电子、语音版

·综述·

神经重症多模态脑监测的研究进展

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摘 要：神经重症监护室(NICU)患者多存在继发性损伤，如脑水肿、颅高压、癫痫及灌注异常，因此，预防、诊断及治疗继发性脑损伤是影响患者临床转归和结局的重要因素。多模态脑监护(MMM)采用多种监护手段，系统性、全面性评估脑生理功能和病理改变，以期实现精准化管理。目前常用的MMM技术包括脑组织氧监测、颅内压监测、脑代谢监测、脑血流监测、脑电监测和多模态影像学，并可分为有创性和无创性，这些监测技术可评估不同角度的脑生理及病理改变。近红外光谱(NIRS)可用于脑组织血氧饱和度，评估颅内灌注情况及血管调节功能。有创颅内压监测可精准监测患者颅内压变化，预测颅内压变化，指导脱水降颅压药物用量。脑微透析(CMD)可对颅内细胞外液进行采样，实时监测颅内代谢产物含量，明确颅内代谢情况。经颅多普勒超声(TCD)可用于监测颅内外大血管的血流量。脑电监测可直接反映脑电活动，也可间接反映脑血流量，用于预测继发性损伤中癫痫及脑缺血情况，而其中的连续脑电图(cEEG)监测在神经重症中应用较为多见，脑电波形的改变与患者临床症状及预后密切相关。多模态影像学作为新兴的监测技术，可客观反映脑结构、功能及病理改变。该文系统梳理了目前应用于NICU中MMM的各类监测技术的应用原理及监测特点，归纳总结了不同监测技术指标与临床预后的相关性，并浅谈这些监测技术目前存在的问题和挑战。

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关键词：神经系统疾病；神经重症医学；多模态脑监测；脑电监测；多模态神经影像学

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Research advances in multimodal brain monitoring of neurocritical diseases

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Abstract: Patients with severe neurological diseases in the neuroscience intensive care unit (NICU) often suffer from various secondary injuries, such as cerebral edema, intracranial hypertension, epilepsy, and abnormal perfusion, and therefore, the prevention, diagnosis, and treatment of secondary brain injury are important influencing factors for clinical prognosis and outcome. Brain multimodal monitoring (MMM) uses various methods to systematically and comprehensively evaluate the physiological function and pathological changes of the brain, so as to realize precise management. At present, commonly used MMM techniques include brain tissue oxygen monitoring, intracranial pressure monitoring, cerebral metabolism monitoring, cerebral blood flow monitoring, electroencephalographic monitoring, and multimodal neuroimaging, which can be classified as invasive and noninvasive techniques, and these monitoring techniques can evaluate pathological and physiological changes of the brain from different perspectives. Near-infrared spectroscopy (NIRS) can be used to evaluate blood oxygen saturation in brain tissue, intracranial perfusion, and the regulatory function of vessels. Invasive intracranial pressure

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monitoring can accurately monitor and predict the change in intracranial pressure and guide the amount of drugs used for dehydration and reducing intracranial pressure. Cerebral microdialysis (CMD) can perform sampling of intracranial extracellular fluid and monitor the content of intracranial metabolites to clarify intracranial metabolism. Transcranial Doppler (TCD) can be used to monitor the blood flow volume of intracranial and extracranial major blood vessels. Electroencephalographic monitoring can reflect brain electrical activity directly and cerebral blood flow indirectly and is used to predict epilepsy and cerebral ischemia; continuous electroencephalographic (cEEG) monitoring is often used in severe neurological diseases, and the change in brain waves is closely associated with clinical symptoms and prognosis. As an emerging technique, multimodal neuroimaging can objectively reflect the structural, functional, and pathological changes of the brain. This article introduces the application principles and monitoring characteristics of each MMM technique currently used in the NICU, summarizes the association of different monitoring indicators with clinical prognosis, and discusses existing problems and challenges in these techniques.　[Journal of International Neurology and Neurosurgery, 2022, 49(6): 92-96]

Keywords: nervous system diseases; neurocritical medicine; brain multimodal monitoring; electroencephalographic monitoring; multimodal neuroimaging

神经重症医学是新兴的神经病学及神经外科亚专业,其综合了神经病学、神经外科学、重症医学、急诊医学及神经影像等多学科知识和技能,为神经系统病危重症患者提供系统、全面而高质量的医疗监护及救治[1]。由于中枢神经系统复杂,脑组织耐受缺血缺氧能力差,与此同时,神经功能评价及治疗手段有限,因此监测及管理神经系统重症患者的脑功能至关重要[2]。急性脑损伤患者往往存在原发性及继发性脑损伤[3],而患者预后与脑缺血、颅内压增高、脑水肿、癫痫发作、颅内低/高灌注这一系列继发性的损伤密切相关[4]。

