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**Brief Report** 

# Subjective Cognitive Decline Correlates With Depression Symptoms and Not With Concurrent Objective Cognition in a Clinic-Based Sample of Older Adults

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#### Abstract

**Objectives:** Subjective cognitive decline (SCD) is common in older adults; however, its utility in clinic-based samples remains controversial given its strong associations with mood symptoms.

**Methods:** Five hundred nineteen individuals aged 60–95 with a wide range of cognitive performance scores were referred by community health clinics for brief screening of cognitive complaints. Linear regression models examined the cross-sectional associations between SCD (5-item self-reported questions), symptoms of depression (Beck Depression Inventory [BDI]), and concurrent objective cognitive performance (Cognitive Composite) adjusting for demographics.

**Results:** There was not a significant association between SCD and concurrent objective cognition after adjusting for demographics and depression. In contrast, there was a significant association between SCD and depression after adjusting for demographics and objective cognition. There was also a consistent association between SCD and depression, but not between SCD and objective cognition, in those with high and low levels of SCD reporting, in all ranges of cognitive performance, and in those with mild to moderate depression.

**Discussion:** Results are consistent with previous findings and suggest that SCD does not accurately reflect concurrent cognitive performance in a clinic-based sample of older adults. Clinical interpretation of SCD should account for the role of depression.

Keywords: Cognitive function—Depression—Memory complaints—Mood—Neuropsychology—Subjective cognitive decline—Subjective cognitive complaints

Subjective cognitive decline (SCD) (Jessen et al., 2014) is common in older adults and is thought to be a risk factor for future cognitive decline (Glodzik-Sobanska et al., 2007; Haley et al., 2009) and progression to mild cognitive impairment (MCI) and Alzheimer's Disease (AD) (Buckley et al., 2015; Donovan et al., 2014; Dufouil, Fuhrer, & Alperovitch, 2005; Jonker, Geerlings, & Schmand, 2000; Reid & MacLullich, 2006). In contrast, the relationship between SCD and concurrent objective cognitive performance is weak and limited by SCD's association with mood symptoms rather than objectively measured cognition (Buckley et al., 2013; Pearman & Storandt, 2004). A recent study from our research group found that SCD correlated with depression and not with objective cognition in a large randomly-selected cohort of community-dwelling adults (Zlatar, Moore, Palmer, Thompson, & Jeste, 2014). This same pattern of associations was observed in other cohorts of community-dwelling older adults, in cognitively normal elders, and in patients with epilepsy (Alegret et al., 2015; Balash et al., 2013; Buckley et al., 2013; Donovan et al., 2014; Galioto, Blum, & Tremont, 2015; Minett, Da Silva, Ortiz, & Bertolucci, 2008).

The present study examined associations between SCD, symptoms of depression, and objective cognition in a large sample of older adults referred by primary care physicians or geriatricians for screening for possible cognitive impairment. Determining the veracity and potential reason for SCD in this sample is a major concern. It may be the case that associations between objective cognition, depression, and SCD in this clinic-based sample differ from those in population-based samples. All individuals in this sample, or their physicians, have concerns about their cognition that rise to the level of actively seeking help, and the sample covers a wide range of cognitive abilities, from normal to MCI. Based on previous findings (Zlatar et al., 2014), we hypothesized that SCD would be associated with symptoms of depression rather than concurrent objective cognitive performance. However, these associations could vary when the sample is stratified by level of cognition or severity of symptoms of depression.

#### Methods

#### Participants

Participants (or family members) who reported to their primary care physicians that they were worried about their memory or thinking were referred to our community clinic program for a brief objective evaluation of cognitive function. Those with frank cognitive impairment (scored < 24 on the Mini-Mental State Exam) were excluded from our analyses since our interest focused on those with questionable cognitive impairment, and because those with dementia often develop anosognosia and would not accurately report SCD (Clement, Belleville, & Gauthier, 2008). We did not exclude participants with mild or questionable cognitive impairment to maintain a range of cognitive performance that would generalize to a primary care clinicbased population. We did not exclude participants based on depression scores in order to include a diverse and representative sample of older adults. Analyses included 519 older adults (57% women) between the ages of 60 and 95, out of which 11% reported moderate to severe symptoms of depression (Beck Depression Inventory [BDI] scores  $\geq$ 20). Informed consent was obtained from each participant in accordance with Federal guidelines for the protection of human subjects and the University of California, San Diego Institutional Review Board.

