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综 述

基于神经影像技术认识膝骨关节炎慢性疼痛的复杂性

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摘 要：膝骨关节炎(knee osteoarthritis, KOA)慢性疼痛极大影响患者的生活质量及功能活动，明确KOA疼痛的机制及不同疗法的镇痛效应是目前研究的重要任务。近年来，神经影像技术在疼痛的基础和临床研究中发挥了重要作用。随着神经影像技术在KOA慢性疼痛研究中的应用和发展，学者们发现KOA的慢性疼痛不仅包含伤害感受性疼痛，也含有神经病理性疼痛成分。参与KOA疼痛的神经病理性疼痛机制复杂，可能是外周或中枢敏化引起的，但在临床诊疗中未引起足够的重视，针对合并神经病理性疼痛KOA的治疗方法也尚未形成共识。因此，本综述基于磁共振成像(magnetic resonance imaging, MRI)、脑电图(electroencephalogram, EEG)、脑磁图(magnetoencephalogram, MEG)、近红外光谱(near-infrared spectroscopy, NIRS)等神经影像技术研究成果，回顾KOA疼痛引起的大脑病理生理学相关区域变化，梳理疼痛评估和预测方面的最新成果，明确KOA不同疗法的脑中枢镇痛机制，希望为KOA疼痛的治疗提供新思路，以利于制定KOA的早、中期合理治疗方案，促进临床镇痛疗效的提高。

关键词：神经影像技术；膝骨关节炎；慢性疼痛；神经病理性疼痛；伤害感受性疼痛
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Complex mechanisms of chronic pain in knee osteoarthritis identified by neuroimaging technology

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Abstract: Chronic pain of knee osteoarthritis (KOA) greatly affects the quality of life and functional activities of patients. It is important to clarify the underlying mechanisms of KOA pain and the analgesic effect of different therapies. Neuroimaging technology has been widely used in the basic and clinical research of pain. In the recent years, neuroimaging technology has played an important role in the basic and clinical research of KOA pain. Increasing evidence demonstrates that chronic pain in KOA includes both nociceptive and neuropathic pain. The neuropathic mechanism involved in KOA pain is complex, which may be caused by peripheral or central sensitization. In this paper, we review the regional changes of brain pathophysiology caused by KOA pain based on magnetic resonance imaging (MRI), electroencephalogram (EEG), magnetoencephalogram (MEG), near-infrared spectroscopy (NIRS) and other neuroimaging techniques. We also discuss the central analgesic mechanism of different KOA therapies, with a focus on the latest

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achievements in the evaluation and prediction of pain. We hope to provide new thoughts for the treatment of KOA pain, especially in the early and middle stages of KOA.

Key words: neuroimaging technology; knee osteoarthritis; chronic pain; neuropathic pain; nociceptive pain

疼痛严重影响膝骨关节炎 (knee osteoarthritis, KOA) 患者的生活质量及功能活动，随着全球老年化，其发病率和致残率逐渐上升 [1–5]。其中，大约有 21.1%~66.7% 的 KOA 患者表现为神经病理性疼痛 [6–9]，在患侧膝关节的远端表现出异常疼痛敏感性或疼痛抑制 [10]。神经影像技术在疼痛复杂机制的识别中发挥了重要作用 [11]，并且在 KOA 的伤害感受性疼痛和神经病理性疼痛研究上取得新进展 [12]，但是在国内外临床医疗领域尚未引起足够的重视。

在不明确 KOA 疼痛的复杂机制的情况下，KOA 患者经受镇痛药物的过多服用和承担副作用发生率较高的风险 [13]，并且该病最终进展为持续性疼痛和严重残疾，患者最终被迫选择手术 [4]。但是，镇痛药物和手术并不能完全消除疼痛，甚至有部分患者对非甾体抗炎药等一线药物和常规手术产生了耐受 [4, 14, 15]，仍遭受难以忍受的疼痛 [16, 17]。此外，之前 KOA 疼痛的临床评估和治疗中主要依靠量表等主观评估，敏感性较差 [18, 19]。近年来，神经影像技术的应用使 KOA 疼痛的机制更加清楚，进一步明确了其神经病理性疼痛成分 [1, 20]，可为 KOA 疼痛临床治疗、诊断、评估和预测提供更客观的技术和方法，促进临床诊疗的规范化进程，有利于改善预后，提高临床疗效和安全性。

