

Yates JA, Clare L, Woods RT, Matthews FE, CFAS Wales.

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Mood and Mild Cognitive Impairment.](#)

Journal of Alzheimer's Disease 2015, 48(S1), S115-S123.

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This is the authors' accepted manuscript of an article that has been published in its final definitive form by IOS Press, 2015.

DOI link to article:

<http://dx.doi.org/10.3233/JAD-150371>

Date deposited:

15/06/2015



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Subjective memory complaints are involved in the relationship between mood and MCI

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Abstract

Subjective memory complaints (SMC) are a criterion in many definitions of mild cognitive impairment (MCI). However, there is controversy over whether this is useful and appropriate, as previous research has suggested that SMC may be a function of mood problems such as anxiety and depression. This paper aimed to establish the relationship between MCI and mood in older people and to investigate the role that SMC play in the relationship. Structured interviews were conducted with community dwelling older people in Wales to collect information regarding cognitive functioning, mood and well-being. A widely-used algorithm was used to categorise 3173 participants into three groups: not cognitively impaired, MCI including SMC (MCI), and MCI without SMC (MCIW). The odds of experiencing anxiety or depression were calculated for each cognitive group. Participants with MCI had increased odds of experiencing symptoms of both anxiety and depression, but the odds were not changed for participants in the not cognitively impaired or MCIW categories. A mediation analysis was performed on the whole sample using cognition as a dichotomous variable, grouped using an age-, education-, and gender-adjusted median cut off point. This showed that SMC partially mediated the relationship between anxiety and cognition, and depression and cognition. Mood problems may be related to SMC rather than objective cognitive impairment, as only participants with MCI that included SMC showed increased odds of experiencing anxiety and depression. SMC are likely to play a mediating role in the relationship between mood and cognitive functioning.

Keywords: Anxiety, depression, mild cognitive impairment, memory

Introduction

Mild cognitive impairment (MCI) is a categorisation that may be applied to older people who experience a level of cognitive decline considered more severe than normal ageing but not thought sufficient in extent or severity to constitute dementia [1]. The broader MCI definition encompasses the following criteria: an objective impairment in memory or other cognitive domains such as language, a subjective memory complaint, absence of dementia, intact general cognition and intact activities of daily living [2-5]. Currently, several variants of this definition exist, and such variations differ in the extent to which they endorse the criteria above [6].

The role of subjective memory complaints (SMC) in the MCI definition is questioned by researchers as some studies have found it to lack accuracy as a diagnostic criterion [7] and level of awareness has been found to vary amongst individuals with MCI, with some over- and others under-estimating extent of difficulties [8]. SMC are common in the healthy older population [9] but show little relationship with either informant reports or cognitive test results [10]. Previous research has also found that as many as 62% of individuals experiencing cognitive decline do not report it [11], suggesting that whilst SMC can be experienced by those without impairments, and often may not be experienced by those with impairments. Older people in advanced stages of cognitive decline may experience anosognosia, and lack awareness of memory problems. This may be for several reasons, such as neurological changes within the brain which may disrupt cognitive processes required for attention, or perhaps due to social cognitive processes, where an individual may attempt to cover up the extent of their memory problems in order to minimise their difficulties [12].

Investigating SMC is important as evidence has shown a link between SMC and future cognitive decline. Schmand et al. [13] found that SMC were associated with greater

odds of having a dementia diagnosis after four years. Reisberg et al. [14] reported that otherwise healthy community dwellers presenting at outpatient departments with subjective cognitive impairment (SCI) were more likely to experience subsequent cognitive decline than people without SCI. There is also a growing body of research investigating subjective cognitive decline as a distinct stage on the cognitive continuum between normal ageing and dementia. Subjective cognitive decline is thought to occur before MCI and potentially represents a stage when the person is aware of changes in cognitive functioning, but these changes are not detected by formal testing. Jessen et al [15] suggest a model of three consecutive stages whereby an individual progresses from subjective memory impairment (SMI) to MCI, and on further to dementia, finding that participants presenting with SMI were at increased risk of conversion to any form of dementia at follow-up time points of 18 months and three years from baseline.

One plausible explanation for the discrepancy in the relationship between SMC and cognitive decline could be the influence of mood, such as symptoms of anxiety or depression. Anxiety and depression are related to MCI [16, 17] and also to SMC [18, 19]. This study will accordingly address the following questions:

1. Are people with MCI more likely to have symptoms of anxiety or depression than people without cognitive impairment?
2. Are people with SMC more likely to report symptoms of anxiety and depression than those without SMC?
3. Do SMC mediate the relationship between cognitive impairment and symptoms of anxiety or depression?

