RESEARCH ARTICLE

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Longitudinal stability of subsyndromal symptoms of depression in individuals with mild cognitive impairment: relationship to conversion to dementia after 3 years†

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Objective: To evaluate the degree to which longitudinal stability of subsyndromal symptoms of depression (SSD) is associated with conversion to dementia in patients with mild cognitive impairment (MCI).

Methods: Data from 405 MCI participants from the Alzheimer's Disease Neuroimaging Initiative (ADNI) study were analyzed. Participants were evaluated at baseline and 12-month intervals over 3 years. Participants were designated as MCI converters if dementia was diagnosed within 3 years or as cognitively stable MCI if dementia was not diagnosed during this interval. SSD were evaluated utilizing the 15-item Geriatric Depression Scale (GDS). Endorsement of specific SSD at baseline and the stability of SSD over 36 months were compared between the two MCI groups.

Results: Baseline symptom endorsement and stability of total GDS scores did not differentiate MCI groups. Worsening of four individual items from the GDS over time (memory problems, feelings of helplessness, loss of interest, and preference for staying at home) differentiated MCI converters from cognitively stable MCI ($p < 0.05$ for all). However, only increased endorsement of memory symptoms over time was associated with progression to dementia after controlling for other clinical variables ($p = 0.05$).

Conclusions: SSD in MCI participants largely consist of cognitive symptoms and activity limitations, and the stability of SSD over time differentiated the MCI groups better than baseline endorsement of symptoms. However, the only significant predictor of conversion to dementia was increased endorsement of memory problems, which likely represents insight into cognitive problems more than depressive symptomatology in MCI individuals. Copyright © 2011 John Wiley & Sons, Ltd.

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Introduction

Subsyndromal symptoms of depression (SSD) (Judd *et al.*, 1994), or depressive symptoms not of the severity or frequency to meet the criteria for major or minor depression, can include feelings of sadness, helplessness or worthlessness, decreased energy, sleep disturbance, concentration problems, weight gain, loss of interest in activities, or psychomotor retardation (APA, 1994). SSD occur in up to 30% of older

community dwelling adults (Cohen *et al.*, 2005), and SSD are increasingly being recognized as significant contributors to disability in older adults (Chopra *et al.*, 2005; Barry *et al.*, 2009). SSD are also among the most commonly reported neuropsychiatric symptoms in mild cognitive impairment (MCI) occurring in up to 50% of MCI individuals (Lyketsos *et al.*, 2002; Gabryelewicz *et al.*, 2004; Geda *et al.*, 2008; Abizanda *et al.*, 2009). As such, both major depression and SSD are often conceptualized as being prodromal features of incipient dementia (Brommelhoff *et al.*, 2009). However, differentiating symptoms of depression from cognitive symptoms in MCI has remained a significant challenge in older adults because of overlapping symptom criteria, particularly with respect to cognitive symptoms and activity limitations (Steffens, 2008). As a result, the degree to which depressive symptoms may serve as phenotypic markers of individuals at increased risk for dementia remains unclear.

Evaluation of the specific types of SSD endorsed by MCI individuals at baseline and the longitudinal stability of these symptoms in relation to conversion to dementia are two significant avenues to clarify this relationship. Previous reports have suggested that anhedonia, sleep disturbance, and concentration problems are all common SSD associated with MCI (Gabryelewicz *et al.*, 2004; Stepaniuk *et al.*, 2008; Edwards *et al.*, 2009). Further, among MCI individuals with major depression, symptoms of depressed affect, in contrast to neurovegetative symptoms or cognitive symptoms, have been shown to differentiate individuals who progressed to dementia from those who remained cognitively stable over time (Houde *et al.*, 2008). However, to our knowledge, differential patterns of depressive symptom endorsement for MCI individuals who progress to dementia have not been evaluated specifically among individuals with SSD. Similarly, although several previous studies have demonstrated that cumulative ratings of depressive symptom severity in MCI are relatively stable over time (Li *et al.*, 2001; Steinberg *et al.*, 2004), one recent study has demonstrated that worsening of total depressive symptom severity over time represents a risk for dementia (Rovner *et al.*, 2009). Therefore, there is preliminary evidence to suggest that baseline SSD characteristics and stability of SSD over time may differentiate MCI individuals who will develop dementia from those who remain cognitively stable.