1 KOA疼痛引起的病理生理学变化

KOA 是由关节软骨破坏、滑膜病变等多种因素导致的病理改变，引发进行性疼痛和功能障碍的骨关节病 [4]。在轻、中度 KOA 患者中，软骨碎片可被滑膜细胞吞噬，引发滑膜炎症反应和疼痛 [21]。导致 KOA 疼痛的重要因素，不仅包括膝关节局部的炎性改变，而且还有中枢神经递质水平及伤害感受通路的异常，外周和中枢神经敏化 [22, 23]。KOA 疼痛可能受免疫系统和神经系统的共同调控 [24, 25]，涉及心理、社会和生物机制，依赖于外周神经、脊髓和脑中枢神经的上行传导通路，以及下行抑制通路 [26]。

疼痛是 KOA 的主要症状，尤其是慢性疼痛，其对身体残障、运动功能、负向情绪的影响可明显降低患者的生活质量，甚至可导致决策失误等认知障碍，引发机体感觉、情感和认知等脑功能活动的异常 [16, 27]。最新研究显示，影响 KOA 患者生理状态的因素有 Kellgren & Lawrence 影像学分级、病程及身体质量指数 (body mass index, BMI)，影响心理状态的因素主要为病程 [28]。

尽管膝关节退行性改变是引起 KOA 慢性疼痛的最初诱因，但膝关节局部影像学表现存在与患者的疼痛不一致现象 [29, 30]。在最新的研究中，中枢敏化和神经可塑性等因素逐渐被关注 [31]。KOA 疼痛由急性转化为慢性疼痛后，引起的大脑病理生理学变化比较复杂，慢性中、重度疼痛可能同时存在脑结构和脑功能改变 [20, 32]。KOA 慢性疼痛的中枢敏化和神经可塑性变化在脑电图 (electroencephalogram, EEG)、脑磁图 (magnetoencephalogram, MEG)、功能磁共振成像 (functional magnetic resonance imaging, fMRI)、结构磁共振成像 (structural magnetic resonance imaging, sMRI) 等神经影像学研究中逐渐被揭示 [23, 31, 33–36]。

KOA 慢性疼痛涉及到自我情感评估的大脑区域，这促进了对膝关节疼痛的正确理解与认识。KOA 的自发性慢性疼痛与膝关节机械性压痛不同，与机械性压痛刺激相关的脑活动可与自发性疼痛相关的脑活动区分开；KOA 相关的临床特征可映射到前额叶 - 边缘区，在接受环氧化酶 -2 抑制剂 (伐地昔布) 治疗后，血液和脑脊液中药物含量与前额叶 - 边缘的脑活动程度呈正相关 [37]。丘脑是“疼痛矩阵”的关键脑区，fMRI 研究结果印证了丘脑在 KOA 疼痛的上下行调控通路中发挥着重要作用 [38]。KOA 的慢性疼痛可导致右丘脑灰质体积缩小，并且右丘脑与中央后回的静息态功能连接 (functional connectivity, FC) 与疼痛程度密切相关 [32]，Liao 等采用 sMRI 体素形态学对 KOA 慢性疼痛患者进行研究，发现优先涉及前额叶皮质 (prefrontal cortex, PFC) 的慢性疼痛可能是认知状态，涉及情感和认知功能 [39]。磁共振波谱 (magnetic resonance spectroscopy, MRS) 可量化 KOA 慢性疼痛患者丘脑神经炎症的脑化学和细胞过程，可用肌醇 (myoinositol, mIns)、胆碱 (Choline, Cho) 和 N- 乙酰天冬氨酸 (N-acetylaspartate, NAA) 等神经代谢产物进行标记 [23]。Z 变换格兰杰因果关系 (zGC) 值表示兴趣区 (region of

