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医学影像物理

磁共振影像技术在卒中后抑郁疾病的研究进展

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【摘 要】卒中后抑郁(Post-Stroke Depression, PSD)是由缺血性卒中引起的情感障碍性疾病,卒中后发病率高,危害大。为了揭示PSD病因学机制,近年来不少研究小组利用磁共振成像技术对该疾病进行了多角度研究。本文分别从磁共振结构成像、磁共振弥散张量成像以及静息态磁共振功能成像对该领域的研究进展进行了综述,并讨论了影像学发现与PSD病理机制的关系,最后总结了基于磁共振成像的PSD研究成果并对未来的研究方向进行了展望。

【关键词】卒中后抑郁;磁共振成像;弥散张量成像;静息态功能成像;综述
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Research progress on MRI technology in post-stroke depression

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Abstract: Post-stroke depression (PSD) is defined as a mood disorder due to ischeemic stroke. PSD has a high incidence and great damage. In order to disclose the etiological mechanism of PSD, magnetic resonance imaging (MRI) technology is used by multiple groups to research on PSD from different perspectives in recent years. In this paper, the research progress of structural MRI, diffusion tensor imaging and resting-state functional MRI in PSD is reviewed. The relationship between the imaging results and the pathological mechanism of PSD is also discussed. Finally, the research results of PSD based on MRI are summarized and the prospect of the study is put forward.

Key words: post-stroke depression; magnetic resonance imaging; diffusion tensor imaging; resting-state functional magnetic resonance imaging; review

前 言

卒中后抑郁(Post-Stroke Depression, PSD)是指由缺血性卒中引起的一种情感障碍性疾病,属于一种继发性抑郁,通常表现为情绪低落、活动功能减退、思维功能迟缓,39%~52%的卒中患者在卒中后前5年内出现过抑郁症状[1]。1977年,Folstein等[2]首次发现卒中患者中抑郁发病率显著高于由矫形外壳损伤引起的抑郁发病率,该疾病严重影响患者的社交功能与认知功能,乃至增加卒中患者的死亡率。PSD的病因学机制并无定论,目前认为该疾病与血管性抑郁相关[3]。依据DSM-IV国际标准的定义,PSD的确认需满足患者卒中后出现包括情绪低落在内的4种情绪失调症状且持续两周以上。目前PSD的流行病学、治疗方案的研究较多,而病因学机制方面的研究匮乏且缺少定论。

磁共振成像(MRI)技术的出现与发展,为无创观察大脑内部结构提供了新的可能,已经越来越多地应用到脑血管疾病与精神心理疾病的临床检查与诊断。随着MRI技术的发展,可量化成像方法为神经科学研究和临床应用提供了更多可能性,如弥散张量成像(Diffusion Tensor Imaging, DTI)以及静息态功能成像(Resting-State Functional MRI, rs-fMRI)技术的出现为脑疾病研究提供了从白质纤维性状、功能连接到生物代谢的多角度研究工具。这些MRI新

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技术在PSD的发病机理、病灶定位、早期诊断与临床预后等方面具有重大意义。本文将以MRI技术在PSD疾病的研究为核心，分别从不同的成像方式概述MRI在PSD疾病的研究和临床应用的现状，包括磁共振结构成像（sMRI）、DTI、rs-fMRI在PSD疾病研究的进展，并重点综述国际上不同研究小组利用以上MRI技术在PSD领域的研究工作，最后讨论当前领域面临的挑战，并对未来可能的研究方向进行展望。

1 sMRI

常规sMRI（T_1/T_2加权成像、FLAIR成像等）凭借其高分辨率能够清楚地揭示PSD患者的梗塞灶位置与大小，因此该成像方式在PSD领域的研究重点关注疾病与卒中部位及其偏侧性的关系。Bhogal等于2004年综述了PSD与病灶偏侧性关系，结果表明病灶部位与疾病的关系存在较大争议。

