Relationships Between Cognitive Complaints and Quality of Life in Older Adults With Mild Cognitive Impairment, Mild Alzheimer Disease Dementia, and Normal Cognition

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Purpose: To examine in persons with varying degrees of cognitive impairment the relationship between self-reports of cognitive complaints and quality of life (QOL).

Methods: Older adults (n = 259) with normal cognition, mild cognitive impairment (MCI), and mild stage Alzheimer disease (AD) dementia completed tests of cognition and self-report questionnaires about QOL and 3 kinds of cognitive complaints: cognitive difficulties, distress from cognitive difficulties, and believing you had more memory problems than most people. Bivariate, multivariable, and multivariate regression analyses assessed relationships between domains of QOL and each cognitive complaint.

Results: Bivariate and multivariable analyses controlling for severity of cognitive and functional impairment found that cognitive complaints were related to relatively lower quality of daily life (QOL-AD, Dementia Quality of Life Scale), greater depression (GDS), more anxiety (BAI), higher perceived stress (PSS), and lower general mental well-being (SF-12 MCS).

Discussion: Cognitive complaints have robust associations with QOL. These findings have implications for AD prevention trials and management of clinical populations.

Key Words: self-rated health, Alzheimer disease, self-reported symptoms, mild cognitive impairment, quality of life

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In the United States, over 5 million older Americans have Alzheimer disease (AD) dementia (DEM), and that number is expected to nearly triple in the next 2 decades.[1] To address this leading cause of disability that has no therapies to stop or slow its progression, the US national Alzheimer's plan seeks to discover an effective therapy by 2025.[1] To achieve this goal, older adults are being identified early in the disease process, either with mild cognitive impairment (MCI) or with no cognitive impairment but with ≥ 1 biological risk factors. The premise is that to prevent or slow cognitive decline through both novel targeted pharmaceutical treatments and lifestyle changes, we need to detect the disease early.[2]

A plan to diagnose and treat AD early means patient-reported outcomes are becoming of even more important.[3–7] Traditionally, patient self-report data have had limited use in AD research and clinical practice because the disease often causes problems in insight that can limit accurate self-report of disability.[6,8,9] This is arguably less likely early in the disease process.[9,10] Currently, much of the information about the patient's health status and symptoms comes from the patient's informant. However, with earlier diagnosis, patients may expect to provide reports of their health status and symptoms.

Cognitive complaints are self-report data about the experience of cognitive symptoms. These self-report data can reflect one's beliefs about functioning, which in turn, can affect willingness to seek diagnosis and care.[11–13] They can also convey information about subjective difficulties and distress that can guide treatment planning and affect treatment adherence.[14–16] Although it is unclear whether cognitive complaints correspond to objective measures of cognitive impairment and pathology,[10,17–21] patient-reported data about beliefs, perceived difficulties, and distress related to cognitive symptoms can offer useful information about the subjective experience and quality of life (QOL) of a patient.

QOL is a multidimensional construct. It is typically evaluated across both personal and situational domains to encompass a person's overall functioning.[22] For individuals with DEM, the conceptual framework for QOL often integrates cognitive functioning, physical functioning, social interactions, mental well-being, and mood.[22] Previous QOL studies in persons with AD DEM have tended to evaluate multiple domains. However, when assessing cognitive symptoms these studies have focused almost exclusively on neuropsychiatric symptoms.[7,23–27] These are symptoms that often occur at severe stages of disease and are uncommon in early stages.

Many QOL studies have been conducted with patients with AD DEM, MCI, and normal cognition (NC),[7,23–40] but few studies have examined the relationships between cognitive complaints and QOL across the continuum from NC, to MCI, to mild stage AD DEM.[35–37] Understanding these relationships may help characterize the patient experience in at-risk or early clinical stages. The more we

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understand the relationships between subjective cognitive complaints and QOL domains, the better we can explain the symptom patterns early in the disease course. Problems in some domains—such as depression and impairments in instrumental activities of daily living (IADLs)—can reflect some of the earliest symptoms of DEM to be reported by patients.[10,11,17–21,41,42]

QOL domains are distinct but given that impairments in one could influence another, it is important to understand how cognitive complaints might relate to a QOL domain independent of that domain's relationships to other QOL domains. This type of analysis, referred to as a "multivariate" analysis, may help inform assessment by showing how domains are or are not associated with cognitive complaints while statistically adjusting for relationships among domains. This simultaneous analysis of multiple outcomes can also help minimize spurious findings that can result from multiple comparisons of individual outcomes.

