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1 摘 要

中文摘要

运动训练对下丘脑—垂体—卵巢轴的作用效应

运动及训练将导致女性下丘脑—垂体—卵巢（hypothalamus pituitary ovarian，HPO）功能轴激素水平发生变化已为众多研究所证实，但由于诸多因素的影响，报道结果大相径庭。要全面认识运动应激中HPO轴激素变化的效应，必须对运动中HPO轴功能激素变化的特点、规律进行系统研究；对HPO轴的影响因素进行同步研究；对靶细胞的相应反应进行同步研究。而运动应激状态下，主要抗生殖激素、生殖激素水平是HPO轴功能的重要影响因素；HPO轴功能激素受体是靶细胞反应性高低的决定性因素；HPO轴各环节结构的改变则是影响其功能变化的根本因素。由于HPO轴功能激素水平的紊乱将导致女运动员发生运动性月经失调（Athletic Menstrual Irregularity，AMI），而AMI可能与过度训练密切相关，因此，上述问题的探讨，将有助于阐释AMI的病理机制过程。由于人体实验方法学的限制，本研究采用动物实验的方法对上述问题进行逐一探讨。

实验一，运动性动情周期紊乱动物模型的建立及其评价：本实验采取递增负荷的跑台运动形式，以雌性SD大鼠为实验对象，大鼠随机分为运动组及对照组，辅以检测指标：体重、疲劳程度、血清总T和T/C比值、Hb、BLA、BUN及阴道脱落细胞指标为评价依据，建立了模拟运动性动情周期紊乱动物模型。结果发现，持续9周的递增负荷跑台运动过程中，大鼠体重呈现渐进性降低，降低幅度超过1/30；疲劳程度均≥3级；血清总T和T/C比值随负荷增大而大幅下降；Hb呈现波动性降低，至训练结束时，运动性贫血的症状已非常明显；BUN呈现波动性升高；BLA水平持续升高；阴道脱落细胞学监测出现白细胞与有核上皮细胞比例交替升高、白细胞比例高于有核上皮细胞的卵巢功能

持续严重受挫、功能低下现象。各项指标的综合分析表明，持续9周的递增负荷跑台运动过程中，大鼠体重的显著减少、血清总T和T/C比值的大幅下降、BLA及BUN水平的明显改变、Hb的敏感性降低、日益加深的疲劳程度及阴道脱落细胞学出现特征性的变化，均可作为运动性动情周期紊乱的诊断参考依据。大鼠陆续发生动情周期总时间延长、各时相紊乱及动情周期抑制现象，而这些现象均为动情周期紊乱的明显征象，其发生过程具有显著的个体差异特点。因此，本研究所建立的运动性动情周期紊乱动物模型符合过度训练的诊断标准，模型的准确性较高。

实验二，递增负荷运动过程中生殖激素、抗生殖激素水平的变化特点及其作用：本部分实验通过对运动性动情周期紊乱大鼠模型建立过程及运动后4个周期的恢复过程中，HPO轴功能激素、抗生殖激素及HPA轴激素水平的动态追踪测定，探讨运动性动情周期紊乱发生过程中，生殖激素、抗生殖激素及HPA轴激素水平变化的特点、规律及影响作用关系。检测指标：下丘脑、垂体GnRH及β—EP采用平衡饱和放射免疫分析法测定；血清FSH、LH、PRL、血浆β—EP及下丘脑和垂体CRH均采用液相顺序饱和放射免疫分析法测定；E_2、P、T采用液相平衡竞争放射免疫分析法；血浆GC水平采用竞争蛋白结合分析法测定。结果发现，递增负荷训练至过度训练过程中，随着运动负荷的加大及训练周期的加长，下丘脑及垂体GnRH，血清LH、E_2、P、T及FSH水平呈现逐渐降低态势，表现出明显的强度及时间效应，并以低促性腺激素及低性腺类固醇水平为特征；长期运动训练下丘脑及垂体CRH及血浆GC水平随运动负荷量的加大而显著升高；下丘脑、垂体及血浆β—EP水平、血清PRL水平，随训练周期的加长而显著升高。结果表明，持续9周的递增负荷运动训练过程中，HPO轴功能激素的正常调控关系发生改变，HPO轴功能全面受抑，体内生殖激素与抗生殖激素水平的正常平衡被破坏。HPO轴功能受抑与HPA轴功能亢进、抗生殖激素水平异常增高密切相关，但HPO轴功能受抑的确切部位尚需进一步确定。同时，生殖激素及抗生殖激素水平的变化可在停训后的恢复期内逐渐得以恢复，说明这种变化是可以逆转的。

