

焦虑障碍的脑电生理研究进展

袁丹凤 杨祥云 李占江

100088 首都医科大学附属北京安定医院 国家精神心理疾病临床医学研究中心 精神疾病
诊断与治疗北京市重点实验室

通信作者: 李占江, Email: lizhj8@ccmu.edu.cn

DOI: 10.3969/j.issn.1009-6574.2024.06.008

【摘要】 焦虑障碍临床表现复杂, 目前缺乏诊断以及疗效预测相关的神经生物学指标。脑电图是一种非侵入性的神经电生理检测工具, 具有较高的时间分辨率, 能锁时反映焦虑障碍认知损害的时间进程。现对焦虑障碍的时域、频域、功能连接脑电特征的相关研究进行综述, 探索焦虑障碍自上而下和自下而上的认知加工异常, 为进一步明确焦虑障碍的神经心理机制以及探索焦虑障碍预测、诊断、预后相关的神经生物学客观指标提供参考。

【关键词】 焦虑障碍; 脑电图; 脑电描记术; 综述

基金项目: 科技创新2030-“脑科学与类脑研究”重大项目(2021ZD0202004); 首都卫生发展科研专项重点攻关项目(2020-1-2121)

Research progress of electroencephalography in anxiety disorders Yuan Danfeng, Yang Xiangyun, Li Zhanjiang

Beijing Key Laboratory of Mental Disorders, National Clinical Research Center for Mental Disorders, Beijing Anding Hospital, Capital Medical University, Beijing 100088, China

Corresponding author: Li Zhanjiang, Email: lizhj8@ccmu.edu.cn

【Abstract】 The clinical manifestations of anxiety disorders are complex, and there is currently a lack of neurobiological indicators related to diagnosis and efficacy prediction. Electroencephalogram (EEG) is a non-invasive neurophysiological detection tool with high temporal resolution, which can reflect the temporal progression of cognitive impairment in anxiety disorders. This article reviews the relevant research on the temporal, frequency, and functional connectivity EEG characteristics of anxiety disorders, exploring the cognitive processing abnormalities of anxiety disorders from top-down and bottom-up. The aim of this review was to provide reference for further clarifying the neuropsychological mechanisms of anxiety disorders and exploring objective neurobiological indicators related to the prediction, diagnosis, and prognosis of anxiety disorders.

【Key words】 Anxiety disorders; Electroencephalogram; Electroencephalography; Review

Fund programs: Science and Technology Innovation 2030 - "Brain Science and Brain-Like Research" Major Project (2021ZD0202004); Special Scientific Research Project of Capital Health Development (2020-1-2121)

焦虑障碍是常见的精神疾病之一, 具有高共病率和高复发率的特点, 其诊断主要依据患者的临床表现, 但在治疗方面缺乏指导个体化治疗的指标以及疗效预测的客观指标。脑电图是探索焦虑障碍病理、认知神经机制、诊断及预后相关生物学标志物的重要非侵入性工具, 可探测大脑皮层神经元自发、节律性电生理活动, 具有毫秒级别的时间分辨率, 方便易行, 对采集环境无特殊要求^[1-2]。由于焦虑障碍病因不明以及其在诊断、治疗方面的复杂性, 探索脑电指标与焦虑症状的关联, 以及焦虑障碍的诊断、预

后相关脑电图特征具有重要意义。本文综述焦虑障碍的脑电生理研究, 将脑电信号分为时域特征、频域特征、功能连接进行分别阐述, 为探索焦虑障碍预测、诊断和预后相关的脑电生理指标提供参考。

一、时域特征

时域特征主要包括事件相关电位(event-related potential, ERP)和诱发电位(evoked potentials, EP)。ERP是一种特殊的EP, 具有锁时锁相的特点, 可准确追踪神经元对不同刺激的反应时间进程, 并与特定认知加工过程相关^[3]。焦虑障碍的ERP研究主

要涉及注意偏向、认知控制、情绪反应等认知加工过程。

1. P1、N170: 是早期视觉相关ERP, 主要起源于视觉皮层^[4]。其中, N170是面孔识别的特异性ERP成分, 能够敏感识别面孔表情。P1、N170成分常被用于探索焦虑障碍患者的注意偏向和早期情绪信息的加工过程。研究表明, 焦虑障碍患者存在威胁性/负性情绪刺激的注意偏向, 表现为P1波幅增高、潜伏期缩短^[5]。而一些研究并未发现焦虑障碍患者存在威胁性/负性刺激的注意偏向^[6-7]。以上研究结果的异质性可能来源于研究间的方法学差异以及接受刺激的个体差异^[5,8]。

