May 2nd, 12:00 AM

Relationship Between Gut Microbiota and Dementia

Saad Ahmed
Rowan University

Zackary Harris
Rowan University

Russell David Levi
Rowan University

Relationship Between Gut Microbiota and Dementia

Saad Ahmed (OMS-III), Russell Levi (OMS-III), Zack Harris (OMS-III)

Rowan-Virtua School of Osteopathic Medicine

Introduction

- **Gut bacteria, diet, and dementia are linked.** [1, 2, 3]
- Our gut microbiome has trillions of bacteria that affects our health. [1, 4]
- **Diet shapes gut bacteria:** unhealthy choices such as high processed foods and sugar can raise dementia risk. Studies show a decrease in gut bacteria diversity in dementia patients compared to healthy controls [2, 5].
- **Good diet → good gut:** High fiber and fermented foods promote a healthy microbiome, likely protecting the brain. Certain bacteria produce anti-inflammatory compounds and short-chain fatty acids that may improve memory and reduce dementia risk factors [3, 6].
- **Work in progress:** the exact link between gut bacteria and brain health is being actively researched. [1, 7]
- **Diet plays a role:** Improving your diet and thus gut bacteria may help prevent dementia. Some studies suggest a Mediterranean diet or high-fiber diet may be beneficial [6, 8].

Methods

Methods: Exploring the Link Between Gut Microbiota and Alzheimer's Disease

This study examines the potential role of gut microbiota in Alzheimer's disease (AD). We explored existing research on the relationship between diet, gut microbiota, and dementia risk.

Literature Review:

- A wholistic search was conducted using scientific databases to identify only the most relevant publications.
- Keywords included "gut microbiota," "Alzheimer's disease," "diet," "dementia," and "microbiome."
- More recent articles, especially within the last five years, were prioritized, including ones written in english.
- The search yielded articles that explained varying microbiota in AD patients compared to healthy controls [2].
- There was also research that proved the benefits of mediterranean and high fiber diet on reducing Alzheimers risk [3, 6].

Data Analysis:

- The selected articles were critically reviewed to evaluate the research methodology, results, and conclusions.
- A narrative synthesis approach was employed to identify common themes and formulate the contemporary understanding of the gut-brain axis in AD.

Results

Study type	Model	Treatment	Main findings	Reference
In vitro	Rotenone-treated SH-SY5Y neurons	Rotenone (100 μM) for 24 h, followed by grape seed extract liposomes (400 μg/ml) for 48 h	Rescues neuronal viability; Reduces intracellular ROS production	Marino et al. (2021)
In vitro	LPS-treated Caco-2 cell model of intestinal barrier	Resveratrol-3-O-sulfate (100 μM)	Improves intestinal barrier integrity; Upregulates mRNA expression of occludin, ZO-1, claudin-1, and claudin-4	Zhang et al. (2021)
In vitro	PD patient-derived fibroblasts	Resveratrol (25 μM) for 24 or 48 h	Rescues mitochondrial function; Increases gene expression of TFAM and cytochrome c; Reduces ROS production	Ferretta et al. (2014)
Animal	Mouse model of stress by immobilization	Oral pretreatment with grape juice for 5 days prior to stress	Reduces proinflammatory mediators; Normalizes oxidative stress indicators	Bobadilla et al. (2021)
Animal	6-OHDA mouse model of PD	Grape seed extract prior to 6-OHDA insult	Improves neuron survival; Enhances motor function	Ben Youssef et al. (2021)
Animal	Senescence-accelerated mouse model of aging	Daily oral resveratrol (25–100 mg/kg) for 8 weeks	Restores cognitive functions; Increases antioxidant activity; Protects from oxidative stress-induced mitochondrial DNA damage	Liu et al. (2012)
Human clinical trials	Elderly persons with mild cognitive impairment	Grape powder in water twice daily for 6 months	Preserves metabolic activity in specific brain regions	Lee et al. (2017)
Human clinical trials	Patients with mild to moderate AD	Daily resveratrol consumption for 52 weeks	Stabilizes decline in plasma and CSF Aβ40 levels; Stabilizes decline in CSF Aβ40 and Aβ42 levels	Turner et al. (2015); Moussa et al. (2017)

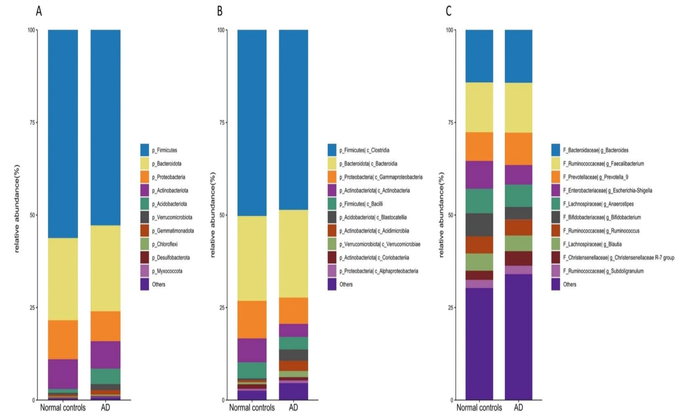
Table 1: The effects of different treatments on brain plasticity and health