The short form of the Geriatric Depression Scale (GDS) is one of the most frequently utilized measures of self-reported depressive symptoms for older adults (Yesavage *et al.*, 1982; Geda *et al.*, 2006; Chopra *et al.*, 2008; Debruyne *et al.*, 2009; Lach *et al.*, 2010). However, to date, relatively little is known about baseline characteristics and longitudinal stability of SSD obtained from the GDS in MCI populations, particularly with respect to dementia outcomes. Given the prevalence of SSD in MCI populations, such evaluations are warranted and could improve treatment outcomes through earlier identification of individuals at higher risk for developing dementia. However, despite studies that have validated the short form of the GDS in MCI populations (Debruyne *et al.*, 2009), item 10 of this scale, that is, 'Do you feel you have more problems with memory than most', is often viewed more as a cognitive symptom of MCI rather than a symptom of depression. As a result, many researchers have excluded this item from analyses conducted to evaluate the impact of SSD on cognitive decline (Rovner *et al.*, 2009). Given that memory impairment is a core feature of both MCI and dementia, and not a symptom of depression, the degree to which endorsement and stability of this symptom differentiates individuals who progress to dementia from those who remain cognitively stable in contrast to other depressive symptoms is of particular interest.

The present study was conducted with three primary aims: (i) to identify the most common types of SSD endorsed on the short form of the GDS in a large sample of older adults diagnosed with MCI; (ii) to evaluate if SSD endorsement at baseline differentiates individuals who progress to dementia within 3 years from those who remain cognitively stable during this interval; and (iii) to compare the longitudinal stability of SSD endorsement on the GDS (total scores, individual items) between MCI individuals who convert to dementia relative to cognitively stable MCI participants. Based on previous studies, we hypothesize that SSD will be common in MCI, that individuals who progress to dementia will endorse more affective symptoms at baseline than stable MCI participants, and that SSD of individuals who convert to dementia will exhibit less stable responses (i.e. show worsening over time) on GDS total scores and individual items of the GDS evaluating affective symptoms. Additionally, we hypothesize that the majority of MCI participants in this sample will endorse memory problems on the GDS and therefore this item will have limited utility in differentiating individuals who develop dementia from cognitively stable MCI participants.

Methods

Setting

The Alzheimer's Disease Neuroimaging Initiative. The Alzheimer's Disease Neuroimaging Initiative (ADNI) was launched in 2004 by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering, the Food and Drug Administration, private pharmaceutical companies, and non-profit organizations. More than 800 participants, ages 55–90 years, have been recruited from 59 sites across the USA and Canada to be followed for 2–3 years. The primary goal of ADNI is to determine whether serial magnetic resonance imaging, positron emission tomography, other biological markers, and clinical and neuropsychological assessment can accurately measure the progression of MCI and early Alzheimer's disease (AD). The identification of specific biomarkers of early AD and disease progression will provide a useful tool for researchers and clinicians in both the diagnosis of early AD and in the development, assessment and monitoring of new treatments. For additional information about ADNI, see www.adni-info.org. Demographic information and clinical data utilized for this study were downloaded from the ADNI clinical data repository (https://www.loni.ucla.edu/ADNI/Data/ADCS_Download.jsp). The 19 July 2009 version of the ADNI clinical database was used for all analyses.

Participants

Four hundred five participants who met the criteria for MCI at baseline constituted the sample for this study. The criteria for diagnosis of MCI included the following: (i) age between 55 and 90 years; (ii) complaints of memory loss by the patient and confirmed by a family relative; (iii) Mini mental state examination (MMSE; Folstein *et al.*, 1983) score of 24 and higher; (iv) overall Clinical Dementia Rating (CDR) Scale (Morris, 1993) score of 0.5; and (v) quantitative evidence of memory impairment relative to age and education-matched peers. Exclusion criteria at baseline included the following: (i) the presence of major depressive disorder or significant symptoms of depression (GDS (Yesavage *et al.*, 1982) score of 6 or higher); (ii) modified Hachinski ischemia score greater than 5; (iii) significant neurological or psychiatric illness; (iv) use of antidepressant drugs with anticholinergic side effects; and (v) high dose of neuroleptics or chronic sedatives or hypnotics, antiparkinsonian medication, and use of narcotic analgesics. Diagnoses of dementia were made by consensus panel of experts based on the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association criteria (McKhann *et al.*, 1984).

