·综述·

帕金森病视觉损害特点研究进展

魏垦慧，马涛

摘要 帕金森病是第二大神经退行性疾病，临床表现包括运动症状和非运动症状。非运动症状对患者的生活质量影响较大，并可能预测疾病进展和可能的结局。视觉功能障碍是其中一种，包括视力、对比敏感度、色觉、视野、立体视觉、眼球运动、瞬目反射、瞳孔反应、视幻觉等，对患者的生活质量影响较大。本文主要对帕金森病视觉功能障碍临床表现、病理表现、辅助检查及药物治疗等进行简要综述，以利早期诊断。

关键词 帕金森病；视觉功能障碍；早期诊断

中图分类号 R741；R741.02；R742 **文献标识码** A **DOI** 10.16780/j.cnki.sjssgncj.20210778

本文引用格式：魏垦慧，马涛. 帕金森病视觉损害特点研究进展[J]. 神经损伤与功能重建, 2023, 18(6): 349-352.

Research Progress on the Characteristics of Visual Impairment in Parkinson's Disease *WEI Ken-hui, MA Tao. Department of Neurology, The Second Wuxi Hospital Affiliated to Nanjing Medical University, Jiangsu Wuxi 214000, China*

Abstract Parkinson's disease (PD) is the second most common neurodegenerative disease, and its clinical manifestations include motor and non-motor symptoms. Non-motor symptoms have a significant impact on the quality of life of patients and may predict disease progression and possible outcomes. Visual impairment is one of them, including visual acuity, contrast sensitivity, color vision, visual field, stereoscopic vision, eye movement, blink reflex, pupillary response, visual hallucination, etc., which has a significant impact on the life quality of patients. This article provides a brief review of the clinical manifestations, pathological manifestations, auxiliary examinations, and drug treatment of visual impairment in PD, which helps to facilitate early diagnosis of PD.

Keywords Parkinson's disease; visual impairment; early diagnosis

作者单位
无锡市第二人民医院（江南大学附属中心医院）神经内科
江苏 无锡 214000

基金项目
无锡市"双百"中青年医疗卫生拔尖人才（BJ2020023）
收稿日期
2022-08-19

通讯作者
马涛
tmadoc@126.com

帕金森病（Parkinson Disease，PD）是最常见的神经退行性疾病之一，其患病率随着年龄的增长而增加，65岁以上人群中PD患病率达1%，80岁以上人群中PD患病率达3%[1]。除震颤、强直等运动症状外，患者还会出现多种非运动症状。视觉功能障碍是PD非运动症状中的一种，本文即对PD患者的视觉功能障碍进行简要综述。

1 视觉功能改变

研究报道78%的PD患者至少有一种视觉症状，PD视觉功能改变包括视敏度、对比敏感度、色觉、视野、立体视觉、眼球运动、瞬目反射、瞳孔反应、视幻觉等方面，显著影响患者的日常生活质量[2]。

1.1 视敏度

视敏度是分辨物体细微结构能力。一项研究发现视敏度降低的人患PD的风险更高，视敏度降低可能是PD的一种运动前征象。视网膜改变可能是视敏度降低的原因之一[3]。认知损害可导致PD患者视敏度下降，视敏度降低是视幻觉的风险因素[4]。

1.2 对比敏感度

视觉对比敏感度是区分视觉对象与背景的能力，在日常活动中极其重要[5]，如在驾驶、阅读和导航等任务中均需要[6]。研究表明PD的对比敏感度降低与疾病的严重程度、冻结步态风险增加[7]和认知障碍相关[6]，可能会引起摔倒、阅读困难及影响驾驶能力，是视幻觉的强烈预测因子[8]。

1.3 色觉

在疾病早期，PD患者可出现颜色鉴别障碍。PD中的色觉障碍主要影响蓝黄色轴[9]，是多巴胺功能障碍的早期征象，与临床症状的严重程度和疾病进展有关，PD色觉障碍与认知损害和白质改变相关[8]。目前认为色觉受损是神经退行性变的临床前标志[6]，是PD的早期诊断指标[10]。Farnsworth-Munsell 100 Hue和D-15检测在临床应用最广泛，在检测PD色觉缺陷上具有最强鉴别力[8]。