社交焦虑障碍(social anxiety disorder, SAD)作为一种常见的焦虑障碍亚型, 常表现为对社会线索存在认知偏差。P1、N170成分常被用于探索SAD患者的早期面孔、情绪信息加工注意偏向。研究发现, 在SAD患者中, 面孔刺激诱发的P1、N170波幅显著高于健康对照, 提示SAD患者对面孔表情刺激存在高警觉性^[9]。然而, 也有研究认为SAD患者的面孔刺激诱发N170与健康人群不存在差异, 但经认知行为治疗(cognitive behavior therapy, CBT)后患者的N170波幅降低, 提示CBT治疗可能降低了患者对面孔的高敏感性^[10]。

2. N2: 主要起源于扣带回, 出现在N170成分后, 反映认知控制和冲突监测过程。注意控制理论认为, 焦虑障碍患者, 特别是广泛性焦虑障碍(generalized anxiety disorder, GAD)患者的认知控制受损较明显。N2成分可用于鉴别GAD患者和健康人群。GAD患者的N2波幅明显高于健康人群, 反映GAD患者存在认知控制功能异常^[11-13]。此外, 有研究探索认知负荷对于认知控制的影响, 并发现焦虑个体在高认知负荷任务下会收集更多认知资源来处理任务无关刺激, 因而在高工作记忆负荷下的Flanker任务中表现为N2波幅增高^[14]。

3. 晚期正成分(late positive potential, LPP): 是一个中央顶叶分布的正相慢波, 源定位分析显示该成分与杏仁核活动相关^[15], 可反映成人和儿童对刺激的持续注意和情绪反应、情绪调节过程^[16]。LPP对刺激的唤醒度敏感, 也可用于评估焦虑障碍患者的注意偏向^[17]。此外, LPP成分会受到认知负荷及情绪调节指令的影响。因此, 也可反映焦虑障碍自上而下的控制加工损害^[18]。由于焦虑会影响认知功能, 在工作记忆任务中, 认知负荷对LPP波幅的调节作用可能被减弱。此外, 在被试采取情绪调节策略时,

LPP的波幅降低^[19]。由于SAD患者在预期阶段、情景暴露阶段存在过度的自我关注, LPP成分也被用于探究SAD患者对自我形象刺激的动机显著性^[20]。LPP成分由于在刺激下的反应时间相对较长, 不同焦虑障碍亚型在LPP早期和晚期的时间窗可能存在差异。MacNamara等^[19]研究发现, 惊恐障碍(panic disorder, PD)患者早期时间窗的LPP波幅增高, 而晚期时间窗的LPP波幅降低。而SAD患者在整个时间窗表现为LPP波幅增高。Bylsma等^[21]的研究提示, LPP早期时间窗主要反映注意定向过程, 与焦虑障碍患者的威胁性注意偏向有关。而LPP晚期时间窗主要反映注意脱离困难, 与焦虑障碍患者的担忧和思维反刍症状相关。此外, LPP可能是焦虑障碍疗效相关的电生理指标^[22-24]。研究显示, 焦虑障碍患者LPP波幅在CBT、针刺治疗、认知重评、注意偏向矫正治疗后降低, 提示这些方法可能通过情绪调节发挥治疗作用^[25-26]。

4. 错误相关负波(error related negativity, ERN): 是错误刺激后100 ms达到峰值, 分布于额中央区域的负相成分, 主要反映前扣带回产生的错误监测反应, 具有良好的心理测量特性。焦虑障碍患者的ERN波幅显著增高^[27]。前瞻性研究显示, ERN波幅增高可能预示未来更高的焦虑障碍患病风险, 特别是GAD和SAD^[28-29]。家族性研究提示, 在焦虑障碍的未患病一级亲属中也可见ERN波幅增高, 提示ERN增高可反映焦虑障碍的易感性^[30]。然而, 有研究发现, ERN对焦虑障碍的疗效预测作用不佳, ERN波幅增高并不随治疗后焦虑症状改善而降低, 基线期ERN波幅与焦虑障碍症状改善无明显相关性^[31-32]。心理维度研究认为, ERN可能是一种跨诊断标记物, 与担忧、难以耐受不确定威胁有关^[33-35]。