Method

Design

Mood, cognitive functioning and SMC were examined using cross-sectional data from a large sample of community dwelling older people who participated in the Cognitive Functioning and Ageing Study Wales (CFAS Wales). CFAS Wales is a longitudinal population-based study which has gathered information about participants drawn from two research centres in urban and rural areas of Wales, investigating changes that people may experience as they age. Participants took part in face-to-face interviews, which were usually conducted in their own homes, with trained interviewers through the medium of English or Welsh, depending on the participant's preference. Ethical approval was granted by the appropriate NHS Ethics committee. This paper presents data from the first wave of interviews.

Participants

Individuals over 65 years and living in the Gwynedd, Ynys Môn and Neath Port Talbot areas of Wales were randomly sampled from general practice lists between 2011 and 2013, with equal numbers drawn from the age groups 65-74 and 75 and above. Participants were excluded from the analyses reported here if they had a diagnosis of dementia (n=129), impaired activities of daily living (ADLs) (n=52) or cognitive decline greater than that expected for a classification of MCI, but not meeting the criteria for dementia for other reasons (other cognitive impairment no dementia; OCIND; n=152) resulting in n=3173 participants included in this analysis.

Definition of subjective memory complaints

Subjective memory complaints were indicated by a self-report of memory problems by the participant. This was assessed using the following questions asked during the structured interview: “Have you ever had any difficulty with your memory?” and “Have you tended to forget things recently?” A positive answer to either question resulted in a participant being categorised as having SMC, which was a dichotomous category.

Assessment of mood

Symptoms of anxiety and depression were assessed during the structured interview. Anxiety and depression were defined using the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) algorithm [20], where a score of two indicated mild symptoms and a score of three or above indicated a case-level anxiety or depression. For the purposes of this study, scores of 0 and 1 were considered in the ‘normal’ range.

Classification of cognitive status

MCI was defined using the cognitive status algorithm [21] (see Figure 1). Participants classified as having MCI displayed an objective cognitive impairment, intact general cognitive functioning (indicated by a score greater than or equal to 22 on the MMSE), intact ADLs, an absence of dementia and SMC. Objective cognitive impairment was defined using the CAMDEX CAMCOG [22] which formed a section of the structured interview. A score falling one standard deviation below age-adjusted norms [23] on any cognitive domain measured in the CAMCOG represented impairment.

A further group of participants was created using the cognitive status algorithm (Figure 1) that included all participants who would otherwise meet criteria for MCI, except that they did not report SMC. This group was referred to as MCI-without (MCIW).

Participants in the OCIND, ADL or dementia categories, defined using the cognitive status algorithm (Figure 1) were excluded from analyses as they represented a level of impairment greater than would be expected for a classification of MCI.

For use in mediation analyses, a median split on the total CAMCOG score was used adjusting for age, gender and education

Statistical analyses

Analyses were conducted using SPSS 20.0. Differences between participants with and without SMC were described. Logistic regression was conducted to determine the odds of experiencing symptoms of anxiety or depression for each cognitive status and for participants with and without SMC. Mediation analyses were conducted to investigate the amount of variance in the relationship between MCI and mood problems that could be explained by the presence of SMC. The mediation analyses were conducted using the median split of the CAMCOG, symptoms of anxiety or depression as the outcome variable and the presence of SMC as the mediating variable, using logistic regression. Sobel's test was used to determine mediation analyses were significant, and that any reduction in variance attributed to the mediating variable was a significant amount. Sensitivity analyses were also conducted and can be found in the supplementary material, in order to identify an appropriate index of cognition that met the criteria for mediation i.e. was significantly related to both SMC and mood.

Results

The characteristics of the study sample are shown in Table 1 and Table 2. Data were analysed from 3173 participants who were classified according to cognitive status as having no cognitive impairment (NCI), MCI or MCIW. SMC were reported by 1050 participants (33.1%), with 200 participants (6.3%) meeting criteria for MCI and 329 participants (10.4%) being categorised as MCIW.

((Table 1 here))

((Table 2 here))

Are people with MCI more likely to have symptoms of anxiety or depression compared to people without cognitive impairment?