1.4 立体视觉

立体视觉是又称深度感知，是一种感知三维世界的视觉能力[10]。有研究报道PD的立体视觉患病率为42%[6]。存在立体视异常的PD患者运动能力较差，统一帕金森病评估量表（unified Parkinson's disease rating scale，UPDRS）运动评分更高，认知能力下降更快[11,12]。色觉障碍、对比敏感度恶化和立体视觉损伤均与PD的进展相关[5]。

1.5 视幻觉

大约50%的PD患者出现视幻觉[13]，发病20年后患病率高达74%[5]。视幻觉与视敏度下降、视觉认知损害、疾病持续时长、REM睡眠行为障碍、痴呆、对比敏感度受损、颜色鉴别下降有关[14]。多巴

胺能药物及抗胆碱能药物为重要触发因素[16,17]。视幻觉是未来进展为痴呆的重要预测因子，是PD痴呆发作的先兆[15]。

1.6 眼球运动异常

眼球运动异常包括会聚不足、异常扫视和平滑跟踪及上视受限。研究表明PD患者的会聚幅度降低[5]，会聚不足可能导致近视模糊和复视，从而干扰阅读。随着疾病进展，PD复视发病率增高[14]。75%的PD患者报告眼跳和平滑追踪眼球运动异常[18]。PD患者中最佳眼的会聚不足，融合范围和视敏度均与疾病的严重程度相关[19]。

1.7 瞳孔反应

在PD的早期，副交感神经系统受累，瞳孔反应表现为光适应后瞳孔直径增大，双侧瞳孔不等大[20]，暗适应后瞳孔无明显异常改变[21]；瞳孔对光反射潜伏期延长、瞳孔收缩幅度减小和最大收缩速度减慢[8]。

1.8 瞬目反射

PD患者的瞬目反射减少，导致泪膜脂质成分在角膜上的分布减少，水性成分快速蒸发，引起干眼症，甚至视力下降[21]，影响日常生活。

2 PD视觉功能障碍相关病理

PD视网膜病理改变包括细胞损失（通常影响视网膜的外周节段最严重）和视网膜多巴胺的减少[22]。多巴胺是一种存在于视网膜中的重要神经递质，参与视网膜发育、视觉信号传递和屈光等多种功能。多巴胺的缺乏与视网膜中无长突细胞的减少相关，通过改变神经节细胞的输入而导致视觉处理的改变[20]。有研究认为眼视觉变化是由于视网膜神经元丧失、α突触核蛋白沉积和视网膜上多巴胺不足所引起[15]。视网膜上无长突细胞的丢失和α突触核蛋白的聚集可能是PD患者视觉对比敏感度下降的原因。神经节细胞层中的细胞大量丢失可能与PD的色觉功能障碍有关[20]。视力差可能是由于视网膜中缺乏多巴胺，眼球运动异常或眨眼不佳引起的[18]。多巴胺对视网膜功能和调节影响广泛，多巴胺能细胞在调节视网膜暗光适应和昼夜节律中起重要作用[22]。枕叶皮质产生眼球扫视运动；在基底神经节内，黑质网部、丘脑底核和尾状核都参与眼跳运动[18]。

铁与α-突触核蛋白和视网膜的关系在PD相关的视力损害中起重要作用。铁是神经递质合成的辅助因子，在视觉光转导级联反应中起重要作用。铁沉积改变了PD患者中α突触核蛋白的表达，导致α突触核蛋白聚集和毒性。α突触核蛋白的翻译后修饰影响铁和多巴胺依赖的氧化应激，从而增加α突触核蛋白聚集的趋势，将多巴胺转变为一种有毒化合物，最终导致α突触核蛋白和多巴胺活性低下。α突触核蛋白的定位以及与视网膜层中铁的相互作用可能参与PD的视力损害[20]。

