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Research progress in sensitivity to inhalation anesthetics

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Abstract: Inhalation anesthetics have both sedative, analgesic and muscle relaxing effects, and are widely used in clinical practice. Hypersensitivity to inhalation anesthetics predicts poor postoperative outcomes. Current studies have shown that some genetic mutations, ion channels or receptor, changes in metabolites, mitochondrial function are all related to the sensitivity of inhalation anesthetics in human or experimental animals. Therefore, this paper will briefly review the research progress in the mechanism of inhalation anesthetic sensitivity from gene mutation, ion channels or receptors, metabolites, and mitochondrial function.

Keywords: Inhalation anesthetics; Sensitivity; Gene mutation; Ion channels; Receptor; Metabolites; Mitochondria

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Inhalation anesthetics are characterized by their sedative, analgesic, and muscle relaxant properties. Therefore, they are particularly suited for surgeries or diagnostic procedures that are less stimulating and short-duration. Moreover, inhalation anesthetics are often preferred for patients with obesity, the elderly, and those with liver or kidney dysfunction. Variations in sensitivity to inhalation anesthetics are not only closely related to the depth of anesthesia but also affect postoperative outcomes [1]. Increased sensitivity to inhalation anesthetics can lead to overly deep anesthesia, circulatory suppression, delayed awakening, impaired neurological function, and even increased mortality [2]. Conversely, reduced sensitivity to inhalation anesthetics may result in too-light anesthesia, leading to intraoperative awareness, interference with surgical procedures, circulatory and neurological complications, and even death [3]. However, the mechanisms underlying the sensitivity to inhalation anesthetics are not fully understood.

Research has shown differences in sensitivity to inhalation anesthetics in experimental animals and humans. Specific genetic mutations have been linked to the inhalation anesthetics sensitivity in experimental animals such as fruit flies, nematodes [4], and mice [5], as well as in humans [6-7]. Studies indicate that ion channels or receptors [8], metabolites [9], and mitochondrial function [10-11] can influence the sensitivity to inhalation anesthetics in both experimental animals and humans. Investigating these areas could further elucidate the mechanisms underlying the sensitivity to inhalation anesthetics and the overall mechanism of general anesthesia. In light of this, this article will review the mechanisms of inhalation anesthetic sensitivity from the perspectives of gene mutations, ion channels or receptors, metabolites, and mitochondrial function.

1. Sensitivity to inhalation anesthetics and genetic

mutations

1.1 Sensitivity to inhalation anesthetics and non-mitochondrial related genetic mutations

Syntaxin, a protein involved in the docking and fusion of synaptic vesicles in the presynaptic active zones, can undergo mutations due to various genetic deletions. However, different gene deletions result in distinct sensitivities to isoflurane in fruit flies. For instance, the deletion of syxKARRAA leads to a mutation in syntaxin-1A protein, making fruit flies sensitive to isoflurane, whereas the deletion of syxH3-C results in a mutation in syntaxin 1A protein that makes fruit flies tolerant to isoflurane. This mechanism may be related to isoflurane targeting synaptic release and sleep pathways [12-13]. Knocking out or mutating the shank3 gene significantly reduces the minimum alveolar concentration (MAC) and median effective concentration (EC_{50}) of isoflurane in mice, thereby increasing their sensitivity to isoflurane. This mechanism may be related to the reduced expression of the NR1 and postsynaptic density protein-95 (PSD-95) genes in the central nervous system [14]. The js127, an allele of acetylcholinesterase-1, encodes adenylyl cyclase in nematodes, the mutation of js127 can increase the levels of adenosine monophosphate (AMP). Research has found that the EC_{50} of isoflurane for js127 mutant nematodes is three times that of wild type, significantly increasing their sensitivity to isoflurane. Thus, specific genetic mutations are related to the sensitivity of experimental animals to inhalation anesthetics.

A study involving 500 patients undergoing abdominal surgery, using whole-exome sequencing (WES) to analyze venous blood from patients with different sensitivities to sevoflurane, identified four genes with eight single nucleotide polymorphism (SNP) sites: FAT2 (SNP rs174272, rs174271, and rs174261), ADI1 (SNP rs117278), NEDD4 (SNP rs70048, rs70049, and rs70056), and FOXRED2 (SNP rs144281), which were related to the sensitivity to sevoflurane [7,15].