5. 反馈相关负波(feedback-related negativity, FRN): 是由外部反馈诱发的负偏向成分^[36]。焦虑障碍患者对反馈刺激的心理预期与健康人群存在差异, 患者更倾向于负性预期, 因此表现出FRN的异常。研究显示, 高焦虑个体在负性反馈下表现为FRN波幅下降, 与焦虑的负性预期、负性解释偏向有关^[37]。FRN可用于探索SAD患者在社交反馈刺激下的异常加工模式。研究发现, 由于SAD患者对社交反馈刺激存在更高的拒绝预期, 患者在社交接纳刺激下的FRN波幅可能高于社交拒绝刺激^[38-39]。

6. 基于稳态视觉诱发电位(steady-state visual evoked potential, ssVEP): 是视觉系统对外部视觉刺激响应, 与刺激信号的频率有关^[40]。相比ERP、

fMRI、眼动追踪, ssVEP可动态、持续测量视觉皮层参与威胁相关的注意加工过程。研究发现,在愤怒面孔刺激下SAD患者的ssVEP波幅增高,且患者对情绪面孔表现出的警觉性会持续增高。面孔刺激诱发的ssVEP与社交焦虑症状的严重程度呈正相关^[41-42]。此外,ssVEP也常被用于研究焦虑障碍患者对威胁刺激的预测情况。研究发现,高焦虑个体对不确定威胁刺激存在过度警觉,且恐惧记忆的消退减缓,在不同情景下威胁性刺激引起的ssVEP波幅比较差异无统计学意义^[43-44]。

7. 失匹配负波(mismatch negativity, MMN): 主要反映听觉中枢对声信息变化的处理^[45]。研究显示,焦虑障碍患者以及高特质焦虑个体可诱发更高的MMN反应^[46-47]。过高的MMN响应可能与焦虑障碍患者的高警觉性和焦虑相关听觉门控通道损害有关^[48]。对PD患者进行的研究表明,对惊恐相关声音刺激的过度警觉以及对其他声音变化的敏感性降低可能与PD的发病机制相关^[49]。

焦虑障碍的时域特征研究多关注特质焦虑等亚临床个体,而临床焦虑障碍患者中的ERP研究相对较少。此外,尚不明确不同的焦虑障碍亚型个体对不同类型的刺激是否存在差异性反应。以上研究显示,焦虑障碍患者存在自上而下的认知控制和注意转移加工异常,表现为ERN、N2增高;以及自下而上的基于显著性注意的加工过强,表现为P1、N170、MMN等成分增高。其中,ERN可能是焦虑障碍诊断相关的电生理标志物,而LPP可能与焦虑障碍的疗效相关。

二、频域特征

1. 相对功率: theta/beta 比值(theta/beta ratio, TBR)是反映神经认知控制功能的神经电生理标志物,且与焦虑症状相关。研究显示,高焦虑会导致持续性担忧,并影响大脑自上而下的注意控制功能^[50]。高焦虑水平的个体TBR高于低焦虑水平的个体,且TBR与焦虑严重程度呈正相关^[51]。

2. 额叶 α 非对称性(frontal α asymmetry, FAA): 主要反映左右两侧大脑半球的 α 功率差异,是与情绪和动机相关的电生理指标。有关抑郁障碍FAA的研究较多,低FAA主要反映低接近动机,且与抑郁症状相关,因此有研究认为FAA可作为抑郁障碍的诊断标志物^[52]。而有关焦虑障碍FAA的研究较少。由于低FAA与高回避动机有关,一些研究认为,焦虑症状主要与低FAA相关^[53-55]。然而,也有相关研究未发现焦虑障碍患者双侧大脑半球的 α 功率存

在显著差异,研究结果间的异质性与任务诱发的焦虑程度不同有关^[56]。目前,有研究探索FAA与焦虑障碍跨诊断症状维度的关系,认为焦虑性担忧和唤醒症状与大脑半球不同的活动模式有关^[57]。

3. Delta-beta耦合(delta-beta coupling, DBC): 可反映皮层与皮层下脑区,特别是边缘系统、杏仁核与前额叶皮层间的相互作用。既往研究发现,前额叶DBC可能与甾体激素(皮质醇)水平相关。高皮质醇水平的个体以及SAD患者的前额叶DBC增高,提示神经内分泌应激反应、社交焦虑与DBC有关^[58]。研究认为,预期阶段的高DBC可能是SAD的内表型,反映了SAD过度控制的神经认知特点^[59]。

