科学通报 2025 年 第 70 卷 第 8 期: 1018 ~ 1028
疼痛与共情专辑 论 文
《中国科学》杂志社 SCIENCE CHINA PRESS

人体穴位会更疼吗? 行为和ERP研究

魏子龙[1,2†], 刘晓翠[1,2,3†], 江进[1,2,4], 李滟婷[1,2], 邵民[1,2], 孟景[1,2*]

1. 重庆师范大学脑与认知科学研究中心, 重庆 401331
2. 重庆师范大学应用心理学重点实验室, 重庆 401331
3. 重庆市江北区第二人民医院, 重庆 400026
4. 重庆五一职业技术学院, 汽车工程学院, 重庆 401320

† 同等贡献
* 联系人, E-mail: qufumj@qq.com

2023-12-18 收稿, 2024-02-28 修回, 2024-02-29 接受, 2024-03-01 网络版发表
重庆市教育委员会人文社会科学研究项目(23SKGH082)资助

摘要 穴位是中医理论中的重要概念, 是针灸治疗过程中插入和操作针灸针的位置点. 通过刺激特定穴位来镇痛的方法已在国内外疼痛治疗中广泛使用. 然而, 人体穴位本身是否有特殊的疼痛感知及其认知神经机制尚知之甚少. 因此, 本研究设计两项实验来探讨这个问题. 实验1采用小步递增法对36名被试穴位(内关、足三里)与非穴位(穴位外侧3厘米)对不同刺激强度的电刺激的感知差异进行初步探索, 发现穴位对较高强度电刺激感知显著低于非穴位, 而对较低强度电刺激的感知与非穴位无显著差异. 实验2采用事件相关电位(event-related potential, ERP)技术对32名被试穴位与非穴位处的3类电刺激(无痛、低痛和高痛)的感知差异进行研究, 发现相较于非穴位, 穴位对高痛刺激的疼痛感知较低、情绪反应较积极、N1波幅较小, 而对低痛和无痛刺激则不存在上述差异. 总之, 本研究表明穴位存在特异性的疼痛感知, 从行为和脑科学层面为穴位的存在提供了实证依据, 为中医发展提供了重要支撑.

关键词 疼痛, ERP, 穴位, 认知神经机制

穴位是传统中医理论中的重要概念, 是人体经络的关键节点的特定部位[1,2], 由肥大细胞、血管以及神经组成的动态复合结构[3]. 在组织结构和生理特征方面, 穴位与非穴位具有显著差异. 穴位通常位于特定的解剖位置, 如神经、血管密集区域, 表现为血管、神经束、神经支以及各种神经感受器的丰富分布[4]. 在生理反应方面, 穴位与体内的经络系统相连接, 其刺激可引发局部或远端的显著反应, 如疼痛减轻和血液循环改善[5]. 相较于非穴位, 穴位具有温度较高、电阻较低等特点[6,7]. 在临床研究中, 穴位也被定义为机体病变的反射点, 也是针灸的重要刺激点[8~10]. 刺激某些穴位可以调节人体特定的生理机能[11]. 近年来, 穴位疗法在抑郁症治疗[12]、免疫功能调节[13]和疼痛缓解[14,15]等方面展现出可靠疗效, 并成为一种备受中外广泛认可与采用的治疗方法[16]. 虽然随着穴位疗法的普及, 穴位相关研究越来越受到重视[17]. 但是, 穴位存在的证据和机制尚未完全清楚. 尽管已有研究探讨了穴位与非穴位在组织结构和生理特征方面上的差异, 但关于穴位和非穴位在疼痛感知上的差异研究, 还不是十分充分, 因此有必要对穴位本身的疼痛感知特点和认知神经机制进行深入探索.

疼痛是一种与实际或潜在的组织损伤相关的, 或类似的不愉快的感觉和情感体验[18], 它不仅是一种普遍的临床疾病, 更是全球范围内公认的健康问题[19~22].

引用格式: 魏子龙, 刘晓翠, 江进, 等. 人体穴位会更疼吗? 行为和ERP研究. 科学通报, 2025, 70: 1018–1028
Wei Z L, Liu X C, Jiang J, et al. Do we feel more pain at acupoints? Behavior and ERP study (in Chinese). Chin Sci Bull, 2025, 70: 1018–1028, doi: 10.1360/TB-2023-1298

尽管很多药物可以缓解疼痛，但药物成瘾等副作用对人体的影响不可忽视[23,24]. 因此, 当前亟需寻求有效的非药物镇痛方法[25,26]. 穴位镇痛疗法, 因其不良反应较少、适用广泛和见效迅速等优势，已在全球范围内广泛使用[27,28]. 前人研究表明, 刺激足三里等穴位可以显著提高个体的疼痛阈限[29]、减轻神经性疼痛[30]以及减少术后阿片类镇痛药物的消耗量[31]. 神经影像学研究表明，刺激内关、阳陵泉、足三里等穴位会激活疼痛调节脑区，包括前扣带回皮层、躯体感觉皮层、脑岛、脑干以及导水管周围灰质等[32~36]. 此外，刺激曲池、足三里等穴位后内源性阿片类物质(如β-内啡肽)的释放增加[37].

在穴位镇痛的研究中，内关(PC6)和足三里(ST36)因其显著的镇痛效果而备受关注[38,39]. 刺激内关能够引发周围细胞外液中的多巴胺、血清肾上腺素和去甲肾上腺素水平的上升[40]，促进大脑分泌γ-氨基丁酸、内源性阿片类物质以及5-羟色胺等抑制性神经递质, 从而减弱交感神经元的活动, 有效抑制疼痛[41]. 足三里是治疗肌肉骨骼疾病、减轻神经炎症以及缓解疼痛的常用穴位[42,43]，刺激足三里不仅能增加穴位周围细胞外液中的谷氨酸水平，也会引起脑脊液中谷氨酸和γ-氨基丁酸水平的显著变化[41]. 刺激内关和足三里不仅会影响神经递质水平，还可以减少穴位周围肌肉中P2X2受体的表达，表明穴位镇痛的机制可能与感觉传入神经密切相关[40]. 尽管前人研究已证实刺激穴位可对身体其他部位产生镇痛作用，但穴位镇痛的生理机制尚未完全阐明. 其镇痛作用可能源于穴位独特的生理和分子机制，这些机制也可能导致穴位本身在疼痛感知与加工方面与身体其他部位存在显著差异. 然而, 穴位是否具备疼痛感知特殊性尚未完全清楚. 因此, 本研究的主要目的是探索穴位的疼痛感知特点及其认知神经机制.