实验三，递增负荷运动过程中ER及PR水平的变化：激素通过其特定的靶细胞来发挥生理作用，靶细胞对激素的相应反应是决定激素作用效果的又一重要因素。在该作用过程中，靶细胞受体是最为重要的一环。性腺类固醇激素通过与靶细胞中ER及PR的结合，使受体活化，并与靶基因中的特定DNA片段——激素反应元件（HREs）结合，促进或抑制靶基因的表达，从而引起生物学效应。持续的递增负荷训练导致大鼠出现以低性腺类固醇水平为主要特征的运动性动情周期紊乱。为了搞清这种极具特点的性激素水平与其相应受体间

的变化是否同步，其变化的机制、意义等问题，在实验3中，我们从递增负荷运动过程中大鼠卵巢、子宫ER及PR变化入手，探讨低性腺类固醇水平与ER及PR之间的作用关系。检测指标：以单点法对大鼠训练期间ER及PR结合量进行测定。发现，递增负荷运动过程中，大鼠卵巢、子宫ER及PR结合量呈渐进性升高，PR水平的显著升高先于ER出现，受体的升高程度与负荷强度、量度及运动训练持续时间有关，表现出强度、量度及时间依赖性。ER及PR结合量的升高与血清E_2水平变化无明显的正向依存关系，表明受体水平的变化可能为非激素依赖性升高。这种改变或许是机体对长期运动训练造成的低性腺类固醇激素环境的一种特征性反应。ER及PR水平上调的意义可能在于提高其对低性腺类固醇激素的“敏感性”，保持受体与激素的平衡状态，维持机体的内环境自稳态。运动结束后的恢复过程中，受体水平出现波动性回落，并渐趋正常，表明持续递增负荷运动所造成的ER及PR水平升高是可逆的，受体水平的回落与E_2水平的恢复性升高具有直接关系。

实验四，递增负荷运动过程中GnRHR mRNA及ER mRNA表达的变化：本部分实验通过检测大鼠在递增负荷训练7周、9周及恢复2、4个动情周期后，HPO轴各环节GnRHR mRNA及ER mRNA的动态变化，从基因表达水平探讨持续运动应激导致动情周期紊乱后GnRHR及ER水平变化的机制。检测指标：采用定量RT—PCR检测下丘脑、垂体、卵巢、子宫各环节GnRHR mRNA及ER mRNA的表达。结果发现，下丘脑、垂体GnRHR mRNA在训练7周结束时开始显著降低，并持续至恢复2期；而卵巢仅在过度训练周显著减少，子宫GnRHR mRNA虽亦呈现降低态势，但与对照组相比自始至终无显著差异。持续递增负荷训练7周后，大鼠下丘脑及垂体ER mRNA与对照组相比均明显减少；这种显著减少一直持续至恢复2期结束；卵巢及子宫ER mRNA则显著高于对照组，并持续至恢复2期结束。结果表明，GnRHR mRNA及ER mRNA表达的减少与血清性腺类固醇水平的降低具有密切关系。GnRHR mRNA及ER mRNA经过4个动情周期的恢复过程，其水平基本恢复至正常，而导致恢复的主要原因与血清E_2水平的复原密切相关。