Assessment of disability

The Functional Activities Questionnaire (Pfeffer *et al.*, 1982). The Functional Activities Questionnaire (FAQ) evaluates the ability of participants to complete 10 domains of complex activities (e.g. managing finances), and scores range from 0 to 20, with higher scores representing increased disability.

Clinical Dementia Rating Scale (Morris, 1993). The CDR is a screening measure utilized to assess functional declines in older adults caused by cognitive impairments in order to classify stages of dementia.

Assessment of symptoms of depression

Geriatric Depression Scale (Yesavage *et al.*, 1982). The short form of the GDS consists of 15 'yes'/'no' questions, and total scores range from 0 to 15, with higher scores exhibiting more depressive symptoms. For this study, individuals scoring >0 and ≤5 on the GDS were classified as exhibiting SSD. At follow up evaluations, individuals scoring ≥6 on the GDS were classified as exhibiting symptoms of major depression (Marc *et al.* 2008).

Assessment of cognitive functioning

The Alzheimer's Disease Assessment Scale-Cognitive (Rosen *et al.*, 1984). The Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) is a widely utilized 11-item instrument devised to assess the severity of cognitive impairment in patients with AD. The total score range is 0 to 70 points, with a higher score indicating poorer cognitive performance.

Statistical analyses

Participants were classified 'MCI converters' if they were diagnosed with dementia within 3 years of their baseline evaluation or 'MCI cognitively stable' if they did not progress to dementia during this interval. Diagnoses of dementia were evaluated at 12-month intervals over this 36-month period. The MCI groups were compared with respect to demographic and

clinical characteristics using Wilcoxon rank sum tests (age, education, MMSE, CDR, ADAS-Cog, FAQ) and a Fisher's exact test (gender). To evaluate if the endorsement of specific symptoms or GDS total score differed between the MCI groups at baseline, a Fisher's exact test was utilized. Subsequently, a linear mixed effects model was employed to evaluate if MCI group status influenced total GDS scores over 3 years after accounting for the contributions of age and time. To evaluate the longitudinal stability of depressive symptoms over 3 years for the MCI groups, two approaches were utilized. First, the proportion of individuals who remained stable, declined, improved, or fluctuated with respect to SSD categorical status over 3 years was calculated and compared between groups utilizing Fisher's exact test. SSD categories were defined as 'depression free' GDS = 0, SSD; GDS = 1–5, and major depression; GDS > 5. Second, the stability (item endorsed, not endorsed) of each of the 15 GDS items was calculated for the 3-year interval relative to baseline between MCI groups utilizing odds ratios (95% confidence interval). Lastly, for each item of the GDS that showed differential stability of symptom endorsement between the two MCI groups, a generalized linear mixed model was utilized to evaluate the degree to which symptom endorsement on individual items of the GDS was predicted by MCI group, age, and time.

Results

Of the total sample, 312 participants (77%) exhibited SSD at baseline utilizing responses to all 15 items of the GDS, and 43% of the sample endorsed item 10 ('Do you have more problems with memory than most?'). Excluding item 10 from analyses resulted in SSD being reported by 55% of the sample. Three-year follow-up data was available for 227 participants, and 103 (45%) individuals converted to dementia during this interval. At baseline, MCI converters exhibited poorer performance on measures of overall cognitive functioning (MMSE, $p < 0.01$; ADAS-Cog, $p < 0.01$) and disability (CDR, $p < 0.01$; FAQ, $p < 0.01$) than cognitively stable MCI participants, but the two groups did not differ with respect to age, education, gender, or overall depression severity (Table 1). Of individuals completing a 3-year follow up evaluation, cognitively stable MCI participants did not differ from MCI converters with respect to endorsement of any of the specific GDS items at baseline (Table 2), and the most commonly endorsed SSD for the sample included memory problems, lack of energy, preference for staying at home, and dropping of activities and interests. No differences in GDS total score rate of change were found between the two MCI groups ($\beta_{\text{years:converter}} = 0.09$, $p = 0.19$, Figure 1). Over 36 months, stability of depressive symptom categories did not differ between the cognitively stable MCI participants and MCI converters ($p = 0.61$), and 49% of the sample exhibited stable SSD symptoms, 16% exhibited worsening symptoms, 8% improved, and 27% of the sample demonstrated fluctuations between depression categories. Further, 11 (9%) of MCI cognitively stable and 16 (16%) of MCI converters developed symptoms of major depression over 3 years, but the proportion of individuals developing major depression did not differ between groups (OR = 1.88, $p = 0.15$).