由于前人研究发现对穴位进行不同强度的刺激的镇痛效果不同，高强度刺激可以更好地起到镇痛效果[44]. 这表明穴位可能对不同强度的刺激反应不同, 穴位可能对高强度刺激更不敏感. 因此, 本研究假设穴位受到高强度刺激时的疼痛感知应显著低于非穴位. 疼痛事件相关电位(event-related potential，ERP)研究表明，N1和P2成分是编码疼痛刺激的神经指标. N1成分与疼痛刺激的强度相关，反映了大脑对疼痛刺激的初级处理[45,46]. 较低的疼痛感知会导致大脑对疼痛刺激的初级处理和认知加工进程减弱，并诱发较小的N1波幅[47]. 因此，如果穴位比非穴位具有较低的疼痛感知, 那么在受到同等物理强度刺激时，穴位可能会诱发更小的N1波幅. P2成分则可能与疼痛刺激的身体部位有关[48,49]. 因此，如果穴位具有身体部位特异性的机制, 那么穴位和非穴位对相同物理刺激诱发的P2波幅可能会不同.

1 实验1: 穴位的疼痛感知差异: 行为研究

1.1 方法

1.1.1 被试

实验1共招募36名被试(女性18名，年龄21.44±2.18岁). 所有被试均为右利手, 视力或矫正视力正常, 无神经或精神疾病史, 不存在急性、慢性疼痛, 当前未使用任何药物. 所有被试在实验前均被告知了实验程序, 并签署了知情同意书，实验程序经重庆师范大学研究伦理委员会批准(CNU-EDU-20210612-004).

1.1.2 刺激部位

根据前人研究[41]，本研究选择了内关和足三里作为穴位刺激部位(内关: PC6，位于前臂内侧，手腕皱褶上方约三指宽处; 足三里: ST36, 膝盖下方约四指宽处, 胫骨外侧). 此外, 研究选取了两个与所选穴位外侧相距约3厘米的非穴位区域作为对照刺激位置, 见图1(a). 两名中医类别执业医师在确定每名被试的穴位和非穴位位置时提供了专业指导，以确保整个研究中刺激位置的准确性和一致性.

1.1.3 仪器与刺激

刺激由一台多通道恒流电刺激器(SXC-4A, 北京三侠科技有限公司)产生. 在被试的内关和足三里以及相应的非穴位贴上电极贴片, 一系列电流(500~5000 μA, 50 ms正向恒流)通过电极贴片传递给被试.

1.1.4 实验程序

实验在一间温度适宜，安静隔音的实验室里进行. 被试在内关和足三里两个穴位及对应的非穴位贴上电极贴片后, 坐在一台24英寸的彩色液晶显示器前, 距离屏幕大约100 cm, 如图1(b)所示.

采用小步递增法[50~52]呈现一系列电刺激(强度范围: 500~5000 μA, 步长为500 μA, 50 ms正向恒流). 每个trial开始时，呈现50 ms的电刺激，然后要求被试用9点Likert量表(1=没有感觉，2=开始有感觉，4=开始疼痛，9=疼痛极限)判断刺激强度. 两个trial之间间隔为4000~6000 ms. 每个刺激在每个部位上呈现两次，刺激

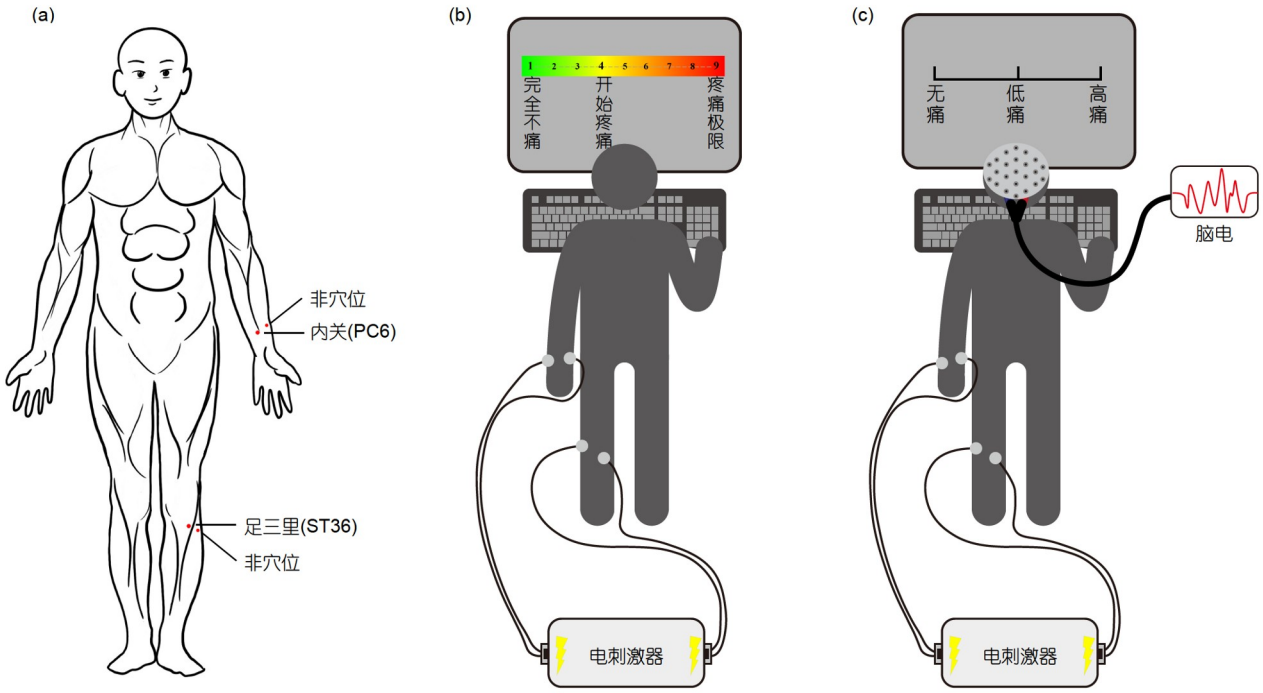

图 1 (网络版彩色)实验1和实验2实验设置示意图. (a) 穴位和非穴位刺激位置. (b) 实验1实验设置示意图, 被试在穴位与非穴位受刺激时使用9点Likert量表进行强度评分. (c) 实验2实验设置示意图, 被试在穴位与非穴位受刺激时进行刺激类型判断, 同时采集脑电(electroencephalography, EEG)数据

Figure 1 (Color online) Experimental setup schematic. (a) Figure depicting the locations of acupoints and non-acupoint sites. (b) Participants were instructed to rate the perceived pain intensity on a 9-point Likert scale, both at acupoints and non-acupoints. (c) Participants were instructed to rate the pain level of the stimuli they received at both acupoints and non-acupoints while electroencephalography (EEG) data was simultaneously collected

位置采用伪随机排列, 共80个trial, 分为两个block呈现. 两个block之间休息10 min, 以尽量减少电刺激的潜在影响. 在实验前告知被试, 如果他们无法忍受疼痛或不再愿意继续实验, 可以按键盘上的“ESC”键退出. 实验使用E-prime 3.0控制刺激呈现并记录被试的刺激强度评分.

1.1.5 统计分析

数据分析使用SPSS 15.0软件(IBM Corp., Armonk, NY, USA)进行. 对刺激强度评分进行2(刺激部位: 穴位, 非穴位)×10(刺激强度: 500~5000 μA, 步长为500 μA)两因素重复测量方差分析. 若重复测量方差分析球形检验不通过则采用Greenhouse-Geisser法校正. 统计结果中简单效应的两两比较采用Bonferroni法进行校正.