The purpose of this study was to understand relationships between self-reported cognitive complaints and QOL in older adults with NC, MCI, or mild stage AD DEM. On the basis of previous studies of samples with AD and MCI,[7,23–31,33–35,43] we anticipated strong negative relationships between cognitive complaints and QOL. A previous study found lower QOL among older adults with MCI compared with those with either NC or AD.[40] This suggests that both cognitive complaints and self-reported QOL do not follow a pattern of linear change with declining cognition. We hypothesized therefore, that in moderator analyses, the relationships between cognitive complaints and QOL would be stronger for persons with a diagnosis of MCI compared with those with either a diagnosis of AD or NC. In a multivariate analysis, we sought to understand whether these relationships would persist after controlling for associations among QOL domains. Understanding these associations may help inform the choice and use of patient-reported outcomes in AD prevention trials and help guide management and intervention in clinical populations.

METHODS

Study Participants

The sample of 259 older adults with mild stage probable AD DEM (n = 68), MCI (n = 92), and NC (n = 99) was recruited from the Penn Memory Center (PMC) cohort study. Eligible adults were: age 65 and above, native English speakers, able to read from a handheld visual acuity card, able to hear conversational speech, completed at least the 6th grade, scored 20 or higher on the Mini Mental Status Examination (MMSE), and lived within 1-hour drive of the PMC. Individuals with AD and MCI were required to participate with a knowledgeable informant. Individuals with NC did not meet clinical criteria for either MCI or AD DEM and showed performance on neuropsychological testing commensurate with similarly aged and educated peers. All participants provided written informed consent or, as appropriate, assent with the written informed consent of their knowledgeable informant.

Participant Interviews

All participants completed a pair of face-to-face interviews. Interviews were conducted over 2 sessions to avoid fatigue and were completed within 3 months of the most recent cohort assessment. Each session lasted 1 to 1.5 hours. Participants received a $20 gift card after each visit.

Measures

Three cognitive complaints were measured. Cognitive difficulties were assessed with the Cognitive Difficulties Scale (CDS), which estimates how many and how often cognitive symptoms impact daily life.[6,12] Distress due to cognitive problems was assessed using the Global Distress Index (GDI), which was adapted from the Memorial Symptom Assessment Scale Short Form.[44] Belief that one experienced more memory problems than most others was obtained from a single item on the Geriatric Depression Scale (GDS).

QOL was appraised across: physical functioning, social interactions, mood, mental well-being, and functioning in activities of daily life.[22] Physical and mental well-being were assessed with the Physical Composite Scale (PCS) and Mental Composite Scale (MCS) from the Short Form Health Survey (SF-12).[45] Depression, anxiety, and subjective stress were assessed using the GDS,[46] Beck Anxiety Inventory (BAI),[47] and Perceived Stress Scale (PSS).[48] Physical functioning was assessed by the Lawton-Brody Basic and Instrumental Activities of Daily Living scales (B/IADLs).[49]

Multiple validated measures captured distinct aspects of QOL in daily life. Difficulty in daily life related to health, well-being, cognitive functioning, social relationships, daily activities, and self-concept was measured by the DEM-QOL.[50] Satisfaction about physical health, living situation, family, marriage, and finances was assessed with the QOL-AD.[51] Health-related QOL linked to mobility, self-care, usual activity, pain, and anxiety was measured by the Euro-QOL (EQ-5D), which included a single visual analogue scale for overall "health state"(EQ-VAS).[52]

Cognitive functioning was appraised with a battery of performance-based assessments. Global cognitive functioning was measured with the MMSE[53] and Montreal Cognitive Assessment (MoCA).[54] Verbal and nonverbal memory were measured with the Philadelphia Verbal Learning Task (PVLT)[55] and Biber Figure Learning Task (BFLT).[56] Executive function was assessed with Graphic Pattern Generation (GPG) test.[57] Cognitive reserve and premorbid crystalized intelligence were assessed by the Wechsler Test of Adult Reading (WTAR)[58] and Wechsler Adult Intelligence Scale third edition (WAIS-III) Information subtest.[59]

Standard demographics were collected directly from NC participants and from knowledgeable informants of AD and MCI participants. All procedures were approved by the local Institutional Review Board. A fuller description of the methods is available elsewhere.[40]

Statistical Analyses

We used descriptive statistics to characterize the sample based on the report of 3 cognitive complaints. Cognitive complaints were analyzed as dichotomies as this aided interpretation and utility of the results. Because subjective memory complaints are common,[60] dichotomizing the measures at the median values of the NC group also helped mitigate ceiling effects. CDS and GDI scores were dichotomized so that the higher category represented endorsement above that of 50% of NC individuals. For cognitive difficulties, the median was a score of 72, whereas for distress it was 18.

