

# 帕金森病抑郁中西医结合诊断与治疗 专家共识(2021年版)

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帕金森病抑郁中西医结合诊断与治疗专家共识写作组

**【摘要】** 抑郁是帕金森病最常见的非运动症状,帕金森病抑郁发病机制尚未完全阐明。为规范疾病诊断体系并提高临床疗效,通过组织全国7个省、直辖市中医和西医领域相关专家进行多次讨论和修改,共同制定《帕金森病抑郁中西医结合诊断与治疗专家共识(2021年版)》(以下简称共识)。共识中西医并重,参考帕金森病、抑郁症等相关诊断标准制定帕金森病抑郁西医诊断、评估量表和西医治疗的专家共识;同时参考中医颤证、郁证等相关中医诊断标准制定帕金森病抑郁中医辨证诊断体系和辨证论治的专家共识,并针对疾病早期和进展期采取不同的中西医结合治疗方法,有确切的临床优势且安全性较高,可供临床医师参考应用。

**【关键词】** 帕金森病; 抑郁; 中西医结合疗法; 专家共识(非MeSH词)

## Expert consensus on diagnosis and treatment of depression in Parkinson's disease with integrated traditional Chinese and Western medicine (2021 edition)

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**【Abstract】** Depression is the most common non-motor symptom of Parkinson's disease. However, the pathogenesis of depression in Parkinson's disease (DPD) remains undetermined. In order to further standardize and improve clinical diagnosis and treatment of DPD, relevant domestic experts of traditional Chinese and Western medicine from Jiangsu, Anhui, Shandong, Guangdong and Tianjin, Beijing, Shanghai jointly developed "Expert consensus on diagnosis and treatment of depression in Parkinson's disease with integrated traditional Chinese and Western medicine (2021 edition)" after detailed discussions both online and offline. With integrated traditional Chinese and Western medicine, the consensus sorts out diagnosis, evaluation tools and treatment of Western medicine according to the diagnostic criteria of Parkinson's disease and depression, and traditional Chinese medicine diagnosis and treatment system based on syndrome differentiation of Parkinson's disease according to the traditional Chinese medicine diagnosis of

doi:10.3969/j.issn.1672-6731.2021.12.002

基金项目:国家重点研发计划重大慢性非传染性疾病防控研究重点专项项目(项目编号:2016YFC1306600);国家重点研发计划重大慢性非传染性疾病防控研究重点专项项目(项目编号:2017YFC1310302);江苏省2019年省重点研发计划项目(项目编号:BE201961);江苏省2020年度中医药科技发展专项项目(项目编号:2020ZX17)

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tremor syndrome and depression syndrome. Different treatment methods are provided for the early and advanced stages of Parkinson's disease according to the treatment principles of integrated traditional Chinese and Western medicine. The expert consensus is superior in clinic and relatively safe, which can be used as a reference for clinicians.

**【Key words】** Parkinson disease; Depression; TCM WM therapy; Expert consensus (not in MeSH)

This study was supported by National Key Research and Development Program Major Chronic Non-Communicable Disease Prevention and Control Research Key Special Project (No. 2016YFC1306600, 2017YFC1310302), Key Research and Development Program of Jiangsu Province in 2019 (No. BE201961), and Special Project of Traditional Chinese Medicine Technology Development Program of Jiangsu Province in 2020 (No. 2020ZX17).

**Conflicts of interest:** none declared

## 前　　言

抑郁是帕金森病最常见的非运动症状(NMS)。由于不同研究纳入对象、诊断标准不一致,文献报道的帕金森病抑郁(DPD)发病率约为40%<sup>[1]</sup>。帕金森病抑郁在帕金森病早期即呈高峰出现。临床表现为持续性情绪低落,注意力集中困难,工作和生活兴趣降低等<sup>[2-4]</sup>。长期抑郁可以加重帕金森病运动症状,形成恶性循环,严重影响患者生活质量,且增加家庭和社会经济负担,因此应早期发现并及时治疗帕金森病抑郁。

帕金森病抑郁的病因及发病机制尚未完全阐明,目前确定的是难以用一种病因和发病机制解释,更倾向于多因素作用的结果。一方面,与原发性抑郁相同,神经递质紊乱发挥重要作用,然而对于帕金森病抑郁,多巴胺和去甲肾上腺素在发病机制中的作用较5-羟色胺更重要<sup>[5-7]</sup>;另一方面,疾病自身的心因性反应亦发挥一定作用,患者无法接受帕金森病导致的生活能力和生活状态改变,易产生情感障碍。

