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·论著·

## BOLD-fMRI联合DTI在侵及运动区肿瘤中的临床应用

林超群,曹作为

(中南大学湘雅医学院附属海口医院,海南 海口 570208)

**【摘要】目的** 研究血氧水平依赖功能磁共振技术(Blood oxygenation level dependent functional magnetic resonance imaging, BOLD-fMRI)联合弥散张量成像技术(Diffusion tensor imaging, DTI)指导运动区肿瘤手术切除的临床意义。**方法** 2010年3月到2011年10月,术前常规行MRI和肌力检查诊断为侵及运动区肿瘤22例,进行术前随机分组;实验组10例,实验组术前行BOLD-fMRI及DTI检查,对照组12例,对照组术前仅行DTI检查。实验组及对照组均由同一术者阅读检查结果后设计手术方法和手术入路,以及术中确定切除范围;并由同一术者主刀完成肿瘤切除手术。术后第三天复查MRI,用于计算两组病例的肿瘤全切率。术后一周行肌力检查,用于判断术后两组病例的运动功能情况。采用Fisher精确概率法对两组的肿瘤全切率和术后致残率进行统计学分析。**结果** 10例实验组病例中,9例为全切,1例为次全切。12例对照组病例中,5例为全切,7例为次全切。统计学分析结果显示实验组的肿瘤全切率明显高于对照组的肿瘤全切率( $P<0.05$ );10例实验组病例中,术后均无肌力下降,12例对照组病例中,5例出现术后肌力下降,统计学分析结果显示实验组的手术致残率明显低于对照组的手术致残率( $P<0.05$ )。**结论** BOLD-fMRI联合DTI相对单纯的使用DTI,可以更加清晰的显示侵及运动区肿瘤患者的皮层运动功能区及皮层下白质纤维束的解剖学位置,从而使术者能够设计出最佳的手术入路和手术方法,并计划出切除范围,有助于提高肿瘤的全切率和最大限度的保留患者的运动功能。

**【关键词】** 血氧水平依赖功能磁共振;弥散张量成像;运动功能;脑肿瘤

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**Clinical application of BOLD-fMRI combined with DTI in tumors involving motor cortex.** LIN Chao-qun, CAO Zuo-wei. Department of Neurosurgery, Haikou Hospital Affiliated to Xiangya School of Medicine, Central South University, Haikou 570208, Hainan, CHINA

**【Abstract】 Objective** To investigate the clinical significance of blood oxygenation level dependent functional magnetic resonance imaging (BOLD-fMRI) combined with diffusion tensor imaging (DTI) in guiding resection of brain tumors involving motor cortex. **Methods** From March 2010 to October 2011, 22 patients of tumors involving motor cortex were diagnosed by preoperative MRI and myodynamic examination. The patients were randomized into two groups preoperatively: the study group (10 patients) received preoperative BOLD-fMRI and DTI examination, while the control group (12 patients) only received preoperative DTI examination. The test results of the two groups were read by a surgeon, and then the surgical techniques and surgical approach was designed by the same surgeon. All the patients were determined the extent of resection during the surgery and performed tumor resection by the same surgeon. The total tumor removal rate were calculated in the two groups by MRI examination on the third day after surgery, and motor function was evaluating in the two groups by myodynamic examination one week after surgery. The total tumor removal rate and surgically maimed rate of the two groups were analyzed by Fisher precise probabilistic method. **Results** In the study group, 9 cases were found with total resection and 1 case was found with subtotal resection. In the control group, 5 cases were with total resection and 7 cases were with subtotal resection. Statistical analysis showed that the total tumor removal rate of the study group was significantly higher than that of the control group ( $P<0.05$ ). No decline of postoperative muscle strength was found in the study group, while 5 cases showed decline of postoperative muscle strength in the control group. Statistical analysis showed that surgically maimed rate of the study group was significantly lower than that of the control group ( $P<0.05$ ). **Conclusion** BOLD-fMRI combined with DTI can reveal the anatomical location of motor cortex functional areas and subcortical white matter fiber bundles more clearly, as compared with using DTI only, so that the surgeon can design the best surgical approach and evaluate the extent of resection. This method can contribute to improve the total tumor removal rate and maximize the retention of motor function.

