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# CORRELATION BETWEEN MRI-BASED BRAIN VOLUME CHANGES AND COGNITIVE DECLINE IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT: A PROSPECTIVE OBSERVATIONAL STUDY.

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## Abstract

### Background

Mild Cognitive Impairment (MCI) is an intermediate stage between normal cognitive aging and dementia, characterized by subtle cognitive decline. MRI-based brain volumetry, particularly of the hippocampus and entorhinal cortex, has been proposed as a potential biomarker for predicting cognitive deterioration. This study aimed to assess the relationship between structural brain volume changes and cognitive decline among patients diagnosed with Mild Cognitive Impairment (MCI).

### Methods

A prospective cohort of 100 patients diagnosed with MCI (mean age 68.5 ± 6.7 years; 54% male) was enrolled. Baseline cognitive function was assessed using the Mini-Mental State Examination (MMSE), and MRI-based volumetric analysis of the hippocampus and entorhinal cortex was conducted. Participants were followed for 12 months, with cognitive status reassessed. Pearson correlation and multiple linear regression analyses were performed to examine associations between brain volume and cognitive performance.

### Results

Baseline MMSE scores averaged 26.2 ± 1.8. Pearson correlation revealed a significant positive association between hippocampal volume ($r = 0.58$, $p < 0.001$) and entorhinal cortex volume ($r = 0.51$, $p < 0.001$) with MMSE scores. Participants with cognitive decline ($n = 40$) exhibited significantly greater hippocampal volume reduction (5.2% ± 1.1%) compared to stable participants (2.1% ± 0.9%; $p < 0.001$). Multiple regression analysis identified hippocampal ($\beta = 0.43$, $p < 0.001$) and entorhinal cortex volumes ($\beta = 0.37$, $p = 0.002$) as independent predictors of cognitive performance (adjusted $R^2 = 0.42$, $p < 0.001$).

### Conclusions

MRI-based volumetric reductions in the hippocampus and entorhinal cortex are significantly correlated with cognitive decline in MCI patients, suggesting their potential as predictive biomarkers for disease progression.

### Recommendations

Recommend integrating MRI-based hippocampal and entorhinal cortex volumetry into routine MCI assessments for early detection and intervention.

**Keywords:** Mild Cognitive Impairment, Cognitive Decline, Magnetic Resonance Imaging (MRI) Volumetry, Hippocampal Volume, Entorhinal Cortex, Mini-Mental State Examination (MMSE), Neuroimaging Biomarkers
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## Introduction

Mild Cognitive Impairment (MCI) is widely recognized as an intermediate stage between normal cognitive aging and dementia, most notably Alzheimer's disease (AD). It is characterized by noticeable impairments in memory, executive function, or other cognitive domains while maintaining independence in daily functional activities, distinguishing it from dementia [1,2]. However, individuals with MCI exhibit a significantly higher risk of progressing to dementia, with annual conversion rates estimated at 10–15%, compared to 1–2% in cognitively healthy elderly populations [3].

Recent advancements in neuroimaging, particularly magnetic resonance imaging (MRI)-based volumetric techniques, have shown promise in detecting structural brain changes associated with cognitive decline. Among the most vulnerable regions, the hippocampus and entorhinal cortex play crucial roles in memory consolidation and learning, and are frequently affected in the early stages of neurodegenerative processes [4,5]. Several studies have consistently demonstrated that atrophy in these

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regions correlates with the severity of cognitive impairment in both MCI and AD populations [5,6].

Despite this evidence, there remains considerable variability in the rate and pattern of neurodegeneration among individuals with MCI. This heterogeneity emphasizes the need for reliable biomarkers to predict disease progression accurately. Early identification of at-risk individuals using such biomarkers could facilitate timely intervention and improve clinical outcomes.

The present study aimed to investigate the correlation between MRI-based volumetric changes in the hippocampus and entorhinal cortex with cognitive decline, as measured by the Mini-Mental State Examination (MMSE), in a cohort of patients with MCI. Furthermore,The study also aimed to evaluate whether these structural brain changes independently predict cognitive deterioration over a 12-month follow-up period.

