综述

情感性触觉干预早期应激相关的焦虑障碍的研究进展

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［摘要］焦虑障碍是以持续过度的恐惧、焦虑和忧虑为特征，并伴有回避行为以及心率加快、呼吸急促和肌肉紧张等躯体症状的精神障碍，也是常见的精神障碍之一。研究显示，早期应激（early life stress，ELS）可通过改变脑结构和功能，增加个体在幼年和成年后罹患焦虑障碍的易感性。目前已有大量文章就ELS相关焦虑障碍的病理生理学机制进行综述，但鲜有关于该类焦虑障碍的干预技术的报道。在经历ELS的个体中，触觉剥夺现象普遍存在。现有的关于情感性触觉与焦虑障碍的研究中，多数提示情感性触觉可作为一种干预ELS相关焦虑障碍的方法。基于此，该文首先对经历ELS的个体的触觉剥夺现象进行介绍，随后就情感性触觉干预ELS相关焦虑障碍的作用进行探讨，接着从神经环路和神经内分泌方面对情感性触觉的作用机制进行总结，以期为ELS相关的焦虑障碍的辅助干预治疗提供参考。

［关键词］触觉；早期应激；焦虑

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Research progress of affective touch intervention on early life stress-related anxiety disorders

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[Abstract] Anxiety disorders are characterized by persistent and excessive fear, anxiety and concern, accompanied by avoidance behaviors and physical symptoms such as increased heart rate, shortness of breath and muscle tension, which is one of the most prevalent psychiatric disorders. Research has shown that early life stress (ELS) can increase individual susceptibility to developing anxiety disorders during childhood and adulthood by modifying brain structure and functions. A large number of papers have reviewed the pathophysiological mechanisms of ELS-related anxiety disorders, while only a few have reviewed interventional techniques for ELS-related anxiety disorders. The phenomenon of tactile deprivation is prevalent in individuals experiencing ELS. Most current researches on affective touch and anxiety disorders suggest that affective touch is an intervention for ELS-related anxiety disorders. The review firstly introduces the phenomenon of touch deprivation in individuals experiencing ELS, discusses the effect of affective touch intervention on ELS-related anxiety disorders, and then summarizes the mechanism of affective touch in terms of neural circuits and neuroendocrinology, in order to provide reference for complementary intervention treatment of ELS-related anxiety disorders.

[Key words] touch; early life stress (ELS); anxiety

焦虑障碍是常见的精神障碍之一，据流行病学调查数据显示我国成人焦虑障碍的终生患病率为7.57%[1]。早期应激（early life stress，ELS）是指个体在发育早期遭受的超出其应对能力的不良事件，包括情感虐待、躯体虐待、性虐待等[2]。ELS被广泛认为与焦虑障碍的发病有密切的关联。FERNANDES等[3]发现，经历早期情绪创伤的个体成年后患焦虑障碍的风险是健康个体的2.6倍。同时，TEICHER等[4]发现，相较于没有ELS经历的抑郁症、焦虑障碍、物质使用障碍类患者，有ELS经历的患者的发病年龄更早、症状更严重、合并症更多且自杀风险更高。临床上，焦虑障碍的相关药物在疗效方面尚存在

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争议，且认知行为疗法也存在普及性相对较低等缺点[5]，因此探索潜在的焦虑障碍的干预和治疗方案十分必要。近年来，已有不少学者就情感性触觉对焦虑障碍的干预作用和机制研究进行分析，本文拟对该相关研究进行综述，以期为ELS相关焦虑障碍的临床干预技术的开发提供新的方向。

1 ELS的个体经历触觉剥夺

触觉是人类最早发育的感觉，是个体感知世界最基本的方式。触觉存在2种类型：辨别性触觉被位于皮肤和关节的低阈值机械感受器感知，经有髓的A-β传入神经快速传至体感皮层[6]；情感性触觉被有毛皮肤的低阈值机械感受器感知，经无髓的C类触觉传入纤维缓慢传至情感和认知相关的脑区[6]。其中，情感性触觉包含触摸、按摩等。

在胎儿时期，胎毛在羊水中的震荡可激活C类触觉传入纤维，这可能是人类最早获得的触觉体验[7]。早产儿由于被过早地剥夺了与母体的羊水、子宫壁的触觉体验，其神经系统发育会受到一定影响。研究[8]发现，早产可增加个体学龄期患焦虑障碍的风险。袋鼠式护理（kangaroo mother care，KMC）是一种将裸体的婴儿俯卧在母亲裸露的胸前进行皮肤接触的护理方式。FELDMAN等[9]在针对接受KMC的早产儿的10年随访中发现，KMC可促进早产儿迷走神经成熟，有益于早期自主神经系统发育和昼夜节律形成；在10岁时，接收KMC的个体可表现出对压力的良好适应能力、更成熟的自主神经功能以及认知控制能力。