**【Key words】** Blood oxygenation level dependent functional magnetic resonance imaging; Diffusion tensor imaging; Motor function; Brain tumor

对于侵及运动区的肿瘤患者,术前能够掌握肿瘤侵犯的范围,以及皮层运动功能区及皮层下白质纤维束的解剖学位置,对患者进行全面的评估,设计出最佳的手术方案是每一个神经外科医师的愿望。BOLD-fMRI能显示皮层运动区的情况,DTI能提供皮质下白质纤维束的信息,因此联合二者可以观察肿瘤、皮层运动区、皮层下纤维束之间的关系。国外对BOLD-fMRI联合DTI的研究已经开展,Holodny等<sup>[1]</sup>将两种成像方法联合应用于脑肿瘤,结果显示联合二者指导手术的切除,能明显减少术后并发症。Schulder等<sup>[2]</sup>联合二者来鉴别脑肿瘤患者移位的脑白质,结果显示联合二者能使种子兴趣区的选择更加靠近客观。Smits等<sup>[3]</sup>将fMRI和DTI联合应用于指导9例颅内肿瘤手术,结果发现联合二者不仅弥补了它们各自临床应用的局限性,而且肿瘤全切率及术后患者运动功能保存均较满意。国内联合二者共同研究也陆续展开,刘强等<sup>[4]</sup>发现联合应用BOLD-fMRI与DTI有助于邻近脑运动功能区肿瘤患者的术前评估。北京天坛医院谢坚等<sup>[5]</sup>联合应用BOLD-fMRI和DTI及术中脑皮层电刺激技术,手术治疗大脑半球运动功能区胶质瘤,发现联合三者不仅可活体、无创地在术前描绘出脑运动功能区皮层、锥体束与运动区胶质瘤的功能解剖关系,指导制定手术方案,而且唤醒麻醉下开颅,术中应用脑皮层电刺激技术可以实时监测、直接定位、标记脑运动功能区皮层和皮层下纤维束的准确位置,为在保护运动中枢的前提下尽量切除肿瘤提供保证。研究结果示三者联合手术治疗大脑半球运动功能区胶质瘤,患者术后运动功能得以保存,术后生活质量较好。本研究通过联合二者对侵及运动区肿瘤患者进行检查,探讨二者联合在运动区肿瘤中的临床应用价值。

## 1 资料与方法

1.1 研究对象 2010年3月到2011年10月门诊收入院的侵及运动区肿瘤患者共22例,年龄23~70岁,平均45岁,男性14例,女性8例。患者神志清醒,经过指导后均能配合医师较好的完成DTI及BOLD-fMRI检查。22例患者随机分为两组,实验组10例,对照组12例,术前两组均完善常规MRI检查(图1)及肌力检查(0~V级)。实验组行BOLD-fMRI及DTI检查及图像处理融合,对照组术前行DTI检查。完善相关检查后,两组患者均由同一术者设计手术方法和手术入路,以及术中确定切除范围并由同一术者主刀完成肿瘤切除手术。术后第三天复查MRI,术后一周行肌力检查(0~V级)。

1.2 MRI设备及成像方法 使用设备为美国GE Signa HDx 3.0T医用磁共振扫描仪,所用接收线圈为8通道高密度头线圈(HRBRAIN),梯度线圈TweenSpeed(GE)参数为梯度爬升率150 mT/S,梯度切换率为50 mT·S<sup>-1</sup>·m<sup>-1</sup>。为了避免头部运动,术前均由医师与患者沟通,令其行MRI检查时保持头部及