从脑科学研究角度上，关注梗塞位置、大小与PSD的关系将有助于对该疾病发病机制的深入理解[4]；从临床角度上，提前知道患者发展为PSD的风险将可以帮助卒中患者的治疗与康复[5]。Altieri等[6]对105个轻度卒中病人（NIHSS Score<5）做了前瞻性研究，其中43（41%）个病人在梗塞发作30个月内发展为PSD。研究结果发现卒中发展为PSD的风险与卒中严重程度无关，同时指出PSD患者的4类梗塞灶位置（前脑、后脑、深灰质和小脑）与PSD无关，且PSD不存在偏侧性现象，由此推断PSD的发展与患者对于卒中后痛苦症状的自发反应相关。Zhang等[7]利用T_2加权成像对梗塞位置、大小、偏侧性与PSD的关系做了系统分析，结果显示来自内囊后肢、内囊膝部、颞叶中皮层到皮层下结构的病灶以及急性梗塞灶数量与PSD相关，推测是因为顶叶、内囊膝、内囊前肢所属的前额叶-皮层下神经回路与颞叶、内囊后肢所属的额叶-内囊-纹状体环神经回路都与情绪、认知、行为控制有关，提示特定位置的病灶可能会增加PSD的概率。Choi-Kwon等[8]同时对PSD与卒中后情绪失禁患者进行病灶位置研究，结果仅发现卒中后情绪失禁患者在基底节-内囊-脑桥片区发生梗塞的概率显著增加，并推测该结果与该区域汇集了大量5-羟色胺能神经纤维有关，基底节-内囊-脑桥片区的损伤可能导致5-羟色胺神经递质分泌降低从而引起抑郁症状。最近，Shi等[9]对收集的PSD病例进行了更细致的病灶分类（早期抑郁发作组与晚期抑郁发作组），但两个组别都未发现病灶位置或偏侧性与PSD存在相关性。

sMRI同样支持利用脑功能区图谱对大脑神经回路进行活体直接定位。神经回路由于比单纯的脑解剖学结构更具有与脑功能连接传递的相关性，在神经心理性疾病的作用逐渐受到重视。Vataja等[4]首次针对脑神经回路与PSD的关系提出猜想，发现PSD患者中位置涉及到前额叶-皮层下回路的病灶具有相当高的比例。随后，Terroni等[10]采用sMRI手段分析了68个PSD患者的神经回路，发现涉及到大脑左侧的边缘系统-皮质-纹状体-苍白球-丘脑（LCSPT）神经回路的病灶大小与急性卒中患者具有显著相关性，该发现与Drevets等[11]通过动物实验证实LCSPT神经回路在重度抑郁症具有独特作用的结果相一致。然而该研究提取LSCPT神经回路的方式是利用Brodmann脑功能区图谱，而Brodmann图谱由于并不包含皮层下神经解剖结构使得对LSCPT神经回路的分析并不完整，且Brodmann图谱不能为不同脑皮层区的研究提供可靠的横向对比[12]。

此外，不同种族可能会对病灶与PSD的关系产生不同影响。Zhang等[13]针对102个中国卒中患者进行病灶偏侧性研究，在筛选出的25个PSD患者中并未发现病灶偏侧性现象。Rajashekaran等[14]针对109个印度PSD患者的研究发现病灶区更多分布在左侧前额叶-皮层下回路区域。Metoki等[15]结合T_2加权成像与FLAIR成像对71个日本PSD患者的研究发现病灶分布在额叶与颞叶的梗塞病人更易发展为抑郁。此外，5-HTTLPR基因对个体的抑郁水平及神经回路的影响均具有显著的种族差异性，且抑郁症的治疗需考虑种族差异性[16]。考虑到5-HTTLPR与PSD的发病率也密切相关，研究认为种族差异性对PSD影像学结果的影响不可忽视[17]。

