

· 癫痫及发作性疾病 ·

血管性眩晕和头晕临床诊断方法研究进展

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【摘要】 眩晕和头晕临床常见,尽管大部分患者预后良好,但血管性眩晕和头晕如不能及时识别,可能导致灾难性后果。目前血管性眩晕和头晕漏诊、诊断泛化和过度检查等问题仍十分显著,《血管性眩晕和头晕:诊断标准》的发布为临床诊断与治疗提供了依据,但实际工作中可能面对更复杂的情况。本文从临床特征、影像学和实验室检查三方面综述血管性眩晕和头晕临床诊断研究进展,以为血管性眩晕和头晕的临床诊断与治疗以及构建更准确的预测模型提供依据。

【关键词】 眩晕; 头晕; 卒中; 诊断; 综述

Advances on clinical identification of vascular vertigo and dizziness

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【Abstract】 Vertigo and dizziness are common clinical symptoms. Although most patients have a good prognosis, vascular vertigo and dizziness can have catastrophic consequences if not recognized promptly. At present, vascular dizziness and vertigo are still very significant problems in clinical missed diagnosis, diagnosis generalization and over examination. The publication of the international "Vascular vertigo and dizziness: diagnostic criteria" provides a basis for clinicians' diagnosis and treatment behavior. However, in practical clinical work, clinicians might have to deal with more complicated situations. This paper reviews the progress of clinical diagnosis of vascular vertigo and dizziness from the aspects of clinical features, imaging and laboratory examination, so as to provide a basis for the clinical diagnosis and treatment of vascular vertigo and dizziness as well as the construction of a more accurate prediction model.

【Key words】 Vertigo; Dizziness; Stroke; Diagnosis; Review

Conflicts of interest: none declared

眩晕和头晕是急诊常见症状,约占全部就诊患者的3.3%^[1]。德国神经病学调查数据显示,每年约1.8%的成人因眩晕或头晕首次就诊,其中50%为前庭性眩晕^[2]。约5%的急性眩晕或头晕最终病因诊断为脑血管病,即血管性眩晕和头晕^[3-4],其病因分为缺血性卒中和出血性卒中,后者发病率较低,头部CT检查敏感性较高,临床易于识别;前者发病率较高,且导致眩晕和头晕绝大部分为后循环卒中,症状出现的24小时内头部MRI平扫联合DWI的漏诊率高达20%^[5],故缺血性卒中致血管性眩晕和头晕临床易漏诊。尽管大部分血管性眩晕和头晕患者临床还表现为头面部麻木、肢体麻木无力、头痛、

呕吐、复视、短暂性意识丧失、视力障碍、行走不稳或跌倒等中枢神经系统症状与体征,但近年研究显示,脑干和(或)小脑卒中导致的血管性眩晕和头晕也可不伴有明显的肢体麻木、无力、共济失调等后循环卒中症状与体征,而仅表现为孤立性眩晕和头晕^[6-7]。约22%的后循环卒中患者发病前90天可见短暂性轻度神经系统症状,尤以孤立性眩晕最为常见^[8],此类患者极易误诊为前庭神经炎(VN)、前庭性偏头痛(VM)、良性复发性眩晕(BRV)和梅尼埃病(MD)等周围性眩晕或其他良性眩晕。血管性眩晕和头晕临床漏诊可错失静脉溶栓与血管内治疗的最佳时机,以孤立性眩晕为表现的短暂性血管性眩晕和头晕临床漏诊则可因未启动必要的脑卒中二级预防而导致脑卒中复发,造成不良预后;反之,如果诊断泛化,患者将面临非针对性治疗带来的潜在损害和心理负担,且过度诊断与治疗也造成大量社

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会医疗资源浪费,给国家医疗体系及患者和家庭带来不必要的经济负担。本文拟从临床特征、影像学和实验室检查三方面对《血管性眩晕和头晕:诊断标准》^[9]涉及的临床症状与体征、辅助检查进行综述,同时介绍疾病临床诊断与预测模型及其研究进展,以为血管性眩晕和头晕的临床诊断与治疗以及构建更准确的模型提供依据。