Author, year	Study design	Human subjects or AD mouse/rat model	Serotonin receptor (ant)agonist	Behavioral tests	Overall outcome effect
Afshar et al. (2018)	Multiple-armed randomized controlled trial	Male Wistar rats (adult), injected with streptozotocin	5-HT1A receptor antagonist (5 micrograms/day), intracerebrally injected	Novel object recognition test, open field test and passive avoidance task	Decreased Aβ plaques in cortex and HC, decreased neural loss in HC, decreased memory loss
Afshar et al. (2019)	Multiple-armed randomized controlled trial	Male Wistar rats (adult), injected with streptozotocin	5-HT1A antagonist and 5-HT2A agonist (5 micrograms/day), intracerebrally injected	–	Decreased hippocampal oxidative stress, damage and connection loss
Giannoni et al. (2013)	Multiple-armed randomized controlled trial	Male APP/PS1 mice (1–2 months)	5-HT4 receptor antagonist and/or partial agonist RS67333 (2mg/kg/week), intraperitoneal	Novel object recognition test	Agonist reduced Aβ plaques in frontal cortex, HC and entorhinal cortex; agonist reduced micro- and astrogliosis, prevented cognitive dysfunction
Hashemi-Firouzi et al. (2017)	Multiple-armed randomized controlled trial	Male Wistar rats (adult), injected with streptozotocin	5-HT7 receptor agonist; AS19 (1 microgram/day), intracerebrally injected	–	Decreased hippocampal apoptosis, improved neural plasticity in DG

Table 2: Serotonin agonist effect on dementia patterns

Author, year	Population	Total sample size	Duration (days)	Pre- and/or probiotic	Overall outcome effect
Barrera-Bugueño et al. (2017)	Male Sprague–Dawley rats (3 weeks)	59	14	Lactobacillus casei 54-2-33 and inulin (synbiotic)	The synbiotic decreased 5-HT1A receptor density, increased 5-HT1A mRNA, anxiogenic
Borrelli et al. (2016)	Male and female zebrafish (4–6 months)	24	28	Lactobacillus rhamnosus IMC 501	The probiotic increased gene expression of TPH1/2, SLC6A4a and MAO, enhanced behavior
Chen et al. (2019)	Male SPF BALB/c mice (3–4 weeks)	24	30	Lactobacillus reuteri	Probiotic enhanced whole brain 5-HT and the number of 5-HT-positive cells
Corpuz et al. (2018)	Senescence-accelerated mouse prone 8 (14 weeks)	36	280–301	Lactobacillus casei subsp. casei 327 and Lactobacillus paracasei K71	Probiotic increased brain 5-HT levels, reduced cognitive decline
Davis et al. (2016)	Wild-type zebrafish (adult)	Unclear	±30	Lactobacillus plantarum	Probiotic induced upregulation of SLC6A4a, had anxiolytic effect
Engevik et al. (2021)	Swiss Webster germ-free mice (adult)	50	14	Bifidobacterium dentium	Probiotic increased 5-HT2A expression, fecal acetate levels

Table 3: Effects of diet (probiotics) on Serotonin which subsequently has an effect on dementia



Relative abundance of the bacterial types in the stool samples. Normal control (healthy controls), AD (individuals with Alzheimer's disease). (**A**) Phylum level, (**B**) class level, (**C**) genus level.

Graph 1: Alzheimers disease patients have different microbiota compositions

Discussion/Conclusion

The growing body of evidence suggests a significant link between gut microbiota, diet, and AD. While the field is still emerging, the potential for dietary and gut microbiota-based interventions to prevent or manage AD is exciting. Future research should focus on unraveling the complex mechanisms at play and developing effective strategies to target the gut microbiome for improved brain health in aging populations. Based on the current data, we are not only sure of there being a clear relationship between Alzheimers and an altered microbiota, but we are also aware of the role that probiotics, and serotonin levels have in neuroplasticity, and thus alzheimer severity. Finally, there are certain dietary treatments that can protect against the oxidative stressors and plaque build up seen in Alzheimers disease.

Future Directions

- Further research is needed to elucidate the precise mechanisms by which gut bacteria influence brain health in AD.
- Larger clinical trials are necessary to validate the efficacy and safety of FMT for AD treatment.
- Identifying specific dietary patterns that promote a beneficial gut microbiome for brain health is crucial.
- Investigating the potential of prebiotics and probiotics as targeted therapies to manipulate the gut microbiota and potentially prevent or slow AD progression holds promise.

References

SCAN ME