We assessed relationships between cognitive complaints and QOL domains in older adults with mild AD, MCI, and NC using bivariate and multivariable regression analyses. We report results from only the multivariable analyses as the bivariate results were similar. The multivariable models controlled statistically for participant characteristics that were unbalanced between study groups.

Adjustment for imbalances in cognitive performance was determined by the cognitive measure that contributed to the best model fit of all potential candidates.[61] In multivariable analyses of cognitive difficulties, models controlled for diagnostic category and Cognitive Composite Score (CCS), which was an objective measure of memory performance calculated as the average of the *z*-scores from the PVLT immediate memory, PVLT long-term memory, BFLT immediate memory, and BFLT long-term memory standardized to the NC group (mean = 0, SD = 1). Multivariable analyses of cognitive distress included global cognitive impairment (MMSE), college education, and diagnostic category. Multivariable analyses of more memory problems than most others controlled for global cognitive impairment (MMSE) and diagnostic category.

To understand the clinical significance of differences in the multivariable analyses, we examined the means and mean differences of measures with interpretable clinical thresholds: anxiety (BAI), depression (GDS), mental well-being (SF-12 MCS), and physical well-being (SF-12 PCS). In addition, we examined how diagnosis modified these relationships using interaction effects. We did this for cognitive difficulties and distress from cognitive problems but not more memory problems than most others because of small cell size. We used multivariate analysis of variance (MANOVA) to assess whether associations retained their significance controlling for the variance shared among QOL domains. We report the variance explained in these models either as the reciprocal of Wilks' λ or R^2 as appropriate.

In all analyses B/IADL scales were entered as binary variables. The cut point for these variables separated one third of the sample into the high group. We used a log transformation on the GDS to improve model fit. All analyses were conducted in Stata 14.

RESULTS

In a sample of 259 older adults with NC, MCI, and AD DEM, we examined 3 self-reported cognitive complaints: cognitive difficulties, distress due to cognitive problems, and belief of experiencing more memory problems than most others. Older adults reporting high cognitive difficulties—that is endorsement above half of similarly aged peers with NC—were similar to those endorsing low cognitive difficulties on all assessed demographic characteristics (all $P \geq 0.13$; Table 1). But, those reporting high distress from cognitive symptoms were more likely to be college educated and to have a diagnosis of MCI than to have a diagnosis of AD or to have NC (both $P < 0.05$). This pattern was similar for those who believed they had more memory problems than most others (both $P < 0.05$).

TABLE 1. Demographic Characteristics and Diagnostic Label by Cognitive Complaint (N = 259)

	n (%)		
Variables	**High**	**Low**	***P***
Cognitive difficulties (CDS)†	137 (52.9)	122 (47.1)	0.03
Age [mean (SD)] (y)	78.5 (6.6)	78.6 (6.9)	0.99
Female	81 (59.1)	76 (62.3)	0.60
White	128 (93.4)	108 (88.5)	0.36
College graduate	90 (65.7)	69 (56.6)	0.13
Right handed	128 (93.4)	112 (91.8)	0.68
AD	35 (25.6)	33 (27.0)	0.23
MCI	55 (40.1)	37 (30.3)	—
CN	47 (34.3)	52 (42.6)	—
Cognitive symptom distress (GDI)‡	147 (56.8)	112 (43.2)	< 0.001
Age [mean (SD)] (y)	78.4 (6.9)	78.7 (6.5)	0.91
Female	85 (57.8)	72 (64.3)	0.29
White	138 (93.9)	98 (87.5)	0.19
College graduate	99 (67.3)	60 (53.6)	0.02
Right handed	137 (93.2)	103 (92.0)	0.81
AD	34 (23.1)	34 (30.4)	0.04
MCI	62 (42.2)	30 (26.8)	—
CN	51 (34.7)	48 (42.9)	—
More memory problems than most others§	71 (27.4)	187 (72.2)	< 0.001
Age [mean (SD)] (y)	77.5 (7.0)	78.9 (6.6)	0.12
Female	39 (54.9)	117 (62.6)	0.26
White	68 (95.8)	167 (89.3)	0.24
College graduate	48 (67.6)	110 (58.8)	0.20
Right handed	63 (88.7)	176 (94.1)	0.20
AD	24 (33.8)	43 (23.0)	< 0.001
MCI	41 (57.7)	51 (27.3)	—
CN	6 (8.5)	93 (49.7)	—

High = at or above median. Low = below median.

