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苏俄太空动物实验研究发展历程

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【摘要】 太空动物实验研究是人类航天科技发展中至关重要的一环。二十世纪以来,前苏联和俄罗斯在人类航天事业取得诸多重大成就,离不开太空动物实验的巨大贡献。太空动物实验可以评估地球生物深入探索太空的可能性,加速人类太空探索时代的来临。一批批"动物宇航员"被航天飞行器送上太空,成为了人类探索太空的"先驱者"以及航天事业发展的里程碑,为载人航天和空间站建设事业奠基。因此,本文就二十世纪以来前苏联和俄罗斯的太空动物研究的发展历程进行综述。

【关键词】 苏联;俄罗斯;航天;动物实验
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A review of space animal experiments conducted by the former Soviet Union and Russia

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【Abstract】 Animal experiments have always been an important component of space exploration. Since the 20th century, the former Soviet Union and Russia have achieved major advances in the human space industry, which would not have been possible without the knowledge gained from animal experiments. Animal experiments were initially used to evaluate the possibility of humankind exploring space. "Animal astronauts" were sent into space as the "pioneers" of human space exploration. Such events were milestones in the development of the aerospace industry and greatly contributed to the construction of crewed spacecraft and space stations. This article reviews the development of space animal experiments in the former Soviet Union and Russia since the 20th century.

【Keywords】 former Union of Soviet Socialist Republics; Russia; space flight; animal experiments
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太空动物实验研究为人类开辟探索太空的道路保驾护航。人类太空探索早期,研究人员用太空动物实验评估载人航天的安全性与可能性,之后又利用太空动物实验对宇航员建立空间站的安全可行性和太空长期作业适应性进行预测。“动物宇航员”作为人类探索太空“先驱者”,为载人航天和太空空间站建设事业做出巨大贡献。

上世纪,苏维埃社会主义共和国联盟(以下简称苏联)处于人类航天事业发展领先地位。1957 年,苏联成功发射世界第一颗人造地球卫星,拉开了太空航行时代序幕。随后,苏联又成功发射了世界第一个月球探测器、载人飞船和火星探测器。截至 1988 年,苏联共发射各类航天器 2461 个,居世界首位,同时也实现了世界首个进入太空的动物、首次载人航天、首位女宇航员、首次太空舱外活动等创造性成就[1-2]。1992 年俄罗斯联邦航天局(Russian Federal Space Agency, RFSA)成立并承接苏联太空计划,继续在人造卫星和太空航行方面保持领先优势。1998 年俄罗斯和美国等 16 个国家共同参与国际空间站建设工作,并支持建造了“曙光号”功能舱、“星辰号”服务舱、“码头号”对接舱、“黎明号”实验舱等[3]。2011 年美国航天飞机全部退役后,俄罗斯的“联盟-FG”等运载火箭继续承担国际空间站运输任务。

1 太空动物实验发展历程

苏联和俄罗斯的太空探索过程中,实验生物被送往 100 ~ 500 公里亚轨道和近地轨道以及深空“旅行”,用以检验地球生物在航天环境生存的可行性和安全性[4],为载人航天奠定科学基础[5-6],(见表 1)。

1.1 高空、亚轨道动物实验预演

1917 年之前,苏联科学家就开始探讨太空航行的理论和实现途径问题。为评估地球生物太空飞行可能性,自 1951 年起苏联空军航空医学研究所开展高空物理火箭生物实验,同年 7 月 2 只犬跟随 R-1V 型火箭成功进入亚轨道。其后 2 个月,苏联共发射 6 枚火箭搭载犬进行实验。因缺乏动物逃生系统而饱受诟病,苏联多次探索后通过 R-1D 上弹射逃生系统让 2 条犬成功返航,标志着第一代航天逃生系统研制取得重大进展[6]。

1.2 近地轨道动物实验预演

第二次世界大战后,美、苏“太空竞赛”加速了全球载人航天计划进程[52]。为了研究安全的载人航天飞行所必要的客观条件,苏联率先发射搭载“太空犬”Лайка 的人造卫星 Sputnik 2 号穿越“卡门线”,虽然 Лайка 因加压舱过热而丧生,它仍然标志着空间生物学的开端[1,6]。

随着生命维持系统进步,1960 年 2 条犬搭乘 Sputnik-5 号人造卫星完成了 17 次环绕地球轨道飞行后安全返回。1966 年为研究辐射带对宇航员的影响,2 条犬在近地轨道破纪录飞行 22 d 后成功返航[6]。

1.3 太空在轨生物载荷实验

1973 ~ 1997 年,前苏联和俄罗斯在 11 个 Bion 系列飞船中通过 12 只猴子和 212 只大鼠和若干其它生物研究动物的失重和放射生物学实验[53]。2005 年开始,Bion-M 系列生物卫星实验用于研究人造重力和长期辐射对生物健康影响,为建立可长期作业的太空空间站和更远距离星球探测做准备[5,53]。俄罗斯计划将恒河猴送往火星,通过前庭-动眼相互作用系统中揭示规律性,用以研究宇航员视线的中心区域部署视觉目标。

2 太空动物实验的动物品系

相比于美国使用灵长类动物黑猩猩作为“宇航员”,苏联对太空实验动物的选择首先基于可控性与易得性。苏联在早期测试航天系统安全性与载人航天可行性时选择了雌性健康流浪犬,因为犬类便于训练,18 月龄 ~ 6 岁的小型流浪犬普遍易得,可适应狭小环境,对航天艰苦端环境适应性强[6]。

随着航天装置与实验科技发展,“动物宇航员”品系更加丰富。啮齿类大鼠、小鼠、沙鼠被广泛用于研究太空环境对代谢、脏器、细胞、骨骼影响[23-25,54-57];日本鹌鹑、非洲爪蟾及大鼠的胚胎主要被用于研究胚胎发育重力感应[58-60];爬行动物如草原龟、海龟、壁虎等主要被用于检测失重适应性[9-10,30,32-35];蝾螈被用于研究细胞增殖变化[61];恒河猴、黑腹果蝇、蚕被用于研究昼夜节律、发育过程、遗传及环境适应等[6,43-48,62]。

表 1　前苏联与俄罗斯有公开报道的太空生物运载情况

Table 1　Publicly reported space bio-loading situations in the Soviet Union and Russia