一、诊断标准

2022年,Bárány协会前庭疾病分类委员会在*J Vestib Res*发布《血管性眩晕和头晕:诊断标准》^[9]。先根据患者临床表现,以症状持续时间作为分界线分为急性持续性血管性眩晕和头晕(症状持续时间≥24小时)、短暂性血管性眩晕和头晕(症状持续时间<24小时)和急性进展性血管性眩晕和头晕(评估时症状持续时间虽<24小时,但症状未缓解,最终持续时间无法确定)。又根据诊断证据力度分为确定的(definite)和很可能的(probable)两个级别,若存在与症状、体征或其他检查相符的前庭系统(脑或内耳)缺血或出血相关影像学责任病灶,则诊断为确定的急性持续性血管性眩晕和头晕、确定的短暂性血管性眩晕和头晕或者确定的急性进展性血管性眩晕和头晕;若无明确的影像学证据,但有高度提示血管性眩晕和头晕的体征、血管危险因素、影像学检查辅助证据,则诊断为很可能的急性持续性血管性眩晕和头晕、很可能的短暂性血管性眩晕和头晕或者很可能的急性进展性血管性眩晕和头晕。依据该诊断标准,对于符合很可能的血管性眩晕和头晕的患者,可及时予以脑血管病相关治疗,并复查影像学以获取诊断证据;对于不符合很可能的血管性眩晕和头晕的患者,可避免过度医疗,节省社会医疗资源。此外,该诊断标准还首次规范“椎动脉压迫综合征(VACS)”的命名和诊断,椎动脉压迫综合征临床较少见,诊断标准的提出为临床诊断和相关研究的一致性提供依据,是提高临床诊断与治疗水平的第一步。

二、临床特征在血管性眩晕和头晕诊断中的价值

1. 床旁检查 (1) HINTS (Head Impulse test, direction changing gaze-evoked Nystagmus, and Test of pronounced Skew deviation)/HINTS plus(HINTS+)测验:HINTS测验包括三项眼动体征的评估,即头脉冲试验(Head Impulse)、凝视诱发眼震(Nystagmus)和眼球垂直反向偏斜(Test of Skew)。急性眩晕和

头晕患者头脉冲试验阴性并出现明显的凝视诱发眼震和眼球垂直反向偏斜,存在其中一项或以上即定义为HINTS阳性,其中,头脉冲试验阴性诊断中枢性眩晕的敏感性最高、凝视诱发眼震的特异性最高,而近年发现眼球垂直反向偏斜并非中枢性病变的特异性体征^[10],约1/4的急性单侧前庭疾病患者存在眼球垂直反向偏斜,垂直反向偏斜角度>3.3°提示中枢性病变,灵敏度为15%、特异度98.2%,经红外摄像头进行眼球追踪的眼球垂直反向偏斜的灵敏度为29.2%、特异度75.5%^[10],因此,临床实践中应关注眼球垂直反向偏斜的角度,辨证分析该体征对中枢性眩晕的鉴别诊断价值。HINTS+测验在HINTS测验基础上进一步结合听力检查、位置性眼震和共济失调等体征。目前认为,HINTS/HINTS+测验是鉴别诊断后循环卒中致血管性眩晕和头晕与其他良性眩晕最有效的方法。2009年的一项针对急性前庭综合征(AVS)患者(至少合并一项血管危险因素)的研究显示,HINTS测验作为床旁检查,诊断中枢性急性前庭综合征的灵敏度为100%、特异度96%,敏感性优于早期头部MRI平扫联合DWI检查^[11]。该项研究奠定了HINTS测验的诊断地位,此后有多项临床研究验证HINTS/HINTS+测验在血管性眩晕和头晕诊断与鉴别诊断中的价值^[12-16]。近年来,随着视频头脉冲试验(vHIT)和眼震视图(VNG)的临床应用,视频及软件支持下的HINTS测验(vHINTS)可有效提高诊断的准确性,其诊断血管性眩晕和头晕的总体准确率为94.2%,灵敏度为100%、特异度88.9%,其中灵敏度较临床医师的床旁诊断高1.09倍^[17]。人工智能(AI)可利用未处理的vHIT试验时间序列准确诊断前庭卒中,通过机器学习(ML)等人工智能算法对眼球和头部运动进行量化分析,可自动诊断急诊患者的急性头晕^[18]。但应注意的是,目前仅在表现为急性前庭综合征(发病时间>24小时,伴自发性眼震以及一种或多种血管危险因素)患者中验证HINTS测验对后循环卒中的诊断准确性,尚无法推广至其他类型血管性眩晕和头晕。例如,大部分短暂性血管性眩晕和头晕患者就诊时临床症状与体征已不同程度缓解,故HINTS/HINTS+测验等依赖眼部体征的检查方法不适用此类疾病的诊断。(2)严重躯干性共济失调:Carmona等^[19]将躯干性共济失调分为3级,1级,可在无支撑的情况下独立行走;2级,无法在无支撑的情况下独立行走,站立时出现严重不平衡,但可自