†Endorsed greater cognitive difficulties than most individuals who were known to have normal cognition (CDS; cut point ≥ 72 score).

‡Endorsed greater distress from cognitive difficulties than most individuals who were known to have normal cognition (GDI; cut point ≥ 18 score).

§Single "yes" or "no" item from Geriatric Depression Scale.

AD indicates Alzheimer disease; CDS, Cognitive Difficulties Scale; CN, cognitively normal; GDI, Global Distress Index; MCI, mild cognitive impairment.

Associations Among Self-reported Cognitive Complaints and QOL Domains

In multivariable analyses, we assessed how each of the 3 self-reported cognitive complaints related to QOL domains. All 3 complaints were related to lower satisfaction in daily life (QOL-AD), more difficulties in daily life (DEM-QOL), greater depression (GDS), more anxiety (BAI), higher perceived stress (PSS), and lower mental well-being (SF-12 MCS; all $P < 0.05$; Table 2).

High cognitive difficulties and high distress from cognitive problems were related to lower ratings of general physical health (EQ-5D), physical well-being (SF-12 PCS), and instrumental functioning (IADLs; all $P < 0.05$). High distress from cognitive problems was additionally associated with lower ratings of global health (EQ-VAS, $P < 0.05$). No other statistically significant differences were observed (all $P > 0.05$).

Assessment of Clinical Differences

On an average, older adults reporting high cognitive difficulties endorsed mild anxiety (BAI = 8.0), which was substantively higher than that of those reporting low cognitive difficulties (BAI = 4.1; Table 3). About 43% (n = 52 of 122) who reported high cognitive difficulties endorsed severe anxiety (BAI ≥ 10). Differences between the 2 groups on other measures appeared clinically unremarkable.

On an average, older adults reporting high distress from cognitive difficulties showed clinically similar endorsement of anxiety and depression, which fell within normal limits. However, on an average, endorsement of anxiety among those reporting high distress (BAI = 7.6) was almost twice that of individuals reporting low distress (BAI = 4.3). This pattern was similar for depression, where average endorsement of depression among those who reported high distress was 6.4, whereas among individuals who reported low distress it was 3.8.

TABLE 2. Multivariable Regression Analyses of Self-reported Cognitive Complaints Associations to Domains of QOL (n = 259)

	Mean Difference		
Outcomes	**Cognitive Difficulties†‡**	**Cognitive Symptom Distress§‖**	**More Memory Problems than Most Others¶#**
QOL			
EQ-5D	−0.05**	−0.04*	−0.03
EQ-VAS	−3.68	−3.91*	−2.62
QOL-AD	−2.33***	−3.64***	−2.73***
DEM-QOL	−7.60***	−8.72***	−7.19***
Mood and Well-being			
GDS††	1.60***	1.74***	2.08***
BAI	3.95***	3.50**	2.64***
PSS	4.81***	5.37***	3.73***
SF-12 MCS	−2.67**	−3.57***	−4.96***
Physical well-being			
IADL Scale‡‡	0.18**	0.13*	0.08
BADL Scale‡‡	0.08	0.01	0.04
SF-12 PCS	−3.42**	−2.52*	0.39

†Endorsed greater cognitive difficulties than most individuals who were known to have normal cognition (CDS; cut point ≥72 score).

‡Model statistically controls for memory impairment (Cognitive Composite Score).

§Endorsed greater distress from cognitive difficulties than most individuals who were known to have normal cognition (GDI; cut point ≥18 score).

‖Model statistically controls for global cognitive impairment (MMSE), college education, and diagnostic group (AD or MCI).

¶Single "yes" or "no" item from GDS.

#Model statistically controls for global cognitive impairment (MMSE) and diagnostic group (AD or MCI).

††Log link back transformed.

‡‡Entered as binary variables. The cut point for these variables separated one third of the sample into the high group.

AD indicates Alzheimer disease; BADL, basic activities of daily living; BAI, Beck Anxiety Inventory; CDS, Cognitive Difficulties Scale; EQ, Euro-QOL; GDI, Global Distress Index; GDS, Geriatric Depression Scale; IADL, instrumental activities of daily living; MCI, mild cognitive impairment; MCS, Mental Composite Scale; MMSE, Mini Mental Status Examination; PCS, Physical Composite Scale; PSS, Perceived Stress Scale; QOL, quality of life; SF-12, Short Form Health Survey; VAS, Visual Analog Scale.