太空动物实验阶段 Phase of space animal experiments	研究对象 Animal subject	实验舱运载火箭发射时间(年) Launch time (Years)	实验舱运载载体 Launch vehicle	动物情况 Animal information
高空、亚轨道动物实验预演阶段 High-altitude or suborbital animal experiment rehearsal phase	犬 Dogs	1951 ~ 1957	R-1、R-2 系列火箭[6] R-1, R-2 series rockets	20 次(失败 3 次),每次 2 只犬 20 times(failed 3 times), 2 dogs at a time
近地轨道动物实验预演阶段 Low-earth orbit animal experiment rehearsal phase	犬 Dogs	1957	Sputnik(伴侣)-2/R-7 火箭[6] Sputnik-2/R-7 rockets	雌,Лайка Female, Лайка
		1958 ~ 1960	R-5A、R-2A、R-7 火箭[6] R-5A, R-2A, R-7 rockets	未进轨道 10 次(失败 1 次),每次 2 只犬 Not in orbit 10 times, failed 1 time, 2 dogs at a time
		1960 ~ 1966	R-7 火箭;Vostok(东方)-3/Космос(宇宙)-110 卫星式飞船[6] R-7 rocket. Voskho-3/Cosmos-110 Sputnik satellite spacecraft	轨道飞行 7 次(失败 2 次),每次 1 ~ 2 只犬 In orbit 7 times, failed 2 times, 1 ~ 2 dogs at a time
	兔 Domestic rabbits	1959	未知[7] Unknown	2 次,每次 1 只兔 2 times, 2 rabbits at a time
		1960	Sputnik-5 卫星式飞船[7] Sputnik-5 satellite spcecraft	
	大鼠 Rats	1960	Sputnik-5 卫星式飞船[7-8] Sputnik-5 satellite spacecraft	2 只大鼠 2 rats
		1960	Sputnik-6 卫星式飞船[6-8] Sputnik-6 satellite spacecraft	未知 Unknown
		1961	Sputnik-9 卫星式飞船[6-8] Sputnik-9 satellite spacecraft	
	小鼠 Mice	1960	Sputnik-5 卫星式飞船[7-8] Sputnik-5 satellite spacecraft	40 ~ 42 只小鼠 40 ~ 42 mice
	豚鼠 Cavy	1960	Sputnik-6 卫星式飞船[7-8] Sputnik-6 satellite spacecraft	未知 Unknown
		1961	Sputnik-9 卫星式飞船[7-8] Sputnik-9 satellite spacecraft	
	爬行动物 Reptiles	1968	Zond-5 探测器[6,9] Zond-5 detectors	2 只草原龟 2 prairie turtles
		1969	Zond-7 探测器[10] Zond-7 detectors	4 只海龟 4 turtles
	昆虫 Insects	1960	Sputnik-5 卫星式飞船[7-8] Sputnik-5 satellite spacecraft	15 瓶果蝇 15 vials of fruit flies
		1961	Vostok-2 Sputnik 卫星式飞船[11] Voskhod-2 Sputnik satellite spacecraft	酒蝇 Wine flies
		1968	Zond-5 探测器[12] Zond-5 detectors	257 个 D-32 系黑腹果蝇卵 257 the D-32 Drosophila melanogaster eggs
太空在轨生物载荷实验阶段 Space on-orbit bio-loading experiment phase	恒河猴 Rhesus monkey	1983 ~ 1996	Bion 6-11 生物卫星[6] Bion 6-11 biosatellites	6 次,每次 2 只 6 time, 2 monkeys at a time, *Macaca mulatta*
	大鼠 Rats	1973 ~ 1982	Космос-605、690、936、1129 号生物卫星[6,13-17] Cosmos-605、690、936、1129 biosatellite	分别搭载 45,30,30,30 只大鼠 Carried 45, 30, 30, 30 rats respectively
		1975 ~ 1989	Космос-782、1667、1887、2044、1669 生物卫星;Rocmoc-1669[6,18-21] Cosmos-782、1667、1887、2044、1669 biosatellite;Rocmoc-1669	SPF 级 Wistar 大鼠 SPF-Wistar rats
		1983	Космос-1514 生物卫星[6,22] Cosmos-1514 biosatellite	10 只 SPF 级 Wistar 孕鼠 10 pregnant SPF-Wistar rats

续表 1

太空动物实验阶段 Phase of space animal experiments	研究对象 Animal subject	实验舱运载火箭发射时间(年) Launch time (Years)	实验舱运载载体 Launch vehicle	动物情况 Animal information
太空在轨生物载荷实验阶段 Space on-orbit bio-loading experiment phase	沙鼠 Gerbils	2007	Foton-M3 科研卫星[23-24] Foton-M3 research satellite	35 只雄性蒙古沙鼠 35 male Mongolian gerbils
		2013	Bion-M1 生物卫星[25] Bion-M1 biosatellite	8 只蒙古沙鼠 8 Mongolian gerbils
	小鼠 Mice	2013	Bion-M1 生物卫星[26-27] Bion-M1 biosatellite	45 只雄性 C57BL/6 45 male C57BL/6 mice
		2017	国际空间站俄罗斯段[28] The Russian Segment of the ISS	21 ~ 24 d C57BL/6J 小鼠 21 ~ 24 d C57BL/6J mice
	禽类 Bird species	1979	Космос-1129 生物卫星[6,29-30] Cosmos-1129 Bion-5 biosatellite	日本鹌鹑胚胎 Japanese quail eggs
		1990 ~ 1999	"和平号"空间站[6,30-31] "Mir" space station	8 次成功孵化日本鹌鹑 8 successful hatchings of Japanese quail
	爬行动物 Crawler	2005 ~ 2013	Foton-M2、Foton-M3、Bion-M1 科研卫星[30,32-35] Foton-M2, Foton-M3, Bion-M1 research satellite	分别搭载 5,5,15 只厚趾壁虎 Carried 5, 5, 15 thick-toed geckos respectively
		2014	Foton-M4 科研卫星[30] Foton-M4 research satellite	5 只昼行壁虎 5 diurnal geckos, *Phelsuma ornata*
	两栖动物 Amphibians	1971	联盟-10 航天飞船[30] Soyuz-10 space shuttle	青蛙 Frogs, *Rana temporaria*
		1975 ~ 1993	联盟号、联盟-礼炮系列火箭 5 次, Bion-10 卫星[30] Soyuz, Soyuz-Salyut series rockets 5 times, Bion-10 biosatellite	非洲爪蟾 *Xenopus laevis*
		1990	"和平号"空间站[6] "Mir" space station	6 只青蛙 6 Frogs, *Litoria caerulea*
		1992 ~ 1998	Космос-2229 Bion-11 生物卫星[36-37] Cosmos-2229 Bion-11 biosatellite	成年欧非肋突螈 Adult newts, *Pleurodeles waltl*
		1996 ~ 1999	"和平号"空间站[38] "Mir" space station	欧非肋突螈胚胎 Newts embryos, *Pleurodeles waltl*
		2005 ~ 2007	Foton-M2、Foton-M3 科研卫星[39] Foton-M2, Foton-M3 research satellite	欧非肋突螈 *Pleurodeles waltl*
	鱼类 Fish	1974–1977	联盟、联盟-礼炮系列火箭 3 次[30] Soyuz, Soyuz-Salyut series rockets 3 times	斑马鱼 Zebrafish, Brachidanio rerio
		1975	Космос-782 生物卫星[30,40] Cosmos-782 biosatellite	鳉鱼卵 Killifish eggs, *Fundulus heteroclitus*
		1987	Космос-1887 生物卫星[41] Cosmos-1887 biosatellite	藻类-细菌-鱼类系统 Algo-bacterial cenosis-fish system
		2007	Foton-M3 科研卫星[42] Foton-M3 research satellite	26 条罗非鱼幼鱼 26 Tilapia larvae, *Oreochromis mossambicus*
	昆虫 Insects	1971 ~ 1979	Союз(联盟号)10,Космос-573、782、936、1129 人造卫星[43-47] Soyuz-10, Cosmos-573, 782、936、1129 satellites	黑腹果蝇 *Drosophila melanogaster*
		2014	Foton-M4 科研卫星[48] Foton-M4 research satellite	第三代 Canton S 黑腹果蝇 The third generation of Canton S, *Drosophila melanogaster*
		2014	国际空间站俄罗斯段[48] the Russian Segment of the ISS	第五代 Canton S 黑腹果蝇 The fifth generation of Canton S, *Drosophila melanogaster*
		1992	Космос-2229 生物卫星[49] Cosmos-2229 biosatellite	蚕 Silkworms, Bombyx mori *L.*
		2007	Foton-M3 科研卫星[50] Foton-M3 research satellite	缓步动物 Macrobiotus richtersi
		2013	Bion-M1 生物卫星[51] Bion-M1 biosatellite	甲壳类动物 Crustaceans
	软体动物 Mollusks	2005 ~ 2014	Foton-M2、M3 和 Bion-M1 科研卫星[39] Foton-M2, M3 and Bion-M1 research satellite	散大蜗牛和欧洲蜗牛 Helix lucorum and Helix aspera