帕金森病抑郁属于中医学颤证与郁证合病<sup>[8]</sup>。中医学有“因郁致病”和“因病致郁”之说,对于帕金森病抑郁,郁证出现于颤证之后。部分帕金森病患者前驱期即出现抑郁症状,而后再出现运动症状,貌似“因郁致病”;目前认为,与前驱期抑郁症状和多巴胺水平降低后机体启动运动代偿机制,引起多种单胺递质紊乱有关,应属于“因病致郁”范畴。总体而言,帕金森病的基本病机为肝肾两虚,风痰瘀阻<sup>[9]</sup>,而帕金森病抑郁系帕金森病导致的抑郁状态,故中医治疗帕金森病抑郁须以帕金森病的基本病机贯穿始终。

## 共识制定依据

参考美国精神障碍诊断与统计手册第5版(DSM-5)抑郁症诊断标准<sup>[10]</sup>,国际运动障碍学会(MDS)2011和2019年帕金森病非运动症状治疗循证指南<sup>[11-12]</sup>;同时参考2013年中华医学会神经病学分会心理学与行为神经病学组、帕金森病及运动障碍学组制定的《帕金森病抑郁、焦虑及精神病性障碍的诊断标准及治疗指南》<sup>[13]</sup>,2016和2020年中华医学会神经病学分会帕金森病及运动障碍学组、中国医师协会神经内科医师分会帕金森病及运动障碍专业委员会制定的《中国帕金森病的诊断标准(2016版)》<sup>[14]</sup>,《帕金森病非运动症状管理专家共识(2020)》<sup>[15]</sup>,《中国帕金森病治疗指南(第四版)》<sup>[16]</sup>,以及1992年中华全国中医学会老年医学会发布的《中医老年颤证诊断和疗效评定标准(试行)》<sup>[17]</sup>、2011年由中华中医药学会脑病专业委员会,国家中医药管理局全国脑病重点专科抑郁症协作组制定的《抑郁症中医证候诊断标准及治疗方案》<sup>[18]</sup>中有关颤证和郁证诊断与治疗标准,2017年出版的新世纪(第二版)全国高等中医药院校规划教材《中医内科学》<sup>[19]</sup>,2020年由中华中医药学会组织发布的《中医治未病·帕金森抑郁和/或焦虑专家共识》<sup>[20]</sup>、中国中西医结合学会神经科专业委员会制定的《抑郁症中西医结合诊疗专家共识》<sup>[21]</sup>。共识写作组按照循证医学原则,在分析和评价帕金森病抑郁中西医结合诊断与治疗临床研究证据的基础上,充分考虑疾病中西医结合诊断与治疗的现状和经验,兼顾疗效、风险、经济因素以及临床可操作性,制定《帕金森病抑郁中西医结合诊断与治疗专家共识》(以下简称共识),并组织江苏省、安徽省、山东省、广东省

以及北京市、上海市、天津市等中医和西医领域相关专家进行多次讨论和修改,于2020年11月28日在江苏省南京市进行了最后一次共识写作组现场讨论会并最终定稿。共识属阶段性的专家意见,今后将根据该领域的国内外学术发展进一步完善。