在ELS动物模型中，母婴分离和筑巢材料模型可减少母代对子代的舔舐梳理[10-11]，这提示经历ELS的子代存在触觉剥夺现象。SIMPSON等[12]发现，新生儿期接受更多触摸的猕猴在出生后前3个月会表现出更好的运动、社交和认知能力。WEI等[13]发现，触摸可减少经历母婴分离的棕色田鼠的焦虑样行为，改善其受损的新物体识别能力和社交互动。ANTONIAZZI等[14]发现，在幼儿发育关键期给予触摸可减少大鼠成年后的恐惧、焦虑样行为以及对兴奋性药物的成瘾性。

综上，经历ELS的个体常伴随着触觉剥夺，然而在发育过程中提供触觉刺激可调节个体早期甚至成年后的行为模式，改善ELS对个体的情绪和认知的影响，从而对个体发挥积极作用。

2 情感性触觉在ELS相关的焦虑障碍中的应用

在临床护理中，从情感性触觉衍生出的KMC、按摩已被推荐为新生儿的护理方式。PICKLES等[15]发现，KMC可改善个体在儿童期的焦虑和抑郁情绪。此外，GUZZETTA等[16]发现，以1 h/次、1次/5 d的频率，以适度的压力按摩和触摸早产儿的躯体和四肢各2次，可促进早产儿脑电活动的成熟及脑功能的发育。这些研究提示，情感性触觉可促进早产儿的神经系统发育。

在情感性触觉干预ELS相关的焦虑障碍的研究方面，尽管国内还相对不足，但现有的国外研究表明情感性触觉可能具有治疗焦虑障碍的潜力。GONSALVES等[17]使用温和的机械震动刺激模拟情感触摸，以20 min/次、2次/d的频率对成年焦虑障碍患者进行为期4周的触觉治疗，结果发现患者的杏仁核与默认模式网络的功能连接有所增强，焦虑情绪也得到了缓解。同样地，CARPENTER等[18]发现情感触摸可改善中度广泛性焦虑障碍患者的焦虑和抑郁情绪，同时还能通过增加患者枕骨区域的θ波来增强正念。WEZE等[19]发现，以60 min/次、1次/周的频率触摸受试者4~6周可减少其自我报告的焦虑和抑郁情绪。此外，作为一种特殊的触觉疗法，以轻压为特点的瑞典式按摩在焦虑障碍的治疗中也得到了初步研究。RAPAPORT等[20]发现，以45 min/次、2次/周的频率对广泛性焦虑障碍患者进行为期6周的瑞典式按摩可在治疗的第3周改善患者的焦虑和抑郁情绪。

综上，现有的研究初步表明情感性触觉在治疗焦虑障碍方面具有潜在应用价值，但有关焦虑障碍治疗中的操作范式、使用频率和触摸时长等技术要点尚未形成共识。因此，未来的研究需进一步探索情感性触觉在焦虑障碍治疗的最佳治疗模式，为其应用提供更全面科学的理论依据。

3 情感性触觉干预ELS相关焦虑障碍的神经调控机制

3.1 神经环路机制

3.1.1 丘脑 丘脑在触觉信息的处理中发挥了较关键的作用，如丘脑腹后核（ventral posterior nucleus，

VP）可接收来自C类触觉传入纤维的投射[6]。研究[21]发现，经历虐待的儿童在成年后显示出丘脑纤维束长度有显著减少。ZHANG等[22]发现，患有社交焦虑症的未成年人的丘脑体积存在不对称。此外，SHEFFIELD等[23]发现，精神障碍患者的体感皮层-丘脑功能连接较强，而前额叶-丘脑功能连接较弱。BENOIT等[24]发现，发育阶段抑制丘脑的神经元活动可长期减少丘脑神经元向前额叶的兴奋性输入，从而导致个体成年后出现认知缺陷，这表明丘脑感觉输入的减少可影响丘脑-皮质环的功能。触觉刺激可增加丘脑皮质的输入，因此未来可进一步研究在发育敏感期提供触觉刺激对ELS相关焦虑障碍的干预效果。