多模态脑监护(brain multimodality monitoring, MMM)采用脑组织氧监测、颅内压监测、脑代谢监测、脑血流监测、脑电监测及影像技术的监护手段,从不同角度评价脑功能,将数据进一步整合分析,系统而全面地评估脑生理功能/病理改变,从而实现患者个体化管理[5-6]。本文通过回顾MMM不同监测技术的机制、应用、临床意义及不足等方面,以期为神经重症监护室(neuro-intensive care units, NICU)临床医师提供借鉴。

1　脑组织氧监测

神经重症患者存在脑灌注减少及血流动力学改变引发的低氧血症,可导致血脑屏障受损[7]、脑微循环障碍、炎症因子活化,可诱发脑水肿和癫痫发作。脑组织氧饱和度降低与机械通气时间呈正相关,当患者48 h内平均脑组织血氧饱和度低于56%时,提示预后不良。近红外光谱(near-infrared spectroscopy, NIRS)通过监测局部脑组织血氧饱和度,实时无创地反映颅内氧代谢情况及有效血流灌注[8-9],现已广泛应用于不同疾病状态下脑血流灌注监测及功能的评估[10]。NIRS基于生物组织对波长为700~1 000 nm的红外光透射性,以及血红蛋白、肌红蛋白和细胞色素氧化酶对光谱的不同吸收率,利用郎伯—比尔定律和光散射理论,计算还原血红蛋白和氧合血红蛋白吸光系数,计算吸收谱比值,得出局部的血红蛋白氧饱和度[11]。NIRS已广泛应用在新生儿重症监护室、心内科重症监护室以及心胸外科手术中。然而,在不同的NIRS检测环境下,颅内外光源的改变可干扰光线透过颅骨的深度,得出不同的氧含量结果,因而存在一定的局限性。

2　颅内压监测

正常成年人颅内压为10~15 mmHg,当颅内压增高持续大于20 mmHg时,病死率明显增高[12]。目前临床上有创颅内压监测是将探头置于脑室、蛛网膜下腔、硬膜外及硬膜下,实时监测颅内压变化,包括脑室内导管监测、脑实质颅内压监测、蛛网膜下隙监测、硬膜下监测及硬膜外监测这5种手段,其中,脑室内导管监测在临床最为常见。颅内压监测操作较为简单,结果比较准确,在监测颅内压同时还可引流脑脊液,如在蛛网膜下腔出血患者中还可以起到引流血性脑脊液,减少红细胞分解产物对脑组织的毒性作用[13-14]。1项多中心研究显示,中度颅脑损伤患者24 h内进行有创颅内压监测可准确预测6个月后神经功能的恢复情况[15],同时发现成年患者颅内压下降20~25 mmHg提示治疗有效。与此同时,在临床上常用的降颅内压药物,如甘露醇、甘油果糖、呋塞米等对肾脏损伤较大,因此与无颅内压监测的患者相比,有创颅内压监测患者的肾功能损伤发生率明显降低。这是由于在颅内压监测后,检测降颅压药物量效与颅内压之间关系,最大限度防止降颅压药物的不良反应。然而,有创颅内压监测的诊疗费用高,人力资源投入多,操作风险高,限制了其广泛应用[16]。

3　脑代谢监测

重度颅脑损伤患者大脑对葡萄糖的利用率降低,酮体及乳酸合成增加,颅脑内微循环代谢障碍,因此对于脑代谢监测可评估脑内局部病理生理状态。脑微透析(cerebral microdialysis，CMD)[17]通过双腔透析导管插至脑皮髓质开窗中，对细胞外液连续采样，实时监测丙酮酸、葡萄糖、乳酸、甘油及谷氨酸等代谢产物含量，实时了解颅内代谢情况[18]。当颅内丙酮酸及乳酸水平较高时，伴随颅内压增高、脑组织氧饱和度降低及远期额叶萎缩[19]；当谷氨酸含量持续升高，提示癫痫的风险增高，预后较差[20]。CMD可对脑内微循环进行准确检测，临床价值较高，但其实际操作技术较为复杂，应用受到了一定限制。

4　脑血流监测

多数神经重症患者在应用镇静麻醉药物后，体循环血压降低、脑血管收缩、脑灌注不足，继而出现脑组织缺血缺氧。因此，脑血流量监测至关重要。经颅多普勒超声(transcranial doppler，TCD)通过超声探头测定颈内动脉及椎动脉的血流速度[21]，同时可监测微栓子，已广泛应用于脑血管病[22]、中枢神经系统感染[23]、颅高压及脑死亡评定[24]。TCD对于脑血流监测没有标准参考值[25]，不同患者变异性较大[26]，需要结合其他检查手段综合判断，也有部分患者超声无法透过颅骨，不能顺利完成TCD检查。