### 中西医结合诊断

采用西医辨病与中医辨证相结合的诊断方式,首先根据西医诊断标准确定帕金森病抑郁的辨病诊断,在此基础上通过中医审证求机、辨证分型方法进行辨证诊断。

#### 一、帕金森病抑郁的西医诊断

1. 诊断标准 目前尚无帕金森病抑郁的专用诊断标准。共识主要参照《中国帕金森病的诊断标准(2016版)》<sup>[14]</sup>和DSM-5抑郁症诊断标准<sup>[10]</sup>,同时符合上述两项标准即可诊断为帕金森病抑郁。其中,抑郁症的诊断标准为:(1)连续2周内有5项或以上下述症状,且为原有功能的改变,其中至少包括1项为①或②,不包括明显因一般躯体症状或者与心境协调的妄想或幻觉所致症状。①几乎每天大部分时间心境抑郁,主观感到悲伤或空虚或他人观察到流泪,儿童和青少年可以表现为易激惹。②几乎每天大部分时间对所有或几乎所有活动的兴趣或愉快感明显降低(主观体验或他人观察)。③未节食但体重明显下降或体重明显增加(1个月内体重变化>5%),或者几乎每天有食欲减退或增加,儿童应考虑体重未达到预期的增加。④几乎每天有失眠或睡眠增多。⑤几乎每天有精神运动性激越或者迟滞(主观感到并他人观察到坐立不安或迟滞)。⑥几乎每天感到疲倦乏力。⑦几乎每天自感无用,或者有不恰当或过分的内疚(可达罪恶妄想程度,不仅仅是因患病而自责或内疚)。⑧几乎每天有思维能力或注意集中能力减退,或者犹豫不决(主观体验或他人观察)。⑨反复有死亡想法(不仅仅是怕死),反复出现自杀意念但无特定计划或自杀未遂或有特定的自杀计划。(2)症状不符合双相情感障碍标准。(3)症状可以引起有临床意义的苦恼或者社交、职业或其他重要功能障碍。(4)症状并非由物质(如成瘾药物、处方药物)或躯体疾病(如甲状腺功能减退症)的直接生理效应所致。(5)症状不可以丧恸反应(失去亲人的反应)进行解释,症状持续>2个月,或症状特征为明显的功能障碍、病态沉

浸于自身无用感、自杀意念、精神病症状或精神运动性迟滞。其中,条目(1)为症状标准,条目(2)和(4)为排除标准,条目(3)为痛苦或功能障碍标准,条目(5)为严重程度标准。符合条目(1)的9项中至少5项(须包括①或②)且同时符合条目(2)~(5)诊断为重度抑郁;符合条目(1)的9项中2项(须包括①或②)且同时符合(2)~(5)诊断为轻度抑郁。

2. 评估量表 神经心理学测验是临床和科研工作常用的帕金森病抑郁评估量表,包括老年抑郁量表15项(GDS-15)、汉密尔顿抑郁量表(HAMD)、Beck抑郁量表(BDI)、Montgomery-Asberg抑郁等级量表(MADRS)等,其中,BDI和MADRS量表适用于帕金森病抑郁症状的筛查;GDS-15量表因具有较好的适用性且相对简洁(15个问题,每个问题2项选项)以及较高的灵敏度(81%)和特异度(91%),广泛应用于帕金森病抑郁症状的筛查,评分0~4为正常、5~8为轻度抑郁症状、9~11为中度抑郁症状、12~15为重度抑郁症状<sup>[16]</sup>。

#### 二、帕金森病抑郁的中医辨证诊断

共识主要参考《中医内科学》<sup>[19]</sup>、《中医老年颤证诊断和疗效评定标准(试行)》<sup>[17]</sup>、《抑郁症中医证候诊断标准及治疗方案》<sup>[18]</sup>中颤证和郁证诊断与治疗标准,并结合近年发表的中医药诊断与治疗帕金森病抑郁文献,再由写作组讨论最终确定。帕金森病抑郁的各证型均符合头摇肢颤、行缓拘痉、情绪低落、寡言懒动的主症,同时根据不同临床表现拟定分为6个证型。(1)肝郁风动扰神证:症见为胸闷、善太息、胁肋胀满、脘闷嗳气、症状随情绪波动、舌苔薄、脉弦,伴急躁易怒、烦热口苦、面红目赤、头目胀痛、大便干结、舌红苔黄、脉弦,属肝郁化火扰神证。(2)肾虚髓空痰蒙证:症见为眩晕或头昏,善忘易呆,困倦喜睡,腰膝酸软,身体困重,舌淡或舌红,苔多白厚腻,脉沉细。(3)痰热动风扰神证:症见为焦虑烦躁不安,胸脘痞闷,口苦口黏,失眠多梦,恶心,便秘,面色油腻,舌红,舌苔黄腻,脉弦滑或滑数。(4)血虚神衰风动证:症见为眩晕或头昏,面色萎黄,多思善虑,神疲乏力,心悸健忘,舌淡苔白,脉细弱。(5)心肾阴虚风动证:症见为形体消瘦,心慌,烦热,咽干口燥,目花干涩,耳鸣耳聋,盗汗,遗精早泄,月经不调,舌红苔少,舌体瘦小,脉细数。(6)瘀阻风动扰神证:症见为肢体疼痛,夜间尤甚,痛处拒按,面色晦暗,口唇暗或紫,肌肤时有青紫瘀斑,口