3.1.2　岛叶皮层　岛叶皮层（insular cortex，IC）分为前岛叶皮层（anterior IC，aIC）、中岛叶皮层和后岛叶皮层（posterior IC，pIC）。pIC可直接接收来自丘脑和体感皮层的投射，参与躯体感觉的处理。MORRISON等[25]发现，以令人愉悦的速度抚摸皮肤可增加对侧pIC的血氧水平依赖性信号，这提示pIC是C类触觉传入纤维的目标脑区。MAIER等[26]发现，有重度儿童虐待经历的成年人被触摸时存在pIC的过度激活。CRAIG[27]曾提出猜想，pIC至aIC投射的神经元可对C类触觉传入纤维传导的信息进行更高层次的整合。DAVIDOVIC等[28]进一步发现，带有愉悦感的抚摸可增加pIC与aIC的功能连接；而后者与边缘系统、额叶和颞叶连接，参与情感、认知和执行功能的加工。NICOLAS等[29]发现焦虑样行为增加的小鼠存在aIC的异常激活，这提示岛叶参与焦虑的加工。综上，我们认为pIC和aIC可能共同参与情感性触觉的整合，且与焦虑情绪加工相关。

3.1.3　前额叶皮层　前额叶皮层（prefrontal cortex，PFC）在情感性触觉的加工中发挥重要作用，即通过对情感性触觉信息的处理和整合，影响个体对情感性触觉的认知和情感反应。NGUYEN等[30]发现，母婴自发的深情触摸互动可增强双方在外侧PFC和内侧PFC的神经元同步性。LÓPEZ-SOLÀ等[31]发现，触摸可减少产妇的背腹侧PFC的活动，发挥镇痛作用。进一步地，RICHARDS等[32]发现，触摸可显著增加大鼠PFC和杏仁核的树突分支、树突长度和突触连接。而ELS可导致大鼠PFC的锥体神经元树突棘数目和长度发生异常，增加成年后的焦虑样行为[33]。因此，触摸可能通过重塑PFC神经元的结构，改善ELS对情感和认知的损害。

3.1.4　前扣带回皮层　前扣带回皮层（anterior cingulate cortex，ACC）是调节情感的重要脑区。ROKITA等[34]发现，ELS与成年后ACC体积减少有关。进一步地，FONZO等[35]发现在处理愤怒情绪时，经历ELS的焦虑障碍患者的腹侧ACC激活增加而背侧ACC激活减少，这提示ACC不同亚区在处理情感时具有不同的效应。KRAUS等[36]发现，与伴侣握手可削减ACC的反应性，减弱前岛叶-ACC的功能连接。同时，GORDON等[37]发现，情感性触摸可以特异性激活内侧PFC/背侧ACC，增强其与对侧IC和杏仁核的功能连接，继而提示ACC、PFC、杏仁核等脑区共同参与情绪的加工。因此，在触摸时，ACC与其他脑区之间存在协同作用，共同调节个体的情绪反应。

3.1.5　杏仁核　作为边缘系统的重要组成部分，杏仁核参与了情绪（如恐惧、焦虑等）效价的编码。有研究[38]发现，ELS可导致儿童和青少年的杏仁核的灰质体积减少，因此大脑可能通过加速杏仁核的成熟以应对压力。然而杏仁核过早成熟可缩短其神经可塑性窗口，使其无法与PFC、海马等脑区建立稳定连接，继而影响个体成年后的情绪调节。CHOI等[39]发现，触觉信息经脊髓旁臂的上行神经元投射到臂旁核，而臂旁核至杏仁核的环路与压力反应相关。此外，有研究[40]发现触觉感觉缺陷的小鼠的基底外侧杏仁核过度激活。而QIN等[41]发现，ELS可显著增加基底外侧杏仁核神经元兴奋性突触传递和内在神经兴奋性，从而增加小鼠的焦虑样行为。综上，触摸可能通过特异调控ELS异常激活的杏仁核亚区来调控焦虑情绪。

3.1.6　海马　大量研究已证实ELS对海马存在长期毒性。TEICHER等[42]在回顾性队列研究中发现，成年人的海马亚区的体积减少与其童年虐待经历强相关。同样地，HERRINGA等[43]在纵向队列研究中发现，童年虐待经历与个体青少年时期海马和膝下ACC的功能连接降低有关。DELPECH等[44]发现，ELS可通过扰乱小胶质细胞的成熟过程来改变海马神经元的轴突生长、髓鞘形成和突触修剪。RODRIGUES等[45]发现早期接受触觉刺激可防止大鼠在出生后因缺血、缺氧诱发的海马损伤，这可能与触觉可防止海马神经损伤或诱导神经元或神经胶质细胞生成有关。WANG等[46]发现，在成年时给ELS的小鼠提供触觉体验可增强小鼠的海马齿状回的突触可

