

doi: 10.3978/j.issn.2095-6959.2021.08.036

View this article at: <https://dx.doi.org/10.3978/j.issn.2095-6959.2021.08.036>

振幅整合脑电图在新生儿脑损伤临床应用中研究的进展

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[摘要] 振幅整合脑电图(amplitude-integrated electroencephalography, aEEG)是新生儿重症监护室(neonatal intensive care unit, NICU)床旁神经功能监护的重要措施。它可以识别早期脑损伤及脑损伤程度, 指导干预及疗效评价, 动态监测可预测神经发育结局。

[关键词] 新生儿; 脑损伤; 振幅整合脑电图

Research progress in clinical application of amplitude-integrated electroencephalogram in neonatal brain injury

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Abstract Amplitude-integrated electroencephalography (aEEG) is very important in bedside nerve function monitoring in neonatal intensive care unit (NICU). It can identify early brain damage and the degree of brain damage, instruct the intervention and efficacy evaluation, and its dynamic monitoring can forecast the neurodevelopmental outcomes.

Keywords neonatal; brain injury; aEEG

振幅整合脑电图(amplitude-integrated electroencephalography, aEEG)是连续脑电图(electroencephalography, EEG)记录的简化形式, 通过分析背景活动及综合评分等评估脑功能有无异常以及预测其神经学预后。最初用于监测成人癫痫持续状态或心脏骤停后的脑功能, 80年代初开始用于新生儿, 现已在全球许多新生儿重症监护病房中作为临床标准监护项目。多项研究表明: aEEG可用于监测新生儿脑病^[1]、癫痫发作^[2]、亚低温治疗期间^[3]的脑功能情况、监测早产儿的脑成熟

度及判断早产儿脑损伤。患有心脏畸形、代谢性疾病、脑室内出血等均可有脑皮质电活动改变。

1 aEEG 的特点

EEG可反映大脑半球的基本功能状态和发育成熟水平, 具有敏感、可靠、无创、可动态随访等优点, 在临床应用广泛。但是EEG是低振幅的, 常被伪迹所干扰, 且它的判读需要医生有丰富的经验, 间断的记录难以判断长时间的脑电活动。

收稿日期 (Date of reception): 2020-06-30

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基金项目 (Foundation item): 云南省新生儿疾病研究中心课题 (2017NS116)。This article was supported by the Project of Yunnan Neonatal Disease Research Center, China (2017NS116).

同时在新生儿重症监护室(neonatal intensive care unit, NICU)中容易受其他机器干扰,无法长时间监测阻抗。

aEEG是通过脑电波幅整合观察脑电趋势,为常规EEG连续简化形式,评价的基本指标包括上边界振幅、下边界振幅、睡眠觉醒周期(sleep-wake cycling, SWC)、异常放电、暴发间期、暴发次数和连续性,具有记录电极少、连续记录、图形直观等优点,且aEEG电极放在双顶骨处,此处是大脑中动脉灌注的边缘带,对缺血敏感,有利于预测缺血缺血性脑病(hypoxie-ischemic encephalopathy, HIE)预后等。近年来aEEG在NICU的应用增多。

2 aEEG在新生儿惊厥早期诊断、治疗及早期预后评估中的应用

新生儿惊厥及可疑发作是aEEG监测的重要指征。在aEEG中,典型的新生儿单次癫痫发作看起来像“驼峰”,代表癫痫发作的典型起伏和减弱特征。重复性癫痫发作,例如癫痫持续状态,通常看起来像锯齿状的重复“驼峰”,每个代表一次癫痫发作^[2]。研究^[4]发现:由KCNQ2基因突变引起的新生儿癫痫有典型的aEEG模式,在癫痫发作末期振幅下降,反映严重的发作后抑制。因为aEEG趋势中的时间压缩,以及使用的电极数量有限,所以观察者通常会错过罕见的、局灶的、低振幅的短暂性癫痫发作。研究^[5]发现:aEEG对单次癫痫发作的检测灵敏度为33.7%,对反复癫痫发作的婴儿的检测灵敏度为86%。aEEG监护时应至少有一次EEG,以便能更全面地监测。

aEEG可以区分未镇静的患者,但无法准确区分药物镇静程度。aEEG参数下降与镇静和镇痛药物剂量增加有关,在一小部分深度镇静的患者中发现爆发抑制活动^[6]。对于难治性的惊厥持续状态,应在aEEG监测下调整静脉内给予抗惊厥药物的剂量,以观察对发作的控制情况^[7]。目前许多研究应用aEEG作为评价惊厥药物疗效的方法,例如一项应用对aEEG的研究^[8]发现:利多卡因作为二线或三线抗惊厥药物,对71.4%的新生儿具有不错的抗惊厥作用,提示aEEG对临床应用及减停抗惊厥药有一定的指导价值。

aEEG结果正常的儿童通常预后较好,一项关于新生儿癫痫aEEG结果与神经系统损伤预后的研究^[9]表明:神经系统结局与aEEG背景模式、aEEG周期性、癫痫的病因相关,在预测重度异常的神经系统结局方面,aEEG背景模式具有最高的预测