#### Procedures

Participants were individually assessed by a psychometrist in a quiet, well-lit room at one of two community primary care or geriatric clinics in San Diego County. The Wechsler Memory Scale Revised (WMS-R) Logical Memory Test Story A, the Trail Making Test (Parts A and B), and the

Animal Fluency test were administered and scores were normed using the means and standard deviations published by The Alzheimer's Disease Centers' Uniform Data Set (UDS) (Weintraub et al., 2009). Trail Making Test A and B z-scores were multiplied by -1 so that higher scores reflect better performance. Test z-scores were then averaged to derive the Cognitive Composite used in subsequent analyses. Symptoms of depression were assessed with the BDI (score range = 0-63). SCD was assessed by asking participants to answer five Yes/No questions concerning current presence of: (a) persistent memory difficulties, (b) difficulty finding words, (c) difficulty in remembering people's names, (d) misplacing belongings, and (e) difficulty completing complex tasks. Each positive response was assigned a value of 1 and a total score was derived by summing across the five questions (score range = 0-5). These questions were developed by our research team to have face validity based upon our extensive experience with typical complaints from those with mild dementia. Their properties as a formal SCD scale have not been reported.

#### Data Analysis

All analyses were conducted using IBM SPSS version 21. Two hierarchical linear regression models (bootstrapped on 1,000 samples) were conducted. The first model examined the association between SCD score and objective cognition after adjusting for age, education, sex, and depression (i.e., BDI) scores. The second model examined the association between SCD score and depression (i.e., BDI) scores after adjusting for age, education, sex, and objective cognition (i.e., cognitive composite score). Results were Bonferroni corrected with a critical significance level set at p < .025 to correct for family-wise error (.05/2).

For stratification by cognitive status, those with cognitive composite scores  $\leq -1.5$  SD from the mean of the sample were assigned to the "Significant Cognitive Impairment" (SCI) group and the rest to the "No Cognitive Impairment" (NCI) group. For stratification by depression status, those with BDI scores  $\geq 20$  were assigned to the "Moderate-Severe Depression" group and the rest to the "Minimum-Mild Depression" group. For stratification by cognitive complaints status, individuals were divided into "Low SCD" and "High SCD" categories based on a median split of the SCD total score (median = 4). Pearson correlations (bootstrapped on 1,000 samples) examined associations between SCD, depression, and cognition within stratified groups. Bonferroni correction was set at p < .016 (.05/3).

#### Results

For participant characteristics see Table 1. The frequency with which each SCD item was endorsed is depicted in Table 2.

The first model, SCD predicting cognitive composite scores, was significant [F(5,513) = 30.62; p < .001; Adjusted

	Minimum	Maximum	Mean	Standard deviation	Possible range
Age	60	95	76.05	7.78	
Years of education	7	20	15.08	2.89	_
Mini-Mental State Exam	24	30	27.50	1.86	0-30
Logical Memory Story A Immediate	0	22	10.52	4.77	0-25
Logical Memory Story A Delayed	0	23	7.09	5.17	0-25
Trail Making Test: Part A <sup>a</sup>	15	150	54.69	24.34	0-150
Trail Making Test: Part B <sup>a</sup>	31	300	151.61	76.71	0-300
Category Fluency: Animals	4	33	16.13	5.34	_
Cognitive Composite Z-Score	-4.02	1.25	-1.07	0.97	_
Beck Depression Inventory	0	43	10.26	7.89	0-63
Subjective cognitive decline	0	5	3.30	1.45	0–5

Table 1. Participant Characteristics and Performance Scores (N = 519)

<sup>a</sup>Higher score = worse performance.

