

[DOI] 10.12016/j.issn.2096-1456.202660020

· 基础研究 ·

微波辐射加重实验性牙周炎小鼠认知功能损伤的研究

周虹瑾^{1,2}, 王健辉³, 刘琳¹, 李鸿波¹

1. 中国人民解放军总医院第一医学中心口腔科, 北京(100853); 2. 中国人民解放军医学院, 北京(100853); 3. 军事医学研究院, 北京(100850)

【摘要】 目的 探讨微波辐射对实验性牙周炎小鼠认知功能及神经炎症的影响, 为理解环境暴露如何通过调控慢性炎症这一共同病理机制, 进而与神经退行性疾病风险相关联提供实验依据。**方法** 本研究获得军事医学研究院动物伦理委员会批准。将C57BL/6J小鼠随机分为对照组(C组, 未做处理)、微波辐射组(R组, 仅微波辐射暴露)、牙周炎组(P组, 仅结扎造模)和牙周炎+微波辐射组(PR组, 结扎造模及微波辐射暴露)。采用丝线结扎法建立牙周炎模型, 并于造模8周后对R组与PR组进行2 800 MHz、10 mW/cm²的微波全身辐射, 10 h/d, 持续7 d。进行行为学测试: 采用旷场实验和高架十字迷宫实验评估小鼠的焦虑样情绪, 通过Y迷宫实验评估小鼠的空间记忆能力, 并利用新物体识别实验评估小鼠的学习记忆能力。采用Micro-CT、苏木精-伊红染色法(HE)和实时荧光定量(qPCR)分析牙周组织病理与局部炎症; 通过酶联免疫吸附实验(ELISA)检测血清及脑组织中脂多糖(LPS)、白细胞介素-1 β (IL-1 β)、白细胞介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平; 基于16S rRNA测序分析口腔菌群组成。**结果** 行为学测试表明, R组与PR组小鼠焦虑样行为显著加剧, 且PR组与P组的空间与识别记忆损伤分别较R组与C组加重($P<0.05$)。组织与分子生物学分析显示, PR组与P组牙周炎症浸润、牙槽骨吸收及局部促炎因子TNF- α 、IL-1 β 、IL-6表达均分别较R组与C组进一步加剧($P<0.05$)。ELISA结果显示, 血清中, P组与PR组LPS水平分别较C组与R组升高, PR组TNF- α 、IL-1 β 、IL-6水平显著高于P组及R组, 且TNF- α 水平协同性升高($P<0.05$); 脑组织中, P组LPS及TNF- α 、IL-1 β 、IL-6水平显著高于C组, PR组上述指标显著高于P组及R组, 且LPS与IL-6水平协同性升高($P<0.05$)。口腔菌群分析发现, 微波辐射在牙周炎基础上进一步降低了菌群多样性, 并导致乳杆菌属、肠球菌属等菌群相对丰度增加, 而葡萄球菌属等菌群相对丰度减少。相关性分析证实, 这些差异菌群与脑组织炎症水平正相关, 与认知功能指标负相关。**结论** 微波辐射暴露可加剧实验性牙周炎小鼠的认知功能损伤, 其机制可能与加重牙周局部破坏、扰乱口腔菌群稳态进而诱导全身及中枢神经炎症的级联反应有关。

【关键词】 微波辐射; 牙周炎; 认知功能; 口腔菌群; 神经炎症; 协同作用; 16S rRNA; 系统性炎症

【中图分类号】 R78 **【文献标志码】** A **【文章编号】** 2096-1456(2026)06-0541-15

【引用著录格式】 周虹瑾, 王健辉, 刘琳, 等. 微波辐射加重实验性牙周炎小鼠认知功能损伤的研究[J]. 口腔疾病防治, 2026, 34(6): 541-555. doi:10.12016/j.issn.2096-1456.202660020.

Study on microwave radiation aggravating the impairment of cognitive functions in mice with experimental periodontitis ZHOU Hongjin^{1,2}, WANG Jianhui³, LIU Lin¹, LI Hongbo¹.

1. Department of Stomatology, The First Medical Center, Chinese PLA General Hospital, Beijing 100853, China; 2. Chinese PLA Medical School, Beijing 100853, China; 3. Academy of Military Medical Sciences, Beijing 100850, China

Corresponding author: LI Hongbo, Email: hongbo_l@sina.com

【Abstract】 Objective To explore the effects of microwave radiation on cognitive function and neuroinflammation



微信公众号

【收稿日期】 2026-01-13; **【修回日期】** 2026-04-20

【作者简介】 周虹瑾, 硕士研究生在读, Email: zhouhongjin0928@163.com

【通信作者】 李鸿波, 主任医师, 博士, Email: hongbo_l@sina.com

in mice with experimental periodontitis, providing experimental evidence for understanding how environmental exposure may be linked to the risk of neurodegenerative diseases by modulating chronic inflammation as a shared pathological mechanism. **Methods** This study was approved by the Animal Ethics Committee of the Academy of Military Medical Sciences. C57BL/6J mice were randomly divided into a control group (C group, untreated), a microwave radiation group (R group, exposed to microwave radiation only), a periodontitis group (P group, ligation-induced periodontitis only), and a periodontitis + microwave radiation group (PR group, ligation-induced periodontitis plus microwave radiation exposure). A periodontitis model was established using the silk ligation method. Eight weeks after modeling, the R and PR groups were subjected to whole-body microwave radiation at 2 800 MHz and 10 mW/cm² for 10 h/day for 7 consecutive days. Behavioral tests were conducted: the open field test and elevated plus maze test were used to assess anxiety-like behavior, the Y-maze test to evaluate spatial memory, and the novel object recognition test to assess learning and memory abilities. Micro-CT, hematoxylin & eosin staining (HE), and quantitative real-time polymerase chain reaction (qPCR) were used to analyze periodontal tissue pathology and local inflammation. Serum and brain levels of lipopolysaccharide (LPS), interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor- α (TNF- α) were measured using enzyme-linked immunosorbent assay (ELISA). The composition of the oral microbiota was analyzed based on 16S rRNA sequencing. **Results** Behavioral tests showed that anxiety-like behavior was significantly exacerbated in the R and PR groups, and spatial and recognition memory impairments in the PR and P groups were more severe compared with the R and C groups, respectively ($P < 0.05$). Histological and molecular biological analyses revealed that periodontal inflammation infiltration, alveolar bone resorption, and local expression of pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6) were further exacerbated in the PR and P groups compared with the R and C groups, respectively ($P < 0.05$). ELISA results showed that in serum, LPS levels in group P and group PR were increased compared with group C and group R, respectively. The levels of TNF- α , IL-1 β , and IL-6 in group PR were significantly higher than those in group P and group R, with a synergistic increase in TNF- α level ($P < 0.05$). In brain tissue, LPS and TNF- α , IL-1 β , IL-6 levels in group P were significantly higher than those in group C; all the above indicators in group PR were significantly higher than those in group P and group R, and LPS and IL-6 levels showed a synergistic increase ($P < 0.05$). Oral microbiota analysis found that microwave radiation further reduced microbial diversity on the basis of periodontitis, leading to increased relative abundances of *Lactobacillus* and *Enterococcus*, and decreased relative abundances of *Staphylococcus*. Correlation analysis confirmed that these differential bacterial genera were positively correlated with brain inflammation levels and negatively correlated with cognitive function indicators. **Conclusion** Microwave radiation exposure can exacerbate cognitive impairment in mice with experimental periodontitis, and its mechanism may be related to aggravated local periodontal damage, disruption of oral microbiota homeostasis, and subsequent induction of systemic and central neuroinflammatory cascades.

【Key words】 microwave radiation; periodontitis; cognitive function; oral microbiota; neuroinflammation; synergistic effect; 16S rRNA; systemic inflammation

J Prev Treat Stomatol Dis, 2026, 34(6): 541-555.

【Competing interests】 The authors declare no competing interests.

牙周炎是全球范围内最常见的慢性炎症性疾病之一,影响着近半数成年人口,不仅是中老年人牙齿丧失的主要原因,更被视为多种系统性疾病的重要风险因素^[1]。其病理本质在于口腔菌群失调引发的持续性免疫炎症反应,可导致牙槽骨吸收和牙周附着丧失^[2]。牙周炎并非局限于口腔局部,致病菌及其代谢产物脂多糖(lipopolysaccharides, LPS)可突破黏膜屏障进入循环系统,诱发全身性炎症状态^[3]。大量流行病学研究揭示了牙周炎与认知功能下降及阿尔茨海默病(alzheimer's

disease, AD)风险增加之间的统计学关联,然而,其确切的因果关系及机制尚未完全阐明,且部分研究结论存在不一致^[4-5]。因此,深入探讨连接牙周炎与神经功能障碍的具体病理生理机制具有重要的科学价值。

随着无线通信技术的普及,环境中的电磁辐射暴露日益普遍,其潜在的健康效应备受关注^[6]。在多种电磁波中,微波作为无线通信常用的频段,已被证实可穿透生物组织,并对中枢神经系统产生非热效应^[7]。研究表明,微波辐射可能通过影响

血脑屏障完整性、诱导氧化应激以及激活神经胶质细胞等机制,促进神经炎症,进而导致学习记忆等认知功能损伤^[8]。然而,现有研究多聚焦微波辐射在生理状态下对健康机体的影响^[9],而在机体已存在慢性炎症负荷的条件下,微波辐射是否会产生协同或加剧效应,目前尚不明确。

此外,微生物在环境应激与宿主健康交互作用中扮演着关键角色^[10]。初步证据提示,职业性电磁辐射暴露人群的口腔菌群结构与正常人存在差异^[11];动物实验也发现,长期微波暴露可伴随焦虑样行为及肠道菌群改变^[12]。这提示菌群可能在微波辐射影响认知功能的过程中起中介或调节作用。然而,在牙周炎与微波辐射双重暴露背景下,口腔菌群的变化是否与神经炎症及行为表型相关,仍有待阐明。因此,本研究旨在系统探讨微波辐射是否会加剧牙周炎相关的认知功能障碍,并初步揭示其与神经炎症及口腔菌群紊乱的潜在关联。

