Self and informant memory concerns align in healthy memory complainers and in early stages of mild cognitive impairment but separate with increasing cognitive impairment

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Abstract

Background: information provided by an informant about a patient with cognitive change is an essential component of clinical history taking. How an informant’s report relates to the patient’s phenomenological experience of memory loss is yet to be understood. The aim was to examine patterns of relationships between self and informant reports from a phenomenological perspective.

Methods: forty-three healthy non-memory complainers (HC-NMC), 37 healthy subjective memory complainers (HC-SMC) and 43 individuals with mild cognitive impairment (MCI) were administered a semi-structured interview, which measured their concerns of frequency of memory lapses and impact on mood. Informants responded to questionnaires.

Results: self-reported concerns of increasing frequency and impacted mood related to informant concerns in HC-SMCs. MCI with lower informant concern showed a similar pattern to HC-SMCs on complaints of increasing frequency. In those with higher informant concern, self-reports markedly separated from informant concern. The MCI group with greater informant concern performed comparatively poor on verbal and non-verbal memory measures.

Conclusions: our results suggest that the association between self-reported and informant memory concerns is moderated by MCI severity. Self and informant reports of increasing memory lapse frequency aligned in HC-SMC and MCIs with low informant concern, suggesting a similar dyadic experience of memory change. In MCIs with greater informant concern, the pattern changed exposing a changing insight with advancing memory impairment. These individuals are potentially reflecting a ‘forgetting that they forget’ phenomenon in elements of their concern.

Keywords: subjective memory complaints, mild cognitive impairment, Alzheimer’s disease, memory, older people
Introduction

Concern about declining cognitive abilities in older adults, or by those who are close to them, is what most often brings them to seek an opinion about the likelihood that they are suffering the early stages of dementia. In otherwise healthy older adults, cognitive complaints do not always indicate neurodegeneration; they may also reflect change in mood or the experience of stress [1]. The importance of subjective cognitive concerns to the recognition of early dementia is made clear by the standardised criteria for mild cognitive impairment [MCI; 2], which if accompanied by high levels of β-amyloid burden is considered as a prodromal stage of Alzheimer’s disease (AD). Subjective cognitive concerns increase risk of future dementia [3], particularly if the self-report is corroborated by an informant [4].

The relationship between self and informant reported cognitive concerns might also inform diagnostic decision-making. Much of the subjective cognitive concern literature is focused on the quantification of this phenomenological experience [5]. The focus of this study, however, is to determine how an informant’s report might relate to self-endorsed concern themes, previously shown to be associated with AD biomarkers [6], such as β-amyloid burden. In healthy adults, levels of concern about cognitive complaints are generally reflected accurately by informants [7]. In the case of MCI, on the other hand, the nature and frequency of self and informant concerns become discrepant. That is, while the concerns of informants become increasingly pronounced, self-appraisal of cognitive impairment becomes progressively muted [8]. This lack of congruence between self and informant accounts predicts progression to a clinical classification of dementia [9, 10], but studies have yet to measure this relationship from a phenomenological perspective. This approach has the potential to produce a more refined understanding of the changing pattern of relationships between these two forms of subjective reports, and how they could be evaluated in diagnostic decision-making. We aimed to investigate relationships between self and informant concerns in healthy older adults and those with MCI. Self-reported concern themes relating to increasing frequency and impact on mood were chose for study, because behaviours relating to these concerns are observable. We hypothesised that an informant’s report would align with self-reported cognitive concern themes in healthy older adults, but not in individuals with MCI.

Methods

Participants

The current cross-sectional study recruited a subgroup of 80 healthy controls (HC) and 43 participants with MCI from the 36-month follow-up of the Australian Imaging, Biomarkers and Lifestyle (AIBL) Study of Ageing cohort [11]. HC were further divided into two groups of healthy non-memory complainers (HC-NMC; n = 43) and healthy subjective memory complainers (HC-SMC; n = 37) in response to the question, ‘Do you have difficulties with your memory?’ Human Research Ethics Committee approval was obtained in Victoria from St Vincent’s Hospital, the Austin Hospital and the University of Melbourne, and from Hollywood Private Hospital and Edith Cowan University in Western Australia. All participants for the current study were recruited via telephone, and invited to participate in a semi-structured interview in their home. 142 individuals were initially contacted, 9 were unable to be contacted, 2 were deceased, 5 did not want to participate and 3 lived in rural areas that were unfeasible for access for an assessment. Participants gave informed consent before participating, and the interviews were recorded with permission.

