

威胁评价和慢性疼痛后果关联的神经基础: 左侧背外侧前额叶皮层和后扣带回皮层

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摘要 慢性疼痛, 即持续或反复发作超过3个月及以上的疼痛。近年来, 慢性疼痛在年轻人中的患病率显著上升, 严重影响其身心健康。疼痛是人类健康和生存受到威胁的重要信号, 但是, 如果个体总是将其评价为威胁, 可能会导致慢性疼痛的发生、持续和加剧。威胁评价是指个体将疼痛信号解读为存在实际或潜在的躯体损伤风险。然而, 威胁评价与慢性疼痛后果关联的神经基础还不清楚。为此, 本研究采用体素形态学分析(VBM)技术, 通过问卷调查收集人口学信息、慢性疼痛后果(包括疼痛强度和疼痛干扰)及威胁评价的数据, 并利用核磁共振成像(MRI)扫描大脑结构, 探究48名年轻慢性疼痛患者(含34名女性, 平均年龄22.51岁, 范围19~30岁)中威胁评价与慢性疼痛后果的关系及其潜在关联的神经基础。行为分析结果显示, 威胁评价与疼痛强度和疼痛干扰之间呈显著正相关。在神经影像学层面, VBM分析结果表明, 左侧背外侧前额叶(DLPFC)和左侧后扣带回皮层(PCC)的灰质体积与威胁评价均呈负相关。中介分析进一步揭示了威胁评价在上述脑区与疼痛后果之间的中介作用。综上所述, 左侧背外侧前额叶和后扣带回皮层可能是威胁评价和慢性疼痛后果关联的神经基础。这些发现为理解慢性疼痛的心理神经机制提供了实证依据, 有助于慢性疼痛早期预防与干预策略的发展。

关键词 慢性疼痛, 威胁评价, 疼痛强度, 疼痛干扰, 体素形态学分析(VBM)

国际疼痛研究协会(International Association For the Study of Pain, IASP)将慢性疼痛定义为持续或反复发作超过3个月及以上, 超越正常组织愈合期, 并与实际或潜在的组织损伤相关的疼痛现象^[1]。在欧美国家, 20%~50%的成年人受到慢性疼痛的影响^[2,3], 而在中国, 这一比例约为31.54%~42.2%^[4,5]。值得注意的是, 慢性疼痛的主要患病群体并不仅限于老年人, 年轻人中也相当普遍。例如, 英国18~25岁人群中有14.3%受其困扰, 而中国19~29岁人群中有17.1%受影响^[3,5]。作为成年人就医的常见原因之一, 慢性疼痛常导致行动受限、睡眠障碍以及焦虑、抑郁等心理问题, 严重影响国民

的健康和生活方式^[6,7]。此外, 心理和行为因素(如对疼痛的威胁认知, 对疼痛的恐惧和回避)也显著加剧慢性疼痛的后果, 包括疼痛强度增加、日常生活干扰及功能丧失^[8~10]。深入探究影响慢性疼痛的相关风险因素, 揭示慢性疼痛的内在认知神经机制, 对于预防其发生或缓解其负面影响具有重要意义。

疼痛的恐惧-回避模型(fear-avoidance model)强调, 对疼痛的威胁和灾难化认知会引起个体对疼痛及其相关线索的注意警觉, 并回避可能引发疼痛的日常活动, 从而导致身体活动减少、功能下降及疼痛加剧, 最终引起急性疼痛向慢性疼痛的转变^[8,11]。高疼痛恐惧者往

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往将疼痛视为实际或潜在组织威胁信号,对疼痛相关信息表现出过度警觉。这一过程始于对疼痛的威胁评价(threat appraisal),即将疼痛视为潜在躯体损伤的初始评价过程^[12],并继而影响慢性疼痛患者对疼痛的感知和采取的应对方式。一项关于疼痛初始评价和慢性疼痛后果关系的元分析发现,将疼痛视为潜在组织损伤来源的威胁评价,与疼痛严重程度、功能损伤以及情绪困扰的显著增加密切相关^[10]。基于22项实验室研究($N=2031$)的元分析也指出,暴露于威胁评价操作会显著降低疼痛耐受性^[10]。高威胁评价的个体更倾向于采取灾难化思维等消极应对策略^[13,14]。实验室研究进一步证实,高威胁评价条件下,积极认知应对策略减少,疼痛灾难化增加,从而削弱疼痛耐受性^[15]。因此,威胁评价这一消极认知评价过程可能会对慢性疼痛的后果产生显著影响。然而,目前尚未有研究考查疼痛的威胁评价与慢性疼痛关联的内在神经基础。