T_2或FLAIR图像上的脑白质高信号（White Matter Hyperintensity, WMH）由小血管病变（Small-Vessel Disease, SVD）引发，被认为是卒中患者梗塞灶的起源[18]。因此，推测WMH在PSD的发病机制中可能参与了重要作用。Vataja等[19]最早针对109个PSD患者分析了不同白质区域（脑室周、分水岭、半卵圆中心和皮质下）WMH与PSD的关系，但并未发现两者存在明显相关性。Tang等[20]针对78个PSD患者脑室周与皮质下区域WMH的严重程度做了4级评分[21]，结果发现PSD患者组别存在严重的皮质下区域WMH。类似的，脑室周区域的WMH被发现与卒中患者的整体认知损伤相关[22]，而老年抑郁症患者更容易发现皮质下区域的WMH[23]。对此，一种可能的解释是皮质下区域的损伤主要阻断了较短的联络纤

维，而脑室周区域的损伤阻断了较长的联络纤维，从而更加影响卒中后神经可塑性的恢复程度[24]。另一种解释是脑室周区域的损伤会导致血管收缩反映障碍，进而产生血流灌注不足，而皮质下区域损伤与微血管病变相关[25]。然而该研究回归分析中缺少对协变量的校正，推测患者身体障碍、认知功能损伤等其它因素可能参与到了调节卒中与抑郁症状的关系[26]。此外，利用T_2*图像检测PSD患者脑微出血灶（Cerebral Microbleeds, CMB）的研究同样发现了PSD受试群体中，PSD患者中包含的CMB组别相比无CMB组别显示出更高的抑郁评分（P=0.01）[27]。由于CMB不仅与血铁黄素沉积有关，而且会引起周围神经细胞坏死，推测当更多的细胞坏死影响到额叶-皮层下回路时将导致抑郁症状的升级[28]。本文将近年来发表的基于sMRI的PSD相关研究结果汇总于表1。

表1 基于sMRI的PSD研究

Tab.1 Study of PSD based on sMRI

Reference	Study plan	History of depression excluded	Severe aphasia excluded	Assessment of PSD	Subject	Key result
Vataja (2004)[4]	Lesion location & WML	Y	Y	DSM-IV	PSD: 26; N-PSD: 44	Lesions affecting the prefronto-subcortical circuits were correlated with PSD.
Altieri (2012)[6]	Lesion location	Y	Y	DSM-IV	PSD: 43; N-PSD: 62	No correlation was observed between lesion site or side and the development of PSD.
Zhang (2012)[7]	Lesion location	Y	Y	DSM-IV	Ma-PSD:29; Mi-PSD:10; NC:124	Lesions at posterior limb and genu of internal capsule and the temporal lobe may correlate with the PSD.
Choi-Kwon (2012)[8]	Lesion location	Y	Y	BDI score	PSD: 70; N-PSD: 438	Locations which were closely related to PSD were the basal ganglia/internal capsule and the pons.
Shi (2015)[9]	Lesion location	Y	NG	DSM-IV	PSD: 221; N-PSD: 334	No correlation was observed between lesion site or side and the development of PSD.
Terroni (2011)[10]	Lesion location	Y	Y	DSM-IV&WHO-1989	PSD: 21; N-PSD: 47	PSD was etiologically related to the disruption of the left LCSPT circuit.
Zhang (2013)[13]	Lesion location	Y	Y	HAMD& WHO-CIDI3.0	PSD: 25; NC: 66	No correlation was observed between lesion site or side and the development of PSD.
Pooja (2013)[14]	Lesion location	NG	NG	DSM-IV	PSD: 28	Left-sided cortical infarcts and sub cortical infarcts showed some association with PSD.
Metoki (2016)[15]	Lesion location	Y	Y	JSS-D	PSD: 71; N-PSD: 350	Frontal and temporal infracts were significantly independent risk factors of early PSD.
Vataja (2001)[19]	Lesion location & WML	NG	NG	DSM-IV	PSD: 275; N-PSD: 211	No correlation was observed between WML and the development of PSD.
Tang (2010)[20]	Lesion location & WML	Y	Y	DSM-IV	PSD: 78; N-PSD: 78	Severe deep WMH remained an independent predictor of PSD.