1.2 结果

如图2所示, “刺激强度”的主效应显著, $F_{(9,315)}$=724.42, P<0.001, η_p^2=0.95, 高强度刺激的评分显著高于低强度刺激(P<0.01). “刺激部位”和“刺激强度”的交互作用显著, $F_{(9, 315)}$=6.97, P<0.001, η_p^2=0.17. 简单效应分析表明, 当刺激强度为500~4000 μA时, 穴位与非穴位之间的刺激强度评分无显著差异(P>0.05), 而当刺激强度为4000~5000 μA时, 穴位的疼痛强度评分低于非穴位(P<0.05), 具体统计结果见表1. 内关、足三里与其对照非穴位的图表统计结果见表S1、表S2与图S1.

2 实验2: 穴位对疼痛感知的影响: ERP研究

2.1 方法

2.1.1 被试

实验2的被试从实验1中招募. 实验1结束一周后, 邀请被试参与实验2. 其中4名被试没有参加实验2, 因此实验2共包含32名被试(16名女性, Mean±SD=21.44±2.26岁).

2.1.2 刺激部位

与研究1一致.

2.1.3 仪器与刺激

实验2使用的仪器与实验1相同, 并且实验2中刺激是根据实验1结果确定的. 与前人研究中刺激选择方法

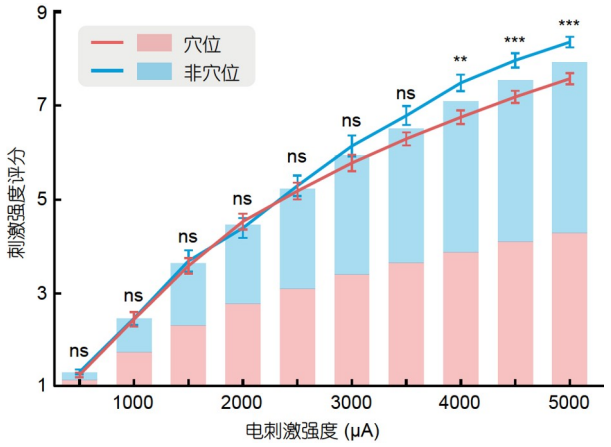

图 2 电刺激强度与刺激强度评分的刺激-反应曲线. 折线图表示为平均值(mean)±标准误(SE), 柱状图表示为1/2平均值. ns, P>0.05; **, P<0.01; ***, P<0.001

Figure 2 Line charts describing the stimulus-response function. Data are expressed as mean±standard error (SE), and the bar graphs represent half of the mean. ns, P>0.05; **, P<0.01; ***, P<0.001

一致[53,54], 根据每位被试的刺激-反应曲线, 选择穴位和非穴位评分为3(有明显感觉但不痛)、5(明显但可忍受的疼痛)、7(强烈但不极端的疼痛)的电刺激的平均值分别作为无痛、低痛、高痛刺激. 全部被试的平均刺激强度为1658.07±60.70 μA(无痛)、2479.84±79.95 μA(低痛)和3452.25±95.53 μA(高痛).

2.1.4 实验程序

实验在一间温度适宜、安静隔音的实验室里进行. 被试在内关和足三里两个穴位及对应的非穴位贴上电极贴片后, 坐在一台24英寸的彩色液晶显示器前, 距离屏幕大约100 cm, 研究2的实验设置如图1(c)所示.

每个trial开始时, 呈现50 ms的电刺激, 被试需要在刺激出现时又快又准确地按1、2或3键(按键进行被试间平衡)判断刺激是无痛、低痛还是高痛. 两个trial之间间隔为4000~6000 ms. 每类刺激呈现30次, 刺激位置和刺激类型采用伪随机排列, 共360个trial, 分为6个block呈现. 每两个block之间休息3~5 min. 实验过程中, 采用E-prime 3.0控制刺激呈现并记录被试的行为数据. 实验过程中记录EEG数据.

EEG记录结束之后, 让被试根据自己的主观感受对刺激进行评分. 每个trial首先呈现一个50 ms的电刺激, 然后依次呈现感觉标尺和情绪标尺, 要求被试根据9点Likert 量表对每个刺激的刺激强度(1=没有感觉, 4=开始疼痛, 9=疼痛极限)以及自身对刺激的情绪反应(1=非常不开心, 5=中性, 9=非常开心)进行评分.

2.1.5 脑电数据采集与分析

采用德国Brain Products公司的ERP记录系统, 使用安装在actiCHamp系统(Brain Vision LLC, Morrisville, NC, US)上的按国际10-20系统扩展的64导电极帽同时记录被试的脑电活动, 记录时参考电极位于Fz处, 接地电极位于前额接地点上. EEG活动采用DC采集, 带通范围DC~280 Hz, 连续采样频率为1000 Hz. 电极与头皮间的阻抗小于5 kΩ.

使用MATLAB R2016a (MathWorks, Natick, MA, USA)和EEGLAB工具箱[55]对EEG数据进行预处理和分析. 分析时以两侧乳突平均值作为参考, 滤波带通为0.1~30 Hz. 分析时程截取电刺激呈现前200 ms至呈现

表 1 穴位与非穴位之间的刺激强度评分结果(mean±SE)[a)]

Table 1 Stimuli intensity scores between acupoints and non-acupoints (mean±SE)

刺激强度(μA)	刺激部位		F	P	η_p^2
	穴位	非穴位			
500	1.24±0.05	1.30±0.05	0.78	0.383	0.02
1000	2.42±0.15	2.44±0.14	0.01	0.914	<0.01
1500	3.56±0.16	3.66±0.23	0.16	0.694	<0.01
2000	4.50±0.17	4.36±0.21	0.32	0.576	0.01
2500	5.15±0.18	5.26±0.22	0.22	0.642	0.01
3000	5.74±0.17	6.10±0.22	1.90	0.177	0.05
3500	6.26±0.14	6.75±0.20	3.76	0.061	0.10
4000	**6.72±0.15**	**7.44±0.18**	**9.53**	**0.004**	**0.21**
4500	**7.15±0.13**	**7.92±0.15**	**16.76**	**<0.001**	**0.32**
5000	**7.54±0.12**	**8.31±0.11**	**23.03**	**<0.001**	**0.40**

a) 加粗表示显著(P<0.05)

后1000 ms, 并以电刺激呈现前200 ms作为基线. 眼动伪迹通过独立主成分分析(independent components analysis, ICA)算法进行校正[56].

本研究分析的ERP成分为疼痛刺激诱发的N1和P2平均波幅(图3). 根据地形图、波形图以及相关文献选取电极点和时间窗[46,57]. N1分析的电极点为FCz、FC2、FC4、Cz、C2、C4, 时间窗为72~92 ms. P2分析的电极点为Cz、C1、C2、CPz、CP1、CP2, 时间窗为244~264 ms.