Logistic regression showed that the odds of experiencing symptoms of anxiety were significantly increased in people who had been classified as having MCI (OR=1.93, CI=1.16-3.22, $p=.012$) but not for people classified as MCIW (OR=0.68, CI=0.37-1.23, $p=.199$) or people without cognitive impairment (OR=0.88, CI=0.59-1.32, $p=.542$). The same pattern was found for the odds of experiencing symptoms of depression, where the risks were significantly increased in people who had been classified as having MCI (OR=2.04, CI=1.52-2.74, $p<.001$) but not for people classified as MCIW (OR=1.01, CI=0.77-1.31, $p=.968$), and the odds were significantly decreased in participants with no cognitive impairment (OR=0.72, CI=0.59-0.88, $p=.002$).

Are people with SMC more likely to report symptoms of anxiety and depression than those without SMC?

The odds of experiencing symptoms of anxiety and depression were significantly increased in participants who had reported subjective memory complaints (anxiety OR=2.25, CI=1.64-3.09, $p<.001$; depression OR=2.02, CI=1.71-2.39, $p<.001$), regardless of their cognitive status. The number of people reporting SMC for each AGE-CAT level of anxiety and depression are shown in Table 3. Data from participants in the NCI group were also analysed separately to determine whether the presence of SMC changed the odds of anxiety or depression in people without cognitive impairment. Logistic regression showed that the odds of both anxiety (OR=2.17, CI=1.53-3.08, $p<.001$) and depression (OR=2.02, CI=1.68-2.43, $p<.001$) were significantly increased in participants without cognitive impairment who reported SMC.

(((Table 3 here)))

Do SMC mediate the relationship between cognition and symptoms of anxiety or depression?

Logistic regression was used to investigate whether SMC mediate the relationship between cognition and anxiety in the whole sample (MCI, MCIW & NCI). Sensitivity analyses conducted prior to mediation analyses indicated that using cognition as a dichotomous variable created by an age-, education- and gender-adjusted median split of the total CAMCOG score would be most appropriate, as this variable had a relationship with anxiety (OR=0.65, CI=0.47-0.89, $p=.008$), whereas cognition as a continuous variable did not (see Supplementary Material, Table S1). Mediation analyses suggested that the

association between cognition and anxiety is partially mediated by the presence of SMC (Figure 2A), and the results of the Sobel test suggest that the mediation effect was significant, $z'=-2.30$, $p=.021$.

The CAMCOG median split variable was also used as the measure of cognition in testing for mediation between cognition and depression in order to maintain continuity, although other measures of cognition were assessed in sensitivity analyses (see Supplementary Material, Table S2). In this analysis, the total effect of cognition on depression was significant (OR=0.70, CI=0.59-0.82, $p<.001$). Mediation analyses show that the association between cognition and depression was partially mediated by the presence of SMC (Figure 2B) and the results of the Sobel test suggest that this mediation was also significant, $z'=-2.48$, $p=.013$.

((Figure 2 here)))

Discussion

This study aimed to investigate the relationship between MCI, mood and SMC, using data from a large population study of people over 65 years old living in Wales. The findings suggest that the odds of experiencing symptoms of both anxiety and depression were significantly increased in people categorised as having MCI (where SMC are part of the criteria), but the odds are not changed for people with no cognitive impairment or for those otherwise meeting criteria for MCI who do not report SMC. Reports of SMC were also associated with increased odds of having symptoms of anxiety and depression across all cognitive status groups compared to people who did not report SMC. Mediation analyses

suggested that the relationship between cognition and mood may be partly accounted for by their mutual relationship with SMC.

The findings from the present study echo the results of previous studies that have also shown an association between MCI and mood [24-27]. SMC may occur due to an individual's attributional style and may therefore be related to depression as a function of negative attributions, rather than due to cognitive impairment [10, 18]. The relationship between MCI and anxiety may operate in two directions. On one hand, concerns over memory may influence general levels of anxiety, as memory problems can be frightening and anxiety provoking [28]. However, anxiety could be a risk factor for reports of SMC [29] as older people may become more vigilant about their cognitive processes and aware of very subtle changes that are not detected by neuropsychological tests. Previous research has also shown that people reporting SMC were also more likely to report symptoms of anxiety and depression even after controlling for actual cognitive performance [30]. The findings of this study are in line with this research, as participants reporting SMC were more likely than those without SMC to experience mood problems regardless of cognitive status.