体素形态学分析(voxel-based morphometry, VBM)是一种先进的神经影像分析技术,广泛应用于评估全脑灰质密度及体积差异,尤其在疼痛和精神障碍研究中价值显著,是揭示个体心理特质与潜在大脑结构关联的有效手段^[16]。慢性疼痛可能会重塑大脑结构^[17]。VBM研究发现,慢性疼痛患者与健康对照组相比,在特定脑区的灰质体积(gray matter volume, GMV)存在差异^[18,19]。尽管不同类型的慢性疼痛导致的灰质异常模式可能有所不同,而在某些脑区,如背外侧前额叶皮质(dorsolateral prefrontal cortex, DLPFC),灰质体积显著减少,这一现象在不同慢性疼痛类型(如腰痛、偏头痛及髌关节炎等)中均有所体现^[20,21]。DLPFC,作为一个庞大且功能多样的脑区^[22],广泛参与认知、情感及感觉处理过程^[23],尤其在疼痛认知控制方面发挥着重要作用^[24-26]。实验室研究表明,疼痛热刺激下,DLPFC的活动强度与被试主观感受到的疼痛强度和不适感呈显著负相关^[27],同时与疼痛灾难化也呈负相关^[28],这表明了DLPFC在疼痛应对中的重要作用。进一步研究发现,慢性偏头痛患者的疼痛灾难化倾向与DLPFC灰质体积减小之间存在显著关联^[29]。此外,这些患者表现出双侧DLPFC与后扣带回皮层(posterior cingulate cortex, PCC)之间功能连接的减弱,而这种减弱的连接强度与疼痛灾难化水平呈正相关^[29]。PCC作为默认网络的核心结点之一,主要负责编码自我参照的认知加工过程^[30],不仅深度参与疼痛威胁信息的处理^[31],还具有评估情绪事件自我相关性的功能^[32]。在纤维肌痛患者

中,PCC在编码自我参照的疼痛灾难化过程中扮演着重要角色,且其活动强度与临床疼痛强度相关,呈正相关关系^[33]。研究还发现,慢性疼痛患者大脑的前额内侧皮层与默认网络模式(特别是PCC)之间的功能连接增强与疼痛反刍行为存在正向关联^[34]。这些发现强调了对疼痛信息的认知评估在影响慢性疼痛后果中的重要作用。基于此,我们推测,DLPFC和PCC可能是威胁评价和慢性疼痛后果关联的神经基础。

本研究旨在运用VBM技术探讨威胁评价和慢性疼痛后果关联的神经基础,以及威胁评价、慢性疼痛后果与相关脑区的潜在关系。首先,我们采用慢性疼痛等级量表(chronic pain grade, CPG)全面评估参与者的慢性疼痛后果,包括疼痛强度和疼痛对日常生活的干扰程度。同时,通过疼痛评价量表-简表(pain appraisal inventory-short form, PAI-SF)的威胁评价分量表评估威胁评价水平。接着,我们采用核磁共振成像(MRI)扫描大脑结构,并使用VBM技术来识别与威胁评价水平显著相关的灰质体积变化脑区。最后,我们采用了中介分析的方法探讨在特定脑区(即DLPFC和PCC)与慢性疼痛后果的关系中,威胁评价是否起着中介作用,从而为我们理解这一关系提供神经生物学层面的证据。

1 资料与方法

1.1 被试

本研究由西南大学心理学部伦理委员会批准同意(编号: H21068)。在校园及其周边社区广泛招募被试,采用慢性疼痛筛查问卷筛选出符合条件的参与者,邀请他们参与本研究,并要求在实验前两天不服用镇痛药物和酒精。纳入标准包括:(1)年龄在18~30岁之间;(2)符合慢性疼痛诊断标准(疼痛持续或反复发作时间超过3个月);(3)自愿参与并签署知情同意书。明确排除患有神经系统疾病、脑血管疾病,以及精神障碍的个体。最终,本研究招募了48名年轻的慢性疼痛患者,其中女性34人,男性14人,年龄跨度为19~30岁,平均年龄为 22.51 ± 2.60 岁。所有被试均表示每天或大部分时间内,能明显感觉到身体某一个或多个部位的疼痛,这种疼痛状态已持续3或3个月以上(中位数=34.79个月,标准差=28.57个月,范围=6~128个月)。主要的疼痛部位包括颈部、颈椎及肩部(41%)、背部(35%)、四肢(21%)和胸部(3%)。其中,超过六成(65%)的被试报告了多部位疼痛,也有少数被试(18%)报告使用过处方药来