PSD: Post-stroke depression; MRI: Magnetic resonance imaging; WML: White matter lesion; DSM: Diagnostic and statistical manual of mental disorders; Y: Yes; N: No; WMH: White matter hyperintensity; WHO: World health organization; BDI: Beck depression inventory; CIDI: Composite international diagnostic interview; NG: Not given; NC: Normal control; N-PSD: Stroke patients without depression; Ma-PSD: Post-stroke depression with major depression; Mi-PSD: Post-stroke depression with minor depression; JSS-D: Japan stroke scale-depression; sMRI: Structural resonance imaging

2 DTI

DTI是目前唯一能无创绘制活体大脑白质神经纤维通路的方法。该技术利用组织中水分子弥散的各向异性，能够探测组织微观结构的成像方法，能够从若干特征性参数变化反映中枢神经系统正常或异常改变。脑白质的水分子弥散各向异性是由于平行

走行的髓鞘所致，脑白质的弥散在平行神经纤维方向最大，这一特性用彩色标记可反映出脑白质的空间方向性。基于这样的弥散特性，DTI可以提供各向异性分数（Fractional Anisotropy, FA）、表观扩散系数（Apparent Diffusion Coeffieient, ADC）等。相比于传统的sMRI，DTI能从若干图像特征性参数变化中反映中枢神经系统正常或异常改变，为医生的诊断和治疗提供更具功能性的生理影像。在不同病理条件下，脑白质病变部位的弥散特性指标与正常组织指标有不同程度的量化差别，这些差别可以借助DTI技术辅助进行PSD的病理学机制研究与早期诊断。

通过提取感兴趣区域（Region of Interest, ROI）的方法，DTI技术能够从白质纤维束完整性的角度更深入地探寻WMH对PSD发展的影响。Taylor等[29]研究小组首先通过证实老年抑郁症患者常伴随出现的WMH区域的FA值下降与ADC值上升，基于白质纤维束完整性遭受破坏的理论建立了WMH的脑白质微结构损伤的生理学解释；2007年，该小组利用提取ROI方法发现82个老年人群体中前脑WMH体积与额叶、中央区白质FA和ADC信号存在相关，首次证实了大脑缺血高信号灶与更大范围的白质结构异常改变存在关联[30]。理论上，局部的缺血高信号灶若中断了影响情绪调节或认识功能的神经回路，将会通过直接性的轴突损伤或非直接的远端损伤机制引起更大范围的失神经效应[31]。因此sMRI发现的缺血高信号灶只是大脑损伤程度的“冰山一角”，而DTI技术则能够揭示sMRI检测不到的远端白质结构异常，为PSD患者情绪调节回路受损的理论提供新的依据。最近，我们利用FA、ADC与径向弥散性（Radial Diffusivity, RD）的多种信号分布特征分析PSD患者梗塞灶以外的脑解剖学结构变化，发现扣带回的结构异常变化与PSD的发病机理具有紧密联系[32]。该研究的结果将有可能为PSD的影像学诊断提供生物标记。