2.1.6 统计分析

采用SPSS 15.0进行统计分析, 对行为数据(反应时和正确率)、主观等级评分(刺激强度评分和情绪效价)和ERP数据(N1和P2平均波幅)进行2(刺激部位: 穴位、非穴位)×3(刺激类型: 无痛、低痛、高痛)两因素重复测量方差分析. 若重复测量方差分析球形检验不通过则采用Greenhouse-Geisser 法校正. 交互作用如果显著则进行简单效应分析, 两两比较采用Bonferroni法进行校正. 为了探索穴位的主观等级评分与特定脑电成分是否有相关性, 采用皮尔逊积差相关评估被试的刺激强度评分和情绪效价与ERP数据(N1和P2平均波幅)之间的相关性, 采用FDR程序校正*P*值[58].

2.2 结果

2.2.1 行为数据

反应时方面, “刺激部位”的主效应显著, $F_{(1,31)}$=5.58, P=0.025, η_p^2=0.15, 穴位的反应时(1086.21±21.72 ms)

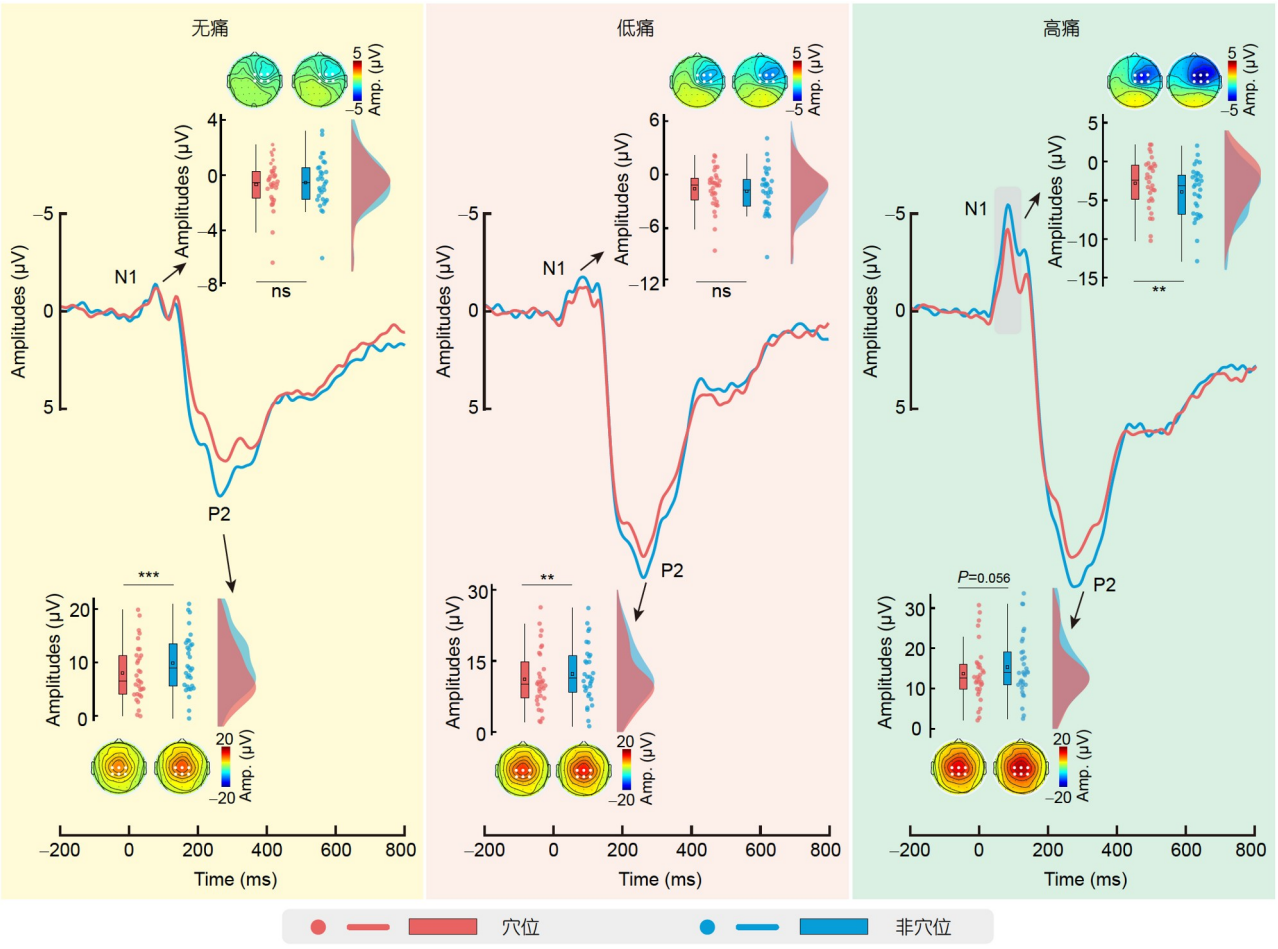

图 3 穴位和非穴位接受三种刺激类型诱发的ERP波形图、地形图和条形图. 在波形图中, 红色实线代表穴位处接受刺激, 蓝色实线代表非穴位处接受刺激. 地形图中白点标记的区域表示该成分所纳入分析的电极点. 平均波幅差异性检验结果如柱形图所示, 用Mean±SE表示柱形图中的数据. ns, P>0.05; **, P<0.01; ***, P<0.001

Figure 3 The effect of stimuli intensity (non-pain, low-pain, and high-pain) on ERP responses for both acupoints and non-acupoints. ERP waveforms, bar charts, and scalp topography distributions elicited on the acupoints (red) and the non-acupoints (blue). Electrodes used to estimate ERP amplitudes are marked with points on their respective scalp maps. Data in the bar charts are expressed as mean±SE. ns, P>0.05; **, P<0.01; ***, P<0.001.

长于非穴位的反应时(1053.41±25.70 ms).

正确率方面, “刺激类型”的主效应显著, $F_{(2,62)}$=19.81, P<0.001, η_p^2=0.39, 高痛刺激(87.76%±0.97%)的正确率高于低痛刺激(80.90%±1.52%; P<0.001)和无痛刺激(78.15%±1.31%; P<0.001), 低痛刺激与无痛刺激之间无显著差异(P=0.356).

刺激强度评分方面, “刺激部位”的主效应显著, $F_{(1,31)}$=7.82, P=0.009, η_p^2=0.20, 穴位(4.16±0.12)的刺激强度评分显著低于非穴位(4.59±0.13). “刺激类型”的主效应显著, $F_{(2,62)}$=598.79, P<0.001, η_p^2=0.95, 高痛刺激(6.06±0.19)的刺激强度评分显著高于低痛刺激(4.72±0.12; P<0.001)与无痛刺激(1.93±0.08; P<0.001), 低痛刺激的刺激强度评分显著高于无痛刺激(P<0.001). “刺激部位”和“刺激类型”的交互作用显著, $F_{(2,62)}$=8.03, P=0.001, η_p^2=0.21. 简单效应分析发现, 在高痛刺激条件下, 穴位(6.06±0.19)的刺激强度评分显著低于非穴位(6.90±0.21; P=0.001), 但在低痛和无痛刺激条件下, 穴位与非穴位之间的刺激强度评分无显著差异(P>0.05).