控制疼痛。表1呈现了被试的年龄、疼痛特征描述和威胁评价得分情况。皮尔逊积差相关分析显示,被试的威胁评价水平和疼痛强度、疼痛干扰程度均呈现显著正相关关系,即个体对疼痛信息的威胁感知水平越高,其报告的疼痛感受也越强烈,且疼痛对日常生活的负面影响也更为显著。

1.2 测量工具

(1) 慢性疼痛等级(chronic pain grade, CPG)^[35]。包括7个题目,用于测量被试在过去的3个月内慢性疼痛的特征。其中,一个题目用来评估疼痛持续的时间(天数)。3个题目评估慢性疼痛严重程度,包括当前的、最严重以及过去3个月平均的疼痛强度,评分标尺从0(完全不痛)~10(最严重的疼痛),计算这3个题目的平均值即为疼痛强度(pain intensity)。慢性疼痛干扰(pain interference)包括3个项目,分别测量了过去3个月中疼痛对日常活动、社交活动和工作能力的负面影响情况,评分标尺从0(无干扰/无变化)~10(无法进行活动/极度变化),计算这3个题目的平均值即为疼痛干扰评分。CPG的原始因素结构已在中国慢性疼痛样本中得到验证^[36],并报告了较好的信效度^[37]。在当前研究中,疼痛严重程度和疼痛干扰的内部一致性系数 α 分别为0.86和0.82。

(2) 疼痛评价量表-简表(pain appraisal inventory-short form, PAI-SF)^[38,39]。本研究采用PAI-SF的威胁评价分量表来考察被试把持续疼痛视作威胁来源和负面结果的程度,包括5个题目,评分标尺从1(非常不同意)~6(非常同意)。PAI-SF在中国样本中具有较好的信效度^[38]。在本研究中,威胁评价量表的内部一致性系数 $\alpha=0.86$ 。

1.3 MRI数据采集

采用西门子3T磁共振成像系统(3.0 T Siemens Trio

MRI)来获取高分辨率的T1加权结构像。在正式扫描之前,被试平躺并把头部调整到舒适的位置,随后使用海绵垫固定头部以确保其在扫描过程中尽量保持不动。采用快速梯度回波成像(magnetization prepared rapid acquisition gradient echo sequences, MPRAGE)收集结构像,扫描参数为:层数为128,回波时间(echo time, TE)=3.39 ms,重复时间(repetition time, TR)=2530 ms,翻转角(flip angle, FA)=7°,视场(field of view, FOV)=256 mm×256 mm,扫描矩阵(acquisition matrix)=256×192,体素大小=1.33 mm×1.0 mm×1.0 mm。

1.4 影像数据预处理

使用基于Matlab R2014a平台上运行的SPM12工具箱(<http://www.fil.ion.ucl.ac.uk/spm/>)中的VBM8工具箱(<http://dbm.neuro.uni-jena.de/vbm8/>)对获取的结构图像进行VBM预处理。在数据预处理之前,两名心理学专业博士对结构像数据进行了初级的视觉筛查。由于发现大量伪影,剔除了一个男性被试的数据。结构图像预处理的步骤参考前人建议(Ashburner, 2007)。首先,为了改善图像配准,将所有被试的T1加权结构图像的前联合点(anterior commissure)手动重新定位于蒙特利尔神经研究所(Montreal neurological institute, MNI)三维空间的坐标原点(0, 0, 0)。其次,从结构图像中分离出灰质(gray matter, GM)、白质(white matter, WM)和脑脊液(cerebral spinal fluid, CSF)三种组织类型^[40]。再次,采用DARTEL算法生成一系列组模板和形变场,并将组模板标准化到MNI空间,并将对准后的图像进行Jacobian调制得到灰质体积图像。接着对标准化后的图像进行质量检查,以排除分割配准不佳的受试者数据。最后,采用8 mm半高全宽(full-width at half-maximum, FWHM)高斯核对图像进行平滑(smooth)处理,以提高信噪比,并在MNI空间中重新采样为1.5 mm×1.5 mm×1.5 mm的体素大小。