渴不欲饮水,舌黯红,舌下脉络青紫,脉涩或弦紧。

### 中西医结合治疗

帕金森病抑郁的治疗较原发性抑郁症更复杂,不仅需根据严重程度分层治疗,还需注意共病情况、抑郁与运动症状的关系、是否存在“开关”现象及其他影响因素。常用治疗方法包括抗抑郁西药、中药、中成药、针灸、心理疗法、物理治疗等。

#### 一、帕金森病抑郁的西医治疗

1. 轻度抑郁 建议采用非药物治疗,包括心理疏导、体育锻炼、睡眠指导、参与团体或社交网络活动等。对于剂末有明显抑郁的患者,可尝试左旋多巴,联合儿茶酚-O-甲基转移酶(COMT)抑制剂、单胺氧化酶B(MAO-B)抑制剂或多巴胺受体激动剂<sup>[19]</sup>。

2. 重度抑郁 参考2019年国际运动障碍学会帕金森病非运动症状治疗循证指南<sup>[12]</sup>以及国外随机对照临床试验结果<sup>[22]</sup>,推荐帕金森病抑郁的治疗药物主要为普拉克索(pramipexole)和文拉法辛(venlafaxine),循证医学证据表明为“有效”或“临床有用”,其他选择性5-羟色胺再摄取抑制剂(SSRI)如西酞普兰(citalopram),虽然目前尚缺乏有力证据证实其有效性<sup>[11]</sup>,但是由于不良反应较轻微,也考虑用于帕金森病抑郁的治疗。单胺氧化酶B抑制剂司来吉兰(selegiline)治疗帕金森病抑郁的有效性尚无明确证据支持<sup>[13]</sup>,因此临床应用时应注意监测精神症状,由于其与选择性5-羟色胺再摄取抑制剂联用可能诱发5-羟色胺综合征,因此禁止二者联用。

3. 其他 其他治疗方法还包括认知行为疗法(CBT)、重复经颅磁刺激(rTMS)等。一项随机对照临床试验显示,认知行为疗法可以有效改善帕金森病抑郁症状<sup>[23]</sup>,但是由于无法进行双盲治疗,因此循证医学证据为“可能有效”或“临床可能有用”。两项随机对照临床试验采用重复经颅磁刺激治疗帕金森病抑郁,其疗效存有差异<sup>[24-25]</sup>,因此循证医学证据为“证据不足”。由于重复经颅磁刺激治疗抑郁症是有效的,故循证医学证据为“临床可能有用”,但疗效维持时间短,需重复治疗。

#### 二、帕金森病抑郁的中医治疗

1. 治疗原则 帕金森病抑郁为帕金森病基础上伴发的抑郁,肝肾亏虚为其病理生理学基础,本虚基础上产生的气郁、风、火、痰、瘀等病理因素与肝肾亏虚相夹杂,因此,治疗始末应重视补益肝肾、治病求本,在辨证治疗的同时予以补益肝肾的药物。

共识写作组检索2005年1月至2020年12月中国知网中国知识基础设施工程(CNKI)、万方数据库和维普数据库关于帕金森病补益肝肾为基础治疗的临床研究和中医经验总结,共获得47篇文献,选取代的35篇<sup>[26-60]</sup>,并剔除重复发表、类似发表、数据不完整文献,按照中药君、臣、佐的出现频次,并结合写作组中医专家的经验,得出帕金森病抑郁补益肝肾的基础方,同时共识写作组中医专家结合郁证的致病特点加用醋柴胡、生龙骨、生牡蛎三味药材,最终得出帕金森病抑郁的基础方为天麻、钩藤、制首乌、熟地、炒白芍、柴胡、生龙骨、生牡蛎。