三、功能连接

功能连接是指不同脑区间神经活动的相互作用。与fMRI相比,脑电功能连接更侧重于不同频段下神经振荡活动的相关性,可弥补fMRI时间分辨率不足的缺陷。焦虑障碍患者和亚临床焦虑人群可能存在多个神经网络的功能损害,如腹侧注意网络和扣带回-盖神经网络的活性增高以及额-顶神经网络的活性降低。然而也有研究倾向于通过全脑脑电功能连接矩阵来检测焦虑障碍的脑网络功能活动,并认为与既往基于先验知识的方法相比,全脑功能连接矩阵能更全面地利用大脑功能连接特征。

默认网络(default mode network, DMN)是焦虑障碍静息态功能连接研究最常关注的神经网络。研究认为,SAD患者由于高度的自我关注,DMN区域功能连接异常,轻中度SAD患者的DMN功能连接增强,而重度SAD患者的DMN功能连接降低^[60]。

突显网络(salience network, SN)主要参与监测内外环境的刺激并启动认知控制。研究发现,高特质焦虑个体 α 频段下SN功能连接减弱,与焦虑个体的显著性目标检测异常和认知控制功能受损有关^[61]。

在全脑水平中,高广泛性焦虑个体的低频 α 波的功能连接减弱,可能与焦虑个体的抑制功能降低有关。此外,高广泛性焦虑个体在 θ 节律下的脑网络聚类系数显著降低,特征路径长度增加,说明GAD患者的信息处理能力下降^[62]。而SAD患者在静息条件下的 θ 节律功能连接增强,可能与SAD患者的自我关注相关^[63]。基于 θ 节律的脑网络聚类系数增加、特征路径长度减小,说明SAD患者具有较高的信息加工效率^[64]。

四、总结与展望

脑电图是研究焦虑障碍认知加工脑机制的重要手段。时域分析能实时反映注意加工的时间进

程。P1、N170、MMN 主要与自下而上的信息自动加工相关,而ERN、FRN、N2则涉及中枢对内部、外部威胁信息自上而下的监控过程。LPP 主要与情绪反应、情绪调节功能有关。在频域分析方面,相对功率和跨频域耦合可用于反映焦虑障碍自上而下的认知控制缺陷。而额叶 α 不对称性主要与趋近动机加工、负性情绪、焦虑情绪相关。在功能连接方面,DMN 在静息状态时的活跃度增加,被认为参与自我意识、自我加工、情绪调节等过程。而SN 则与焦虑相关的显著性检测、情绪调节、认知控制等过程相关。ERN 由于其稳定性特质,可能作为焦虑障碍诊断的生物学标志物。治疗前负性情绪刺激下 LPP 高反应的患者在 CBT/SSRIs 治疗后焦虑症状改善更显著,LPP 有望作为焦虑障碍预后相关电生理标志物。

然而,目前焦虑障碍的脑电研究结果存在一定的异质性,可能与研究样本量小、范式不统一等原因有关。未来可扩大样本量,进行纵向随访观察焦虑障碍患者脑电指标的动态变化。由于脑电信号具有非线性和非稳态特性,传统的时、频域分析在处理脑电信号方面存在一定的局限性,在此基础上,Lyapunov 指数、复杂度等非线性分析方法受到了越来越多的关注。随着人工智能技术的发展,机器学习、深度学习算法被应用于基于脑电图特征的模型建立。通过不同的脑电特征可区分焦虑障碍患者和健康人群、不同严重程度的焦虑障碍患者以及高焦虑特质和低焦虑特质个体。然而,目前缺乏临床和亚临床的焦虑人群以及焦虑障碍亚型的分类模型。多维度脑电信号有望进一步提高模型的整体性能。多模态的神经成像技术,如脑电图和 fMRI、脑磁图、近红外光学脑成像系统可提供更高时间、空间分辨率的数据,更准确地反映大脑的动态变化过程。此外,目前的相关研究多聚焦于分类模型的构建,较少有研究进行焦虑障碍的预后模型构建,模型的泛化能力有待提高。未来需要融合多模态的数据,进一步提高模型预测和诊断焦虑障碍的准确度、可靠性,并建立对疗效有指导意义的模型以改善患者的预后。

利益冲突 文章所有作者共同认可文章无相关利益冲突

作者贡献声明 文献收集与分析、论文撰写为袁丹凤,论文修订为杨祥云,李占江审校

参 考 文 献

[1] 汤翔嵘,王晓刚,陈桃林,等.精神障碍的神经电生理循证医学证据[J].生物化学与生物物理进展,2021,48(10):1157-1176. DOI:10.16476/j.pibb.2020.0399.

Tang XR, Wang XG, Chen TL, et al. Evidence-based medicine biomarkers of neuroelectrophysiology for mental disorders[J]. Progress in Biochemistry and Biophysics, 2021, 48(10): 1157-1176.