**Table 2.** Subjective Cognitive Decline (SCD) Questions:Frequency of Endorsed Items

SCD item	Number of participants endorsed (% of total sample)		
1. Persistent memory difficulties	416 (80.2)		
2. Difficulty finding words	340 (65.5)		
3. Difficulty in remembering	389 (75)		
people's names			
4. Misplacing belongings	325 (62.6)		
5. Difficulty completing complex	244 (47)		
tasks			
Number of SCD items endorsed (0-	-5)		
0 SCD items endorsed	31 (6)		
1 SCD item endorsed	39 (7.5)		
2 SCD items endorsed	63 (12.1)		
3 SCD items endorsed	116 (22.4)		
4 SCD items endorsed	149 (28.7)		
5 SCD items endorsed	121 (23.3)		

 $R^2$  = .22]; however, SCD scores were not associated with objective cognition after adjusting for co-variates and BDI (Table 3). The second model, SCD predicting BDI, was also significant [*F* (5,513) = 17.89; *p* < .001; Adjusted  $R^2$  = .14] and SCD scores contributed significant variance to the model ( $R^2 \Delta = .09$ , *p* < .001) after adjusting for demographics and cognitive composite scores (Table 3; Figure 1).

Within the NCI and the SCI groups, SCD was not associated with objective cognition after Bonferroni correction (NCI: N = 352, r = .11, p = .039; SCI: N = 167, r = .03, p = .69), but it was significantly associated with BDI scores (NCI: r = .32, p < .001; SCI: r = .33, p < .001). Within the "Minimum-Mild Depression" group, SCD was not significantly associated with objective cognition (N = 461, r = .07, p = .16), but it was with BDI scores (r = .3, p < .001). In those with "Moderate-Severe Depression", SCD was not significantly associated with objective cognition (N = 58, r = .02, p = .91) or BDI scores (r = .01, p = .92). SCD was significantly associated with BDI scores in both the "Low SCD" (N = 249, r = .24, p < .001) and "High SCD" (N = 270, r = .23, p < .001) groups, but not with objective cognition (Low SCD: r = .07, p = .24; High SCD: r = -.1, p = .103).

#### Discussion

The present results show that SCD was associated with self-report of depressive symptoms, but not with concurrent objective cognitive performance, in a large sample of older adults referred for cognitive screening by their primary care physician or geriatrician. The lack of association between SCD and concurrent objective cognitive performance is consistent with previous findings (Alegret et al., 2015; Balash et al., 2013; Buckley et al., 2013; Donovan et al., 2014; Galioto et al., 2015; Hohman, Beason-Held, & Resnick, 2011; Ryu, Lee, Kim, & Lee, 2015; Zlatar et al., 2014) and extends them to a primary care clinicbased sample of older individuals with cognitive concerns that rise to the level of actively seeking help. In contrast to previous studies, cognitive abilities in the present sample ranged from cognitively normal to MCI, and depression scores ranged from minimal to severe. There was no significant association between SCD and objective cognitive performance even when analyses were limited to those with significant cognitive impairment. This may reflect a mild level of anosognosia even though patients with frank dementia were excluded from the study.

The relationship between SCD and depression scores was evident in those with no objective cognitive impairment and those with significant cognitive impairment (to the level of MCI), as well as in those with minimum to mild levels of self-reported symptoms of depression. It was also evident in those with low levels of SCD and high levels of SCD. These findings highlight the consistency of the association between symptoms of depression and SCD (Zlatar et al., 2014) and indicate that clinicians should assess and take into account these symptoms in patients who present with SCD in a clinical setting.

