·专题综述·

7T超高场强MRI在耐药性癫痫诊断与治疗中的应用进展

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【摘要】 7T超高场强MRI(简称7T MRI)的高分辨率、高信噪比和高对比度特点,使其在海马硬化和局灶性皮质发育不良诊断、辅助鉴别二者病理亚型、定位手术切除范围等临床应用中优于常规场强MRI,并已在耐药性癫痫病因诊断与治疗中取得进展。本文综述7T MRI的临床应用价值及研究进展,以推动其在癫痫诊断与治疗领域的应用。

【关键词】 耐药性癫痫; 磁共振成像; 综述

Application progress of 7T ultra-high field MRI in diagnosis and treatment of drug-resistant epilepsy

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【Abstract】 7T ultra-high field MRI (7T MRI), with its high resolution, high signal-to-noise ratio (SNR) and high contrast, is superior to conventional field intensity MRI in clinical applications such as diagnosis of hippocampal sclerosis (HS) and focal cortical dysplasia (FCD), assisting in the identification of pathological subtypes of the both, locating the scope of surgical excision, and has made progress in the diagnosis and treatment of drug-resistant epilepsy (DRE). This paper aims to review the clinical application value and research progress of 7T MRI in order to promote its application in the field of diagnosis and treatment of epilepsy.

【Key words】 Drug resistant epilepsy; Magnetic resonance imaging; Review

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癫痫是临床常见中枢神经系统疾病,全球人群患病率约为7‰[1],我国约有1000万例癫痫患者[2],其中近1/3患者经两种或两种以上抗癫痫发作药物(ASM)规范治疗后仍无法有效控制发作,称为耐药性癫痫(DRE)[3]。目前,癫痫外科手术是耐药性癫痫的有效治疗方法[4],手术方案的制定与疗效最大程度取决于术前对致痫灶的准确定位。MRI是癫痫外科手术前评估的重要手段,亦是定位致痫灶不可或缺的方法[5]。但仍有约30%患者在MRI上无法发现明确的致痫灶,称为MRI阴性或无灶性癫痫[6]。研究显示,MRI检出致痫灶的患者术后无发作概率是阴性患者的2~3倍[7]。因此,提高致痫灶检出率是耐药性癫痫患者术前评估的关键环节。近年来,7T超高场强MRI(以下简称7T MRI)凭借其高分辨率、高信噪比和高对比度之优势(图1),在癫痫临床诊断与治疗中发挥辅助作用,尤其对致痫灶的术前定位至关重要[8]。本文旨在对近年来7T MRI在不同类型耐药性癫痫诊断与治疗中的应用进展进行总结,以期促进7T MRI在癫痫领域的应用。

一、7T MRI在海马硬化型颞叶癫痫中的应用

颞叶癫痫是好发于成人的耐药性癫痫,而海马硬化(HS)则是颞叶癫痫常见病理类型[9],包括神经

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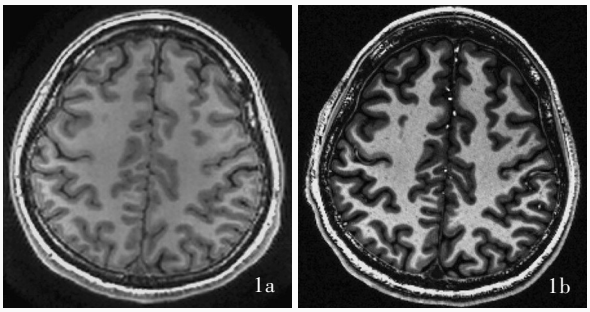

图1　横断面T_1WI灰白质对比可见7T图像较3T图像灰白质对比度更高(灰质信号更低、白质信号更高),灰白质交界更清晰　1a　3T MRI　1b　7T MRI

Figure 1　Gray-white matter contrast on axial T_1WI showed 7T images had higher gray-white contrast (lower gray matter signal and higher white matter signal) and clearer gray-white matter junction than 3T images. 3T MRI (Panel 1a). 7T MRI (Panel 1b).

