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DATA NOTE

Shotgun metagenomics data from faecal samples of 47 patients with mild cognitive impairment: Insights from the memoir study

[version 1; peer review: awaiting peer review]

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Abstract

This Data Note describes the MEMOIR dataset, consisting of shotgun metagenomics data from faecal samples of 47 individuals over the age of 65 diagnosed with mild cognitive impairment (MCI). The dataset was generated to investigate the relationship between gut microbiota functionality and cognitive impairment through the gut-brain-microbiota axis. The dataset includes sequencing data that can be used to explore gut microbiota gene profiles linked to MCI. The dataset was generated using high-throughput shotgun metagenomics technology to identify microbial genes and their potential involvement in cognitive health. This allows for functional interrogation of the gut microbial community and its impact on MCI progression, providing a rich resource for future research. The dataset supports analyses aimed at understanding how dietary interventions (Mediterranean diet and WHO diet) and probiotic treatments influence MCI progression, as well as the potential sex-based differences in response to these interventions. The MEMOIR dataset adheres to the FAIR principles and is intended to facilitate reproducibility and data reuse in studies exploring the gut microbiota's role in cognitive

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decline. No conclusions or analyses are presented in this note, but the dataset offers potential for novel insights into personalised treatment strategies for MCI in ageing populations. Future publications from the MEMOIR project will explore the results from these analyses in detail, contributing to a better understanding of the role of gut microbiota in cognitive decline and identifying potential microbial targets for intervention.

ClinicalTrials.gov, identifier NCT05029765, registration date of 2021-09-01. For further details, please refer to: https://clinicaltrials.gov/study/NCT05029765?term=NCT05029765&rank=1

Plain language summary
This Data Note presents the MEMOIR dataset, which contains data from faecal samples of 47 people over the age of 65 who have mild cognitive impairment (MCI). MCI is a disorder that impacts memory and cognitive abilities and has the potential to progress to dementia. The data collected aims to investigate the relationship between gut bacteria (gut microbiota) and their influence on cognitive health, mediated by the gut-brain-microbiota axis. Through the application of cutting-edge DNA sequencing techniques, the dataset offers comprehensive insights into the genetic profiles of gut bacteria that may contribute to cognitive decline. This information is crucial for researchers examining the role of gut microbiota in conditions such as MCI. Additionally, the dataset facilitates exploration of the effects of dietary patterns, specifically the Mediterranean diet and the World Health Organization (WHO) recommended diet, along with probiotic interventions, on MCI, including potential gender-based differences in treatment response.

The MEMOIR dataset follows high standards to make sure it is easy to use and share, and no conclusions are drawn from the data in this report. However, this data will support future studies that aim to find new ways to prevent or treat MCI by targeting the gut microbiota. Upcoming publications from the MEMOIR project will explore these findings in more detail, helping us better understand how the gut bacteria might play a role in cognitive decline and how we can develop treatments to slow or reverse it.

Keywords
Mild Cognitive Impairment (MCI), Gut Microbiota, Shotgun Metagenomics, Gut-Brain Axis, Mediterranean Diet, Probiotic Treatment, Cognitive Decline, Aging Population



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Introduction

The MEMOIR project (MEtagenomic Modelling of cOgnitive ImpaiRment) was launched to explore the potential link between gut microbiota and mild cognitive impairment (MCI), a condition that affects perception, memory, and language abilities in senior population[1–3]. MCI is frequently viewed as an early indicator of dementia, significantly affecting the quality of life for the elderly[4]. Addressing and comprehending cognitive decline associated with aging has emerged as a critical public health challenge[5]. The MEMOIR project was developed to address this increasing concern, concentrating specifically on the potential impact of dietary interventions and probiotic treatments on the gut-brain-microbiota axis within the framework of MCI.

MCI is a complex, multifactorial condition influenced by both physiological and environmental factors, including oxidative stress, advanced glycation end-products, and lifestyle factors such as diet, smoking, and cognitive activity[6]. Recent research has also linked gut microbiota—the diverse microbial community residing in the gastrointestinal tract—to a range of neurological conditions, including Alzheimer's and Parkinson's disease[7,8]. The gut-brain axis, a bidirectional communication network between the gut and central nervous system, plays a crucial role in this relationship[9,10]. Evidence suggests that gut microbiota can affect brain function through neural, endocrine, and immune pathways[11], and that interventions targeting the gut microbiota could have therapeutic potential for neurodegenerative patients[12–14].