3　太空动物实验装置

3.1　犬类

“太空犬”会穿上带有密封“犬袖”、树脂玻璃头盔的“太空服”，在环境控制室内设置摄像头、温湿度传感器等进行监测[2,6]。发明“弹射车”帮助返回故障时犬及设备通过降落伞逃生。随着绕地飞行时间延长，太空舱开始配备生命维持系统，包括空气再生、自动定时喂食、“太空厕所系统”等[6]。

3.2　啮齿动物

生物卫星 Foton-M3 使用自我维持生命支持系统(life support system, LSS)的 Kontur-L 模块装载可录像沙鼠铁笼，供给饲料及水[63-64]。生物卫星 Bion-M1 搭载的 Block Obespecheniya Soderzhaniya (BOS)装置由 Bion 计划中大鼠栖息模块改装[56]，提供 12 h 明暗循环及糊状饲料，每个单元可饲养 3 只小鼠，需单笼饲养时使用通风笼(GM 500)，由中央生命保障系统维持环境[56-57]。

3.3　卵生禽类(鹌鹑)

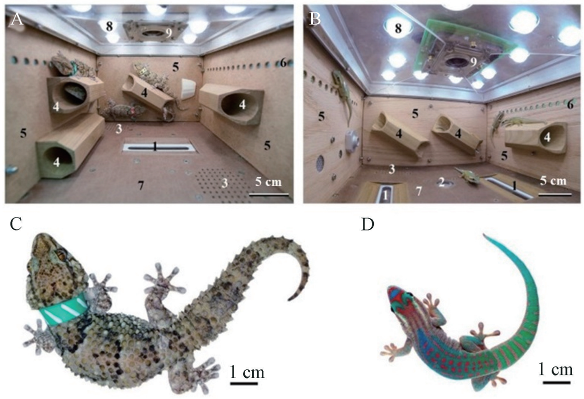
禽类生殖周期研究设备包括孵化器 Slovakian (1M-02 型)、含固定液培养皿和鸟巢[65]。生物卫星 Космос-1299 内部安装恒温恒湿孵化箱放置鹌鹑胚胎。“和平号”空间站使用陆地生物群落简化的自主封闭生态系统和胚胎存放装备(refrigerator stowage kit for eggs, RSKE)培养成年鹌鹑和鹌鹑胚胎[58,65-67]。

3.4　爬行动物(壁虎)

2005 ~ 2014 年进行了多项壁虎航天轨道实验用于检测其特异适应性[68]。Foton-M2 使用未提供再生空气、水与食物，温控 16.5℃ 的壁虎实验舱[32]，2007 年 Foton-M3 开始配置维生系统，提供水与食物，提高温控[35,69]。Bion-M1 增加了空气再生系统用于更久航行[21,70]。Foton-M4 搭载小型壁虎消耗小，未进行空气再生[71]见图 1。

3.5　昆虫(果蝇)

“联盟”10 号飞船将带有培养基和 D-32 黑腹果蝇的饲养管放置在小型搭载恒温器(Biotherm Ⅱ)里[43]。Foton-M4 航天飞机搭载的 BB-1F 设备含有 3 个 BB-2 模块(放置被动充氧饲养管，含有用于繁殖果蝇的营养介质：水、琼脂、糖、粗面粉、酵母、丙酸[48])。



注：A：厚趾壁虎及其实验生存舱(搭载于 Bion-M1 飞船)；B：花斑昼行壁虎及其实验生存舱(搭载于 Foton-M4 飞船)；C：雌性厚趾壁虎；D：雄性花斑昼行壁虎；1：料箱，2：水碗，3：加热区，4：壁虎橡木栖息管，5：生存舱内壁，6：通风口和废料存积处，7：纺织层压板，8：照明灯，9：摄像机和风扇；仅花斑昼行壁虎生存舱提供饲料和水。

图 1　Bion-M1 和 Foton-M4 壁虎及其实验生存舱[68]

Note. A. Hardboard RSB with thick-toed geckos (Bion-M1). B. Oak RSB with ornate day geckos (Foton-M4). C. Thick-toed gecko female. D. Ornate day gecko male. 1. Feedbox. 2. Water bowl. 3. Heating zones. 4. Oak tubular shelter. 5. RSB wall. 6. Ventilation and waste collection vents. 7. Textile laminate floors. 8. LEDs. 9. Video camera and a fan. Only the RSB for ornate day geckos was equipped with feedbox and water bowl.

Figure 1　Research and support block (RSB) and geckos for Bion-M1 and Foton-M4

4　太空动物实验研究

4.1　犬

候选犬航行前通过模拟实验舱训练适应空间限制、撞击声与离心机旋转及极端情况。“太空犬”Лайка 的皮下、心脏、颈动脉和胸腔内被植入生理监测仪，并通过心电图(胸前导联)、血压、呼吸频率和运动活动监测其生命体征[3]。加速升空后 Лайка 多项生理参数下调，心率倍增，入轨后恢复，表明它对发射和太空环境有足够耐受性[2]。苏联计划 1 周后对 Лайка 实施安乐死，但由于降温系统故障，惊吓、压力与高温导致 Лайка 脉搏骤增，器官衰竭而亡[5-6]。早在此次航行前，国际舆论曾强烈谴责牺牲 Лайка 进行太空生物实验。苏联由此倍加重视实验动物返回舱的建设。随着航天安全设施进步，后续太空舱开始搭载返回系统，并于 1958 年成功让 2 只犬从“卡门线”以上安全返航。1960 年 Strelka 成为第一批绕地飞行后返航的“太空犬”，它返回后

生育的 6 只幼崽中 Pushinka 被送给美国时任总统肯尼迪,并成功诞下 4 只幼崽[6]。

4.2　啮齿动物(大鼠)