An evaluation of stability of specific GDS items for each of the two MCI groups (Table 3) revealed that four individual items from the GDS were less stable for MCI converters than MCI cognitively stable participants (memory problems, feelings of helplessness, preference for staying at home, dropped activities and interests) and in each case, increased endorsement of these symptoms over time (i.e. worsening of symptoms) was evident in the MCI converter group. A generalized linear mixed model (Table 4) was subsequently utilized to evaluate the degree to which symptom endorsement on these four GDS items was predicted by MCI group, age, and time, and only stability of memory symptoms was predicted by MCI group ($\text{Log(OR)}_{\text{years:converter}} = 0.34$, $p = 0.05$; Figure 2).

Discussion

Our major findings include the following: (i) SSD are common in MCI, and the most frequently endorsed symptoms from the GDS included memory problems, lack of energy, preference for staying at home, and limitations in activities; (ii) total SSD severity and endorsement of specific depressive symptoms did not differ at baseline between MCI groups; (iii) the majority of MCI participants demonstrated either stable or fluctuating SSD, and stability of SSD total severity scores did not differ between MCI groups; and (iv) stability of four specific depressive symptoms from the GDS (memory problems, activity and interest limitations, preference for staying at home, and feelings of helplessness) over 36 months differentiated cognitively stable MCI participants from MCI converters.

Table 1 Demographic and clinical characteristics of MCI groups at baseline ($n = 227$)

	Cognitively stable MCI		MCI converters		p
	n	Female (%)	n	Female (%)	
Gender	124	37 (29.8)	103	34 (33)	0.67[a]
	n	Mean (SD)	n	Mean (SD)	
Age (years)	124	74.9 (7.6)	103	74.8 (6.7)	0.69[b]
Education (years)	124	16.0 (2.8)	103	15.9 (2.9)	0.72[b]
MMSE	124	27.7 (1.7)	103	26.7 (1.6)	<0.01[b]
ADAS-Cog	124	9.4 (3.9)	103	12.7 (3.9)	<0.01[b]
GDS	124	1.5 (1.4)	103	1.6 (1.3)	0.38[b]
CDR[b]	124	1.4 (0.7)	103	1.8 (1.0)	<0.01[b]
FAQ	122	2.0 (3.1)	102	5.7 (4.7)	<0.01[b]

MMSE, Mini mental state examination; ADAS-Cog, Alzheimer's Disease Assessment Scale-Cognitive; GDS, Geriatric Depression Scale; CDR, Clinical Dementia Rating Scale; FAQ, Functional Activities Questionnaire.
[a]Fisher's Exact test.
[b]Wilcoxon Rank Sum tests.

Table 2 Endorsement of the 15 Geriatric Depression Scale items at baseline for mild cognitive impairment (MCI) groups ($n = 227$)

	Stable MCI n (%)	MCI converters n (%)	OR	p
1. Basically satisfied with your life?	6 (5)	5 (5)	1.00	1.00
2. Dropped many of your activities and interests	16 (13)	21 (20)	1.72	0.15
3. Feel your life is empty	2 (2)	4 (4)	2.46	0.41
4. Often get bored	8 (7)	8 (8)	1.22	0.80
5. In good spirits most of the time	6 (5)	3 (3)	1.69	0.52
6. Afraid something bad is going to happen	8 (7)	9 (9)	1.39	0.62
7. Feelings of happiness	6 (5)	4 (4)	1.26	1.00
8. Feelings of helplessness	4 (3)	4 (4)	1.21	1.00
9. Preference for staying at home	32 (26)	23 (22)	0.83	0.64
10. More problems with memory than most	61 (49)	55 (53)	1.18	0.59
11. Think wonderful to be alive	1 (1)	3 (3)	0.27	0.33
12. Feelings of worthless	2 (2)	1 (1)	0.60	1.00
13. Feel full of energy	29 (23)	27 (26)	0.86	0.63
14. Situation is hopeless	1 (1)	0 (0)	—	1.00
15. Better off than others	4 (3)	1 (1)	0.30	0.38

However, only endorsement of memory problems was associated with conversion to dementia after accounting for other clinical variables. Each of these findings will be discussed below.

