·临床研究·

良性伴海马硬化的颞叶癫痫临床特点分析

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【摘要】 **目的** 观察伴海马硬化的颞叶癫痫(TLE-HS)对药物治疗的反应性,分析药物反应良好的良性伴海马硬化的颞叶癫痫的临床特点。**方法** 46例颞叶癫痫患者经MRI证实伴海马硬化,抗癫痫药物治疗至少随访2年,超过发作周期无癫痫发作,与51例对抗癫痫药物耐药的患者比较人口学资料、早期突发损伤因素、癫痫家族史、临床症状、发作间期脑电图痫样放电、海马硬化侧别、药物治疗方案等特征,并采用多因素前进法Logistic回归分析筛选药物治疗反应良好的影响因素。**结果** 良性TLE-HS组与对照组患者发病年龄($P=0.041$)、病程($P=0.001$)、热性惊厥史($P=0.019$)、癫痫发作频率($P=0.001$)和药物治疗方案($P=0.000$)差异有统计学意义,而性别、年龄、出生史异常、脑炎史、颅脑创伤史、癫痫家族史、癫痫持续状态、认知功能障碍、精神障碍,以及发作类型、先兆、是否存在发作间期和发作间期脑电图痫样放电、海马硬化侧别差异均无统计学意义($P>0.05$);其中,热性惊厥史是药物治疗反应良好的危险因素($OR=3.405$,95%CI:1.080~10.737;$P=0.037$),而低癫痫发作频率($OR=0.275$,95%CI:0.100~0.758;$P=0.013$)和单药治疗($OR=0.135$,95%CI:0.049~0.373;$P=0.000$)是药物治疗反应良好的保护因素。**结论** 良性伴海马硬化的颞叶癫痫多于青少年后期发病,发病初期癫痫发作频率低,较少伴热性惊厥史,单药治疗特别是卡马西平或奥卡西平疗效较好。

【关键词】 癫痫,颞叶; 海马; 硬化; 回归分析

Clinical analysis on benign temporal lobe epilepsy with hippocampal sclerosis

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【**Abstract**】 **Objective** To observe the drug response of patients with benign temporal lobe epilepsy with hippocampal sclerosis (TLE-HS), and to summarize the clinical characteristics of patients with good drug response. **Methods** A total of 46 benign TLE-HS patients who were treated by anti-epileptic drugs (AEDs) and followed-up for at least 2 years with seizure-free periods longer than 12 months were enrolled in benign TLE-HS group and 51 AEDs-resistant patients were enrolled in control group. Demographic data, early sudden damage factor, family history of epilepsy, clinical symptoms, interictal EEG abnormality, side of hippocamal sclerosis and drug strategy were noted and compared between 2 groups. Multivariate forward Logistic regression was used to analyze the influencing factors of good drug response to TLE-HS. **Results** Age of onset ($P=0.041$), duration ($P=0.001$), history of febrile seizure ($P=0.019$), initial seizure frequency ($P=0.001$) and drug strategy ($P=0.000$) were statistically different between 2 groups. Age, sex, perinatal injury, encephalitis, traumatic brain injury (TBI), family history of epilepsy, status epilepticus (SE), cognitive impairment, mental disturbance, seizure type, aura, interictal EEG abnormality and side of hippocamal sclerosis were not statistically different between 2 groups ($P>0.05$, for all). History of febrile seizure was risk factor for benign TLE-HS ($OR=3.405$, 95%CI: 1.080–10.737; $P=0.037$), while low initial seizure frequency ($OR=0.275$, 95% CI: 0.100–0.758; $P=0.013$) and monotherapy ($OR=0.135$, 95% CI: 0.049–0.373; $P=0.000$) were protective factors for good drug response. **Conclusions** Benign TLE-HS often occurs in late adolescence. In the early stage, seizure frequency is low and the occurrence of febrile

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seizure is rare. Monotherapy of carbamazepine or oxcarbazepine may achieve good therapeutic effect.