生物卫星 Космос-605、782、1129、1667、1887、2044 号上开展大鼠实验研究短期太空暴露骨骼、肌肉、脏器等变化。组织形态学检查发现多个飞行组大鼠出现骨骼钙、磷流失,基质蛋白质含量下降,胫骨近端干骺、腰椎海绵体骨减少等骨质疏松症早期迹象[16,18,72-77]。观察膈肌突触区肌纤维、神经肌肉连接和微血管等超微结构组织,发现失重对膈肌结构破坏性变化主要出现太空飞行早期[19,78]。Космос-1669 搭载实验发现基于破坏性再生的肌肉突触重组主要表现在比目鱼肌[79]。此外,长期太空飞行、急性应激等因素导致淋巴细胞减少退化,胸腺中核碎屑积累及脾中性粒细胞浸润,骨髓中红细胞、粒细胞和巨噬细胞祖细胞数量减少[18,21]。暴露于超负荷重力后,大鼠胰腺出现血管过度填充,外分泌细胞减少等代偿适应性和破坏性变化[80]。近期国家空间站研究发现失重时皮肤肥大细胞分泌活性增加,拮抗细胞间信号传导,减弱胶原纤维形成强度[28]。

4.3　啮齿动物(小鼠)

Bion-M1 小鼠实验选用成年雄性 C57BL/6N 小鼠分为飞行、地面对照和两个实验室对照组,每组包括体内外组[26,56]。采用自动数据采集系统(TSE Pheno Master)和植入式遥测技术监测;一部分返回后进行记忆和学习、前庭功能、体力活动等行为测试;一部分即时采集皮肤、血液、大脑、眼部、骨骼、肌肉及脏器进行形态学、免疫组织化学、生物化学等多种分子生物学分析;一部分恢复期后通过微原子学评估骨微观结构和质量等[26-27,56-57,81-86]。结果发现在轨飞行诱导关节软骨蛋白聚糖水平降低,软骨细胞及细胞外基质合成相关基因表达下调,出现软骨分解早期症状[81],骨细胞死亡导致骨衰老特征出现,恢复期后成骨细胞数增加、活性恢复,但骨恢复不明显[27]。椎体骨体积分数、骨密度和小梁厚度显著降低[82]。股骨肌肉萎缩严重[83],诱导肌纤维凋亡[27,81],通过 α-肌动蛋白-1、α-肌动蛋白-4 启动信号通路影响心肌结构等[84-85]。同时检测出微重力易感基因[86]。胰腺出现外分泌颗粒堆积和胰岛肥大[57]。证实了微重力与运动缺乏和糖尿病表现相关。动物在喂食附近出现高度聚集行为,推测食物供应装置故障导致 50%小鼠死亡[56]。

4.4　啮齿动物(沙鼠)

Foton-M3 任务中沙鼠分为飞行、地面同步对照两组,采用形态、细胞、组织化学等方法对心肌、肝叶、空肠、胫骨进行分析。12 d 飞行后沙鼠心肌亚型与二级结构改变,肌联蛋白 N2BA、肌联蛋白磷酸化增加,对离体肌动球蛋白 ATP 酶激活减少[87]。肝小叶各功能区糖原水平降低,静脉多糖分布降低,肝细胞高糖原异质性,细胞内糖原形态改变,代谢紊乱[23];肝细胞质扩大,肝实质细胞质 RNA 含量降低[88],出现功能代偿性无丝分裂加剧和双核肝细胞增加[89]。胃粘膜出现微灶性病变,腺体营养不良,粘液屏障、解离功能减退[90]。空肠粘液脂质细胞种类减少[91],粘膜绒毛、棱柱形上皮、杯状细胞结构改变,间质屏障功能减退[92]。胫骨纵向生长抑制和早期骨质减少,微重力影响骨形成减慢导致骨量损失[93]。

4.5　卵生禽类(鹌鹑)

“和平号”空间站搭载实验研究微重力对成年日本鹌鹑和胚胎发育影响。成年鹌鹑能较快适应太空环境并学会无重力飞行和正常进食。检测鹌鹑胚胎发育中期测量飞行组与地面对照组胚胎的胚胎,眼睛,骨骼发育情况差异[65,94]。太空飞行没有影响发育胚胎的钙利用[67,95],部分正常发育孵化[66,94,96],但矿物质供应不足使软骨细胞钙化以及骨化延迟[94],甲状腺发育迟缓[97],肾上腺皮质脂肪积累,胆固醇转化降低,类固醇生成受阻[66],食物摄入减少导致小肠功能发育延迟[98]。鹌鹑幼仔无法稳定站立自由吞咽,最后被执行安乐死[5,99]。

4.6　爬行动物(壁虎)

Foton-M2 到 M4、Bion-M1 均采用 4 ∶ 1 的雌雄比例,Foton-M4 选用小型昼行壁虎进行行为观测,其他实验中选用体型较大的夜行厚趾壁虎研究行为、血液、内脏、中枢神经系统、刚毛、骨骼、排泄物等[30,32-35]。

飞行恢复期后组织学,免疫组织化学和 X 射线显微计算机断层扫描(micro-computer tomography, MCT)检测骨密度和骨结构等[33]。Foton-M 系列和 Bion-M1 卫星上所有实验中壁虎体重均下降,推断环境温度对新陈代谢影响较大。Foton-M2 飞行组壁虎外肝区出现肝细胞器官萎缩和肝细胞退化,Foton-M3 则无;与对照组动物相比,Foton-M3 飞行、对照组动物的糖原减少是缺乏营养导致的正常反应[68]。Foton-M2 和 M3 粪便糖皮质激素水平升高,

Foton-M3 壁虎大脑中神经胶质破坏主要位于皮质和上丘脑[33]。Foton-M2 飞行后,壁虎红细胞和暗核粒细胞减少,小肠高血球细胞含量升高[33,68]。推断 Foton-M2 栖息条件导致壁虎骨质变化[32]。Foton-M3 飞行组缺乏营养导致小肠壁厚度增加[68]。Foton-M2 和 M3 飞行壁虎仍保持正常生理情况,其生物学特性帮助它们较好地适应太空飞行条件[69]。Bion-M1 飞行组前庭小脑浦肯野细胞发生可逆性变化[35]。肝重量与体重比略高,肝细胞糖原减少,部分壁虎外周区有胆汁外流困难并伴有坏死,胆囊中出现粘性实质,但胃肠道结构没有显著改变[68]。微重力引起飞行组肺部毛细血管高度充血和内皮细胞空泡化,肺间隔壁数增加,肺充血等[33]。

4.7 昆虫(果蝇)

"联盟"10 号飞船搭载的黑腹果蝇雌性死亡比率大,与性别相关的隐性致死与配子发生阶段有关,卵母细胞阶段对太空飞行因素的敏感性高[43]。Zond-5、Космос-573 上果蝇也发现性别相关隐性致死性突变[12,44]。Foton-M4 上培育的第三代果蝇飞行结束后 0 ~ 1、12、24 h 采集 BB-2 区生物材料,其余培养成虫繁育第四代并在国际空间站孕育第五代。飞行结束进行转录组学研究,发现从缺氧到常氧的转变以及失重增加了果蝇代谢基因和角质层成分转录,减少了形态、分化相关转录,微重力暴露导致以上基因转录变化更显著,从微重力到重力环境转变则情况相反[48]。

