

**Morbus Alzheimer: Wird die Erkrankung durch Parodontitis beeinflusst?**

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**Literatur**

- [1] Chen CK, Wu YT, Chang YC. Association between chronic periodontitis and the risk of Alzheimer's disease: a retrospective, population-based, matched-cohort study. *Alzheimers Res Ther.* 2017 Aug 8;9(1):56. doi: 10.1186/s13195-017-0282-6.
- [2] Choi S, Kim K, Chang J, Kim SM, Kim SJ, Cho HJ, Park SM. Association of Chronic Periodontitis on Alzheimer's Disease or Vascular Dementia. *J Am Geriatr Soc.* 2019 Jun;67(6):1234-1239. doi: 10.1111/jgs.15828.
- [3] Deutsche Alzheimer Gesellschaft e.V. Die Häufigkeit von Demenzerkrankungen. Informationsblatt 1. [https://www.deutsche-alzheimer.de/fileadmin/alz/pdf/factsheets/infoblatt1\\_haeufigkeit\\_demenzerkrankungen\\_dalzg.pdf](https://www.deutsche-alzheimer.de/fileadmin/alz/pdf/factsheets/infoblatt1_haeufigkeit_demenzerkrankungen_dalzg.pdf), abgerufen am 25.01.2020
- [4] Díaz-Zúñiga J, Muñoz Y, Melgar-Rodríguez S, et al. Serotype b of *Aggregatibacter actinomycetemcomitans* triggers pro-inflammatory responses and amyloid beta secretion in hippocampal cells: a novel link between periodontitis and Alzheimer's disease?. *J Oral Microbiol.* 2019;11(1):1586423. Published 2019 Apr 15. doi:10.1080/20002297.2019.1586423
- [5] Dioguardi M, Gioia GD, Caloro GA, Capocasale G, Zhurakivska K, Troiano G, Russo LL, Muzio LL. The Association between Tooth Loss and Alzheimer's Disease: a Systematic Review with Meta-Analysis of Case Control Studies. *Dent J (Basel).* 2019 May 1;7(2). pii: E49. doi: 10.3390/dj7020049.
- [6] Dominy SS, Lynch C, Ermini F, Benedyk M, Marczyk A, Konradi A, Nguyen M, Haditsch U, Raha D, Griffin C, Holsinger LJ, Arastu-Kapur S, Kaba S, Lee A, Ryder MI, Potempa B, Mydel P, Hellvard A, Adamowicz K, Hasturk H, Walker GD, Reynolds EC, Faull RLM, Curtis MA, Dragunow M, Potempa J. *Porphyromonas gingivalis* in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. *Sci Adv.* 2019 Jan 23;5(1):eaau3333. doi:10.1126/sciadv.aau3333.
- [7] Dunn N, Mullee M, Perry VH, Holmes C. Association between dementia and infectious disease: evidence from a case-control study. *Alzheimer Dis Assoc Disord.* 2005;19(2):91–94. doi:10.1097/01.wad.0000165511.52746.1f
- [8] Feres M, Teles F, Teles R, Figueiredo LC, Faveri M. The subgingival periodontal microbiota of the aging mouth. *Periodontol 2000.* 2016 Oct;72(1):30-53. doi: 10.1111/prd.12136.