3 PD视觉功能障碍与基因的关系

近年来，PD基因突变的发现，使人们对PD的异质性有了重要的认识，其中一些基因突变与确定的分子途径有关，与特定突变相关的视觉知觉功能障碍可能涉及潜在的病理生理机制。与特发性PD患者相比，携带PARK2基因突变的PD患者与线粒体系统功能障碍有关，具有更局限的神经病理学分布，在认知测试中的表现更优[8]；携带LRRK2基因突变的PD患者具有更好的颜色辨别力[23]和较少的认知缺陷[24]；携带GBA基因突变显示视觉空间的任务缺陷[25]，有视觉记忆受损[26]，具有较高的认知缺陷和快速眼动睡眠障碍风险，易出现视幻觉[8]。

与这些基因相关的视觉缺陷可能共享病理生理机制，溶酶体功能障碍与皮质视觉功能障碍有关。基因多态性可能在PD的认知障碍易感性中起作用[15]。

4 辅助检查

4.1 光学相干断层扫描技术（optical coherence tomography，OCT）

OCT是一种新兴的医学成像技术，用于评估视网膜神经纤维层（retinal nerve fibre layer，RNFL）的厚度，黄斑中央、视网膜内外层、黄斑中央体积和黄斑总体积[27]。很多研究报道PD患者的RNFL变薄[28]，且常常影响颞侧[8]。RNFL变薄与视幻觉有关，并与PD的进展相关[29]。研究表明RNFL损伤较大的PD患者往往生活质量更低、症状更严重[30]。视网膜中央凹厚度与疾病严重程度相关。OCT可以增进对PD视网膜损伤机制的了解，提供潜在的与PD治疗相关的标志物[31]。PD患者中央凹视力受损，故评估黄斑体积/厚度可能比RNFL厚度有更高的诊断率[8]。在有视幻觉的PD患者中，RNFL似乎更薄，这是较强的死亡预测因子[32]。此外，黄斑厚度也可作为PD和阿尔茨海默病以及其他神经退行性疾病的鉴别诊断[33]。

4.2 光学相干断层摄影血管造影术（optical coherence tomography angiography，OCT-A）

OCT-A是一种新兴的无创眼血管成像技术，用于广泛的视网膜血管疾病中视网膜血管系统的完整性评估，可提供视网膜血管解剖的定量测量，为评估疾病中的血管病理提供了一种客观的方法[34]。Kwapong等[35]报道PD患者整个视网膜大部分区域的微血管密度降低，视网膜浅层血管密度降低与内丛状细胞层和神经节细胞层变薄相关。

4.3 视觉诱发电位（visual-evoked potentials，VEP）

在PD患者中，VEP对有色刺激尤其是蓝黄色水平光轴的反应会受到影响[20]，PD患者的VEP的N75、P100、N145的潜伏期明显延长[36]，P100波振幅更低[27]。且P100潜伏期很少受多巴胺药物影响，与HY分级及UPDRS评分正相关[36]。

4.4 视网膜电图（ electroretinograms，ERG）

ERG目前主要有3种：闪光ERG、图形ERG和多聚焦ERG。临床使用闪光ERG可以诊断影响视网膜的疾病，更精确地诊断视网膜的前两层（光感受器和双极细胞）。但闪光ERG测量缺乏敏感性，只有在视网膜广泛病变的情况下才受影响。闪光ERG提供视网膜对光刺激的反应。视网膜反应是由双相波形支配的光诱发电位。它的2个成分是负a波（光感受器的超极化）和正b波（双极细胞的去极化）。闪光ERG可以提供光感受器和双极细胞在暗（适应黑暗）或光（适应光）条件下的反应。