值,缺失aEEG周期性具有次高预测值。严重的HIE、脑梗死、早产儿颅内出血等引起的癫痫常预后更差。在对围产期缺血性动脉卒中婴儿的研究^[10]中,发现与有正常认知能力的儿童相比,有不良预后的患儿,患病侧及对侧大脑半球达到正常连续电压的时间都更长,提示aEEG结果异常与不良预后相关。aEEG评分系统将使儿科医生能更好地评估癫痫患儿神经发育受损的风险,并有助于对发生癫痫发作的新生儿进行早期干预。

3 aEEG在新生儿HIE及亚低温治疗中的应用

aEEG可以早期对HIE进行准确预测,从而为早期干预提供可靠依据。研究^[11]发现:出生6h内的aEEG预测中重度HIE的特异性为53.57%,敏感性为78%,aEEG监测能有效评估新生儿早期脑损伤,但随着时间的推移,敏感性降低,特异性更高。有研究^[1]对比aEEG、头颅MRI、脑干听觉诱发电位、闪光视觉诱发电位颅压监测、血神经组织蛋白质及脐动脉血气分析监测HIE患儿的效果,发现脐动脉血气分析敏感度及阴性预测率最高,头颅MRI和aEEG特异度及阳性预测率最高。随着HIE临床程度加重,aEEG背景活动连续性变差、振幅降低^[12]。

aEEG波谱带呈现正弦曲线样变化,由活动睡眠期和安静睡眠期构成SWC。SWC是由下丘脑-苍白球环路及脑皮层神经元电活动参与维持的,是大脑完整性的指征。aEEG显示的SWC形式是预后预测的重要指标,HIE患儿亚低温治疗时降温期间SWC的存在和早期发现可预示良好的预后。虽然有研究^[5]发现:低温加上抗惊厥药物会影响EEG的癫痫波,进而可能影响aEEG的结果。但在低温治疗过程中对aEEG背景模式分类具有预后价值^[13]。多项研究表明,尽管在6h时aEEG活动降低,但结局仍可能是正常的,48h时aEEG持续下降与长期不良预后相关^[3]。研究^[6]表明:接受低温治疗的HIE婴儿第三天和第四天的aEEG振幅下降和SWC出现延迟与脑部MRI严重性评分有关,并且可能与异常结局的风险增加有关。

4 aEEG在新生儿急性胆红素脑病中的应用

新生儿急性胆红素脑病(acute bilirubin encephalopathy, ABE)是由于游离的间接胆红素通过血脑屏障沉积在脑干、海马等部位,脑干功

能受损在aEEG表现为SWC不成熟或缺失。研究^[14]发现: aEEG在ABE早期诊断中敏感性为87.88%, 特异性为59.66%。另有研究^[15]表明: aEEG对诊断ABE的敏感度达87.9%, 高于脑干听觉诱发电位(brainstem auditory evoked potential, BAEP), 并与BAEP呈正相关。胆红素所致神经损伤(bilirubin-induced neurologic damage, BIND)评分是精神状态、肌张力、哭声表现的分数相加获得的总分, 有利于评估ABE严重程度(1~3分提示轻度ABE, 4~6分提示中度, 7~9分提示进展期ABE)。aEEG联合BIND评分可协助ABE分级, 对其远期神经系统不良预后有一定的预测价值^[16]。而应用ABE的研究^[17]发现早期SWC的变化有助于预测患儿的神经损伤预后。

5 aEEG在新生儿先天性心脏病围手术期中的应用

脑损伤是婴儿期接受手术治疗的先天性心脏病(congenital heart disease, CHD)患儿的常见并发症^[18]。近年来国外有学者提出EEG监测有助于预测围手术期脑损伤^[19]。有研究^[20]在新生儿大手术术前监测aEEG, 发现有36.2%的患儿有轻度或严重背景活动异常, 且显示出与脑病一致的模式。对CHD术后的新生儿进行aEEG监测, 有27.4%的SWC不成熟, 3.5%缺乏SWC, 且出生时缺氧程度、延迟关胸、术后严重感染是影响术后SWC的重要因素^[21]。研究^[22]表明: 监测到异常aEEG脑活动是早期床旁监测CHD术后脑损伤的新方法, 背景模式异常和发作性放电是明显的脑病理征, 与定量aEEG和EEG测量相比, 定性aEEG特征能更好预测脑损伤。