情绪效价方面, “刺激部位”的主效应显著, $F_{(1,31)}$=5.40, P=0.027, η_p^2=0.15, 非穴位(5.11±0.18)比穴位(5.35±0.19)的情绪反应更消极. “刺激类型”的主效应显著, $F_{(2,62)}$=35.98, P<0.001, η_p^2=0.54, 高痛刺激(4.40±0.20)的情绪反应比低痛刺激(5.27±0.18; P<0.001)和无痛刺激(6.02±0.24; P<0.001)更消极, 低痛刺激的情绪反应比无痛刺激(P<0.001)更消极. “刺激部位”和“刺激类型”的交互作用显著, $F_{(2,62)}$=6.78, P=0.004, η_p^2=0.18. 简单效应分析发现, 对高痛刺激, 非穴位(4.19±0.22)比穴位(4.62±0.19, P=0.001)更消极, 但对低痛和无痛刺激, 穴位与非穴位之间的情绪效价评分无显著差异(P>0.05).

2.2.2 电生理数据

不同条件下的波形图、地形图以及条形图见图3, ERP数据方差分析结果见表2.

(1) N1. “刺激部位”的主效应显著, $F_{(1,31)}$=4.38, P=0.045, η_p^2=0.12, 穴位(−1.69±0.39 μV)的平均波幅显著小于非穴位(−2.10±0.42 μV). “刺激类型”的主效应显著$F_{(2,62)}$=46.77, P<0.001, η_p^2=0.60, 高痛刺激(−3.37±0.56 μV)诱发的N1波幅显著大于低痛刺激(−1.70±0.40 μV; P<0.001)和无痛刺激(−0.61±0.29 μV; P<0.001), 低痛刺激诱发的N1波幅显著大于无痛刺激(P<0.001). “刺激部位”和“刺激类型”的交互作用显著, $F_{(2,62)}$=5.73, P=0.005, η_p^2=0.16, 简单效应分析发现, 在高痛刺激条件下, 穴位(−2.81±0.57 μV)诱发的N1波幅显著小于非穴位(−3.93±0.59 μV; P=0.002), 但在低痛和无痛刺激条件下, 穴位与非穴位之间的平均波幅无显著差异(P>0.05).

(2) P2. “刺激部位”的主效应显著, $F_{(1,31)}$=12.03, P=0.002, η_p^2=0.28, 穴位刺激(10.97±1.04 μV)诱发的P2波幅显著小于非穴位(12.50±1.08 μV). “刺激类型”的主效应显著, $F_{(2,62)}$=63.28, P<0.001, η_p^2=0.67, 高痛刺激(14.53±1.24 μV)诱发的P2波幅显著大于低痛刺激(11.69±1.05 μV; P<0.001)和无痛刺激(8.98±0.91 μV; P<0.001), 低痛刺激诱发的P2波幅显著大于无痛刺激(P<0.001).

2.2.3 主观等级评分与电生理数据相关分析结果

主观等级评分与电生理数据相关分析见表3. 结果显示, 在高痛刺激条件下, 穴位刺激的N1波幅与刺激强度评分之间存在显著负相关(r=−0.50, P=0.024). 说明被试的N1波幅越大, 其刺激强度评分越高. 其他主观等级评分与电生理数据无显著相关(P>0.05).

3 讨论

本研究结合行为与ERP实验, 探讨穴位与非穴位是否存在电刺激感知的差异. 实验1通过行为实验发现, 穴位受到高强度刺激时的疼痛感知显著低于非穴位, 而对低强度刺激则无感知差异; 实验2通过ERP实

表 2 ERP数据方差分析结果[a)]

Table 2 Results of the statistical analyses of the ERP amplitudes

变量	N1			P2		
	F	P	η_p^2	F	P	η_p^2
刺激部位	**4.38**	**0.045**	**0.12**	**12.03**	**0.002**	**0.28**
刺激类型	**46.77**	**<0.001**	**0.60**	**63.28**	**<0.001**	**0.67**
刺激部位×刺激类型	**5.73**	**0.005**	**0.16**	0.71	0.44	0.02

a) 加粗表示显著(P<0.05)

表 3 主观等级评分与电生理数据相关分析结果

Table 3 Correlation between subjective rating scores and ERP amplitudes

变量		脑电成分	刺激强度评分[a)]	情绪效价
穴位	非痛	N1	−0.26	0.31
		P2	0.08	−0.10
	低痛	N1	−0.20	0.31
		P2	0.29	−0.24
	高痛	N1	−0.50*	0.20
		P2	−0.02	−0.14
非穴位	非痛	N1	−0.17	0.13
		P2	0.25	−0.12
	低痛	N1	−0.05	0.15
		P2	0.33	−0.21
	高痛	N1	−0.13	0.02
		P2	0.26	−0.11

a) *, $P<0.05$

验发现, 与非穴位相比, 穴位对高痛刺激的疼痛感知较低、情绪反应较积极, 并且诱发的N1波幅较小, 而对低痛和无痛刺激则无上述差异. 这些结果从行为和神经科学的角度证实了穴位与非穴位在高痛刺激感知上存在显著差异, 并支持了穴位作为一个独特身体部位的存在. 这为中医理论中穴位的存在提供了实证依据, 并为关于穴位存在与否的争议提供了新的实验证据.

与前人研究一致[51,59,60], 实验1通过小步递增法发现, 被试接受的电刺激强度越大, 刺激强度感受越高, 表明实验中使用的电刺激强度具有可靠性和有效性. 此外, 当电刺激强度超过4000 μA时, 穴位处的疼痛强度评分显著低于非穴位, 而当电刺激强度低于4000 μA时, 穴位与非穴位之间的刺激强度评分无显著差异. 表明穴位与非穴位对低强度刺激可能不存在感知上的差异, 但穴位对高强度刺激具有更低的疼痛感知, 这与以往研究结果相似[61]. 说明穴位可能能够减轻对高痛刺激的疼痛感知.

与前人研究一致[57,62,63], 实验2发现“刺激类型”的主效应, 随着刺激强度的提高, 被试对刺激判断更准确、主观感受更痛、情绪反应更消极, 以及N1、P2波幅更大. “刺激部位”的主效应发现相较于非穴位, 被试在穴位接受刺激时反应更慢、主观感受更不痛、情绪反应更积极, N1、P2波幅较小. N1波幅与躯体感觉的主观体验相关[47], 穴位处刺激激活较小的N1波幅可能反映了穴位在感觉处理的早期阶段对电刺激的较低感知水平. 而P2波幅与刺激的身体部位相关[48,49], 穴位处刺激激活较小的P2波幅可能是因为穴位在身体的特定区域, 因而具有不同的反应机制.

