Decisional Capacity for Research Participation in Individuals with Mild Cognitive Impairment

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OBJECTIVES: To assess decisional capacity performance and the neuropsychological correlates of such performance to better understand higher-level instrumental activities of daily living in individuals with mild cognitive impairment (MCI).

DESIGN: Cross-sectional.

SETTING: Research center, medical center, or patient's home.

PARTICIPANTS: Forty participants with MCI and 40 cognitively normal older controls (NCs) aged 60 to 90 (mean age ± standard deviation 73.3 ± 6.6; 54% female).

MEASUREMENTS: Capacity to provide informed consent for a hypothetical, but ecologically valid, clinical trial was assessed using the MacArthur Competence Assessment Tool for Clinical Research. Neuropsychological functioning was assessed using a comprehensive protocol.

RESULTS: Adjusted between-group comparisons yielded significant differences for most decisional capacity indices examined, including Understanding ($P = .001$; NC > MCI) and Reasoning ($P = .002$; NC > MCI). Post hoc analyses revealed that participants with MCI who were categorized as capable of providing informed consent according to expert raters had higher levels of education than those who were categorized as incapable.

CONCLUSION: The findings suggest that many individuals with MCI perform differently on a measure of decisional capacity than their NC peers and that participants with MCI who are incapable of providing informed consent on a hypothetical and complex clinical trial are less edu-cated. These findings are consistent with prior studies documenting functional and financial skill difficulties in individuals with MCI. **J Am Geriatr Soc 2008.**

Key words: mild cognitive impairment; memory; executive function; cognition; decision analysis; informed consent

Decisional capacity describes a person's abilities to understand, appreciate, reason, and make a choice.[1] It informs the judgment of whether an individual is competent to make a decision.[2] Prior research has shown that even patients with mild Alzheimer's disease (AD) have a diminished capacity to make decisions.[2,3] However, little is known about decisional capacity in individuals with mild cognitive impairment (MCI), a condition that is widely regarded as a precursor to AD.[4]

According to recent research diagnostic criteria, individuals with MCI lack traditionally defined functional dependence.[5] Nevertheless, some persons with MCI exhibit more difficulty performing instrumental activities of daily living[6] and higher-level functional skills, such as financial decision-making,[7] than cognitively normal older controls (NCs). These data suggest that persons with MCI may have clinically significant impairments in their decision-making capacity.

There are at least two reasons why it is important to better understand the ability of individuals with MCI to make complex decisions, particularly their ability to make decisions concerning research participation. First, the clinical significance of cognitive impairments observed in persons with MCI needs to be better understood. Specifically, it is important to determine whether individuals with MCI differ from cognitively normal elderly people on decisional capacity and the cognitive correlates of such decision-making. Prior work focused on persons with AD has suggested that decisional capacity and judgments of competency are associated with measures of language,[8,9] executive func-

tioning,[8–10] and memory,[10] but limited research is available linking cognitive functioning to decisional capacity in participants with MCI. Recent work focusing on financial capacity suggests that attention and executive functioning are most relevant,[7] despite the common amnestic features of the MCI diagnosis. Increasing understanding of the cognitive correlates of capacity will aid in the design of interventions that address those cognitive deficits and, in turn, improve or maintain capacity.

Second, the more that is known about the clinical significance of cognitive impairments in individuals with MCI, the more informed ethical and policy issues in this area can be. Individuals with MCI are increasingly recruited for clinical trials to evaluate interventions that might slow progression of cognitive impairment. These clinical trials often involve a commitment of time[11] or procedures that some regulatory boards may judge to pose more than minimal risk.[12] Understanding the nature and extent of decisional capacity impairments in people with MCI for enrolling in such research will guide researchers and policymakers to determine whether persons with MCI, like persons with AD, are a vulnerable population in need of additional subject protections.

The MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR), a well-known measure of decisional capacity, was used to assess whether persons with MCI would perform worse than NCs on understanding, appreciation, and reasoning elements of capacity for research participation. It was hypothesized that of the people with MCI, measures assessing elements of executive functioning would be most strongly associated with decisional capacity performance.[7–10] Furthermore, it was hypothesized that people with MCI who were incapable of providing informed consent would have worse neuropsychological performances than people with MCI who were capable, particularly on measures of executive functioning.[7–10]

METHODS

Participants

Participants for this study were prospectively recruited from the Boston University Alzheimer's Disease Core Center research registry, which is funded by the National Institute on Aging (NIA). As part of this research registry, participants are followed longitudinally with annual visits, including an in-depth clinical interview with the participant and a reliable informant, neurological and physical examinations, and a comprehensive neuropsychological assessment. Based on this information, cognitive diagnoses for participants are reached through a multidisciplinary consensus conference that includes neurologists, neuropsychologists, and a nurse practitioner. Diagnoses are based on widely accepted criteria[5,13,14] and are consistent with procedures put forth by the National Alzheimer's Coordinating Center for all NIA-funded Alzheimer's Disease Centers.[15] Specifically, MCI diagnoses are based on relative preservation of functional abilities, subjective report of cognitive change, and objective cognitive impairment, defined as performance ≥1.5 standard deviations below normative data.[5,13] NCs are free of any reported functional difficulties or subjective or objective cognitive impairment.

Participants enrolled in this prospective, cross-sectional study were aged 60 to 90, community dwelling, and English speakers. Exclusion criteria included a history of major psychiatric illness (e.g., schizophrenia, bipolar disorder), neurological illness (e.g., stroke, epilepsy, dementia), or head injury with significant loss of consciousness. Participants included 40 individuals diagnosed with MCI[5,13] and 40 NCs. (See Table 1 for sample characteristics.) Participants with MCI met one of four diagnostic subtypes based on the cognitive profile of their most recent registry visit, including amnestic single domain (n = 18), amnestic multiple domain (n = 14), nonamnestic single domain (n = 3), and nonamnestic multiple domain (n = 5).[5] However, participants with MCI were analyzed as a single group for the present study.

Procedures

After approval by the appropriate local institutional review boards, study visits were conducted at the Boston University Medical Center General Clinical Research Center, the Edith Nourse Rogers Memorial Veterans Affairs Medical Center, or participants' homes. Participants and their study partners (e.g., spouse or adult child) provided written informed consent before beginning the testing procedures. The entire protocol was administered in a single session that generally lasted 3 to 4 hours. Participants completed neuropsychological testing and then a decisional capacity evaluation.

Decisional Capacity Assessment

The MacCAT-CR evaluates decision-making capacity using a semistructured interview customizable for any research protocol[1] and contains 21 items assessing four abilities that constitute decisional capacity: Understanding (13 items), Appreciation (3 items), Reasoning (4 items), and Expression of a Choice (1 item).[16] Each item is scored 0 to 2, and higher scores indicate better performance.

For the present study, the MacCAT-CR was customized for a hypothetical, but ecologically relevant, Food and Drug Administration Phase III clinical trial of a hypothetical

Table 1. Sample Characteristics of Cognitively Normal Older Controls (NCs) and Participants with Mild Cognitive Impairment (MCI)

Characteristic	NC n = 40	MCI n = 40
Age, mean ± SD (range)	72.3 ± 5.5 (60–82)	74.3 ± 7.5 (60–90)
Education, years, mean ± SD (range)	16.5 ± 2.5 (12–21)	15.8 ± 2.9 (12–21)
Wide Range Achievement Test-3 Reading, mean ± SD (range)*	54.6 ± 1.9 (50–57)	50.1 ± 5.6 (34–57)
Mini-Mental State Examination, mean ± SD (range)*	29.3 ± 0.9 (27–30)	27.8 ± 1.8 (22–30)
Female, %	60	48
White, %	83	78

* Significant between-group difference, $P < .001$.
SD = standard deviation.

drug, M-360, whose purpose was to treat or prevent memory decline in NCs and people with MCI. The research protocol consisted of a randomized, double-blind, placebo-controlled study that involved multiple study visits, brain magnetic resonance imaging, lumbar puncture, neuropsychological assessment, blood draw, and electrocardiogram. The nine-page consent statement contained approximately 4,000 words and was structured according to the principal investigator's (ALJ) institutional template for clinical trial research, including appropriate language and format.