1.2 Sensitivity to inhalation anesthetics and mitochondrial genome mutations

The literature reports that knocking out the NDUFS4 subunit of mitochondrial complex I in mice significantly increases their sensitivity to inhalation anesthetics, reducing their MAC value by more than 50%. This is the most considerable change in the potency of inhalation anesthetics at the whole-animal level in research *in vivo* [16]. The gas-1 gene encodes a subunit of mitochondrial complex I, and mutations in the gas-1 gene can affect mitochondrial function. Studies using *Caenorhabditis elegans* as the research subjects found that oxidative phosphorylation and ATP production were not related to the sedative effects of inhalation anesthetics. However, accompanying mutations in the gas-1 gene, oxidative phosphorylation and ATP production increased the sensitivity of inhalation anesthetics [17]. Thus, changes in mitochondrial function by oxidative damage are related to the sensitivity of *Caenorhabditis elegans* to inhalation anesthetics. Another study showed that the gas-1 gene in mitochondrial complex I and the mev-1 gene in mitochondrial complex II were involved in the electron transfer process of the mitochondrial respiratory chain. Mutations in these two genes affect mitochondrial function, affecting the susceptibility to inhalation anesthetics in *Caenorhabditis elegans*. This suggests that mitochondrial complex I and mitochondrial complex II affect the behavior of experimental animals, which is similar to the mechanism of the organ-protective effect of inhalation anesthetics. Mitochondrial complex I and mitochondrial complex II affect the behavior of experimental animals, similar to the organ protective mechanism of inhalation anesthetics [18].

2. Sensitivity to inhalation anesthetics and ion channels or receptors

2.1 Sensitivity to inhalation anesthetics and ion channels

In excitable cells, the two-pore domain potassium (K_{2P}) channels are crucial for background potassium currents. K_{2P} consists of two subunits, each with four transmembrane spanning regions and two pore-forming regions. Numerous studies have indicated K_{2P} channels are involved in the mechanism of sensitivity to inhalation anesthetics. TRESK channels, a subtype of K_{2P} channels, were found to be related to sensitivity to isoflurane in mice. Morphological and behavioral methods were used to assess the differences in sensitivity to inhalation anesthetics between TRESK channel knockout mice (using homologous recombination techniques) and wild-type mice, and found that compared to wild-type mice, TRESK channel knockout mice had increased sensitivity to pain and an increased MAC value, indicating that the TRESK channel is related to the sensitivity of mice to isoflurane. This study also demonstrated that the TRESK channel was a target of inhalation anesthetics [19]. TREK-1 is the most extensively studied K_{2P} channel and plays a critical role in the cellular mechanisms of neuroprotection, anesthesia, pain, and depression. Recent research has shown that mice with TREK-1 and TREK-2 gene knockouts are not resistant to halothane or isoflurane, suggesting that the absence of TREK channels does not alter the sensitivity to inhalation anesthetics in mice. Therefore, the influence on sensitivity to inhalation anesthetics might be mediated by other channels [8].

In the central and peripheral nervous systems, the Nav1.6 ion channels are the major voltage-gated sodium channels, encoded by the *Scn8a* gene. The Nav1.6 ion channel plays a significant role in generating persistent and resurgent currents and is expressed throughout the entire mouse brain, including the cerebellum, hippocampus, frontal cortex, and basal ganglia [20]. One

study using mice with reduced activity of Nav1.6 ion channels due to mutations in the Scn8a$^{medJ/medJ}$ and Scn8a$^{9J/9J}$ genes showed that these mice exhibited significantly increased sensitivity to inhaled anesthetics. Thus, the Nav1.6 ion channel is involved in the mechanism of sensitivity to inhalation anesthetics in mice, and may serve as a target for inhalation anesthetics [20].

2.2 Sensitivity to inhalation anesthetics and receptors

Scholars found that changes in glutamate receptors with age were associated with increased sensitivity of dog to inhaled anesthetics [21]. They also discovered that the MAC value for isoflurane was approximately 1.82% in dogs aged 2-3 years, whereas it was approximately 1.45% in dogs with 11-year-olds. Further studies found that elderly dogs had reduced binding sites for glutamate and diazepam on NMDA receptors in the cerebral cortex and hippocampus, which may be related to differences in MAC values in experimental animals. This could be one of the reasons for the differences in sensitivity to inhalation anesthetics among experimental animals [21]. Varnäs *et al.* [22] observed that metabolic glutamate receptor 5 (mGluR5) radioligands might have an affinity for monoamine oxidase-B (MAO-B), and their binding could be sensitive to sevoflurane anesthesia in a positron emission tomography study. This observation suggests that sevoflurane anesthesia can inhibit the binding of radioligands to MAO-B in primate brains, which might be related to the mechanism of action and sensitivity to sevoflurane. Research has also confirmed that glycine receptors are one of the targets for the anesthetic effect of inhalation anesthetics [5]. In summary, the impact of specific receptor functions is related to the sensitivity of experimental animals to inhalation anesthetics.