振荡电位也是闪光ERG记录的一部分，模式ERG研究神经节细胞反应和黄斑完整性。所采用的刺激是一个黑白可逆的棋盘。主要的视网膜反应是P50波和N95波。最后，多聚焦ERG可以对黄斑区域的视网膜功能进行地形图测绘，并反映双极细胞和光感受器的活动[37]。PD患者的视网膜电图测量显示视网膜电活动降低[15]，图形ERG表现为a波、振荡电位和b波振幅的降低以及振荡电位潜伏期延长。P1的振幅密度结合黄斑体积可以对PD患者有较高的诊断效果。说明多聚焦ERG和SD-OCT联合应用可为PD的诊断提供良好的临床生物标志物[38]。中央凹厚度和图形视网膜电图N95成分为预测PD生活质量和疾病严重程度的良好生物标记物[30]。视网膜电生理测量可能比OCT测量有更少的缺陷[37]。

5 药物治疗

多巴胺能药物治疗可影响视敏度，在药物治疗周期内引起屈光变化[6]。在早期和中期PD中，左旋多巴治疗可部分逆转对比敏感度，但随着疾病的发展，这种敏感性最终再次恶化。左旋多巴可增强PD患者的色觉和对比度敏感性和改善PD患者的异常视觉诱发电位[15]。左旋多巴可能对PD患者的视网膜具有保护作用[39]。普拉克索治疗似乎可以预防视网膜变性，但是需要进一步的研究来证实这一发现[40]。胆碱酯酶抑制剂如卡巴拉汀控制PD痴呆的视幻觉是有用的[16]。ERG的损失及视网膜电图表现可通过左旋多巴疗法得到改善。

综上所述，视觉功能障碍可作为PD的早期诊断标志，可预测疾病的发展和预后。对比敏感度变化、色觉障碍与临床症状的严重程度和疾病进展有关，可作为PD病情发展的指标。对视觉症状的早期识别有助于PD的早期诊断，早期管理及积极治疗，可改善患者生活质量及预后。