interest, ROI) 到全脑及全脑到 ROI 的有效 FC；低频振幅 (amplitude of low frequency fluctuation, ALFF) 可用来检测与分析人体自发性脑活动，其两个延伸指标分别是比率低频振幅 (fractional amplitude of low frequency fluctuation, fALFF) 和 z 转换后的低频振幅 (z amplitude of low frequency fluctuation, zALFF)。研究显示，在慢性中、重度疼痛 KOA 患者中存在脑功能改变，右侧丘脑 zALFF 值减低，并且右侧丘脑到右侧中央前回、中央后回、顶上小叶、楔前叶的 FC 增强，从右侧顶上小叶、楔前叶到右侧丘脑的有效 FC 减低，疼痛视觉模拟评分 (visual analogue scale, VAS) 评分与右侧楔前叶到右侧丘脑间的有效 FC 的 zGC 值呈负相关 [40]。

除了认知控制，KOA 慢性疼痛中枢可发生伤害性记忆、情绪调节、感觉加工的信息整合。KOA 慢性疼痛存在中脑导水管周围灰质 (periaqueductal gray matter, PAG)、内侧额叶皮质 (medial frontal cortex, MFC)、双侧海马 (hippocampus, Hpc)、伏隔核 (nucleus accumbens, NAc)、头端前扣带回皮质 (rostral anterior cingulate cortex, rACC) 和背外侧前额叶皮质 (dorsolateral prefrontal cortex, DLPFC) 等脑区静息态 FC 异常，常伴有情绪反刍、伤害性记忆和回避学习等方面的复杂变化 [41, 42]。基于 fMRI 的研究显示，中枢多巴胺系统相关脑区 NAc 与认知控制、情绪调节、感觉加工相关脑区及默认网络 FC 异常，这可能是 KOA 疼痛的脑功能机制 [43]。KOA 慢性疼痛患者的 DLPFC 和“疼痛矩阵 (pain matrix)”有不同的脑激活模式和异常脑 FC [44]。基于局部一致性 (regional homogeneity, ReHo) 的脑功能成像研究显示，KOA 慢性疼痛患者的双侧前扣带回 ReHo 值与 VAS 呈负相关 (AlphaSim correction, $P < 0.01$)，提示双侧前扣带回脑功能活动的紊乱与疼痛关系密切 [45]。ReHo 可作为模型驱动方法的补充，度量给定体素时间序列与最近邻体素时间序列的相似性，有助于揭示人脑功能的复杂性 [46]。此外，预期也会影响KOA患者的疼痛。Brown等研究显示，对于相同强度的激光热痛刺激，KOA 患者的预期引起的脑岛 (insula) 活动与 KOA 疼痛和压痛点数量相关，DLPFC 的激活在预期过程中降低 [47]。目前已有研究运用脑灰质体积检测技术评估骨关节炎疼痛及其敏感性 [39, 48, 49]，在以后研究中可应用多变量模型区分 KOA 的神经病理性疼痛成分，并检测出比以往更精细的大脑皮质解剖结构差异，从而可更客观地分析 KOA 疼痛的脑中枢机制。

KOA 慢性疼痛会降低弥漫性伤害性抑制控制 (diffuse noxious inhibitory controls, DNIC) 强度 [50]。MEG 和 EEG 技术可在神经元水平研究疼痛调控机制 [33, 34]。在短暂的电刺激引起 KOA 患者出现典型疼痛时，患者的中扣带回 (mid-cingulate cortext, MCC) 显示出激活减少，次级体感皮层 (secondary somatosensory cortex, SII) 的活动没有明显变化，提示 DNIC 的强度在慢性疼痛的发展过程中减弱，受下行抑制性疼痛系统的神经元可塑性的影响 [37]。KOA 患者的疼痛特征无法用纯粹的外周机制来解释，因为也可能存在中枢敏化等神经病理性成分。Lockwood 等对骨关节炎大鼠疼痛模型进行镇痛研究时，发现他喷他多和普瑞巴林在联合应用时镇痛效应更好，提示该镇痛效应可能是中枢性镇痛药他喷他多调节了 DNIC 诱导的神经元抑制，同时普瑞巴林抑制了神经元异常的反应，共同调整了中枢敏化状态 [34]。这与相关实验性 KOA 疼痛模型的动物研究结果相互补充，例如 Im 等研究显示，随着 KOA 病情进展，动物的脊髓及脊髓背角小胶质细胞出现逐渐增殖现象，印证了 KOA 的神经病理性疼痛成分 [51]。

