

癫痫发作与非癫痫性发作的鉴别诊断研究进展

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【摘要】 癫痫发作是大脑神经元过度同步化异常放电引起的阵发性神经功能障碍,发作时伴脑电图痫样放电。非癫痫性发作是多种原因引起的,与癫痫发作有类似临床表现的一组疾病,不伴与发作同步的发作期脑电图痫样放电,与癫痫发作鉴别诊断存在一定困难。视频脑电图已广泛应用于神经系统疾病的诊断与治疗,对癫痫发作与非癫痫性发作的鉴别诊断具有重要意义。本文综述症状学特征和脑电图特征对癫痫发作与非癫痫性发作的鉴别诊断意义,以及与癫痫发作相鉴别的常见非癫痫性发作,为癫痫的精准诊断与治疗提供理论依据。

【关键词】 癫痫; 诊断,鉴别; 脑电描记术; 综述

Progress on distinguishing in epileptic and non-epileptic seizure

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【Abstract】 Epileptic seizure is a paroxysmal brain dysfunction caused by the abnormal discharge of excessive synchronization of brain neurons, accompanied by epileptiform discharge of EEG. Non-epileptic seizure (NES) is a group of diseases caused by various reasons. Although they are not accompanied by epileptiform discharges of EEG, they have similar clinical manifestations to seizures, rendering the differentiation from seizures difficult. Video electroencephalography (VEEG) technology, which has been widely used in the diagnosis and treatment of nervous system diseases, is key to the differential diagnosis of epileptic seizures. This article reviews the role of symptomatic and EEG features in the differential diagnosis of epileptic seizure and NES, as well as common NES that can be differentiated from epileptic seizure, so as to provide theoretical basis for accurate diagnosis and treatment of epilepsy.

【Key words】 Epilepsy; Diagnosis, differential; Electroencephalography; Review

Conflicts of interest: none declared

癫痫发作(ES)系大脑神经元过度同步化异常放电引起的阵发性神经功能障碍,具有一过性、反复性、刻板性特点,伴脑电图痫样放电。癫痫发作的临床表现具有异质性,取决于受累脑区,包括肌强直、肌阵挛等运动症状以及感觉障碍、自主神经功能障碍、认知功能障碍、情绪障碍等非运动症状,可伴意识障碍,发作后可出现癫痫后状态(PIS),即癫痫发作停止至恢复为发病前水平的异常状态^[1]。非癫痫性发作(NES)指多种原因引起的,与癫痫发作有类似临床表现的一组疾病,如偏头痛、屏气发作等^[2],包括心因性非癫痫性发作(PNES)和器质性

非癫痫性发作,不伴与发作同步的发作期脑电图痫样放电,无癫痫后状态。由于二者临床表现相似,鉴别诊断具有一定困难,有20%~30%经癫痫中心诊断的癫痫为误诊^[3]。本文拟综述症状学特征和脑电图特征鉴别诊断癫痫发作与非癫痫性发作的临床价值,以及与癫痫发作相鉴别的常见非癫痫性发作,为癫痫的精准诊断与治疗提供理论依据。

一、症状学特征的鉴别诊断价值

癫痫发作与非癫痫性发作均属于发作性疾病,临床表现相似,主要包括以下鉴别要点。(1)刻板行为:刻板行为是一类反复刻板的动作、言语或姿势,包括肌强直和肌阵挛等简单动作以及游走、骑车、摸索、咀嚼、痴笑等复杂动作。既往认为刻板行为是癫痫发作的主要特征,近年有刻板行为见于心因性非癫痫性发作的报道,但其导致的刻板行为可通