## Methodology

### Study Design and Setting

A prospective observational study was conducted over a 12-month period from November 2023 to October 2024 to evaluate the relationship between brain volumetric changes and cognitive decline in patients with Mild Cognitive Impairment (MCI). The study was carried out in a clinical setting, with magnetic resonance imaging (MRI) and volumetric analysis performed in the Department of Radiodiagnosis at Late Smt. Indira Gandhi Memorial Government Medical College, Kanker, Chhattisgarh, India

### Participants

A total of 100 patients diagnosed with Mild Cognitive Impairment (MCI) were recruited based on the Peterson criteria, which include: (1) subjective memory complaints, (2) objective memory impairment for age and education, (3) preserved general cognitive function, (4) intact daily living activities, and (5) absence of dementia.

### Study Size

A total of 100 participants were enrolled, based on feasibility during the 12-month study period and previous similar neuroimaging studies in MCI populations. This sample size was deemed adequate to detect meaningful associations between brain volume changes and cognitive decline with acceptable statistical power.

### Bias Control

To minimize selection bias, participants were enrolled consecutively based on predefined inclusion and exclusion criteria. Information bias was reduced by using standardized tools for cognitive assessment (MMSE) and automated volumetric software (FreeSurfer) for MRI analysis. All MRI evaluations were conducted by radiologists blinded to participants' cognitive status.

### Inclusion criteria

- Age between 60 and 80 years
- Diagnosis of MCI confirmed by a neurologist
- MMSE score between 24 and 27
- Ability to undergo MRI scanning

### Exclusion criteria

- History of major psychiatric illness or stroke
- Diagnosis of Alzheimer's disease or other dementias
- Structural abnormalities on MRI unrelated to MCI
- Contraindications to MRI (e.g., pacemaker, metallic implants)

### Cognitive Assessment

Cognitive function was assessed at baseline and at 12-month follow-up using the Mini-Mental State Examination (MMSE). A decline of ≥2 points in MMSE score over 12 months was considered significant cognitive decline.

### MRI Imaging and Volumetric Analysis

All participants underwent MRI brain scans at baseline using a 3T MRI scanner. High-resolution T1-weighted images were analyzed using automated volumetric software (FreeSurfer) to quantify hippocampal and entorhinal cortex volumes bilaterally. Volumes were normalized to intracranial volume to account for inter-individual variability.

### Grouping of Participants

Based on MMSE score change at follow-up, participants were categorized into:
**Stable MCI Group** (n = 60): No significant decline in MMSE
**Declining MCI Group** (n = 40): Decline of ≥2 points in MMSE over 12 months

### Statistical Analysis

Data were analyzed using SPSS Version 25.0. Descriptive statistics were used to summarize demographic variables and baseline scores. Pearson correlation analysis was performed to evaluate the relationship between brain volume and MMSE scores. Independent t-tests compared volumetric and cognitive changes between groups. Multiple linear regression was used to identify independent

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predictors of cognitive performance, adjusting for age, sex, and education. A p-value < 0.05 was considered statistically significant.

## Ethical Considerations

The study received approval from the Institutional Ethics Committee of Late Smt. Indira Gandhi Memorial Government Medical College, Kanker. Written informed consent was obtained from all participants after explaining the study objectives, procedures, and confidentiality measures.

## Results

A total of 132 patients with suspected MCI were initially screened. Of these, 112 met preliminary eligibility based on age and clinical suspicion. Following application of inclusion/exclusion criteria and neurologist confirmation, 100 participants were enrolled in the study. All 100 completed baseline MRI and cognitive assessments. During the 12-month follow-up, 96 participants completed the second MMSE assessment. Four participants were lost to follow-up due to relocation or health issues. Data from 96 participants were included in the final analysis

A total of 100 patients diagnosed with Mild Cognitive Impairment (MCI) were enrolled in the study. The mean age of the participants was 68.5 ± 6.7 years, with 54% being male and 46% female. The baseline cognitive function, assessed using the Mini-Mental State Examination (MMSE), had a mean score of 26.2 ± 1.8 (Table 1).