- [9] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975; 12:189–198.
- [10] Hajishengallis G. Immune evasion strategies of *Porphyromonas gingivalis*. *J Oral Biosci.* 2011;53(3):233–240. doi:10.2330/joralbiosci.53.233
- [11] Hajishengallis G. Periodontitis: from microbial immune subversion to systemic inflammation. *Nat Rev Immunol.* 2015 Jan;15(1):30-44.
- [12] Han EC, Choi SY, Lee Y, Park JW, Hong SH, Lee HJ. Extracellular RNAs in periodontopathogenic outer membrane vesicles promote TNF- $\alpha$  production in human macrophages and cross the blood-brain barrier in mice. *FASEB J.* 2019;33(12):13412–13422. doi:10.1096/fj.201901575R
- [13] Han YW, Wang X. Mobile microbiome: oral bacteria in extra-oral infections and inflammation. *J Dent Res.* 2013 Jun;92(6):485-91. doi: 10.1177/0022034513487559. Epub 2013 Apr 26.
- [14] Hashioka S, Inoue K, Miyaoka T, Hayashida M, Wake R, Oh-Nishi A, Inagaki M. The Possible Causal Link of Periodontitis to Neuropsychiatric Disorders: More Than Psychosocial Mechanisms. *Int J Mol Sci.* 2019 Jul 30;20(15). pii: E3723. doi: 10.3390/ijms20153723.
- [15] Hayashi K, Hasegawa Y, Takemoto Y, Cao C, Takeya H, Komohara Y, Mukasa A, Kim-Mitsuyama S. Continuous intracerebroventricular injection of *Porphyromonas gingivalis* lipopolysaccharide induces systemic organ dysfunction in a mouse model of Alzheimer's disease. *Exp Gerontol.* 2019 Jun;120:1-5. doi: 10.1016/j.exger.2019.02.007.
- [16] Hill AB. The environment and disease: association or causation? *Proc R Soc Med.* 1965;58:295-300.
- [17] Holmer J, Eriksdotter M, Schultzberg M, Pussinen PJ, Buhlin K. Association between periodontitis and risk of Alzheimer's disease, mild cognitive impairment and subjective cognitive decline: A case-control study. *J Clin Periodontol.* 2018;45(11):1287–1298. doi:10.1111/jcpe.13016
- [18] Holmes C, El-Okli M, Williams AL, Cunningham C, Wilcockson D, Perry VH. Systemic infection, interleukin 1beta, and cognitive decline in Alzheimer's disease. *J Neurol Neurosurg Psychiatry.* 2003;74(6):788–789. doi:10.1136/jnnp.74.6.788
- [19] Ide M, Harris M, Stevens A, Sussams R, Hopkins V, Culliford D, Fuller J, Ibbett P, Raybould R, Thomas R, Puenter U, Teeling J, Perry VH, Holmes C. Periodontitis and Cognitive Decline in Alzheimer's Disease. *PLoS One.* 2016 Mar 10;11(3):e0151081. doi: 10.1371/journal.pone.0151081.
- [20] Ilievski V, Zuchowska PK, Green SJ, et al. Chronic oral application of a periodontal pathogen results in brain inflammation, neurodegeneration and

- amyloid beta production in wild type mice. PLoS One. 2018;13(10):e0204941. Published 2018 Oct 3. doi:10.1371/journal.pone.0204941
- [21] Kadowaki T, Baba A, Abe N, et al. Suppression of pathogenicity of Porphyromonas gingivalis by newly developed gingipain inhibitors. Mol Pharmacol. 2004;66(6):1599–1606. doi:10.1124/mol.104.004366
- [22] Kamer AR, Craig RG, Dasanayake AP, Brys M, Glodzik-Sobanska L, de Leon MJ. Inflammation and Alzheimer's disease: possible role of periodontal diseases. Alzheimers Dement. 2008 Jul;4(4):242-50. doi: 10.1016/j.jalz.2007.08.004.
- [23] Kamer AR, Craig RG, Pirraglia E, Dasanayake AP, Norman RG, Boylan RJ, Nehorayoff A, Glodzik L, Brys M, de Leon MJ. TNF-alpha and antibodies to periodontal bacteria discriminate between Alzheimer's disease patients and normal subjects. J Neuroimmunol. 2009 Nov 30;216(1-2):92-7. doi: 10.1016/j.jneuroim.2009.08.013.
- [24] Kamer AR, Dasanayake AP, Craig RG, Glodzik-Sobanska L, Bry M, de Leon MJ. Alzheimer's disease and peripheral infections: the possible contribution from periodontal infections, model and hypothesis. J Alzheimers Dis. 2008 May;13(4):437-49.
- [25] Kaulen H. Bakterien im Gehirn – Was hat Zahnfleisch mit Alzheimer zu tun? FAZ 18.02.2019. <https://www.faz.net/aktuell/wissen/medizin-ernaehrung/neue-stossr...eisch-mit-alzheimer-zu-tun-hat-16048243.html?service=printPreview>, zuletzt abgerufen am 18.01.2020
- [26] Kubota T, Maruyama S, Abe D, Tomita T, Morozumi T, Nakasone N, Saku T, Yoshie H. Amyloid beta (A4) precursor protein expression in human periodontitis-affected gingival tissues. Arch Oral Biol. 2014 Jun;59(6):586-94. doi: 10.1016/j.archoralbio.2014.03.004.
- [27] Kumar PS. From focal sepsis to periodontal medicine: a century of exploring the role of the oral microbiome in systemic disease. J Physiol. 2017 Jan 15;595(2):465-476.
- [28] Maldonado A, Laugisch O, Bürgin W, Sculean A, Eick S. Clinical periodontal variables in patients with and without dementia-a systematic review and meta-analysis. Clin Oral Investig. 2018;22(7):2463–2474. doi:10.1007/s00784-018-2523-x
- [29] Ming Y, Hsu SW, Yen YY, Lan SJ. Association of oral health-related quality of life and Alzheimer disease: A systematic review [published online ahead of print, 2019 Nov 18]. J Prosthet Dent. 2019;S0022-3913(19)30545-1. doi:10.1016/j.prosdent.2019.08.015
- [30] Molloy DW, Standish TI. A guide to the standardized Mini-Mental State Examination. Int Psychogeriatr. 1997;9 Suppl 1:87–150. doi:10.1017/s1041610297004754