【Key words】 Epilepsy, temporal lobe; Hippocampus; Sclerosis; Regression analysis

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伴海马硬化的颞叶癫痫(TLE-HS)极易转变为药物难治性癫痫,2010年国际抗癫痫联盟(ILAE)将其归入适宜外科手术治疗的癫痫综合征之一。同时也有学者关注到,一些颞叶癫痫(TLE)患者呈现良性临床过程,对药物治疗反应良好,其中部分患者伴海马硬化(HS),提示可能有部分良性伴海马硬化的颞叶癫痫被忽视[1]。鉴于此,笔者拟对抗癫痫药物(AEDs)反应良好的良性伴海马硬化的颞叶癫痫的临床特点进行分析,以为临床鉴别诊断与治疗提供参考。

对象与方法

一、研究对象

顺序纳入2009年1月1日–2011年3月31日在广东三九脑科医院神经内科就诊的97例伴海马硬化的颞叶癫痫患者,分别进行病史采集、神经系统检查、视频脑电图和头部MRI检查。

1. 纳入标准 (1)颞叶癫痫诊断标准:根据国际抗癫痫联盟1989年提出的颞叶癫痫诊断性特征,即发作特征[单纯部分性发作特点为神经症状和(或)精神症状,以及某些特殊感觉如嗅觉、听觉(包括错觉)减退,以上腹部气向上涌为主;复杂部分性发作特点为动作突然中止,随后出现口-消化道自动症,持续时间>1 min]和头皮脑电图特征(无异常,背景活动轻度或显著不对称,颞区单侧和双侧同步或非同步性痫样放电,颞区以外脑区痫样放电)。(2)海马硬化的影像学诊断依据:冠状位FLAIR成像显示海马信号明显增高,海马萎缩[2];双侧海马信号改变或体积缩小,尤以单侧严重;双侧均明显受累诊断者为双侧海马硬化。(3)仅行抗癫痫药物治疗且随访时间≥24个月。

2. 排除标准 (1)于2009年前在广东三九脑科医院首诊并于2009年后复诊的伴海马硬化的颞叶癫痫患者。(2)非颞叶癫痫患者。(3)影像学显示海马硬化伴同侧颞叶灰白质分界不清,并且其他脑区存在癫痫相关结构异常患者。(4)随访时间<24个月患者。

二、研究方法

1. 视频脑电图检查 检测用Nicolet(V32)脑电图仪为美国Natus公司产品。所有患者入组后至少接受1次21导头皮电极24 h视频脑电图监测,分别记录单侧和双侧颞区痫样放电,以及其他脑电改变。检查结果经2位专业脑电图医师确认。

2. MRI检查 采用荷兰Philips公司生产的Intera 1.5T MRI扫描仪、8通道敏感头部线圈进行全头部和海马扫描。(1)横断面T_1WI:重复时间(TR)488 ms、回波时间(TE)15 ms,反转角(FA)69°,视野(FOV)230 mm×183 mm,矩阵256×512,体素前后距(AP)×左右距(RL)为1.50×1.52,层厚5.50 mm、层间距1 mm,扫描范围116 mm。(2)横断面T_2WI:重复时间3980 ms、回波时间110 ms,反转角90°,视野230 mm×183 mm,矩阵256×512,体素前后距×左右距为0.90×0.95,扫描层厚5.50 mm、层间距1 mm,扫描范围116 mm。(3)横断面T_2-FLAIR成像:重复时间为6000 ms、回波时间120 ms、反转时间(TI)2000 ms,视野230 mm×183 mm,矩阵256×512,体素前后距×左右距为1.20×1.49,层厚5.50 mm、层间距1 mm,扫描范围116 mm。(4)垂直于海马长轴的斜冠状位T_2-FLAIR成像:重复时间为8000 ms、回波时间125 ms、反转时间2450 ms,视野200 mm×160 mm,矩阵256×512,体素头足距(FH)×左右距为1.33×1.68,扫描层厚3 mm、层间距为零,扫描范围54 mm。成像结果由2位神经影像学专业医师分别判读以确认海马硬化改变。

3. 药物治疗方案分组 (1)良性伴海马硬化的颞叶癫痫组(良性TLE-HS组):共46例患者,均接受抗癫痫药物治疗,在观察期(24个月)内至少达到12个月无发作并持续至观察终点。药物治疗方案为患者入组后根据发作类型选择初始抗癫痫药物,以单药治疗开始,逐渐增至恰当的治疗剂量。观察3个发作周期仍无法控制发作者改用其他单药治疗或添加其他抗癫痫药物。良性TLE-HS组包括单药治疗有效和2种及以上药物联合治疗有效。(2)对照组:51例患者均为观察期内耐药性癫痫,即采用至