The MCIW category and mood problems were not significantly related, suggesting that it is likely that SMC mediate the relationship between MCI and mood, as the only difference between the MCI and MCIW categories is the presence of SMC. This idea is confirmed by mediation analyses, although it is probable that other factors also influence the relationship as the analyses suggest that SMC operate only as a partial mediator, and further investigation is required. Older people without cognitive impairment may report SMC despite a lack of objective evidence. Such complaints may be related to mood problems, or could instead reflect a greater awareness of their own cognitive abilities and represent underlying metacognitive processes. It may be that the MCIW group includes people with lower levels of neuroticism who self-monitor less, and are generally less concerned about

health and other difficulties. If they notice cognitive difficulties, perhaps they are attributed to the effects of age, and not seen as noteworthy or worth reporting; others may more actively minimise problems as a defensive process. Others may show difficulty on objective tests, but not encounter difficulties in daily life. Whilst this group may be said to show a degree of anosognosia, a neurological basis for this is more likely in those showing more advanced stages of cognitive decline than apparent in this study.

There are several limitations to the present study. The response rate to the interviews from which the data were collected was approximately 46% and it could be suggested that potential participants with anxiety, depression or cognitive impairment may have refused to participate, leaving a sample that is not entirely representative, however for this analysis which uses relative rather than absolute differences this effect is attenuated. The measure of SMC is fairly crude, and may not have picked up changes in function sufficiently, rather than a general disposition to complain. Unlike a clinical population, the sample was not defined by participants identification of a difficulty and help-seeking behaviour.

The number of participants reporting symptoms of anxiety was small and this could indicate that the questions included in the interview to assess anxiety may not have been sensitive enough. In addition, the AGE-CAT algorithm [20] used to categorise the level of anxiety may not be effective at classifying people with less severe but more frequent anxiety problems and consequently may miss individuals with sub-clinical levels of anxiety. In addition, older people may not report anxiety, as they may trivialise the symptoms or regard these as a normal part of the ageing process. The present study does, however, have several strengths. Firstly, the data were collected from a large sample which incorporated community dwellers and older people living in institutions, from both urban and rural areas in Wales. In addition, the measures used within the interview to assess cognition such as the MMSE [31] and the CAMCOG [22] are very well established tools for use with older people. Lastly, the

use of the MCI and MCIW categories for classifying the cognitive status of the participants made it possible to directly compare how SMC operate in relation to mood.

The findings from this study have several possible applications. From a theoretical perspective, the results raise questions regarding the inclusion of SMC as a criterion within the MCI definition. By insisting on the presence of SMC, many people with objective cognitive impairment who could benefit from timely intervention may go undetected by healthcare professionals. In addition, the MCI and MCIW categories may represent different points on the continuum between normal ageing and pathological ageing. Research suggests that symptoms of anxiety and depression are associated with progression from MCI to dementia, and the lack of relationship between mood and the MCIW category compared to the relationship shown with the MCI category could indicate that MCI is a step further along on the pathway to pathological ageing. Alternatively, the MCIW category may represent a separate trajectory, on which participants may progress to further cognitive decline, remain stable or even improve their cognitive performance. It would be informative to follow this sub-sample of participants over time and observe their cognitive journey.

Clinical applications of the findings could include the identification of symptoms of anxiety or depression in older people who report SMC, as the present study suggests that SMC may be related to mood rather than objective cognitive performance. Previous research found that an improvement in mood was associated with a decline in the reporting of SMC [28]. Coupled with research that suggests that SMC are related to a lower quality of life [32], this could mean that detecting and addressing mood problems could reduce SMC and in turn improve quality of life. Interventions to improve mood problems may in turn also help to reduce the chances of progression from MCI to dementia.

The findings of this study highlight the requirement for more research in this area. The association between MCI and anxiety could be investigated with more comprehensive measures of anxiety, such as a scaled measurement tool, instead of using the AGE-CAT algorithm [20]. Further investigation could aim to determine the nature of anxiety in older people, and the worries or concerns that affect them. Understanding anxiety better in older people may help to develop a better understanding of how mood, cognitive function and SMC interact.

This study has shown that the odds of experiencing symptoms of anxiety and depression are increased in participants categorised as having MCI, but the odds are not increased in those without cognitive impairment, or those categorised as MCIW, suggesting that SMC are more likely to be related to mood problems rather than objective cognitive impairment. The results suggest that SMC may play a mediating role in the relationship between cognition and mood problems. Awareness of the interplay between SMC and mood may help older people to obtain targeted assistance for both memory and mood problems which may in turn positively affect their quality of life.

Acknowledgements

The CFAS Wales study was funded by the ESRC (RES-060-25-0060) and HEFCW as ‘Maintaining function and well-being in later life: a longitudinal cohort study’. The grant holders are Professors Woods (CI), Clare (Bangor), Brayne, Matthews (Cambridge), Burholt, Phillips (Swansea) and Drs Windle (Bangor), Bennett and McCracken (Liverpool). We are grateful to the NISCHR Clinical Research Centre for their assistance in tracing participants and in interviewing and in collecting blood samples, and to general practices in the study areas for their cooperation. We would like to thank the CFAS Wales population, their families and carers for their participation.