实验五，递增负荷运动大鼠HPO轴超微结构变化及其恢复过程观察：本部分实验对训练及恢复不同阶段大鼠下丘脑、垂体、卵巢及子宫组织细胞的超微结构，进行了透射及扫描电镜观察，试图从形态结构变化的角度对功能变化的特点机制予以阐释。结果发现，长期递增负荷运动训练，可致大鼠下丘脑、垂体、卵巢及子宫细胞超微结构发生异常改变，这种改变与训练周期的增长及运动负荷的增大具有显著递进关系。训练过程中，大鼠下丘脑弓状核神经元出现渐进性的细胞器变性、轴突髓鞘分离，突触小泡及微管微丝减少、树突棘减少

等异常变化，表明细胞功能受抑，神经元间的相互联系减弱，促性腺激素释放激素的合成及分泌均受到干扰。垂体促性腺细胞及生长激素细胞出现渐进性的细胞器变性及核膜异常，溶酶体增多等异常改变，而ACTH细胞形态结构变化较小，与同期测定的较低FSH、LH水平和较高CRH及GC水平具有一致性。说明垂体促性腺细胞合成和分泌激素的功能均受到抑制。递增负荷运动中，卵巢上皮细胞形态由隆起渐趋平坦，上皮细胞层由完整至不完整，出现斑剥缺损，细胞间微绒毛由多渐少等表面结构改变。卵泡膜内层细胞及颗粒细胞异染色质边聚，核膜破裂，线粒体空泡化或溶解，内质网明显扩张，环形板结构及次级溶酶体增多等异常结构变化。与同期测定的低E_2、P水平呈同步变化。子宫结构的变化主要表现在内膜上皮细胞超微结构的异常改变。扫描电镜下可见上皮细胞微绒毛由轻度脱落过渡到几乎完全缺失，胞膜破裂，形成漏洞，表明细胞的分泌功能下降。细胞器结构异常改变，出现包含物空泡，核内常染色质减少，异染色质边聚呈块状。表明细胞合成机能受阻，细胞成熟受到抑制，细胞呈现动情间期状态。表现出与低性激素水平及动情周期紊乱和抑制的依从关系。HPO轴各环节组织细胞超微结构，随训练周期增长及运动负荷量增大出现渐进性异常改变的结果表明，运动性动情周期紊乱以结构变化为基础，HPO轴结构和机能的改变以下丘脑为核心。而持续9周的递增负荷训练所造成的下丘脑、垂体、卵巢、子宫结构的改变经过4个周期的恢复，逐渐复原。提示持续9周递增负荷运动造成的动情周期紊乱是可逆的，这种可逆性的变化是以结构恢复为基础、以下丘脑为核心的恢复过程。

关键词

下丘脑—垂体—卵巢轴；动情周期紊乱大鼠；生殖激素；雌孕激素受体；促性腺激素释放激素受体；抗生殖激素；下丘脑—垂体—肾上腺皮质轴；递增负荷运动；过度训练；放射免疫测定；放射配体结合分析；单点法；逆转录；聚合酶链式反应；超微结构

英文摘要

Title: The effects of training on the hypothalamus — pituitary — ovarian axis

Abstract:

Most studies have confirmed that hormone levels of hypothalamus—pituitary—ovarian axis (HPO axis) will change in exercise and training in women. Because many factors affect the functions of HPO axis, the study results are quite different. For comprehensive understanding the effects of changes of HPO axis hormones in exercise stress, it is necessary to systematically investigate the peculiarity and rule of HPO axis hormones; to investigate the influencing factors to HPO axis; and to investigate the reaction of target cells to HPO axis hormones as the same time. Main anti— reproductive hormones and reproductive hormones are the important influencing factors to HPO axis function. HPO axis hormone receptors are the deciding factors to target cells reaction. Structure changes of every segment of HPO axis are the ultimate factors to HPO axis function. AMI will take place when HPO axis hormone level is disturbed. AMI may be related to overtraining. So resolving of these problems will be help to explain the pathological mechanisms of AMI. Animal experiment was adopted in this study, as human experiment is impossible.