少2种药物联合治疗(每种药物剂量达有效治疗剂量)仍未达到3个发作周期无发作,包括观察期内符合手术指征进行癫痫外科手术患者。抗癫痫药物主要为卡马西平(得理多)、奥卡西平(曲莱)、拉莫三嗪(利必通)、托吡酯(妥泰)、丙戊酸镁(神泰)、丙戊酸钠(德巴金)、左乙拉西坦(开浦兰)。观察期内仅用单药治疗(一种或多种不同单药)者归入单药治疗组,采用2种或以上药物联合治疗者归入联合治疗组。

4.观察指标 观察两组患者性别、年龄、发病年龄、病程、早期突发损伤因素[如出生史异常、热性惊厥(FS)史、脑炎史、颅脑创伤(TBI)史],以及癫痫家族史、癫痫持续状态(SE)、认知功能障碍、精神障碍、发作类型(部分性发作或继发全面性发作)、发作频率(≥4或<4次/月)、是否存在先兆、病程中是否存在发作间期(病程中>12个月无发作)、发作间期脑电图异常放电的单双侧性、MRI显示海马硬化侧别、药物治疗方案(单药治疗或联合治疗),定期随访至2013年8月31日,随访时间≥24个月。

5.统计分析方法 采用SPSS 17.0统计软件进行数据计算与分析。呈正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,采用两独立样本的t检验;呈非正态分布的计量资料以中位数和四分位数间距[$M(P_{25}, P_{75})$]表示,采用秩和检验;计数资料以相对数构成比(%)或率(%)表示,采用χ^2检验。具有统计学意义的参数进一步行多因素前进法Logistic回归分析筛查药物反应良好的良性伴海马硬化的颞叶癫痫的影响因素。以$P \leq 0.05$差异具有有统计学意义。

结 果

一、良性伴海马硬化的颞叶癫痫临床特点

本研究共收集资料完整的经抗癫痫药物治疗后无发作患者46例(良性TLE-HS组),男性33例,女性13例;年龄7~54岁,平均(21.76±10.79)岁;发病年龄1~49岁,中位年龄15.50(8.75,20.25)岁;病程0~23年,中位病程2.50(0.83,8.00)年;随访时间24~53个月,中位时间40(33,48)个月;无发作时间12~48个月,平均(29.16±12.39)个月。选择同期就诊且对抗癫痫药物耐药的患者51例(对照组),男性33例,女性18例;年龄10~46岁,平均(20.80±8.46)岁;发病年龄1~44岁,中位年龄11(7,16)岁;病程1~22年,中位病程6.00(3.50,11.00)年;随访时间0~47个月,中位时间4(1,14)个月。两组患者人口学资料(性别、年龄、发病年龄、病程)、早期突发损伤因素(出生史、热性惊厥史、脑炎史、颅脑创伤史)和其他重要病史(癫痫家族史、癫痫持续状态、认知功能障碍、精神障碍)比较,仅发病年龄($P = 0.041$)、病程($P = 0.001$)和热性惊厥史($P = 0.019$)差异有统计学意义,其他各项差异均无统计学意义($P > 0.05$,表1)。

对良性TLE-HS组与对照组癫痫发作频率、发作类型、先兆、是否存在发作间期、发作间期脑电图痫样放电和海马硬化侧别等临床特征进行比较,仅癫痫发作频率组间差异有统计学意义($P = 0.001$),其他临床特征差异均无统计学意义($P > 0.05$,表2)。

二、良性伴海马硬化的颞叶癫痫抗癫痫药物治疗方案

1.药物选择 良性TLE-HS组46例患者中34例(73.91%)为单药治疗、12例(26.09%)为联合治疗,抗癫痫药物起效时间为0~43个月,平均(11.51±12.90)个月;对照组单药治疗14例(27.45%)、联合治疗37例(72.55%)。两组患者抗癫痫药物治疗方案差异有统计学意义($\chi^2 = 21.032$, $P = 0.000$)。由表3可见,良性TLE-HS组34例单药治疗患者中25例(73.53%)予钠离子通道阻断剂(卡马西平或奥卡西平)治疗、9例(26.47%)接受其他抗癫痫药物(拉莫三嗪、丙戊酸钠、托吡酯或苯妥英钠)治疗;12例联合治疗患者中6例以丙戊酸钠为主、6例以卡马西平或奥卡西平为主,同时辅助托吡酯(4例)、左乙拉西坦(2例)或氯硝西泮(2例)。