Conflicts of interest

None declared.

References

- [1] Matthews FE, Stephan BCM, McKeith IG, Bond J, Brayne C (2008) Two year progression from mild cognitive impairment to dementia: To what extent do different definitions agree? *Journal of the American Geriatrics Society* **56**, 1424 - 1433.
- [2] Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E (1999) Mild cognitive impairment: Clinical characterization and outcome. *Archives of Neurology* **56**, 303-308.
- [3] Petersen RC, Doody R, Kurz A, Mohs RC, Morris JC, Rabins PV, Winblad B (2001) Current concepts in mild cognitive impairment. *Archives of Neurology* **58**, 1985 - 1992.
- [4] Petersen RC (2004) Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine* **256**, 183 - 194.
- [5] Portet F, Ousset PJ, Visser PJ, Frisoni GB, Nobili F, Scheltens P, Vellas B, Touchon J, MCI Working Group of the European Consortium on Alzheimer's Disease (EADC) (2006) Mild cognitive impairment (MCI) in medical practice: a critical review of the concept and new diagnostic procedure. Report of the MCI Working Group of the European Consortium on Alzheimer's Disease. *Journal of Neurology, Neurosurgery & Psychiatry* **77**, 714-718.
- [6] Stephan BCM, Brayne C, McKeith IG, Bond J, Matthews FE (2008) Mild cognitive impairment in the older population: Who is missed and does it matter? *International Journal of Geriatric Psychiatry* **23**, 863 - 871.
- [7] Lenehan ME, Klekociuk SZ, Summers MJ (2012) Absence of a relationship between subjective memory complaint and objective memory impairment in mild cognitive impairment (MCI): is it time to abandon subjective memory complaint as an MCI diagnostic criterion? *International Psychogeriatrics* **24**, 1 - 10.
- [8] Roberts JL, Clare L, Woods RT (2009) Subjective memory complaints and awareness of memory functioning in mild cognitive impairment: A systematic review. *Dementia and Geriatric Cognitive Disorders* **28**, 95 - 109.
- [9] Podewils LJ, McLay RN, Rebok GW, Lyketsos CG (2003) Relationship of self-perceptions of memory and worry to objective measures of memory and cognition in the general population. *Psychosomatics* **44**, 461-470.
- [10] Jorm AF, Christensen H, Korten AE, Henderson AS, Jacomb PA, Mackinnon A (1997) Do cognitive complaints either predict future cognitive decline or reflect past cognitive decline? A longitudinal study of an elderly community sample. *Psychological Medicine* **27**, 91-98.
- [11] Iliffe S, Pealing L (2010) Subjective memory problems. *BMJ* **340**, 703-706.
- [12] Clare L, Markova IS, Roth I, Morris RG (2011) Awareness in Alzheimer's disease and associated dementias: Theoretical framework and clinical implications. *Aging & Mental Health* **15**, 936-944.
- [13] Schmand B, Jonker C, Geerlings MI, Lindeboom J (1997) Subjective memory complaints in the elderly: Depressive symptoms and future dementia. *The British Journal of Psychiatry* **171**, 373-376.
- [14] Reisberg B, Shulman MB, Torossaian C, Leng L, Zhu W (2010) Outcome over seven years of health adults with and without subjective cognitive impairment. *Alzheimer's & Dementia* **6**, 11-24.
- [15] Jessen F, Wiese B, Bachmann C, Eifflaender-Gorfer s, Haller F, Kolsch H, Luck T, Mosch E, van den Bussche H, Wagner M, Wollney A, Zimmerman T, Pentzek M, Reidel-Heller SG, Romberg H-P, Weyerer S, Kaduszkiewicz H, Maier W, Bickel H (2010) Prediction of dementia by subjective memory complaints: Effects of severity