2 KOA不同疗法的脑中枢镇痛机制

神经影像学技术在 KOA 疼痛中的应用使不同疗法的中枢镇痛机制更加清晰，为临床合理运用健康教育、针灸、推拿、药物及手术等疗法提供了依据。

2.1 健康教育

健康教育属于 KOA 临床治疗指南中的基础疗法 [4]，在健康教育过程中，无论是否包括运动都是有益的 [52, 53]。同时，预期和安慰剂等可有效激发正向预期以及强烈的安慰剂效应 [54, 55]，因此在 KOA 镇痛治疗中要对健康教育中的类似内容予以重视。NAc、前扣带回皮质 (anterior cingulate cortex, ACC) 和内侧前额叶皮质 (medial prefrontal cortex, mPFC) 是调节奖赏预期系统和动机系统相互作用的关键大脑区域 [56–59]。其中，预期对奖赏通路的作用受到 NAc 中的多巴胺神经传递的影响，并与富含阿片样物质的 ACC 等脑区密切相关 [57]。研究表明，提高预期可加强 KOA 疼痛的治疗效果 [54]。fMRI 研究数据显示，以 NAc 为种子点的静息态 FC 在 mPFC、rACC 和 DLPFC 脑区的强度增加，提示奖赏预期系统和动机系统对镇痛过程的调节作用，而缓解疼痛可被视为奖赏的特种情况 [57, 59]。一项双盲、

随机、安慰剂对照、三交叉试验 fMRI 研究 [35] 显示，神经性疼痛中安慰剂的脑中枢镇痛机制与吻侧前扣带回和脑干的 FC 增强有关，这项研究为解决 KOA 疼痛检测提供了可能的客观指标，避免过度依赖主观报告，有利于减少镇痛药的过量应用。

2.2 非药物疗法

针灸、运动、推拿等非药物疗法是《膝骨关节炎中医诊疗指南 (2020 年版)》推荐疗法 [60]，对 KOA 神经病理性疼痛的防治有一定的潜力，可依据作用效应在临床治疗中合理运用。

针刺等相关技术不仅能缓解 KOA 疼痛，对于关节僵硬、功能活动障碍等也有不同程度改善作用 [61]。针刺可能通过恢复大脑 PAG-MFC 和 PAG-Hpc 等关键疼痛区域静息态 FC 的平衡，改变与疼痛相关的注意力和记忆来发挥镇痛作用 [41]，通过调节右额顶神经网络 (right frontoparietal network, rFPN) 和执行控制网络 (executive control network, ECN) 与 rACC/mPFC (下行疼痛调节系统的关键区域) 的 FC 来缓解 KOA 疼痛 [62]。研究显示，在提高预期的基础上进行针刺治疗 KOA，KOA 疼痛的缓解比标准针刺更好，这种改善作用的机制与 NAc 和 mPFC、rACC 和 DLPFC 之间的静息态 FC 增加有关，使大脑区域的 FC 恢复正常，为促进 KOA 疼痛的治疗提供了新思路 [42]。fALFF 对自发性脑活动的检测有较高的敏感性和特异性 [63]。Xie 等应用 fMRI 研究艾灸对 KOA 患者的大脑作用机制，发现艾灸可使右侧大脑、外核、左侧小脑、左侧大脑和脑白质的 fALFF 值升高，中央前回、额叶和枕叶的 ALFF 值降低，同时使丘脑、外核和顶叶的 ReHo 值升高，右侧大脑、左侧大脑和额叶的 ReHo 值降低，提示艾灸对大脑的影响不是单个区域，而是引起多个脑区协同的复杂调节 [64]。一项基于 fMRI 技术的臭氧水临床研究显示，KOA 患者治疗前后的右岛叶 ReHo 变化与 VAS 变化呈负相关 ($r = -0.657$)，提示岛叶可能是臭氧水镇痛作用的关键脑区 [65]。