利用基于体素的分析方法（Voxel Based Analysis, VBA）和基于纤维束的空间统计（Tract Based Spatial Statistics, TBSS）能够更全面地发挥DTI技术在PSD研究中的价值。VBA主要利用统计推断来描述多个被试之间的脑形态学差异，通过空间标准化、图像平滑、统计建模与假设检验等步骤实现全脑弥散特性的定量分析[33]。Yasuno等[34-35]通过对卒中患者与健康对照的VBA组间分析发现，患者组大脑双侧内囊前肢的FA值显著下降，RD不变，且急性梗塞发病6个月后该结构FA值产生了轻度上升并且与抑郁评分的下降具有相关性。一般认为，内囊前肢是额叶-皮层下回路的一个节点，与皮质和皮层下结构都有广泛的结构连接[36]。值得注意的是，该研究中卒中患者的梗塞灶并不包含内囊前肢，因此该结构的FA与RD的联合变化模式暗示梗塞灶导致远端结构的神经细胞集中退化（沃勒变性）[37]而非失髓鞘[38]。此外，结合内囊前肢的微结构损伤与重度抑郁症的相关性，推测内囊前肢白质纤维的异常改变可能导致卒中患者负面情绪的出现[39]。针对VBA方法在各向通行滤波后无法保证某一体素的信息仍保留对应解剖结构信息的局限性，TBSS方法则可以通过将受试群体FA图像配准到目标模板后提取脑白质纤维束，可得到大脑骨架[40]。利用该方法，Brookes等[41]发现具有SVD的PSD患者的全脑白质纤维束平均FA值的下降与抑郁症状相关，该结果提示白质损伤可作为SVD与抑郁的调节因子。

由于DTI可以根据水分子各向异性弥散方向追踪白质纤维束走向，因此可以获得脑区之间的白质纤维的结构位置[42]，描绘出大脑内部结构连接的特点，从而构建出脑结构网络[43]。在脑结构网络中，可将特定的脑区表示成一个点，脑区间的白质纤维连接强度表示为边[44]，用图论分析对脑网络的拓扑属性进行全面描述[45]。目前已有基于1 000节点构造的大脑结构连接网络图谱[46]，并发现人脑具有“小世界”性质[47]，并且节点度服从幂律分布。借助该技术，Yang等[48]基于40个PSD患者的FA值，筛选了自由度与抑郁评分（Hamilton Rating Scale, HAMD）显著相关的17个网络节点（包括双侧上纵沟、双侧岛叶、双侧尾状核、双侧梭状回、双侧楔前叶、双侧后扣带回、左侧上纵束、右侧壳核等）构建抑郁相关子网络，并进行了网络拓扑分析，其结果表明抑郁子网络的局部效率下降是卒中后重度抑郁的风险因素（relative risk=0.84）（P=0.027）。该结果提示卒中导致的大脑局部神经组织损伤会引起该区域的结构连接退化，进一步印证了情绪相关网络的损伤可能导致PSD症状的出现。

3 rs-fMRI

近年来，rs-fMRI为检测认知与情绪失调提供了有效的新工具。相比于传统的基于任务的脑功能成像，rs-fMRI既不需要复杂的任务激发设备，也不需要患者的主动配合，因此非常适合伴随物理或认知功能损伤的PSD患者进行成像[49]。Wang等[50]首次通过rs-fMRI技术提取大脑感觉运动区网络的自发低频血氧依赖水平（Blood Oxygen Level-Dependent, BOLD）波动，从而获取其功能连接（Functional Con-

nectivity, FC)。FC被认为是解剖学上的分离,但功能相关脑区之间的自发波动信号的时域相关性,而这些相互具有FC的脑区集合可构建特殊的脑功能网络[51]。

目前被探索最为广泛的脑功能网络是默认网络(Default Mode Network, DMN)[52-54]。DMN已被证实和走神、自我参照处理[55]以及认知与情感处理相关[56]。同时,抑郁患者的DMN已观察到了受损的FC,这进一步强化了关于DMN在情绪失调的发病机理中起到关键作用的假设[57]。侯晶晶等[58]研究发现PSD患者的多个脑区(双侧额中回、左侧岛叶、左侧尾状核、左侧海马、右侧扣带回等)存在异常升高或降低的局部一致性(Regional Homogeneity, ReHo),而这些区域与DMN包含的区域吻合,提示DMN异常可能参与到PSD的发病机制中,然而该研究的受试对象缺少非抑郁的卒中病人作为对照。Lassalle-Lagadec等[59]在研究中发现,卒中患者在发病10 d后的焦虑严重程度与中央颞叶和脑中前扣带的FC显著相关(P<0.01);而在卒中发作3个月后,PSD患者的HAMD与左侧中央颞叶和楔前叶的FC显著相关(P<0.01)。该结果为早期DMN的FC损伤与卒中后病人情绪失调风险之间的联系提供了支持,并提示卒中后早期的焦虑表现相比早期的抑郁表现更能促成后期的抑郁症状[60]。不足的是,该研究仅使用了1个独立分量分析(ICA)识别DMN,结合老年人群体中rs-fMRI检测的BOLD信号拥有多个ICA分量的发现,该研究的有效性还需进一步验证[61]。