3. Sensitivity to inhalation anesthetics and metabolites

Study found that after 2 h of sevoflurane anesthesia, the types of polyunsaturated fatty acids in monkey decreased significantly, and the body showed an inflammatory response, indicating that sevoflurane anesthesia disturbed lipid metabolism [23]. Another study using sevoflurane anesthesia to induce unconsciousness in patients, observed that sevoflurane anesthesia affected cerebral blood flow in patients, altering metabolites and metabolic connections in regions such as the frontal lobe and hypothalamus using electroencephalography (EEG), positron emission tomography scanning, and functional magnetic resonance imaging techniques [24]. These findings indicate that changes in systemic or local tissue metabolites may be involved in the mechanism of sevoflurane anesthesia. Glutamate, one of the primary excitatory neurotransmitters in the central nervous system, is involved in the mechanism of action of inhalation anesthetics [25]. Studies have shown that intermittent exposure to hypoxia reduces the sensitivity of mice to sevoflurane anesthesia by enhancing the O-GlcNAc-dependent regulation of the glutamate-glutamine cycle in the brain [26]. This suggests that glutamate and its related metabolism may be related to the sensitivity of experimental animals to inhalation anesthetics.

A study of 500 patients undergoing abdominal surgery, metabolomics techniques were used to examine the preoperative 2-hour plasma of patients with different sensitivities to sevoflurane. The levels of L-glutamine, pyroglutamic acid, L-selenocysteine, and sphingosine were related to patients' sensitivity to sevoflurane [9]. This indicates that changes in metabolites are involved in the differences in human sensitivity to sevoflurane.

Nitric oxide (NO) is a neurotransmitter in the central nervous system that regulates receptors related to general anesthesia, including γ-aminobutyric acid (GABA) [27], NMDA [28], and acetylcholine receptors [29]. NO can induce various downstream targets, including guanylate cyclase (GC), the activation of NO, and cyclic guanosine monophosphate (cGMP) produced by GC. cGMP is a second messenger that can regulate synaptic plasticity in the mammalian brain. Studies have shown that the NO-cGMP signaling pathway is related to the sensitivity of mice to isoflurane by observing the concentration of isoflurane required for the loss and recovery of the righting reflex in mice [30].

4. Sensitivity to inhalation anesthetics and mitochondrial function

Inhalation anesthetics have been confirmed to exert organ-protective effects by affecting mitochondrial function and producing organ protection. An animal study found that inhibiting mitochondrial complex I was an essential mechanism for the differences in sensitivity to inhalation anesthetics [11]. Ninety-one children aged 6 months to 16 years undergoing diagnostic muscle biopsy for mitochondrial diseases were selected for a clinical trial, and sevoflurane was used as the only sedative for anesthesia and maintenance. The end-tidal concentration of sevoflurane required to maintain the same depth of anesthesia was significantly lower in patients with mitochondrial complex I defect compared with patients with other mitochondrial defects and normal patients. This indicates that patients with mitochondrial complex I defect have an increased sensitivity to sevoflurane [10]. In summary, mitochondrial function is involved in the sensitivity of animals and humans to inhalation anesthetics.

5. Outlook

In conclusion, the sensitivity to inhalation anesthetics is related to the postoperative outcomes of patients, making the study of this scientific issue of significant clinical importance. Current research indicates that the sensitivity to inhalation anesthetics is associated with various factors, including genetic mutations, ion

channels or receptors, metabolites, and mitochondrial energy metabolism. Focusing research efforts on these areas not only promises to further reveal the mechanisms behind the sensitivity to inhalation anesthetics but also lays the foundation for guiding the rational use of inhalation anesthetics, achieving personalized general anesthesia, optimizing clinical outcomes, and developing more effective general anesthetic drugs.