行站立;3级,无法自行站立。他们评估躯干性共济失调与脑卒中的关系,发现无一例急性单侧前庭疾患或前庭神经炎患者出现3级躯干性共济失调或姿势不稳,2~3级躯干性共济失调诊断小脑前下动脉(AICA)和小脑后下动脉(PICA)缺血性卒中的灵敏度为92.9%、特异度为61.1%,中枢性眼震+2~3级躯干性共济失调诊断缺血性卒中的灵敏度为100%、特异度为61.1%^[19]。Kattah等^[20]进一步发现,2~3级躯干性共济失调区分前庭神经炎与缺血性卒中的灵敏度为92%(95%CI:0.790~1.000)、特异度为67%(95%CI:0.470~0.860),屈曲不协调区分前庭神经炎与缺血性卒中的灵敏度为70%(95%CI:0.470~0.920)、特异度为88%(95%CI:0.690~1.000)。由于躯干性共济失调临床检查简单易行,遂于2022年将其纳入血管性眩晕和头晕的诊断标准^[9]。(3)眼动障碍:扫视和平滑追踪是临床最常用的眼动检查。脑干或小脑特定区域卒中表现为不同类型的眼动障碍^[17,21-22]。扫视异常主要指扫视速度和精确性异常,提示中枢性病变,其中,垂直扫视速度减慢提示中脑内侧纵束嘴侧核损害,水平扫视速度减慢提示脑桥旁中央网状结构损害;扫视过冲(saccadic overshoot)提示小脑(顶核)和延髓外侧部受损,扫视欠冲(saccadic undershoot)提示小脑蚓部受损^[23]。平滑追踪异常被认为是中枢性病变的体征,提示小脑绒球功能障碍,但是由于平滑追踪受药物、患者配合度等多种因素的影响,临床应谨慎判断。临床实践中,血管性眩晕和头晕患者急性期常伴明显眼震,可影响临床医师对眼动的评估,同时患者常因恶心呕吐等自主神经症状而无法配合精细的眼动检查,故限制眼动检查在急性眩晕中的定位价值,而是更多应用于慢性前庭综合征或不伴明显眼震的急性前庭综合征的定位诊断。孤立的单侧小脑绒球病变临床十分罕见,可表现为自发性眼震、对侧眼偏斜反应(OTR)、单侧平滑追踪异常和凝视诱发眼震^[24],同时,头脉冲试验呈双侧阳性^[25]。小脑扁桃体病变可在去固视抑制的情况下表现为同侧自发性眼震和平滑追踪异常、对侧主观视觉垂直(SVV)偏移、双侧凝视诱发眼震和中枢性位置性眼震^[26]。小脑后蚓部病变可引起中枢性位置性眼震和扫视过冲^[27]。