1 材料和方法

1.1 实验动物

选择8周龄的雄性C57BL/6J小鼠48只,体重22~26 g。小鼠由北京华阜康生物科技股份有限公司提供[许可证号:SCXK(京)2020-0008]。将它们饲养在(24±2)°C、40%~70%湿度、12 h明/暗循环的环境下,同时允许自由获取食物和水。本研究已获得军事医学研究院动物伦理委员会批准(IACUC-No: sq2021590)。

1.2 主要实验仪器与试剂

旷场实验箱(XR-XZ301,上海欣软信息科技有限公司)、新物体识别箱(XR-XX117,上海吉量软件科技有限公司)、高架十字迷宫实验装置(XR-XG201,上海欣软信息科技有限公司)、Y迷宫实验装置(XR-XY1032,上海欣软信息科技有限公司)、Anymaze动物视频分析系统(6000, Stoelting, 美国)、辐射混响室(中国信息通信研究院环境与安全部)、非吸收性外科缝线(扬州环宇医疗器械有限公司)、多功能酶标检测仪(EnSpire 2300, PerkinElmer, 美国)、实时荧光定量PCR仪(7500, ThermoFisher, 美国)、台式高速冷冻离心机(3K15, Eppendorf, 德国)、Micro-CT(德国 Siemens, vivaCT80)、测序仪(美国 Illumina, NextSeq 2000)。3%戊巴比妥钠(MP0787, 北京博奥派克生物科技有限公司)、FastPfu Polymerase(AP221-01, 北京全式金生物技

术有限公司)、小鼠脂多糖(LPS)酶联免疫吸附实验(enzyme-linked immunosorbent assay, ELISA)试剂盒(JL20691-96T, 江莱生物)、白细胞介素(interleukin, IL)-1 β ELISA试剂盒(E-EL-M0037, 武汉伊莱瑞特生物科技股份有限公司)、IL-6 ELISA试剂盒(E-EL-M0044, 武汉伊莱瑞特生物科技股份有限公司)、肿瘤坏死因子- α (tumor necrosis factor, TNF- α) ELISA试剂盒(E-EL-H0109, 武汉伊莱瑞特生物科技股份有限公司)、RNA simple Total RNA Kit(DP419, 北京天根生化科技有限公司)

1.3 实验分组和设计

适应性喂养1周后随机分为对照组(C组)、牙周炎组(P组)、微波辐射组(R组)和牙周炎+微波辐射组(PR组),每组12只。3%戊巴比妥钠(50 mg/kg)腹腔注射麻醉小鼠,麻醉成功后在P组和PR组小鼠双侧上颌一二磨牙之间放置两端打结的5-0非可吸收性外科缝线进行牙周炎造模。结扎状态维持8周,每周检查,如有脱落则重新进行结扎。C组和R组进行同样处理,丝线放置后即刻去除。

微波辐射环境暴露:牙周炎诱导8周后,将R组和PR组小鼠置于辐射混响室,接受2 800 MHz、功率密度10 mW/cm²的微波全身辐射,每天10 h间歇性暴露,持续7 d。C组和P组置于相同环境但不开启辐射。

1.4 小鼠体重及温度检测

通过检测R组及PR组小鼠体重与温度,明确微波辐射对小鼠的影响是非热效应引起的。体重:分别于辐射开始前一天以及辐射结束后一天记录R组及PR组小鼠体重。温度:采用便携式智能数字体温计监测微波辐照前后R组及PR组小鼠肛门温度。

1.5 行为学测试

辐射结束后,依次进行以下行为学测试。所有测试前,小鼠均在实验房间适应30 min。每只动物测试结束后,均用75%酒精彻底清洁设备。为评估微波辐射对牙周炎小鼠焦虑样情绪及空间、识别记忆能力的影响,本研究在辐射结束后系统开展四项行为学测试。

1.5.1 旷场实验(open field test, OFT) 用于评估小鼠焦虑样情绪。记录10 min内小鼠在中心区域的运动距离、停留时间及进入次数。

1.5.2 高架十字迷宫(elevated plus maze, EPM)实验 用于评估小鼠焦虑样情绪。记录5 min内小鼠进入开放臂的次数百分比、时间百分比和距离

百分比。

1.5.3 Y 迷宫(Y maze, YM)实验 用于评估小鼠空间记忆能力。记录 7 min 内的进臂序列,计算自发交替率(%)。自发交替率(%)=[正确交替次数/(总进臂次数-2)]×100 %。

1.5.4 新物体识别实验(novel object recognition test, NORT) 用于评估小鼠识别记忆能力。分 3 d 进行适应(第 1 天)、学习(第 2 天)和测试(第 3 天)阶段,记录测试期小鼠探索新旧物体的时间,计算识别指数。测试阶段小鼠探索旧物体 A 的时间(TA)和探索新物体 B 的时间(TB)。识别指数(discrimination index, DI)=TB/(TA+TB)。

1.6 样本收集

行为学测试结束后,于动物处死采集样本前 24 h,将 P 组及 PR 组小鼠丝线拆除,同时在各组小鼠上颌第一、二磨牙之间统一重新放置全新的无菌结扎丝线。24 h 后,收集这些丝线作为口腔菌群样本,放入 -80 °C 保存。腹腔麻醉小鼠后,眼球取血,离心分离血清。脱颈处死后,快速分离脑组织、上颌骨及牙龈组织,部分用 4 % 多聚甲醛固定,部分液氮速冻后 -80 °C 保存。

1.7 Micro-CT 分析

扫描固定后的上颌骨,三维重建后,测量双侧上颌第一磨牙颊腭侧近中、中央、远中 6 个位点的釉牙骨质界至牙槽嵴顶的距离(cemento-enamel

junction to alveolar bone crest, CEJ-ABC),计算平均值以评估牙槽骨吸收。

1.8 组织学染色

采用苏木精-伊红染色法(hematoxylin-eosin staining, HE)观察牙周及脑组织病理变化:经 4 % 多聚甲醛固定、流水冲洗后,梯度乙醇脱水、二甲苯透明、石蜡包埋;切成 4 μm 切片,展片烘干后进行 HE 染色:苏木精染 5 min,盐酸乙醇分化,流水冲洗,返蓝 15 min,伊红染 1~2 min,脱水透明,中性树胶封片,光镜观察。

1.9 小鼠血清和脑组织中脂多糖及炎症因子含量检测

为探究微波辐射对系统性与中枢神经炎症的影响,本研究严格按照 ELISA 试剂盒说明书检测小鼠血清和脑组织匀浆中 LPS、TNF-α、IL-1β 和 IL-6 的浓度。

1.10 小鼠牙龈组织中炎症因子含量检测

使用实时荧光定量(quantitative real-time PCR, qPCR)法测定小鼠牙龈组织中炎症因子(TNF-α、IL-1β、IL-6)浓度,步骤如下:使用试剂盒提取牙龈组织总 RNA,逆转录合成 cDNA。以 GAPDH 为内参,SYBRGreen 法进行 qPCR,检测 TNF-α、IL-1β 和 IL-6 mRNA 的相对表达水平。以 GAPDH 为内参计算目的基因相对表达水平,引物序列见表 1。

表 1 PCR 引物序列

Table 1 PCR primer sequences

Gene	Forward primer (5'-3')	Reverse primer (5'-3')
GAPDH	TGATGGGTGTGAACACGAG	AGTGATGGCATGGACTGTGG
TNF-α	ACGCTCTTCTGTCTACTGAACCTTCG	TGGTTTGTGAGTGTGAGGGTCTG
IL-1β	GGGCTGCTTCCAAACCTTTG	AAGACACAGGTAGCTGCCAC
IL-6	GCCTTCTGGGACTGATGCT	AGCCTCCGACTTGTGAAGTG

GAPDH: glyceraldehyde-3-phosphate dehydrogenase; TNF-α: tumor necrosis factor-alpha; IL-1β: interleukin-1 beta; IL-6: interleukin-6

1.11 小鼠口腔菌群 16S rRNA 基因高通量测序

为阐明微波辐射对口腔微生态的影响及与全身表型的潜在关联,本研究对小鼠口腔结扎丝线样本进行 16S rRNA 基因测序。具体方法:使用试剂盒提取口腔基因组 DNA,PCR 扩增 16S rRNA 基因 V3-V4 区,Illumina NextSeq 2000 平台测序;基于 QIIME 2 流程生成扩增子序列变异(amplicon sequence variant, ASV)。在此基础上,从 α 多样性的 Chao1 和 Shannon 指数、β 多样性的主坐标分析(principal coordinate analysis, PCoA)和非度量多维

尺度分析(non-metric multidimensional scaling, NMDS)、群落结构的物种组成分析、差异物种的线性判别分析效应大小(linear discriminant analysis effect size, LEfSe)通过计算线性判别分析(linear discriminant analysis, LDA)得分来筛选各组标志物种,通过 Spearman 相关性热图评估菌群结构变化与宿主整体表型的关联。

1.12 统计学分析

采用 GraphPad Prism 10 软件进行统计分析。符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)

表示。为分析牙周炎与微波辐射两个因素的独立效应及交互作用,采用双因素方差分析(Two-way ANOVA)进行析因分析,LSD检验进行组间分析。体重及温度数据采用配对样本 t 检验分析。采用Spearman相关分析评估细菌相对丰度与其他实验结果的相关性。所有统计分析以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 微波辐射对小鼠体重及肛温的影响

微波辐射前后记录R组与PR组小鼠的体重,R组与PR组小鼠辐射7 d前后体重差异无统计学意义;R组与PR组小鼠辐射前后肛温差异无统计学意义(表2)。

表2 微波辐射对小鼠体重及肛温的影响

Table 2 Effects of microwave radiation on body weight and rectal temperature in mice

Time	Weight/g		Rectal temperature/°C	
	R group	PR group	R group	PR group
Before irradiation	29.95±1.44	29.97±1.36	37.15±0.30	37.17±0.34
After irradiation	30.91±1.82	30.5±1.83	37.41±0.38	37.45±0.36
t	0.031	2.113	0.561	1.820
P	0.976	0.058	0.586	0.096

R group: microwave radiation exposure only; PR group: ligation modeling and microwave radiation exposure. $n=12$