Conflict of Interest: None

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· 学术前沿 ·

吸入麻醉药物敏感性的研究进展

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摘要：吸入麻醉药物同时具备镇静、镇痛和肌肉松弛作用，被广泛用于临床麻醉，吸入麻醉药敏感性增加预示着患者不良的术后结局。目前的研究表明，一些基因突变、离子通道或受体、代谢物的变化、线粒体功能等均与人或实验动物对吸入麻醉药的敏感性有关。因此，本文将从基因突变、离子通道或受体、代谢物、线粒体功能等方面，概述吸入麻醉药敏感性机制的研究进展。

关键词：吸入麻醉药；敏感性；基因突变；离子通道；受体；代谢物；线粒体
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Research progress in sensitivity to inhalation anesthetics

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Abstract: Inhalation anesthetics have both sedative, analgesic and muscle relaxing effects, and are widely used in clinical practice. Hypersensitivity to inhalation anesthetics predicts poor postoperative outcomes. Current studies have shown that some genetic mutations, ion channels or receptors, changes in metabolites, mitochondrial function are associated with the sensitivity of human or experimental animals to inhalation anesthetics. Therefore, this paper will briefly review the research progress in the mechanism of inhalation anesthetics sensitivity from gene mutation, ion channels or receptors, metabolites, and mitochondrial function.

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吸入麻醉药同时具备镇静、镇痛和肌肉松弛作　　用。因此，在刺激小、持续时间短的手术或诊疗操作

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中，可仅选用吸入麻醉药。同时，针对肥胖、老年、肝和肾功能障碍患者，也可以优先选择吸入麻醉药。吸入麻醉药敏感性的差异，不仅与麻醉深度密切相关，同时还关系到患者的术后结局[1]。吸入麻醉药敏感性增加，容易导致麻醉过深，抑制循环，导致苏醒延迟、神经功能受损，甚至增加患者死亡率[2]。患者对吸入麻醉药的敏感性降低，在麻醉中可能导致麻醉过浅，出现术中知晓，干扰手术操作，引起循环系统、神经系统并发症，甚至导致死亡[3]。然而，目前对于吸入麻醉药物敏感性的机制，并不十分清楚。

研究发现，实验动物以及人类对吸入麻醉药存在敏感性差异，一些基因突变与果蝇、线虫[4]和小鼠[5]等实验动物以及人类[6-7]对吸入麻醉药的敏感性有关。研究表明，离子通道或受体[8]、代谢物[9]、线粒体功能[10-11]等影响实验动物或人对吸入麻醉药的敏感性。以这些方向为突破口，有望进一步揭示吸入麻醉药敏感性的机制以及全身麻醉机制。鉴于此，本文将从基因突变、离子通道或受体、代谢物、线粒体功能等方面，对吸入麻醉药敏感性的机制做一介绍。

1　吸入麻醉药敏感性与基因突变

1.1　吸入麻醉药敏感性与非线粒体相关基因突变　突触融合蛋白（syntaxin）是一种在突触前区参与突触小泡泊靠与融合的蛋白质，不同基因缺失均可导致 syntaxin 1A 蛋白突变，然而不同基因缺失却使得果蝇对异氟烷的敏感性有明显差异，例如 syxKARRAA 缺失致 syntaxin 1A 蛋白突变，果蝇表现为对异氟烷敏感，而 syxH3-C 缺失致 syntaxin 1A 蛋白突变，果蝇却表现为对异氟烷耐受，其机制可能与异氟烷靶向突触释放和睡眠通路有关[12-13]。敲除 shank3 基因或者使其突变，小鼠对异氟烷的最低肺泡有效浓度（minimum alveolar concentration，MAC）和半数有效浓度（median effective concentration，EC_{50}）明显降低，因此，小鼠对异氟烷的敏感性增加，其机制可能与中枢神经系统中 NR1 和 PSD95 基因表达降低有关[14]。js127 是乙酰胆碱酯酶-1 的一个等位基因，在线虫编码腺苷酸环化酶，js127 基因突变能增加一磷酸腺苷的水平。有学者通过测量成年线虫的移动情况来判断其对异氟烷的敏感性，发现 js127 基因突变的线虫 EC_{50} 是野生型线虫的 3 倍，因此其对异氟烷的敏感性显著增加。可见，某些基因突变与实验动物对吸入麻醉药的敏感性有关。