2. ABCD²评分 ABCD²评分是一种脑血管风险分层方法,主要用于预测短暂性脑缺血发作患者的脑卒中复发,其敏感性和特异性显著低于HINTS测

验^[12]。近年来,ABCD²评分广泛应用于血管性眩晕和头晕的临床诊断。有研究发现,ABCD²评分≥4分诊断血管性眩晕和头晕的灵敏度为55.7%~71.4%,特异度为60.6%~95.3%^[28-30],但样本量较小。Navi等^[31]对907例急诊就诊的眩晕或头晕患者进行回顾分析,仅37例(4.08%)病因为脑血管病;ABCD²评分≤3分者512例,其中仅5例(0.98%)最终诊断为脑血管病,ABCD²评分4~5分者369例,其中25例(6.78%)最终诊断为脑血管病,ABCD²评分6~7分者26例,其中7例(26.92%)最终诊断为脑血管病,因此认为ABCD²评分可用于识别急诊眩晕和头晕患者中脑血管病风险人群,但该项研究具有明显局限性:(1)为单中心回顾性研究,部分患者信息不全,仅35%进行神经影像学评估,很可能存在诊断医师的经验性偏倚。(2)所有患者均默认核心症状持续时间≥60分钟,基线ABCD²评分均为2分,故研究结论仅适用于临床症状持续时间≥60分钟的患者,并不适用于发病时间短的患者。(3)ABCD²评分不包括对血管性眩晕和头晕有预测价值的性别、症状主诉、高脂血症和冠心病等因素,而作为ABCD²评分项目的糖尿病并未显示出预测价值。因此,ABCD²评分虽为非眩晕专科医师快速评估血管性眩晕和头晕提供有力依据,但单纯应用ABCD²评分可能并非床旁检查的最优方案,联合应用ABCD²评分和HINTS测验筛查急诊非选择性眩晕患者的敏感性较高、特异性较低,而剔除诊断不确定患者(包括短暂性脑缺血发作)后临床特异性显著提高^[32]。

3. STANDING 四步检查法以及TriAGE+评分

(1)STANDING四步检查法:2017年,Vanni等^[33]提出STANDING四步检查法用于中枢性眩晕的诊断,包括自发性与位置性眼震的区分(the discrimination between Spontaneous and positional nystagmus)、眼震方向的评估(the evaluation of the Nystagmus Direction)、头脉冲试验(the head Impulse test)和姿势平衡的评估(the evaluation of equilibrium,图1),该方法的总体准确率为88%,灵敏度95%、特异度87%,阴性预测值99%,对非神经耳科医师排除脑卒中及其他中枢性眩晕有较高的准确性和可靠性。Nakatsuka和Molloy^[34]的Meta分析显示,接受过培训的急诊科医师采用STANDING四步检查法区分中枢性与非中枢性眩晕的灵敏度为0.96(95%CI:0.870~1.000),特异度0.88(95%CI:0.850~0.910),表明该检查法可辅助急诊科医师进