5 结语

太空动物实验在太空探索的安全可行性、太空环境对生物影响、长期太空环境作业影响等方面研究有着突出贡献,在航天事业发展中起着举足轻重的作用。太空动物的牺牲令人惋惜和敬佩,"首位太空乘客"犬 Лайка 意外丧生让苏联和国际航天更加重视动物实验安全及返回舱的建设,随着航天科技发展,人类也越来越重视太空实验动物权利。"太空动物"人文关怀也越来越受重视,前苏联与俄罗斯也通过纪念馆、书籍、邮票、歌曲纪念这些"太空小英雄"。

近年来国际空间站活动中俄罗斯主要进行微生物研究,并计划 2024 年发射"方舟"号生物卫星继续进行航天生物学探索,利用微重力、辐射等太空特殊生物学效应开展更为丰富严谨的空间生物实验和生物安全技术研究。同时,太空动物实验也将是远程探测和空间站建设过程中的航天医疗、安全保障的重要研究手段。为此,本文综述了俄罗斯太空动物实验发展历程,以期对我国下一阶段在中国空间站开展的动物实验和模拟航天动物研究有所启示。

参　考　文　献(References)

[1] West JB. Historical aspects of the early Soviet/Russian manned space program [J]. J Appl Physiol (1985), 2001, 91(4): 1501-1511.

[2] 林来兴. 苏联航天研究 [J]. 科技导报, 1989, 5: 52-57.
Lin LX. Soviet space research [J]. Sci Technol Rev, 1989, 5: 52-57.

[3] 庞之浩. 俄罗斯对国际空间站的贡献 [J]. 航天员, 2011, 6: 65-68.
Pang ZH. Russia's contribution to the International Space Station [J]. Astronaut, 2011, 6: 65-68.

[4] 张万周. 俄罗斯航天生物医学研究所及其科研活动 [J]. 中国航天, 1998,7: 34-37.
Zhang WZ. Russian Aerospace Biomedical Research Institute and its scientific research activities [J]. Aerospace Chin, 1998,7: 34-37.

[5] Morey-Holton ER, Hill EL, Souza KA. Animals and spaceflight: from survival to understanding [J]. J Musculoskelet Neuronal Interact, 2007, 7(1): 17-25.

[6] Burgess C, Dubbs C. Animals in space: from research rockets to the space shuttle [M]. U.K.: Praxis Publishing Ltd; 2007.

[7] Burgess C. The greatest adventure: a history of human space exploration [M]. U.K.: Reaktion Books; 2021.

[8] Hall R, David S. The rocket men: Vostok & Voskhod. The first soviet manned spaceflights [M]. U.K.: Springer Science & Business Media; 2001.

[9] Amtinov VV, Gaidamakin NA, Parfenov GP, et al. Pathomorphological and histochemical changes in the organs of tortoises carried onboard the spacecraft Zond 5 (Atrophic changes in tortoises during roundtrip to moon on Zond 5 ascribed to hunger and space flight factors) [J]. Cosmic Res, 1969, 7: 834-841.

[10] Sutulov LS, Kulkin SG, Saxonov PP, et al. Post-flight histological analysis of turtles aboard Zond 7 [J]. Life Sci Space Res, 1971, 9: 125-128.

[11] Antipov VV, Kozlov VA, Parfenov GP, et al. The results of biological studies made on board the Voskhod and Voskhod 2 spaceships [J]. Life Sci Space Res, 1967, 5: 119-121.

[12] Glembozky JL, Grozdova TJ, Parfenov GP. Experiments with Drosophila on board the spacecraft Zond-5 [J]. Life Sci Space Res, 1970, 8: 1-3.

[13] Ilyin EA, Serova LV, Portugalov VV, et al. Preliminary results of examinations of rats after a 22-day flight aboard the Cosmos-605 biosatellite [J]. Aviat Space Environ Med, 1975, 46(3): 319-321.

[14] Plakhuta-Plakutina GI. State of spermatogenesis in rats flown

aboard the biosatellite Cosmos-690 [J]. Aviat Space Environ Med, 1977, 48(1): 12-15.

[15] Gurovsky NN, Gazenko OG, Adamovich BA, et al. Study of physiological effects of weightlessness and artificial gravity in the flight of the biosatellite Cosmos-936 [J]. Acta Astronaut, 1980, 7(1): 113-121.

[16] Prokhonchukov AA, Desiatnichenko KS, Tigranian RA, et al. Sostoianie mineral'noĭ fazy I belkovogo matriksa kostnoĭ tkani krys posle poleta na biosputnike "Космос-1129" [Mineral phase and protein matrix status of rat bony tissue after a flight on the Kosmos-1129 biosatellite] [J]. Kosm Biol Aviakosm Med, 1982, 16(2): 61-64.

[17] Aĭzikov GS, Markin AS, Mokrousova AV. Osobennosti liftnoĭ reaktsii u belykh krys posle dlitel'nogo kosmicheskogo poleta (vliianie nevesomosti i iskusstvennoĭ sily tiazhesti) [Features of the lifting reflex in the white rat following prolonged space flight (effect of weightlessness and artificial gravity)] [J]. Biull Eksp Biol Med, 1981, 92(12): 722-725.

[18] Durnova GN, Kaplanskiĭ AS, Portugalov VV. Izmeneniia limfoidnykh organov krysy pri kosmicheskikh poletakh [Changes in the lymphoid organs of rats during space flight] [J]. Arkh Anat Gistol Embriol, 1977, 72(5): 14-20.

[19] Il'ina-Kakueva EI. Issledovanie skeletnykh myshts krys posle kratkovremennogo kosmicheskogo poleta na biosputnike "Космос-1667" [Examination of skeletal muscles of rats after a short-term flight on Cosmos-1667] [J]. Kosm Biol Aviakosm Med, 1987, 21(6): 31-35.

[20] Il'ina-Kakueva EI. Morfogistokhimicheskoe issledovanie skeletnykh myshts krys v éksperimente na biosputnike "Космос-1887" [Morphohistochemical study of skeletal muscles in rats after experimental flight on "Космос-1887"] [J]. Kosm Biol Aviakosm Med, 1990, 24(4): 22-25.

[21] Vacek A, Michurina TV, Serova LV, et al. Decrease in the number of progenitors of erythrocytes (BFUe, CFUe), granulocytes and macrophages (GM-CFC) in bone marrow of rats after a 14-day flight onboard the Cosmos-2044 Biosatellite [J]. Folia Biol (Praha), 1991, 37(1): 35-41.

[22] Serova LV, Denisova LA, Apanasenko ZI, et al. Obshchaia kharakteristika éksperimenta po izucheniiu ontogeneza krys na biosputnike "Космос-1514" [General characteristics of an experiment to study the ontogeny of rats on board the Космос-1514 biosatellite] [J]. Kosm Biol Aviakosm Med, 1985, 19(2): 49-53.

[23] Atiakshin DA, Bykov EG, Il'in EA, et al. Glycogen content in gerbil's liver following the spacecraft Foton-M3 mission [J]. Aviakosm Ekolog Med, 2009, 43(5): 18-22.

[24] Il'in EA, Smirnov IA, Soldatov PE, et al. Gerbil experiment in the flight of spacecraft" Foton-M3" [J]. Aviakosm Ekolog Med, 2009, 43(4): 21-25.