参考文献

[1] Homayoun H. Parkinson Disease[J]. Ann Intern Med, 2018, 169(5): ITC33-ITC48.
[2] Armstrong RA. Visual Dysfunction in Parkinson's Disease[J]. Int Rev Neurobiol, 2017, 134: 921-946.
[3] Han G, Han J, Han K, et al. Visual Acuity and Development of Parkinson's Disease: A Nationwide Cohort Study[J]. Mov Disord, 2020, 35 (9): 1532-1541.
[4] Archibald NK, Clarke MP, Mosimann UP, et al. Visual symptoms in Parkinson's disease and Parkinson's disease dementia[J]. Mov Disord, 2011, 26(13): 2387-2395.
[5] Ming W, Palidis DJ, Spering M, et al. Visual Contrast Sensitivity in Early-Stage Parkinson's Disease[J]. Invest Ophthalmol Vis Sci, 2016, 57 (13): 5696-5704.
[6] Borm CDJM, Smilowska K, de Vries NM, et al. How I do it: The Neuro-Ophthalmological Assessment in Parkinson's Disease[J]. Parkinsons Dis, 2019, 9(2): 427-435.
[7] Davidsdottir S, Cronin-Golomb A, Lee A. Visual and spatial symptoms in Parkinson's disease[J]. Vision Res, 2005, 45(10): 1285-1296.
[8] Guo L, Normando EM, Shah PA, et al. Oculo-visual abnormalities in Parkinson's disease: Possible value as biomarkers[J]. Mov Disord, 2018, 33(9): 1390-1406.
[9] Brandt AU, Zimmermann HG, Oberwahrenbrock T, et al. Self-perception and determinants of color vision in Parkinson's disease[J]. Neural Transm (Vienna), 2018, 125(2): 145-152.
[10] Turcano P, Chen JJ, Bureau BL, et al. Early ophthalmologic features of Parkinson's disease: a review of preceding clinical and diagnostic markers [J]. J Neurol, 2019, 266(9): 2103-2111.
[11] Sun L, Zhang H, Gu Z, et al. Stereopsis impairment is associated with decreased color perception and worse motor performance in Parkinson's disease[J]. Eur J Med Res, 2014, 19(1): 29.
[12] Kwon KY, Kang SH, Kim M, et al. Nonmotor Symptoms and Cognitive Decline in de novo Parkinson's Disease[J]. Can J Neurol Sci, 2014, 41(5): 597-602.
[13] Gibson G, Mottram PG, Burn DJ, et al. Frequency, prevalence, incidence and risk factors associated with visual hallucinations in a sample of patients with Parkinson's disease: a longitudinal 4-year study[J]. Int J Geriatr Psychiatry, 2013, 28(6): 626-631.
[14] Ekker MS, Janssen S, Seppi K, et al. Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked[J]. Parkinsonism Relat Disord, 2017, 40: 1-10.
[15] Weil RS, Schrag AE, Warren JD, et al. Visual dysfunction in Parkinson's disease[J]. Brain, 2016, 139(11): 2827-2843.
[16] Poewe W. When a Parkinson's disease patient starts to hallucinate[J]. Pract Neurol, 2008, 8(4): 238-241.
[17] Diederich NJ, Goetz CG, Stebbins GT. Repeated visual hallucinations in Parkinson's disease as disturbed external/internal perceptions: focused review and a new integrative model[J]. Mov Disord, 2005, 20(2): 130-140.
[18] Armstrong RA. Visual signs and symptoms of Parkinson's disease[J]. Clin Exp Optom, 2008, 91(2): 129-138.
[19] Visser F, Vlaar AMM, Borm CDJM, et al. Diplopia in Parkinson's disease: visual illusion or oculomotor impairment[J]? J Neurol, 2019, 266 (10): 2457-2464.
[20] Mohana Devi S, Mahalaxmi I, Aswathy NP, et al. Does retina play a role in Parkinson's Disease[J]? Acta Neurol Belg, 2020, 120(2): 257-265.
[21] Armstrong RA. Oculo-Visual Dysfunction in Parkinson's Disease[J]. Parkinsons Dis, 2015, 5(4): 715-726.
[22] Ortuño-Lizarán I, Sánchez-Sáez X, Lax P, et al. Dopaminergic Retinal Cell Loss and Visual Dysfunction in Parkinson Disease[J]. Ann Neurol, 2020, 88(5): 893-906.
[23] Marras C, Schüle B, Munhoz RP, et al. Phenotype in parkinsonian and nonparkinsonian LRRK2 G2019S mutation carriers[J]. Neurology, 2011, 77(4): 325-333.
[24] Alcalay RN, Mirelman A, Saunders-Pullman R, et al. Parkinson disease phenotype in Ashkenazi Jews with and without LRRK2 G2019S mutations[J]. Mov Disord, 2013, 28(14): 1966-1971.
[25] Alcalay RN, Caccappolo E, Mejia-Santana H, et al. Cognitive performance of GBA mutation carriers with early-onset PD: the CORE-PD study[J]. Neurology, 2012, 78(18): 1434-1340.
[26] Zokaei N, McNeill A, Proukakis C, et al. Visual short-term memory deficits associated with GBA mutation and Parkinson's disease[J]. Brain, 2014, 137(Pt8): 2303-2311.
[27] Mailankody P, Lenka A, Pal PK. The role of Optical Coherence Tomography in Parkinsonism: A critical review[J]. Neurol Sci, 2019, 403: 67-74.
[28] Hasanov S, Demirkilinc Biler E, Acarer A, et al. Functional and morphological assessment of ocular structures and follow-up of patients with early-stage Parkinson's disease[J]. Int Ophthalmol, 2019, 39(6): 1255-1262.
[29] Gupta S, Zivadinov R, Ramanathan M, et al. Optical coherence tomography and neurodegeneration: are eyes the windows to the brain[J]? Expert Rev Neurother, 2016, 16(7): 765-775.
[30] Garcia-Martin E, Rodriguez-Mena D, Satue M, et al. Electrophysiology and optical coherence tomography to evaluate Parkinson disease severity[J]. Invest Ophthalmol Vis Sci, 2014, 55(2): 696-705.
[31] Tian T, Zhu XH, Liu YH. Potential role of retina as a biomarker for progression of Parkinson's disease[J]. Int J Ophthalmol, 2011, 4(4): 433-438.
[32] Lee JY, Kim JM, Ahn J, et al. Retinal nerve fiber layer thickness and visual hallucinations in Parkinson's Disease[J]. Mov Disord, 2014, 29(1): 61-67.
[33] Cubo E, Tedejo RP, Rodriguez Mendez V, et al. Retina thickness in