* < 0.05.

** ≤ 0.01.

*** ≤ 0.001.

TABLE 3. Mean Scores and Mean Differences in Anxiety (BAI), Depression (GDS), Mental Well-being (SF-12 MCS), and Physical Well-being (SF-12 PCS) by High and Low Endorsement of Cognitive Complaints

Variables	**High Mean (SD)**	**Low Mean (SD)**	**Mean Difference (SD)**
Cognitive difficulties (CDS) [n (%)]†			
BAI	8.0 (6.3)	4.1 (4.0)	4.0 (0.7)***
GDS	6.4 (5.0)	4.0 (3.9)	2.4 (0.6)***
SF-12 mental	53.4 (7.3)	55.2 (6.3)	−2.8 (0.9)***
SF-12 physical	46.1 (10.1)	49.3 (9.9)	−3.2 (1.2)**
Cognitive symptom distress (GDI) [n (%)]‡			
BAI	7.6 (6.2)	4.3 (4.4)	3.3 (0.7)***
GDS	6.4 (5.0)	3.8 (3.7)	2.6 (0.6)***
SF-12 mental	55.7 (6.2)	52.2 (7.2)	3.5 (0.8)***
SF-12 physical	49.0 (10.2)	46.5 (10.0)	2.5 (1.3)*
More memory problems than most others [n (%)]§			
BAI	8.2 (6.1)	5.4 (5.4)	2.8 (0.8)***
GDS	8.5 (5.1)	4.1 (3.9)	4.5 (0.6)***
SF-12 mental	50.0 (7.1)	55.1 (6.5)	−5.1 (0.9)***
SF-12 physical	48.4 (9.9)	47.2 (10.3)	1.2 (0.4)

High = at or below median. Low = below median

†Endorsed greater cognitive difficulties than most individuals who were known to have normal cognition (CDS; cut point ≥72 score).

‡Endorsed greater distress from cognitive difficulties than most individuals who were known to have normal cognition (GDI; cut point ≥18 score).

§Single "yes" or "no" item from GDS.

BAI indicates Beck Anxiety Inventory; CDS, Cognitive Difficulties Scale; GDI, Global Distress Index; GDS, Geriatric Depression Scale; MCS, Mental Composite Scale; SF-12, Short Form Health Survey.

* < 0.05.

** < 0.01.

*** < 0.001.

On an average, older adults who believed they had more memory problems than most others reported mild depression (GDS = 8.5), which was substantively higher than that endorsed by those who did not believe this about themselves (GDS = 4.1). About 22% (n = 27 of 122) of those who believed they had more memory problems than most endorsed severe depression (GDS ≥ 10). Mental well-being (SF-12 MCS) and physical well-being (SF-12 PCS) appeared clinically similar between those who endorsed high versus low symptoms.

MCI and AD Dementia Diagnoses Effects on Relationships Between Self-report Symptoms and QOL

Among older adults reporting high cognitive difficulties, those with MCI reported more difficulties in daily life [Dementia Quality of Life Scale (DEM-QOL)], greater depression (GDS), greater subjective stress (PSS), and greater impairment in instrumental functioning (IADLs) than those who were cognitively normal (all $P < 0.05$; Fig. 1). Those with a diagnosis of AD DEM reported more difficulties in daily life (DEM-QOL) and greater subjective stress than those with this symptom but cognitively normal (PSS; both $P < 0.05$). No other statistically discernible interactions were observed based on cognitive difficulties or distress from cognitive symptoms (all $P > 0.05$).

Associations Among Self-reported Cognitive Complaints and QOL Domains Statistically Adjusting for Relationships Among QOL Domains

In multivariate analysis of cognitive difficulties, the model was not significant for explaining health-related QOL (EQ-5D; Table 4). MCI diagnosis was associated with lower satisfaction in daily life (QOL-AD), greater difficulty in daily life (DEM-QOL), greater depression (GDS), more subjective stress (PSS), and lower mental well-being (SF-12 MCS; $P < 0.05$). AD DEM was associated with lower satisfaction in daily life (QOL-AD), greater difficulties in daily life (DEM-QOL), and greater impairments in IADLs (all $P < 0.05$).