有研究以 500 例腹部手术患者为对象，以筛选出的对七氟烷具有敏感差异性的患者的静脉血进行全外显子组测序（WES）后，发现 4 个基因，共 8 个单核苷酸多态性（single nucleotide polymorphism，SNP）位点：即 FAT2（SNP rs174272、rs174271 和 rs174261）、ADI1（SNP rs117278）、NEDD4（SNP rs70048、rs70049 和 rs70056）和 FOXRED2（SNP rs144281），与患者对七氟烷的敏感性有关[7,15]。

1.2　吸入麻醉药敏感性与线粒体相关基因突变　文献报道，敲除小鼠线粒体复合体 I 的亚基 NDUFS4，小鼠对吸入麻醉药的敏感性显著增加，其 MAC 值降低超过 50%，这是目前在整体动物水平上观察到的吸入麻醉药效价变化最大的动物实验[16]。文献显示，gas-1 基因是编码线粒体复合体 I 的一个亚基，gas-1 基因突变会影响线粒体的功能。以线虫为研究对象，发现氧化磷酸化和 ATP 的生成本身与吸入麻醉药的镇静作用无关。然而在 gas-1 基因突变的情况下，氧化磷酸化和 ATP 的生成却可以增加线虫对吸入麻醉药的敏感性[17]。可见，氧化损伤引起线粒体的功能改变，与线虫对吸入麻醉药的敏感性有关。另有研究显示，线粒体复合体Ⅰ中的 gas-1 基因和线粒体复合体Ⅱ中的 mev-1 基因均参与了线粒体呼吸链的电子传递过程，这两个基因突变均会影响线粒体的功能，进而影响线虫对吸入麻醉药的敏感性，提示线粒体复合体Ⅰ及线粒体复合体Ⅱ对实验动物的行为学有影响，这与吸入麻醉药的器官保护作用机制相似[18]。

2　吸入麻醉药敏感性与离子通道或受体

2.1　吸入麻醉药敏感性与离子通道　在可兴奋细胞，双孔钾通道（K_{2P}）对于背景钾电流极为重要，K_{2P} 由两个亚基构成，每一个亚基都有 4 个跨膜区域和两个孔排列构成。大量的研究表明，双孔钾通道（K_{2P}）参与了吸入麻醉药敏感性的作用机制。TRESK 通道是一种 K_{2P} 通道亚型，有研究通过同源重组的方法敲除小鼠体内的 TRESK 通道，利用形态学和行为学的方法评估 TRESK 通道敲除小鼠与野生型小鼠对吸入麻醉药敏感性的差异，发现与野生型小鼠比较，TRESK 通道敲除小鼠增加了对疼痛的敏感性，增加了 MAC 值，可见 TRESK 通道与小鼠对异氟烷的敏感性有关，该研究还证明 TRESK 通道是吸入麻醉药的作用靶点[19]。TREK1 是研究最透彻的 K_{2p} 通道，在神经保护、麻醉、疼痛和抑郁的细胞机制中具有关键作用。最新的研究显示，TREK-1 和 TREK-2 基因敲除小鼠对氟烷或异氟烷没有抗性，这表明 TREK 通道缺失不会改变小鼠对吸入麻醉药物的敏感性，那么对吸入麻醉药敏感性的影响，可能是由其他通道发挥这种作用[8]。

在中枢和外周神经系统中，Nav1.6 离子通道是主要的电压门控钠离子通道，由 Scn8a 基因编码。Nav1.6 离子通道在持续和复活电流的产生中发挥重要作用，它在小鼠整个大脑中均有表达，如小脑、海马、前额叶皮质和基底节等[20]。有研究利用 $Scn8a^{medJ/medJ}$ 和 $Scn8a^{9J/9J}$ 突变的小鼠，降低 Nav1.6 离子通道的活性后，吸入麻醉药诱导小鼠致意识消失，观察小鼠翻正反射消失时对异氟烷和七氟烷的浓度需求，发现 Nav1.6 离子通道活性降低的小鼠对吸入麻醉药的敏感性显著增加。可见，Nav1.6 离子通道参与了小鼠对吸入麻醉药的敏感性机制，且该通道可能是吸入麻醉药的作用靶点[20]。