The research coordinator (SL), blinded to diagnostic category, served as the interviewer for all 80 decisional capacity interviews. The research coordinator was formally trained on the administration of the MacCAT-CR, following procedures previously outlined.[17] Administration of the MacCAT-CR deviated slightly from the manual to enhance the ecological validity of the consent process by allowing participants to retain a copy of the consent disclosure while answering all items. Participants were told that the M-360 study was hypothetical, and they were asked to imagine that they were being invited to enroll in the study. If at any time during the interview, a participant forgot that the study was hypothetical, the interviewer reminded him or her of its hypothetical nature. Before the interview, the participant read the consent statement in its entirety. Next, the research coordinator read aloud four disclosures from the consent statement, one at a time, including (1) purpose and overview; (2) potential benefits; (3) risks and discomforts; and (4) alternatives, subjects' rights, and rights to refuse or withdraw. After reading aloud each disclosure, the research coordinator posed the general query, "In your own words, tell me your understanding of what I just said." If the participant did not state the target answers, the research coordinator followed up with specific queries (e.g., "What is the goal of the research study that I described to you?"). Participants were allowed to consult their consent form copy as needed, although for full credit, participants were required to paraphrase information rather than to read the information verbatim from the form provided.

Interviews were digitally recorded. Research assistants who did not conduct or score the decisional capacity interview and who were blinded to all clinical information transcribed these recordings. The principal investigator and the research coordinator scored the interviews blinded to participant diagnoses, and scoring discrepancies were resolved in a conference on a case-by-case basis. Interrater reliability for the MacCAT-CR dimensions ranges from 0.65 to 0.96.[17]

Competency Determinations

To better understand the clinical significance of the MCI participant scores on the MacCAT-CR, a criterion standard of competent versus not competent was used, based on the agreement of two expert raters' competency judgments.[3,17] Two clinical neuropsychologists with experience in competency assessment were asked to independently review the decisional capacity interview transcripts (n = 40) and answer the question, "Based on the content of the transcript, does this person have sufficient capacity to provide informed consent to participate in the hypothetical drug trial?" The raters selected from one of the following

categories: definitely capable, probably capable, probably incapable, and definitely incapable. These responses were collapsed into "capable" (definitely capable and probably capable) and "incapable" (probably incapable and definitely incapable) categories. Experts were blinded to the participants' demographics and clinical information, including performance on neuropsychological tests and diagnoses. Discrepancies between raters (n = 6) were resolved in a telephone conference.

Neuropsychological Evaluation

Participants completed a neuropsychological protocol of sufficient length to tap multiple cognitive components but brief enough to increase participant compliance. Measures included have strong reliability and validity and are sensitive to cognitive functions mediated by frontal-subcortical and cortical systems, which have previously been related to decisional capacity performance.[8–10] Tests were carefully selected so that a range of performance (premorbid intelligence, global cognition, learning and memory, language, and executive functioning/information processing) may be documented, precluding floor or ceiling effects. See Table 2 for a description of measures.

Data Analyses

Before hypothesis testing, between-group comparisons were conducted for demographic variables (age, education, sex, race) and global cognitive functioning (Mini-Mental State Examination (MMSE)). Between-group comparisons (NC vs MCI) were conducted using analysis of variance (ANOVA) for all neuropsychological measures. To test the hypothesis that individuals with MCI differ from NCs, ANOVAs were conducted for three of the MacCAT-CR dimensions (Understanding, Appreciation, and Reasoning) and the total score. Between-group comparisons for each item were conducted using post hoc Mann-Whitney tests. Effect sizes were calculated according to Cohen's d formula and interpreted according to published guidelines.[18] MacCAT-CR performance impairment cutoffs were established based on the NCs' mean scores. Specifically, impairment for each decisional capacity dimension was defined as performance ≥ 1.5 standard deviations below the NCs' mean performance. To better understand the cognitive correlates of decisional capacity performance in the MCI groups, Pearson correlations were conducted between three of the MacCAT-CR dimensions (Understanding, Appreciation, and Reasoning) and the neuropsychological protocol (described in Table 2). No analyses were conducted for the fourth MacCAT-CR dimension (Expression of Choice) because of restriction of range.[2]