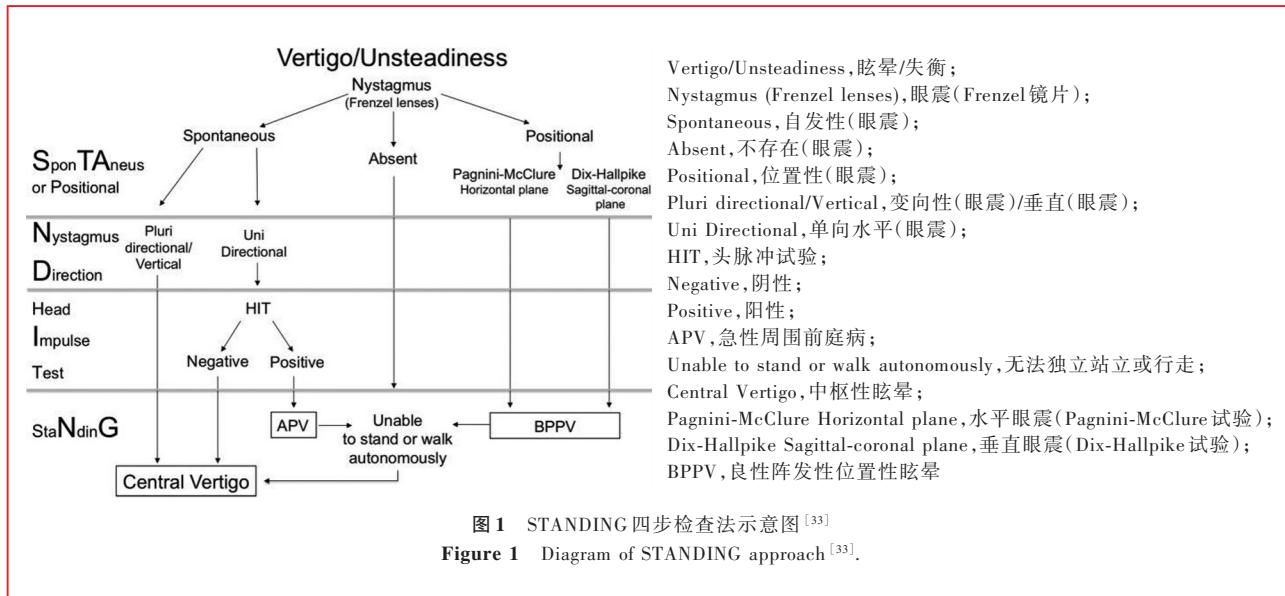


图1 STANDING四步检查法示意图^[33]
Figure 1 Diagram of STANDING approach^[33].

行血管性眩晕和头晕的快速诊断。(2)TriAGE+评分:Kuroda等^[35]的单中心观察性研究评估TriAGE+评分的诊断效能,该评分包括无促发因素(2分)、房颤(2分)、男性(1分)、血压≥140/90 mm Hg(2分)、脑干或小脑功能障碍(1分)、局灶性无力或语言障碍(4分)、无头晕/眩晕或迷路/前庭疾病病史(2分)、非旋转性头晕(3分)共8项内容,临界值定义为5分时灵敏度达96.6%,其预测脑卒中优于ABCD²评分。Bi和Cao^[36]通过前瞻性多中心队列研究研发出一款用于脑卒中风险预测的网络在线服务工具(<https://neuroby.shinyapps.io/dynnomapp/>),该模型包括性别、触发因素、孤立症状、恶心、短暂性头晕史、高血压、指鼻试验和串联步态试验共8项内容,具有较好的诊断效能且优于ABCD²评分,由于该模型部分内容与TriAGE+评分相似,因此提示TriAGE+评分涉及的危险因素对血管性眩晕和头晕可能具有较高的预测价值。

4. 社会人口学特征及血管危险因素 血管危险因素是急诊缺血性卒中危险因素分层的重要组成部分,对诊断血管性眩晕和头晕亦具有重要预测价值。Kim等^[37]系统性回顾分析77 993例因失衡/头晕/眩晕急诊入院患者的社会人口学和临床特征,发现以下因素与急性缺血性卒中呈正相关:以失衡为主要表现,非洲裔美国人,罹患高血压、糖尿病、高胆固醇血症、房颤,吸烟,颅外动脉粥样硬化;以下因素与急性缺血性卒中呈负相关关系:以眩晕为主要表现,女性,年龄>81岁,罹患贫血、冠状动脉疾患、哮喘,抑郁症和焦虑症。该项研究明确多种急

性缺血性卒中潜在的阳性和阴性预测因素,从而为血管性眩晕和头晕提供更准确的危险分层依据。Chen等^[38]进行眩晕病因分析,选择贡献较大的因素作为后循环缺血评分系统的危险因素并根据相对优势比(OR)制定分值,最终选择9项危险因素,包括高血压(1分)、糖尿病(1分)、缺血性卒中(1分)、旋转和摇晃(-1分)、语言障碍(5分)、耳鸣(-5分)、肢体和感觉缺陷(5分)、步态共济失调(1分)和肢体共济失调(5分),总评分≤0分为低风险(后循环缺血发生率<37.4%)、1~5分为中风险(37.4%~95.0%)、≥6分为高风险(>95.0%),选择0分作为区分后循环与非后循环缺血的截断值,灵敏度为94.1%、特异度41.4%,曲线下面积为0.82(95%CI:0.770~0.870, P=0.000),高于ABCD²评分的0.69 (P=0.000)和Essen脑卒中风险评分(ESRS)的0.67 (P=0.000),提示后循环缺血评分系统有助于临床医师迅速区分血管性眩晕和头晕与其他眩晕和头晕,且临床诊断效能优于ABCD²评分和ESRS评分。