Experiment 1, Establishment and evaluation of animal model about athletic estrous cycle dysfunction:

Female SD rats were assigned randomly to training and control groups. Training groups ran on a treadmill according to the protocal in progressive increasing training load manner. Evaluation parameters included body weight, fatigue classification serum total T and T/C, Hb, BLA, BUN and vagina shedding cells. The results found that, during 9 weeks training period, weight gradually decreased, and the range was over 1/30; fatigue degree graded ≥3; serum total T and T/C greatly reduced with load volume increasing; Hb level undulately decreased, and distinctly appeared athletic aneamic symptoms; BUN level enhanced; BLA level continually increased; ovarian function frustration and downfall phenomena appeared (the ratio of white cells and nucleus epithelia alternately increased; white cells were over nucleus epithelia) in vagina shedding cells monitoring. The results indicated that these parameters may be used to diagnose athletic estrous cycle

dysfunction. Phenomena appeared in succession in rats, including total duration of estrous cycle prolonged, each cycle was disturbed, and estrous cycle was inhibited. These phenomena were distinct signs of estrous cycle dysfunction, and there were significant individual difference in the process. The modal accord with diagnosis criterion of overtraining, and was quietly correct.

Experiment 2, Changes and roles of reproductive hormone and anti—reproductive hormone levels during progressive increasing load volume training periods in rats:

In order to explore characteristics, rule, and influencing effects, this study dynamically traced the changes of reproductive hormone, anti—reproductive hormone, and HPA axis hormone levels. Equation saturation RIA was used in GnRH and β —EP determining in hypothalamus and pituitary; fluid order saturation RIA was used in serum FSH, LH, PRL, plasma β —EP, and hypothalamus and pituitary CRH; fluid equation competition RIA was used in serum E_2, P, and T; competition protein binding assay was used in plasma GC. The results found that GnRH of hypothalamus and pituitary, serum LH, E_2, P, T, and FSH level showed significant fall/ downfall trend, and appeared relation to intensity and duration. The obvious characteristics were lower gonadotropin and female steroids levels. CRH of hypothalamus and pituitary, and plasma GC markedly increased with training load volume increasing. β —EP of hypothalamus, pituitary and plasma, greatly enhanced with the training duration, similarly to the serum PRL level. The results indicated that normal relations of regulation and controlling of HPO axis hormones were disturbed; the function of HPO axis was fully inhibited; the balance of reproductive hormones and anti—reproductive hormones was destroyed. Inhibition of HPO axis was related to HPA axis enhancing and anti—reproductive hormones increasing. But the true position of HPO axis inhibition required further to be confirmed. Reproductive and anti—reproductive hormone level gradually recovered during recovering phase. The results suggested that these changes were reversed after training stopped.

Experiment 3, Changes of ER and PR levels during progressive increasing load volume training periods in rats:

Hormone exerts its physiological action by its target cells. The target cells reaction to hormone is another important factor of deciding hormone effects. The receptor of target cells is the main part in hormone roles in this course. Female steroids activate receptors by binding with ER and PR. Receptor—hormone

complexes bind to the special DNA segment—hormone response elements (HREs), as a consequence, the target gene expression is improved or inhibited, which brings out biological effects. In experiment 2, we found that continually progressive increasing load volume training resulted in athletic estrous cycle dysfunction, which went with lower steroids level (the main characteristics). In experiment 3, we examined the relationship between lower steroids level and ER and PR of ovarian and uterus, so that we can explain whether the change is consistent, its mechanism, and significance. ER and PR binding capacity was detected by radioligand binding (one—point) assay. The main results were: ER and PR binding capacity of ovarian and uterus was gradually elevated during progressive increasing load training. The elevation of PR level was prior to ER, and the extent depended on load intensity, volume, and training duration. There was no obvious "up—regulation" of serum E_2 to steroids receptors. These results showed that the elevation of receptors level may be related to non—hormone dependence path, which was a character reaction of body to lower steroids during long—term training. The significance may consist in improving body's sensitivity to lower steroids, keeping the balance between receptors and steroids, and holding body inner environment balance. Receptor levels undulately fell down and tended to become normal levels after training, which indicated that the elevation of receptor levels was reversible, and the recovery was attribute to the elevation of E_2 concentration.