The recruitment and diagnostic methods of the AIBL Study of Ageing have been published elsewhere [11, 12]. In brief, volunteers responded to a media appeal or were referred to the study by their medical practitioner. They were screened via telephone for basic demographic information, and the following exclusion criteria were applied: psychiatric illness (such as significant current but not past depression, which was determined by a Geriatric Depression Scale [GDS: 13] score of greater than 5), obstructive sleep apnoea, Parkinson’s disease, cancers within recent years, symptomatic stroke, uncontrolled diabetes and alcohol consumption greater than Australian recommended levels. A diagnostic review panel of neurologists, geriatricians, psychiatrists and neuropsychologists, chaired by author DA, oversaw the classification into HC and MCI groups according to well-established criteria [14]. MCI classification was made based on performance falling 1.5 SD or more below age-adjusted levels in formal cognitive assessment, expressed cognitive complaint/subjective memory concern and current preservation of activities of daily living, as described previously [12].

Informants were invited to participate by the participant, and the informant in most cases filled out a questionnaire at the same time as the participant. In the case of an absent informant, the questionnaire was mailed to their home address.

Observer Memory Questionnaire

This questionnaire has been administered in our previous work on subjective memory complaints in temporal lobe epilepsy patients [15]. This 30-item questionnaire measures informant concern. Questions pertain to certain memory lapses (i.e. does he/she remember to relay messages to you about missed phone calls) and overall memory performance (i.e. his/her memory function is the same as my own). The items involved Likert-style responses, and all items sum together to create a total score, with a larger score indicating greater informant concern. A good internal consistency (Cronbach’s α = 0.90) has been reported previously for the Observer Memory Questionnaire (OMQ) [15], and in the current study, the OMQ performed similarly (α = 0.94).

Qualitative analysis: semi-structured interview

The semi-structured interview was developed, using clinical experience and aligning with previous interviews constructed
by the second author, M.S., to elicit a rich description of the participant’s subjective experience of memory changes [16]. Informants were not given the semi-structured interview. Administration of the interview took approximately 30–45 min. It was structured to probe circumstances in which memory lapses were likely to occur. Eight scenarios were developed to probe the subjective frequency of memory lapses, whether the individual could provide details about a set of elicited scenarios, and how the individual recovers from acknowledged lapses in memory. The procedure for this interview has been described previously [6]. The themes were arrived at from discussions between the coders, R.B. and M.S., which were held until a consensus was reached for each theme. As stated in the introductory section, we specifically chose two qualitative themes that would be easily observable by an informant. The theme of impacted mood pertains to how memory lapses might impinge on an individual’s mood and could refer to either the positive or negative mood expressions, such as repeatedly laughing or expressing frustration. The increasing frequency theme, on the other hand, reflects the participant’s perception of the frequency of memory lapses. Participants could receive a score of one for the endorsement of a theme on each of the eight questions, up to a maximum score of eight.

Memory and executive function measures

The California Verbal Learning Test–Second edition (CVLT-II) Short Delay recall and Long Delay recall [17], the Wechsler Memory Scale (WMS) Logical Memory (LM) immediate and delayed recall (Story 1 only), the Rey Complex Figure Test (RCFT) 30-min long delay, the CANTABeclipse v3.0 Paired Associate Learning (PAL) ‘stage 6 errors’ adjusted score [18] and the Stroop test.