Table 1: **Demographic and Baseline Characteristics of the Study Population (n = 100)**

| Variables | Mean ± SD / n (%) |
|---|---|
| Age (years) | 68.5 ± 6.7 |
| Gender | Male: 54 (54%)<br>Female: 46 (46%) |
| Years of Education | 10.2 ± 2.8 |
| Baseline MMSE score | 26.2 ± 1.8 |

## Correlation Between Brain Volume and Cognitive Function

Pearson correlation analysis revealed a statistically significant moderate positive correlation between hippocampal volume and MMSE scores (r = 0.58, p < 0.001), indicating that greater hippocampal volume was associated with higher cognitive performance. Similarly, a positive correlation was found between entorhinal cortex volume and MMSE scores (r = 0.51, p < 0.001) (Table 2). These findings suggest that volumetric reductions in these regions may reflect cognitive deterioration in MCI patients.

Table 2: **Pearson Correlation Between Brain Volumes and MMSE Scores**

| Brain Region | Correlation Coefficient (r) | p-value |
|---|---|---|
| Hippocampal Volume | 0.58 | < 0.001 |
| Entorhinal Cortex Volume | 0.51 | < 0.001 |

## Group-wise Comparison Based on Cognitive Decline

Participants were stratified into two subgroups based on longitudinal changes in MMSE scores over a 12-month follow-up period: Stable MCI (n = 60) and Declining MCI (n = 40). The Declining MCI group demonstrated a significantly larger reduction in MMSE scores (mean change = -2.3 ± 0.8) compared to the Stable group (-0.4 ± 0.6; p < 0.001). Additionally, hippocampal volume reduction was more pronounced in the Declining MCI group (5.2% ± 1.1%) than in the Stable MCI group (2.1% ± 0.9%; p < 0.001), as shown in Table 3.

Table 3: **Comparison of Cognitive Decline and Brain Volume Reduction Between MCI Groups**

| Variables | Stable MCI (n = 60) | Declining MCI (n = 40) | p-value |
|---|---|---|---|
| Change in MMSE score (12 months) | -0.4 ± 0.6 | -2.3 ± 0.8 | < 0.001 |
| Hippocampal Volume Reduction (%) | 2.1 ± 0.9 | 5.2 ± 1.1 | < 0.001 |

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## Regression Analysis of Cognitive Predictors

Multiple linear regression analysis was conducted to identify predictors of cognitive performance (MMSE score) while adjusting for age, sex, and educational status. The results indicated that both hippocampal volume ($\beta = 0.43$, $p < 0.001$) and entorhinal cortex volume ($\beta = 0.37$, $p = 0.002$) were independent predictors of cognitive status. The overall model explained 42% of the variance in MMSE scores (Adjusted $R^2 = 0.42$, $p < 0.001$) (Table 4).This analysis addressed the secondary objective of the study, assessing whether hippocampal and entorhinal cortex volumes independently predict cognitive performance over 12 months

Table 4: **Multiple Linear Regression Analysis Predicting MMSE Scores**

| Predictor Variable | β Coefficient | p-value |
|---|---|---|
| Hippocampal Volume | 0.43 | < 0.001 |
| Entorhinal Cortex Volume | 0.37 | 0.002 |
| Adjusted $R^2$ | 0.42 | < 0.001 |

## Discussion

The present study examined the association between structural brain volume changes and cognitive performance. Study findings demonstrated that reductions in hippocampal and entorhinal cortex volumes were significantly correlated with Mini-Mental State Examination (MMSE) scores. Specifically, participants with declining cognition exhibited greater hippocampal volume loss (5.2% ± 1.1%) compared to stable individuals (2.1% ± 0.9%; $p < 0.001$), alongside a significant decrease in MMSE scores (−2.3 ± 0.8 vs −0.4 ± 0.6; $p < 0.001$). These findings suggest that structural atrophy in these brain regions may reflect underlying neurodegenerative processes and can serve as early predictors of cognitive deterioration in individuals with Mild Cognitive Impairment (MCI).