In multivariate analysis of cognitive distress, the model was not significant for explaining health-related QOL (EQ-

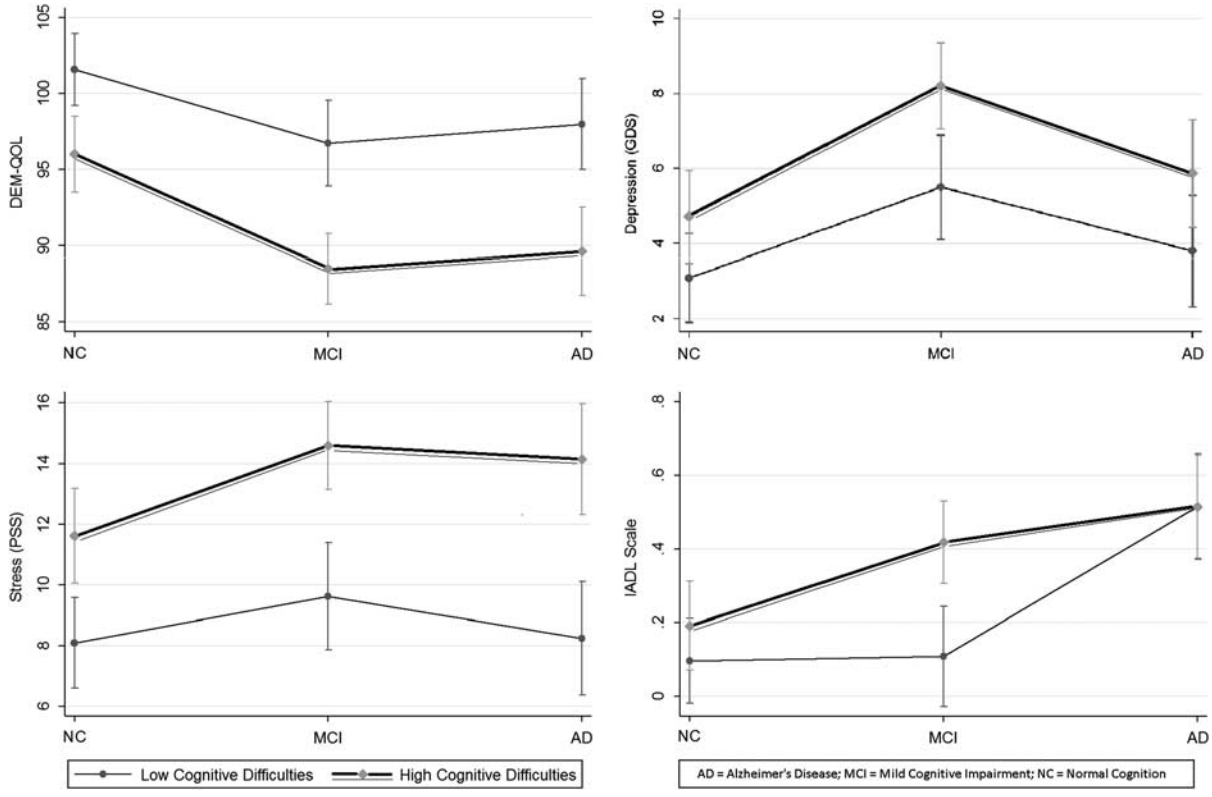

FIGURE 1. Comparisons of QOL domains by older adults reporting high versus low cognitive difficulties. All models statistical control for memory impairment (Cognitive Composite Score). Error bars denote 95% confidence intervals. Intervals that do not overlap represent statistically significant between-group differences ($P < 0.05$). AD indicates Alzheimer disease; GDS, Geriatric Depression Scale; IADL, instrumental activities of daily living; MCI, mild cognitive impairment; NC, normal cognition; PSS, Perceived Stress Scale; QOL, quality of life.

5D) or ratings of global health (EQ-VAS). MCI diagnosis was associated with lower satisfaction in daily life (QOL-AD), greater difficulty in daily life (DEM-QOL), greater depression (GDS), more subjective stress (PSS), and lower mental well-being (SF-12 MCS; $P < 0.05$). AD DEM was associated with lower satisfaction in daily life (QOL-AD), more difficulties in daily life (DEM-QOL), and greater impairment in IADLs (all $P < 0.05$).

In multivariate analysis of one's belief about the severity of memory problems, MCI diagnosis was associated with greater difficulty in daily life (DEM-QOL) and greater depression (GDS; both $P < 0.05$). AD DEM was not independently associated with domains of QOL (all $P > 0.05$).

DISCUSSION

This study investigated relationships between cognitive complaints and QOL in 259 older adults with varying degrees of cognitive decline. On the basis of previous studies in samples with AD and MCI,[7,23–31,33–35,43] we anticipated strong negative relationships between cognitive complaints and QOL. We found all 3 cognitive complaints were related to relatively lower quality of daily life (QOL-AD, DEM-QOL) and worse psychological outcomes—depression (GDS), anxiety (BAI), stress (PSS), and mental well-being (SF-12 MCS).