2.影响因素 将上述具有统计学意义的参数[发病年龄、病程、热性惊厥史、癫痫发作频率、药物治疗方案(单药治疗或联合治疗)]作为自变量,以药物治疗反应是否良好为因变量,进行多因素前进法Logistic回归分析。表4结果显示,热性惊厥史是药物治疗反应良好的危险因素($OR = 3.405$, 95%CI: 1.080~10.737; $P = 0.037$),而低癫痫发作频率($OR = 0.275$, 95%CI: 0.100~0.758; $P = 0.013$)和单药治疗($OR = 0.135$, 95%CI: 0.049~0.373; $P = 0.000$)是药物治疗反应良好的保护因素。

讨 论

根据一项四级癫痫中心的流行病学调查显示,在2200例癫痫患者中局灶性癫痫约占62.2%,而颞叶癫痫则占66%,占该项研究所纳入全部病例的

表1 良性TLE-HS组与对照组患者人口学资料和病史特征的比较

Table 1. Comparison of demograhpic data and medical history between benign TLE-HS group and control group

Item	Benign TLE-HS (N = 46)	Control (N = 51)	Statistic value	*P* value
Sex [case (%)]			1.086	0.397
Male	33 (71.74)	33 (64.71)		
Female	13 (28.26)	18 (35.29)		
Age ($\bar{x} \pm s$, year)	21.76 ± 10.79	20.80 ± 8.46	0.489	0.626
Age of onset [*M* (P_{25}, P_{75}), year]	15.50 (8.75, 20.25)	11.00 (7.00, 16.00)	-2.043	0.041
Duration [*M* (P_{25}, P_{75}), year]	2.50 (0.83, 8.00)	6.00 (3.50, 11.00)	-3.328	0.001
Perinatal injury [case (%)]	2 (4.35)	3 (5.88)	-0.340	0.734
FS [case (%)]	10 (21.74)	23 (45.10)	5.879	0.019
Encephalitis [case (%)]	5 (10.87)	8 (15.69)	0.999	0.382
TBI [case (%)]	4 (8.70)	7 (13.72)	0.165	0.772
Family history of epilepsy [case (%)]	3 (6.52)	4 (7.84)	-0.250	0.803
SE [case (%)]	2 (4.35)	1 (1.96)	-0.675	0.500
Cognitive impairment [case (%)]	9 (19.57)	11 (21.57)	0.059	1.000
Mental disturbance [case (%)]	4 (8.70)	5 (9.80)	0.192	0.737

t test for comparison of age, rank sum test for comparison of age of onset and duration, and χ^2 test for comparison of others. TLE-HS, temporal lobe epilepsy with hippocampal sclerosis, 伴海马硬化的颞叶癫痫; FS, febrile seizure, 热性惊厥; TBI, traumatic brain injury, 颅脑创伤; SE, status epilepticus, 癫痫持续状态。The same for Table 2

表2 良性TLE-HS组与对照组患者临床特征的比较[例(%)]

Table 2. Comparison of clinical characteristics between benign TLE-HS group and control group [case (%)]

Item	Benign TLE-HS (N = 46)	Control (N = 51)	χ^2 value	*P* value
Seizure frequency			11.111	0.001
≥ 4 per month	16 (34.78)	35 (68.63)		
< 4 per month	30 (65.22)	16 (31.37)		
Seizure type			0.819	0.400
Focal	14 (30.43)	20 (39.22)		
Focal + secondarily generalized	32 (69.57)	31 (60.78)		
Aura			2.342	0.156
Yes	19 (41.30)	29 (56.86)		
No	27 (58.70)	22 (43.14)		
Seizure free period			0.599	0.585
Yes	9 (19.57)	7 (13.73)		
No	37 (80.43)	44 (86.27)		
Interictal discharges			-0.441	0.659
One side of temporal lobe	29 (63.04)	34 (66.67)		
Both sides of temporal lobe	14 (30.43)	15 (29.41)		
Extra-temporal lobe	3 (6.52)	2 (3.92)		
Side of hippocampal sclerosis			1.403	0.496
Right	17 (36.96)	19 (37.25)		
Left	17 (36.96)	24 (47.06)		
Bilateral	12 (26.09)	8 (15.69)		