Between-group comparisons of the competency determinations for the "capable" and "incapable" participants with MCI were made using ANOVAs for demographic (age, education) and neuropsychological test variables (MMSE, Wide Range Achievement Test-3 (WRAT-3) Reading, Boston Naming Test, Token Test, Controlled Oral Word Association, Similarities, Matrix Reasoning, Delis Kaplan Executive Function System Trail Making Test-A (TMT-A, Number Sequencing) and Trail Making Test-B (TMT-B, Number-Letter Sequencing), Judgment, and California Verbal Learning Test-II (CVLT-II) Trials 1–5 and Long-

Table 2. Neuropsychological Performances of Cognitively Normal Older Controls (NCs) and Participants with Mild Cognitive Impairment (MCI)

Domain	Variable (Range)	Test Description	NC n = 40	MCI n = 40	P-Value*	d
			Mean ± Standard Deviation (Range)			
Language	Boston Naming Test[27] (0–60)	Assesses confrontation naming and lexical retrieval abilities	58.2 ± 1.8 (53–60)	52.9 ± 6.7 (32–60)	<.001	1.1
	Token Test[28] (0–44)	Measures verbal comprehension of single and multiple step commands	43.5 ± 1.1 (39–44)	41.0 ± 3.4 (30–44)	<.001	1.0
Executive Functioning and Information Processing	Controlled Oral Word Association[29,30]	Assesses rapid word generation	50.9 ± 10.8 (28–71)	36.3 ± 10.9 (10–57)	<.001	1.4
	Similarities[31] (0–33)	Measures verbal abstract reasoning	28.2 ± 3.0 (19–33)	22.9 ± 6.1 (0–30)	<.001	1.1
	Matrix Reasoning[31] (0–26)	Assesses nonverbal abstract reasoning	17.1 ± 4.2 (8–24)	11.7 ± 5.2 (4–23)	<.001	1.2
	DKEFS Trail Making Test Part A[32]	Measures visual-scanning and attention abilities; higher scores indicate worse performance	41.4 ± 13.8 (21–86)	51.8 ± 31.8 (24–208)	.06	0.4
	DKEFS Trail Making Test Part B[32]	Assesses sequencing and mental flexibility; higher scores indicate worse performance	83.8 ± 26.9 (39–153)	164.2 ± 91.4 (75–551)	<.001	1.2
	Judgment[33] (0–20)	Measures judgment pertaining to home safety, health, and medication issues	17.6 ± 1.6 (14–20)	17.1 ± 2.0 (12–20)	.27	0.3
Learning and Memory	CVLT-II Trials 1–5[34] (0–80)	Assesses verbal learning abilities	52.4 ± 9.7 (32–71)	33.7 ± 10.9 (16–67)	<.001	1.8
	CVLT-II Long-Delay Free Recall[34] (0–16)	Measures verbal retrieval abilities	11.9 ± 2.8 (6–16)	5.8 ± 3.3 (0–14)	<.001	2.0

* Significance based on analysis of variance.
DKEFS = Delis Kaplan Execution Function Scale; CVLT-II = California Verbal Learning Test-II; d = effect size based on Cohen's d.

Delay Free Recall). Because of the multiple comparisons, significance for all analyses was set a priori at $P < .01$.

RESULTS

Sample Characteristics
Table 1 summarizes the sample characteristics. There were no between-group differences for participants with MCI and NCs in terms of age ($F_{(1,79)} = 1.8$, $P = .18$), education level ($F_{(1,79)} = 1.2$, $P = .27$), sex (chi-square (χ^2)$_{(1)} = 1.3$, $P = .26$), or race ($x^2_{(1)} = 2.1$, $P = .56$). As expected, the NC group performed significantly better than the MCI group on the MMSE ($F_{(1,79)} = 20.3$, $P < .001$), a pattern of differential performance that was similarly observed for most other neuropsychological measures included in the protocol (Table 2). However, participants with MCI had lower WRAT-3 Reading scores than NCs ($F_{(1,79)} = 23.0$, $P < .001$), so this variable was used as a covariate in subsequent secondary analyses comparing the MCI and NC groups.