5　脑电监测

连续脑电图监测技术(continuous electroencephalograghy，cEEG)是一种动态、实时脑电图监测，用于发现及预测癫痫发作、评估脑损伤程度、指导治疗、预测预后的监测技术[27]。在神经重症患者中，cEEG可通过脑电波的变化监测继发的颅脑损伤[28]。脑电图不同波形是基于脑血流量变化，正常脑血流量约为每分钟50 mL/100 g，当脑血流量下降到每分钟25~30 mL/100 g时，脑电图节律性的4~7 Hz慢波增加；当脑血流量下降到每分钟12~18 mL/100 g时，脑电图节律变得更慢；当脑血流量少于每分钟10~12 mL/100 g时，电波抑制，电活动减少，提示预后不良。相比于常规脑电图，cEEG监测持续时间较长，因而对亚临床痫性发作及癫痫临床识别率显著提高[29]。cEEG定量分析可提高对癫痫及脑缺血的敏感度[30]，例如α节律比值提示颅内血管痉挛程度；快波减少提示脑缺血；普遍的节律失调高度提示颅高压或脑疝形成[31]。而这些脑电波的改变往往先于患者临床症状的出现，而且在颅内压增高的情况下更为明显。Witsch等[32]在蛛网膜下腔出血患者中应用cEEG及深部电极监测脑血流量，发现2 Hz为组织缺氧的警戒脑电频率。cEEG电极安放简单，对患者相对舒适、脑电信号采集较为稳定，更适合在重症监护病房中应用。

颅内深部电极(depth electrodes，DE)是将电极置于颅内，监测颅内的异常放电波[33]，相较于头皮脑电图，颅内深部电极可发现常规头皮脑电图不能监测的微小棘波或尖波[34]。1项基于14例成年脑外伤患者的研究发现，颅内深部电极对于痫性波发放和继发性脑损伤的监测较为敏感[35]。颅内深部电极在神经外科术前及术后的应用较广泛[36]。

6　多模态影像学

多模态神经影像学包括正电子发射计算机断层扫描(positron emission computed tomography，PET)[37]、单光子发射计算机断层扫描(single-photon emission computed tomography，SPECT)，以及功能神经影像学(包括磁共振灌注扫描、弥散张量成像、三维结构磁共振及磁共振波谱成像)[38]。神经影像学可辅助临床医师评价患者颅内解剖及生理功能，可协助诊断如急性脑卒中、脑外伤、癫痫、中枢神经系统感染等在内的中枢神经系统疾病[39-40]。

PET利用正电子放射性药物(核素^{11}C、^{13}N、^{15}O和^{18}F等)标记人体内糖、氨基酸、脂肪、核酸、配基或抗体，示踪人体内特定生物物质活动，获得正常/病灶组织在特定时刻的血流灌注、糖、氨基酸、核酸、氧代谢、受体分布及活性等功能信息。PET可在分子水平上揭示机体生物活动，并用客观的解剖影像形式及生理参数显示，广泛应用在肿瘤、基因及代谢疾病中。PET可较早捕获重症脑损伤中的代谢异常、功能失调及结构改变，在临床症状出现之前发现病变并及时应对。SPECT可将γ光子转化为光信号，再转为电信号，通过计算机计算信号强度，实现人体断层图像重建。PET和SPECT监测的颅内高代谢及局部血流量的升高，均提示血流速度增快，病变血运丰富。1项基于脑容量分析的功能磁共振研究，发现脑外伤患者磁共振显示的脑萎缩与昏迷时间及预后存在密切的相关性[41]。

磁共振弥散张量成像可评估大脑白质结构及神经纤维束的完整性，在神经解剖、纤维连结和脑发育中应用较广阔。在重度脑外伤中，弥散张量成像可发现脑白质中异常断裂的神经纤维束，定量显示脑损伤的范围及严重程度[42]。随着影像学技术的发展，基于磁共振扫描得到的表面形态学数据，应用软件包对大脑皮质进行三维重建分析，可清晰展现大脑皮质的结构和发育轨迹。三维结构磁共振可通过测量全脑/局部脑区皮质厚度、皮质表面积及局部折叠系数，明确脑生理结构及病理改变。

7　总结与展望

神经重症中的MMM在协助患者个体化管理、及早修正治疗、评估治疗效果、判定病情转归及防治继发损伤具有重要作用。在利用脑代谢监测、脑氧含量监测、脑电图监测、神经影像、脑血流量监测及多种生理学参数等监护技术为临床医师提供更多的参考依据。然而，MMM仍面临较大的挑战，尚缺乏大规模的临床验证，因此迫切需要多中心队列研究验证MMM对继发性脑损伤的识别。

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