表1 慢性疼痛个体的年龄、疼痛特征和威胁评价及其相关性($N=48$, 其中34名女性)^{a)}

Table 1 Age, pain characteristics, and threat appraisal of individuals with chronic pain, along with their correlations ($N=48$; 34 female)

	<i>M(SD)</i>	范围	1	2	3	4
1. 年龄(岁)	22.67 (2.79)	19~30	—			
2. 疼痛持续时间(月)	34.52 (28.33)	6~128	<0.001	—		
3. 疼痛强度	4.99 (1.45)	2~7.67	0.15	0.14	—	
4. 疼痛干扰	4.32 (1.47)	2~7	0.02	0.15	0.83***	—
5. 威胁评价	13.75 (4.61)	6~26	-0.20	0.14	0.45**	0.40**

a) *M(SD)*=平均数(标准差); ** $P<0.01$, *** $P<0.001$

1.5 灰质体积分析

为了探索慢性疼痛个体威胁评价的神经解剖学基础,采用SPM12软件对预处理后的灰质体积数据进行多元线性回归模型的组水平分析(second-level modeling analysis),以确定灰质体积与个体威胁评价的相关性。具体而言,个体报告的威胁评价分数作为预测变量纳入多元线性回归模型。研究表明成年人的大脑灰质总体积随年龄增长呈线性下降趋势,并与性别存在交互效应^[41,42]。因此,在本研究中,被试的年龄、性别和颅内总体积(the total intracranial volume, TIV)作为协变量纳入模型,以排除可能的混淆效应。基于以往研究^[43,44],为了限制整个大脑的灰质体积,在本研究中采用了0.2的绝对阈值mask。最后,使用 T -contrast检验来确定与慢性疼痛个体威胁评价显著相关的体素。采用Dpabi(<http://restfmri.net>)对统计结果进行基于高斯随机场(Gaussian random field, GRF)理论的多重比较校正(体素水平 $P<0.001$, 团块水平 $P<0.05$, 双尾检验)^[45]。

1.6 中介效应分析

为了深入探索威胁评价和慢性疼痛后果之间的复杂关联,并揭示它们共同作用的大脑结构基础,我们采用基于SPM12的REX工具箱(<http://web.mit.edu/swg/software.htm>)提取了与威胁评价显著相关的脑区灰质体积的平均值。随后,采用SPSS 24.0对提取出的局部灰质体积分别与慢性疼痛结果(疼痛强度和疼痛干扰)进行皮尔逊积差相关分析以探究其相关性。此外,为了探究威胁评价在其中的中介效应,采用INDIRECT程序包中的PROCESS宏^[46,47],构建中介效应模型,分别将疼痛强度和疼痛干扰定义为结果变量,与威胁评价相关的脑区灰质体积定义为预测变量,而威胁评价为中介变量。我们采用Bootstrap方法进行5000次的重采样以检验中介效应模型的显著性。

2 结果

2.1 灰质体积分析结果

以威胁评价为预测变量,性别、年龄和颅内总体积作为协变量进行多元回归分析,探究与威胁评价显著相关的灰质体积变化所在的大脑区域。图1和表2呈现了经多重比较校正的VBM分析结果(GRF校正, voxel $P<0.001$, cluster $P<0.05$, cluster size >585)。分析结果显

示,左侧背外侧前额叶皮层(the left dorsolateral prefrontal cortex, DLPFC, MNI-coordinates: $x=-11$, $y=35$, $z=45$, 图1(a))和左侧后扣带回皮层(the left posterior cingulate cortex, PCC, MNI-coordinates: $x=-3$, $y=-55$, $z=50$, 图1(b))的灰质体积与威胁评价呈显著负相关。该结果说明,左侧背外侧前额叶和左侧后扣带回的灰质体积越小,其威胁评价水平越高。

2.2 中介分析结果

接下来,我们分别对左侧背外侧前额叶和左侧后扣带回灰质体积与疼痛强度及疼痛干扰之间的关系进行皮尔逊积差相关分析,统计显著性水平设定为 $P<0.05$ (未校正)。结果显示,左侧背外侧前额叶灰质体积与疼痛强度($r=-0.33$, $P<0.05$)以及疼痛干扰($r=-0.34$, $P<0.05$)均呈负相关。左侧后扣带回灰质体积与疼痛干扰存在负相关关系($r=-0.33$, $P<0.05$),但与疼痛强度的相关性并未达到显著性水平($r=-0.11$, $P=0.464$)。