Decisional Capacity Comparison for MCI and NC Groups
ANOVAs revealed significant differences for the MacCAT-CR dimensions of Understanding ($F_{(1,79)} = 26.0$, $P < .001$), Appreciation ($F_{(1,79)} = 7.4$, $P = .008$), and Reasoning ($F_{(1,79)} = 6.3$, $P = .01$), as well as total score ($F_{(1,79)} = 21.9$, $P < .001$). In all cases, the NC group had better scores than the MCI group. Post hoc analyses of covariance, adjusting

for WRAT-3 Reading, showed that between-group differences remained for Understanding ($F_{(1,79)} = 8.4$, $P = .005$), Reasoning ($F_{(1,79)} = 9.8$, $P = .002$), and total score ($F_{(1,79)} = 12.2$, $P = .001$). However, between-group differences for Appreciation did not reach the a priori significance level ($F_{(1,79)} = 5.5$, $P = .02$), suggesting that inclusion of the WRAT-3 Reading measure as a covariate attenuated Appreciation differences. Post hoc comparisons yielded several between-group differences for individual MacCAT-CR items, particularly for those items that constitute the Understanding dimension. See Table 3 for means, standard deviations, and effect sizes for all MacCAT-CR dimensions and items, including Expression of Choice.

To illustrate between-group differences in MacCAT-CR performances, Table 4 juxtaposes the range of each group's decisional capacity scores according to dimension. An impairment cutoff was calculated for each dimension (i.e., ≥1.5 standard deviations below the NC group's mean performance and rounded up to the closest whole number). Impairment was defined as scores for Understanding of 21.6 or less, for Appreciation of 4.7 or less, and for Reasoning of 4.6 or less. In Table 4, the dotted line separating impaired from intact scores for each dimension denotes cutoff score values.

Neuropsychological and Decisional Capacity Correlations for Participants with MCI
For participants with MCI, multiple significant associations emerged between the neuropsychological measures and the

Table 3. Decisional Capacity Performances for Cognitively Normal Older Controls (NCs) and Participants with Mild Cognitive Impairment (MCI)

Decisional Capacity Ability (Range)	Description	Variable	NC n = 40 Mean ± Standard Deviation	MCI n = 40 Mean ± Standard Deviation	P-Value
Understanding (0–26)	Assesses understanding of the nature of the study and procedures, such as the study's purpose, methodology (e.g., double-blind, placebo-controlled), and risks and benefits	**Understanding total**	24.2 ± 1.7	21.3 ± 3.2	.001*
		1. Nature of research project	7.8 ± 0.6	6.6 ± 1.5	<.001[†]
		2. Understanding study purpose	1.7 ± 0.5	1.5 ± 0.6	.14[†]
		3. Effects on individualized care	5.7 ± 0.5	5.1 ± 1.1	.004[†]
		4. Risks and benefits of participating	7.0 ± 1.1	6.2 ± 1.4	.003[†]
Appreciation (0–6)	Measures recognition of the effects that participating (or not participating) will have on the participant's care and well-being	**Appreciation total**	5.6 ± 0.6	5.0 ± 1.2	.02*
		1. No personal medical benefit	1.7 ± 0.6	1.4 ± 0.7	.07[†]
		2. Possibility of reduced benefit	2.0 ± 0.0	1.8 ± 0.5	.04[†]
		3. Withdrawal possible	1.9 ± 0.3	1.7 ± 0.5	.08[†]
Reasoning (0–8)	Assesses the participant's comparative analysis regarding the study's benefits and risks	**Reasoning total**	6.4 ± 1.2	5.7 ± 1.3	.002*
		1. Consequential reasoning	1.8 ± 0.4	1.7 ± 0.5	.08[†]
		2. Comparative reasoning	1.2 ± 0.7	0.9 ± 0.6	.05[†]
		3. Generating consequences	1.5 ± 0.7	1.3 ± 0.7	.22[†]
		4. Logical consistency of choice	2.0 ± 0.2	1.9 ± 0.3	.65[†]
Expression of choice (0–2)	Participant's ability to express their decision	**Expression of Choice total**	2.0 ± 0.2	1.9 ± 0.3	NA[‡]
Total score			38.1 ± 2.7	33.8 ± 5.1	.008*

* Between-group comparisons for all MacArthur Competence Assessment Tool for Clinical Research dimensions reflect analysis of covariance results, adjusting for Wide Range Achievement Test-3 Reading.

[†] Between-group item analyses are based on unadjusted Mann-Whitney comparisons.