These results are consistent with previous studies highlighting the role of structural brain changes in predicting cognitive deterioration in MCI and Alzheimer's disease (AD) [7,8]. Combining volumetric measurements from multiple brain regions has been shown to improve the predictive accuracy for Alzheimer's disease and MCI progression. Significant associations have also been observed between automated MRI-based volumetry and neuropsychological test performance, highlighting the clinical relevance of hippocampal and entorhinal cortex atrophy in cognitive assessments [7,8].

The study findings are further supported by evidence showing that volumetric MRI effectively predicts the rate of cognitive decline associated with AD and cerebrovascular disease [9]. Hippocampal atrophy has been identified as a robust biomarker for early detection of MCI in population-based samples [10], reinforcing the value of MRI volumetry in diverse clinical settings.

The moderate positive correlations observed in this study between hippocampal volume ($r = 0.58$) and entorhinal cortex volume ($r = 0.51$) with MMSE scores align with previous research highlighting the significance of brain imaging markers in distinguishing MCI from both AD and healthy aging [11]. Furthermore, the greater hippocampal volume reduction in the Declining MCI group (5.2% vs. 2.1%, $p < 0.001$) supports its utility as an early structural indicator of cognitive impairment [12].

Moreover, multiple regression analysis confirmed that hippocampal and entorhinal cortex volumes are independent predictors of cognitive status (adjusted $R^2 = 0.42$, $p < 0.001$), consistent with prior research advocating the integration of volumetric imaging with clinical cognitive assessments [7–12]. These findings are particularly relevant in light of emerging disease-modifying therapies, where identifying individuals at high risk for progression could enable more effective targeting and earlier intervention strategies

## Generalizability

The findings of this study are potentially generalizable to other clinical settings with access to MRI and standardized cognitive testing. However, as the study population was derived from a single center in central India, results may not fully represent broader geographic, ethnic, or socio-economic populations. Replication in multi-center and community-based cohorts is essential to validate the predictive utility of volumetric MRI across diverse populations.

## Conclusion

This study demonstrated that MRI-based volumetric reductions in the hippocampus and entorhinal cortex are significantly associated with cognitive decline in patients with Mild Cognitive Impairment (MCI). Participants with declining cognitive function exhibited greater reductions in hippocampal volume over 12 months, and volumetric measures independently predicted cognitive performance. These findings highlight the potential of structural

MRI biomarkers in identifying MCI patients at risk of progression to dementia. Incorporating brain volumetry into routine clinical assessments may enhance early diagnosis and guide timely interventions. Future studies should explore combining neuroimaging with molecular biomarkers for comprehensive risk prediction and therapeutic monitoring in MCI populations.

## Limitations

The relatively short follow-up duration (12 months) may not capture long-term cognitive trajectories. Additionally, reliance on MMSE alone, while widely used, may not fully reflect subtle changes in specific cognitive domains. Incorporating comprehensive neuropsychological batteries and biomarkers such as amyloid PET or cerebrospinal fluid (CSF) analyses could provide further insights.

## Recommendations

It is recommended that clinicians incorporate MRI-based volumetric assessments of the hippocampus and entorhinal cortex into routine evaluations of patients with Mild Cognitive Impairment (MCI) to enhance early detection of individuals at high risk for cognitive decline. These structural biomarkers can serve as valuable tools for predicting disease progression and guiding timely clinical decisions. Future research should aim to validate these findings in larger and more diverse populations, and explore the added value of combining neuroimaging with molecular biomarkers for more accurate and comprehensive risk stratification in MCI management.

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## List of Abbreviations

MCI – Mild Cognitive Impairment
MRI – Magnetic Resonance Imaging
MMSE – Mini-Mental State Examination
AD – Alzheimer's Disease
CSF – Cerebrospinal Fluid
PET – Positron Emission Tomography

## Source of funding

The study had no funding.

## Conflicts of interest

Author declares no conflict of interest.

## Data Availability

Available up on request

## Author's contribution:

KKS-Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript

## Author Biography

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