H. PYLORI INFECTION AS A CAUSAL AGENT FOR THE NEUROINFLAMMATION CHARACTERISTIC OF ALZHEIMER’S DISEASE

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What is Alzheimer’s Disease (AD)?
• Progressive neurodegenerative disorder, characterized by neuroinflammation and amyloid deposition, responsible for deterioration of cognitive and behavioral functions
• Inadequate treatment and diagnostic method attributed to incomplete understanding of AD etiology
• Inflammatory hypothesis recently favored (contrasting traditional amyloid cascade hypothesis)

What is Helicobacter Pylori (H. pylori)?
• Gram- negative bacterium in gut microbiome
• Suggested to stimulate systemic and neuroinflammation, influencing CNS activity

Study Objective
I aim to evaluate a causal relationship between H. pylori and Alzheimer’s disease by emphasizing neuroinflammation as a potential mechanism and indicator of AD.

Proposed Study Aims
• A1: Correlation between H. pylori, neuroinflammation, and incidence and severity of AD in AD patients relative to long-term care patients
• A2: Causal sequence from H. pylori infection to neuroinflammation to AD using germ-free version of standard APP-PS1 AD model
• A3: Interventions (antibiotic and anti-inflammatory) to prevent AD or alter AD progression

Proposed Experiments and Outcomes
A1:
• Giemsa stain to diagnose H. pylori infection; monitor microbiome via stool samples and sequencing analyses
• Quantify neuroinflammation via flow cytometric analysis of microglia activity
• Approximately incidence and severity of AD with ADAS-Cog test; verify with immunohistochemical staining for amyloid plaque and neuronal loss post-mortem
• Compare parameters

A2:
• Feed germ-free APP-PS1 mice with microbiota essential to immune function; infect treatment group with H. pylori (strain B47)
• Assess incidence and severity of AD via NOR test
• Post-mortem analysis of neuroinflammation, AD, similar to A1

A3:
• Administer clarithromycin (antibiotic) to treatment group (H. pylori infected APP-PS1 mice), and compare cognitive scores, severity of neuroinflammation and AD onset to controls
• Administer indomethacin (anti-inflammatory) to treatment group and compare parameters as described above

Fig.1 Global AD cases expected to increase exponentially
Fig.2 H. pylori located on lining of stomach
Fig.3 Inflammatory hypothesis of AD in context of microbiota-gut-brain axis

References