With respect to the overall prevalence of SSD at baseline in this sample, 77% exhibited one or more symptoms of depression on the GDS. If item 10 (memory problems) was excluded from analysis, 55% of the sample endorsed SSD on this measure, demonstrating that 22% of the sample endorsed isolated memory problems. Our results suggest that in addition to memory problems, lack of energy, preference for staying at home, and dropping of activities and interests were the most commonly endorsed SSD for the sample.

Overall, the prevalence of SSD obtained from the entire GDS in our sample was higher than estimates of SSD in MCI using other measures of depression, which typically report the prevalence of SSD of approximately 30–50% (Lyketsos *et al.*, 2002; Gabryelewicz *et al.*, 2004; Geda *et al.*, 2008; Abizanda *et al.*, 2009). However, if item 10 of the GDS was removed from analysis, our results would be more consistent with these previous estimates. As memory problems are not considered to be symptoms of depression by most diagnostic criteria (APA, 1994), we would recommend that when utilizing the GDS to estimate the prevalence of SSD in MCI populations, item 10 should be excluded (Rovner *et al.*, 2009). However, we also recognize that endorsement of this item may in fact represent

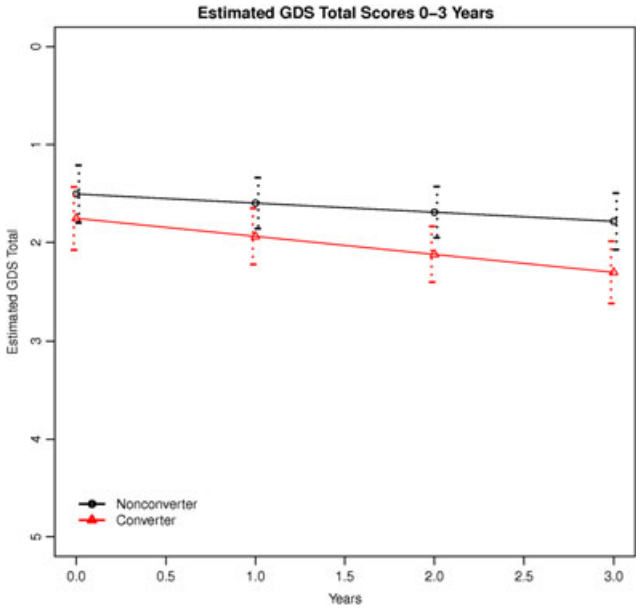

Figure 1 Estimated Geriatric Depression Scale (GDS) total score over 3 years ($n = 227$).

difficulties with concentration, which is a symptom of depression (APA, 1994), and further research may be necessary to determine the validity of this item of the GDS for use in MCI populations. Further, although there is not a consensus criterion for defining SSD, our methodology for designating SSD included individuals with only one reported depressive symptom, which is consistent with many previous studies evaluating neuropsychiatric symptoms in MCI (Lyketsos *et al.*, 2002; Gabryelewicz *et al.*, 2004; Abizanda *et al.*, 2009). However, we do recognize that SSD are also often utilized to denote individuals with two or more depressive symptoms (Judd *et al.*, 1994) (Lyness *et al.*, 2009), a distinction which is particularly important when comparing the prevalence of SSD across different patient populations.

Our findings also suggested that at baseline, individuals with stable MCI do not differ from individuals who progress to dementia with respect to overall severity of SSD or the endorsement of specific items. These findings were unexpected given recent findings that depressive symptom severity and endorsement of specific affective symptoms at baseline differentiated individuals who converted to dementia from cognitively stable MCI participants in other studies (Houde *et al.*, 2008; Boyle *et al.*, 2010). We interpret our findings to suggest that SSD in MCI, unlike more significant symptoms of depression, are primarily a generalized consequence or concurrent feature of the MCI syndrome, but these symptoms are not pathognomic features of individuals at higher risk for dementia. Further, given that the most commonly endorsed SSD in this sample included items that could be attributed to cognitive decline and resulting activity limitations, our results could be interpreted to suggest that SSD in MCI populations do not represent a concurrent affective component and instead reflect a significant overlap in symptoms between the two syndromes.