6 aEEG在早产儿脑功能监测中的应用

6.1 早产儿脑成熟度

aEEG可以较好地反映早产儿脑成熟度, 随着胎龄增大, 脑电背景活动趋于成熟^[23]。随胎龄增加, 背景活动连续性逐渐增强, 下界电压升高, 上界电压降低, 带宽变窄, 睡眠周期时程变短。早产儿在胎龄32周时, aEEG开始有较为明显的连续性。胎龄36周时开始出现宽带与窄带相交替的睡眠周期, 这与正常足月儿相近^[24]。有研究^[25]表明: 早产小于胎龄儿在第3天和第14天显示出与早产适于胎龄儿相似的总aEEG成熟评分, 但在第7天评分较低, 表明早产儿在出生后的第1周

成熟延迟。

6.2 早产儿脑损伤

脑室周围白质软化(periventricular leukomalacia, PVL)的早产儿aEEG上边界电压增高、下边界电压显著降低及SWC延迟, 且aEEG异常程度与PVL病情严重程度显著相关。严重颅内出血的早产儿aEEG表现为下边界电压显著降低(多 $<2\ \mu\text{V}$), SWC不成熟或延迟^[26]。脑室周围-脑室内出血的早产儿aEEG表现为背景模式不成熟, 可出现连续性电压延迟^[27]。另有研究^[28]指出: aEEG不能预测早产儿脑室内出血。aEEG监测小于28周出生的早产儿, 发现在生命的前3天内, 癫痫发作的发生率在13%~20%^[29]。aEEG监测早产儿缺氧性脑病的结果与临床分级相关, 敏感性为100%, 特异性为82.5%^[30]。

早产儿aEEG振幅与儿童认知结局之间存在关联^[31], 早产儿在前72 h内出现癫痫发作与2岁时语言得分较低有关。有研究^[32]表明: aEEG信号的改变与5岁时识字能力低下有关。在极低出生体重的早产儿中, 早期aEEG背景活动的中度至重度异常与新生儿期影像学检查中发现的严重脑损伤有关, aEEG有助于确定患者是否需要进一步MRI检查以帮助早期诊断脑损伤^[33]。通过研究32周胎龄早产儿出生72 h内aEEG监测和MRI, 发现aEEG或MRI改变与大脑成熟度有关^[34]。

7 其他

1) 化脓性脑膜炎常有脑损伤后遗症, EEG作为神经功能监测的重要方法, 在脑膜炎中广泛应用, 曾有报道^[35]指出: 新生儿细菌性脑膜炎EEG总异常率为61.4%。另有针对90例新生儿化脓性脑膜炎的研究^[36]表明aEEG异常率为31.03%。对比常规脑电图(routine electroencephalography, REEG)与aEEG在儿童病毒性脑炎中的应用, 发现REEG异常率为53.2%, aEEG异常率为80.9%, aEEG组在重度异常儿童的检出率明显高于REEG组, aEEG可以更成功地将重度病毒性脑炎的儿童与中度和轻度分开。随着EEG异常程度的加深, 儿童的住院时间和EEG恢复正常的时间相应延长^[37]。

2) 低血糖是新生儿常见的代谢紊乱疾病, 严重的低血糖会影响脑细胞代谢和发育, 造成神经系统不可逆的损伤。改良aEEG评分(参照徐文慧等^[38]制定的改良aEEG评分量化工具)对区分不同程度脑损伤有重要作用, 脑损伤组评分明显低于无

脑损伤组, 并且症状性脑损伤组评分最低^[39]。有研究^[40]发现: 低血糖脑损伤的aEEG常表现为帽状或锯齿状的癫痫持续状态及频繁癫痫发作, 低血糖纠正后恢复期aEEG仍有散发或频发的癫痫发作, 伴或不伴癫痫的临床发作。

8 结语

aEEG检测的适用范围: 有脑损伤表现或存在脑损伤高危因素的新生儿、新生儿脑发育的评估、新生儿惊厥和可疑发作的监测以及脑损伤治疗效果的评估^[41]。aEEG在脑损伤早期诊断及预后评估方面有很高的价值, 但由于记录部位有限, 缺少波形、频率、节律等重要信息, 故aEEG在临床应与EEG互补应用, aEEG可用于对高风险新生儿的长期监测, 而EEG则可用于评估更细微的情况。aEEG联合其他检查手段, 能有效评估新生儿的脑功能情况及预后, 随着对aEEG更深的研究, aEEG在新生儿脑损伤还会发挥更大的作用。

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本文引用: 周君, 崔珊, 赵晓芬, 和灿琳, 赵朋娜, 李杨方. 振幅整合脑电图在新生儿脑损伤临床应用中研究的进展[J]. 临床与病理杂志, 2021, 41(8): 1952-1957. doi: 10.3978/j.issn.2095-6959.2021.08.036

Cite this article as: ZHOU Jun, CUI Shan, ZHAO Xiaofen, HE Canlin, ZHAO Pengna, LI Yangfang. Research progress in clinical application of amplitude-integrated electroencephalogram in neonatal brain injury[J]. Journal of Clinical and Pathological Research, 2021, 41(8): 1952-1957. doi: 10.3978/j.issn.2095-6959.2021.08.036