全身处于静止仰卧位,并用海绵垫填塞头部与MRI头罩之间的空隙。

1.2.1 解剖定位像 T1 3D MPRAGE(Fast gradient echo with Invert restore pulse) FOV=24, 矩阵320×256, IR=450 ms, 带宽=31.25 HZ; IR反转恢复准备时间=450 ms, 反转角=15°。

1.2.2 BOLD-fMRI 检查方法 采用Gradient Echo EPI, 检查方法为交替对掌运动, 模式采用组块设计法。忽略的循环数(base)=8 cycle, active phase = 10, base phase=10, 重复次数=5。

1.2.3 DTI检查方法 采集序列为SE-EPI(弥散方向=15), B值=1 000, TR=8 000 ms, TE=88, 采集时间=2 min 16 s。

1.3 图像处理及融合 使用BrainVoyage 12.0的DTI处理软件包,计算FA图。实验组患者首先行BOLD-fMRI,确定M1区(初级运动皮层)后,分别于BOLD-fMRI确定的M1区下方及内囊后肢皮质脊髓束(CST)走行区层面放置ROI,进行弥散张量纤维束成像(Diffusion tensor tractography, DTT)。对照组患者分别于正常解剖学M1区下方及内囊后肢CST走行区层面放置感兴趣区(ROI),进行DTT。然后使用BrainVoyage 12.0融合模块对图像进行融合处理。

## 1.4 手术方法及手术入路、术中切除范围的确定

所有患者完善术前检查后,均由同一术者根据两组病例所得的影像学资料设计手术方法及手术入路,术中确定切除范围,并由其主刀完成肿瘤切除术。

1.5 术后MRI检查及肌力检查 两组病例均于术后3 d行MRI增强扫描,计算肿瘤全切率。两组病例于术后一周行肌力检查(0~V级),统计手术致残率。

1.6 统计学方法 实验数据采用Fisher精确概率法进行分析处理。分别统计出两组患者的肿瘤全切数据和手术致残数据,检验数据使用SPSS13.0统计软件处理,P<0.05为差异具有显著统计学意义。

## 2 结果

2.1 实验组 实验组病理结果显示4例胶质瘤,6例脑膜瘤。术前通过BOLD-fMRI检查(见图2,图3),发现10例运动区肿瘤病例的M1区与正常解剖位的M1区对照,均发生了移位,行DTT成像发现皮层下纤维束被完全破坏的1例,皮层下纤维束被浸润的1例,皮层下纤维束仅被推移的8例。术后3 d行MRI增强扫描(见图4),9例为全切,1例为次全切。术后一周行肌力检查(0~V级),所有病例术后均无肌力下降。

2.2 对照组 对照组病理结果显示5例胶质瘤,7例脑膜瘤。行DTT成像发现皮层下纤维束被完全破坏的2例,皮层下纤维束被浸润的2例,皮层下纤维束仅被推移的8例。术后3 d行MRI增强扫描,5例为全切,7例为次全切。术后一周行肌力检查(0~V级),术后有5例病例出现肌力下降,见表1。