Experiment 4, Changes of ultrastructure of HPO axis in rats during progressive increasing load volume training and recovery periods:

The aims of experiment 4 were to elucidate the potential mechanisms of effects of structure changes on functions in rats' hypothalamus, pituitary, ovarian, and uterus during progressive increasing training load and recovery periods. Transmission and scanning electron microscopes were used to observe the ultrastructure in HPO axis. We found that long—term progressive increasing load volume training resulted in ultrastructure changes in hypothalamus, pituitary, ovarian, and uterus, and this changes successively related to training period and training load volume. Gradually, organelles denaturalized, myelin sheath of axons separated, synapse vesicles, microtubule, microneme, and dendritic spine reduced in the neurons of arcuate hypothalamic nucleus in rats during training courses. These changes indicated that cell functions were inhibited, connections of neurons weakened, GnRH synthesizing and secreting were disturbed. Organelles

denaturalized and nuclear membrane was abnormal, lysosomes increased in gonadotroph (Gn) and somatotroph (GH) cells, but ultrastructure less changed in corticotroph (ACTH) cells in pituitary. These ultrastructure changes were consistent in lower gonadotrophin, and higher CRH and GC levels in the same phase. The results showed that hormones synthesizing and secretion were restrained in pituitary. The surface structure changes of epithelium were from promontory to flatness, from integrity to imperfect; microvilli on cells from richness to fewness in ovarian. Separate chromatin migrated towards the side, nuclear membrane breaked, mitochondria became vacuole or dissolving, endoplasmic reticulum dilated, ring board appeared, and lysosome increased in follicular theca interna cells and granular cells. These changes were consistent in lower E_2 and P levels. The surface structure changes of epithelium of endometrium may find: microvilli on cells decreased from lightness to seriousness, cell membrane breaked and had leak, which showed that secretion role of cells weakened. Organelles were abnormal, containing organelles vacuole presented, constant chromatin became sparseness, separate chromatin migrated towards the side and became clump, which indicated synthesizing function was inhibited, and cell mature was restrained, so that endometrium were in diestrus. Changes of endometrium were attribute to lower estrogen level. These results suggested that athletic estrous cycle dysfunction based on the structural changes. Hypothalamus was the center and initial segment of structure and function changes of HPO axis. The structure changes of hypothalamus, pituitary, ovarian, and uterus were progressively recovered after rest in 4 estrous cycles, which suggested that athletic estrous cycle dysfunction was reversible, and the recovery course was based on structural recovery and focused on hypothalamus structure and function.

Experiment 5, Changes of GnRHR mRNA and ER mRNA expression during progressive increasing load volume training periods in rats:

The purpose of this experiment was to explore the change mechanisms of GnRHR and ER levels by gene expression in estrous cycle dysfunction in continuous exercise stress. We examined dynamic changes of GnRHR mRNA and ER mRNA in each segment of HPO axis after 7th , 9th week training, 2nd , and 4th estrous cycle recovery courses. GnRHR mRNA and ER mRNA expression were detected by reverse transcription—polymerase chain reaction (RT—PCR). The results obtained were as following: GnRHR mRNA in hypothalamus and pituitary markedly decreased after 7th week training, the lower level went on 2nd recovery period.

Ovarian GnRHR mRNA significantly reduced in overtraining week. Uterus GnRHR mRNA was no difference with control group, although it showed a decreasing state. After 7th week training, ER mRNA in hypothalamus and pituitary obviously reduced; ER mRNA level in ovarian and uterus increased compared with control group, and went on 2nd recovery period. The results indicated that GnRHR mRNA and ER mRNA expression were related to lower serum steroids concentrations, especially, E_2 concentration. GnRHR mRNA and ER mRNA approximately recovered to normal level through 4 estrous cycles. Serum estrogen concentration may be responsible for the recovering course.