此外, N1波幅的“刺激部位”和“刺激类型”交互作用显著, 被试在穴位接受高痛刺激时比非穴位表现出更不痛的主观感受、更积极的情绪反应以及更小的N1波幅, 而在低痛刺激与无痛刺激条件下则没有发现这种刺激部位差异. N1波幅反映的是处理躯体感觉信息的输入, 与躯体感觉的主观体验密切相关[47]. N1波幅的减弱表明对躯体感觉信息的反应相应减弱[53,64]. 这说明, 穴位对高痛刺激确实存在感知水平较低的现象. 前人关于穴位镇痛的研究曾发现, 高痛穴位刺激比低痛穴位刺激更能有效缓解个体的疼痛[44], 说明刺激强度可能是影响穴位感知和功能的重要因素.

本研究的两项实验结果表明, 相较于非穴位, 穴位对高痛刺激呈现出较低的疼痛感知. 这表明穴位与非穴位在生理特征方面可能存在差异, 可能涉及特殊的神经机制, 从而影响对疼痛信号的处理. 根据中医理论, 穴位是经络系统的关键部位[9]. 对特定穴位进行刺激可以通过经络系统影响远处部位的身体生理机能[11]. 现代科学研究表明, 刺激穴位可以引发大脑活动的变化, 并且能够激发机体产生内源性阿片类物质以及其他神经递质, 从而对身体产生镇痛效果[33,35,40,65]. 然而本研究在同一个实验内对穴位与非穴位进行随机刺激, 因此得以直接比较穴位与非穴位在不同条件下的疼痛感知差异, 因此内源性阿片类物质分泌的角度可能无法完全解释本研究的结果.

研究表明, 穴位是由肥大细胞、血管以及神经组成的动态复合结构[3]. 在穴位的肥大细胞中, 存在一种被称为瞬时受体电位香草酸亚型(transient receptor potential vanilloid subtype, TRPV1)的核心成分. 该成分在皮肤功能和疼痛感觉传递中发挥着重要作用, 特别是在疼痛感知过程中[66,67]. 当穴位受到高强度刺激时, TRPV1的表达水平显著上调. 这种生理反应可能会导致感觉神经元脱敏, 产生局部镇痛效应, 使穴位处的疼痛感知低于非穴位[68]. 因此, 相较于非穴位, 穴位较低的疼痛感知可能源自穴位内部独特的生理和分子机制.

本研究存在一些局限性. 首先, 本研究的被试都是健康的年轻人, 目前还不清楚这些研究结果在多大程度上适用于老年人或患有慢性疼痛以及其他疾病的人. 其次, 本研究选择了内关和足三里作为研究穴位, 未来

的研究可能会考虑探索更多的穴位. 最后, 尽管研究努力控制无关变量的影响, 但可能还有其他外部因素会影响研究结果.

4 结论

为了探究穴位本身的疼痛感知特点, 本研究结合心理物理学与电生理技术, 采集了穴位和非穴位受到不同强度电刺激时的行为和神经反应数据, 发现相较于非穴位, 穴位接受高痛刺激时其疼痛感知较弱. 本研究表明穴位对高痛刺激存在特异性的疼痛感知, 从行为和脑科学的角度为穴位的存在提供了实证证据, 为中医发展提供了重要支撑.

致谢 衷心地感谢参与本研究的所有被试. 感谢重庆市高校哲学社会科学协同创新团队·特殊儿童心理健康研究协同创新团队(重庆师范大学)的支持.

参考文献

1 Furlan A D, van Tulder M, Cherkin D, et al. Acupuncture and dry-needling for low back pain: An updated systematic review within the framework of the cochrane collaboration. Spine, 2005, 30: 944–963
2 Li Y, Yu Y, Liu Y, et al. Mast cells and acupuncture analgesia. Cells, 2022, 11: 860
3 Luo M F, Dong X T, Song X J, et al. Study on the dynamic compound structure composed of mast cells, blood vessels, and nerves in rat acupoint. Evid Based Complement Alternat Med, 2013, 2013: 160651
4 Zhang Z J, Wang X M, McAlonan G M. Neural acupuncture unit: A new concept for interpreting effects and mechanisms of acupuncture. Evid Based Complement Alternat Med, 2012, 2012: 1–23
5 Kim S Y, Min S, Lee H, et al. Changes of local blood flow in response to acupuncture stimulation: A systematic review. Evid Based Complement Alternat Med, 2016, 2016: 1–11
6 Li J, Wang Q, Liang H, et al. Biophysical characteristics of meridians and acupoints: A systematic review. Evid Based Complement Alternat Med, 2012, 2012: 1–6
7 Zheng H D, Wang Z Q, Li S S, et al. Effect of acupoints on acupuncture-moxibustion and its therapeutic mechanism. World J Tradit Chin Med, 2020, 6: 239–248
8 Fu L, Li B J, Yao K Y, et al. Exploration of the construction of semantic framework of meridians and acupoints based on top-level ontology (in Chinese). Zhongguo Zhen Jiu Chin Acupunct Moxibust, 2022, 42: 1064–1072 [付璐, 李宝金, 姚克宇, 等. 顶层本体指导下的经络腧穴语义框架构建探索研究. 中国针灸, 2022, 42: 1064–1072]
9 Li F, He T, Xu Q, et al. What is the acupoint? A preliminary review of acupoints. Pain Med, 2015, 16: 1905–1915
10 Zhu B. On the acupoint and its specificity (in Chinese). Zhongguo Zhen Jiu Chin Acupunct Moxibust, 2021, 41: 943–950 [朱兵. 论穴位与穴位特异性. 中国针灸, 2021, 41: 943–950]
11 Liu S, Wang Z, Su Y, et al. A neuroanatomical basis for electroacupuncture to drive the vagal-adrenal axis. Nature, 2021, 598: 641–645
12 Tu M, Wu X, Qu S, et al. The effective on intradermal acupuncture based on changes in biological specificity of acupoints for major depressive disorder: Study protocol of a prospective, multicenter, randomized, controlled trial. Front Psychiatry, 2023, 14: 1183127
13 Liu F, Wang Y, Lyu K, et al. Acupuncture and its ability to restore and maintain immune homeostasis. QJM, 2024, 117: 167–176
14 Cao J, Tu Y, Wilson G, et al. Characterizing the analgesic effects of real and imagined acupuncture using functional and structure MRI. Neuroimage, 2020, 221: 117176
15 Coutaux A. Non-pharmacological treatments for pain relief: TENS and acupuncture. Joint Bone Spine, 2017, 84: 657–661
16 Brondino N, Fusar-Poli L, Rocchetti M, et al. Complementary and alternative therapies for autism spectrum disorder. Evid Based Complement Alternat Med, 2015, 2015: 1–31
17 Zhang L, Chu Q, Wang S, et al. Is sham acupuncture as effective as traditional Chinese acupuncture? It's too early to say. Chin J Integr Med, 2016, 22: 483–489
18 Raja S N, Carr D B, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. Pain, 2020, 161: 1976–1982
19 Goldberg D S, McGee S J. Pain as a global public health priority. BMC Public Health, 2011, 11: 770
20 Wang Y, Li L, Cai J, et al. Incidental physical pain reduces brain activities associated with affective social feedback and increases aggression. Soc Cogn Affect Neurosci, 2023, 18: nsac048
21 Wei Z X, Zhang M, Kong Y Z. Neural similarities and differences between pain and itch: Reception, transmission and modulation (in Chinese).