为了进一步探讨威胁评价、慢性疼痛后果及相关脑区间的关系,我们构建了以左背外侧前额叶和左侧后扣带回灰质体积为预测变量,疼痛强度和疼痛干扰为结果变量,威胁评价为中介变量的中介模型。结果表明,威胁评价在左背外侧前额叶灰质体积对疼痛强度和疼痛干扰的关系中起着中介作用,95%的置信区间分别为 $[-0.24, -0.01]$ 和 $[-0.21, -0.01]$,如图2(a)所示。威胁评价在左侧后扣带回灰质体积和疼痛强度以及疼痛干扰的关系中起着中介作用,95%置信区间分别为 $[-0.33, -0.02]$ 和 $[-0.27, -0.01]$,如图2(b)所示。

3 讨论

在本研究中,我们采用基于体素的形态测量方法考察了慢性疼痛个体威胁评价和疼痛后果关联的神经机制,并通过中介分析探究了威胁评价在特定脑区(左侧背外侧前额叶和左侧后扣带回)和慢性疼痛后果关系间的作用。行为结果显示,慢性疼痛个体的威胁评价与疼痛强度、疼痛对生活干扰程度均显著正相关。在神经层面,VBM分析发现,左侧背外侧前额叶(DLPFC)和左侧后扣带回皮层(PCC)的灰质体积与威胁评价呈显著负相关。进一步的中介分析表明,威胁评价在左侧DLPFC、左侧PCC的灰质体积与疼痛后果(即疼痛强度和疼痛干扰)之间均起着中介作用。