- and temporal association with cognitive impairment. *Archives of General Psychiatry* **67**, 414-422.
- [16] Barnes DE, Alexopoulos GS, Lopez OL, Williamson JD, Yaffe K (2006) Depressive symptoms, vascular disease, and mild cognitive impairment: findings from the Cardiovascular Health Study. *Archives of General Psychiatry* **63**, 273-279.
- [17] Yates JA, Clare L, Woods RT (2013) Mild cognitive impairment and mood: a systematic review. *Reviews in Clinical Gerontology* **23**, 317-356.
- [18] Dux MC, Woodard JL, Calamari JE, Messina M, Arora S, Chik H, Pontarelli N (2008) The moderating role of negative affect on objective verbal memory performance and subjective memory complaints in healthy older adults. *Journal of the International Neuropsychological Society* **14**, 327-336.
- [19] Minett TSC, Da Silva RV, Ortiz KZ, Bertolucci PHF (2008) Subjective memory complaints in an elderly sample: a cross-sectional study. *International Journal of Geriatric Psychiatry* **23**, 49-54.
- [20] Copeland JRM, Dewey ME, Griffiths-Jones HM (1986) A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGE-CAT. *Psychological Medicine* **16**, 89-99.
- [21] Matthews FE, Stephan BCM, Bond J, McKeith I, Brayne C, on behalf of the Medical Research Council Cognitive Function and Ageing Study. (2007) Operationalisation of mild cognitive impairment: A graphical approach. . *PLoS Medicine* **4**, e304.
- [22] Huppert FA, Brayne C, Gill C, Paykel ES, Beardsall L (1995) CAMCOG - a concise neuropsychological test to assist dementia diagnosis: socio-demographic determinants in an elderly population sample. *British Journal of Clinical Psychology* **34**, 529-541.
- [23] Williams JG, Huppert FA, Matthews FE, Nickson J (2003) Performance and normative values of a concise neuropsychological test (CAMCOG) in an elderly population sample. *International Journal of Geriatric Psychiatry* **18**, 631-644.
- [24] Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S (2002) Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. *JAMA : the journal of the American Medical Association* **288**, 1475-1483.
- [25] Kruger TM, Abner EL, Mendiondo M, Schmitt FA, Smith CD, Jicha GA (2012) Differential reports of pain and depression differentiate mild cognitive impairment from cognitively intact elderly participants. *Journal of Geriatric Psychiatry and Neurology* **25**, 107 - 112.
- [26] Fernandez-Martinez M, Molano A, Castro J, Zarranz JJ (2010) Prevalence of neuropsychiatric symptoms in mild cognitive impairment and Alzheimer's disease, and its relationship with cognitive impairment. *Current Alzheimer research* **7**, 517-526.
- [27] Van der Linde R, Stephan BCM, Matthews FE, Brayne C, Savva GM (2010) Behavioural and psychological symptoms in the older population without dementia – relationship with socio-demographics, health and cognition. *Biomed Central Geriatrics* **10**.
- [28] Antikainen R, Hanninen T, Honkalampi K, Hintikka J, Koivumaa-Honkanen H, Tanskanen A, Viinamaki H (2001) Mood improvement reduces memory complaints in depressed patients. *European Archives of Psychiatry and Clinical Neuroscience* **251**, 6-11.
- [29] Derouesne C, Lacomblez L, Thibault S, LePoncin M (1999) Memory complaints in young and elderly subjects. *International Journal of Geriatric Psychiatry* **14**, 291-301.

- [30] Comijs HC, Deeg DJ, Dik MG, Twisk JW, Jonker C (2002) Memory complaints; the association with psycho-affective and health problems and the role of personality characteristics. A 6-year follow-up study. *Journal of Affective Disorders* **72**, 157-165.
- [31] Folstein MF, Folstein SE, McHugh PR (1975) 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* **12**, 189 - 198.
- [32] Mol MEM, van Boxtel MPJ, Willems D, Jolles J (2006) Do subjective memory complaints predict cognitive dysfunction over time? A six-year follow-up of the Maastricht Aging Study. *International Journal of Geriatric Psychiatry* **21**, 432–441.