2.2 微波辐射诱发小鼠焦虑样行为并加重牙周炎小鼠学习记忆损伤

微波辐射对牙周炎小鼠焦虑样行为及认知功能的影响见图1。旷场实验显示(图1a~1c),与C组相比,R组小鼠在中心区域的运动距离、停留时间及进入次数均降低,差异有统计学意义(均 $P<0.05$)。与P组相比,PR组小鼠的上述3项指标亦进一步下降(均 $P<0.05$)。高架十字迷宫实验结果(图1d~1g)可知R组小鼠在开放臂的进入距离与停留时间百分比均较C组减少($P<0.05$),且PR组小鼠的这些指标均低于P组($P<0.05$)。相较于C组,R组小鼠开放臂进入次数百分比差异无统计学意义($P>0.05$),PR组小鼠上述指标较P组降低($P<0.05$)。

在空间记忆方面,Y迷宫实验表明(图1h~1i),与C组相比,P组小鼠自发交替率降低($P<0.05$),R组相较C组差异无统计学意义;而PR组小鼠的自发交替率下降更为明显,显著低于P组与R组(均 $P<0.05$)。在新物体识别实验中(图1j),P组与R

组小鼠的识别指数均较C组下降($P<0.05$),而PR组小鼠的识别指数进一步降低,低于P组和R组($P<0.05$)。

综上,微波辐射可独立诱发小鼠焦虑样行为并损害其识别记忆,且微波辐射可使牙周炎小鼠空间记忆与识别记忆能力进一步下降。

2.3 微波辐射加重牙周炎小鼠牙周组织炎症

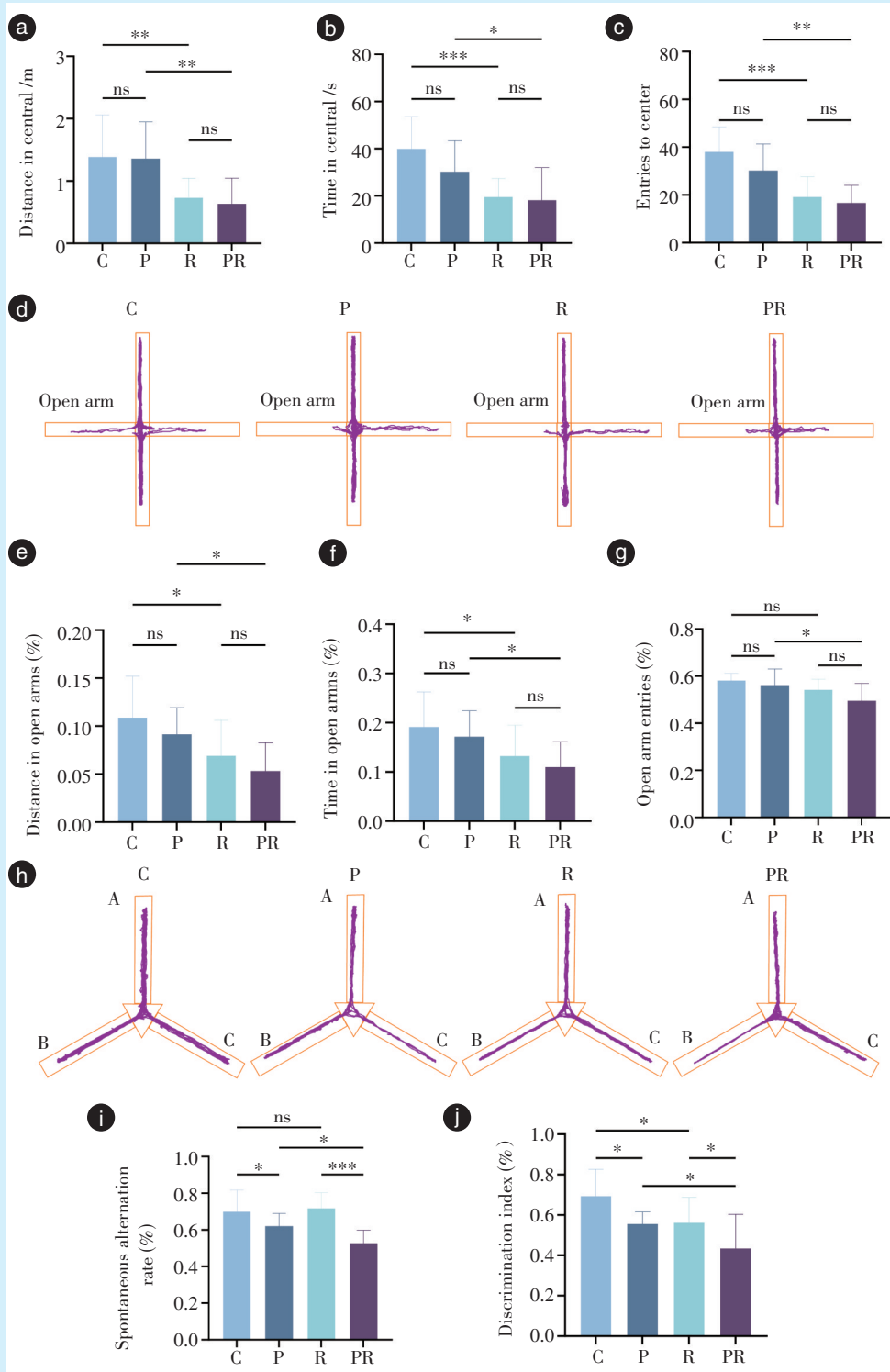
微波辐射对牙周炎小鼠牙周组织的影响见图2。HE染色结果显示,C组为正常牙周组织,牙龈上皮完整,结合上皮位置正常;与C组相比,P组牙龈组织出现明显萎缩及炎症细胞浸润;R组仅见轻微炎症;PR组小鼠牙龈组织萎缩及炎症细胞浸润较P组更为严重。Micro-CT三维重建及定量分析进一步揭示,C组无牙槽骨吸收;与C组相比,P组牙槽骨吸收明显,R组未见明显吸收;PR组小鼠牙槽骨吸收较P组更为严重。CEJ-ABC定量分析显示,P组的CEJ-ABC距离大于C组($P<0.001$),R组与C组之间差异无统计学意义;而PR组的CEJ-ABC距离较P组进一步增加($P<0.01$),表明微波辐射加剧了牙周炎所致的骨吸收。

qPCR检测结果显示,P组中TNF- α 、IL-1 β 及IL-6的mRNA水平均较C组升高,PR组中上述3种炎症因子的表达水平进一步上调,高于P组与R组(均 $P<0.05$)。

综上,组织学、影像学及分子生物学证据一致表明,微波辐射暴露能加重实验性牙周炎小鼠的牙龈炎症浸润、促进牙槽骨吸收并上调局部促炎因子表达,从而加速牙周炎的病理进展。

2.4 微波辐射加重小鼠血清以及脑组织中脂多糖及炎症水平

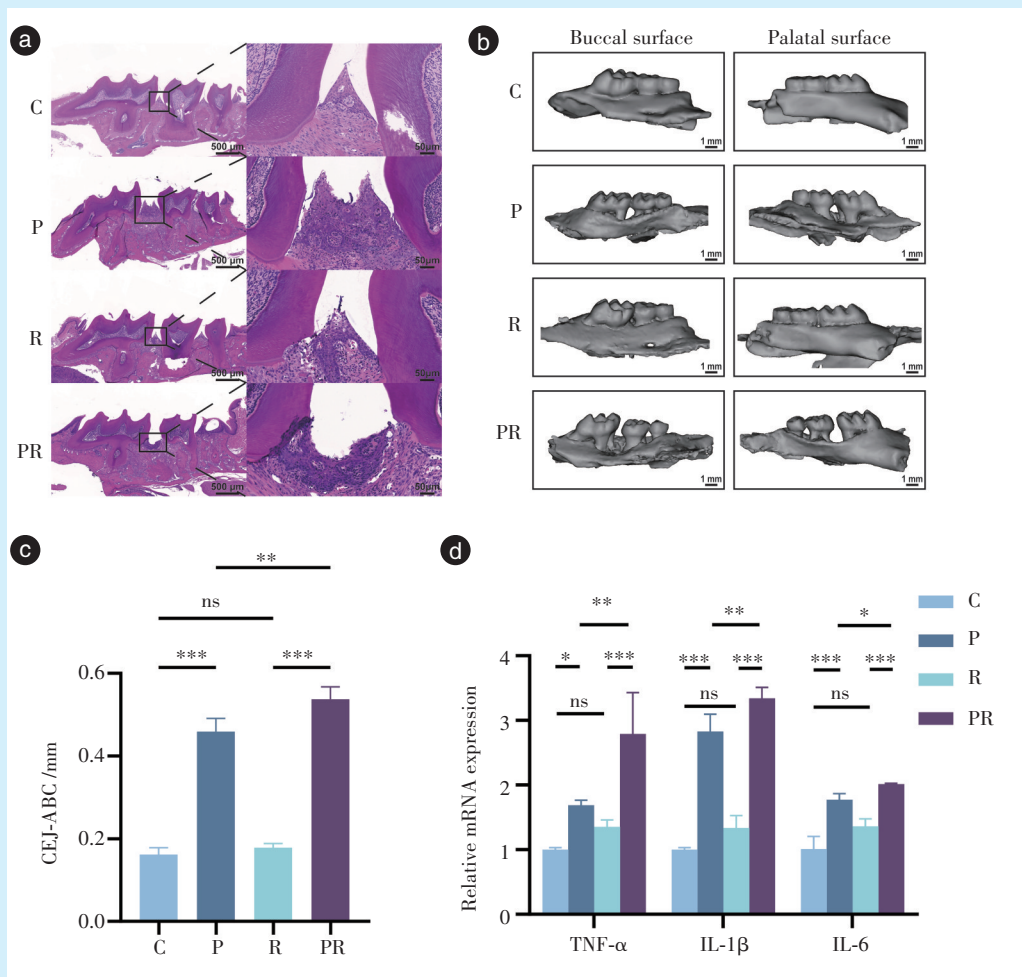
微波辐射对牙周炎小鼠血清、脑组织LPS及炎症因子含量影响见图3、表3、表4。血清检测结果显示(图3a、3b),相较于C组,P组小鼠的LPS水平升高($P<0.01$),R组与C组相比差异无统计学意义。PR组的血清LPS水平与P组相比,差异无统计学意义;而与R组相比,PR组的血清LPS水平则明显升高($P<0.05$)。相较于C组,P组TNF- α 水平明显升高($P<0.05$),R组与C组TNF- α 水平差异无统计学意义,P组及R组与C组IL-1 β 及IL-6水平差异无统计学意义;PR组TNF- α 、IL-1 β 及IL-6水平高于P组与R组(均 $P<0.05$)。双因素方差分析进一步表明,牙周炎与微波辐射对血清TNF- α 水平存在交互作用(表3; $P=0.038$),提示二者在升高血清TNF- α 方面具有协同效应。



a-c: the open field test. a: distance in central; b: time in central; c: entries to the center. d-g: the elevated plus maze test. d: elevated plus maze tracking plot; the trajectory map of the PR group shows that the distance mice traveled in the open arms was significantly shortened; e: percentage of distance in the open arms; f: percentage of time in the open arms; g: percentage of open arm entries. h&i: the Y maze test. h: Y-maze trajectory map; in the trajectory map of the PR group, the lines representing the mice's entries into arm B are thinner, indicating a significant reduction in the number of entries; i: spontaneous alternation rate (%). j: the novel object recognition test, discrimination index (%); * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, ns: no statistical significance, $n = 10-12$. C group: control group, no treatment; P group: ligation modeling only; R group: microwave radiation exposure only; PR group: ligation modeling and microwave radiation exposure