二、影像学检查在血管性眩晕和头晕诊断中的价值

CT对急性缺血性卒中特别是后循环缺血性卒中的敏感性极低,故其诊断血管性眩晕和头晕的作用主要在于脑出血的病因诊断,而对缺血性卒中的病因诊断价值有限^[39]。急性后循环梗死症状出现24~48小时MRI平扫联合DWI的漏诊率为15%~20%^[40-41],特别是梗死灶较小(直径<10毫米)时漏诊率高达50%^[42]。由此可见,常规影像学检查在急诊血管性眩晕和头晕诊断中的价值有限,过度依赖

影像学检查是造成急性血管性眩晕和头晕漏诊的主要因素之一。灌注成像(PWI)有助于识别缺血性卒中,一项关于急性缺血性卒中的前瞻性研究显示,26例早期(发病24小时内)DWI阴性的急性缺血性卒中患者中12例PWI显示脑灌注降低^[43]。采用神经系统检查+HINTS+测验+平衡评估预测脑卒中的灵敏度为83%,联合应用PWI使灵敏度增至100%^[43]。Choi等^[30]发现,急性短暂性前庭综合征患者罹患脑卒中的概率为27%,其中12%PWI显示单侧小脑低灌注,DWI无梗死;9.3%存在局限性椎动脉狭窄或发育不良,表明PWI有助于诊断表现为急性短暂性前庭综合征的急性脑卒中。因此认为,CTA结合PWI理论上可以更好地辅助诊断血管性眩晕和头晕。此外,血管超声也是一种诊断血管性眩晕和头晕的高度特异性方法,但考虑其敏感性较低,不适用于急诊筛查^[44-45]。

三、实验室检查在血管性眩晕和头晕辅助诊断中的价值

业已证实,血清学标志物具有区分血管性眩晕和头晕与周围性眩晕的潜在价值。尽管早期研究并未显示出血清D-二聚体、C-反应蛋白(CRP)和纤维蛋白原(FIB)区分血管性眩晕和头晕与周围性眩晕的价值^[46],但是最近研究显示,血管性眩晕患者血清S-100蛋白B(S-100B)^[47]和神经元特异性烯醇化酶(NSE)^[48-49]水平显著高于周围性眩晕患者,进一步绘制受试者工作特征(ROC)曲线,NSE的曲线下面积为0.843(95%CI:0.753~0.932),S100-B为0.787(95%CI:0.687~0.886)。中性粒细胞/淋巴细胞比值(NLR)是急性缺血性卒中致眩晕与周围前庭疾病致眩晕的重要鉴别诊断要点^[50],NLR>2.8诊断急性缺血性卒中致眩晕的灵敏度为85.7%、特异度为78.0%,联合无水平眼震可将特异度增至81.0%,但应注意,NLR<2.8并不能排除缺血性卒中。

综上所述,对于不伴其他中枢神经系统症状与体征的血管性眩晕和头晕,临床诊断具有挑战性,临床特征、影像学检查和实验室检查均未发现可兼顾敏感性和特异性的诊断标志物,仅单一依靠上述标志物影响临床诊断与鉴别诊断。以证据链的思维模式整合临床症状与体征、社会人口学特征、影像学检查和实验室检查是提高临床诊断准确性的主要方法。未来采用多中心临床数据,构建血管性眩晕和头晕的临床预测模型,将有助于量化危险分层,提高血管性眩晕和头晕的快速诊断能力。

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· 小词典 ·

中英文对照名词词汇(五)