Parkinson’s disease and essential tremor[J]. Mov Disord, 2010, 25(14): 2461-2462.
[34] Asanad S, Mohammed I, Sadun AA, et al. OCTA in neurodegenerative optic neuropathies: emerging biomarkers at the eye-brain interface[J]. Ther Adv Ophthalmol, 2020, 12: 2515841420950508.
[35] Kwapong WR, Ye H, Peng C, et al. Retinal Microvascular Impairment in the Early Stages of Parkinson's Disease[J]. Invest Ophthalmol Vis Sci, 2018, 59(10): 4115-4122.
[36] Liu C, Zhang Y, Tang W, et al. Evoked potential changes in patients with Parkinson’s disease[J]. Brain Behav, 2017, 7(5): e00703.
[37] Bernardin F, Schwan R, Lalanne L, et al. The role of the retina in visual hallucinations: A review of the literature and implications for psychosis[J]. Neuropsychologia, 2017, 99: 128-138.
[38] Huang J, Li Y, Xiao J, et al. Combination of Multifocal Electroretinogram and Spectral-Domain OCT Can Increase Diagnostic Efficacy of Parkinson’s Disease[J]. Parkinsons Dis, 2018, 2018: 4163239.
[39] Sen A, Tugcu B, Coskun C, et al. Effects of levodopa on retina in Parkinson disease[J]. Eur J Ophthalmol, 2014, 24(1): 114-119.
[40] Mello LGM, Bissoli LB, Saraiva FP, et al. Retinal Layers and Choroid Measurements in Parkinson’s Disease With or Without Pramipexole Treatment[J]. Mov Disord, 2020, 35(12): 2357-2359.