元丢失和神经胶质细胞增生,MRI表现为海马体积缩小、伴T_2WI和FLAIR成像高信号及内部结构紊乱,以及侧脑室颞角扩大等征象。据海马硬化程度和受累范围,国际抗癫痫联盟(ILAE)将其分为4种经典亚型,即海马硬化1型、海马硬化2型、海马硬化3型和无海马硬化仅胶质增生型[10]。海马硬化形成可能与婴幼儿期外伤、脑炎、高热惊厥等有关[11],早期(<3岁)损伤所致海马硬化表现为海马各亚区神经元严重丢失,通过1.5T MRI即可识别[12];部分患者海马神经元丢失范围局限且程度较轻,1.5T MRI甚至3T MRI很难识别,易误诊为MRI阴性颞叶癫痫[12]。

1.提高海马硬化检出率　7T MRI具有较高的海马硬化检出率,可以通过海马亚区自动分割对常规场强(1.5T和3T)MRI阴性颞叶癫痫患者的海马体积变化进行分析,此类患者各亚区体积均呈萎缩征象,并且病程越长(>10年)CA1区体积不对称指数越高[13]。Canjels等[14]报告8例常规场强呈MRI阴性耐药性癫痫患者的7T MRI分析结果,显示所有患者患侧海马体积均较对侧明显缩小;Santyr等[15]对9例常规场强MRI阴性颞叶癫痫患者行7T MRI检查,其中1例(1/9)患侧海马亚区萎缩,最终经病理证实为海马硬化。因此,通过7T MRI进行海马体积分析可于部分常规场强MRI阴性颞叶癫痫患者中发现隐匿性海马硬化病例。近期开展的一项7T MRI磁敏感加权成像(SWI)对比研究对常规场强MRI阴性内侧颞叶癫痫患者行血管密度分析,与正常对照组相比,癫痫组患侧海马血管密度不仅显著降低且明显不对称($P<0.05$),但海马体积组间无明显差异($P>0.05$),提示除海马萎缩外,海马血管密度降低或不对称同样具有鉴别诊断意义[16]。

2.辅助鉴别海马硬化病理亚型　不同病理亚型患者手术预后存在一定差异,若术前明确海马硬化病理亚型,对指导制定手术方案、判断预后具有重要意义。与常规场强MRI相比,7T MRI具有高分辨率、高信噪比和高对比度优势,故具备术前预测病理亚型、判断预后的可能性。体外研究显示,7T MRI T_2WI可以清晰辨识无硬化海马组织标本从外至内的7层组织,而硬化海马组织仅可分辨出4层组织,进一步的扩散张量成像(DTI)分析,海马硬化1型组织切片的平均扩散率(MD)显著高于海马硬化2型,可资鉴别[17]。Gillmann等[18]的研究发现,测量7T MRI T_2WI图像中平行和垂直于分子层的锥体细胞层的宽度乘积,可以有效区分海马硬化1型(0.43 mm^2)、海马硬化2型(1.67 mm^2)以及无海马硬化型(2.91 mm^2)。此外,亦可利用半定量分析辅助鉴别海马硬化病理亚型,有研究将海马各亚区的7T MRI特征(如体积、传导信号、内部结构、齿状回颗粒细胞层宽度等)与术后组织病理学结果(海马神经元丢失、星形胶质细胞增生等)进行半定量分析,结果显示,7T MRI预测海马硬化各亚型的准确度高达12/13[19]。表明利用7T MRI于术前预测海马硬化病理亚型具有可行性。

3.检测颞叶癫痫相关代谢与功能异常　7T MRI不仅可以发现海马组织微小病灶,在观察颞叶癫痫功能及代谢异常方面也具有一定优势。MRS借助于不同物质间化学位移程度显示人体不同代谢物及其表达水平,与常规场强MRI相比,其信噪比和分辨率提高,区分相邻波峰的能力增强,如区分低代谢物产生的化学位移[20]。与正常人群相比,颞叶癫痫患者随年龄的增长出现后扣带回/楔前叶γ-氨基丁酸(GABA)水平降低,而该脑区谷氨酸水平升高则是药物治疗后短期(3个月)无发作的预测因素[21]。通过谷氨酸化学交换饱和度转移技术可以发现,7T MRI呈阴性的颞叶癫痫患者患侧海马和下托组织中谷氨酸化学交换饱和度较对侧升高,可以此辅助定位致痫灶[22]。