When we evaluated the stability of depressive symptoms categorically over time, we found that the majority of patients in the sample demonstrated stable, fluctuating, or improving SSD, with only a relatively small proportion of the sample (16%) exhibiting worsening of SSD. This finding was consistent with previous studies demonstrating that cumulative ratings of depressive symptom severity in MCI are relatively stable over time (Li *et al.*, 2001;

Table 3 Stability of depressive symptoms of the 15 Geriatric Depression Scale items for mild cognitive impairment (MCI) groups ($n = 227$)

	Stable MCI (%)	MCI converters (%)	Test	*p*
1. Basically satisfied with your life?	84.7	80.6	0.75	0.48
2. Dropped many of your activities and interests	71.0	48.5	0.39	<0.01
3. Feel your life is empty	88.7	89.3	1.06	1.00
4. Often get bored	81.5	75.7	0.71	0.33
5. In good spirits most of the time	91.1	87.4	0.68	0.39
6. Afraid something bad is going to happen	81.5	82.5	1.07	0.86
7. Feelings of happiness	86.3	85.4	0.93	0.85
8. Feelings of helplessness	87.9	71.8	0.35	<0.01
9. Preference for staying at home	68.5	51.5	0.49	0.01
10. More problems with memory than most	59.7	42.7	0.51	0.01
11. Think wonderful to be alive	94.4	93.2	0.82	0.79
12. Feelings of worthless	91.1	84.5	0.53	0.15
13. Feel full of energy	58.9	59.2	1.01	1.00
14. Situation is hopeless	91.9	88.3	0.67	0.38
15. Better off than others	90.3	91.3	1.12	1.00

Table 4 Comparison of worsening on selected Geriatric Depression Scale items for mild cognitive impairment (MCI) groups ($n = 227$)

	$Log(OR)_{years:converter}$	SD	Z	p
Dropped many activities and interests	0.01	0.29	0.04	0.97
Feelings of helplessness	0.05	0.34	0.16	0.16
Preference of staying at home	-0.08	0.19	-0.44	0.66
Feelings of increased memory problems	0.34	0.17	1.94	0.05

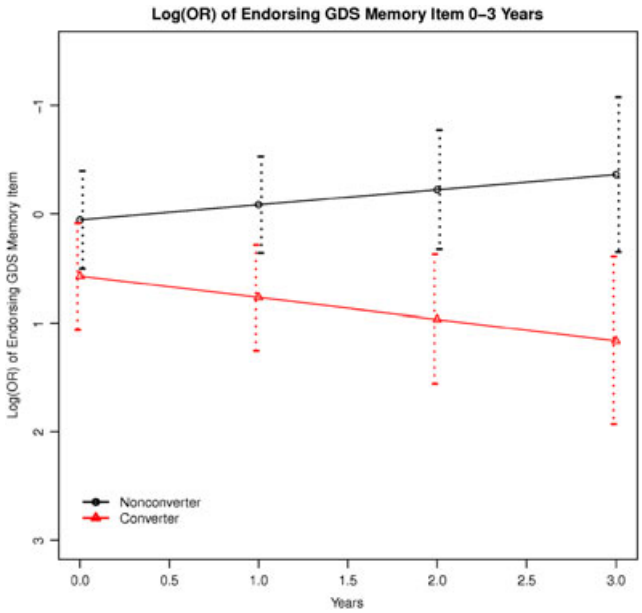

Figure 2 Endorsement of memory problems over 3 years for mild cognitive impairment groups ($n = 227$); GDS, Geriatric Depression Scale.

Steinberg *et al.*, 2004). However, unexpectedly, we did not see significant differences between our two MCI groups with respect to categorical evaluations of stability of total SSD severity as might be expected given a recent study suggesting that increased SSD severity over time represented a risk for dementia (Rovner *et al.*, 2009). Unlike this previous study, however, we utilized categorical ratings of SSD rather than total symptom score, which may have contributed to our divergent findings. We utilized this categorical approach as we felt that this represented the most clinically meaningful analysis of the data as by definition, SSD represent subthreshold symptoms of depression.