与前人研究一致^[10,48,49],我们的结果表明,慢性疼痛个体的威胁评价水平越高,其疼痛后果越严重,表现

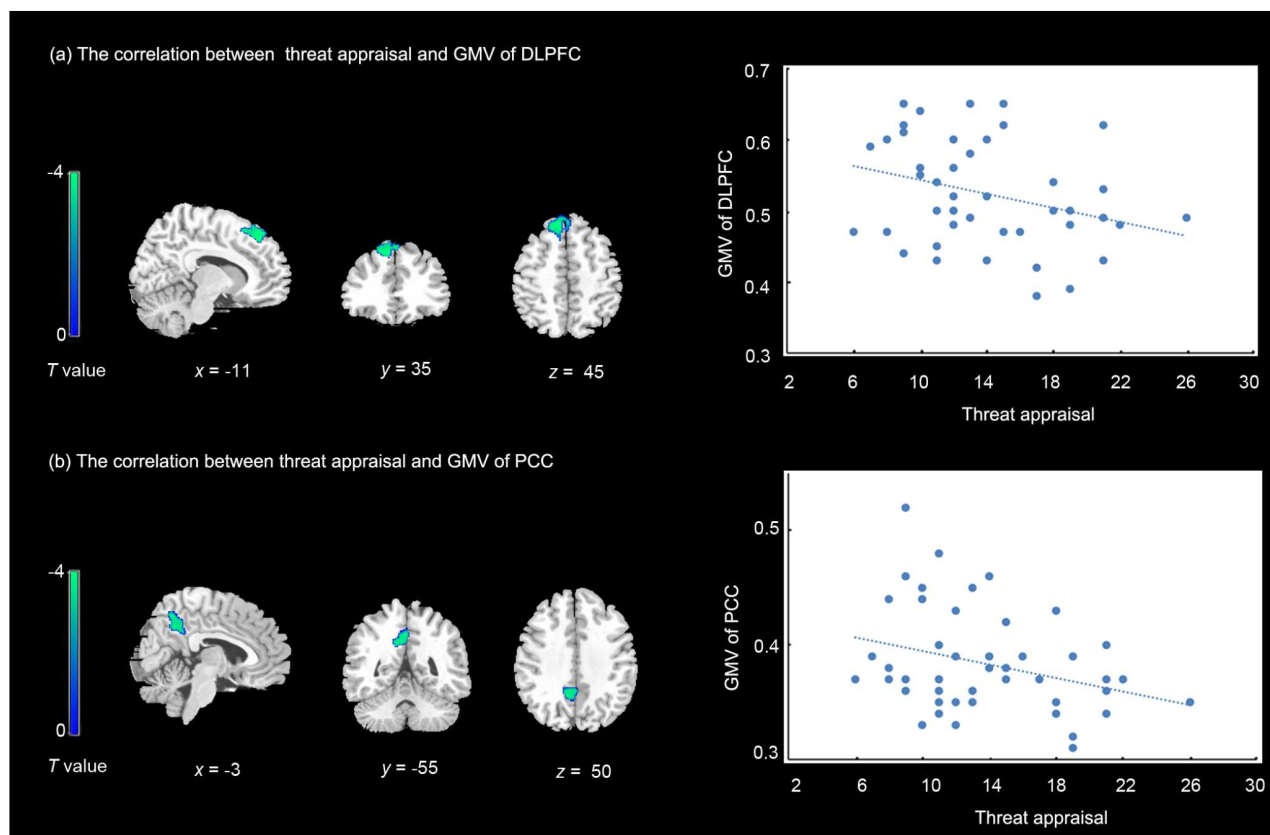


图1 (网络版彩色)灰质体积与威胁评价显著相关的大脑区域. GRF多重比较校正, voxel $P < 0.001$, cluster $P < 0.05$, cluster size > 585

Figure 1 (Color online) Brain regions where gray matter volumes (GMV) were significantly associated with threat appraisal ratings. Multiple comparison corrected with GRF; voxel $P < 0.001$, cluster $P < 0.05$, cluster size > 585

表2 灰质体积与慢性疼痛威胁评价显著相关的大脑区域^{a)}

Table 2 Brain regions where gray matter volumes (GMV) were significantly associated with threat appraisal ratings in individuals with chronic pain

大脑区域	BA	Hem	No. voxels	MNI-coordinates			<i>T</i>
				<i>x</i>	<i>y</i>	<i>z</i>	
背外侧前额叶皮层DLPFC	9/8	L	782	-11	35	45	-4.91
后扣带回皮层PCC	7/31	L	675	-3	-55	50	-3.94

a) GRF多重比较校正, voxel $P < 0.001$, cluster $P < 0.05$, cluster size > 585

为疼痛强度增加以及疼痛对生活 and 社交的干扰程度提高。对疼痛的评价及其相关信念强烈影响个体对疼痛刺激的情绪和行为反应。威胁评价将疼痛信息解读为一种与实际或潜在的组织损伤相关的威胁,从而使得疼痛刺激可能被感知为更强烈和不愉快,引发更多非适应性的回避行为^[50]。威胁评价水平较高的个体更容易对疼痛信息表现出注意偏向^[51],他们往往较少采用积极的应对方式(如重新评估、接受挑战),而更多采用消极的应对方式(如灾难化、回避)^[14,15]。上述消极的应对方式可能导致他们的日常活动水平降低,最终引发

功能性失能^[9],这一结果支持了恐惧-回避模型^[8]。此外,疼痛的回避行为可能通过提升威胁评价水平而增加与疼痛相关的恐惧^[13],最终形成一种恶性循环。

VBM分析显示,左侧背外侧前额叶(DLPFC)和左侧后扣带回皮层(PCC)的灰质体积与慢性疼痛个体的威胁评价呈负相关,即左侧DLPFC和左侧PCC的灰质体积越小,威胁评价水平越高。DLPFC参与自上而下的注意控制,能够抑制对任务无关的威胁刺激的选择性注意^[52,53],并参与或维持疼痛抑制^[21]。研究发现,在要求抑制疼痛的条件下,长时间的疼痛刺激会引发双侧,