二、7T MRI在局灶性皮质发育不良型颞叶外癫痫中的应用

局灶性皮质发育不良(FCD)是难治性颞叶外癫痫的常见病理类型[23],可发生于不同脑叶,以额叶

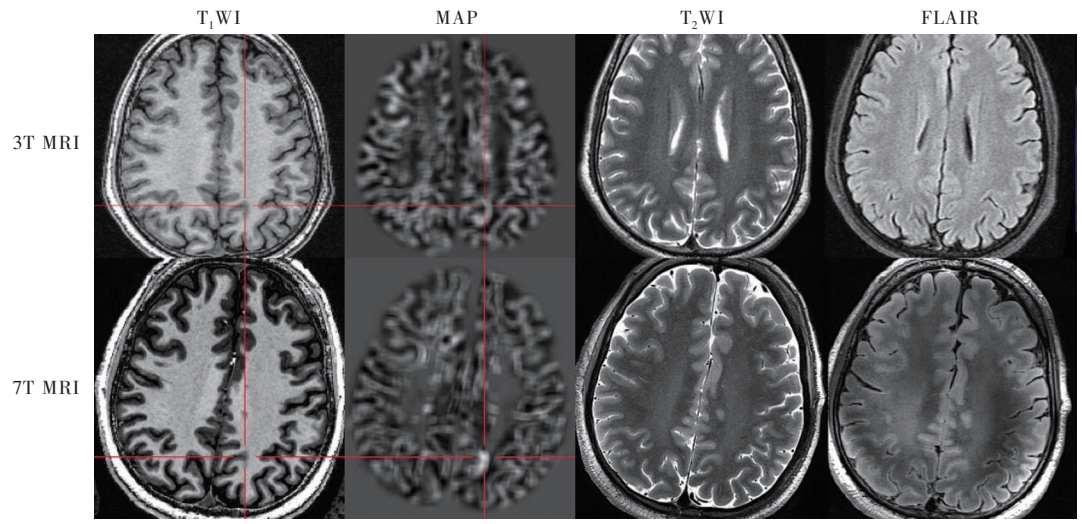

图2　局灶性耐药性癫痫患者，男性，32岁。3T MRI图像经MAP后处理未发现病灶；7T MRI图像经MAP后处理发现左侧额顶叶交界区微小病灶，病理证实为FCD Ⅱa型

Figure 2　A 32-year-old male with focal drug-resistant epilepsy. 3T MRI images with MAP post-processing revealed non-lesional. 7T MRI images with MAP post-processing revealed a suspected subtle lesion in left frontoparietal junction, and pathology confirmed as FCD Ⅱa.

高发。其典型MRI表现为局部皮质增厚、灰白质交界不清、灰质向白质深部异常延伸，以及T_2WI和FLAIR成像高信号等[24]。国际抗癫痫联盟最新分类标准将其分为FCD Ⅰ型、FCD Ⅱ型和FCD Ⅲ型，其中FCD Ⅱ型根据是否存在“气球”样细胞进一步分为Ⅱa和Ⅱb亚型[25]。临床约有40%的FCD Ⅱ型、85%的FCD Ⅰ型在常规场强MRI上无法被识别[26]，导致患者可能失去及时手术切除病灶的机会。

1. 提高局灶性皮质发育不良检出率　7T MRI图像清晰，能够很好地显示局灶性皮质发育不良病灶特征[27]，与常规场强MRI相比，7T MRI对致痫灶的识别率可提高31%[28]。一项采用7T MRI对常规场强MRI阴性耐药性局灶性癫痫的研究显示，新发可疑致痫灶检出率约28.57%(6/21)，术后经病理证实为局灶性皮质发育不良[29]。7T MRI的诊断价值主要体现在T_2*WI和FLAIR成像[29]。局灶性皮质发育不良在常规场强MRI呈阴性的原因是病灶微小或缺乏异常征象，隐匿存在的异常特征在图像辨识过程中易忽略。形态学分析程序(MAP)是基于体素的形态学分析(VBM)开发的一种局灶性皮质发育不良检测程序，通过对患者大脑皮质厚度、脑沟深度以及皮质灰白质交界清晰度与正常受试者模板的定量对比，突显出潜在的可疑病灶，以提高检出率(图2)。MAP应用于常规场强MRI可显著提高局灶性皮质发育不良检出率，但在7T MRI上的表现尚待进一步验证。Wang等[30]对67例3T MRI阴性耐药性癫痫患者进行7T MRI研究，其中22.39%(15/67)发现微小致痫灶；经T_1WI图像MAP后处理，可使致痫灶检出率提高至43.28%(29/67)，16/17例手术患者经病理证实为局灶性皮质发育不良。Chen等[31]对35例经MAP后处理(3T MRI)和PET等多模态影像学评估的耐药性癫痫患者的观察发现，11例3T MRI疑似局灶性皮质发育不良的患者中9例经7T MRI证实诊断；而24例3T MRI阴性病例即使对7T MRI图像进行MAP后处理，也仅重新检出4例(16.67%)局灶性皮质发育不良。以上研究有关7T MRI检出率存在的差异可能与不同研究纳入的病例数或MRI阴性判断标准不同有关，不同癫痫中心所用MRI序列不同也是导致检出率差异的原因，如大多数专业人员行MAP分析时倾向应用高分辨率3D T_1WI图像寻找病灶，而在肉眼识别过程中FLAIR成像异常高信号更易被注意到。