另一方面,大脑情感网络(Affective Network, AN)在PSD发病机理中的作用也受到关注。Zhang等[62]选取前扣带回作为AN的种子节点,研究发现PSD患者AN的FC相比于非抑郁组合健康对照组有显著改变,并且FC值与PSD患者的HAMD相关(P=0.05),提示AN的损伤将增加卒中病人在亚急性阶段发展为抑郁的风险。国内学者也有一致的发现。朱祖福等[63]利用rs-fMRI技术针对PSD与非抑郁脑梗患者的ReHo值进行对比,发现情绪回路状态异常与PSD的产生具有紧密联系。本文将近年来发表的基于DTI与rs-fMRI的PSD相关研究结果汇总于表2。

表2 基于DTI与rs-MRI的卒中后抑郁研究

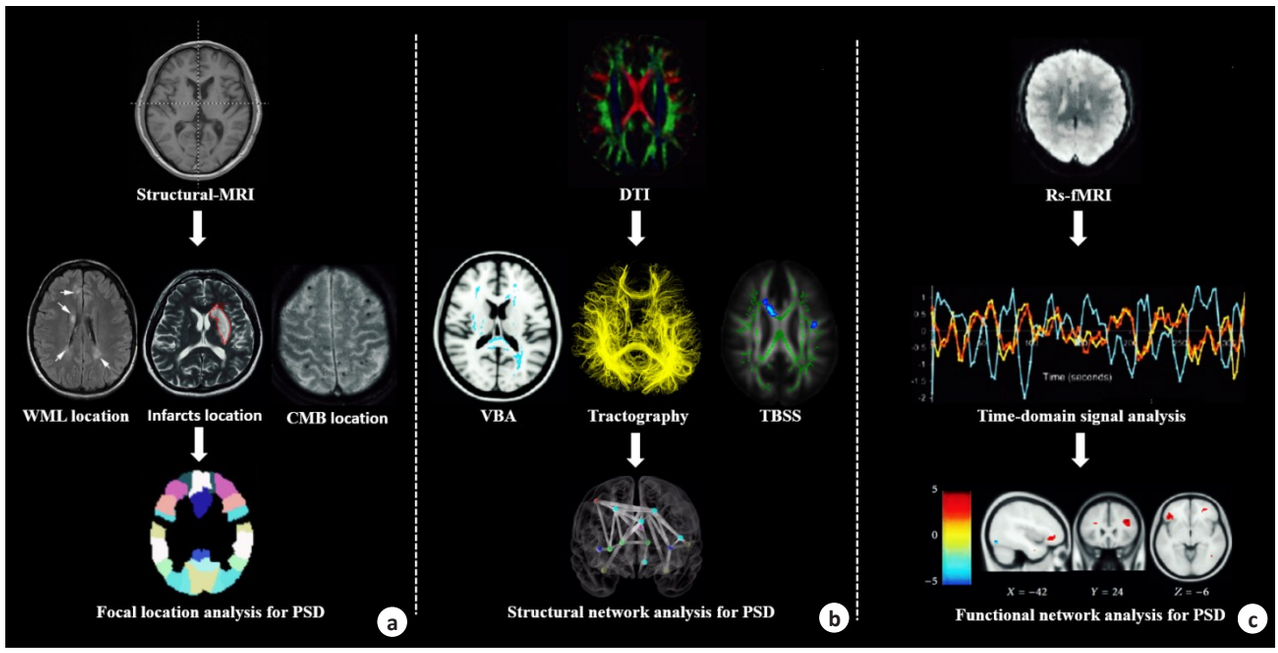
Tab.2 Study of PSD based on DTI and rs−fMRI