蹬车运动、太极拳和八段锦等多种运动方式对于缓解 KOA 慢性疼痛有着积极的作用 [66, 67]，基于运动方式的共同和独特机制可能有助于创建基于运动的慢性疼痛干预措施。Shanahan 等采用 fMRI 发现，KOA 患者膝关节和踝关节运动任务表现质量与运动皮质组织的差异有关 [68]。八段锦、太极拳等多种运动能调节认知控制网络来缓解 KOA 疼痛 [69]，可同时调节下行阿片能通路的静息态 FC、奖赏 / 动机系统，提高血清程序性死亡 1 (programmed death 1, PD-1) 浓度，并且右侧眶内侧前额叶皮质与 PAG 的静息态 FC 降低程度和膝关节疼痛改善有关，眶内侧前额叶皮质灰质体积均显著增加，此外太极拳和八段锦运动使左腹侧被盖区和眶内侧前额叶皮质之间的静息态 FC 显著降低 [70]。

推拿是一种古老的中医外治法，临床研究认为推拿可改善 KOA 疼痛 [71, 72]，而随着神经影像学研究深入，推拿干预后引起的广泛镇痛效应被逐渐揭示。推拿对 KOA 慢性疼痛的瞬时效应表现为对大脑扣带回、额中回、中央前回、额内侧回独立成分信号的增强，偏向于镇痛，其长期累积效应偏向于调整情绪、认知，可使梭状回和颞中回的独立成分信号增强 [32]。

2.3 药物疗法

随着对 KOA 神经病理性疼痛成分的深入研究，针对 KOA 中枢敏化的治疗药物也逐渐被重视，并为手术后长期疼痛的解决提供了新思路。普瑞巴林、曲马多、加巴喷丁作为神经病理性镇痛药物，镇痛效应更强 [35, 73]，逐渐被应用于 KOA 神经病理性疼痛的镇痛研究中 [1, 74, 75]。其中，加巴喷丁作为钙离子通道调节剂，被国际疼痛学会 (International Association for the Study of Pain, IASP) 药物治疗指南推荐为治疗神经病理性疼痛的一线药物，在 KOA 慢性疼痛的临床研究中已有报道 [73]。艾瑞昔布等非甾体抗炎药主要针对伤害性疼痛，而加巴喷丁是钙离子通道调节剂，在单用时仅可缓解 KOA 的部分疼痛，当两者联合运用时镇痛效果更加明显 [1]。此外，仅用颅电刺激或萘普生来缓解 KOA 疼痛时，采用 fMRI、功能近红外光谱 (functional near-infrared spectroscopy, fNIRS) 等研究显示，腹侧脑、扣带回等脑区的激活伴随疼痛症状改善 [76, 77]。

2.4 手术疗法

手术是针对 KOA 病情严重患者的推荐疗法之一，但是也可能会留下术后持续疼痛的问题，这可能是神经病理学疼痛没能得到科学处理的结果。Lan 等用静息态 fMRI 研究老年 KOA 患者全膝关节置换术 (total knee arthroplasty, TKA) 引起的脑功能变化与疼痛及神经心理评估的关系，发现 KOA 患者的 DMN 的 ALFF 较低，而双侧杏仁核和小脑后叶的 ALFF 较高，即使是 TKA 术后 1 周脑区的这种变化特征仍持续存在 [78]。Lewis 等研究显示，终末期 KOA 患者双侧 NAc 和杏仁核以及同侧 S1 等

大脑区域发生特异性灰质萎缩，在 TKA 术后双侧杏仁核等脑灰质体积恢复，白质完整性也得到改善 [79]，但是伤害性抑制和促进过程引起的脑结构变化与伤害性系统的功能关系有待进一步证实。