Figure 1 Effects of microwave radiation on anxiety-like behavior and cognitive function of mice with periodontitis

图1 微波辐射对牙周炎小鼠焦虑样行为及认知功能的影响



a: HE staining of periodontal tissue; the PR group exhibited more severe periodontal attachment loss and inflammatory cell infiltration; b: three-dimensional reconstruction results from micro-CT; a significant increase in alveolar bone resorption was evident in the PR group; c: quantitative analysis of CEJ-ABC distance; d: qPCR detection results of periodontal tissues; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, ns: no statistical significance, $n = 3$. CEJ-ABC: cemento-enamel junction to alveolar bone crest. C group: control group, no treatment; P group: ligation modeling only; R group: microwave radiation exposure only; PR group: ligation modeling and microwave radiation exposure. TNF-α: tumor necrosis factor-α; IL-1: interleukin-1; IL-6: interleukin-6

Figure 2 Effects of microwave radiation on periodontal tissues of mice with periodontitis

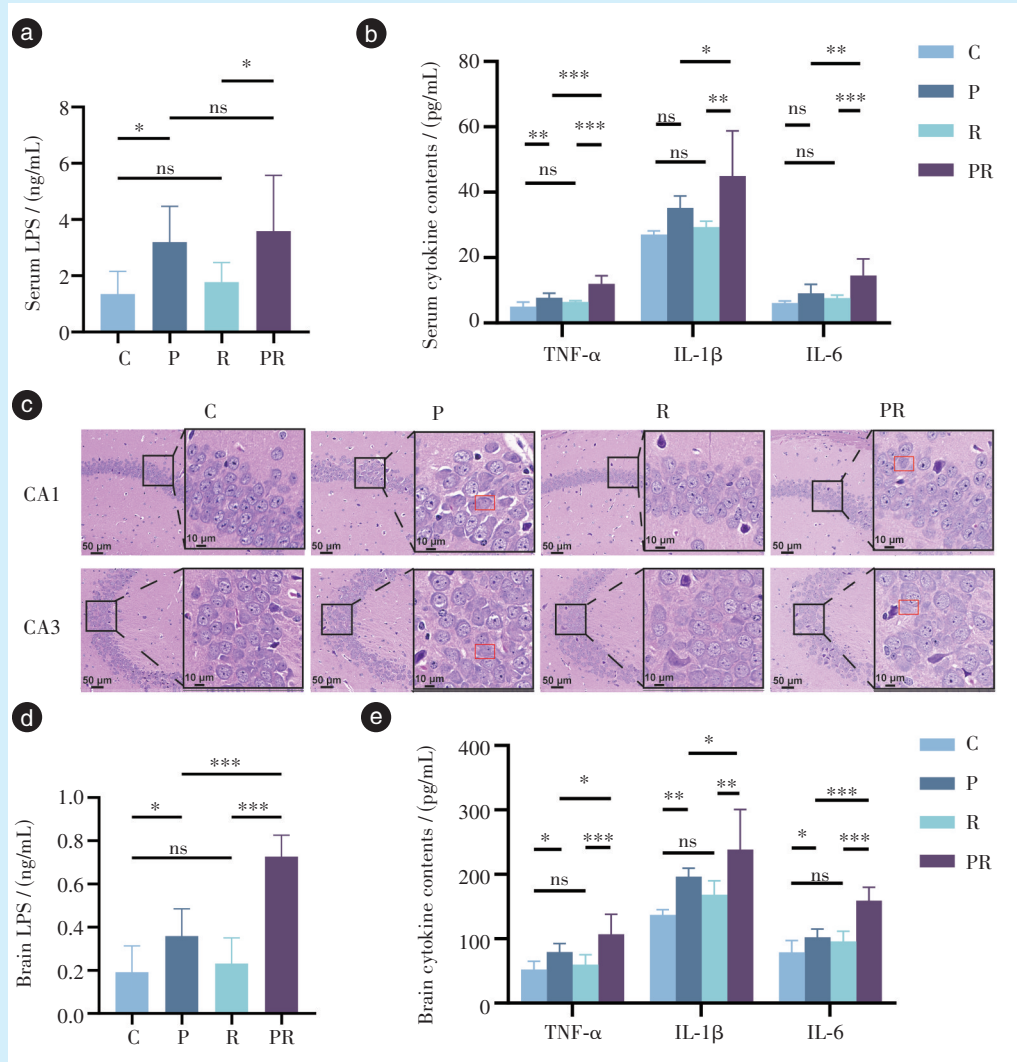
图2 微波辐射对牙周炎小鼠牙周组织的影响

脑组织 HE 染色结果显示(图 3c),与 C 组相比, P 组小鼠海马 CA1 区及 CA3 区神经元排列疏松,部分神经元胞体出现固缩; R 组可见神经元排列紧密、胞体轻微固缩; PR 组可见神经元胞体固缩、神经元数量进一步减少。相较于 C 组, P 组 LPS、TNF-α、IL-1β 及 IL-6 含量均增加(均 $P < 0.05$); R 组上述指标与 C 组相比差异均无统计学意义; PR 组上述各项指标的水平均高于 P 组与 R 组(均 $P < 0.05$)(图 3d、3e)。双因素方差分析提示,牙周炎与微波辐射对脑组织 LPS 及 IL-6 含量均存在交互作用(表 4; $P = 0.003$; $P = 0.01$),说明两者在诱发脑组织炎症反应方面同样表现协同作用。

综上,微波辐射暴露不仅加剧了牙周炎小鼠的外周炎症状态,而且与牙周炎协同作用,显著加重了脑组织的炎症负荷。

2.5 微波辐射可改变牙周炎小鼠口腔菌群

2.5.1 微波辐射对牙周炎小鼠口腔菌群多样性的影响 微波辐射对牙周炎小鼠口腔菌群多样性的影响见图 4。在 α 多样性方面, Chao1 指数与 Shannon 指数分析显示,组间菌群丰富度与多样性存在差异。与 C 组相比, P 组的菌群丰富度与多样性均降低, R 组与 C 组差异无统计学意义。PR 组与 R 组相比,亦呈现相同的降低趋势($P < 0.001$),提示微波辐射和牙周炎共同作用进一步削弱了口腔菌群



a: LPS content in serum; b: inflammatory cytokine content in serum; c: HE staining of brain tissue; neurons in the cornu ammonis (CA) 1 and CA3 regions of the PR group were loosely arranged with pyknotic cell bodies (red boxes); d: LPS content in the brain; e: inflammatory cytokine content in the brain; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; ns: no statistical significance, $n = 6$. LPS: lipopolysaccharide; TNF-α: tumor necrosis factor-α; IL-1β: interleukin-1β; IL-6: interleukin-6. C group: control group, no treatment; P group: ligation modeling only; R group: microwave radiation exposure only; PR group: ligation modeling and microwave radiation exposure

Figure 3 Effects of microwave radiation on levels of LPS and inflammatory cytokines in the serum and brain tissues of mice with periodontitis

图3 微波辐射对牙周炎小鼠血清及脑组织LPS及炎症因子含量影响

表3 血清中LPS及炎症因子含量析因分析结果

Table 3 Results of factorial analysis of LPS and inflammatory factor levels in serum

Factor	Serum LPS		Serum TNF-α		Serum IL-1β		Serum IL-6	
	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>
R	0.64	0.430	19.53	0.003	4.184	0.054	8.421	0.009
P	12.82	0.002	42.66	<0.001	16.30	<0.001	16.95	<0.001
P×R	<0.001	0.980	4.929	0.038	1.615	0.218	2.756	0.113

P group: ligation modeling only; R group: microwave radiation exposure only; P×R: interaction between periodontitis group and microwave radiation group. LPS: lipopolysaccharide; TNF-α: tumor necrosis factor-α; IL-1β: interleukin-1β; IL-6: interleukin-6

表 4 脑组织中LPS及炎症因子含量析因分析结果

Table 4 Results of factorial analysis of LPS and inflammatory factor levels in brain tissues