In contrast, our findings indicate that the worsening of four specific items of the GDS (memory problems, dropped activities and interests, preference for staying at home, and feelings of helplessness) over time relative to baseline endorsement were associated with conversion to dementia. As we feel these four items are most strongly associated with cognitive problems and functional limitations, which are core aspects of a diagnosis of dementia, these findings are not surprising but do illustrate the complexity of distinguishing mood symptoms from cognitive symptoms among individuals with MCI (Steffens, 2008). However, after accounting for other clinical features, only worsening of memory problems over time was associated with conversion to dementia. Again, as memory problems are not typically viewed as a symptom of depression and represent a core feature of dementia, this finding is not surprising. However, a lack of association between the stability of other SSD that are more reflective of affective symptoms, such as feelings of depressed mood and worthlessness, and conversion to dementia suggests that worsening of affective symptoms are not core depressive features of a prodromal phase of incipient dementia.

Although we expected memory symptoms to be common in MCI individuals, our finding that 42% of the sample endorsed memory problems is significant for several reasons. First, we expected a higher rate of endorsement for this item given that all participants in the study were diagnosed with MCI and demonstrated memory impairments on testing. Our findings indicate that less than one half of participants in the sample reported an awareness of cognitive symptoms that are core diagnostic features of MCI. Given this, we feel that endorsement of memory problems on the GDS may represent a mechanism for evaluating the participant's awareness or insight into cognitive deficits, and recent studies have suggested that patient awareness of cognitive symptoms may be a particularly useful in differentiating individuals with different forms of neurodegenerative disease (Barnes *et al.*, 2006; Williamson *et al.*, 2009). Our results could extend these previous studies to suggest that awareness of memory problems in MCI, although not typically viewed as SSD, may also be a significant clinical attribute associated with increased risk for conversion to dementia. In addition, previous studies evaluating the agreement between self-reported symptoms of depression and informant ratings of depression in

MCI and dementia patients have found that item 10 represents the single item of the GDS for which patients and informants show high degrees of agreement (Chopra *et al.*, 2008). In combination, these findings would suggest that self-report measures of awareness of memory problems obtained from commonly utilized measures of depression may be particularly useful, in combination with measures of cognitive functioning and activity limitations, in identifying individuals at risk for continued cognitive decline.

Overall, this study has several strengths including a large sample size, thorough ascertainment of MCI status, and a relatively long follow-up period. Despite these strengths, there are several limitations to the study, which also should be discussed. First, it is important to note that for our designation of SSD, we did not require specific depressive symptoms to be endorsed and we did not exclude any individual items of the GDS from our statistical analyses. Although our intent for this study was not to validate the short form of the GDS or to demonstrate the incidence of SSD in MCI populations, this methodological consideration will limit the generalizability of our findings. Similarly, diagnostic evaluations of minor depression were not conducted, and therefore it is possible that some of the patients that we designated as exhibiting SSD may have in fact met diagnostic criteria for minor depression. Further, as we excluded participants with major depression and significant cerebrovascular disease, our ability to generalize our findings to the larger population is limited. Additionally, although not specific to our study, measurement error may have resulted in the inclusion of some individuals with normal cognitive function or dementia in our baseline sample or the misdiagnosis of dementia over the 36-month interval. Lastly, by design, we utilized only one self-report measure of depression to evaluate SSD. Given previous studies demonstrating that ratings of depressive symptoms in MCI often differ from clinician ratings and informant ratings (Chopra *et al.*, 2008), this represents a further limitation to our findings.

Conclusions

Subsyndromal symptoms of depression in this MCI sample were primarily characterized by cognitive complaints, activity limitations, and decreased energy. Neither baseline SSD nor longitudinal stability of SSD total scores differentiated cognitively stable MCI participants from those who developed dementia. Worsening of specific GDS items associated with memory problems, decreased energy, feelings of helplessness, and activity limitations was more common in individuals who developed dementia; however, only increased endorsement of cognitive complaints over time was associated with progression to dementia after accounting for other clinical variables. Therefore, our results suggest that SSD may have limited utility in identifying MCI individuals at increased risk for dementia.

Key points

- Subsyndromal symptoms of depression (SSD) are common in Mild Cognitive Impairment (MCI).
- The stability of SSD over time differentiated the MCI groups (converters, non-converters) better than baseline endorsement of SSD but the only significant SSD predictor of conversion to dementia was increased endorsement of memory problems.
- Cognitive complaints may be more useful in predicting conversion to dementia than other types of SSD.

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