2. 辨证论治 (1)疏肝解郁,熄风安神:用于肝郁风动扰神证。推荐方为柴胡疏肝散(《景岳全书》)加减。常用药物有醋柴胡、川芎、炒白芍、香附、枳壳、天麻、钩藤、熟地黄、制首乌、生龙骨、生牡蛎、茯神。肝郁化火扰神证推荐方为丹栀逍遥散(《内科摘要》)加减。常用药物有牡丹皮、栀子、黄芩、醋柴胡、川芎、炒白芍、香附、枳壳、天麻、钩藤、制首乌、生龙骨、生牡蛎、茯神。(2)补肾填精,开窍化痰:用于肾虚髓空痰蒙证。推荐方为涤痰汤(《证治准绳》)加减。常用药物有姜半夏、陈皮、茯苓、胆南星、枳实、党参、石菖蒲、竹茹、大枣、制首乌、天麻、钩藤、炒白芍、醋柴胡、生龙骨、生牡蛎。(3)清热化痰,熄风安神:用于痰热动风扰神证。推荐方为黄连温胆汤(《六因条辨》)加减。常用药物有黄连、法半夏、茯苓、陈皮、枳壳、竹茹、胆南星、制首乌、天麻、钩藤、炒白芍、醋柴胡、生龙骨、生牡蛎、茯神。(4)补血养心,熄风安神:用于血虚神衰风动证。推荐方为归脾汤(《济生方》)加减。常用药物有黄芪、白术、龙眼肉、酸枣仁、党参、当归、远志、制首乌、天麻、熟地黄、炒白芍、醋柴胡、生龙骨、生牡蛎、茯神。(5)补益心肾,熄风安神:用于心肾阴虚风动证。推荐方为天王补心丹(《摄生秘剖》)加减。常用药物有党参、茯苓、玄参、桔梗、远志、当归、五味子、麦门冬、柏子仁、生地黄、制首乌、天麻、钩藤、熟地黄、炒白芍、醋柴胡、生龙骨、生牡蛎。(6)活血熄风,定颤安神:用于瘀阻风动扰神证。推荐方为血府逐瘀汤(《医林改错》)加减。常用药物有桃仁、红花、当归、生地黄、川芎、桔梗、赤芍、枳壳、制首乌、天麻、钩藤、熟地黄、醋柴胡、生龙骨、生牡蛎。

3. 针刺疗法 针刺等体表刺激疗法已广泛应用于临床实践。无论是手工针刺还是电针刺激特定穴位均可缓解帕金森病运动和非运动症状,尽管

尚缺乏循证医学证据较高的临床研究,但在实际工作中有一定的应用价值。推荐方案为:(1)针刺特定穴位,取哑门、双侧风池、完骨、天柱穴<sup>[61-62]</sup>。(2)以电针刺激头部八穴为主,取双侧风池、头临泣、率谷、百会、印堂穴为主,配穴取肩髃、曲池、太溪、太冲、足三里、关元、三阳络<sup>[63]</sup>。(3)针刺结合药物治疗:如服用普拉克索的基础上针刺双侧风池、百会、印堂穴<sup>[64]</sup>。

### 三、帕金森病抑郁的中西医结合治疗

临床主要根据帕金森病分期和抑郁程度予以中西医结合治疗。

**1. 疾病早期治疗原则** 帕金森病早期运动症状较轻微时,轻度抑郁患者可优先采用中药治疗以及认知行为疗法、重复经颅磁刺激等,如果效果欠佳,可选择普拉克索等多巴胺受体激动剂,有改善运动症状和改善抑郁症状的双重作用<sup>[65]</sup>;对于重度抑郁患者,普拉克索等多巴胺受体激动剂应达足剂量,同时根据循证医学证据推荐帕罗西汀或文拉法辛等抗抑郁药联合用药。中医治疗采用中药基础方,并对抑郁证型进行辨证论治。同时应同步采用其他治疗方法。

**2. 疾病进展期治疗原则** 帕金森病出现运动并发症如剂末现象和异动症时,首先优化左旋多巴治疗,减轻因运动并发症导致的抑郁,注意多种药物的合理搭配,积极减少引起抑郁的危险因素。采取个性化心理疗法和物理治疗,让患者家属参与疾病管理和药物管理。轻度抑郁患者可继续服用普拉克索等多巴胺受体激动剂,同时加用中药基础方;重度抑郁患者可增加文拉法辛或其他选择性5-羟色胺再摄取抑制剂如帕罗西汀等。中医治疗在西医治疗的基础上添加中药基础方,并对抑郁证型进行辨证论治。