The MEMOIR dataset was carried out to investigate this potential by focusing on the gut microbiota of individuals with MCI. Faecal samples from 47 individuals over the age of 65 were collected at IMIBIC (Maimonides Institute for Biomedical Research of Córdoba), providing a valuable resource for exploring the genetic composition and functional capabilities of the gut microbiome in relation to cognitive health. This project intends to go beyond taxonomic profiling, which determines the kinds of bacteria present in a sample, to comprehend the functional genes that they carry and how these genes may contribute to the progression of MCI through the use of high-throughput shotgun metagenomics sequencing. The primary objectives of generating the MEMOIR dataset were threefold: (i) to identify the effects of probiotic treatment on gut microbiota and its potential impact on MCI; (ii) to assess the influence of dietary interventions, specifically the Mediterranean diet, on cognitive decline; and (iii) to investigate potential sex-based differences in response to these interventions.

This dataset was generated not only to provide insights into the gut microbiota's role in MCI but also to facilitate the discovery of potential microbial targets for future therapeutic interventions. Finally, the broader goal of MEMOIR is to develop personalised treatment strategies aimed at mitigating the effects of MCI and improving cognitive health in aging populations.

Methods

This dataset resulted from a randomized, double-blind, controlled dietary intervention trial with a Latin-square crossover design (this trial is registered at ClinicalTrials.gov under the identifier NCT05029765, with the registration date of 2021-09-01) involving 47 patients with MCI. No significant deviations from the original trial protocol were made during the course of the study. Each participant was randomly assigned to one of three dietary interventions, each lasting 24 weeks: (1) a Mediterranean diet, (2) a Healthy diet aligned with World Health Organization (WHO) recommendations, and (3) a Mediterranean diet supplemented with probiotics (specifically, 109 colony-forming units of *Lactobacillus rhamnosus* and *Bifidobacterium longum*). Participants were assessed both before and after each of the three 24-week intervention periods, resulting in a total evaluation timeframe of 72 weeks. These assessments considered: blood tests, dietary adherence, cognitive performance metrics, and analyses of gut microbiota. Briefly, patients were eligible for the study if they were aged 60 years or older and met the following criteria: a Clinical Dementia Rating (CDR) scale score of 0.5; a Mini Mental State Examination (MMSE) score greater than 23; a score of 85 or less on the delayed memory subtest of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS); a Geriatric Depression Scale score of less than 6, indicating no mild or major depression; and the ability to complete neuropsychological tests, along with sufficient visual and auditory capacities, a minimum level of education, and the availability of a family member or caregiver to assist with clinical visits. This data note relates solely to the shotgun metagenomics data generated during the MEMOIR study.

Sample collection

A total of 47 individuals over the age of 65, all diagnosed with MCI, were included in this study. Each individual provided faecal samples at four distinct time points: at baseline (time 0) and during the intervention (visit 1, 2 and 3), which included dietary modifications (under two different version, Mediterranean diet and the Healthy diet recommended by WHO) and a Mediterranean diet + a probiotic treatment. Four faecal samples were collected per participant, resulting in a total of 177 samples (baseline=47, visit 1 =43, visit 2 =44, visit 3 =43). All samples were stored in a -80ºC freezer until the time when they were shipped to GenomeScan for further processing.

Sample quality assessment

Upon receipt at GenomeScan (Plesmanlaan 1d, 2333 BZ, Leiden), the 177 samples were evaluated for quality. Concentration and integrity were measured using the Fragment Analyzer to ensure they met the quality criteria for sequencing. All samples passed the quality checks.

DNA extraction and library preparation

Shotgun metagenomic sequencing of the gut microbiota in faecal samples was outsourced to GenomeScan (Leiden, The Netherlands), this company owns the equipment and necessary licenses to execute the sequencing of the samples. The DNA libraries were prepared using the NEBNext® Ultra II FS DNA Module (Cat# NEB #E7810S/L) and the NEBNext® Ultra II Ligation Module (Cat# NEB #E7595S/L) (New England Biolabs, Ipswich, MA, USA), following the manufacturer's protocols. Procedures for DNA fragmentation, A-tailing, and the ligation of sequencing adapters were conducted in

accordance with the protocols outlined by the manufacturer for both the NEBNext Ultra II FS DNA module and the NEBNext Ultra II Ligation module (New England Biolabs, Ipswich, MA, USA). After library preparation, quality control was performed using the Fragment Analyzer to assess the size distribution and yield of the prepared libraries, which were found to be in the expected range of 500–700 bp. The libraries were then diluted to a concentration of 1.1 nM before sequencing.

Sequencing and data generation

The prepared libraries were sequenced on the Illumina NovaSeq6000 platform (Illumina, San Diego, CA, USA) according to the manufacturer's guidelines. The sequencing run was managed using the NovaSeq control software NCS v1.7 (https://support.illumina.com/downloads/novaseq-control-software-v1-7.html). Sequencing was conducted to generate high-throughput shotgun metagenomics data, which is essential for the comprehensive profiling of the gut microbiota.