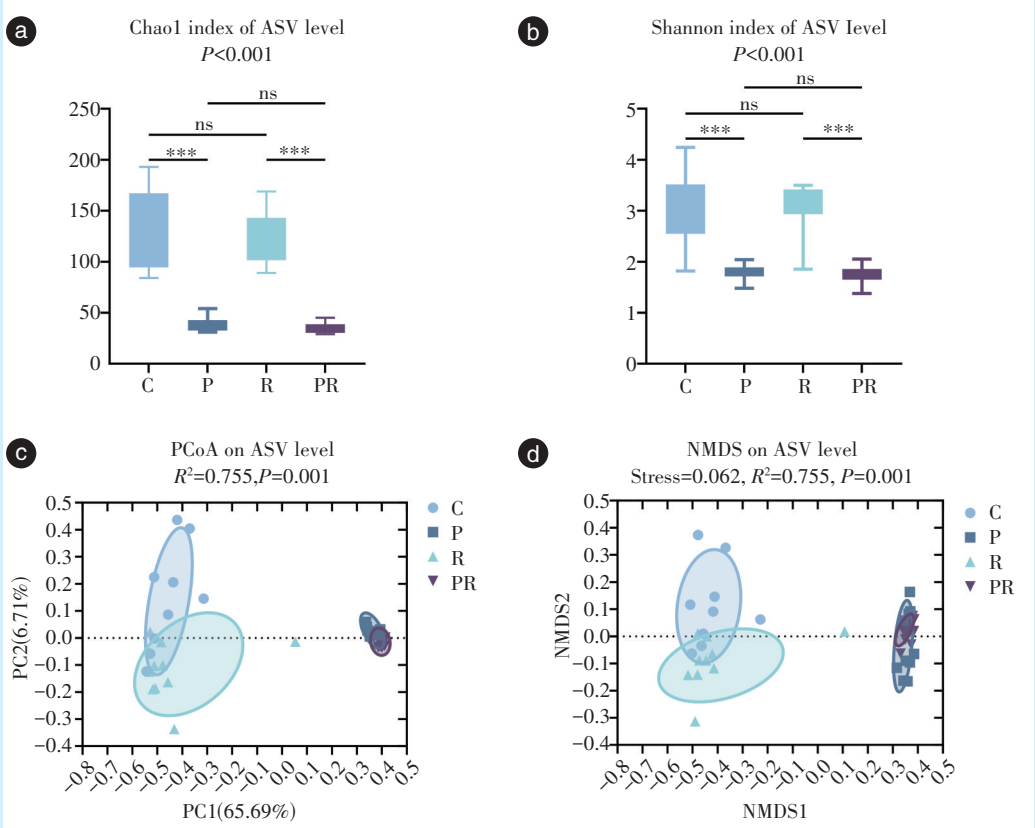
Factor	Brain LPS		Brain TNF-α		Brain IL-1β		Brain IL-6	
	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>
R	18.21	<0.001	4.882	0.039	7.032	0.015	27.71	<0.001
P	47.93	<0.001	21.61	<0.001	21.83	<0.001	37.47	<0.001
P×R	11.74	0.003	1.55	0.228	0.157	0.696	8.027	0.01

P group: ligation modeling only; R group: microwave radiation exposure only; P×R: interaction between periodontitis group and microwave radiation group. LPS: lipopolysaccharide; TNF-α: tumor necrosis factor-α; IL-1β: interleukin-1β; IL-6: interleukin-6

的多样性。

基于 Bray-Curtis 距离的 β 多样性 (PCoA 与 NMDS) 表明, 各组口腔菌群结构分离 ($P=0.001$)。

P 组与 PR 组样本聚集紧密, 说明牙周炎是驱动菌群结构改变的主导因素, 而微波辐射的介入使 PR 组菌群结构发生进一步偏离。



a: alpha diversity analysis (Chao1 index); b: alpha diversity analysis (Shannon index); c: beta diversity analysis (PCoA plot); the samples from the P and PR groups were tightly clustered; d: beta diversity analysis (NMDS plot); the samples from the P and PR groups were tightly clustered; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; ns: no statistical significance. $n=9-12$. ASV: amplicon sequence variant; PcoA: principal coordinate analysis; NMDS: non-metric multidimensional scaling. C group: control group, no treatment; P group: ligation modeling only; R group: microwave radiation exposure only; PR group: ligation modeling and microwave radiation exposure

Figure 4 Effects of microwave exposure on the oral microbiota diversity of mice with periodontitis

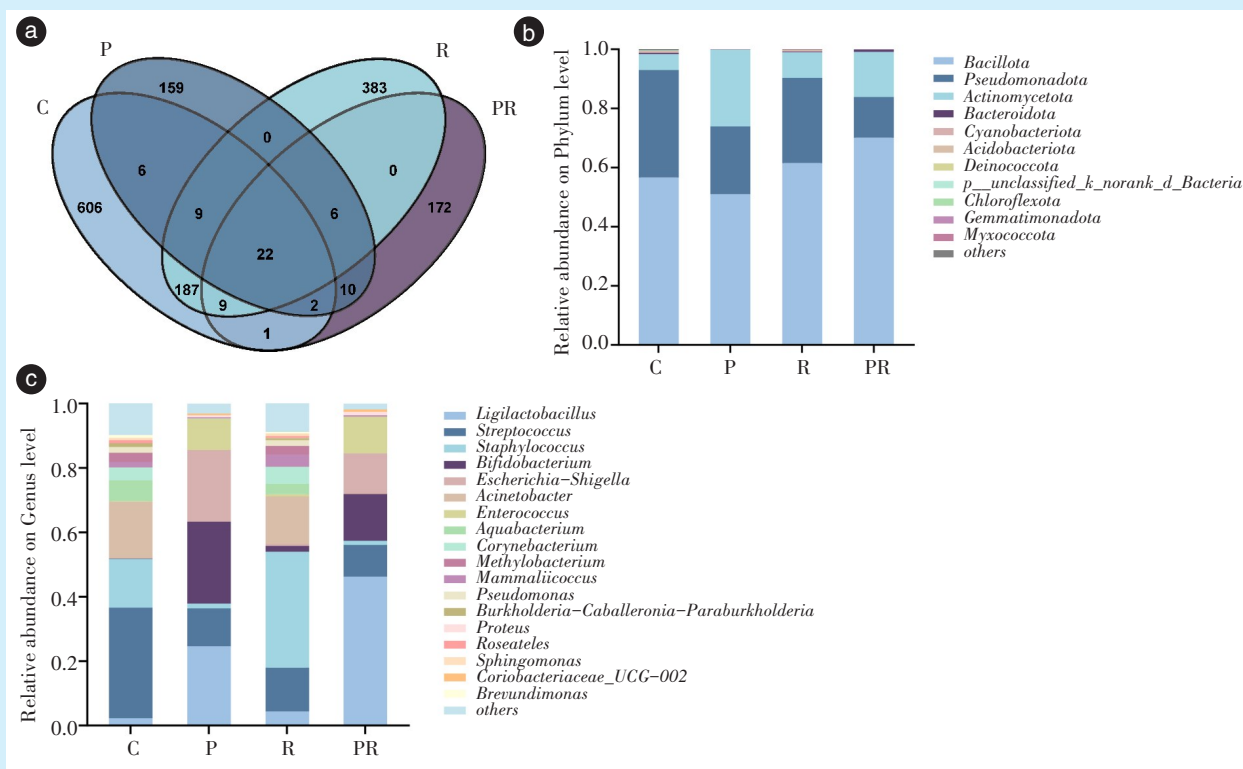
图 4 微波辐射对牙周炎小鼠口腔菌群多样性的影响

2.5.2 微波辐射对牙周炎小鼠口腔菌群群落结构的影响 微波辐射对牙周炎小鼠口腔菌群群落结构的影响见 图 5。所有样本共获得 1 570 个 ASVs。

韦恩图显示, C、P、R、PR 四组分别含有 606、159、383 和 172 个特有 ASVs。其中 P 组与 PR 组共享 40 个 ASVs, 提示二者具有部分共同的核心菌群。门水

平上,所有组别口腔菌群均以厚壁菌门、变形菌门、放线菌门为主导,但其相对丰度发生改变。与C组相比,P组、R组及PR组均可见厚壁菌门比例上升,而变形菌门比例下降,其中PR组变化最明显。属水平进一步揭示了菌群结构的特异性改变。C组及R组均以链球菌属、不动杆菌属、葡萄

球菌属为主;P组则转变为以双歧杆菌属、唾液乳杆菌属、埃希氏菌-志贺氏菌属为主导。而PR组表现出独特的组成模式:唾液乳杆菌属异常增殖成为最优势菌,而双歧杆菌属丰度较P组大幅降低,同时保留了较高丰度的埃希氏菌-志贺氏菌属和肠球菌属。



a: Venn diagram; b: composition of oral microbiota at the phylum level; c: composition of oral microbiota at the genus level; $n = 9-12$. C group: control group, no treatment; P group: ligation modeling only; R group: microwave radiation exposure only; PR group: ligation modeling and microwave radiation exposure

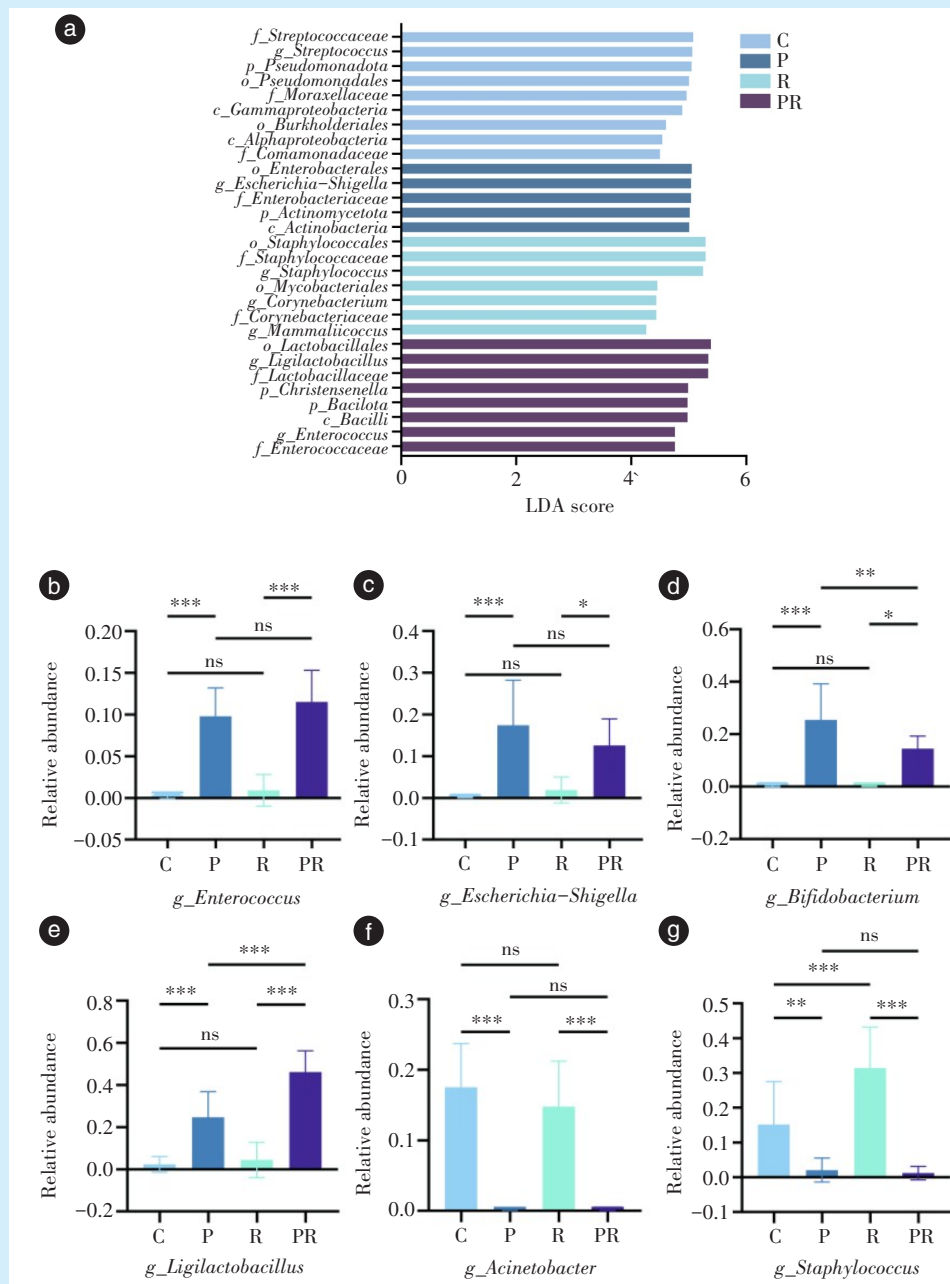
Figure 5 Effect of microwave radiation on the oral microbiota community structure of mice with periodontitis

