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Review

The Role of Oral Microbiota and Glial Cell Dynamics in Relation to Gender in Cardiovascular Disease Risk

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Abstract

The oral microbiota, long recognized for their role in local pathologies, are increasingly implicated in systemic disorders, particularly cardiovascular disease (CVD). This review focuses on emerging evidence linking oral dysbiosis to neuroglial activation and autonomic dysfunction as key mediators of cardiovascular pathology. Pathogen-associated molecular patterns, as well as gingipains and leukotoxin A from *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, *Treponema denticola*, *Aggregatibacter actinomycetemcomitans*, etc., disrupt the blood–brain barrier, activate glial cells in autonomic centers, and amplify pro-inflammatory signaling. This glia driven sympathetic overactivity fosters hypertension, endothelial injury, and atherosclerosis. Crucially, sex hormones modulate these neuroimmune interactions, with estrogen and testosterone shaping microbial composition, glial reactivity, and cardiovascular outcomes in distinct ways. Female-specific factors such as early menarche, pregnancy, adverse pregnancy outcomes, and menopause exert profound influences on oral microbial ecology, systemic inflammation, and long-term CVD risk. By mapping this oral–brain–heart axis, this review highlights the dual role of oral microbial virulence factors and glial dynamics as mechanistic bridges linking periodontal disease to neurogenic cardiovascular regulation. Integrating salivary microbiome profiling with glial biomarkers [e.g., GFAP (Glial Fibrillary Acidic Protein) and sTREM2 (soluble Triggering Receptor Expressed on Myeloid cells 2)] offers promising avenues for sex-specific precision medicine. This framework not only reframes oral dysbiosis as a modifiable cardiovascular risk factor, but also charts a translational path toward gender tailored diagnostics and therapeutics to reduce the global CVD burden.

Keywords: oral microbiome; brain; cardiovascular disease; gender-based differences; microglia; astrocytes

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1. Introduction

1.1. Oral Microbiota, Glial Interaction, and Their Significance in Health and Disease

1.1.1. Overview of the Oral Microbiota

The microbiota comprise living microbes (bacteria, archaea, fungi, protists, and algae), while the microbiome includes these organisms along with their metabolites, structural components, host-derived molecules, and non-living genetic elements such as phages, viruses, plasmids, and extracellular DNA [1]. Among the various microbial communities within the human body, the oral microbiota are the second largest [2]. The oral cavity comprises several ecological niches, including the saliva, tongue, tooth surfaces, gingiva, buccal mucosa,