**3. 中西医结合治疗的优势** 帕金森病抑郁相关影响因素较复杂,药物改善运动症状和抗抑郁具有较强的循证医学证据,但治疗后完全无抑郁症状的比例<50%,大多数患者仍遗留轻度抑郁症状,部分患者无效。改善疲劳、食欲不振、便秘、口干、睡眠障碍等抑郁相关症状的疗效欠佳,部分患者不良反应明显<sup>[66]</sup>。抗抑郁药不良反应发生率达30%~60%<sup>[67]</sup>。中医治疗通过辨证论治,整体调节,降低患者对环境应激的敏感性,同步调治抑郁相关症状等发挥积极预防与治疗作用。然而对于重度抑郁,则存在难以快速缓解、证型分散、诊断与治疗标准

不统一等问题。由此可见,中西医治疗帕金森病抑郁各有优势和不足,需优势互补。共识写作组通过检索2015年1月至2020年11月CNKI、万方数据库和维普数据库,共获得7篇中西医结合治疗帕金森病抑郁的随机对照临床试验计500例患者<sup>[68-74]</sup>,结果显示,中西医结合治疗协同增效,减少不良反应,可以有效改善帕金森病运动症状和抑郁症状,提高患者生活质量,并最终提高临床治愈率和安全性。

**4. 中西医结合治疗的安全性** 中西药联用配伍禁忌十分复杂,协同增效的同时,亦有不良反应增加的可能。目前尚缺乏大样本中西医结合治疗帕金森病抑郁不良反应的临床研究,但任何治疗均存在有效性和安全性两方面,需明确中西药药性,尽可能明确药物所含化学成分、药理作用和体内代谢过程,方能得出联合用药的最佳组合。抗抑郁药的常见不良反应包括消化道症状、锥体外系症状、性功能减退、自主神经功能紊乱、体重增加等,因此有可能增加帕金森病运动和非运动症状,应严格按照药品说明书服药,注意药物配伍禁忌<sup>[75]</sup>,服药过程中注意观察不良反应,及时处理。中药的安全性明显优于西药,但须遵循辨证论治原则,综合考虑年龄、个体差异等因素,遵守配伍禁忌、用法用量,尽量避免不良反应的危险因素<sup>[76]</sup>。帕金森病抑郁患者如果采取较长时间的中西药联用,应注意定期复查,必要时进行相应的实验室检查,根据病情及时调整药物种类和剂量,避免不良反应的发生。

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利益冲突 无

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(收稿日期:2021-11-18)

(本文编辑:彭一帆)

## · 小词典 ·

## 中英文对照名词词汇(二)

- 第二代测序技术 next-generation sequencing(NGS)  
 电子病历 electronic health record(EHR)  
 $\beta$ -淀粉样蛋白 amyloid  $\beta$ -protein(A $\beta$ )  
 动物流畅性测验 Animal Fluency Test(AFT)  
 多导睡眠图 polysomnography(PSG)  
 额叶功能评价量表 Frontal Assessment Battery(FAB)  
 额叶行为量表 Frontal Behavioral Inventory(FBI)  
 儿茶酚-O-甲基转移酶 catechol-O-methyltransferase(COMT)  
 翻转角 flip angle(FA)  
 反应时间 reaction time(RT)  
 反转时间 inversion time(TI)  
 非语言性认知功能评价量表  
 Non-Language-Based Cognitive Assessment(NLCA)  
 非运动症状 non-motor symptom(NMS)  
 符号数字转换测验 Symbol Digit Modalities Test(SDMT)

- Rey-Osterrieth 复杂图形测验  
 Rey-Osterrieth Complex Figure Test(ROCFT)  
 改良 Rankin 量表 modified Rankin Scale(mRS)  
 高斯随机场 Gaussian random field(GRF)  
 工具性日常生活活动能力量表  
 Instrumental Activities of Daily Living(IADL)  
 功能磁共振成像  
 functional magnetic resonance imaging(fMRI)  
 功能性近红外光谱成像  
 functional near-infrared spectroscopy(fNIRS)  
 广泛结节型髓母细胞瘤  
 medulloblastoma with extensive nodularity(MBEN)  
 国际标准化比值 international normalized ratio(INR)  
 国际血管性行为与认知障碍学会  
 International Society for Vascular Behavioral and Cognitive Disorders(VASCOG)  
 国际运动障碍学会 Movement Disorder Society(MDS)