塑性，改善记忆并减少焦虑样行为。综上，触觉干预可保护经历ELS后受损的海马神经元，重塑海马与其他脑区之间的功能连接，从而调节情绪认知。

3.2 神经内分泌机制

3.2.1 下丘脑-垂体-肾上腺轴 由ELS引起的下丘脑-垂体-肾上腺（hypothalamic-pituitary-adrenal，HPA）轴功能紊乱可导致下丘脑过度释放促肾上腺皮质激素释放激素（corticotropin releasing hormone，CRH），从而使CRH受体和糖皮质激素受体（glucocorticoid receptor，GR）表达减少或脱敏，削弱HPA轴的负反馈机制；同时，该轴功能紊乱还可使基础皮质醇维持在高水平，对海马、PFC、杏仁核等应激敏感的脑区产生不可逆损害，从而增加成年后患焦虑障碍的风险[47]。KENTNER等[48]在模拟新生儿炎症和母婴分离的动物模型中发现，触摸可提高海马GR的表达，逆转ELS导致的HPA轴钝化；且VAN OERS等[49]发现，触摸可逆转母婴分离导致的海马亚区的盐皮质激素受体和GR减少。同时，触觉刺激还可降低海马GR的DNA甲基化，增加该受体的表达，进而增强HPA轴的负反馈[50]，降低血浆皮质醇水平。因此，触觉可能通过逆转ELS所致的HPA轴失调，恢复基础皮质醇水平，改善个体焦虑情绪。

3.2.2 催产素 催产素是研究最多的神经肽之一，具有缓解焦虑和亲社会的作用。LABUSCHAGNE等[51]发现，催产素可减弱社交焦虑症患者的杏仁核对恐惧面孔的反应。SHI等[33]发现，ELS可减少大鼠PFC神经元的催产素受体的表达，而补充催产素可增加大鼠对应激的耐受力，并减少其焦虑样行为。这些研究表明催产素具有抗焦虑作用。而TANG等[52]发现，触觉可激活大鼠室旁核（paraventricular nucleus，PVN）的催产素神经元以释放催产素。进一步地，YU等[53]发现，社交触摸可激活中脑导水管投射到PVN的速激肽神经元，进而促进PVN的催产素神经元释放催产素。此外，杏仁核、PFC、ACC、伏隔核等脑区均可表达大量催产素受体并接受来自PVN的催产素神经元的侧支投射[54]。综上，触摸可促进催产素的释放，从而调控表达催产素受体的脑区活动，以实现对情感和认知的调控。

3.2.3 阿片肽-阿片肽受体系统 研究[55-57]发现，ELS可改变导水管周围灰质、延髓腹内侧、杏仁核、外侧缰核等脑区的阿片受体表达，从而诱发焦虑。有研究[58]发现，梳理毛发可促进非人灵长类动物的内啡肽的释放，从而激活奖赏系统；给予吗啡可减少其对毛发梳理的需求，而给予阿片受体拮抗剂可诱导出毛发梳理和社交行为。同样地，MORHENN等[59]发现，按摩受试者上背部可减少其β-内啡肽的释放。NUMMENMAA等[60]发现，触摸可引发受试者的愉悦感，并增加腹侧纹状体、内侧PFC和杏仁核的μ-阿片受体的利用。综上，这些研究提示触摸可能发挥类阿片肽的作用，即通过影响阿片肽的释放和阿片肽受体的表达来调节社会行为和情绪。

4 总结与展望

情感性触觉通过影响情感和认知相关的大脑，重塑受ELS扰乱的脑区结构和功能，调节应激激素和神经肽的分泌，从而改变大脑对应激的反应。触觉作为一种临床干预技术已在临床护理和焦虑障碍防治中得到初步实践。而目前关于触觉干预ELS相关的焦虑障碍的机制研究主要集中在对海马、PVN、前额叶等单个脑区的结构和功能的探索，后续的研究可结合神经调控技术、病毒示踪技术等进一步解析触觉对神经环路的影响。此外，在临床研究中，触觉不可避免地与其他感官体验、社会环境等因素交互影响，因此未来的临床研究需要排除其他因素以明确触摸对情感的影响。

利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。
Both authors disclose no relevant conflict of interests.

作者贡献/Authors' Contributions

廖冰冰负责文献的检索和文章的撰写，王振负责指导文章的写作并参与论文的修改。所有作者均阅读并同意了最终稿件的提交。
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