2.2　吸入麻醉药敏感性与受体　有学者以犬为研究对象，发现随着年龄的增加，谷氨酸受体的变化与犬对吸入麻醉药敏感性增加有关[21]。他们还发现 2~3 岁的犬，异氟烷的 MAC 值约为 1.82%，11 岁的犬，异氟烷的 MAC 值约为 1.45%。进一步研究发现，老龄犬在大脑皮质和海马区域的谷氨酸和地佐环平与 N-甲基-D-天冬氨酸（NMDA）受体的结合位点减少，可能与实验动物的 MAC 值有关，这或许是实验动物对吸入麻醉药敏感性有差异的原因之一[21]。Varnäs 等[22]在正电子发射断层扫描研究中意外观察到代谢性谷氨酸受体 5（mGluR5）放射性配体，可能与单胺氧化酶-B 具有亲和力，两者的结合可能对七氟烷麻醉敏感，由此可见七氟烷麻醉能抑制灵长类动物脑中放射性配体与单胺氧化酶-B 的结合，这可能和七氟烷作用及敏感性机制相关。研究证实甘氨酸受体也是吸入麻醉药发挥麻醉效应的靶点之一[5]。综上可见，某些受体功能的影响与实验动物对吸入麻醉药的敏感性有关。

3　吸入麻醉药敏感性与代谢物

有学者以猴为研究对象，发现七氟烷麻醉 2 h 后，其血清中多不饱和脂肪酸的脂质种类明显减少，机体呈现炎症反应状态，表明七氟烷麻醉扰乱了脂质代谢[23]。有研究通过七氟烷麻醉致患者意识消失，利用脑电图（EEG）、正电子发射断层扫描和功能磁共振技术，观察到七氟烷麻醉影响了患者脑血流，改变了额叶、下丘脑等部位的代谢物和代谢连接[24]。可见，机体全身或者局部组织代谢物的变化可能涉及到七氟烷的麻醉机制。谷氨酸是中枢神经系统中主要的兴奋性神经递质之一，参与吸入麻醉药的作用机制[25]。有研究显示，间歇性低氧暴露通过增强脑部 O-GlcNAc 依赖的谷氨酸—谷氨酰胺循环调控，降低了小鼠对七氟烷麻醉的敏感性[26]。由此可见，谷氨酸和其相关代谢可能与实验动物对吸入麻醉药的敏感性有关。

有研究以 500 例腹部手术患者为研究对象，通过代谢组学技术，对高敏、低敏组患者麻醉前及手术开始 2 h 时间点的血浆进行检测发现：L-谷氨酰胺、焦谷氨酸、L-硒代半胱氨酸，以及鞘氨醇的含量与患者对七氟烷的敏感性有关[9]。可见，代谢物的变化影响了人对七氟烷的敏感性。

一氧化氮（NO）在中枢神经系统是一种神经递质，调节全身麻醉相关的受体，包括 γ-氨基丁酸（GABA）[27]、NMDA[28] 和乙酰胆碱受体[29]。NO 可作用于多种下游靶点，包括鸟苷酸环化酶（GC），激活 NO 和 GC 能够产生鸟嘌呤核苷酸（cGMP）。cGMP 是一种第二信使，在哺乳动物大脑，cGMP 能够调节突触的可塑性。有研究通过观察异氟烷致小鼠翻正反射消失和翻正反射恢复时的异氟烷浓度需求，发现 NO-cGMP 信号通路与小鼠对异氟烷的敏感性有关[30]。

4　吸入麻醉药敏感性与线粒体功能

吸入麻醉药已被证实可通过影响线粒体的功能，进而发挥器官保护作用。在一项动物实验中发现，线粒体复合物 Ⅰ 的抑制是吸入性麻醉剂敏感性差异的重要机制[11]。在一项临床研究中选取 91 例 6 月龄至 16 岁的儿童进行线粒体疾病的诊断性肌肉活检术，以七氟烷作为唯一镇静药物进行麻醉与维持，发现维持在相同麻醉深度下线粒体复合物 Ⅰ 缺陷患者所需要的呼吸末七氟烷浓度明显低于其他线粒体缺陷患者和正常患者，可见线粒体复合物 Ⅰ 缺陷患者对七氟烷敏感性增加[10]。综上可见，线粒体功能涉及到动物和人对吸入麻醉药的敏感性。

5　展　望

综上所述，吸入麻醉药的敏感性关系到患者的术后结局，研究这个问题具有重要的临床意义。目前的研究表明，吸入麻醉药的敏感性与一些基因突变、离子通道或受体、代谢物、线粒体能量代谢等有关。以这些方向为突破口深入研究，不仅有望进一步揭示吸入麻醉药敏感性的机制，同时还可为指导吸入麻醉的合理用药、实现个体化全身麻醉、优化临床效果及开发出效果更好的全身麻醉药物奠定基础。

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