Key words: Hypothalamus—pituitary—ovarian axis (HPO axis); athletic estrous cycle dysfunction rat; reproductive hormone; estrogen and progesterone receptor (ER and PR); Gonadotropin—releasing hormone receptor(GnRHR); anti—reproductive hormone; hypothalamus—pituitary—adrenal cortex axis (HPA axis); progressive increasing load volume training; overtraining; radioimmunoassay (RIA); radioligand binding assay; reverse transcription (RT); polymerase chain reaction (PCR); ultrastructure

缩略词

缩略词	英文名称	中文名称
ACTH	adrenal corticotropic hormone	促肾上腺皮质激素
AMI	athletic menstrual irregularity	运动性月经失调
BLA	blood lactate	血乳酸
BUN	blood urea nitrogen	血尿素
CRH	corticotrophin releasing hormone	促肾上腺皮质激素释放激素
CAE	catecholaminergic estrogen	儿茶酚雌激素
DA	dopamine	多巴胺
E_2	estrodiol	雌二醇
EGF	epidermal growth factor	表皮生长因子
ER	estrogen receptor	雌激素受体
ERE	estrogen response elements	雌激素反应元件
FSH	follicular stimulating hormone	卵泡刺激素
GC	glucocorticoid	糖皮质激素
GH	growth hormone	生长激素
GnRH	gonadotropin relesing hormone	促性腺激素释放激素
GnRHR	gonadotropin relesing hormone receptor	促性腺激素释放激素受体
Hb	hemoglobin	血红蛋白
HPA	hypothalamus pituitary adrenal cortex	下丘脑—垂体—肾上腺皮质
HPO	hypothalamus pituitary ovarian	下丘脑—垂体—性腺
Hsp	heat shock protein	热休克蛋白
IGF— I	insulin growth fator—1	胰岛素样生长因子— I
LH	luteinizing hormone	黄体生成素
MAPK	mitogen activated protein kinase	丝裂原激活的蛋白激酶
MLT	melatonin	降黑素
P	progesterone	孕酮
PKC	protein kinase C system	PKC系统
PR	progesterone receptor	孕激素受体
PRL	prolactin	泌乳素
RIA	radioimmunoassay	放射免疫分析法
RT—PCR	reverse transcription polymerase chain reaction	反转录聚合酶链式反应
T	testosterone	睾酮
β—EP	β—endorpin;	β—内啡肽
β—LPH	β—lipotropin	β—促脂素
α—MSH	α—melanocyte stimulating hormone	促黑激素

2 前 言

月经周期是女性特有的生理现象，每个周期中，卵巢及子宫发生周期性的变化，这种变化受制于下丘脑—垂体—卵巢轴（Hypothalamus—pituitary—ovarian，HPO轴）的调控。下丘脑、垂体、卵巢在不同层面上各自分泌功能激素，通过环节或整个功能轴的交互影响作用，实现对月经周期的调控。女性的正常月经周期与体内内分泌平衡有密切关系，具体表现为体内生殖激素与抗生殖激素水平的动态平衡；各内分泌功能轴间交互效应的动态平衡；这些平衡又受制于各种功能激素产生、代谢转换、清除诸方面平衡状态的维持。HPO轴功能激素水平规律的周期性变化是月经周期稳定的重要标志。当某种因素干预下，导致HPO轴任一环节功能激素水平的正常规律被破坏时，将影响周期的规律和时程，出现月经失调。