Image acquisition: $^{11}$C-PiB, $^{18}$F-flutemetamol and $^{18}$F-florbetapir PET imaging

High or low Aβ burden is reported in Table 1 as an indication of the level of AD pathology in each group. Thirty-nine participants (HC = 30, MCI = 9) underwent PiB-PET imaging, 15 (HC = 10, MCI = 5) underwent $^{18}$F-flutemetamol PET scans and 13 (HC = 12, MCI = 1) had $^{18}$F-florbetapir PET imaging.

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<th>Table 1. Demographic and clinical variables by diagnostic category</th>
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HC-NMC, Healthy non-memory complainer; HC-SMC, Healthy memory complainer; MCI, Mild cognitive impairment; OMQ, Observer Memory Questionnaire; GDS, Geriatric Depression Scale; PAL, Paired Associates Learning; LM, Logical Memory; CVLT, California Verbal Learning Test; RCFT, Rey Complex Figure Test.

*Age-adjusted score.

$^a,b,c$: Variables significantly different (Tukey’s method), adjusting for multiple comparisons (Sidak).

$^*:z$-score.

HC-NMC, Healthy non-memory complainer; HC-SMC, Healthy memory complainer; MCI, Mild cognitive impairment; OMQ, Observer Memory Questionnaire; GDS, Geriatric Depression Scale; PAL, Paired Associates Learning; LM, Logical Memory; CVLT, California Verbal Learning Test; RCFT, Rey Complex Figure Test.

$^a,b,c$: Variables significantly different (Tukey’s method), adjusting for multiple comparisons (Sidak).

$^*:z$-score.
Statistical analysis

Analysis of variance (ANOVA), t-tests and $\chi^2$ tests of independence were used to determine group differences. Kruskal–Wallis $\chi^2$ analyses were used to compare the three diagnostic groups (HC-NMC/HC-SMC/MCI), on the level of endorsement on both complaint themes, and Mann–Whitney U analyses were used for post hoc group comparisons. To determine relationships between self and informant reports, we conducted linear curve regression analyses, which calculate the best-fit parameters using linear and non-linear curve estimation methods [19]. As we found a non-linear (inverse quadratic; see Figure 2B) relationship in the MCI group, we split the group into high and low informant concern according to the median split. We then conducted non-parametric Spearman’s $\rho$ correlations in high and low informant concern groups. Analyses were conducted using SPSS Version 22.0, and all findings were corrected for multiple comparisons using the Sidak method. All data was calculated with effect sizes (see Table 1). Missing data existed for informant responses and affective measures but totalled <10% of the entire data set (see Table 1).

Results

Demographic and clinical variables

Demographic differences can be found in Table 1. All three groups were significantly different in the informant’s report of their memory (see Figure 1A). Informants were of an average age of 68.6 years (range = 34–97 years) and had known the participant for 47 years on average (range = 2–68 years). Males made up 33% of the informant group. 72% were the participants’ spouse, 19% were an immediate relative and 9% were an extended relative or friend. An informant’s OMQ score was not influenced by these variables and were not included as covariates.

Differences in thematic complaints: HC-NMC, HC-SMC and MCI

All three groups differed significantly on endorsements of impact on mood, $\chi^2 = 16.45$, $P < 0.001$, and increasing frequency, $\chi^2 = 16.41$, $P < 0.001$, (see Figure 1B). Post hoc analyses revealed that HC-SMC and MCI groups were not significantly different from one another in endorsement of complaints of impact on mood, $U_{HC-SMC} = 556.50$, $P = 0.02$, and $U_{MCI} = 481.50$, $P < 0.001$, respectively. For increasing frequency, again complaints from HC-SMC and MCI groups were not significantly different from one another, $U = 792.50$, $P = 0.98$, but the groups expressed more complaints in comparison with the HC-NMC group ($U_{HC-SMC} = 462.00$, $P = 0.001$ and $U_{MCI} = 513.00$, $P < 0.001$, respectively). The complaint themes were moderately correlated in healthy controls, Spearman’s $\rho$ (80) = 0.41, $P = 0.006$, but not correlated in MCI participants, $\rho$ (43) = 0.31, $P = 0.06$. We found no influence of depressive symptomatology on the two memory complaint themes in HC-SMC and MCI.