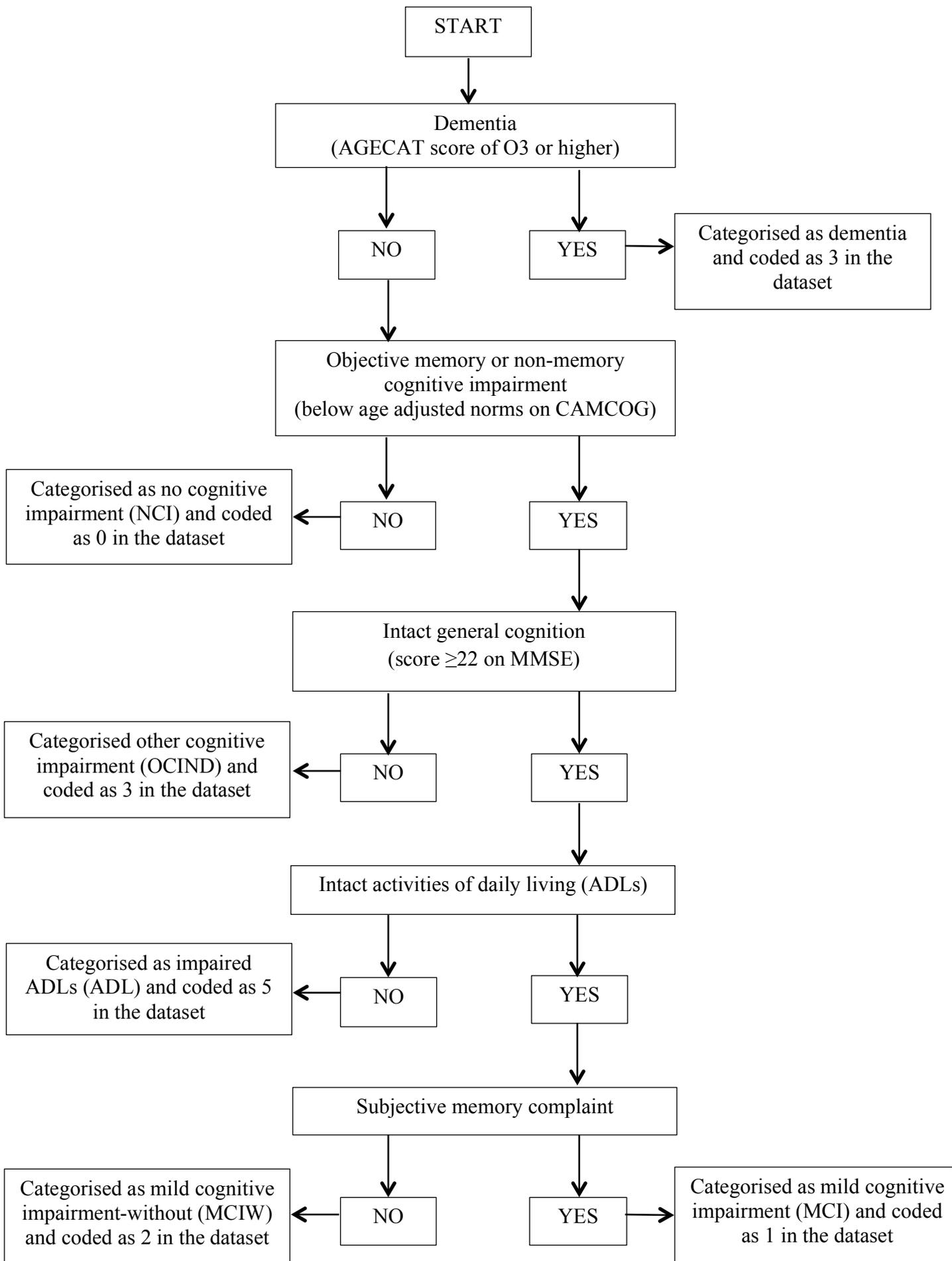


Figure 1: Flow diagram of the cognitive status algorithm

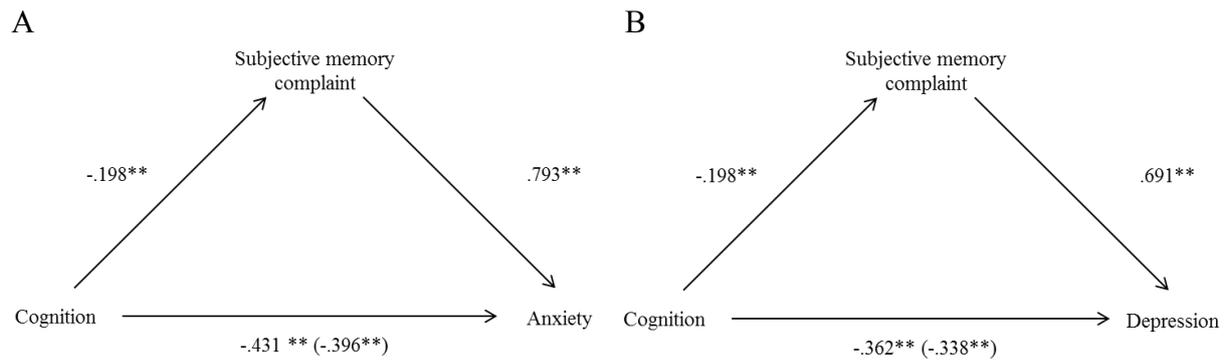


Figure 2: The relationships between cognition and anxiety (A) and cognition and depression (B) are partially mediated by subjective memory complaints. Coefficients without parentheses indicate the direct relationship between each pair of variables; coefficients in parentheses indicate the (reduced) coefficient when subjective memory complaints are added into the regression equation relating cognition and mood