虽然 TKA 是缓解疼痛和改善终末期 KOA 物理性能的有效疗法，但是 TKA 术后的不良预后较差，为了提高镇痛疗效，结合运动制定临床干预方案被逐渐关注 [80]。此外，一项针对 TKA 术后慢性疼痛患者的疼痛、敏化和身体表现的研究显示 [15]，TKA 术后患者在临床疼痛和定量感觉分析结果方面与 KOA 慢性疼痛患者相比没有差异，而体能表现却较低，这与中枢致敏可能有关，表明对患有慢性疼痛的 TKA 患者进行适当的检查和康复非常必要。

3 神经影像技术对KOA疼痛的评估和预测作用

3.1 KOA疼痛的评估

目前，针对 KOA 表型的客观化诊断方法、区分标准及结果判读上存在差异 [81]。神经影像学技术有助于 KOA 患者的疼痛类型诊断，为区分或优化临床治疗方案提供依据 [82]。没有一种功能成像方法同时具有优越的时间和空间分辨率。任务相关或静息状态功能磁共振成像 (fMRI 或 rsfMRI) 主要定量脑功能指标，如 FC、ReHo、ALFF 等，通过血液动力学效应评估脑功能变化，有较高的时间分辨率 [83–85]；基于体素的形态计量学 (VBM) 主要定量大脑解剖结构指标，如灰质密度或体积等，有较高的空间分辨率 [86]。随着神经影像技术的应用，KOA 慢性疼痛的功能和结构变化所代表的确切生理学意义更加明确 [82]。动脉自旋标记方法可独立地评估基线生理状态；通过多模式成像，将 fMRI、EEG 和 MEG 等相结合，有利于确定大脑区域对疼痛刺激做出反应的顺序 [87]。Fox 等将 fMRI 与正电子发射断层扫描相结合，分析大脑活动的激活和抑制模式，这种方法目前已被应用于揭示冥想实践的神经生理学分离性 [88]。

在镇痛效应的研究中，fMRI 在揭示神经病理性疼痛机制上可提供更客观证据，可检测大脑中伤害性和疼痛处理区的神经活动，评估 ACC 和脑干等脑区间的 FC [35]，根据 PAG 的激活程度能敏感、客观地评价 KOA 髌股关节软骨疼痛压力 [84]，也可被用于表征慢性疼痛的中枢神经系统活性 [87, 89]。每个 KOA 表型都包含许多典型的疼痛或病理生理学机制，可以应用神经影像学检测患者的疼痛参数 [81]。Liu 等 [40] 研究显示，慢性中、重度疼痛 KOA 患者在 TKA 术后的 VAS 评分与右侧丘脑到右侧中央后回的 zGC 值呈正相关，在临床中有助于识别术后慢性疼痛高危病人。Vachon-Presseau 等基于 fMRI 技术揭示慢性疼痛患者的脑功能网络特征，从心理学和神经生理学方面为慢性疼痛的评估提供了可借鉴范式 [90]。Monfort 等研究显示，fMRI 可客观量化关节源性疼痛的治疗效果，能敏感地评估硫酸软骨素对髌股关节软骨疼痛压力脑反应的影响 [84]。

通过神经成像技术来量化 KOA 疼痛有很大潜力，基于多模态磁共振的中枢神经系统药物活性评估的通用方案被逐渐关注。有研究通过采用机器学习方法和来自多个已发表研究的数据来确定药物相关活动调节和药物疗效之间的可靠关联，为镇痛药物的发现提供中等到强有力的证据 [89]。Yue 等基于疼痛行为学与 fMRI 数据进行乙酰氨基酚缓释片镇痛效应的研究，发现骨关节炎患者感觉皮层和边缘上回等疼痛通路的 BOLD 信号激活减少 [91]。Sorkpor 等基于 fNIRS 技术探索老年 KOA 患者的实质性脑激活模式，发现不同患者对侧的 PFC 和体感区域 (somatosensory regions) 对刺激的反应强度不同 [92]。