2.3 统计学分析 统计学处理示实验组全切率为

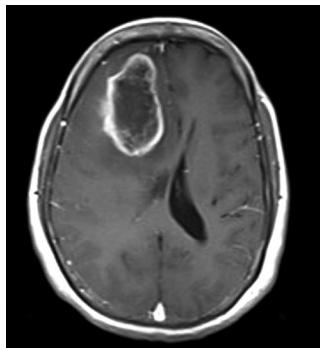


图1 右额叶胶质母细胞瘤

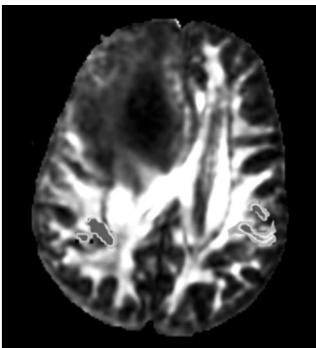


图2 BOLD图与FA图融合



图3 融合图

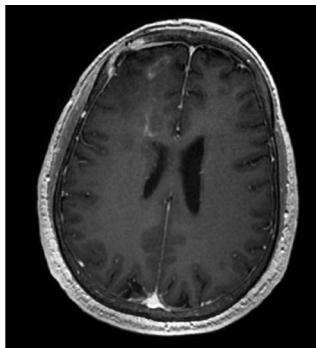


图4 术后MRI示肿瘤全切

注:图1为常规MRI示右额叶有一椭圆形占位;图2为患侧M1区发生推移但信号未减弱,患侧皮质脊髓束被肿瘤推移,但并未破坏;图3为通过BOLD图选择M1区为感兴趣区,行DTT成像后行肿瘤M1区皮质脊髓束3D融合图,示患侧肿瘤推移皮质脊髓束,双侧M1区大小无明显差异;图4为术后MRI示肿瘤全切。

90.00%,对照组为41.67%,两组差异有统计学意义 $P=0.031$ ,见表1。统计学分析显示实验组的全切率明显高于对照组( $P=0.031<0.05$ );实验组术后致残率为0,对照组为41.67%,两组差异有统计学意义( $P=0.040$ )。实验组的术后致残率明显低于对照组( $P=0.040<0.05$ ),见表2。

表1 两种方法指导下手术全切率的比较(例)

组别	全切	次全切	合计	有效率(%)
BOLD-fMRI	9	1	10	90.00
与DTI联合组				
DTI组	5	7	12	41.67

注:由Fisher检验可得 $P=0.031$ ,两组差异有统计学意义。

表2 两种方法指导下术后致残率的比较(例)

组别	致残	未致残	合计	致残率(%)
BOLD-fMRI	0	10	10	0
与DTI联合组				
DTI组	5	7	12	41.67

注:由Fisher检验可得 $P=0.040$ ,两组差异有统计学意义。

### 3 讨论

实验组结果显示M1皮层的受压移位与M1皮层下纤维束的移位具有对应性,M1皮层移位的方向和M1皮层下纤维束移位的方向一致。通过联合二者检查,术者能够清晰的判断功能皮层及皮层下纤维束的位置和肿瘤周围皮层下纤维束的走形,从而在手术中能精确的切除肿瘤而不伤及功能皮层及皮层下纤维束。在对照组中,术者在假定运动功能区没有移位的情况下判断功能皮层及皮层下纤维束的位置和肿瘤周围皮层下纤维束的走形,进行肿瘤切除手术。对照组未做BOLD-fMRI检查,假定皮层运动区没有移位,选择正常解剖位的M1区为ROI区,行DTT成像,实际M1区由于肿瘤的占位效应会发生移位,因此术者在手术中在切除肿瘤时不敢轻易切除实际已被肿瘤侵犯的正常解剖位的M1区,导致全切率低于实验组。由于对照组正常解剖位的M1区的皮层下白质

1,从而使术者能够设计出最佳的手术方法和手术入路,以及切除范围,有助于提高肿瘤的全切率和最大限度的保留患者的运动功能。然而本实验依然存在不少问题有待完善。比如BOLD-fMRI和DTI联合成像方法具有一定的局限性<sup>[10-11]</sup>,部分容积效应的影响、图像伪影的处理、感兴趣区的选择等均受人为因素的影响。实验组及对照组的样本量均不大,后续实验应该增加样本量,使结论能更具有说服力。本实验目前没有与术中导航系统相结合,使术者对肿瘤位置的判断存在一定的主观性。随着医学科技的进步,各项技术的日益成熟,我们联合DTI与BOLD-fMRI,并且与术中导航系统相结合,相信这样的技术在基础研究与临床应用中必将发挥更大的作用。