24%[3]；另一项对接受外科手术治疗的癫痫患者临床特点的分析表明，291例癫痫患者中73%为颞叶癫痫，且伴海马硬化为其常见病理学类型[3]。在2010年国际抗癫痫联盟新分类中，伴海马硬化的颞叶癫痫是具有诊断价值并适宜行外科治疗的癫痫类型[4]。可见该类局灶性癫痫为药物治疗预后不良类型。然而，随着影像学诊断技术的不断进步，发现正常人群和良性颞叶癫痫均存在海马硬化[2,5-6]，提示存在海马硬化的颞叶癫痫并非一定是药物难治性。故有学者将经药物治疗或未经药物治疗达到至少24个月无发作的颞叶癫痫定义为良性颞叶癫痫[1]。该类型以发病年龄较晚为重要临床特征，患者多于青春期至成年中期发病，Aguglia等[7]公布的平均发病年龄为(33.1 ± 19.8)岁；而伴海马硬化者发病年龄显著提前，平均15.7岁，明显早于无海马硬化者的29.5岁。本研究伴海马硬化的良性颞叶癫痫患者平均发病年龄16.76岁，与文献报道相近，但明显晚于耐药性患者。对于抗癫痫药物疗效评价而言，发病初期发作频率可能是除病因外最为重要的有效预测因素[8]。Hitiris等[9]研究显示，抗癫痫药物初始治疗前发作>10次者，进展至耐药性癫痫的可能性是早期治疗的2倍；而且发病初期发作频率较高即平均16次/月的伴海马硬化的颞叶癫痫患者比平均10次/月者发生耐药性的风险明显增加[10]。本研究结果也提示，发作<4次/月患者的疗效明显优于发作≥4次/月者，表明发病初期发作频率低是抗癫痫药物治疗反应良好的保护因素。

此外，热性惊厥史与良性伴海马硬化的颞叶癫痫的相关性值得探讨。据文献报道，约47.1%的良性伴海马硬化的颞叶癫痫患者有热性惊厥史，而仅6.5%的非良性伴海马硬化的颞叶癫痫患者有热性惊厥史[7]；本研究良性TLE-HS组热性惊厥史阳性者约占21.74%(10/46)、对照组占45.10%(23/51)。有热性惊厥史的患者，药物治疗效果较差，热性惊厥史可能预示海马硬化存在致痫性。此外，对有热性惊厥史的良性伴海马硬化的颞叶癫痫的分析显示，

表3 良性TLE-HS组患者抗癫痫药物治疗方案[例(%)]
Table 3. AEDs in benign TLE-HS group [case (%)]

Drug	No. of patients
Monotherapy	
CBZ (0.30–0.60 g/d)	17 (50.00)
OXC (0.53–0.90 g/d)	8 (23.53)
LTG (100–150 mg/d)	4 (11.76)
VPA (0.50–1.00 g/d)	3 (8.82)
TPM (100 mg/d)	1 (2.94)
PHT (0.10 g/d)	1 (2.94)
Total	34 (100.00)
Polytherapy	
VPA (0.50–1.00 g/d) + TPM (62.50 mg/d) / CBZ (0.20 mg/d) / LTG (150 mg/d) / CZP (4 mg/d)	6 (6/12)
CBZ (0.30–0.60 g/d) + TPM (50–100 mg/d) / PB (30 mg/d)	4 (4/12)
OXC (0.60 g/d) + LEV (50 mg/d) / CZP (3 mg/d)	2 (2/12)
Total	12 (12/12)

CBZ, carbamazepine, 卡马西平; OXC, oxcarbazepine, 奥卡西平; LTG, lamotrigine, 拉莫三嗪; VPA, valproic acid, 丙戊酸钠; TPM, topiramate, 托吡酯; PHT, phenytoin, 苯妥英钠; CZP, clonazepam, 氯硝西泮; PB, phenobarbital, 苯巴比妥; LEV, levetiracetam, 左乙拉西坦

表4 药物治疗反应良好相关影响因素的多因素前进法Logistic回归分析
Table 4. Factors influencing good drug response of benign TLE - HS by using multivariate forward Logistic regression analysis

Variable	*b*	*SE*	Wald χ^2	*P* value	*OR*	*OR* 95%CI
Age of onset	0.007	0.030	0.053	0.818	1.007	0.949– 1.068
Duration	0.080	0.043	3.423	0.064	1.083	0.995– 1.178
FS	1.225	0.586	4.371	0.037	3.405	1.080–10.737
Seizure frequency	-1.289	0.516	6.235	0.013	0.275	0.100– 0.758
Therapy	-2.002	0.519	14.900	0.000	0.135	0.049– 0.373
Constant	2.020	0.990	4.167	0.041		