A. Subjective cognitive decline (SCD) predicting cognitive composite score									
	В	Standard error B	Standardized beta	t	p				
Age	-0.054	0.004	432	-10.858	.001				
Sex	0.037	0.080	.019	0.476	.650				
Years of education	0.076	0.014	.227	5.701	.001				
BDI score	-0.001	0.006	011	-0.270	.816				
SCD score	0.014	0.027	.020	0.497	.625				
B. Subjective cognitive decline (S	SCD) predicting Bec	ck Depression Inventory scor	es						
	В	Standard error B	Standardized beta	t	þ				
Age	-0.180	0.050	177	-3.877	.001				
Sex	0.715	0.626	.045	1.074	.246				
Years of education	-0.211	0.118	077	-1.797	.074				
Cognitive composite score	-0.103	0.478	013	-0.270	.836				
SCD score	1.637	0.191	.300	7.272	.001				

 Table 3. Coefficients From Hierarchical Regression Models (N = 519)



Figure 1. Associations between subjective cognitive decline (SCD), Beck Depression Inventory scores, and cognitive composite scores in the entire sample.

It should be noted that the way in which SCD was assessed may have led to an over-endorsement of SCD as compared to questions that ask respondents to compare their cognitive abilities to others their age (Tandetnik et al., 2015). It is possible that this led to a differential association with symptoms of depression. The present study assessed SCD with five questions judged to have face validity based upon our extensive experience with typical complaints from those with mild dementia. Although this is likely better than the use of a single question (Reid & MacLullich, 2006), the validity/reliability of our SCD scale has not yet been reported. Further development of valid and reliable measures to characterize SCD is important for future research.

Given the cross-sectional nature of this study, we cannot address the value that SCD may hold in predicting future cognitive decline. It is also possible that the tests we used to measure cognition are not sensitive enough to detect preclinical AD (Jessen et al., 2014). The value of SCD as a predictor of future cognition is worth continued exploration.

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#### **Conflict of Interest**

The authors report no financial or personal conflicts of interest.

#### References

- Alegret, M., Rodríguez, O., Espinosa, A., Ortega, G., Sanabria, A., Valero, S.,...Boada, M. (2015). Concordance between subjective and objective memory impairment in volunteer subjects. *Journal of Alzheimer's Disease*, 48, 1109–1117. doi:10.3233/ JAD-150594
- Balash, Y., Mordechovich, M., Shabtai, H., Giladi, N., Gurevich, T., & Korczyn, A. D. (2013). Subjective memory complaints in elders: Depression, anxiety, or cognitive decline? *Acta Neurologica Scandinavica*, **127**, 344–350. doi:10.1111/ane.12038
- Buckley, R. F., Ellis, K. A., Ames, D., Rowe, C. C., Lautenschlager, N. T., Maruff, P.,...Saling, M. M. (2015). Phenomenological characterization of memory complaints in preclinical and prodromal Alzheimer's disease. *Neuropsychology*, 29, 571–581. doi:10.1037/neu0000156
- Buckley, R. F., Saling, M. M., Ames, D., Rowe, C. C., Lautenschlager, N. T., Macaulay, S. L.,...Ellis, K. A. (2013). Factors affecting subjective memory complaints in the AIBL aging study: biomarkers, memory, affect, and age. *International Psychogeriatrics*, 25, 1307–1315. doi:10.1017/S1041610213000665
- Clément, F., Belleville, S., & Gauthier, S. (2008). Cognitive complaint in mild cognitive impairment and Alzheimer's disease. *Journal* of the International Neuropsychological Society: JINS, 14, 222– 232. doi:10.1017/S1355617708080260
- Donovan, N. J., Amariglio, R. E., Zoller, A. S., Rudel, R. K., Gomez-Isla, T., Blacker, D.,...Rentz, D. M. (2014). Subjective cognitive concerns and neuropsychiatric predictors of progression to the early clinical stages of Alzheimer disease. *The American Journal of Geriatric Psychiatry: Official Journal of the American Association for Geriatric Psychiatry*, 22, 1642–1651. doi:10.1016/j.jagp.2014.02.007
- Dufouil, C., Fuhrer, R., & Alpérovitch, A. (2005). Subjective cognitive complaints and cognitive decline: Consequence or predictor? The epidemiology of vascular aging study. *Journal of the American Geriatrics Society*, 53, 616–621. doi:10.1111/j.1532-5415.2005.53209.x
- Galioto, R., Blum, A. S., & Tremont, G. (2015). Subjective cognitive complaints versus objective neuropsychological performance in older adults with epilepsy. *Epilepsy & Behavior*, 51, 48–52. doi:10.1016/j.yebeh.2015.06.035
- Glodzik-Sobanska, L., Reisberg, B., De Santi, S., Babb, J. S., Pirraglia, E., Rich, K. E.,...de Leon, M. J. (2007). Subjective memory complaints: presence, severity and future outcome in normal older subjects. *Dementia and Geriatric Cognitive Disorders*, 24, 177– 184. doi:10.1159/000105604
- Haley, A. P., Hoth, K. F., Gunstad, J., Paul, R. H., Jefferson, A. L., Tate, D. F.,...Cohen, R. A. (2009). Subjective cognitive complaints relate to white matter hyperintensities and future cognitive decline in patients