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## • 实验研究 •

## 饲喂高浓度创伤弧菌对小鼠消化道的损伤研究

郑 晶, 翁 阳, 王明华

(海南医学院病理教研室 海南医学院附属医院, 海南 海口 571101)

**【摘要】** 目的 探讨高浓度创伤弧菌(*Vibrio vulnificus*, Vv)经食道感染小鼠的致病特点。方法 22只昆明小鼠, 实验组16只, 均强制性喂食Vv菌液( $4.2 \times 10^{12}$  cfu/ml)0.6 ml/只; 对照组6只, 喂食灭菌液体培养基(Marine broth 2216)0.6 ml/只。观察小鼠一般情况, 分别于实验后12 h及48 h采血并处死8只实验组小鼠和3只对照组小鼠, 进行血液的Vv分离培养并取其消化道及重要脏器组织进行病理学观察。结果 48 h组8只小鼠, 有4只血培养结果为阳性; Vv经食道感染小鼠后导致其出现腹泻等消化道症状, 病理学结果显示实验组小鼠食道及胃黏膜上皮部分缺损, 小肠绒毛明显水肿, 结肠肠壁平滑肌溶解断裂, 消化道黏膜、黏膜下、肌层均可见不同程度的中性粒细胞浸润; 小鼠主要脏器也出现不同程度的损伤, 以肺和肾脏的广泛出血性损伤为主。结论 (1)高浓度Vv经食道进入小鼠胃组织后能部分存活, 并进入肠道繁殖, 从而引起小鼠腹泻症状, 损伤小鼠消化道组织, 并可入血引发败血症, 导致小鼠肺、肾等多脏器的和损伤, 造成小鼠死亡。(2)Vv可经消化道感染, 所致炎症性病变特点为蜂窝织性炎。

**【关键词】** 创伤弧菌; 胃肠道; 感染; 蜂窝织炎**【中图分类号】** R-332   **【文献标识码】** A   **【文章编号】** 1003—6350(2012)09—024—03

**Pathogenicity of infections with *Vibrio vulnificus* in mice through the enteron.** ZHENG Jing, WENG Yang, WANG Ming-hua. Department of Pathology, Hainan Medical College, Haikou 571101, Hainan, CHINA

**【Abstract】** Objective To study the characteristics of infections through the alimentary canal with *Vibrio vulnificus* (Vv) in mice. Methods Twenty-two KM mice (SPF) were randomly divided into two groups, the study group (n=16) and the control group (n=6). The animal model of *Vibrio vulnificus* infections through the alimentary canal was established by feeding Vv inoculum ( $4.2 \times 10^{12}$  cfu/ml, strain 1.175 8) of 0.6 ml to each mouse in the study group. And the mouse in the control group was fed with sterile culture medium (Marine broth 2216). Eight mice in the study group and three mice in the control group were killed 12 h and 48 h after treatment. The Vv from the blood were cultured, and the pathological changes of the alimentary canal and other organs were observed under microscope. Results Of the eight mice killed 48 h after treatment, four showed positive blood cultures. In the study group, The gastric and esophagus mucosa was damaged with degeneration and necrosis of the epidermic cells. The edema of small intestinal villous was also observed. The neutrophil infiltration was observed in each layer of digestive tract. And different degrees of injury were also observed in the main viscera of the mice in study group, which is the most severe in lung and kidney. The pathological changes of lung and kidney were characterized by hemorrhagia, degeneration and necrosis of the cells. Conclusion The injury of digestive tract could be induced by Vv in high concentration. Vv reproduction in digestive tract leads to primary septicemia, resulting in the death of the mice finally. Vv infection in digestive tract was characterized by Phlegmonous inflammation.

**【Key words】** *Vibrio vulnificus*; Gastrointestinal tract; Infection; Phlegmonous inflammation

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作者简介:郑 晶(1979—),女,湖北省黄冈市人,讲师,博士。

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