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过主动或者被动转移注意力终止,不伴意识障碍,多在白天反复出现^[4],可资鉴别。此外,成年期发病的非癫痫性发作刻板行为多继发于皮质-纹状体-丘脑-皮质通路功能障碍或额叶-纹状体通路抑制作用缺失^[5]。(2)发作时睁闭眼:Azar等^[6]对24例心因性非癫痫性发作和23例癫痫发作患者对比分析,前者发作时睁眼发生率显著低于后者(13%对100%, $P < 0.0001$)。发作时睁眼是癫痫发作的强效预测因素,发作时闭眼则是非癫痫性发作的强效预测因素,其预测非癫痫性发作的灵敏度为73.7%、特异度76.9%^[7]。(3)并发症:癫痫发作和非癫痫性发作均有较高的抑郁、焦虑共病率,以及伴随人格改变^[8]。Walsh等^[9]对13项有关癫痫和心因性非癫痫性发作患者抑郁发生率的临床研究进行Meta分析,均采用9条目患者健康问卷(PHQ-9)、Beck抑郁量表(BDI)、医院焦虑抑郁量表(HADS)、抑郁-焦虑-压力量表(DASS)、神经系统疾病伴抑郁量表-供癫痫患者使用(NDDI-E)评价抑郁症状,结果显示,非癫痫性发作患者自评为抑郁的概率(Cohen's $d = 0.51$, 95%CI:0.400~0.620; $P < 0.001$)和睡眠障碍等躯体症状发生率(Cohen's $d = 0.48 \sim 0.88$, $P < 0.01 \sim 0.05$)均高于癫痫患者。Abe等^[10]研究发现心因性非癫痫性发作患者的7条目广泛性焦虑量表(GAD-7)、PHQ-9、BDI-II评分均高于癫痫发作患者(均 $P < 0.05$)。(4)大小便失禁、发作中受伤和舌咬伤:既往认为大小便失禁、发作中受伤和舌咬伤是癫痫发作的特征性表现,但晚近研究显示,约66%的非癫痫性发作患者同样出现上述症状^[4],因此目前无法根据发作期大小便失禁、发作中受伤和舌咬伤情况鉴别诊断癫痫发作与非癫痫性发作。

二、脑电图特征的鉴别诊断价值

脑电图在癫痫诊断与鉴别诊断中发挥重要作用,视频脑电图(VEEG)是鉴别诊断癫痫发作与非癫痫性发作的“金标准”^[11-14]。脑电图碎片化 α 活动、门状棘波、入睡超同步化和过度通气诱发的慢波等良性变异易错误判读为痫样放电^[15],1/3误诊为癫痫的患者系脑电图错误判读为痫样放电所致^[16-17]。过度强调位相倒置亦是错误判读脑电图的重要原因,双极导联描记时,描记同一电极(导入和导出)的两条记录线同步出现波形、波幅相反的现象称为位相倒置,是双极导联定位局灶性痫样放电部位的主要方法。既往认为,位相倒置提示脑电图异常,但实际仅表明倒置处电压最大,需进一步根

据脑电图波形以及各导联异常波形之间关系明确是否为痫样放电。以阵挛为主要表现的非癫痫性发作,发作期脑电图可见大量肌电伪迹和运动伪迹,发作后即刻恢复正常,而癫痫患者的阵挛发作则出现发作后慢波或脑电抑制。以摇头等重复运动为主要表现的非癫痫性发作可诱发节律性波形异常,易错误判读为痫样放电^[15]。以晕厥为主要表现的血管迷走性晕厥患者发作时表现为短暂性意识丧失,平卧数秒或数十秒即可恢复意识,但因其刻板性、可重复性特点,若无同步脑电图监测极易误诊为癫痫发作^[15]。颞叶新皮质癫痫患者发作时可出现幻听,内侧颞叶癫痫(mTLE)患者则可伴随恐惧感,二者均可继发于有精神症状的复杂部分性发作,并出现精神行为异常,易误诊为心因性非癫痫性发作甚至精神疾病。