Chin Sci Bull, 2020, 65: 1556–1568 [魏朝行, 张明, 孔亚卓. 疼痛与痒神经机制的异同: 感受、传导与调控. 科学通报, 2020, 65: 1556–1568]
22 Li Z, Zhang L, Zhang H, et al. Pain-related gamma band oscillations: Progress and prospect (in Chinese). Chin Sci Bull, 2020, 65: 2752–2762 [李镇江, 张立波, 张会娟, 等. 疼痛相关高频振荡信号: 进展与展望. 科学通报, 2020, 65: 2752–2762]
23 Rütgen M, Seidel E M, Pletti C, et al. Psychopharmacological modulation of event-related potentials suggests that first-hand pain and empathy for pain rely on similar opioidergic processes. Neuropsychologia, 2018, 116: 5–14
24 Staahl C, Olesen A E, Andresen T, et al. Assessing analgesic actions of opioids by experimental pain models in healthy volunteers—An updated review. Brit J Clin Pharma, 2009, 68: 149–168
25 Bushnell M C, Frangos E, Madian N. Non-pharmacological treatment of pain: Grand challenge and future opportunities. Front Pain Res, 2021, 2: 696783
26 Li J, Yang H, Xiao Y, et al. The analgesic effects and neural oscillatory mechanisms of virtual reality scenes based on distraction and mindfulness strategies in human volunteers. Br J Anaesth, 2023, 131: 1082–1092
27 Lan L, Gao Y J, Zeng F, et al. A central analgesic mechanism of acupuncture for migraine: An ongoing functional MRI study. Neural Regen Res, 2013, 8: 2649–2655
28 Xie L, Liu Y, Zhang N, et al. Electroacupuncture improves M2 microglia polarization and glia anti-inflammation of hippocampus in Alzheimer's disease. Front Neurosci, 2021, 15: 689629
29 Baeumler P I, Fleckenstein J, Benedikt F, et al. Acupuncture-induced changes of pressure pain threshold are mediated by segmental inhibition—a randomized controlled trial. Pain, 2015, 156: 2245–2255
30 Ma X, Chen W, Yang N N, et al. Potential mechanisms of acupuncture for neuropathic pain based on somatosensory system. Front Neurosci, 2022, 16: 940343
31 Meng D, Mao Y F, Song Q M, et al. Efficacy and safety of transcutaneous electrical acupoint stimulation (TEAS) for postoperative pain in laparoscopy: A systematic review and meta-analysis of randomized controlled trials. Evid Based Complement Alternat Med, 2022, 2022: 9922879
32 Na B, Jahng G H, Park S, et al. An fMRI study of neuronal specificity of an acupoint: Electroacupuncture stimulation of Yanglingquan (GB34) and its sham point. Neurosci Lett, 2009, 464: 1–5
33 Napadow V, Dhond R, Park K, et al. Time-variant fMRI activity in the brainstem and higher structures in response to acupuncture. Neuroimage, 2009, 47: 289–301
34 Qiu K, Yin T, Hong X, et al. Does the acupoint specificity exist? Evidence from functional neuroimaging studies. Curr Med Imaging, 2020, 16: 629–638
35 Sun Z, Pi Y, Zhang J, et al. Effect of acupuncture at ST36 on motor cortical excitation and inhibition. Brain Behav, 2019, 9: e01370
36 Tu Y, Li Z, Zhang L, et al. Pain-preferential thalamocortical neural dynamics across species. Nat Hum Behav, 2023, 8: 149–163
37 Zhang S, Tang H, Zhou J, et al. Electroacupuncture attenuates neuropathic pain after brachial plexus injury. Neural Regen Res, 2014, 9: 1365–1370
38 Kim S, Zhang X, O'Buckley S C, et al. Acupuncture resolves persistent pain and neuroinflammation in a mouse model of chronic overlapping pain conditions. J Pain, 2018, 19: 1384.e1–1384.e14
39 Li C, Wang Y, Li B, et al. Effects of acupuncture at neiguan in neural activity of related brain regions: A resting-state fMRI study in anxiety. Neuropsychiatr Dis Treat, 2022, Volume 18: 1375–1384
40 Nguyen H T M, Lee D Y, Liu C H, et al. Changes in acupuncture-induced specific acupoint neurotransmitters are possibly related to their physiological functions in rats. Evid Based Complement Alternat Med, 2023, 2023: 4849528
41 Lee D Y, Jiu Y R, Hsieh C L. Electroacupuncture at Zusanli and at Neiguan characterized point specificity in the brain by metabolomic analysis. Sci Rep, 2020, 10: 10717
42 Wan C, Xu Y, Cen B, et al. Neuregulin1-ErbB4 signaling in spinal cord participates in electroacupuncture analgesia in inflammatory pain. Front Neurosci, 2021, 15: 636348
43 Yim Y K, Lee H, Hong K E, et al. Electro-acupuncture at acupoint ST36 reduces inflammation and regulates immune activity in collagen-induced arthritic mice. Evid Based Complement Alternat Med, 2007, 4: 51–57
44 Barlas P, Ting S L H, Chesterton L S, et al. Effects of intensity of electroacupuncture upon experimental pain in healthy human volunteers: A randomized, double-blind, placebo-controlled study. Pain, 2006, 122: 81–89
45 Zhang L B, Lu X J, Huang G, et al. Selective and replicable neuroimaging-based indicators of pain discriminability. Cell Rep Med, 2022, 3: 100846
46 Hu L, Valentini E, Zhang Z G, et al. The primary somatosensory cortex contributes to the latest part of the cortical response elicited by nociceptive somatosensory stimuli in humans. Neuroimage, 2014, 84: 383–393
47 Lee M C, Mouraux A, Iannetti G D. Characterizing the cortical activity through which pain emerges from nociception. J Neurosci, 2009, 29: 7909–7916
48 Lagerburg V, Bakkers M, Bouwhuis A, et al. Contact heat evoked potentials: Normal values and use in small-fiber neuropathy. Muscle Nerve, 2015, 51: 743–749