[25] Sychev VN, Ilyin EA, Yarmanova EN, et al. The BION-M1 project: overview and first results [J]. Aviakosm Ekolog Med, 2014, 48(1): 7-14.

[26] Andreev-Andrievsky AA, Shenkman BS, Popova AS, et al. Experimental studies with mice on the program of the biosatellite BION-M1 mission [J]. Aviakosm Ekolog Med, 2014, 48(1): 14-27.

[27] Gerbaix M, Gnyubkin V, Farlay D, et al. One-month spaceflight compromises the bone microstructure, tissue-level mechanical properties, osteocyte survival and lacunae volume in mature mice skeletons [J]. Sci Rep, 2017, 7(1): 2659.

[28] Atiakshin DA, Shishkina VV. Mast cells effect on the condition of skin collagen fibers in microgravity conditions [A]. AIP Conference Proceedings [C]; 2021.

[29] Ilin EA. Main results of the experiments conducted during the flight of the Kosmos-1129 Biosatellite and the status of preparation of studies on the next biosatllite [R]. U. S.: NASA, 1980.

[30] Proshchina A, Gulimova V, Kharlamova A, et al. Reproduction and the early development of vertebrates in space: problems, results, opportunities [J]. Life (Basel), 2021, 11(2): 109.

[31] Sychev VN, Shepelev EY, Meleshko GI, et al. Main characteristics of biological components of developing life support system observed during the experiments aboard orbital complex MIR [J]. Adv Space Res, 2001, 27(9): 1529-1534.

[32] Almeida EAC, Roden C, Phillips JA, et al. Development of the gecko (Pachydactylus turneri) animal model during Foton M-2 to study comparative effects of microgravity in terrestrial and aquatic organisms [J]. J Gravit Physiol, 2006, 13: 193-196.

[33] Nikitin VB, Proshchina AE, Kharlamova AS, et al. Comparative studies of the thick-toed geckos after 16 and 12 days spaceflights in Foton-M experiments [J]. J Gravit Physiol, 2008, 15: 285-288.

[34] Proshchina A, Gulimova V, Kharlamova A, et al. Cytoskeleton markers in the spinal cord and mechanoreceptors of thick-toed geckos after prolonged space flights [J]. Life (Basel). 2022;12(1):100.

[35] Alexandra P, Anastasia K, Valeriy B, et al. Vestibular cerebellum of thick-toed geckos (Chondrodactylus turnery GRAY, 1864) and C57/BL6N mice after the long-term space flight on the biosatellite BION-M1 [J]. J Chem Neuroanat, 2017, 79: 58-65.

[36] Bautz A, Houillon Ch, Aimar C, et al. Fate of the grafted ovaries from female salamander Pleurodeles waltl embarked on the Cosmos 2229 flight [J]. Adv Space Res, 1996, 17(6-7): 269-270.

[37] Grigorian EN, Tuchkova SIa, Poplinskaia VA, et al. Regeneratsiia setchatki posle pererwzki zritel'nogo nerva u tritonov, éksponirovannykh na bortu biosputnika "Bion-11" [Retinal regeneration after dissection of the optic nerve in newts exposed on board the Bion-11 biosatellite] [J]. Aviakosm Ekolog Med, 1999, 33(3): 15-20.

[38] Gualandris-Parisot L, Husson D, Foulquier F, et al. Pleurodeles waltl, amphibian, Urodele, is a suitable biological model for embryological and physiological space experiments on a vertebrate

[J]. Adv Space Res, 2001, 28(4): 569-578.

[39] Ilyin EA. Biological experiments in flights of unmanned space craft Foton-M2 and Foton-M3 [J]. Aviakosm Ekolog Med, 2013, 47(1): 47-54.

[40] Krasnov IB. Quantitative histochemistry of the vestibular cerebellum of the fish Fundulus heteroclitus flown aboard the biosatellite Cosmos-782 [J]. Aviat Space Environ Med, 1977, 48(9): 808-811.

[41] Levinskikh MA, Sychev VN. Rost i Razvitie odnokletochnykh vodorosleĭ v usloviiakh kosmi- cheskogo poleta v sostave ékosistemy "a'lgobakteria'lnyĭ tsenoz- ryby" [Growth and development of unicellular algae in the algae-bacteria-fish biocenosis system during space flight] [J]. Kosm Biol Aviakosm Med, 1989, 23(5): 32-35.

[42] Anken R, Brungs S, Grimm D, et al. Fish inner ear otolith growth under real microgravity (spaceflight) and clinorotation [J]. Microgravity Sci Technol, 2016, 28: 351-356.

[43] Dubinin NP, Glembotsky YL, Vaulina EN, et al. Effects of space flight factors on Drosophila [J]. Life Sci Space Res, 1973, 11: 163-165.

[44] Glembotskiĭ IaL, Vaulina EN, Pal'mbakh LR, et al. Geneticheskie éffekty u drozofily, vyzvannye faktorami kosmicheskogo poleta na "Космос-573" [Genetic effects in Drosophila caused by space flight factors in "Космос-573"] [J]. Genetika, 1975, 11(7): 70-77.

[45] Parfyonov GP, Platonova RN, Tairbekov MG, et al. Biological investigations aboard biosatellite Cosmos-782 [J]. Acta Astronaut, 1979, 6(10): 1235-1238.

[46] Parfyonov GP, Platonova RN, Tairbekov MG, et al. Biological experiments carried out aboard the biological satellite Cosmos-936 [J]. Life Sci Space Res, 1979, 17: 297-299.

[47] Tairbekov MG, Parfyonov GP, Platonova RW, et al. Biological investigations aboard the biosatellite Cosmos-1129 [J]. Adv Space Res, 1981, 1(14): 89-94.

[48] Ogneva IV, Belyakin SN, Sarantseva SV. The development of Drosophila Melanogaster under different duration space flight and subsequent adaptation to Earth gravity [J]. PLoS One, 2016, 11(11): e0166885.

[49] Shi Z, Zhuang D, Ilyin EA. Space flight experiment on Chinese silkworm on board the Russian 10th Biosatellite [J]. Adv Space Res, 1998, 21(8-9): 1145-1150.

[50] Rebecchi L, Altiero T, Guidetti R, et al. Tardigrade resistance to space effects: first results of experiments on the LIFE-TARSE mission on FOTON-M3 (September 2007) [J]. Astrobiology, 2009, 9(6): 581-591.

[51] Hilbig R, Lebert M. OMEGAHAB-XP a bioregenerative aquatic life support system designed to be used in Bion-M1 long term space flight [J]. 38th COSPAR Scientific Assembly, 2010, 38: 3.

[52] 何慧东, 张蕊, 苑艺, 等. 世界载人航天 60 年发展成就及未来展望 [J]. 国际太空, 2021, 4: 4-10.
He HD, Zhang R, Yuan Y, et al. The 60-year development achievements and future prospects of manned spaceflight in the world [J]. Space Int, 2021, 4: 4-10.

[53] Grigor'ev AI, Il'in EA. Animals in space [J]. Herald Russ Acad Sci, 2007, 77(6): 541-549.