[2] Gallinat J, Mulert C, Leicht G. Significance of clinical electroencephalogram in psychiatry[J]. Nervenarzt, 2016, 87(3): 323-339. DOI: 10.1007/s00115-016-0068-2.

[3] Harrewijn A, Schmidt LA, Westenberg PM, et al. Electrocortical measures of information processing biases in social anxiety disorder: a review[J]. Biol Psychol, 2017, 129: 324-348. DOI: 10.1016/j.biopsycho.2017.09.013.

[4] Schindler S, Bruchmann M, Steinweg AL, et al. Attentional conditions differentially affect early, intermediate and late neural responses to fearful and neutral faces[J]. Soc Cogn Affect Neurosci, 2020, 15(7): 765-774. DOI: 10.1093/scan/nsaa098.

[5] Gupta RS, Kujawa A, Vago DR. The neural chronometry of threat-related attentional bias: event-related potential (ERP) evidence for early and late stages of selective attentional processing[J]. Int J Psychophysiol, 2019, 146: 20-42. DOI: 10.1016/j.ijpsycho.2019.08.006.

[6] Steinweg AL, Schindler S, Bruchmann M, et al. Reduced early fearful face processing during perceptual distraction in high trait anxious participants[J]. Psychophysiology, 2021, 58(6): e13819. DOI: 10.1111/psyp.13819.

[7] Yoon S, Shim M, Kim HS, et al. Enhanced early posterior negativity to fearful faces in patients with anxiety disorder[J]. Brain Topogr, 2016, 29(2): 262-272. DOI: 10.1007/s10548-015-0456-0.

[8] Mogg K, Bradley BP. Anxiety and threat-related attention: cognitive-motivational framework and treatment[J]. Trends Cogn Sci, 2018, 22(3): 225-240. DOI: 10.1016/j.tics.2018.01.001.

[9] Cui L, Dong X, Zhang S. ERP evidence for emotional sensitivity in social anxiety[J]. J Affect Disord, 2021, 279: 361-367. DOI: 10.1016/j.jad.2020.09.111.

[10] Cao J, Liu Q, Li Y, et al. Cognitive behavioural therapy attenuates the enhanced early facial stimuli processing in social anxiety disorders: an ERP investigation[J]. Behav Brain Funct, 2017, 13(1): 12. DOI: 10.1186/s12993-017-0130-7.

[11] Yu Y, Jiang C, Xu H, et al. Impaired cognitive control of emotional conflict in trait anxiety: a preliminary study based on clinical and non-clinical individuals[J]. Front Psychiatry, 2018, 9: 120. DOI: 10.3389/fpsy.2018.00120.

[12] Hum KM, Manassis K, Lewis MD. Neural mechanisms of emotion regulation in childhood anxiety[J]. J Child Psychol Psychiatry, 2013, 54(5): 552-564. DOI: 10.1111/j.1469-7610.2012.02609.x.

[13] Cavanagh JF, Meyer A, Hajcak G. Error-specific cognitive control alterations in generalized anxiety disorder[J]. Biol Psychiatry Cogn Neurosci Neuroimaging, 2017, 2(5): 413-420. DOI: 10.1016/j.bpsc.2017.01.004.

[14] Owens M, Derakshan N, Richards A. Trait susceptibility to worry modulates the effects of cognitive load on cognitive control: an ERP study[J]. Emotion, 2015, 15(5): 544-549. DOI: 10.1037/emo0000052.

[15] Bo K, Yin S, Liu Y, et al. Decoding neural representations of affective scenes in retinotopic visual cortex[J]. Cereb Cortex, 2021, 31(6): 3047-3063. DOI: 10.1093/cercor/bhaa411.