Associations between self and informant reports

To determine whether linear or non-linear relationships existed between self and informant reports, we conducted

Figure 1. (A) Informant concern for HC-NMC, HC-SMC and MCI groups. (B) Self-reported memory concerns (Kruskal–Wallis mean ranks) regarding increasing frequency and impact on mood according to group (white = HC-NMC, grey = HC-SMC and black = MCI).
Figure 2. Linear relationships, calculated using curve regression analysis, between self-reported (A) impact on affect and (B) increasing frequency against informant concern in healthy memory complainers (diamonds, unbroken line) and individuals with MCI (filled circles, dashed line). (C) represents the correlational relationship between self-reported concern of increasing frequency and informant concern in MCI with low informant concern (stars, large dashed line), and MCI with high informant concern (filled circles, small dashed line). Linear relationships and their corresponding $r$-squared ($R^2$) parameters are listed in the legend Figure 2A and B, non-parametric relationships and corresponding coefficients are listed in the legend Figure 2C. IoM, impact on mood; IF, increasing frequency; OMQ, Observer Memory Questionnaire.
curve regression analyses. As expected, there were no relationships found between self and informant reports in the HC-NMC group, and data from this group are not depicted in Figure 2. In the HC-SMC group, an informant’s report was linearly related to themes of impact on mood, ($\beta = 0.46$, $P = 0.005$, $R^2 = 0.21$) and increasing frequency, ($\beta = 0.41$, $P = 0.01$, $R^2 = 0.17$; see Figure 2A).

In the MCI group, we found no relationship between self and informant reports for impact on mood. For the complaint theme involving increasing frequency, MCI data was characterised by a quadratic trend (see Figure 2B), disclosing the possibility that participants could be grouped by low and high informant concern. We split the MCI group according to the median split of informant concern (median = 91.8). MCI individuals with high informant concern performed more poorly on the PAL task and the CVLT delayed recall (see Table 1). Those with low levels of informant concern showed a positive association between self and informant concern, $\varrho (22) = 0.42$, $P = 0.05$. MCI individuals with high informant concern exhibited a negative relationship, $\varrho (18) = -0.59$, $P = 0.01$. These relationships are represented by a scatterplot in Figure 2C.

**Discussion**

This is the first study to report on the changing pattern of relationships between informant concerns and subjective cognitive concern themes that are evident on thematic analysis. Our findings suggest a dynamic pattern of relationships between the self-informant dyad. We found evidence of an increasingly disparate relationship between self and informant accounts in those MCI with high informant concern. This raises the notion that the relationship between self and informant accounts have the potential to convey much more diagnostic information beyond the commonly reported congruent/incongruent issue [4, 9, 20, 21]. Importantly, our findings suggest that subjective concerns are related to observed failures in everyday memory function in both healthy memory complainers and MCI individuals who have low informant concern.

In healthy memory complainers, self-reports of increasing frequency and impaired mood exhibited a strong linear relationship with informant reports, supporting previous research [21, 22]. This suggests a shared or corroborated view of memory symptomatology within the healthy self-informant dyad [23]. Dyadic alignment is predictive of future dementia in healthy older adults according to some studies [4], but others argue that this level of corroboration relates solely to increased affective symptomatology [22, 24]. A corroborative account is likely to occur when memory lapses are overtly apparent, but awareness of memory symptoms might be as much a function of lowered informant mood as it is of lowered self-mood [22].