Studies comparing QOL in patients with MCI and mild stage AD DEM have found those with MCI report more difficulties in daily life (DEM-QOL), more mood disturbances, worse general health, and lower vitality.[7,35] In a previous study that compared patients with MCI to both those with NC and AD DEM, those with MCI reported more stress, more difficulties, and lower satisfaction with daily life than those with NC and worse mental well-being and greater depression than those with AD.[40] Thus, we expected a diagnosis of MCI would strengthen inverse relationships between cognitive complaints and QOL. We found support for this hypothesis for depression (GDS), subjective stress (PSS), difficulties in daily life (DEM-QOL), and problems in instrumental functioning (IADLs). We also found that a diagnosis of AD DEM strengthened the relationship between cognitive complaints and both difficulties in daily life (DEM-QOL) and worse mental well-being (SF-12 MCS).

Our results suggest that relationships between cognitive complaints and impairments in QOL are amplified for those diagnosed with MCI and AD and that how these relationships shift differs by diagnosis. These findings were independent of performance-based cognitive impairment. The underlying reasons for these findings warrant study. Understanding whether these relationships might correspond to underlying neuropathology or whether they may reflect psychosocial reactions or a combination of the 2 may be helpful for understanding how early diagnosis may affect individuals.

The conceptual framework for assessing QOL is often multidimensional—cognitive, physical, social, and mental.[22] Fairly consistent documentation of concurrent impairment

TABLE 4. Multivariate Analyses of Mean Differences in Domains of QOL Based on Self-reported Cognitive Complaints, Diagnosis, and Cognitive Impairment (n = 259)

Outcomes	R^2	F	Cognitive Difficulties†	MCI‡	AD‡	MMSE
EQ-5D	0.04	2.33	−0.05**	−0.02	−0.01	−0.004
QOL-AD	0.07	5.02***	−2.24***	−1.87*	−2.16*	−0.12
DEM-QOL	0.24	19.57***	−7.26***	−6.42***	−5.42**	−0.09
GDS§	0.14	10.61***	2.17***	3.16***	1.54	0.13
BAI	0.13	9.54***	3.89***	1.15	1.10	0.02
PSS	0.19	14.87***	4.66***	2.31**	1.46	0.03
SF-12 MCS	0.10	7.02***	−2.43**	−3.48***	−1.18	0.20
IADL Scale‖	0.15	11.34***	0.14**	0.07	0.21*	10.03**
SF-12 PCS	0.05	3.34**	−3.37**	1.28	2.34	−0.30
			Cognitive Symptom Distress¶	MCI‡	AD‡	MMSE
EQ-5D	0.02	1.36	−0.03	−0.02	−0.01	−0.003
EQ-VAS	0.02	1.20	3.80	−0.29	1.48	−0.10
QOL-AD	0.11	7.93***	−3.10***	−1.62*	−2.20*	−0.10
DEM-QOL	0.26	22.65***	−8.08***	−5.89***	−5.51**	−0.03
GDS§	0.14	11.07***	2.31***	3.01***	1.56	0.11
BAI	0.09	6.61***	3.26***	1.04	1.12	−0.02
PSS	0.21	16.87***	5.04***	2.00*	1.51	0.02
SF-12 MCS	0.12	8.39***	−3.09***	−3.24**	−1.22	0.22
IADL Scale‖	0.15	11.06***	0.13*	0.06	0.21*	−0.04**
SF-12 PCS	0.04	2.50*	−2.55*	1.34	2.32	−0.27
			More Memory Problems Than Most#	MCI‡	AD‡	MMSE
QOL-AD	0.07	4.73***	−2.61***	−1.02	−1.13	−0.05
DEM-QOL	0.17	13.14***	−6.34***	4.54**	3.05	0.07
GDS§	0.21	17.04***	3.98***	1.73*	0.06	0.05
BAI	0.05	3.29**	2.53**	0.51	0.21	0.06
PSS	0.09	6.54***	3.34***	1.40	0.05	−0.07
SF-12 MCS	0.14	9.89***	−4.35***	−1.92	0.49	0.29