with cardiovascular disease. *The American Journal of Geriatric Psychiatry*, **17**, 976–985. doi:10.1097/JGP.0b013e3181b208ef

- Hohman, T. J., Beason-Held, L. L., & Resnick, S. M. (2011). Cognitive complaints, depressive symptoms, and cognitive impairment: are they related? *Journal of the American Geriatrics Society*, 59, 1908–1912. doi:10.1111/j.1532-5415.2011.03589.x
- Jessen, F., Amariglio, R. E., van Boxtel, M., Breteler, M., Ceccaldi, M., Chételat, G.,...Wagner, M. (2014). A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimer's & Dementia*, 10, 844–852. doi:10.1016/j.jalz.2014.01.001
- Jonker, C., Geerlings, M. I., & Schmand, B. (2000). Are memory complaints predictive for dementia? A review of clinical and population-based studies. *International Journal of Geriatric Psychiatry*, 15, 983–991.
- Minett, T. S., Da Silva, R. V., Ortiz, K. Z., & Bertolucci, P. H. (2008). Subjective memory complaints in an elderly sample: a crosssectional study. *International Journal of Geriatric Psychiatry*, 23, 49–54. doi:10.1002/gps.1836
- Pearman, A., & Storandt, M. (2004). Predictors of subjective memory in older adults. *The Journals of Gerontology. Series B*, *Psychological Sciences and Social Sciences*, **59**, P4–P6. doi:10.1093/geronb/59.1.P4
- Reid, L. M., & Maclullich, A. M. (2006). Subjective memory complaints and cognitive impairment in older people. *Dementia and Geriatric Cognitive Disorders*, 22, 471–485. doi:10.1159/000096295
- Ryu, S. Y., Lee, S. B., Kim, T. W., & Lee, T. J. (2015). Subjective memory complaints, depressive symptoms and instrumental activities of daily living in mild cognitive impairment. *International Psychogeriatrics*, 28, 487–494. doi:10.1017/ S1041610215001945
- Tandetnik, C., Farrell, M. T., Cary, M. S., Cines, S., Emrani, S., Karlawish, J., & Cosentino, S. (2015). Ascertaining subjective cognitive decline: A comparison of approaches and evidence for using an age-anchored reference group. *Journal of Alzheimers Disease*, 48, S43–55. doi:10.3233/jad-150251
- Weintraub, S., Salmon, D., Mercaldo, N., Ferris, S., Graff-Radford, N. R., Chui, H.,...Morris, J. C. (2009). The Alzheimer's Disease Centers' Uniform Data Set (UDS): The neuropsychologic test battery. *Alzheimer Disease and Associated Disorders*, 23, 91– 101. doi:10.1097/WAD.0b013e318191c7dd
- Zlatar, Z. Z., Moore, R. C., Palmer, B. W., Thompson, W. K., & Jeste, D. V. (2014). Cognitive complaints correlate with depression rather than concurrent objective cognitive impairment in the successful aging evaluation baseline sample. *Journal of Geriatric Psychiatry and Neurology*, 27, 181–187. doi:10.1177/0891988714524628