By contrast, the MCI group exhibited heterogeneity in relation to level of informant concern. Those with greater informant concern manifested greater verbal and non-verbal memory impairment, demonstrating an earlier and later stage of MCI. In those with low informant concern, the self-informant relationship aligned with that of the healthy memory complainers. In those with high informant concern, on the other hand, greater informant concern was related to lesser self-reported concern in relation to the theme of increasing frequency. The selective appearance of a disparate relationship in MCI patients with many observed memory problems evokes the notion of a gradually progressive lack of awareness of memory dysfunction in MCI [10, 25, 26]. It is of particular interest to the authors that MCI individuals with low informant concern mirrored the pattern of relationship shown in healthy memory complainers, suggesting that only for the more advanced MCI, the self-informant relationship changes. While this has been suggested in theoretical conceptualisations [8], ours is one of the first to demonstrate this relationship within the dialogue of MCI patients with advancing levels of impairment. This raises the question as to what might produce this progressively muted complaint. From a speculative standpoint, the progression of non-recollection of memory lapses may well be underpinned by disturbances in the ‘feeling of knowing’, which is known to arise in individuals with MCI [27], particularly for newly acquired information [28]. Inherently linked to this metamemory process of 'feeling of knowing' is a sense of familiarity, which becomes increasingly impaired in individuals with MCI [25]. Progressive atrophy of the rhinal cortices, the first region to be pathologically compromised in AD [29], has a recognised association with decreased familiarity with newly learned information [30]. We argue, from a hypothetical standpoint, that if a sense of familiarity is compromised, it is possible that individuals with MCI might have difficulty conceptualizing what they are unable to recognise as previously known knowledge, and so leading to a more muted complaint. The misalignment between self and informant reports bear important diagnostic information, and classification of MCI cases based on self-appraisal alone is clearly not clinically appropriate, as this has the potential to result in false negatives [31].

The OMQ, used in our previous work on clinical populations, is a fundamentally unidimensional measure, and the domain of observer complaint is likely to be considerably more complex. This measure has highlighted the hypothesised separation between self-informant reports as cognitive impairment advances, but the domain of observer concern deserves further examination.

**Conclusion**

It is often the case that clinicians will refer to the informant when taking a clinical history of the patient. Our findings suggest that an informant’s account aligns in complex ways with self-appraisal in the earliest stages of AD. The emergence of misalignment supports the notion of progressive attenuation of awareness in MCI, which has led some to question the diagnostic utility of subjective expressions of memory loss. We argue that this point of emerging disparity between self and informant accounts in MCI bears clinical
These patterns of divergence are robust even after highly co-morbid affective factors, such as depression, are taken into account.

**Key points**

- Self and informant concerns expressed have been shown to diverge in prodromal stages of Alzheimer’s disease.
- Our study demonstrates that a divergence appears only in certain phenomenological aspects of a concern.
- These patterns of divergence are robust even after highly co-morbid affective factors, such as depression, are taken into account.

**Conflicts of interest**

None declared.

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Eating alone and depression in older men and women by cohabitation status: The JAGES longitudinal survey

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Abstract

Background: eating by oneself may be a risk factor for mental illness among older adults, but may be influenced by cohabitation status. We examined the association between eating alone and depression in the context of cohabitation status in older adults in Japan.

Design: a longitudinal, population-based study.

Setting: data from the Japan Gerontological Evaluation Study.

Subjects: we analysed 17,612 men and 19,581 women aged ≥65 without depression (Geriatric Depression Scale <5) at baseline in 2010.

Methods: eating status was classified into two categories: eating with others and eating alone. The risk of depression onset by 2013 was estimated using Poisson regression.

Results: after adjusting for socioeconomic status, physical health, nutritional status, social support, social participation, frequency of meet friends, employment status and marital status, the adjusted rate ratio (ARR) for depression onset in men who ate alone compared with those who ate with others was 2.36 (95% confidence intervals [CI]: 1.18–4.71) for those living alone and 1.03 (95% CI: 0.81–1.32) for those living with others. Among women, the ARR for depression for those who ate alone compared with those who ate with others was 1.31 (95% CI: 1.00–1.72) for those living alone and 1.21 (95% CI: 1.01–1.44) for those living with others.

Conclusions: eating alone may be a risk factor for depression. Among men, the effect of eating alone on depression may be reinforced by living alone, but appears to be broadly comparable in women living alone and women living with others.

Keywords: eating alone, living alone, depressive symptoms, older people

Introduction

In addition to increased physical health risks, ageing is a risk factor for depression because of the loss of social contact resulting from retirement, the independence of children and limited mobility. Depression may lead to a deterioration in physical and cognitive functioning and increase the risk of premature death (e.g. by suicide) [1, 2].