[54] Popova IA, Grigor'ev AI. Vliianie kosmicheskogo poleta na obmen veshchestv: itogi biokhimicheskikh issledovaniĭ v éksperimentakh s krysami na biosputnikakh "Космос" [The effect of space flight on metabolism: the results of biochemical research in rat experiments on the Космос biosatellites] [J]. Aviakosm Ekolog Med, 1992, 26(5-6): 4-10.

[55] Serova LV. Adaptation to new environments: microgravity [J]. Usp Fiziol Nauk, 2005, 36(2): 3-21.

[56] Andreev-Andrievskiy A, Popova A, Boyle R, et al. Mice in Bion-M1 space mission: training and selection [J]. PLoS One, 2014, 9(8): e104830.

[57] Proshchina AE, Krivova YS, Saveliev SC. Pancreas of C57 black mice after long-term space flight (Bion-M1 Space Mission) [J]. Life Sci Space Res (Amst), 2015, 7: 22-26.

[58] Kostal L, Bilcik B, M Juráni, et al. Behaviour of newly hatched and adult Japanese quail and the feasibility of adaptation to weightlessness [J]. Physiologist, 1993, 36(1): 50-52.

[59] Snetkova E, Chelnaya N, Serova L, et al. Effects of space flight on Xenopus laevis larval development [J]. J Exp Zool, 1995, 273(1): 21-32.

[60] Serova LV. Ontogenesis of mammals and gravity [J]. J Gravit Physiol, 2004, 11(2): 161-164.

[61] Almeida E, Roden C, Phillips JA, et al. Analysis of cell proliferation in newt (Pleurodeles waltl) tissue regeneration during spaceflight in Foton M-2 [J]. J Gravit, Physiol, 2006, 13: 1.

[62] Shi Z, Zhuang D, Ilyin EA. Space flight experiment on Chinese silkworm on board the Russian 10th Biosatellite [J]. Adv Space Res, 1998, 21(8-9): 1145-1150.

[63] Soldatov PE, Smirnov IA, Il'in EA, et al. Handling and maintenance of gerbils during the spacecraft Foton-M3 mission [J]. Aviakosm Ekolog Med, 2009, 43(5): 12-18.

[64] Soldatov PE. Investigation of the main gas-exchange parameters in the Mongolian gerbil in view of a space experiment [J]. Aviakosm Ekolog Med, 2005, 39(4): 53-56.

[65] Barrett JE, Wells DC, Paulsen AQ, et al. Embryonic quail eye development in microgravity [J]. J Appl Physiol (1985), 2000, 88(5): 1614.

[66] Tsigankova V, Zibrin M, Kochishova I, et al. Morfologicheskie izmeneniia v nadpochechnikakh ptentsov iaponskogo perepela, vylupivshikhsia v usloviiakh nevesomosti [Morphological changes in the adrenal gland of Japanese quail chicken hatched out in microgravity] [J]. Aviakosm Ekolog Med, 2002, 36(5): 29-32.

[67] Orban JI, Piert SJ, Guryeva TS, et al. Calcium utilization by quail embryos during activities preceding space flight and during embryogenesis in microgravity aboard the orbital space station MIR [J]. J Gravit Physiol, 1999, 6(2): 33-41.

[68] Gulimova V, Proshchina A, Kharlamova A, et al. Reptiles in space missions: results and perspectives [J]. Int J Mol Sci, 2019, 20(12): 3019.

[69] Nikitin VB, Gulimova VI, Ilyin EA, et al. Comparative analysis of the skeletal changes in tetrapods after brief influence of microgravity [J]. J Gravit Physiol, 2007, 14(1): 103-104.

[70] Barabanov VM, Gulimova VI, Berdiev RK, et al. Individual features of play behavior in thick-toed geckos in weightlessness and normal gravity conditions [J]. Life Sci Space Res (Amst), 2019, 22: 38-46.

[71] Gulimova VI, Barabanov VM, Berdiev RK, et al. Species differences in the ability of geckos to adapt to the conditions of long-term orbital experiment onboard "BION-M1" and "FOTON-M4" biosatellites [J]. Aviakosm Ekolog Med, 2016, 50: 55-57.

[72] Prokhonchukov AA, Tigranian RA, Kolesnik AG, et al. Soderzhanie kal'tsiia, fosfora i vkliuchenie 45Ca v kostiakh i zubakh krys posle 22-sutochnogo kosmicheskogo orbital'nogo poleta na korable-sputnike "Kosmos-605" [Calcium and phosphorus content and the 45Ca incorporation into the bones and teeth of rats after a 22-day orbital space flight on board the "Cosmos-605" satellite ship] [J]. Kosm Biol Aviakosm Med, 1977, 11(1): 26-30.

[73] Ushakov AS, Vlasova TF, Miroshnikova EB. Studies of amino acid metabolism in the muscles of rats flown aboard the biosatellite Cosmos 782 [J]. Life Sci Space Res, 1979, 17: 231-234.

[74] Rogacheva IV, Stupakov GP, Volozhin AI, et al. Kharakteristika kostnoĭ tkani krys posle poleta na biosputnike "Kosmos-1129" [Characteristics of bone tissue of rats after flight aboard biosputnik Kosmos-1129] [J]. Kosm Biol Aviakosm Med, 1984, 18(5): 39-44.

[75] Kaplanskiĭ AS, Durnova GN, Sakharova ZF, et al. Gistomorfometricheskĭ analiz kosteĭ krys, nakhodivshikhsia na bortu biosputnika "Космос-1667" [Histomorphometric analysis of the bones of rats on board the Космос-1667 biosatellite] [J]. Kosm Biol Aviakosm Med, 1987, 21(5): 25-31.

[76] Durnova GN, Kaplanskiĭ AS, Il'ina-Kakueva EI, et al. Gistomorfometricheskiĭ analiz kosteĭ krys, éksponirovannykh na biosputnike "Космос-1887" [Histomorphometric analysis of the bones of rats exposed to "Cosmos-1887" space flight] [J]. Kosm Biol Aviakosm Med, 1990, 24(5): 42-45.

[77] Il'ina-Kakueva EI, Burkovskaia TE. Vliianie nevesomosti na techenie reparativnogo protsessa v myshtsakh krys, éksponirovannykh na biosputnike "Kosmos-2044" [Effect of weightlessness on the course of the reparative process in the muscles of the biosatellite Kosmos-2044 rats] [J]. Kosm Biol Aviakosm Med, 1991, 25(5): 24-29.

[78] Babakova LL, Baranov VM, Pozdnyakov OM. Influence of space flight factors on the ultrastructure of rat diaphragm muscle [J]. Bull Exp Biol Med, 2013, 155(1): 18-21.

[79] Pozdniakov OM, Babakova LL, Demorzhi MS, et al. Izmeneniia ul'trastruktury nervno-myshechnykh sinapsov krys pod vliianiem faktorov kosmicheskogo poleta [Changes in the ultrastructure of neuromuscular synapses in rats under the effects of space flight factors] [J]. Biull Eksp Biol Med, 1988, 105(6): 752-755.

[80] Pashchenko PS, Zakharova IV. Changes in the pancreas structure after exposure of the body to gravitational overloads [J]. Morfologiia, 2006, 129(1): 62-67.