（本文编辑：唐颖馨）

（上接第345页）

[7] Bouchon A, Dietrich J, Colonna M. Cutting edge: inflammatory responses can be triggered by TREM-1, a novel receptor expressed on neutrophils and monocytes[J]. J Immunol, 2000, 164: 4991-4995.
[8] Baruah S, Keck K, Vrenios M, et al. Identification of a Novel Splice Variant Isoform of TREM-1 in Human Neutrophil Granules[J]. J Immunol, 2015, 195: 5725-5731.
[9] Cao C, Gu J, Zhang J. Soluble triggering receptor expressed on myeloid cell-1 (sTREM-1): a potential biomarker for the diagnosis of infectious diseases[J]. Front Med, 2017, 11: 169-177.
[10] De Oliveira Matos A, Dos Santos Dantas P H, Figueira Marques Silva-Sales M, et al. The role of the triggering receptor expressed on myeloid cells-1 (TREM-1) in non-bacterial infections[J]. Crit Rev Microbiol, 2020, 46: 237-252.
[11] Pelham C J, Pandya A N, Agrawal D K. Triggering receptor expressed on myeloid cells receptor family modulators: a patent review[J]. Expert Opin Ther Pat, 2014, 24: 1383-1395.
[12] Natale G, Biagioni F, Busceti C L, et al. TREM Receptors Connecting Bowel Inflammation to Neurodegenerative Disorders[J]. Cells, 2019, 8: 1124.
[13] Colonna M. TREMs in the immune system and beyond[J]. Nat Rev Immunol, 2003, 3: 445-453.
[14] Zhong W J, Duan J X, Liu T, et al. Activation of NLRP3 inflammasome up-regulates TREM-1 expression in murine macrophages via HMGB1 and IL-18[J]. Int Immunopharmacol, 2020, 89: 107045.
[15] Owens R, Grabert K, Davies C L, et al. Divergent Neuroinflammatory Regulation of Microglial TREM Expression and Involvement of NF-kappaB[J]. Front Cell Neurosci, 2017, 11: 56.
[16] Read C B, Kuijper J L, Hjorth S A, et al. Cutting Edge: identification of neutrophil PGLYRP1 as a ligand for TREM-1[J]. J Immunol, 2015, 194: 1417-1421.
[17] Ornatowska M, Azim A C, Wang X, et al. Functional genomics of silencing TREM-1 on TLR4 signaling in macrophages[J]. Am J Physiol Lung Cell Mol Physiol, 2007, 293: L1377-1384.
[18] Pandupuspitasari N S, Khan F A, Huang C J, et al. Novel Attributions of TREMs in Immunity[J]. Curr Issues Mol Biol, 2016, 20: 47-54.
[19] Prufer S, Weber M, Sasca D, et al. Distinct signaling cascades of TREM-1, TLR and NLR in neutrophils and monocytic cells[J]. J Innate Immun, 2014, 6: 339-352.
[20] Xu P, Zhang X, Liu Q, et al. Microglial TREM-1 receptor mediates neuroinflammatory injury via interaction with SYK in experimental ischemic stroke[J]. Cell Death Dis, 2019, 10: 555.
[21] Liu Q, Johnson E M, Lam R K, et al. Peripheral TREM1 responses to brain and intestinal immunogens amplify stroke severity[J]. Nat Immunol, 2019, 20: 1023-1034.
[22] Xu K, Gao X, Xia G, et al. Rapid gut dysbiosis induced by stroke exacerbates brain infarction in turn[J]. Gut, 2021, gutjnl-2020-323263.
[23] Backes F N, De Souza A, Bianchin M M. Biomarkers in the prognostic evaluation of ischemic stroke: Is there benefit in the measurements of TREM-1 and TREM-2 in the acute phase[J]? Clin Biochem, 2021, 98: 10-16.
[24] Tao T, Liu G J, Shi X, et al. DHEA Attenuates Microglial Activation via Induction of JMJD3 in Experimental Subarachnoid Haemorrhage[J]. J Neuroinflammation, 2019, 16: 243.
[25] Xu P, Hong Y, Xie Y, et al. TREM-1 Exacerbates Neuroinflammatory Injury via NLRP3 Inflammasome-Mediated Pyroptosis in Experimental Subarachnoid Hemorrhage[J]. Transl Stroke Res, 2021, 12: 643-659.
[26] Sun X G, Ma Q, Jing G, et al. Early elevated levels of soluble triggering receptor expressed on myeloid cells-1 in subarachnoid hemorrhage patients[J]. Neurol Sci, 2017, 38: 873-877.
[27] Raggi F, Bosco M C. Targeting Mononuclear Phagocyte Receptors in Cancer Immunotherapy: New Perspectives of the Triggering Receptor Expressed on Myeloid Cells (TREM-1) [J]. Cancers (Basel), 2020, 12: 1337.
[28] Kluckova K, Kozak J, Szaboova K, et al. TREM-1 and TREM-2 Expression on Blood Monocytes Could Help Predict Survival in High-Grade Glioma Patients[J]. Mediators Inflamm, 2020, 2020: 1798147.
[29] Liu Y S, Yan W J, Tan C C, et al. Common Variant in TREM1 Influencing Brain Amyloid Deposition in Mild Cognitive Impairment and Alzheimer's Disease[J]. Neurotox Res, 2020, 37: 661-668.
[30] Jiang T, Zhang Y D, Gao Q, et al. TREM1 facilitates microglial phagocytosis of amyloid beta[J]. Acta Neuropathol, 2016, 132: 667-683.
[31] Liang Y B, Song P P, Zhu Y H, et al. TREM-1-targeting LP17 attenuates cerebral ischemia-induced neuronal injury by inhibiting oxidative stress and pyroptosis[J]. Biochem Biophys Res Commun, 2020, 529: 554-561.
[32] Vandestienne M, Zhang Y, Santos-Zas I, et al. TREM-1 orchestrates angiotensin II-induced monocyte trafficking and promotes experimental abdominal aortic aneurysm[J]. J Clin Invest, 2021, 131: e142468.

（本文编辑：唐颖馨）