三、与癫痫发作相鉴别的常见非癫痫性发作

1. 心因性非癫痫性发作 心因性非癫痫性发作是一种临床症状与癫痫相似但不伴脑电图痫样放电的发作性疾病,常误诊为癫痫。心因性非癫痫性发作通常由心理障碍所致,75%~80%为女性,各年龄段均可发病,平均发病年龄(30.5 ± 13.7)岁^[4],其发作有以下特征^[4]:(1)回忆创伤史而诱发。(2)假睡。(3)非持续性、不规则或非同步性向对侧摆头、腕部甩动、颈部后仰、口吃、横扫动作。(4)发作时双侧肢体抽搐,但无意识障碍。(5)发作持续时间超过5分钟,鉴别癫痫发作与非癫痫性发作的最佳发作持续时间为123.5秒,灵敏度65%、特异度93%^[13]。(6)发作时闭眼。(7)主要为舌前部咬伤,而癫痫发作则多表现为单侧舌咬伤。(8)发作后通常呈安静且不规则的浅呼吸,而癫痫发作后为打鼾样呼吸。(9)发作后恢复较迅速,而癫痫发作通常有数分钟至数十分钟的癫痫后状态,这一期间患者可能存在意识模糊。(10)抗癫痫发作药物(ASM)治疗无效。(11)发作期脑电图正常^[14]。癫痫发作与心因性非癫痫性发作可共病,Kutlubaev等^[18]检索美国国立医学图书馆国际性综合生物医学信息书目数据库(MEDLINE)、荷兰医学文摘(EMBASE)、心理学文摘数据库(PsycINFO)、护理学数据库(CINAHL)和补充医学文献数据库(AMED),纳入2016年12月至2018年10月共117项临床研究计17478例癫痫发作与心因性非癫痫性发作共病患者,发现心因性非癫痫性发作患者的癫痫发作平均频率为22%(95%CI:0.200~0.250),而癫痫患者的心因性非癫

痫性发作平均频率为 12% (95%CI: 0.100 ~ 0.140), 与既往文献报道相近 (10% ~ 36%)^[18-19]。此外, 癫痫发作治疗过程中也可出现心因性非癫痫性发作, Asadi-Pooya 等^[20]回顾 697 例接受手术治疗的难治性癫痫患者, 27 例 (3.87%) 术后经视频脑电图证实存在心因性非癫痫性发作, 提示对于癫痫手术治疗后仍频繁发作的患者, 应考虑心因性非癫痫性发作的可能, 必要时行视频脑电图予以鉴别。

2. 晕厥 晕厥系脑低灌注导致的突发性、短暂性意识丧失, 临床表现具有发作性、重复性特点, 应注意与伴意识丧失的癫痫发作相鉴别。晕厥是久站、强烈情绪、咳嗽、排尿、排便等因素刺激后诱发自主神经功能障碍所致^[21], 而癫痫发作较少有明确诱因。晕厥发作前常有黑蒙、语言障碍, 伴或不伴头晕和听力改变; 而癫痫发作仅视觉中枢皮质受累方出现黑蒙, 极少出现语言障碍。晕厥患者表现为不规则双侧肌阵挛, 包括屈肘和旋腕, 持续时间少于 30 秒, 发作频率较低; 而癫痫发作中阵挛发作持续时间较长, 发作频率较高, 可进展为癫痫持续状态 (SE)^[4]。脑电图和心电图是鉴别晕厥与癫痫发作的重要方法^[22]。晕厥患者心电图异常与心脏抑制反射有关, 主要取决于窦房结和房室受抑制程度, 最常见的是窦性心动过缓进展为窦性停搏, 随后出现进行性窦性心律加速。直立倾斜试验 (HUTT) 是诊断非癫痫性发作的重要方法, 患者于安静状态下平卧 10 分钟, 在心电监测和静脉通道开放的情况下, 将直立倾斜床倾斜角度调整至 60° ~ 80°, 共监测 45 分钟, 如果出现晕厥或严重晕厥前表现为恶心、视物模糊、站立不稳、声音刺激反应减慢等, 同时伴低血压 (收缩压 < 80 mm Hg) 或者心动过缓 (< 40 次/min), 则为直立倾斜试验阳性, 神经源性晕厥患者直立倾斜试验阳性率达 57.5%^[23]。Ungar 等^[24]纳入 107 例既往有 2 次以上非惊厥性短暂性意识丧失伴或不伴抽搐或自主运动的患者, 63 例 (58.88%) 诊断为可能的 (possible) 癫痫, 44 例 (41.12%) 为难治性癫痫, 进一步采用欧洲心脏病协会 (ESC) 晕厥指南对患者进行评估, 63 例诊断为可能的癫痫患者中 45 例最终诊断为晕厥。Josephson 等^[25]对转诊至癫痫门诊的 1506 例患者进行回顾分析, 有 194 例 (12.88%) 最终修正诊断为心源性晕厥。