图5 微波辐射对牙周炎小鼠口腔菌群群落结构的影响

2.5.3 微波辐射对牙周炎小鼠口腔菌群差异物种的影响 微波辐射对牙周炎小鼠口腔菌群差异物种的影响见图6。LEfSe分析结果显示,C组的标志物种为芽孢杆菌纲-乳杆菌目-链球菌科-链球菌属、变形菌门- γ -变形菌纲-伯克氏菌目-丛毛单胞菌科。P组具有差异的优势物种为 γ -变形菌纲-肠杆菌目-肠杆菌科-埃希氏菌-志贺氏菌属。R组具有差异的优势物种为芽孢杆菌纲-葡萄球菌目-葡萄球菌科-葡萄球菌属、芽孢杆菌纲-葡萄球菌目-葡萄球菌科-哺乳动物球菌属、放线菌纲-分枝杆菌目-棒状杆菌科-棒状杆菌属。PR组具有差异的优势物种为厚壁菌门-芽孢杆菌纲-乳杆菌目-乳酸杆

菌科-乳杆菌属、厚壁菌门-芽孢杆菌纲-乳杆菌目-肠球菌科-肠球菌属(LDA得分 >4.0 , $P < 0.05$)。

组间比较发现,相较于C组与R组,P组与PR组的口腔菌群结构发生了系统性偏移,表现为埃希氏菌-志贺氏菌属、肠球菌属、双歧杆菌属和乳杆菌属类群的整体性增多(均 $P < 0.05$),而葡萄球菌属与不动杆菌属等常见口腔共生类群则显著减少(均 $P < 0.05$)。且PR组乳杆菌属的相对丰度高于P组($P < 0.001$),同时双歧杆菌属的相对丰度降低($P < 0.01$),提示在微波辐射与牙周炎共同作用下,口腔微生物群落不仅发生了数量变化,更出现了明显的结构重组与生态位更替。



a: LEfSe analysis plot; b: relative abundance of *Enterococcus*; c: relative abundance of *Escherichia-Shigella*; d: relative abundance of *Bifidobacterium*; e: relative abundance of *Ligilactobacillus*; f: relative abundance of *Acinetobacter*; g: relative abundance of *Staphylococcus*; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, ns: no statistical significance, $n = 9-12$; LDA score: linear discriminant analysis score. LEfSe: linear discriminant analysis effect size. C group: control group, no treatment; P group: ligation modeling only; R group: microwave radiation exposure only; PR group: ligation modeling and microwave radiation exposure

Figure 6 Effect of microwave radiation on differential oral microbial species of mice with periodontitis

图6 微波辐射对牙周炎小鼠口腔菌群差异物种的影响

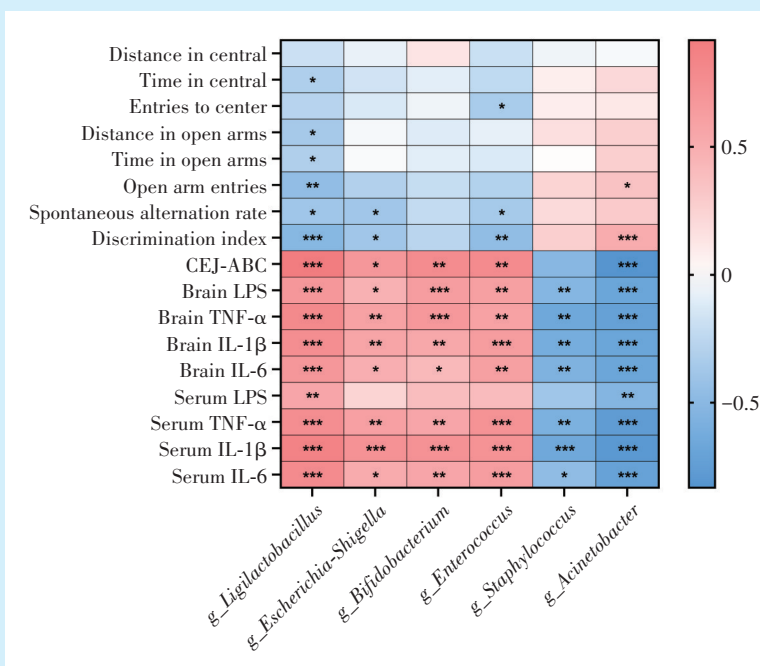
2.6 口腔菌群与宿主整体表型的相关性分析

口腔菌群与宿主整体表型的相关性分析见图7。

Spearman 相关性热图分析结果显示,埃希氏菌-志贺氏菌属、肠球菌属、双歧杆菌属和乳杆菌属与脑组织和血清炎症因子水平呈正相关,与自发交替率和识别指数等认知指标呈负相关。葡萄球菌属

和不动杆菌属与脑组织和血清炎症因子水平表现负相关。

以上结果提示,微波辐射与牙周炎诱导的菌群改变可能与全身炎症反应增强及认知功能下降存在密切联系,口腔菌群紊乱可能是连接环境暴露与神经行为表型的重要桥梁。



Heatmap of correlations between differential oral bacteria and host phenotypic parameters; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, $n = 8-12$; CEJ-ABC: cemento-enamel junction to alveolar bone crest; LPS: lipopolysaccharide; TNF-α: tumor necrosis factor-α; IL-1β: interleukin-1β; IL-6: interleukin-6.

Figure 7 Correlation between oral microbiota and host phenotypic parameters

图7 口腔菌群与宿主整体表型的相关性分析

3 讨论

本研究通过建立牙周炎与微波辐射双重暴露的小鼠模型,旨在探究2 800 MHz微波辐射在牙周炎背景下对认知功能的影响。实验所用辐射参数(2 800 MHz、10 mW/cm²、10 h/d、持续7 d)参考了现代无线通信的典型频段,并与该领域已发表的动物实验研究中所采用的微波暴露条件相接近,同时也模拟了相关职业人群可能面临的高暴露情境^[13-14]。该频段覆盖了多种日常及专业应用场景,例如部分无线电话、蓝牙耳机等电子设备,以及早期2.5G移动通信和4G的部分上行频段^[15];在工业领域,该频率亦用于点对点数字图传、无线遥测等专用数据链路^[16];在军事应用方面,该频段(通常称为S波段)是许多军用雷达系统的工作频率范围,同时也可能应用于电子对抗、战术数据链及部分军事卫星通信地面终端^[17]。结果表明,微波辐射作为一种环境压力源,不仅可单独诱发焦虑样行为与学习记忆损伤,更能加剧牙周炎相关的认知功能损伤。

该损伤过程伴随口腔局部(炎症浸润加重、骨吸收增加)至全身循环(LPS及促炎因子水平升高),再到脑组织炎症负荷加重的级联性病理改变,且在全身及脑组织炎症因子层面均表现出显著的协同效应,而非简单的效应叠加。同时,研究揭示口腔菌群结构的重塑与认知功能损伤及外周/

脑组织炎症因子水平升高密切相关。综上,本研究提示,在疾病状态下,环境微波辐射可能通过加重口腔菌群失调、驱动系统性炎症并加剧脑组织炎症这一系列的病理环节,从而显著放大对脑组织的损伤效应。

3.1 微波辐射加剧小鼠牙周炎相关认知功能损伤

本研究证实,微波辐射本身可诱导小鼠产生焦虑样行为并损害其学习记忆能力,这与既往研究报道的微波辐射对中枢神经系统的非热效应相符^[18-19]。此外,当微波辐射作用于已存在牙周炎的小鼠时,其对认知功能的损伤效应被显著放大。这一发现将环境物理因素的神经毒性研究从“健康机体”模型扩展至“慢性炎症”这一更为普遍且脆弱的内在状态,提示个体的基础疾病负荷是评估环境风险时不可忽视的关键因素^[20]。这为解释在相同环境暴露下,不同健康状态的个体会出现显著差异的神经系统反应提供了实验依据^[21]。这种损伤的神经生物学基础可能涉及环境因素对已处于炎症应激状态的血脑屏障的进一步破坏、对小胶质细胞激活的增强以及对海马突触可塑性的干扰^[22],这有待后续研究在细胞与分子层面进行深入探索。

3.2 微波辐射加剧牙周局部病理进程

本研究首先在局部组织层面证实,微波辐射能显著加剧实验性牙周炎的病理进展。与P组相

比,PR组小鼠的牙龈组织表现出更严重的炎症细胞浸润与软组织破坏,牙槽骨吸收程度进一步增加,局部促炎因子(TNF- α 、IL-1 β 、IL-6)的mRNA表达水平显著上调。这些结果表明,微波辐射对牙周组织具有显著的破坏和炎症促进作用。已有研究发现微波辐射作为一种物理应激,不仅可诱发低水平氧化应激,其非热效应亦可能直接影响细胞膜通透性与细胞内信号转导,造成组织损伤^[23-24]。因此,微波辐射可能通过加剧细胞损伤和组织破坏,并激活炎症相关信号通路,从而加重牙周组织病理改变。此外,加剧的牙周局部炎症与破坏,可能加重了牙周血管通透性,促进口腔细菌及LPS等因子的全身性易位,从而为后续系统性炎症的升高提供了明确的病理基础^[25-26]。