2. 提高局灶性皮质发育不良病灶手术切除范围的准确性　7T MRI不仅可提高局灶性皮质发育不良病灶检出率，还可使病灶边界成像更加清晰。局灶性皮质发育不良好发于额叶和中央区，当累及初级感觉运动皮质或语言皮质等功能皮质时，精准确定病灶范围对实现完整切除病灶、避免术后运动或语言等功能障碍至关重要。但常规场强MRI受限于其分辨率和信噪比较低之缺陷，通常无法精确显

示病灶边界，使术中划定病灶范围、避免医原性功能区损伤难度增加。7T MRI利用白质抑制（WMS）和灰白质组织边界增强（TBE）技术，更精准地确定病灶边界，从而指导并确定手术切除范围[32]。Kelley等[33]报告1例左侧旁中央小叶沟底局灶性皮质发育不良病例，经7T MRI T_1WI证实病灶部位，并以此图像指导电极植入、确定病灶边界，最终精确切除病灶并保留锥体束，术后14个月无发作且避免肢体瘫痪。

3.有助于局灶性皮质发育不良病理亚型的鉴别　在常规MRI图像中，FCDⅡa型病灶较Ⅱb型更为隐匿，漏诊率高达49%[34]。既往认为，皮质发育不良的特征性信号“鼠尾征”（transmantle sign，即在皮质下白质图像中呈“漏斗”状延伸至侧脑室）是FCDⅡb型的特征性影像学表现，诊断时可与其他病理亚型相鉴别，以7T MRI更具优越性[27]。但近年有学者发现“鼠尾征”也可见于FCDⅡa型，为MRI鉴别FCDⅡa型和Ⅱb型带来新的困扰。一项针对FCDⅡ型病理学特征与7T MRI影像学表现关系的研究表明，发育异常的皮质在T_2WI上呈现的异常高信号和信号不均匀与异形神经元数目增加、皮质内纤维损害有关，而皮质下白质异常高信号与髓鞘受损程度相关；FCDⅡa型病灶相关异形神经元数目较FCDⅡb型少且髓鞘发育不良程度较轻，由此可见，MRI异常征象更为隐匿，甚至可以完全呈阴性[35]。该项研究不仅为FCDⅡa型和Ⅱb型的异常MRI表现提供病理学基础，而且为术前预测病理亚型、判断预后提供依据。与常规场强MRI相比，7T MRI突出贡献在于发现发育异常皮质内部存在的信号差异，即“黑线征（black line sign）”，该特征可以用于鉴别局灶性皮质发育不良病理亚型。这一特异性影像学征象由De Ciantis等[29]首次提出，该作者于2016年报告1例7T MRI T_2*WI呈现异常皮质内特征性窄带状低信号区的FCDⅡb型病例；其研究团队之后又报告6例经病理证实的FCDⅡb型患者影像学表现，其中5例异常皮质内存在信号差异，命名为“黑线征”；而4例FCDⅡa型患者无“黑线征”[36]。最近发表在*Neurology*上的一项研究也发现类似现象，该项研究采用7T MRI对20例局灶性皮质发育不良患者的T_2*WI序列进行分析，结果显示，14例为FCDⅡb型患者，其中12例存在“黑线征”；余6例为FCDⅡa型患者，均未发现该征象[37]。此外，MRI“黑线征”脑区的病理表现呈异形神经元和“气球”样细胞聚集，且其不完整切除与术后癫痫复发相关[37]。因此，7T MRI“黑线征”有望成为FCDⅡb型患者术前影像学评估最具典型意义的生物学标志物，为术前定位、确定切除范围提供重要依据。