3. 偏头痛 枕叶癫痫和偏头痛的先兆症状均可表现为视觉症状, 偏头痛的最常见先兆症状主要包括强光闪光、光幻视、视物模糊、视野内出现锯齿形

线或暗点等^[26-27], 多数有先兆偏头痛 (MA) 患者可同时出现多种视觉症状; 如果视觉症状具有刻板性、偏侧性和幻视水平漂移则倾向癫痫发作^[28]。癫痫发作与偏头痛最显著的区别是视觉症状持续时间, 癫痫通常为数秒至数分钟, 偏头痛则为 5 ~ 60 分钟 (平均 30 分钟)^[26-28]。约 76% 有先兆偏头痛患者视觉先兆在病程中逐渐进展, 而癫痫发作的视觉先兆通常突然出现^[29]。有先兆偏头痛有时可诱发癫痫发作^[30-33], 而发作持续时间较长的枕叶癫痫或枕叶癫痫持续状态亦可出现发作后头痛。枕叶癫痫患者脑电图异常, 发作间期可见枕区尖波, 闭眼可诱发, 发作期亦可见枕区尖波, 伴不同程度向前头部扩散, 可资与偏头痛相鉴别^[34]。

4. 发作性睡病 1 型 发作性睡病是一种以白天过度嗜睡 (EDS) 为特征的原发性睡眠障碍, 根据是否发生猝倒分为 1 型和 2 型。发作性睡病 1 型常因白天过度嗜睡导致注意力和反应能力缺乏, 易被误诊为失神癫痫, 而猝倒则易被误诊为多种癫痫发作类型。MacLeod 等^[35]报告 5 例发作性睡病患者, 2 例最初误诊为失神癫痫、2 例为局灶性癫痫、1 例为全面性癫痫, 其中 1 例误诊患儿甚至服用抗癫痫药物数年, 修正诊断并予以恰当治疗后, 所有患儿症状均改善。频繁猝倒发作还可被误诊为非典型癫痫^[36-37]。发作性睡病的诊断主要依靠 *HLA-DQB1*0602* 等位基因阳性、脑脊液促食欲素水平降低, 以及脑电图显示睡眠期启动的快速眼动睡眠期 (REM)。

综上所述, 癫痫发作与非癫痫性发作在症状学上具有诸多相似之处, 仅凭临床表现难以准确鉴别诊断^[38]。脑电图已广泛应用于神经系统疾病的诊断与治疗, 视频脑电图是鉴别诊断二者的“金标准”。临床医师应高度警惕非癫痫性发作的可能, 详细询问患者病史, 进行全面体格检查, 及时完善视频脑电图等, 减少临床误诊, 为癫痫的精准诊断与治疗提供理论依据。

利益冲突 无

参 考 文 献

- [1] Pottkämper JCM, Hofmeijer J, van Waarde JA, van Putten MJAM. The postictal state: what do we know [J]? *Epilepsia*, 2020, 61:1045-1061.
- [2] China Association Against Epilepsy. Clinical guidelines for epilepsy (2015 revision) [M]. Beijing: People's Medical Publishing House, 2015: 23-24. [中国抗癫痫协会. 临床诊疗指南 癫痫病学分册 (2015 修订版) [M]. 北京: 人民卫生出版社,

