ischemic preconditioning provides protection against distant renal ischemia and reperfusion injury in mice. J Korean Med Sci 2012; 27: 547-552 [PMID: 22563222 DOI: 10.3346/jkms.2012.27.5.547]

Figueira ER, Rocha-Filho JA, Nakatani M, Buto MF, Tatede ER, Andre VO, Cecconello I, D’Albuquerque LA. Hepatic ischemic preconditioning increases portal vein flow in experimental liver ischemia reperfusion injury. Hepatobiliary Pancreat Dis Int 2014; 13: 40-47 [PMID: 24463078 DOI: 10.1016/S1999-3872(14)60005-9]

Martin DS, D’Aunno DS, Wood ML, South DA. Repetitive high G exposure is associated with increased occurrence of cardiac valvular regurgitation. Aviat Space Environ Med 1999; 70: 1197-1200 [PMID: 10596774]

Siitonen SL, Kauppinen T, Leino TK, Vanninen E, Kuronen P, Länsimies E. Cerebral blood flow during acceleration in flight measured with SPECT. Aviat Space Environ Med 2003; 74: 201-206 [PMID: 12650265]

Cao XS, Sun XQ, Wei YB, Yao YJ, Feng DY, Yang CB. Effects of repeated lower g exposures on high G-induced memory and balance changes in rats. Space Med Med Eng (Beijing) 2004; 17: 16-19 [PMID: 15005111]

Cao XS, Wu XY, Sun XQ, Liu TS. Effects of low gravity preconditioning on rat learning and memory impairment induced by high gravity exposure. Di Yi Jun Yi Da Xue Xue Bao 2005; 25: 212-215 [PMID: 15699009]

Li JS, Sun XQ, Wu XY, Rao ZR, Liu HL, Xie XP. Influences of repeated lower +Gz exposures on high +Gz exposure induced brain injury in rats. Space Med Med Eng (Beijing) 2002; 15: 339-342 [PMID: 12449138]

Fu FY, Zhan H, Zhang Z, Li T, Xin YM, Wei SH. Effects of low-g preconditioning on contractile ability of left ventricle and contents of endothelin and prostanoyline in myocardium of rats after repeated +10 Gz stress. Space Med Med Eng (Beijing) 2003; 16: 414-417 [PMID: 15008190]

Zhang Z, Zhan H, Lu JY, Xin YM, Li T, Zhang QJ. Effects of repeated high +Gz exposure on several enzyme activities in cardiomyocytes in rats and some protective measures. Space Med Med Eng (Beijing) 2001; 14: 410-413 [PMID: 11887894]

Starr S, Hand H. Nursing care of chronic and acute liver failure. Nurs Stand 2002; 16: 47-54; quiz 55-56 [PMID: 12216300]

Zakaria ZA, Rosiie MS, Somchit MN, Zuraini A, Sulaiman MR, Teh KL, Salleh MZ, Long K. Hepatoprotective activity of dried- and fermented-processed virgin coconut oil. Evid Based Complement Alternat Med 2011; 2011: 142739 [PMID: 2131840 DOI: 10.1155/2011/142739]

Feng S, Wang Q, Wang H, Peng Y, Wang L, Lu Y, Shi T, Xiong L. Electroacupuncture pretreatment ameliorates hypergravity-induced impairment of learning and memory and apoptosis of hippocampal neurons in rats. Neurosci Lett 2010; 478: 150-155 [PMID: 20457216 DOI: 10.1016/j.neulet.2010.05.006]

Reading HW, Isbir T. The role of cation-activated ATPases in transmitter release from the rat iris. Q J Exp Physiol Cogn Med Sci 1980; 65: 105-116 [PMID: 6251506]

Suzuki S, Toledo-Pereyra LH, Rodriguez FJ, Cevaldo D. Neutrophil infiltration as an important factor in liver ischemia and reperfusion injury. Modulating effects of FK506 and cyclosporine. Transplantation 1993; 55: 1265-1272 [PMID: 7685932 DOI: 10.1097/00007890-199306000-00011]

Jones DR. A review of central nervous system effects of G-induced loss of consciousness on volunteer subjects. Aviat Space Environ Med 1991; 62: 624-627 [PMID: 1898296]

Öztürk C, İlbasmış MS, Akın A. Cardiac responses to long duration and high magnitude +Gz exposure in pilots: an observational study. Anadolu Kardiyol Derg 2012; 12: 668-674 [PMID: 22968302 DOI: 10.5152/akd.2012.219]

Yoshizumi T, Yanaka K, Soejima Y, Maeda T, Uchiyama H, Sugimachi K. Amelioration of liver injury by ischaemic preconditioning. Br J Surg 1998; 85: 1636-1640 [PMID: 9876065 DOI: 10.1046/j.1365-2168.1998.00917.x]

Yadav SS, Sindram D, Perry DK, Clavien PA. Ischemic preconditioning protects the mouse liver by inhibition of apoptosis through a caspase-dependent pathway. Hepatology 1999; 30: 1223-1231 [PMID: 10534344 DOI: 10.1002/hep.105300513]

Sindram D, Rüdiger HA, Upadhyag SM, Strasberg SM, Clavien PA. Ischemic preconditioning protects against cold ischemic injury through an oxidative stress dependent mechanism. J Hepatol 2002; 36: 78-84 [PMID: 11804668 DOI: 10.1016/S0168-8278(01)00229-X]

Stevenson AT, Lythgoe DT, Darby CL, Devlin JM, Connelly DM, Scott JP. Garment fit and protection from sustained +Gz acceleration with ‘full-coverage’ anti-G trousers. Aviat Space Environ Med 2013; 84: 600-607 [PMID: 23745288 DOI: 10.3357/ASEM.3487.2013]

Eiken O, Kölegård R, Bergsten E, Grönkvist M. G protection: interaction of straining maneuvers and positive pressure breathing. Aviat Space Environ Med 2007; 78: 392-398 [PMID: 17484342]

Burns JW. Prevention of loss of consciousness with positive pressure breathing and supinating seat. Aviat Space Environ Med 1998; 59: 20-22 [PMID: 3281646]

Cohen MM. Combining techniques to enhance protection against high sustained accelerative forces. Aviat Space Environ Med 1983; 54: 338-342 [PMID: 6847571]

Jing X, Wu P, Liu F, Wu B, Miao D. Guided imagery, anxiety, heart rate, and heart rate variability during centrifuge training. Aviat Space Environ Med 2011; 82: 92-96 [PMID: 21329022 DOI: 10.3357/ASEM.2282.2011]

Wojtkowiak M, Markiewicz L, Kempa G. Effect of low acceleration simulator training on +Gz acceleration tolerance level. J Gravit Physiol 1998; 5: P31-P32 [PMID: 11542353]

Takayama F, Egashira T, Kudo Y, Yamanaka Y. Chemiluminescence and reperfusion injury in the liver of rats. J Gravit Physiol 2011; 18: P31-P32 [PMID: 11542353]

Wojtkowiak M, Markiewicz L, Kempa G. Effect of low acceleration simulator training on +Gz acceleration tolerance level. J Gravit Physiol 1998; 5: P31-P32 [PMID: 11542353]