3.3 系统性炎症与脑组织炎症的级联放大

本研究中,微波辐射加重了牙周炎小鼠的牙龈炎症浸润、牙槽骨吸收及局部促炎因子表达,提示其直接加剧了原发性口腔疾病的病理过程。局部组织的进一步破坏,可能促进了口腔细菌及其代谢产物向循环系统的迁移。在系统层面,PR组小鼠血清中的TNF- α 、IL-1 β 、IL-6水平相较于P组显著升高,说明源自口腔的炎症介质可能已大量进入循环,引发全身性炎症状态。类似机制在其他病理条件下亦有报道,例如肠道菌群失调可通过增加肠道通透性促使炎症因子入血,进而诱发系统性炎症并影响中枢神经系统功能^[27-28]。此外,病程5个月的新冠住院患者中也观察到全身性炎症因子与脑内炎症因子水平呈正相关,进一步支持外周炎症与中枢神经变化之间的密切联系^[29]。

在中枢层面,PR组小鼠脑组织中LPS与IL-6水平呈现协同性升高,提示微波辐射与牙周炎的共同暴露加剧了脑内的促炎环境。现有研究表明,循环中的LPS可进入中枢神经系统并激活小胶质细胞的TLR4受体^[30],进而触发下游NF- κ B、STAT3等炎症信号通路^[31],而持续的小胶质细胞活化及其释放的炎症因子(如IL-1 β 、TNF- α)可损害神经元与突触功能,是多种认知障碍疾病的共同病理基础^[32-33]。尽管本研究未直接观测小胶质细胞活化状态,但脑内LPS与IL-6的协同升高与其可能参与的神经免疫激活机制相一致^[34]。未来研究可通过检测小胶质细胞/星形胶质细胞特异性标志物、血脑屏障完整性及相关信号通路蛋白,进一步明确微波辐射在牙周炎背景下影响中枢免疫应答的具体细胞与分子机制。

3.4 口腔菌群:连接环境暴露与系统炎症的关键环节

本研究的另一个关键发现在于,微波辐射与牙周炎共同作用可显著改变口腔菌群结构与组成,而非仅引起单一菌属的数量波动。本研究中,辐射结束1周后即观察到显著的菌群变化。这一快速改变可能源于实验的复合模型:牙周丝线结扎术首先造成了急性损伤与菌群失衡,创造了不稳定的微环境;随后施加的微波辐射作为“二次打击”,进一步筛选并富集了具有特定耐受性或致病潜能的菌群。这与急性应激可导致黏膜菌群在数天内快速重构的研究相符^[35]。 α 与 β 多样性分析共同表明,微波辐射在牙周炎所致菌群失调的基础上,使口腔微生物的丰富度与均匀度存在显著下降趋势。这一结果与多种慢性炎症状态下微生物群落稳定性受损、多样性丧失的特征相一致^[36]。本研究进一步揭示,牙周炎作为初始应激已破坏口腔微生态的稳定,在微波辐射这一物理应激下被放大,导致微生物群落的恢复力下降,整体结构更趋于单一化和不稳定状态($P=0.001$)。LEfSe分析与组间比较显示,相较于C与R组,P组与PR组口腔菌群呈现出明确的生态位更替趋势:葡萄球菌属与不动杆菌属等菌群相对丰度显著降低,而肠球菌属、埃希氏菌-志贺氏菌属、乳杆菌属等菌群相对丰度显著富集。特别值得注意的是,PR组中乳杆菌属相对丰度显著高于P组,而双歧杆菌属丰度却显著降低,这一变化模式不宜简单归因于“有益菌”的增加或者“有害菌”的减少,而是反映出在微波辐射与慢性炎症的双重压力下,口腔菌群发生了特异性、整体性的结构重组。此外,本研究的菌群观察时间点集中在辐射后1周,虽然观察到了菌群的显著变化,但未能描绘其动态演变过程。未来需要多个时间点的追踪以明确这种变化的持续性与稳定性。

这种重构后的菌群结构,其生物学意义通过与宿主表型的相关性分析得以进一步阐明。乳杆菌属、肠球菌属等异常增殖的菌群,与牙槽骨吸收、系统性及中枢神经炎症水平的升高、以及认知行为表现的下降均存在显著关联。已有研究发现,牙周炎相关的菌群失调可通过加重整体炎症水平加剧中枢神经性疾病的发展进程^[37-38]。同时,微波辐射作为一种物理应激,已被证实可影响微生物的生存状态,其非热效应可能改变细胞膜通透性,直接导致微生物代谢功能紊乱^[39]。这强烈

提示,环境因素与慢性炎症共同塑造的“低多样性、高炎症潜力”的菌群结构,可能具备更强的促炎潜力和更差的功能相容性。

因此,本研究结果提示,“口腔菌群”在环境应激与慢性疾病交互作用中可能处于核心位置。微波辐射与牙周炎的共同作用最终体现为口腔微生态从共生、多样的稳定态,向促炎、单一的失衡态发生结构性转变。这一菌群整体结构的失调,而非单个菌属的孤立变化,可能是连接口腔局部病变与脑组织炎症及认知功能下降的关键中间桥梁,这与其他研究认为口腔微生物生态系统可通过免疫、神经及内分泌途径与大脑进行双向通信、进而影响中枢神经系统健康的观点一致^[40]。近期综述进一步指出,牙周炎可能通过“口腔-肠-脑轴”参与认知相关疾病的病理过程^[41]。在此框架下,本研究将“微波辐射”这一环境因素纳入考察,发现其与牙周炎共同塑造出一种促炎型的口腔菌群结构,且该结构与系统性炎症及脑组织炎症升高、认知功能下降均表现出相关性。

本研究揭示了微波辐射与牙周炎对脑组织的协同损伤作用,并且发现口腔菌群可能为该效应的关键中介,在诱导和放大脑组织炎症中发挥作用。这一发现不仅强调了在慢性疾病背景下重新评估环境电磁辐射健康风险的重要性,并为理解“口腔-脑轴”在环境与疾病交互作用中的机制提供了新的科学视角。

[Author contributions] Zhou HJ was responsible for experimental design and implementation, data curation, manuscript writing and revision. Wang JH, Liu L were responsible for experimental implementation, statistical analysis. Li HB was responsible for experimental design guidance and manuscript review. All authors read and approved the final manuscript as submitted.

参考文献

- [1] Yamaguchi S, Murakami T, Satoh M, et al. Associations of dental health with the progression of hippocampal atrophy in community-dwelling individuals: the ohasama study[J]. *Neurology*, 2023, 101(10): e1056-e1068. doi: [10.1212/WNL.0000000000207579](https://doi.org/10.1212/WNL.0000000000207579).
- [2] Armitage GC. Periodontal diagnoses and classification of periodontal diseases[J]. *Periodontol* 2000, 2004, 34: 9-21. doi: [10.1046/j.0906-6713.2002.003421.x](https://doi.org/10.1046/j.0906-6713.2002.003421.x).
- [3] Villoria GEM, Fischer RG, Tinoco EMB, et al. Periodontal disease: a systemic condition[J]. *Periodontol* 2000, 2024, 96(1): 7-19. doi: [10.1111/prd.12616](https://doi.org/10.1111/prd.12616).
- [4] Fu YD, Li CL, Hu CL, et al. Meta analysis of the correlation between periodontal health and cognitive impairment in the older population[J]. *J Prev Alzheimers Dis*, 2024, 11(5): 1307-1315. doi: [10.14283/jpad.2024.87](https://doi.org/10.14283/jpad.2024.87).
- [5] Mao S, Huang CP, Lan H, et al. Association of periodontitis and oral microbiomes with Alzheimer's disease: a narrative systematic review[J]. *J Dent Sci*, 2022, 17(4): 1762-1779. doi: [10.1016/j.jds.2022.07.001](https://doi.org/10.1016/j.jds.2022.07.001).
- [6] Hardell L, Nilsson M. Case report: the microwave syndrome after installation of 5G emphasizes the need for protection from radiofrequency radiation[J]. *Ann Case Rep*, 2023, 8(1): 1112. doi: [10.29011/2574-7754.101112](https://doi.org/10.29011/2574-7754.101112).
- [7] Wang H, Liu Y, Sun Y, et al. Changes in cognitive function, synaptic structure and protein expression after long-term exposure to 2.856 and 9.375 GHz microwaves[J]. *Cell Commun Signal*, 2023, 21(1): 34. doi: [10.1186/s12964-022-01011-1](https://doi.org/10.1186/s12964-022-01011-1).
- [8] Pophof B, Kuhne J, Schmid G, et al. The effect of exposure to radiofrequency electromagnetic fields on cognitive performance in human experimental studies: systematic review and meta-analyses [J]. *Environ Int*, 2024, 191: 108899. doi: [10.1016/j.envint.2024.108899](https://doi.org/10.1016/j.envint.2024.108899).
- [9] El-Kafoury BMA, Abdel-Hady EA, El Bakly W, et al. Lipoic acid inhibits cognitive impairment induced by multiple cell phones in young male rats: role of Sirt1 and Atg7 pathway[J]. *Sci Rep*, 2023, 13(1): 18486. doi: [10.1038/s41598-023-44134-2](https://doi.org/10.1038/s41598-023-44134-2).
- [10] Honda K, Littman DR. The microbiota in adaptive immune homeostasis and disease[J]. *Nature*, 2016, 535(7610): 75-84. doi: [10.1038/nature18848](https://doi.org/10.1038/nature18848).
- [11] Banerjee S, Singh NN, Sreedhar G, et al. Analysis of the genotoxic effects of mobile phone radiation using buccal micronucleus assay: a comparative evaluation[J]. *J Clin Diagn Res*, 2016, 10(3): ZC82-ZC85. doi: [10.7860/JCDR/2016/17592.7505](https://doi.org/10.7860/JCDR/2016/17592.7505).
- [12] Zhou GQ, Wang X, Gao P, et al. Intestinal microbiota via NLRP3 inflammasome dependent neuronal pyroptosis mediates anxiety-like behaviour in mice exposed to 3.5 GHz radiofrequency radiation[J]. *Sci Total Environ*, 2024, 927: 172391. doi: [10.1016/j.scitotenv.2024.172391](https://doi.org/10.1016/j.scitotenv.2024.172391).
- [13] Melnick RL, Moskowitz JM, Héroux P, et al. The WHO-commissioned systematic reviews on health effects of radiofrequency radiation provide no assurance of safety[J]. *Environ Health*, 2025, 24(1): 70. doi: [10.1186/s12940-025-01220-4](https://doi.org/10.1186/s12940-025-01220-4).
- [14] Zheng R, Zhang X, Gao Y, et al. Biological effects of exposure to 2650 MHz electromagnetic radiation on the behavior, learning, and memory of mice[J]. *Brain Behav*, 2023, 13(6): e3004. doi: [10.1002/brb3.3004](https://doi.org/10.1002/brb3.3004).
- [15] Bosch-Capblanch X, Esu E, Dongus S, et al. The effects of radiofrequency electromagnetic fields exposure on human self-reported symptoms: a protocol for a systematic review of human experimental studies[J]. *Environ Int*, 2022, 158: 106953. doi: [10.1016/j.envint.2021.106953](https://doi.org/10.1016/j.envint.2021.106953).
- [16] Yoo SE, Chong PK, Kim D, et al. Guaranteeing real-time services for industrial wireless sensor networks with IEEE 802.15.4[J]. *IEEE Trans Ind Electron*, 2010, 57(11): 3868-3876. doi: [10.1109/TIE.2010.2040630](https://doi.org/10.1109/TIE.2010.2040630).
- [17] Farooqi A, Ramdhani MA, Andika DD, et al. Design of 2.75-2.85 GHz frequency microstrip band pass filter with square open-loop