三、7T MRI在其他皮质发育畸形中的应用

皮质发育畸形（MCD）是一类以先天性大脑皮质发育异常为主的疾病，临床表现为癫痫发作和不同程度的智力、运动障碍等症状，大部分皮质发育畸形在MRI和PET等影像学检查上均可发现结构和功能异常，其中多小脑回畸形为皮质发育畸形常见类型，多发生于一侧或双侧外侧裂相邻区域，周围皮质常涉及运动和语言等重要功能，需通过术前评估确定手术切除范围。应用7T MRI T_2*加权血管造影和TBE序列可以检出3T MRI无法发现的病灶，例如3T MRI诊断为单侧外侧裂多小脑回畸形者，在7T MRI上则呈双侧病灶，其中TBE图像低信号带可清晰显示灰白质分界，而T_2*加权血管造影则可显示病灶皮质表浅静脉的异常扩张，从而辅助定位多小脑回畸形病灶[38]。脑室旁灰质异位是神经元移行障碍引起的畸形，异位神经元常在脑室旁形成单个或多个灰质结节，也是皮质发育畸形的常见类型。利用对轴突显微扩散各向异性更敏感的扩散磁共振成像（dMRI）技术，可以发现皮质下灰质异位在7T T_1WI和FLAIR成像上显示为均匀一致灰质成分特征的病灶，在dMRI上则可见大量白质成分特征，据此可以辅助确定手术切除范围并减少术后并发症[39]。7T MRI T_1WI和T_2WI对结节性硬化症皮质结节的显示更为清晰，SWI序列则可显示结节周围血管的形态异常，而WMS和TBE技术有利于发现更细微的病灶。由此可见，7T MRI对皮质发育畸形的术前评估也具有辅助诊断作用[40]。

四、小结与展望

7T MRI凭借优越的信噪比、图像分辨率和对比度，可以更清晰地显示致痫灶，在伴海马硬化的颞叶癫痫、伴局灶性皮质发育不良的颞叶外癫痫及在其他皮质发育畸形的术前评估中均具有较大的应用价值。7T MRI的应用在提高隐匿性病灶检出率的同时可辅助鉴别致痫灶病理亚型、确定病灶边界和手术切除范围、预测患者预后。但7T MRI图像也存在显著缺陷，即额底、前颞叶和后颅窝伪影与信号丢失，此与7T MRI射频场不均匀引起的电介质效应伪影以及鼻窦等气腔引起的磁化率效应所致局部场强不均匀有关（图3）；此外，更高的场强和更强

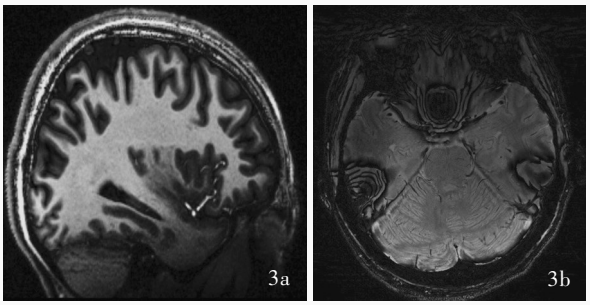

图3 7T MRI伪影示例 3a 矢状面T_1WI可见额底、前颞叶和小脑信号丢失明显 3b 横断面SWI可见不同磁化率物质交界面(空气/骨/软组织)产生的磁敏感伪影

Figure 3 Examples of imaging artifact in 7T MRI findings Sagittal T_1WI showed significant signal loss in the orbital frontal, anterior temporal lobe and cerebellum (Panel 3a). Axial SWI showed susceptibility artifact in the interface (air/bone/soft tissue) of substances for the different susceptibility (Panel 3b).

的磁化率效应可引起头晕、周围神经刺激和皮肤灼伤等不良反应[41-42]。预防方法可于头部两侧应用含钛酸钙电介质垫提高磁场均匀度,以减少颞叶和小脑信号丢失[42];双反转恢复序列、液体和白质抑制序列也可以减轻7T MRI射频场不均匀导致的信号丢失。目前,更多辅助改善超高场强MRI的成像缺陷和安全性问题的新技术与方法已提上日程,虽存在诸多挑战,但可预见7T MRI将进一步普及并完善,在未来将有更多大样本、高质量多中心临床研究评估7T MRI在癫痫诊断与治疗领域的应用价值,推动其在癫痫临床诊断与治疗中的广泛应用。

利益冲突 无

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