1978年Jurkowski首次报道了运动中女运动员性激素水平发生显著变化[1]，国内外众多研究者开始将目光聚焦于运动与女性HPO轴的关系。研究者们发现，女性性激素水平与运动强度、运动持续时间和运动形式等因素密切相关。对这些影响因素控制标准的不统一，导致女性激素水平会发生不同的变化，因此研究报道结果各异[2] [3]。20世纪80年代以来，随着女性参加角逐的运动项目日益增多，运动性月经失调（Athletic Menstrual Irregularity，AMI）的发病率也随之增高。人们注意到，长期运动训练影响下，女运动员出现的最显著、最常见的反应表现为低性腺类固醇和低促性腺激素水平[4] [5] [6]。表明，运动训练对HPO轴功能产生了深刻的影响，这种影响可能通过调整生殖激素及抗生殖激素的基础分泌模式，以及修正其对运动刺激的反应而完成。与运动训练有关的诸多因素（运动负荷强度、量度、营养状况、体脂厚度、体重降低、体温升高、缺氧刺激等）的长期刺激作用，均可能破坏体内正常的激素平衡，导致HPO轴功能失调，发生AMI[7]。由此人们开始思考：运动对女性HPO轴功能的整体影响效应究竟怎样？激素水平的变化是运动刺激下的一过性反应？还是一种持续的不可逆性改变？AMI的病理机制过程与临床常见的女性月经失调

及闭经是否相同或相似？差异又在何处？为此，研究者们陆续对HPO轴各环节激素水平对运动的反应，以及不同运动项目女运动员的激素变化特点进行了较为细致的观察。发现，发生AMI运动员体内的HPO轴激素及抗生殖激素水平变化特点与下丘脑型闭经患者相似。从激素水平变化的角度分析，运动员长期训练出现的低性腺类固醇和低促性腺激素水平的特征性激素变化，似乎是以抗生殖激素水平异常增高，导致下丘脑—垂体环节功能改变为主的变化[8] [9]。因此，有学者提出，AMI的激素失衡学说。针对运动中肾上腺皮质轴功能亢进的特点，有人又提出肾上腺皮质轴活化学说。此外，尚有能耗学说等诸多假说。这些假说分别从不同的侧面，对AMI的特点和病因病理机制进行了描述。由于AMI发生机制的复杂性以及方法学手段的限制，这些研究大多局限于对现象的描述及对机制的推测。

80年代—90年代末期，随着分子生物学技术手段的进步，人们开始注意到HPO轴激素信号转导的中介环节——受体的重要作用。激素在相应受体介导下，通过对靶基因的调控作用，实现信息的转化、放大，完成其生物学效应。受体水平及活性是决定激素生物学效应的关键因素。那么，在以低性腺类固醇和低促性腺激素水平为主要特征的特殊状态下，HPO轴功能激素受体是否也会出现相应的变化？其变化的机制怎样？在AMI发生中又具有什么意义呢？截止目前，这方面的研究报道极为少见，因而大大限制了运动对HPO轴整体功能变化及机制研究的深入。

运动训练对机体的影响是具体而深刻的，一直以来，对于长期的大负荷训练是否能够导致女运动员生殖系统发生不可逆转的器质性改变，进而影响其终生？也成为人们所困扰和顾虑的问题。就已有的研究报道分析，运动训练对机体的影响可能不仅表现为性腺轴功能激素与抗生殖激素水平的变化，而且可能出现激素与受体表达、不同内分泌功能轴间、性腺轴超微结构与功能间的交互影响、相互作用[10] [11] [12]。由于目前对运动训练影响下HPO轴功能受体的研究尚很不全面，对受体变化的机制更缺乏从基因调控水平的进一步分析，这也是AMI病理机制的研究至今未果的原因之一。而对于运动训练恢复过程HPO轴整体功能的变化及机制、HPO轴功能变化与结构改变关系的研究则更为少见，难以回答HPO轴功能变化与运动，特别是与长期运动训练的确切效应关系。也就依然成为当今运动人体科学研究的热点之一。

长期剧烈运动训练将可能导致女运动员AMI发生，已是不争的事实。长跑运动员中AMI发病率达36%[13]，大学生运动员的AMI发病率也高达31%[14]，而普通女性月经失调的发生率仅为2～5%[15]。近年来许多研究报道，AMI状