3.2 KOA疼痛的预测

研究表明大脑的神经影像学标记可以预测疼痛感知以及手术后镇痛效应 [93, 94]。fMRI 分析可能比神经心理学测试更有价值，可检测准备接受 TKA 治疗的老年 KOA 患者的认知能力下降 [39, 43]。膝关节骨性关节炎疾病特异性测量研究显示，前岛叶皮层 (anterior insular cortex, aIC)、前额叶和边缘区参与了预期对疼痛强度对调控。在重度 KOA 女性患者中，aIC 与右眶额皮质 (orbitofrontal cortex, OFC)、胼胝体下区 (subcallosal area) 和双侧额叶极 (bilateral frontal pole) 的静息态 FC 增强，左 aIC 和右 OFC 的静息态 FC 强度与 KOA 疼痛强度呈正相关，预期可使 OFC、胼胝体下区、额极和 aIC 在疼痛刺激过程中被激活，脑区之间的 FC 会影响严重 KOA 持续性术后疼痛的形成，可结合术前特异性疼痛区域的静息态 FC 预测 TKA 后持续疼痛的危险程度 [93]。此外，在外周伤害性刺激的神经影像学研究方面，也有学者认为可通过不同类型的共存 MRI 技术结合有或无关节负荷时 KOA 疼痛情况来预测临床手术的镇痛效果 [94]。

由于 KOA 慢性疼痛常存在脊髓介导的抑制信号减少和伤害性信号增加，因此在疼痛研究中应用

神经影像学检测脊髓介导的信号技术，可为KOA患者疼痛类型的神经生物学分类和术后疗效的准确预测提供支持。对于KOA中枢敏化患者，fNIRS利用血液对近红外光良好的散射性来获得大脑活动时氧合血红蛋白和脱氧血红蛋白的变化情况，可有效地检测和研究非药物、自我给药治疗相关的皮层疼痛神经机制[36]。采用MRS的研究也显示了中前扣带回(mid-anterior cingulate cortex, mACC)在中枢性疼痛敏化中的重要性，受累关节附近的点刺激和冷刺激引起的疼痛会显著增加，rACC的神经活动较低，头端腹内侧髓质(rostral ventromedial medulla, RVM)、同侧楔状核(nucleus cuneiformis, NCF)的神经活动较高，并且rACC与RVM的FC更加显著，神经病理性疼痛的表现和RVM较高的神经活动强度与关节成形术后中、重度长期疼痛相关[20, 31]。应用MRI评估KOA患者TKA术后的脑功能改变，可对脑功能改变患者采取提前干预，使KOA患者术后的疼痛程度减轻[40]。

4 小结与展望

神经影像学技术在KOA疼痛机制研究的应用，为评估和预测KOA的中枢敏化、情感和认知等特征提供了可能。虽然KOA患者的残障、运动功能、负向情绪、生活质量和疼痛之间的具体作用关系仍不明确，但目前的神经影像学研究已初步发现KOA患者的疼痛体验与脑功能、脑结构的介导密切相关，为相关研究的开展奠定了基础。

目前，在临床常规诊疗中，通过神经影像学技术精准检测KOA患者疼痛成分的诊断方法尚未普及，这可能与神经影像学的指标处理难度大、检查费用较高有关。在KOA疼痛的实际诊疗过程中，相同疼痛程度KOA患者的疼痛成分可能不同，即使接受同一KOA疗法，也将出现不一致的镇痛效果。随着技术的创新与发展，在未来针对疼痛个体的临床诊疗中，可基于神经影像学评估KOA患者的疼痛情况，制定合理方案，以便通过神经影像学技术来减少不同疼痛成分对临床疗效的影响，以及临床镇痛措施可能带来的副作用或医源性伤害。

总之，神经影像学技术在KOA疼痛诊疗领域有广阔前景，将在个体化、精准化诊疗方面发挥重大作用，可更好地确定治疗靶点，为KOA疼痛的治疗提供新思路，并利于在KOA的早、中期制定合理方案，提高临床疗效和安全性。

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