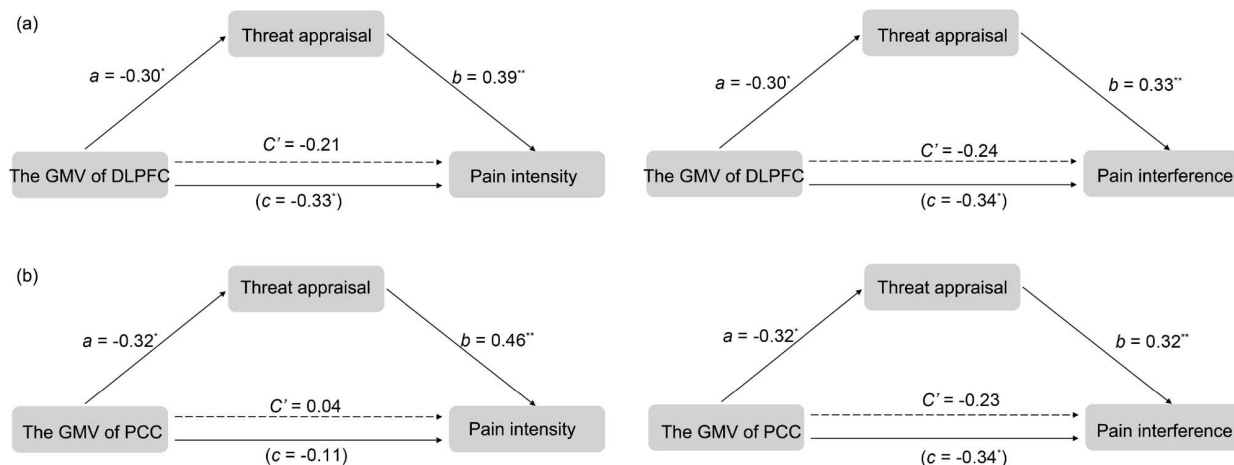


图2 威胁评价的中介效应。*, $P < 0.05$; **, $P < 0.01$

Figure 2 The mediating effect of threat appraisal. *, $P < 0.05$; **, $P < 0.01$

尤其是左侧DLPFC的激活增强^[54], 而双侧DLPFC的激活与热痛的不愉快程度降低相关^[27]。左侧DLPFC参与早期阶段的威胁处理, 对左侧DLPFC的抑制性刺激可导致高焦虑个体出现脱离偏差^[55]。安慰剂镇痛研究也表明, DLPFC在疼痛应对中起重要作用, 抑制DLPFC活动可能会阻断安慰剂反应^[56]。此外, 对疼痛控制的感知与DLPFC的激活相关^[25]。因此, 在本研究中, 慢性疼痛个体在DLPFC的灰质体积减少, 其威胁评价水平增高, 说明他们的疼痛抑制功能可能受损, 这与已有的研究结果一致^[57,58]。而在对潜在威胁环境的探索来评估威胁性质方面, PCC发挥着调节作用^[59]。前人研究发现, 在面临危险环境时, PCC的激活更强^[60,61]。作为默认网络的核心结点之一, PCC负责编码自我参照的认知加工^[30], 并参与处理疼痛威胁信息^[31], 因此具有评估的功能, 特别是评估疼痛与自我的相关性^[32]。此外, PCC的部分区域还参与自主情绪调节^[62,63]。有研究报告显示PCC在情绪疏离过程中激活, 这是一种自主情绪调节策略^[64]。纤维肌痛患者在编码自我参照的疼痛灾难化过程中, PCC起着重要作用, 并与临床疼痛强度呈正相关^[33]。与我们的结果一致, 包括PCC在内的多个脑区的灰质体积与慢性疼痛的威胁评价水平呈负相关^[29]。因此, 本研究中慢性疼痛个体在PCC区域的灰质体积越小, 其威胁评价水平越高, 可能涉及对环境威胁刺激的评估和自我情绪调节方面的损伤。综上, 我们的研究结果表明, 涉及疼痛抑制的背外侧前额叶和参与环境威胁评估及自主情绪调节的后扣带回皮层在慢性疼痛个体的威胁评价中发挥着关键作用。

最后, 本研究发现, 威胁评价在左侧DLPFC、PCC和慢性疼痛后果(即疼痛强度和疼痛干扰)之间的关系中均起着中介作用。研究结果表明, 左侧DLPFC和PCC的灰质体积与慢性疼痛后果之间存在负相关, 这与前人的研究结果一致^[29]。同时如前所述, DLPFC参与疼痛认知控制、维持疼痛抑制^[21], 而PCC则参与环境威胁、自我相关性评估和自主情绪调节^[32,63]。DLPFC和PCC的灰质体积越小, 慢性疼痛个体的威胁评价水平越高, 慢性疼痛带来的负面后果也越严重。威胁评价水平较高的个体可能伴随DLPFC和PCC功能的减弱, 表现为对环境威胁的评估更为敏感、疼痛认知控制能力较弱以及自主情绪调节能力受损等。这些因素可能使个体更倾向于采取消极应对策略, 从而体验到更高的疼痛强度和更严重的生活干扰等负面后果, 不利于慢性疼痛的治愈。综上, 本研究表明, 与疼痛认知控制、环境威胁评估和情绪调节相关的脑区可能是慢性疼痛后果的神经基础, 而威胁评价在其中可能起着中介作用。