Reference	Study plan	History of depression excluded	Severe aphasia excluded	Assessment of PSD	Subject	Key result
Ye (2016)[32]	DTI	N	N	NG	PSD: 22; NC: 20	Neuronal loss occurred in cingulate cortex of PSD patients.
Yasuno (2014)[34]	DTI & VBA	Y	NG	DSM-IV & WHO-1989	PSD: 18; NC: 22	FA reduced in the anterior limb of the internal capsule of PSD patients.
Yasuno (2014)[35]	DTI & VBA	Y	NG	DSM-IV & WHO-1989	PSD: 29; NC: 37	A significant correlation was found between the increased ratio of FA and the depression scale score.
Brookes (2014)[41]	DTI & TBSS	NG	NG	GDS	SVD: 100; N-SVD: 50; NC: 203	White matter damage detected on DTI mediated the association between SVD and depression.
Yang (2015)[48]	DTI & network analysis	Y	Y	DSM-IV & HAMD	Ma-PSD:14; Mi-PSD:26; NC:76	Decreased local efficiency of the subnetwork was a significant risk factor for Ma-PSD.
Hou (2011)[58]	rs-fMRI & ReHo	Y	Y	DSM-IV & HAMD	PSD: 13; NC: 13	Many brain regions had abnormal functions in acute ischemic PSD.
Lassalle (2012)[59]	rs-fMRI & FC	Y	Y	DSM-IV & HAMD	PSD: 24	A dysfunction of DMN functional connectivity was associated with PSD.
Zhang (2014)[62]	rs-fMRI & FC	Y	Y	DSM-IV & HAMD	PSD:26; N-PSD:24; NC:24	Dysfunction of the affective network may cause the development of PSD.
Zhu (2012)[63]	rs-fMRI & ReHo	Y	Y	DSM-IV & HAMD	PSD: 13; NC: 13	PSD had resting-state neural circuit dysfunction.

DTI: Diffusion tensor imaging; rs-fMRI: Resting-state functional MRI; ReHo: Regional homogeneity; HAMD: Hamilton rating scale; DMN: Default mode network; VBA: Voxel based analysis; FA: Fractional anisotropy; TBSS: Tract based spatial statistics; SVD: Small-vessel disease; FC: Functional connectivity; GDS: Geriatric depression scale

4 讨论和展望

MRI技术凭借其多种成像模态与图像后处理方式，能够结合人脑解剖学结构、白质纤维完整性以及功能连接等不同角度综合探索PSD的病理定位、风险因素与发病机制（图1）。本文综述了近年来基于MRI技术的PSD神经影像学重要发现。这些发现尽管为该疾病的影像学特点提供了部分神经生理学解释，但仍存在诸多争议。



a: Lesion location (WML, infarcts and cerebral microbleeds) analysis of structural MRI images; b: VBA, TBSS and tractography-derived depression-related sub-network analysis based on DTI; c: PSD functional network analysis based on rs-fMRI blood oxygen level-dependent signals

图1 针对PSD的MRI成像与分析技术

Fig.1 MRI and analysis technology on PSD

对于PSD的病因学机制研究，血管性抑郁可作为PSD的疾病参照。血管性抑郁被定义为由慢性缺血性损害导致的精神活动迟滞、常伴发认知障碍的抑郁综合症。尽管血管性抑郁通常与体积较小的SVD相关，PSD大多由更大体积的梗塞灶引发，但研究发现两种疾病在执行功能失调、高于老年抑郁症的能力障碍严重程度等方面具有很高的相似性[64-67]。血管性抑郁的发病机制目前包含“失联合综合症假说”、“低灌注假说”以及“炎性反应假说”[68]。梗塞病灶与受损神经回路关系的一系列研究发现[11, 14, 19, 30, 34-35]，也在某种程度上应证了“失联合综合症假说”，即特定位置的血管及其周围神经组织损伤相比其余位置更能决定抑郁症状的发生[31]。此外，WMH不仅与PSD的发生频率具有相关性[20, 30]，也可作为血管性抑郁的风险因子[69]。然而有研究表明，心血管风险因素对于血管性抑郁与PSD的影响并不一致[70]。并且当个体大脑特定白质纤维束的损伤（包括扣带回、钩束、上纵束等）积累到超过一定“阈值”时，会立刻触发血管性抑郁的发生[71]。然而PSD是否也符合该“阈值”模型尚缺少相关研究，针对这两种疾病机理之间的确切关系还有待进一步探索。