- [16] McLean MA, Van den Bergh B, Baart M, et al. The late positive potential (LPP): a neural marker of internalizing problems in early childhood[J]. *Int J Psychophysiol*, 2020, 155: 78-86. DOI: 10.1016/j.jpsycho.2020.06.005.
- [17] Botelho C, Pasion R, Prata C, et al. Neuronal underpinnings of the attentional bias toward threat in the anxiety spectrum: Meta-analytical data on P3 and LPP event-related potentials[J]. *Biol Psychol*, 2023, 176: 108475. DOI: 10.1016/j.biopsycho.2022.108475.
- [18] Cheng Y, Jackson TB, MacNamara A. Modulation of threat extinction by working memory load: an event-related potential study[J]. *Behav Res Ther*, 2022, 150: 104031. DOI: 10.1016/j.brat.2022.104031.
- [19] MacNamara A, Jackson TB, Fitzgerald JM, et al. Working memory load and negative picture processing: neural and behavioral associations with panic, social anxiety, and positive affect[J]. *Biol Psychiatry Cogn Neurosci Neuroimaging*, 2019, 4(2): 151-159. DOI: 10.1016/j.bpsc.2018.04.005.
- [20] Dickey L, Pegg S, Kujawa A. Neurophysiological responses to interpersonal emotional images: associations with symptoms of depression and social anxiety[J]. *Cogn Affect Behav Neurosci*, 2021, 21(6): 1306-1318. DOI: 10.3758/s13415-021-00925-6.
- [21] Bylsma LM, Tan PZ, Silk JS, et al. The late positive potential during affective picture processing: associations with daily life emotional functioning among adolescents with anxiety disorders[J]. *Int J Psychophysiol*, 2022, 182: 70-80. DOI: 10.1016/j.jpsycho.2022.09.009.
- [22] Kinney KL, Burkhouse KL, Chang F, et al. Neural mechanisms and predictors of SSRI and CBT treatment of anxiety: a randomized trial focused on emotion and cognitive processing[J]. *J Anxiety Disord*, 2021, 82: 102449. DOI: 10.1016/j.janxdis.2021.102449.
- [23] Stange JP, MacNamara A, Barnas O, et al. Neural markers of attention to aversive pictures predict response to cognitive behavioral therapy in anxiety and depression[J]. *Biol Psychol*, 2017, 123: 269-277. DOI: 10.1016/j.biopsycho.2016.10.009.
- [24] König N, Steber S, Seebacher J, et al. How therapeutic tapping can alter neural correlates of emotional prosody processing in anxiety[J]. *Brain Sci*, 2019, 9(8): 206. DOI: 10.3390/brainsci9080206.
- [25] Cao D, Li Y, Niznikiewicz MA. Neural characteristics of cognitive reappraisal success and failure: an ERP study[J]. *Brain Behav*, 2020, 10(4): e01584. DOI: 10.1002/brb3.1584.
- [26] Pan DN, Wang Y, Lei Z, et al. The altered early components and the decisive later process underlying attention bias modification in social anxiety: evidence from event-related potentials[J]. *Soc Cogn Affect Neurosci*, 2019, 14(12): 1307-1316. DOI: 10.1093/scan/nsz098.
- [27] Riesel A. The erring brain: error-related negativity as an endophenotype for OCD: a review and meta-analysis[J]. *Psychophysiology*, 2019, 56(4): e13348. DOI: 10.1111/psyp.13348.
- [28] Meyer A, Nelson B, Perlman G, et al. A neural biomarker, the error-related negativity, predicts the first onset of generalized anxiety disorder in a large sample of adolescent females[J]. *J Child Psychol Psychiatry*, 2018, 59(11): 1162-1170. DOI: 10.1111/jcpp.12922.