- 2015: 23-24.]
- [3] Benbadis S. The differential diagnosis of epilepsy: a critical review [J]. *Epilepsy Behav*, 2009, 15:15-21.
- [4] Leibetseder A, Eisermann M, LaFrance WC Jr, Nobili L, von Oertzen TJ. How to distinguish seizures from non - epileptic manifestations[J]. *Epileptic Disord*, 2020, 22:716-738.
- [5] Shukla T, Pandey S. Stereotypies in adults: a systematic review[J]. *Neurol Neurochir Pol*, 2020, 54:294-304.
- [6] Azar NJ, Tayah TF, Wang L, Song Y, Abou-Khalil BW. Postictal breathing pattern distinguishes epileptic from nonepileptic convulsive seizures[J]. *Epilepsia*, 2008, 49:132-137.
- [7] Azar NJ, Pitiyanuvath N, Vittal NB, Wang L, Shi Y, Abou-Khalil BW. A structured questionnaire predicts if convulsions are epileptic or nonepileptic[J]. *Epilepsy Behav*, 2010, 19:462-466.
- [8] Baslet G, Seshadri A, Bermeo-Ovalle A, Willment K, Myers L. Psychogenic non - epileptic seizures: an updated primer [J]. *Psychosomatics*, 2016, 57:1-17.
- [9] Walsh S, Levita L, Reuber M. Comorbid depression and associated factors in PNES versus epilepsy: systematic review and meta-analysis[J]. *Seizure*, 2018, 60:44-56.
- [10] Abe C, Denney D, Doyle A, Cullum M, Adams J, Perven G, Dave H, Dieppa M, Hays R, Agostini M, Ding K. Comparison of psychiatric comorbidities and impact on quality of life in patients with epilepsy or psychogenic nonepileptic spells [J]. *Epilepsy Behav*, 2020, 102:106649.
- [11] Doss RC, LaFrance WC Jr. Psychogenic non-epileptic seizures[J]. *Epileptic Disord*, 2016, 18:337-343.
- [12] Benbadis SR, Tatum WO. Overinterpretation of EEGs and misdiagnosis of epilepsy[J]. *J Clin Neurophysiol*, 2003, 20:42-44.
- [13] Benbadis SR, Lin K. Errors in EEG interpretation and misdiagnosis of epilepsy: which EEG patterns are overread[J]? *Eur Neurol*, 2008, 59:267-271.
- [14] Kerr WT, Zhang X, Hill CE, Janio EA, Chau AM, Braesch CT, Le JM, Hori JM, Patel AB, Allas CH, Karimi AH, Dubey I, Sreenivasan SS, Gallardo NL, Baurjan J, Hwang ES, Davis EC, D'Ambrosio SR, Al Banna M, Cho AY, Dewar SR, Engel J Jr, Feusner JD, Stern JM. Epilepsy, dissociative seizures, and mixed: associations with time to video-EEG[J]. *Seizure*, 2021, 86:116-122.
- [15] Duncan R. Psychogenic nonepileptic seizures: EEG and investigation[J]. *Handb Clin Neurol*, 2016, 139:305-311.
- [16] Seneviratne U, Minato E, Paul E. How reliable is ictal duration to differentiate psychogenic nonepileptic seizures from epileptic seizures[J]? *Epilepsy Behav*, 2017, 66:127-131.
- [17] Benbadis SR. The EEG in nonepileptic seizures [J]. *J Clin Neurophysiol*, 2006, 23:340-352.
- [18] Kutlubaev MA, Xu Y, Hackett ML, Stone J. Dual diagnosis of epilepsy and psychogenic nonepileptic seizures: systematic review and meta - analysis of frequency, correlates, and outcomes [J]. *Epilepsy Behav*, 2018, 89:70-78.
- [19] Hingray C, Biberon J, El-Hage W, de Toffol B. Psychogenic non-epileptic seizures (PNES)[J]. *Rev Neurol (Paris)*, 2016, 172:263-269.
- [20] Asadi-Pooya AA, Asadollahi M, Tinker J, Nei M, Sperling MR. Post - epilepsy surgery psychogenic nonepileptic seizures [J]. *Epilepsia*, 2016, 57:1691-1696.
- [21] van Dijk JG, van Rossum IA, Thijs RD. Timing of circulatory and neurological events in syncope[J]. *Front Cardiovasc Med*, 2020, 7:36.