Base calling and initial quality checks were conducted using the Illumina data analysis pipeline, which included RTA v3.4.4 and Bcl2fastq v2.20 (available via the Illumina support page https://support.illumina.com/). Quality-filtered reads were provided in the 'Raw Data' folder for downstream analysis.

Data processing and availability

The generated raw sequence data include high-quality FASTQ files containing the shotgun metagenomics reads. These data are available for further analysis, focusing on functional profiling of the microbial communities. All raw sequence data are archived and made available in compliance with the FAIR data principles for reproducibility and data reuse. The sequencing data generated in this study have been deposited in the Sequence Read Archive (SRA) of the National Center for Biotechnology Information (NCBI). The data include shotgun metagenomic sequencing of the gut microbiota from fecal samples from human. Accession number PRJNA1219367; https://www.ncbi.nlm.nih.gov/sra/PRJNA1219367 (Mora-Ortiz *et al.*, 2025). The dataset generated and used in this study is publicly available and can be accessed at the NCBI via the following link: https://www.ncbi.nlm.nih.gov/sra/PRJNA1219367.

Abbreviations

- **Bcl2fastq**: Base Call to FASTQ Conversion Software
- **bp**: Base Pairs
- **CIBEROBN**: CIBER Fisiopatología de la Obesidad y Nutrición
- **FAIR**: Findable, Accessible, Interoperable, and Reusable (data principles)
- **FEDER**: Fondo Europeo de Desarrollo Regional
- **GDPR**: General Data Protection Regulation
- **IMIBIC**: Instituto Maimonides de Investigacion Biomedica de Córdoba
- **MCI**: Mild Cognitive Impairment
- **MEMOIR**: MEtagenomic Modelling of cOgnitive ImpaiRment
- **NCS**: NovaSeq Control Software
- **NEB**: New England Biolabs
- **PI**: Principal Investigator
- **RTA**: Real-Time Analysis
- **WHO**: World Health Organization

Ethical approval and consent

The study was conducted in alignment with ethical standards and received clearance from the Ethics Committee of Reina Sofía University Hospital (protocol number 1496). The ethics were approved on 27/03/2009. Prior to enrollment in the trial, all participants provided written informed consent, confirming their voluntary involvement in the research and they kept the right to resign at any point. They were adequately informed about the aims of the study, the methods to be employed, and the potential risks and benefits involved. The ethics committee approved the use of written consent.

Throughout the study, the confidentiality and privacy of participants were maintained rigorously. Personal identification details were anonymized and securely handled. The data collected was processed in accordance with the General Data Protection Regulation (GDPR) and other relevant privacy laws. Participants were entitled to withdraw from the study at any time without facing any negative consequences.

The research involving human subjects was conducted in line with the principles outlined in the Declaration of Helsinki, which governs the ethical conduct of biomedical research. This dietary intervention trial is registered at: clinicaltrials.gov NCT05029765.

Data availability

Underlying data

Accession numbers

National Center for Biotechnology Information (NCBI): The data include shotgun metagenomic sequencing of the gut microbiota from fecal samples. Accession number PRJNA1219367; https://www.ncbi.nlm.nih.gov/sra/PRJNA1219367

Reporting guidelines

Figshare Repository: CONSORT checklist for 'Dental Care Measures for Alleviating Oral Symptoms in Cancer Patients Undergoing Oral Chemotherapy: A Scoping Review Protocol.'

https://doi.org/10.6084/m9.figshare.28450304.v1[15]

Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

Software availability

We have outsourced the sequencing of the samples to GenomeScan (Leiden, Netherlands), some of the software this company used are not open access. NovaSeq control software NCS v1.7 (Illumina, proprietary) was used to operate the

sequencing run. As an alternative, open-source sequencing control software such as ONT MinKNOW (Oxford Nanopore) or OpenFlex could be considered for non-Illumina platforms. Sequencing was conducted to generate high-throughput shotgun metagenomics data, which is essential for the comprehensive profiling of the gut microbiota. Base calling and initial quality checks were conducted using the Illumina data analysis pipeline, which included RTA v3.4.4 (Illumina, proprietary) and Bcl2fastq v2.20 (Illumina, proprietary). Free alternatives for base calling include ONT Guppy (for Nanopore data) or Deepbinner, while quality control can be performed using open-source tools such as FastQC, AfterQC, or Seqtk. Quality-filtered reads were provided in the 'Raw Data' folder for downstream analysis. This project was executed in strict accordance with the guidelines and specifications established by GenomeScan, ensuring full compliance throughout. No deviations or exceptions were made during the processing of samples or the sequencing procedures.

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