FS, febrile seizure, 热性惊厥

热性惊厥史并非预测伴海马硬化的颞叶癫痫药物难治性的唯一因素,还应考虑其他遗传因素和环境因素的共同作用[1]。在良性颞叶癫痫发作期,内脏感觉先兆为常见症状,此与家族性常染色体显性颞叶癫痫之特点极其相似[11]。而在Crompton等[12]报告的51例家族性颞叶癫痫患者中,37例(72.55%)以精神症状为先兆,特别是似曾相识感;本研究中良性TLE-HS组有19例发作前出现先兆,6例即以精神症状为主,而对照组发作前出现先兆的概率并非明显高于良性TLE-HS组。对于先兆是否能够作为伴海马硬化的颞叶癫痫患者对抗癫痫药物治疗反应之预测因素,尚难确定。有研究显示,约94.11%的良性伴海马硬化的颞叶癫痫患者发作间期脑电图呈现痫样放电,其中>70%集中于单侧颞区[7];本研究良性TLE-HS组与对照组患者发作间期脑电图也有上述特点,提示发作间期脑电图不能作为伴海马硬化的颞叶癫痫呈良性或耐药性之预测指标。发病初期经抗癫痫药物单药治疗能够控制发作,是良性颞叶癫痫的重要临床特点,90%以上患者通过单药即可控制发作,一般以低剂量卡马西平或奥卡西平首选[7],丙戊酸钠也可备选[13]。根据Gomez-Ibañez等[14]的晚近报告,对未行手术治疗的47例伴海马硬化的颞叶癫痫患者进行长期抗癫痫药物疗效观察,7例长达7年无发作,其中6例选择卡马西平(2例)、奥卡西平(1例)、丙戊酸钠(1例)、拉莫三嗪(1例)或苯妥英钠(1例)单药治疗,1例予以丙戊酸钠和托吡酯联合治疗。值得注意的是,该项研究纳入的47例患者中39例为耐药性伴海马硬化的颞叶癫痫,其中18例有平均5年的无发作期[14],表明2年以上无发作并不意味着长期无发作。因此,对于良性颞叶癫痫患者即使晚期复发风险较小,长期随访仍至关重要[1];尤其发病年龄小、合并早期突发损伤因素的患者(如长时间复杂热性惊厥)复发风险更大,而发病年龄太晚且不伴早期脑损伤者则病情可长期缓解即无发作[15]。本研究良性TLE-HS组约有13.73%(7/51)患者在病程中出现发作间期,最长者达7年,因此我们将平均随访时间达40个月的患者判断为良性颞叶癫痫,由于随访时间较短,尚待进一步积累资料。

综上所述,在伴海马硬化的颞叶癫痫患者中确实存在相当一部分对抗癫痫药物反应良好的良性伴海马硬化的颞叶癫痫,早期识别良性病程之临床指标对制定治疗方案具有重要意义。良性伴海马硬化的颞叶癫痫多于青少年后期发病,病程短,发病初期癫痫发作频率低,且较少伴热性惊厥史,对单药治疗特别是卡马西平或奥卡西平反应良好。但海马硬化对良性颞叶癫痫致痫性所发挥的作用尚待深入研究,与此同时,遗传因素对良性伴海马硬化的颞叶癫痫的影响亦值得进一步探讨。

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Animal Models of Neurodevelopmental Disorders published

Animal Models of Neurodevelopmental Disorders (ISBN: 978-1-4939-2708-1, eBook ISBN: 978-1-4939-2709-8) was published by Humana Press in September 2015. The editor of this book is Jerome Yager, Division of Pediatric Neurology, University of Alberta.

Providing a spectrum of models that is reflective of the various species that can be utilized in experimentation on disorders across a broad range of developmental disabilities, this volume collects expert contributions involved in investigation of the causes, outcomes, treatment, and prevention. *Animal Models of Neurodevelopmental Disorders* explores models of perinatal hypoxia-ischemia/cerebral palsy and stroke, autism spectrum disorder, fetal alcohol syndrome, as well as mental retardation. Practical and authoritative, *Animal Models of Neurodevelopmental Disorders* serves to introduce and entice those interested in better understanding and treating these disorders to the vital animal model world of investigation.

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Cellular Therapy for Stroke and CNS Injuries published

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