[81] Fitzgerald J, Endicott J, Hansen U, et al. Articular cartilage and sternal fibrocartilage respond differently to extended microgravity [J]. NPJ Microgravity, 2019, 5: 3.

[82] Gerbaix M, White H, Courbon G, et al. Eight days of earth reambulation worsen bone loss induced by 1-month spaceflight in the major weight-bearing ankle bones of mature mice [J]. Front Physiol, 2018, 9: 746.

[83] Radugina EA, Almeida EAC, Blaber E, et al. Exposure to microgravity for 30 days onboard Bion M1 caused muscle atrophy and impaired regeneration in murine femoral Quadriceps [J]. Life Sci Space Res (Amst), 2018, 16: 18-25.

[84] Ogneva IV, Maximova MV, Larina IM. Structure of cortical cytoskeleton in fibers of mouse muscle cells after being exposed to a 30-day space flight on board the BION-M1 biosatellite [J]. J Appl Physiol (1985), 2014, 116(10): 1315-1323.

[85] Berg-Johansen B, Liebenberg EC, Li A, et al. Spaceflight-induced bone loss alters failure mode and reduces bending strength in murine spinal segments [J]. J Orthop Res, 2016, 34(1): 48-57.

[86] Gambara G, Salanova M, Ciciliot S, et al. Gene expression profiling in slow-type calf soleus muscle of 30 days space-flown mice [J]. PLoS One, 2017, 12(1): e0169314.

[87] Vikhlyantsev IM, Okuneva AD, Shpagina MD, et al. Changes in isoform composition, structure, and functional properties of titin from Mongolian gerbil (*Meriones unguiculatus*) cardiac muscle after space flight [J]. Biochemistry (Mosc), 2011, 76(12): 1312-1320.

[88] Atiashkin DA, Bykov EG, Il'in EA, et al. RNA content of gerbil hepatocytes after the flight aboard space platform Foton-M3 [J]. Aviakosm Ekolog Med, 2010, 44(3): 28-32.

[89] Atiakshin DA, Il'in EA, Pashkov AN. Morphofunctional state of hepatocytes nuclear apparatus in Mongolian herbils after the flight on space apparatus Foton-M3 [J]. Aviakosm Ekolog Med, 2010, 44(2): 29-34.

[90] Atiashkin DA, Bykov EG. Morphological changes in gastric wall of mongolian gerbils following the 12-day orbital flight aboard Foton-M3 [J]. Aviakosm Ekolog Med, 2012, 46(5): 26-33.

[91] Atyakshin DA, Bykov EG. Population characteristics of mucous tissue basocytes in the Mon golian gerbil's jejunum following the 12-day orbital flight onboard space platform "Foton-M3" [J]. Aviakosm Ekolog Med, 2013, 47(6): 17-24.

[92] Atiakshin DA, Bykov EG, Il'in EA, et al. Tissue-specific reaction of the mucous coat of herbals' small gut under the influence of spaceflight factors on board biosat "Foton M3" [J]. Aviakosm Ekolog Med, 2011, 45(2): 25-30.

[93] Durnova GN, Kaplansky AS, Orlov OI, et al. Histomorphometric investigation of the shin bones taken from Mongolian gerbille Meriones unguiculatus exposed on satellite "Foton-M" No. 3 [J]. Aviakosm Ekolog Med, 2008, 42: 27-30.

[94] Komissarova DV, Dadasheva OA, Gurieva TS, et al. Histogenesis of Japanese quail bone and cartilage tissues at the final stages of embryonic development in microgravity [J]. Aviakosm Ekolog Med, 2013, 47(6): 24-28.

[95] Komissarova DV, Gur'eva TS, Sychev VN. Dynamics of calcium utilization for skeleton formation in Japanese quail embryos under the microgravity condition [J]. Aviakosm Ekolog Med, 2011, 45(5): 52-53.

[96] Dadasheva OA, Gur'eva TS, Sychev VN, et al. Characteristics of morphogenesis of the Japanese quail embryos during microgravity [J]. Aviakosm Ekolog Med, 1998, 32(3): 38-41.

[97] Dadasheva OA, Gur'eva TS, Iaglov VV. Razvitie shchitovidnoĭ zhelezy u émbrionov iaponskogo perepela, inkubirovannykh v usloviiakh mikrogravitatsii [Thyroid gland development in Japanese quail embryos incubating in microgravity] [J]. Aviakosm Ekolog Med, 2000, 34(1): 29-31.

[98] Lenhardt L, Cigankova V, Zibrin M, et al. Functional development of small intestine of Japanese quail hatched on MIR orbital station [J]. Acta Vet Brno, 2001, 70(2): 127-131.

[99] Meleshko GI, Shepelev EIa, Gur'eva TS, et al. Embrional'noe razvitie ptits v usloviiakh nevesomosti [The embryonic development of birds in weightlessness] [J]. Kosm Biol Aviakosm Med, 1991, 25(1): 37-39.

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综述:肠道微生物与炎性肠病间的关系

炎性肠病(Inflammatory bowel disease, IBD)是一类病因不明确和难以治愈的慢性肠道炎症性疾病,其临床症状表现为腹痛、腹泻和黏液脓血便等。随着病情发展也可以导致肠道致残性改变,包括肠穿孔、肠梗阻和肠癌等。近年来,IBD 的发病率在中国逐年上升,已达到了 14/100 000,且患者年龄呈年轻化的趋势。来自中国农业大学、中国医学科学院、中国农业科学院和北京农业职业学院的研究者从实验小鼠模型和肠道微生物区系平衡两方面,对目前炎性肠病的相关发病机理作一综述。文中提到的炎性肠病临床上主要包括溃疡性结肠炎(Ulcerative colitis, UC)和克罗恩病(Crohn's disease, CD),两者的主要病症均表现为腹痛、腹胀、腹泻以及便血。目前关于炎性肠病发病机理的研究主要集中肠道微生物、免疫、遗传和环境等因素。研究者考虑到肠道微生物可与遗传易感基因、肠道黏膜免疫和环境因素的相互作用,认为肠道微生物区系与炎性肠病的发生和发展密切相关。

在该综述中,作者首先总结了肠道微生物的分类,主要包括细菌、真菌、病毒和原生动物,其中肠道细菌在肠道微生物占据较大比重。其次,作者阐述了健康机体中肠道微生物的功能和作用,随后介绍了用以模拟炎性肠病的四种小鼠模型,包括三种化学诱导(DSS、TNBS 和乙酸)和一种微生物诱导(柠檬酸杆菌)模型。同时,作者对四种小鼠模型的造模方法、剂量、诱导的相关机理做了简要总结,为后续炎性肠病的深入研究提供思路。最后,在探讨肠道微生物区系与炎性肠病的关系时,作者认为肠道微生物区系与炎性肠病之间的关系不是固定的因果关系,而是相互作用的。综上所述,本文首先对炎性肠病的分类、病症和流行病学进行总结,阐明炎性肠病是一种全球性的公共健康问题;同时,剖析影响炎性肠病发病的因素,并表明肠道微生物与炎性肠病的发生和发展密切相关;基于炎性肠病小鼠模型,阐明肠道微生物区系紊乱与炎性肠病的确切关联,为炎性肠病发病机制的深入研究提供思路。

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