- [22] Runser LA, Gauer RL, Houser A. Syncope: evaluation and differential diagnosis[J]. *Am Fam Physician*, 2017, 95:303-312.
- [23] Anderson J, O'Callaghan P. Cardiac syncope[J]. *Epilepsia*, 2012, 53 Suppl 7:34-41.
- [24] Ungar A, Ceccofiglio A, Pescini F, Mussi C, Tava G, Rafanelli M, Langellotto A, Marchionni N, van Dijk JG, Galizia G, Bonaduce D, Abete P. Syncope and Epilepsy coexist in 'possible' and 'drug-resistant' epilepsy (Overlap between Epilepsy and Syncope Study: OESYS)[J]. *BMC Neurol*, 2017, 17:45.
- [25] Josephson CB, Rahey S, Sadler RM. Neurocardiogenic syncope: frequency and consequences of its misdiagnosis as epilepsy[J]. *Can J Neurol Sci*, 2007, 34:221-224.
- [26] Queiroz LP, Friedman DI, Rapoport AM, Purdy RA. Characteristics of migraine visual aura in Southern Brazil and Northern USA[J]. *Cephalalgia*, 2011, 31:1652-1658.
- [27] Viana M, Sances G, Linde M, Nappi G, Khaliq F, Goadsby PJ, Tassorelli C. Prolonged migraine aura: new insights from a prospective diary-aided study[J]. *J Headache Pain*, 2018, 19:77.
- [28] Hartl E, Gonzalez-Victores JA, Rémi J, Schankin CJ, Noachtar S. Visual auras in epilepsy and migraine: an analysis of clinical characteristics[J]. *Headache*, 2017, 57:908-916.
- [29] Viana M, Sprenger T, Andelova M, Goadsby PJ. The typical duration of migraine aura: a systematic review[J]. *Cephalalgia*, 2013, 33:483-490.
- [30] Thabit MN, Sadek AA, Motawe ES, Ali RAE, Mohamed MM. Non-epileptic paroxysmal events in paediatric patients: a single tertiary centre study in Egypt[J]. *Seizure*, 2021, 86:123-128.
- [31] Burrows SAB, Goloubeva O, Keaser ML, Haythornthwaite JA, Seminowicz DA. Differences in gray matter volume in episodic migraine patients with and without prior diagnosis or clinical care: a cross-sectional study[J]. *J Headache Pain*, 2021, 22:127.
- [32] Bandara SMR, Samita S, Kiridana AM, Herath HMMTB. Elevated nitric oxide and carbon monoxide concentration in nasal-paranasal sinus air as a diagnostic tool of migraine: a case-control study[J]. *BMC Neurol*, 2021, 21:407.
- [33] Bassetti CLA, Adamantidis A, Burdakov D, Han F, Gay S, Kallweit U, Khatami R, Koning F, Kornum BR, Lammers GJ, Liblauer RS, Luppi PH, Mayer G, Pollmächer T, Sakurai T, Sallusto F, Scammell TE, Tafti M, Dauvilliers Y. Narcolepsy: clinical spectrum, aetiopathophysiology, diagnosis and treatment[J]. *Nat Rev Neurol*, 2019, 15:519-539.
- [34] Nye BL, Thadani VM. Migraine and epilepsy: review of the literature[J]. *Headache*, 2015, 55:359-380.
- [35] Macleod S, Ferrie C, Zuberi SM. Symptoms of narcolepsy in children misinterpreted as epilepsy[J]. *Epileptic Disord*, 2005, 7: 13-17.
- [36] Singh AK, Saha A, Dutt N, Mohapatra PR, Janmeja AK, Bansal A. Narcolepsy presenting as refractory epilepsy[J]. *Indian J Pediatr*, 2009, 76:1073.
- [37] Zhou J, Zhang X, Dong Z. Case report of narcolepsy in a six-year-old child initially misdiagnosed as atypical epilepsy [J]. *Shanghai Arch Psychiatry*, 2014, 26:232-235.
- [38] Abe C, Denney D, Doyle A, Cullum M, Adams J, Perven G, Dave H, Dieppa M, Hays R, Agostini M, Ding K. Comparison of psychiatric comorbidities and impact on quality of life in patients with epilepsy or psychogenic nonepileptic spells [J]. *Epilepsy Behav*, 2020, 102:106649.

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