- resonator in radar method[J]. *Int J Eng & Technol*, 2018, 7(2): 711-715. doi: [10.14419/ijet.v7i2.29.14003](https://doi.org/10.14419/ijet.v7i2.29.14003).
- [18] Li Y, Deng P, Chen C, et al. 1, 800 MHz radiofrequency electromagnetic irradiation impairs neurite outgrowth with a decrease in Rap1-GTP in primary mouse hippocampal neurons and Neuro2a cells[J]. *Front Public Health*, 2021, 9: 771508. doi: [10.3389/fpubh.2021.771508](https://doi.org/10.3389/fpubh.2021.771508).
- [19] Sun B, Xue T, Gao AN, et al. The CB1R of mPFC is involved in anxiety-like behavior induced by 0.8/2.65 GHz dual-frequency electromagnetic radiation[J]. *Front Mol Neurosci*, 2025, 18: 1534324. doi: [10.3389/fnmol.2025.1534324](https://doi.org/10.3389/fnmol.2025.1534324).
- [20] Ji W, Li L, Cheng Y, et al. Air pollution, lifestyle, and cardiovascular disease risk in northwestern China: a cohort study of over 5.8 million participants[J]. *Environ Int*, 2025, 199: 109459. doi: [10.1016/j.envint.2025.109459](https://doi.org/10.1016/j.envint.2025.109459).
- [21] Ma J, Zhang J, Zhang Y, et al. Causal effects of noise and air pollution on multiple diseases highlight the dual role of inflammatory factors in ambient exposures[J]. *Sci Total Environ*, 2024, 951: 175743. doi: [10.1016/j.scitotenv.2024.175743](https://doi.org/10.1016/j.scitotenv.2024.175743).
- [22] Chen L, Zhang J, Fei X, et al. Hypobaric hypoxia aggravates neuroinflammation in ligature-induced periodontitis mice *via* the STAT3 signaling pathway[J]. *Front Immunol*, 2025, 16: 1600035. doi: [10.3389/fimmu.2025.1600035](https://doi.org/10.3389/fimmu.2025.1600035).
- [23] Haidar J, Nabos P, Orlacchio R, et al. Impact of *in vitro* exposure to 5G-modulated 3.5 GHz fields on oxidative stress and DNA repair in skin cells[J]. *Sci Rep*, 2025, 15(1): 31214. doi: [10.1038/s41598-025-15090-w](https://doi.org/10.1038/s41598-025-15090-w).
- [24] Lai H, Levitt BB. Cellular and molecular effects of non-ionizing electromagnetic fields[J]. *Rev Environ Health*, 2023, 39(3): 519-529. doi: [10.1515/reveh-2023-0023](https://doi.org/10.1515/reveh-2023-0023).
- [25] Singh Solorzano C, De Cillis F, Mombelli E, et al. From gums to moods: exploring the impact of the oral microbiota on depression [J]. *Brain Behav Immun Health*, 2025, 48: 101057. doi: [10.1016/j.bbih.2025.101057](https://doi.org/10.1016/j.bbih.2025.101057).
- [26] Gao C, Li X, Zhao X, et al. Standardized studies of the oral microbiome: from technology-driven to hypothesis-driven[J]. *Imeta*, 2022, 1(2): e19. doi: [10.1002/imt2.19](https://doi.org/10.1002/imt2.19).
- [27] Yang J, Liang J, Hu N, et al. The gut microbiota modulates neuroinflammation in Alzheimer's disease: elucidating crucial factors and mechanistic underpinnings[J]. *CNS Neurosci Ther*, 2024, 30(10): e70091. doi: [10.1111/cns.70091](https://doi.org/10.1111/cns.70091).
- [28] Di Vincenzo F, Del Gaudio A, Petito V, et al. Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review[J]. *Intern Emerg Med*, 2024, 19(2): 275-293. doi: [10.1007/s11739-023-03374-w](https://doi.org/10.1007/s11739-023-03374-w).
- [29] Graf C, Raman B, Manktelow A, et al. Brainstem neurochemical profiles after hospitalisation for COVID-19: a 7T MR spectroscopy study[J]. *Front Neurosci*, 2025, 19: 1617709. doi: [10.3389/fnins.2025.1617709](https://doi.org/10.3389/fnins.2025.1617709).
- [30] Li F, Ma C, Lei S, et al. Gingipains may be one of the key virulence factors of *Porphyromonas gingivalis* to impair cognition and enhance blood-brain barrier permeability: an animal study[J]. *J Clin Periodontol*, 2024, 51(7): 818-839. doi: [10.1111/jcpe.13966](https://doi.org/10.1111/jcpe.13966).
- [31] Hu Y, Zhang X, Zhang J, et al. Activated STAT3 signaling pathway by ligature-induced periodontitis could contribute to neuroinflammation and cognitive impairment in rats[J]. *J Neuroinflammation*, 2021, 18(1): 80. doi: [10.1186/s12974-021-02071-9](https://doi.org/10.1186/s12974-021-02071-9).
- [32] Magni G, Riboldi B, Ceruti S. Modulation of glial cell functions by the gut-brain axis: a role in neurodegenerative disorders and pain transmission[J]. *Cells*, 2023, 12(12): 1612. doi: [10.3390/cells12121612](https://doi.org/10.3390/cells12121612).
- [33] Li R, Wang J, Xiong W, et al. The oral-brain axis: can periodontal pathogens trigger the onset and progression of Alzheimer's disease? [J]. *Front Microbiol*, 2024, 15: 1358179. doi: [10.3389/fmicb.2024.1358179](https://doi.org/10.3389/fmicb.2024.1358179).
- [34] Yuan S, Yang J, Jian Y, et al. Treadmill exercise modulates intestinal microbes and suppresses LPS displacement to alleviate neuroinflammation in the brains of APP/PS1 mice[J]. *Nutrients*, 2022, 14(19): 4134. doi: [10.3390/nu14194134](https://doi.org/10.3390/nu14194134).
- [35] Kelly LS, Apple CG, Gharaibeh R, et al. Stress-related changes in the gut microbiome after trauma[J]. *J Trauma Acute Care Surg*, 2021, 91(1): 192-199. doi: [10.1097/TA.0000000000003209](https://doi.org/10.1097/TA.0000000000003209).
- [36] Dai H, Luo S, Zhang X. Flavonoids from ficus pandurate var. angustifolia W.C. Cheng restore cognitive impairment and regulate the gut microbiota in sleep-deprived mice[J]. *Foods*, 2025, 14(16): 2888. doi: [10.3390/foods14162888](https://doi.org/10.3390/foods14162888).
- [37] Qian X, Lin X, Hu W, et al. Intestinal homeostasis disrupted by periodontitis exacerbates Alzheimer's disease in APP/PS1 mice [J]. *J Neuroinflammation*, 2024, 21(1): 263. doi: [10.1186/s12974-024-03256-8](https://doi.org/10.1186/s12974-024-03256-8).
- [38] Qiu C, Zhou W, Shen H, et al. Profiles of subgingival microbiomes and gingival crevicular metabolic signatures in patients with amnesic mild cognitive impairment and Alzheimer's disease[J]. *Alzheimers Res Ther*, 2024, 16(1): 41. doi: [10.1186/s13195-024-01402-1](https://doi.org/10.1186/s13195-024-01402-1).
- [39] Wang X, Zhou G, Lin J, et al. Effects of 4.9 GHz radiofrequency field exposure on brain metabolomic and proteomic characterization in mice[J]. *Biology (Basel)*, 2024, 13(10): 806. doi: [10.3390/biology13100806](https://doi.org/10.3390/biology13100806).
- [40] Chalmers JC, Hernandez-Kapila YL. The role of the oral microbiome, host response, and periodontal disease treatment in Alzheimer's disease: a primer[J]. *Periodontol 2000*, 2025, 98(1): 220-227. doi: [10.1111/prd.12631](https://doi.org/10.1111/prd.12631).
- [41] Adil NA, Omo-Erigbe C, Yadav H, et al. The oral-gut microbiome-brain axis in cognition[J]. *Microorganisms*, 2025, 13(4): 814. doi: [10.3390/microorganisms13040814](https://doi.org/10.3390/microorganisms13040814).

(编辑 张琳)



Open Access

This article is licensed under a Creative Commons

[Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).

Copyright © 2026 by Editorial Department of Journal of

Prevention and Treatment for Stomatological Diseases



官网