三肽基肽酶1 tripeptidyl peptidase 1(TPP1)	下丘脑错构瘤 hypothalamic hamartoma(HH)
色氨酸羟化酶1 tryptophan hydroxylase 1(TPH1)	纤维肌痛综合征 fibromyalgia syndrome(FS)
伤残调整寿命年 disability adjusted life year(DALY)	纤维母细胞生长因子受体 fibroblast growth factor receptor(FGFR)
射频热凝 radiofrequency thermocoagulation(RFTC)	小脑后下动脉 posterior inferior cerebellar artery(PICA)
神经节细胞胶质瘤 ganglioglioma(GG)	小脑深部核团 deep cerebellar nuclei(DCN)
神经元蜡样质脂褐质沉积病 neuronal ceroid lipofuscinoses(NCLs)	小脑前下动脉 anterior inferior cerebellar artery(AICA)
神经元特异性烯醇化酶 neuron-specific enolase(NSE)	Bárány协会分类委员会 Classification Committee of the Bárány Society(CCBS)
神经系统疾病伴抑郁量表-供癫痫患者使用 Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)	心因性非癫痫性发作 psychogenic non-epileptic seizure(PNES)
α1-肾上腺素受体 α1-adrenergic receptor(α1-AR)	心因性运动障碍 psychogenic movement disorders(PMD)
肾素-血管紧张素系统 renin-angiotensin system(RAS)	新发难治性癫痫持续状态 new-onset refractory status epilepticus(NORSE)
生酮饮食 ketogenic diet(KD)	选择性5-羟色胺和去甲肾上腺素再摄取抑制剂 selective serotonin and norepinephrine reuptake inhibitor (SSNRI)
视觉性眩晕 visual vertigo(VV)	选择性5-羟色胺再摄取抑制剂 selective serotonin reuptake inhibitor(SSRI)
视频脑电图 video electroencephalography(VEEG)	血管内皮生长因子-B vascular endothelial growth factor-B(VEGF-B)
视频头脉冲试验 Video Head Impulse Test(vHIT)	血管中心型胶质瘤 angiocentric glioma(AG)
受试者工作特征曲线 receiver operating characteristic curve(ROC曲线)	眼偏斜反应 ocular tilt reaction(OTR)
双相情感障碍 bipolar affective disorder(BAD)	眼震视图 videonystagmography(VNG)
瞬时钠电流 transient sodium current(INaT)	Toll样受体4 Toll-like receptor 4(TLR4)
丝氨酸/苏氨酸激酶 serine/threonine kinase(AKT)	医院焦虑抑郁量表 Hospital Anxiety and Depression Scale(HADS)
丝裂原激活蛋白激酶 mitogen-activated protein kinase(MAPK)	N-乙酰天冬氨酸 N-acetyl-aspartate(NAA)
羧基末端结构域 carboxy-terminal domain(CTD)	抑郁-焦虑-力量表 Depression-Anxiety-Stress Scale(DASS)
苔藓纤维 mossy fiber(MF)	Beck抑郁量表 Beck Depression Inventory(BDI)
特发性局灶性癫痫 idiopathic focal epilepsy(IFE)	音猬因子 sonic hedgehog(SHH)
特发性震颤 essential tremor(ET)	婴儿痉挛症 infantile spasm(IS) [West综合征 West syndrome(WS)]
9条目患者健康问卷 Patient Health Questionnaire-9(PHQ-9)	婴儿期严重肌阵挛癫痫 severe myoclonic epilepsy in infancy(SMEI) [Dravet综合征 Dravet's syndrome(DS)]
突触囊泡蛋白2A synaptic vesicle protein 2A(SV2A)	有先兆偏头痛 migraine with aura(MA)
网络荟萃分析 network Meta-analysis(NMA)	院前快速抗惊厥药物治疗试验 Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART)
无进展生存期 progression free survival(PFS)	
无特定病原体 specific pathogen free(SPF)	
系统性红斑狼疮 systemic lupus erythematosus(SLE)	
细胞毒性T细胞 cytotoxic T lymphocyte(CTL)	
细胞色素P450 cytochrome P450(CYP450)	
细胞色素P450 3A4酶 cytochrome P450 family 3 subfamily A member 4(CYP3A4)	
下丘脑-垂体-肾上腺 hypothalamic-pituitary-adrenal(HPA)	