†Endorsed greater cognitive difficulties than most individuals who were known to have normal cognition (CDS; cut point ≥72 score).
‡Reference is cognitively normal group.
§Log link back transformed.
‖Entered as binary variable. The cut point separated one third of the sample into the high group.
¶Endorsed greater distress from cognitive difficulties than most individuals who were known to have normal cognition (GDI; cut point ≥18 score).
#Single "yes" or "no" item from GDS.
AD indicates Alzheimer disease; BAI, Beck Anxiety Inventory; CDS, Cognitive Difficulties Scale; DEM-QOL, Dementia Quality of Life Scale; EQ, EuroQOL; GDI, Global Distress Index; GDS, Geriatric Depression Scale; IADL, instrumental activities of daily living; MCI, mild cognitive impairment; MCS, Mental Composite Scale; MMSE, Mini Mental Status Examination; PCS, Physical Composite Scale; PSS, Perceived Stress Scale; QOL, quality of life; SF-12, Short Form Health Survey; VAS, Visual Analog Scale.
* < 0.05.
** ≤ 0.01.
*** ≤ 0.001.

in domains, like depression and quality of daily life (eg, DEM-QOL, QOL-AD)[23,27,28,30,35] have raised the question of whether all domains are useful.[7] We found QOL domains to be independent of one another. In fact, the magitude of some relationships, such as that between cognitive difficulties and depression, appeared stronger in the multivariate analysis that adjusted for relationships shared among domains.

Together, results from the multivariable and multivariate analyses show that associations between cognitive complaints and QOL can vary based on both the specific symptom and QOL domain. Broadly, our findings show older adults with cognitive complaints tended to report lower QOL than their respective counterparts with NC, MCI, or AD DEM. This underscores the import of addressing subjective symptoms during routine clinical practice. Specific findings suggest that cognitive complaints may have clinical value in helping guide providers' assessments. That is, our findings suggest that older patients who report cognitive complaints may also be experiencing problems in other areas of functioning, such as anxiety, depression, and activities in daily life. The degree of impairment, particularly in anxiety and depression, suggests patients reporting significant cognitive complaints may benefit from screening for mood disorders and, as appropriate, psychological treatment. Given our results show patients with MCI or AD who endorsed fewer cognitive symptoms reported, on an average, statistically similar levels of situational stress and anxiety as older adults with NC, they raise the question of whether clinical interventions that improve symptom management may help restore or preserve QOL. In addition, AD prevention trials may benefit from including self-report measures of functioning in daily life (DEM-QOL) and subjective stress (PSS) in addition to the already commonly built-in metrics for depression (GDS), mental well-being (SF-12 MCS), and IADLs. This may help appraise the breadth of effects of an experimental treatment, help measure disease progression, and help characterize effects in sample subgroups.

Previous studies examining relationships between DEM symptoms and QOL have focused largely on neuropsychiatric symptoms.[7,23–27,30] However, self-report

symptom data are gaining importance as advances in AD diagnosis are leading to identifying persons ever earlier in the disease process.[3–5] Our findings show these symptoms that emerge earlier in the disease course may be helpful in identifying treatable problems. Moreover, they suggest that addressing self-report symptoms may aid in mitigating substantive differences in QOL that are observed among individuals with MCI, AD, and NC. Further study of these symptom-related patient-reported outcomes is needed.

We analyzed 3 self-report symptoms as binary variables. To do this, we dichotomized scores on the CDS and GDI. We defined the cut between high and low categories using the respective median value for each that was obtained from our group of older adults who were known to be cognitively normal. For cognitive difficulties, scores of 72 and above on the CDS represented high levels of cognitive difficulties. In the low group, scores ranged from 41 to 71 in our sample. In the general public, the average CDS score is 32 (SD, 15).[12] This suggests that cognitive difficulties in our sample, high or low, was well above what most members of the general public report. The third symptom, believing one had more memory problems than most others, was a single binary item adopted from the GDS. Because of its relationship to the GDS, associations between this item and the full GDS scale should be cautiously interpreted.

We carefully constructed the statistical models to limit the risk of overfitting, and all models passed a test of goodness-of-fit. We found several factors differed between older adults who did and did not believe they experienced more memory problems than most others. These were executive function (GPG unique designs), crystalized intelligence (WAIS IS), memory (CCS), and global cognition (MMSE). Because of the multicollinearity among these factors, model variance was inflated when we added them together. In these models, all effects were larger than those we report. Because of this, our results may underestimate actual effects. In addition, it was not possible to statistically control for all potential confounders, including that our study was conducted at a single site. The results may not generalize to populations with other characteristics. Nonetheless our findings offer information that may be helpful to the design of future studies that can test the generalizability and causality of the relationships that we report.

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