本研究深入揭示了慢性疼痛威胁评价和疼痛后果之间关联的神经基础, 对于慢性疼痛后果有了更深入的理解。但需要注意的是, 本研究在进行脑区灰质体积和心理、行为变量之间的相关和中介分析时, 未经过多重比较校正, 而且无法推断因果关系, 对于结果的解释还需谨慎。未来研究可以采用纵向追踪调查或任务导向的fMRI等方法, 进一步探究慢性疼痛的威胁评价、疼痛后果和大脑神经基础之间的因果关系。此外, 还可以采用或者开发新的技术或方法(如计算建模等), 以探究与慢性疼痛后果相对应的大脑回路以及威胁评价相

关的大脑神经特征, 并检验这两个变量相互影响的所有可能存在的神经通路. 另外, 本研究未考虑到被试服用药物或其他治疗史对威胁评价、慢性疼痛后果以及相关神经基础的潜在影响. 未来研究应进一步探讨这些因素的作用.

4 结论

本研究首次采用体素形态学(VBM)的方法探讨了

年轻慢性疼痛个体的威胁评价和慢性疼痛后果之间的神经机制. 结果表明, 左侧背外侧前额叶和后侧扣带回皮层的灰质体积与威胁评价及疼痛后果存在负相关. 此外, 威胁评价在左侧背外侧前额叶和后扣带回皮层与疼痛后果之间起着中介作用. 本研究不仅为威胁评价和慢性疼痛后果关联的神经基础提供了实证证据, 还为开发慢性疼痛早期预防策略和干预手段提供了重要的理论支持.

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Summary for “威胁评价和慢性疼痛后果关联的神经基础: 左侧背外侧前额叶皮层和后扣带回皮层”

The neural basis linking threat appraisal and pain outcomes in chronic pain: roles of the left DLPFC and PCC

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Chronic pain is defined as pain that persists or recurs for more than three months after the initial healing of a wound. In recent years, the rising prevalence of chronic pain among young people has become a significant concern, profoundly impacting their physical and mental well-being. While pain serves as an important signal of potential harm to health and survival, consistently interpreting it as a threat can contribute to the onset, persistence, and worsening of chronic pain. Threat appraisal, the process of evaluating pain as either actual or potential bodily damage, plays a crucial role in the development and maintenance of chronic pain. However, the neural mechanisms linking threat appraisal to chronic pain outcomes remain unclear. This study aimed to explore these neural correlates using the voxel-based morphometry (VBM) technique. Forty-eight young individuals with chronic pain (34 females, average age 22.51 years, ranging from 19 to 30) completed questionnaires on demographics, threat appraisal, as well as chronic pain outcomes, including pain intensity (current, worst, and average pain intensity over the past three months) and pain interference (the negative impact of pain on daily activities, socialization and work over the past three months). Participants then underwent magnetic resonance imaging (MRI) to obtain structural brain images. Behavioral results revealed significant positive correlations between threat appraisal and both pain intensity and pain interference; specifically, higher threat appraisal levels were associated with more severe chronic pain outcomes. These results align with previous findings, and provide evidence for the fear-avoidance model of chronic pain. At the neuroimaging level, VBM analysis indicated that higher threat appraisal was linked to reduced gray matter volume in the left dorsolateral prefrontal cortex (DLPFC) and the left posterior cingulate cortex (PCC). Individuals with chronic pain exhibited decreased gray matter volume in these regions, suggesting potential impairments in pain inhibition, environmental threat appraisal, and emotional self-regulation, which may be linked to greater levels of threat appraisal, potentially creating a vicious circle. Further mediation analysis showed that threat appraisal mediated the relationships between gray matter volume in the left DLPFC and PCC and pain outcomes. Higher levels of threat appraisal were associated with reduced functioning in these brain areas, leading to increased sensitivity to perceived threats, diminished cognitive control over pain, and impaired emotional regulation. These factors may predispose individuals to adopt negative coping strategies, resulting in greater pain intensity and more significant disruption to daily life, which can hinder the healing process of chronic pain. In conclusion, the left DLPFC and PCC may serve as critical neural substrates linking threat appraisal to chronic pain outcomes. This research provides empirical evidence for the neural mechanisms connecting threat appraisal and chronic pain, supporting the development of early prevention strategies and interventions for managing chronic pain.

chronic pain, threat appraisal, pain intensity, pain interference, voxel-based morphometry

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