- [29] Judah MR, Grant DM, Frosio KE, et al. Electrocortical evidence of enhanced performance monitoring in social anxiety[J]. *Behav Ther*, 2016, 47(2): 274-285. DOI: 10.1016/j.beth.2015.12.002.
- [30] Riesel A, Klawohn J, Grützmann R, et al. Error-related brain activity as a transdiagnostic endophenotype for obsessive-compulsive disorder, anxiety and substance use disorder[J]. *Psychol Med*, 2019, 49(7): 1207-1217. DOI: 10.1017/S0033291719000199.
- [31] Kujawa A, Weinberg A, Bunford N, et al. Error-related brain activity in youth and young adults before and after treatment for generalized or social anxiety disorder[J]. *Prog Neuropsychopharmacol Biol Psychiatry*, 2016, 71: 162-168. DOI: 10.1016/j.pnpbp.2016.07.010.
- [32] Ladouceur CD, Tan PZ, Sharma V, et al. Error-related brain activity in pediatric anxiety disorders remains elevated following individual therapy: a randomized clinical trial[J]. *J Child Psychol Psychiatry*, 2018, 59(11): 1152-1161. DOI: 10.1111/jcpp.12900.
- [33] Meyer A. On the relationship between the error-related negativity and anxiety in children and adolescents: from a neural marker to a novel target for intervention[J]. *Psychophysiology*, 2022, 59(6): e14050. DOI: 10.1111/psyp.14050.
- [34] Abi-Dargham A, Moeller SJ, Ali F, et al. Candidate biomarkers in psychiatric disorders: state of the field[J]. *World Psychiatry*, 2023, 22(2): 236-262. DOI: 10.1002/wps.21078.
- [35] White EJ, Grant DM, Taylor DL, et al. Examination of evaluative threat in worry: insights from the error-related negativity (ERN) [J]. *Psychiatry Res Neuroimaging*, 2018, 282: 40-46. DOI: 10.1016/j.pscychres.2018.10.006.
- [36] Chase HW, Swainson R, Durham L, et al. Feedback-related negativity codes prediction error but not behavioral adjustment during probabilistic reversal learning[J]. *J Cogn Neurosci*, 2011, 23(4): 936-946. DOI: 10.1162/jocn.2010.21456.
- [37] Xia L, Xu P, Yang Z, et al. Impaired probabilistic reversal learning in anxiety: evidence from behavioral and ERP findings[J]. *Neuroimage Clin*, 2021, 31: 102751. DOI: 10.1016/j.nicl.2021.102751.
- [38] Voegler R, Peterburs J, Bellebaum C, et al. Modulation of feedback processing by social context in social anxiety disorder (SAD)-an event-related potentials (ERPs) study[J]. *Sci Rep*, 2019, 9(1): 4795. DOI: 10.1038/s41598-019-41268-0.
- [39] Cao J, Gu R, Bi X, et al. Unexpected acceptance? Patients with social anxiety disorder manifest their social expectancy in erps during social feedback processing[J]. *Front Psychol*, 2015, 6: 1745. DOI: 10.3389/fpsyg.2015.01745.
- [40] Norcia AM, Appelbaum LG, Ales JM, et al. The steady-state visual evoked potential in vision research: a review[J]. *J Vis*, 2015, 15(6): 4. DOI: 10.1167/15.6.4
- [41] McTeague LM, Laplante MC, Bulls HW, et al. Face perception in social anxiety: visuocortical dynamics reveal propensities for hypervigilance or avoidance[J]. *Biol Psychiatry*, 2018, 83(7): 618-628. DOI: 10.1016/j.biopsych.2017.10.004.
- [42] Zheng J, Cao F, Chen Y, et al. Time course of attentional bias in social anxiety: evidence from visuocortical dynamics[J]. *Int J Psychophysiol*, 2023, 184: 110-117. DOI: 10.1016/j.jpsycho.2023.01.002.