- [31] Nezu A, Kubota T, Maruyama S, Nagata M, Nohno K, Morozumi T, Yoshie H. Expression of neprilysin in periodontitis-affected gingival tissues. *Arch Oral Biol.* 2017 Jul;79:35-41. doi: 10.1016/j.archoralbio.2017.03.003.
- [32] Nie R, Wu Z, Ni J, et al. Porphyromonas gingivalis Infection Induces Amyloid- $\beta$  Accumulation in Monocytes/Macrophages. *J Alzheimers Dis.* 2019;72(2):479–494. doi:10.3233/JAD-190298
- [33] Noble JM, Borrell LN, Papapanou PN, Elkind MS, Scarmeas N, Wright CB. Periodontitis is associated with cognitive impairment among older adults: analysis of NHANES-III. *J Neurol Neurosurg Psychiatry.* 2009 Nov;80(11):1206-11. doi: 10.1136/jnnp.2009.174029.
- [34] Noble JM, Scarmeas N, Celenti RS, Elkind MS, Wright CB, Schupf N, Papapanou PN. Serum IgG antibody levels to periodontal microbiota are associated with incident Alzheimer disease. *PLoS One.* 2014 Dec 18;9(12):e114959. doi: 10.1371/journal.pone.0114959.
- [35] Olsen I, Singhrao SK, Potempa J. Citrullination as a plausible link to periodontitis, rheumatoid arthritis, atherosclerosis and Alzheimer's disease. *J Oral Microbiol.* 2018;10(1):1487742. Published 2018 Jun 22. doi:10.1080/20002297.2018.1487742
- [36] Olsen I, Singhrao SK. Is there a link between genetic defects in the complement cascade and Porphyromonas gingivalis in Alzheimer's disease?. *J Oral Microbiol.* 2019;12(1):1676486. Published 2019 Oct 25. doi:10.1080/20002297.2019.1676486
- [37] Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J Periodontol.* 2007;78(7 Suppl):1387–1399. doi:10.1902/jop.2007.060264
- [38] Poole S, Singhrao SK, Kesavalu L, Curtis MA, Crean S. Determining the presence of periodontopathic virulence factors in short-term postmortem Alzheimer's disease brain tissue. *J Alzheimers Dis.* 2013;36(4):665–677. doi:10.3233/JAD-121918
- [39] Rolim Tde S, Fabri GM, Nitrini R, et al. Evaluation of patients with Alzheimer's disease before and after dental treatment. *Arq Neuropsiquiatr.* 2014;72(12):919–924. doi:10.1590/0004-282X20140140
- [40] Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry.* 1984;141(11):1356–1364. doi:10.1176/ajp.141.11.1356
- [41] Sabharwal A, Gomes-Filho IS, Stellrecht E, Scannapieco FA. Role of periodontal therapy in management of common complex systemic diseases and conditions: An update. *Periodontol 2000.* 2018;78(1):212–226. doi:10.1111/prd.12226

- [42] Shoemark DK, Allen SJ. The microbiome and disease: reviewing the links between the oral microbiome, aging, and Alzheimer's disease. *J Alzheimers Dis.* 2015;43(3):725-38. doi: 10.3233/JAD-141170.
- [43] Singhrao SK, Olsen I. Assessing the role of *Porphyromonas gingivalis* in periodontitis to determine a causative relationship with Alzheimer's disease. *J Oral Microbiol.* 2019;11(1):1563405. Published 2019 Jan 29. doi:10.1080/20002297.2018.1563405
- [44] Sochocka M, Sobczyński M, Sender-Janeczek A, Zwolińska K, Błachowicz O, Tomczyk T, Ziętek M, Leszek J. Association between Periodontal Health Status and Cognitive Abilities. The Role of Cytokine Profile and Systemic Inflammation. *Curr Alzheimer Res.* 2017;14(9):978-990. doi: 10.2174/1567205014666170316163340.
- [45] Sparks Stein P, Steffen MJ, Smith C, Jicha G, Ebersole JL, Abner E, Dawson D 3rd. Serum antibodies to periodontal pathogens are a risk factor for Alzheimer's disease. *Alzheimers Dement.* 2012 May;8(3):196-203. doi: 10.1016/j.jalz.2011.04.006.
- [46] Thoden van Velzen SK, Abraham-Inpijn L, Moorer WR. Plaque and systemic disease: a reappraisal of the focal infection concept. *J Clin Periodontol.* 1984 Apr;11(4):209-20.
- [47] Watts A, Crimmins EM, Gatz M. Inflammation as a potential mediator for the association between periodontal disease and Alzheimer's disease. *Neuropsychiatr Dis Treat.* 2008 Oct;4(5):865-76.