

# Comparing the relationship between subjective memory complaints, objective memory performance, and medial temporal lobe volumes in patients with mild cognitive impairment

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## Abstract

**Introduction:** This study examined the relationship between subjective memory complaints (both self- and informant-report), objective memory performance, and medial temporal lobe (MTL) volume.

**Methods:** Mild cognitive impairment (MCI) patients (n = 58) and their informants (n = 51) completed the Memory Assessment Clinics self- (MAC-S) and family (MAC-F)-rating scales as a measure of subjective memory. Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Immediate and Delayed Memory indices were used as objective measures of memory and a subset of MCI participants also underwent magnetic resonance imaging, which was used to measure MTL volume.

**Results:** Patients reported greater difficulty with semantically based information (e.g., word and name recall) relative to informant report. However, the severity of these self-reports was unrelated to objective memory performance and only a single MAC-S scale was related to amygdalar volume. Conversely, several MAC-F indices were related to the RBANS Delayed Memory index and to amygdalar and hippocampal volumes. Measures of executive functioning were associated with MAC-S frequency scales but not any MAC-F scale.

**Discussion:** The results of this study suggest that, in those who are cognitively symptomatic, the frequency of self-reported subjective memory difficulty may reflect executive dysfunction but holds little value for verifying memory impairment. Conversely, informant report provides meaningful information about actual memory deficits in those with MCI.

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## Keywords:

Aging; Diagnosis; Memory complaints; Dementia; Alzheimer's disease

## 1. Introduction

Mild cognitive impairment (MCI) describes an intermediate state between normal aging and dementia and is characterized by significant cognitive deficits, especially in the areas of learning and memory. Specifically, MCI requires (1) subjective memory complaints, preferably corroborated by an informant, (2) objective memory decline, and (3) a

general preservation of everyday functioning [1,2]. Additionally, brain atrophy within the medial temporal lobes (MTL) has been associated with objective learning and memory deficits in MCI [3,4]. The current report addresses a knowledge gap about self- and informant-report of memory complaints and their relationship with objective memory performance and MTL volumes.

Subjective memory complaints help to establish a decline in functioning relative to premorbid status, and existing evidence suggests that the presence of such complaints may be a harbinger of subsequent cognitive decline [5-7]. In addition, studies have reported similar MTL volumes (and

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other brain regions) in patients with MCI and healthy older adults with subjective memory complaints [8]. An important caveat is that these relationships generally appear limited to “cognitively intact” older adults (i.e., those whose objective memory test performances fall within normal limits). A meta-analysis [9] and a review of longitudinal studies [5] revealed inconsistent evidence for the value of subjective memory complaints in those with objective memory impairment (i.e., MCI). Informant-reported memory impairment may hold diagnostic value as it has previously been shown to reflect objective memory test impairment [10–12]. Conversely, some studies have found a relationship between subjective memory complaints and objective test performance [5,13], whereas other studies have not [10,14]. Such discrepant results may arise from the presence or absence of anosognosia, which is a common feature of Alzheimer’s disease (AD) that has been variably reported in MCI [15–17]. It is important to note that such awareness of deficit requires the ability to monitor and evaluate one’s performance in the moment, which literature suggests requires intact executive abilities and associated prefrontal-parietal networks [e.g., 18,19]. Of course, being able to report the nature and/or severity of cognitive impairment requires an accurate memory for the episodes of failure, which certainly relies on the MTL memory system. Thus, MCI patients may experience difficulty due to one or both of these aspects of awareness.

Another reason for the discrepant findings about the value of self-reported complaints is that a range of measures have been used, most of which dichotomize participants based on a single question (i.e., present vs. absent) [5]. Recently, Buckley et al. [14] examined the relationship between subjective memory, affect, and biomarkers of AD in a large sample of healthy controls and MCI patients who were enrolled in the Australian Imaging Biomarkers and Lifestyle study of Aging. Importantly, this study used the memory assessment clinics questionnaire (MAC-Q [20]), which is a brief measure that rates the severity of subjective memory complaints along a continuum. The results demonstrated that complaint severity was unrelated to objective memory test performance or to any biomarkers of AD (gray matter, white matter, or hippocampal volumes; amyloid burden) in either group. Similarly, another recent study found that informant report of overall cognitive impairment in MCI patients was more related to biomarkers of AD than was self-report [12; though see 13 for positive findings]. It is possible that the brevity of the measures used in these studies limited the detection of meaningful relationships in the MCI patients, in which case a more comprehensive measure that assesses perceived difficulty across different situations/contexts will be more reflective of objective impairment.

The current study used the full MAC self-rating scale (MAC-S) and family-rating (MAC-F) questionnaires, which provide continuous measures of functioning across several ecologically relevant contexts, to assess subjective memory complaints in those previously diagnosed with MCI. These

subjective ratings were correlated with objective memory test performances (via the memory indices from the Repeatable Battery for the Assessment of Neuropsychological Status—RBANS), measures of executive functioning, and MTL volumes. Thus, this study allowed us to directly compare the utility of self- vs. informant-report of memory complaints while at the same time examining potential biological explanations for any observed differences.

## 2. Methods

### 2.1. Participants

A total of 58 participants, diagnosed with MCI according to Petersen’s criteria [2], were recruited from the Emory University Alzheimer’s Disease Research Center and surrounding community as part of a larger, multisession study on cognitive rehabilitation. Each patient had been diagnosed with MCI at a consensus conference using all relevant clinical data (e.g., laboratory findings, neuroimaging, neuropsychological testing). Participants were then referred to our study and, after providing written informed consent, completed a brief neuropsychological protocol that included both subjective and objective measures of memory functioning (see Table 1). This protocol was developed to minimize overlap with the tests used during the diagnostic process. For example, we used the RBANS as a brief, yet relatively comprehensive, measure of cognitive functioning (especially for learning and memory) given evidence of its sensitivity to MCI [21] and AD [22]. These results allowed us to ensure persistent cognitive (especially memory) deficits at the time of study enrolment. Informant-based information was obtained for 51 of these participants using the MAC-Family (MAC-F) questionnaire during this screening session. Informants were typically spouses or other family members and all lived and/or interacted with the patient multiple times per week. All neuropsychological and neuroimaging data (see later) included in this study were both independent of those used for the clinical diagnosis and obtained before cognitive rehabilitation was provided.

General exclusion criteria included a history of neurologic injury or disease (e.g., stroke, moderate or severe traumatic brain injury, and epilepsy), psychiatric disorders (e.g., severe depression, bipolar disorder schizophrenia), and current or past alcohol or drug abuse/dependence. The Institutional Review board of Emory University approved the study procedures.

### 2.2. MAC—self and family-rating scale

The MAC-S consists of 21 items that assess one’s perceived functioning (i.e., ability) and that are grouped into five memory areas (Remote, Numeric, Everyday, Semantic, and Spatial) [23]. It also includes another 24 items that assess the frequency of memory concerns and are also grouped into five scales (Semantic, Concentration, Everyday, Forgetfulness, and Facial). There are four global

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