- [43] Stegmann Y, Reicherts P, Andreatta M, et al. The effect of trait anxiety on attentional mechanisms in combined context and cue conditioning and extinction learning[J]. *Sci Rep*, 2019, 9(1): 8855. DOI: 10.1038/s41598-019-45239-3.
- [44] Stegmann Y, Andreatta M, Pauli P, et al. Investigating sustained attention in contextual threat using steady-state VEPs evoked by flickering video stimuli[J]. *Psychophysiology*, 2023, 60(5): e14229. DOI: 10.1111/psyp.14229.
- [45] 朱斌, 孟子坤, 胡萍萍, 等. 正常听力儿童及青年失匹配负波研究[J]. *听力学及言语疾病杂志*, 2021, 29(1): 25-28. DOI: 10.3969/j.issn.1006-7299.2021.01.006.
Zhu B, Meng ZK, Hu PP, et al. Mismatch negativity in normal children and youth[J]. *Journal of Audiology and Speech Pathology*, 2021, 29(1): 25-28.
- [46] Chang Y, Xu J, Pang X, et al. Mismatch negativity indices of enhanced preattentive automatic processing in panic disorder as measured by a multi-feature paradigm[J]. *Biol Psychol*, 2015, 105: 77-82. DOI: 10.1016/j.biopsycho.2015.01.006.
- [47] Fucci E, Abdoun O, Lutz A. Auditory perceptual learning is not affected by anticipatory anxiety in the healthy population except for highly anxious individuals: EEG evidence[J]. *Clin Neurophysiol*, 2019, 130(7): 1135-1143. DOI: 10.1016/j.clinph.2019.04.010.
- [48] Ioakeimidis V, Lennuyeux-Comnene L, Khachatoorian N, et al. Trait and state anxiety effects on mismatch negativity and sensory gating event-related potentials[J]. *Brain Sci*, 2023, 13(10): 1421. DOI: 10.3390/brainsci13101421.
- [49] Zheng Y, Li R, Guo H, et al. Heightened sensitivity to panic-related sounds with reduced sensitivity to neutral sounds in preattentive processing among panic patients[J]. *J Affect Disord*, 2019, 250: 204-209. DOI: 10.1016/j.jad.2019.03.019.
- [50] Putman P, Verkuil B, Arias-Garcia E, et al. EEG theta/beta ratio as a potential biomarker for attentional control and resilience against deleterious effects of stress on attention[J]. *Cogn Affect Behav Neurosci*, 2014, 14(2): 782-791. DOI: 10.3758/s13415-013-0238-7.
- [51] Wei H, Chang L, Huang Q, et al. Relation between spontaneous electroencephalographic theta/beta power ratio and test anxiety[J]. *Neurosci Lett*, 2020, 737: 135323. DOI: 10.1016/j.neulet.2020.135323.
- [52] van der Vinne N, Vollebregt MA, van Putten M, et al. Frontal alpha asymmetry as a diagnostic marker in depression: fact or fiction? A meta-analysis[J]. *Neuroimage Clin*, 2017, 16: 79-87. DOI: 10.1016/j.nicl.2017.07.006.
- [53] Demerdzieva A, Pop-Jordanova N. Relation between frontal alpha asymmetry and anxiety in young patients with generalized anxiety disorder[J]. *Pril (Makedon Akad Nauk Umet Odd Med Nauki)*, 2015, 36(2): 157-177. DOI: 10.1515/prilozi-2015-0064.
- [54] Thoma L, Koller-Schlaud K, Gaudlitz K, et al. Frontolateral alpha power asymmetry in panic disorder[J]. *Int J Psychophysiol*, 2021, 167: 69-76. DOI: 10.1016/j.ijpsycho.2021.06.015.
- [55] Moscovitch DA, Santesso DL, Miskovic V, et al. Frontal EEG asymmetry and symptom response to cognitive behavioral therapy in patients with social anxiety disorder[J]. *Biol Psychol*, 2011, 87(3): 379-385. DOI: 10.1016/j.biopsycho.2011.04.009.
- [56] Harrewijn A, van der Molen MJ, Westenberg PM. Putative EEG measures of social anxiety: comparing frontal alpha asymmetry and delta-beta cross-frequency correlation[J]. *Cogn Affect Behav Neurosci*, 2016, 16(6): 1086-1098. DOI: 10.3758/s13415-016-0455-y.
- [57] Härpfer K, Spychalski D, Kathmann N, et al. Diverging patterns of EEG alpha asymmetry in anxious apprehension and anxious arousal[J]. *Biol Psychol*, 2021, 162: 108111. DOI: 10.1016/j.biopsycho.2021.108111.
- [58] Poole KL, Schmidt LA. Frontal brain delta-beta correlation, salivary cortisol, and social anxiety in children[J]. *J Child Psychol Psychiatry*, 2019, 60(6): 646-654. DOI: 10.1111/jcpp.13016.
- [59] Harrewijn A, van der Molen M, van Vliet IM, et al. Delta-beta correlation as a candidate endophenotype of social anxiety: a two-generation family study[J]. *J Affect Disord*, 2018, 227: 398-405. DOI: 10.1016/j.jad.2017.11.019.
- [60] Al-Ezzi A, Yahya N, Kamel N, et al. Severity assessment of social anxiety disorder using deep learning models on brain effective connectivity[J]. *IEEE Access*, 2021. DOI: 10.1109/ACCESS.2021.3089358.
- [61] Massullo C, Carbone GA, Farina B, et al. Dysregulated brain salience within a triple network model in high trait anxiety individuals: a pilot EEG functional connectivity study[J]. *Int J Psychophysiol*, 2020, 157: 61-69. DOI: 10.1016/j.ijpsycho.2020.09.002.
- [62] Qi X, Fang J, Sun Y, et al. Altered functional brain network structure between patients with high and low generalized anxiety disorder[J]. *Diagnostics (Basel)*, 2023, 13(7): 1292. DOI: 10.3390/diagnostics13071292.
- [63] Hamilton JP, Farmer M, Fogelman P, et al. Depressive rumination, the default-mode network, and the dark matter of clinical neuroscience[J]. *Biol Psychiatry*, 2015, 78(4): 224-230. DOI: 10.1016/j.biopsych.2015.02.020.
- [64] Xing M, Tadayonnejad R, MacNamara A, et al. Resting-state theta band connectivity and graph analysis in generalized social anxiety disorder[J]. *Neuroimage Clin*, 2017, 13: 24-32. DOI: 10.1016/j.nicl.2016.11.009.

(收稿日期: 2023-11-02)

(本文编辑: 郑圣洁)