49 Rosner J, Hostettler P, Scheuren P S, et al. Normative data of contact heat evoked potentials from the lower extremities. Sci Rep, 2018, 8: 11003
50 Pan Z, Zhang C, Su W, et al. Relationship between individual differences in pain empathy and task- and resting-state EEG. Neuroimage, 2023, 284: 120452
51 Yao M, Lei Y, Li P, et al. Shared sensitivity to physical pain and social evaluation. J Pain, 2020, 21: 677–688
52 Zhang W Y, Zhuo S W, Zheng Q Q, et al. Autistic traits influence pain empathy: The mediation role of pain-related negative emotion and cognition (in Chinese). Acta Psychol Sin, 2023, 55: 1501–1517 [张文芸, 卓诗维, 郑倩倩, 等. 自闭特质对疼痛共情的影响: 疼痛负性情绪和认知的中介作用. 心理学报, 2023, 35: 1501–1517]
53 Wei Z, Huang Y, Li X, et al. The influence of aggressive exercise on responses to self-perceived and others' pain. Cereb Cortex, 2023, 33: 10802–10812
54 Zhou L, Wei H, Zhang H, et al. The influence of expectancy level and personal characteristics on placebo effects: Psychological underpinnings. Front Psychiatry, 2019, 10: 20
55 Delorme A, Makeig S. EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J Neurosci Methods, 2004, 134: 9–21
56 Jung T, Makeig S, Westerfield M, et al. Analysis and visualization of single-trial event-related potentials. Hum Brain Mapping, 2001, 14: 166–185
57 Meng J, Jackson T, Chen H, et al. Pain perception in the self and observation of others: An ERP investigation. Neuroimage, 2013, 72: 164–173
58 Benjamini Y, Hochberg Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. J R Stat Soc Ser B-Stat Methodol, 1995, 57: 289–300
59 Li X, Liu Y, Ye Q, et al. The linkage between first-hand pain sensitivity and empathy for others' pain: Attention matters. Hum Brain Mapping, 2020, 41: 4815–4828
60 Peng W, Lou W, Huang X, et al. Suffer together, bond together: Brain-to-brain synchronization and mutual affective empathy when sharing painful experiences. Neuroimage, 2021, 238: 118249
61 Lv Z, Shen L, Zhu B, et al. Effects of intensity of electroacupuncture on chronic pain in patients with knee osteoarthritis: A randomized controlled trial. Arthritis Res Ther, 2019, 21: 120
62 Peng W, Huang X, Liu Y, et al. Predictability modulates the anticipation and perception of pain in both self and others. Soc Cogn Affect Neurosci, 2019, 14: 747–757
63 Zhang M, Zhang Y, Zhu Y, et al. Stigmatized experience is associated with exacerbated pain perception in depressed patients. Behav Res Ther, 2023, 161: 104252
64 Wu B, Zhou L, Chen C, et al. Effects of exercise-induced hypoalgesia and its neural mechanisms. Med Sci Sports Exerc, 2022, 54: 220–231
65 Shi J, Cao W, Zhang X N, et al. Local analgesia of electroacupuncture is mediated by the recruitment of neutrophils and released β-endorphins. Pain, 2023, 164: 1965–1975
66 Dou B, Li Y, Ma J, et al. Role of neuroimmune crosstalk in mediating the anti-inflammatory and analgesic effects of acupuncture on inflammatory pain. Front Neurosci, 2021, 15: 695670
67 Wang L N, Wang X Z, Li Y J, et al. Activation of subcutaneous mast cells in acupuncture points triggers analgesia. Cells, 2022, 11: 809
68 Abraham T S, Chen M L, Ma S X. TRPV1 expression in acupuncture points: Response to electroacupuncture stimulation. J Chem Neuroanat, 2011, 41: 129–136

补充材料

表S1 内关与对照非穴位之间的刺激强度评分结果
表S2 足三里与对照非穴位之间的刺激强度评分结果
图S1 电刺激强度与刺激强度评分的刺激-反应曲线

本文以上补充材料见网络版csb.scichina.com. 补充材料为作者提供的原始数据, 作者对其学术质量和内容负责.

Summary for “人体穴位会更疼吗? 行为和ERP研究”

Do we feel more pain at acupoints? Behavior and ERP study

Zilong Wei[1,2†], Xiaocui Liu[1,2,3†], Jin Jiang[1,2,4], Yanting Li[1,2], Min Shao[1,2] & Jing Meng[1,2*]

[1] *Research Center for Brain and Cognitive Science, Chongqing Normal University, Chongqing 401331, China*
[2] *Key Laboratory of Applied Psychology, Chongqing Normal University, Key Laboratory of Applied Psychology, Chongqing 401331, China*
[3] *Chongqing Jiangbei Second People's Hospital, Chongqing 400026, China*
[4] *Department of Automobile Engineering, Chongqing Wuyi Polytechnic, Chongqing 401320, China*
† Equally contributed to this work
* Corresponding author, E-mail: qufumj@qq.com

The theory of acupoints has existed in traditional Chinese medicine for millennia. Acupoints are specific points on the surface of the human body, comprising dynamic composite structures composed of mast cells, blood vessels, and nerves that reflect pathological information. The stimulation of certain acupoints can regulate specific physiological functions of the body. Pain is a prevalent clinical condition and a globally recognized health problem. While medications can offer effective pain treatment, their use is often associated with negative effects such as addiction and side effects. Therefore, there is an urgent need to explore effective non-pharmacological analgesic methods. Fortunately, interventions like acupoint therapy have shown positive effects on pain management. Acupoint analgesic therapy is widely utilized worldwide due to its advantages of fewer adverse effects, wider applicability, and rapid results. Although studies have explored the differences between acupoints and non-acupoints in terms of tissue structure and physiological characteristics, the distinctions in pain perception between acupoints and non-acupoints have not been adequately investigated. It is necessary to explore pain perception characteristics and the cognitive neural mechanisms of acupoints in-depth. Therefore, the present study combined behavioral and event-related potential (ERP) experiments to investigate whether the perception of electrical stimulation differs between acupoints and non-acupoints.

In Experiment 1, a series of electrical stimuli (intensity range: 500–5000 μA, in ascending steps of 500 μA) were presented to 36 participants in incremental steps. The participants judged the stimulus intensity by self-report using a 9-point Likert scale, initially to explore the difference in perception between acupoints (Neiguan, Zusanli) and non-acupoints (3 cm lateral to the acupoint). It was found that the perception of higher-intensity electrical stimuli (4000–5000 μA) at acupoints was significantly lower than at non-acupoints, while no significant differences were observed in the perception of lower-intensity electrical stimuli (500–4000 μA) between acupoints and non-acupoints.

Experiment 2 employed ERP technology to explore the differences in perceiving three types of electrical stimuli (no-pain, low-pain, and high-pain) at acupoints and non-acupoints in 32 participants. The stimuli in Experiment 2 were determined based on the results of Experiment 1. Specifically, the mean values of electrical stimuli with acupoints and non-acupoints ratings of 3 (significant sensation but no pain), 5 (significant but tolerable pain), and 7 (intense but not extreme pain) were selected as no-pain, low-pain, and high-pain stimuli, respectively, based on the stimulus-response function of each participant.

Compared to non-acupoints, high-pain stimuli were perceived as less painful at acupoints and judged less negatively, with smaller N1 amplitudes. In contrast, these differences did not exist for low-pain and no-pain stimuli. The present study's findings reveal that acupoints induced lower pain perception in response to high-pain stimuli compared to non-acupoints, suggesting inherent physiological distinctions possibly governed by specific neural mechanisms.

In conclusion, the present study provides empirical evidence supporting distinct pain perception at acupoints, thereby advancing our understanding from both behavioral and cognitive neural perspectives and offering valuable insight for advancing traditional Chinese medicine.

pain, ERP, acupoints, cognitive neural mechanisms

doi: 10.1360/TB-2023-1298