Table 1: Sample characteristics for participants with and without SMC

	No SMC	SMC	Total (%)
Age mean (SD)	74.34 (6.89)	74.34 (6.79)	
MMSE mean (SD)	27.55 (2.19)	27.22 (2.30)	
CAMCOG mean (SD)	85.20 (10.65)	84.83 (8.47)	
Years in FT Education mean (SD)	11.73 (2.69)	11.73 (2.83)	
Female N (%)	1205 (56.8)	524 (50.1)	1729 (54.5)
With anxiety N (%)	79 (3.7)	84 (8.0)	163 (5.1)
Without anxiety N (%)	2044 (96.3)	966 (92.0)	3010 (94.9)
With depression N (%)	431 (20.3)	357 (34.0)	788 (24.8)
Without depression N (%)	1692 (79.7)	693 (66.0)	2385 (75.2)
Total (%)	2123 (66.9)	1050 (33.1)	3173 (100)

Table 2: Sample characteristics for participants in each cognitive status group

	NCI	MCI	MCIW	Total (%)
Age mean (SD)	74.31 (6.95)	73.88 (6.12)	74.87 (6.50)	
MMSE mean (SD)	27.65 (2.13)	26.20 (2.43)	26.36 (2.35)	
CAMCOG mean (SD)	86.72 (7.79)	77.81 (12.61)	76.26 (15.67)	
Years in FT Education mean (SD)	11.83 (2.80)	11.44 (2.40)	11.08 (2.31)	
Female N (%)	1444 (54.6)	89 (44.5)	196 (59.6)	1729 (54.5)
With anxiety N (%)	133 (5.03)	18 (9.0)	12 (3.6)	163 (5.1)
With depression N (%)	628 (23.8)	78 (39.0)	82 (24.9)	3010 (94.9)
Subjective memory complaint N (%)	850 (32.1)	200 (100)	0 (0.0)	1050 (33.1)
Total (%)	2644 (83.3%)	200 (6.3%)	329 (10.4%)	3173 (100)

Table 3: SMC reported for each AGEKAT level of anxiety and depression

	No SMC (N)	SMC (N)
Anxiety Level 0	1352	518
Anxiety Level 1	692	448
Anxiety Level 2	32	27
Anxiety Level 3	37	37
Anxiety Level 4	10	15
Anxiety Level 5	0	5

	No SMC (N)	SMC (N)
Depression level 0	1617	620
Depression level 1	75	73
Depression level 2	270	239
Depression level 3	122	81
Depression level 4	39	37

Supplementary material

Various measures of cognition were assessed using logistic regression to investigate the relationship with anxiety in order to select the most appropriate measure to include in the mediation model. The results of the logistic regressions are shown in Table S1. The CAMCOG median split measure of cognition is the only measure of cognition that is significant, and also yields a significant Sobel test statistic. Table S2 shows the sensitivity analyses conducted using logistic regression to investigate the relationship between cognition and depression.

Table S1: Sensitivity analyses using logistic regression to show the relationship between different measures of cognition and anxiety and results of the Sobel test for mediation with SMC as a mediating variable

	OR	CI	P	Sobel test	P
MCItotal	1.14	0.76-1.71	.542	2.25	.025
CAMCOG total score	0.99	0.98-1.00	.176	-0.98	.327
CAMCOG median split	0.65	0.47-0.89	.008	-2.29	.021

MCItotal groups MCI and MCIW together and compares them to no cognitive impairment
 CAMCOG total score is the total score achieved by each participant on the CAMCOG questions asked in the interview
 CAMCOG median split is a dichotomous variable created from splitting the CAMCOG scale into two groups using the median of the scale

Table S2: Sensitivity analyses using logistic regression to show the relationship between different measures of cognition and depression and results of the Sobel test for mediation with SMC as a mediating variable

	OR	CI	P	Sobel test	P
MCItotal	1.39	1.13-1.71	.002	2.40	.016
CAMCOG total score	0.98	0.98-0.99	.000	-0.99	.320
CAMCOG median split	0.70	0.59-0.82	.000	-2.48	.013
<p>MCItotal groups MCI and MCIW together and compares them to no cognitive impairment CAMCOG total score is the total score achieved by each participant on the CAMCOG questions asked in the interview CAMCOG median split is a dichotomous variable created from splitting the CAMCOG scale into two groups using the median of the scale</p>					