目前学界对于卒中患者的梗塞灶中断特定神经回路从而诱发抑郁症状的假说已逐渐上升为共识，然而神经回路损伤如何作用于卒中病人的情绪失调还需要进一步的神经生理学解释[72]。神经回路通过神经元与突触传递生物电信号能够单独地执行某些功能，其损伤可能导致某些心理或精神失调现象的发生。例如连接前额叶、丘脑、杏仁核与基底节等结构的LCSPT神经回路出现信息传导不畅是强迫、焦虑和压抑的病理原因之一[73]。神经递质是神经回路信息传导的重要一环，已有研究发现去甲肾上腺素下降[74]与前扣带回中谷氨酸的异常改变[75]和PSD的严重程度相关。利用MRI多模态成像技术与遗传学方法，采用影像遗传学的研究策略，将在未来加速探

索神经递质系统单基因及基因通路对影像学内表型的作用，更深入地揭示PSD神经回路的损伤机制。

此外，现有的研究还存在一些普遍的方法问题：(1)PSD的诊断标准不一致，患者需符合DSM-IV标准或世界卫生组织WHO-CIDI 3.0标准才能被诊断为PSD，然而不同地区的研究小组沿用了不同的诊断标准[8, 15, 41]；(2)PSD患者常伴随着抑郁、焦虑、冷漠、认知障碍、失语、狂躁、精神错乱等症状[1]，然而失语症患者常因无法正常接受HAMD测试而被剔除出受试群体，导致样本偏差；(3)受试PSD患者常缺乏对于住院病人与社区病人、急性与亚急性梗塞、轻度与重度抑郁的区分，而这些因素对于MRI扫描结果的影响不可忽视，例如住院患者与急性卒中患者的病灶多位于左侧，社区患者与慢性期卒中患者的病灶多位于右侧[76]，抑郁子网络只与PSD重度抑郁患者而非轻度抑郁患者具有相关性[48]等；(4)对PSD受试进行MRI扫描的时间点与HAMD时间点缺少一致性；(5)PSD的轻度抑郁症状是否应当用药存在争论[34]，导致不同研究的用药标准有所区别。以上问题将不可避免地使MRI研究结果产生偏差，需要在今后统一标准。

近年来随着人类基因组计划的不断发展、影像技术的不断革新以及临床数据的不断积累，精准医学将可能通过对PSD患者的组学、组织病理学与影像学的联合检测，为其提供个性化的最优治疗方案。在精准医学中，MRI技术扮演着重要角色。MRI多模态成像的影像学数据结合机器学习策略可为神经类疾病的诊断准确率提升约20%[77]。此外，通过建立影像学特征信息（大脑形态学、结构与功能变化）与基因表达的特殊模式之间的关联，将可能使MRI临床扫描替代依赖于活体组织切片的基因表达微阵列检测，更好地服务于PSD的子类型筛查与临床干预[78]。

尽管MRI成像技术已经改变了人们对PSD的理解，但该疾病的研究仍然处于进展中，相信MRI成像及其后处理技术的不断发展将为该疾病的研究提供更加精准的解读。包含脑结构、弥散特性与脑功能的MRI多模态成像结合基于图论的复杂网络分析方法，将可能为PSD的潜在生物标记的发现提供依据，在未来实现该疾病的早期筛查与辅助诊断。

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