[‡] No statistical analyses were conducted on the "Expression of Choice" dimension because of restriction of range.

decisional abilities (Table 5). Global cognition, as assessed by the MMSE, was significantly associated with all abilities, including Understanding (correlation coefficient (r) = 0.42, $P = .008$), Appreciation ($r = 0.46$, $P = .003$), and Reasoning ($r = 0.44$, $P = .004$). For MacCAT-CR Understanding, more-specific associations were observed with tests of executive functioning, including Similarities ($r = 0.59$, $P < .001$), Matrix Reasoning ($r = 0.47$, $P = .002$), TMT-B ($r = -0.52$, $P = .001$), Judgment ($r = 0.41$, $P = .009$), and TMT-A ($r = -0.63$, $P < .001$). Similarly, the MacCAT-CR Appreciation measure was significantly related to tests of executive functioning, including Similarities ($r = 0.49$, $P = .001$), Judgment ($r = 0.42$, $P = .007$), and TMT-A ($r = -0.68$, $P < .001$). Finally, the MacCAT-CR Reasoning dimension was related to the fewest neuropsychological tests, including a measure of information processing (TMT-A; $r = -0.52$, $P < .007$) and memory (CVLT-II Trials 1–5; $r = 0.41$, $P = .009$).

Experienced Clinician Ratings of Competency

The experienced clinicians' ratings resulted in 16 participants with MCI (40%) being labeled as "incapable" and 24 participants with MCI labeled as "capable" (60%). ANOVAs comparing "incapable" and "capable" participants with MCI yielded few significant between-group differences. Between-group differences were observed for education level ($F_{(1,39)} = 12.6$, $P = .001$), such that the "capable" participants with MCI had more years of formal education ($17.0 ± 2.6$) than their "incapable" peers ($14.0 ± 2.5$). Two neuropsychological test performance differences also emerged for which the "capable" participants with MCI performed significantly better than their "incapable" peers on Similarities ($F_{(1,39)} = 11.1$, $P = .002$; "capable" = $25.3 ± 3.9$; "incapable" = $19.4 ± 7.1$) and Matrix Reasoning ($F_{(1,39)} = 10.4$, $P = .003$; "capable" = $13.7 ± 5.0$; "incapable" = $8.8 ± 4.0$). Additional differences, which did not reach the a priori significance level, were observed for age ($F_{(1,39)} = 4.2$, $P = .05$; "capable" = $72.4 ± 7.9$; "incapable" = $77.1 ± 5.9$), MMSE ($F_{(1,39)} = 5.2$, $P = .03$; "capable" = $28.3 ± 1.1$; "incapable" = $27.1 ± 2.4$), WRAT-3 Reading ($F_{(1,39)} = 4.6$, $P = .04$; "capable" = $51.6 ± 4.9$; "incapable" = $47.9 ± 5.9$), TMT-A ($F_{(1,39)} = 5.3$, $P = .03$; "capable" = $42.8 ± 14.2$; "incapable" = $65.3 ± 44.7$), and Judgment ($F_{(1,39)} = 5.9$, $P = .02$; "capable" = $17.7 ± 1.7$; "incapable" = $16.3 ± 2.1$).

To better understand the influence of educational attainment on these neuropsychological differences, post hoc analyses of covariance were conducted, adjusting for education. Once education was considered in the model, the

Table 4. Breakdown of Decisional Capacity Performances for Cognitively Normal Older Controls (NCs) and Participants with Mild Cognitive Impairment (MCI)

Decisional Capacity Ability	NC n = 40	MCI n = 40
	n (%)	
Understanding		
26	10 (25.0)	3 (7.5)
24–25	17 (42.5)	9 (22.5)
22–23	10 (25.0)	7 (17.5)
20–21	2 (5.0)	11 (27.5)
18–19	1 (2.5)	5 (12.5)
12–17	0 (0.0)	5 (12.5)
Appreciation		
6	25 (62.5)	16 (40.0)
5	12 (30.0)	14 (35.0)
4	3 (7.5)	6 (15.0)
3	0 (0.0)	1 (2.5)
2	0 (0.0)	2 (5.0)
1	0 (0.0)	1 (2.5)
Reasoning		
8	8 (20.0)	1 (2.5)
7	12 (30.0)	11 (27.5)
6	10 (25.0)	13 (32.5)
5	7 (17.5)	7 (17.5)
4	3 (7.5)	5 (12.5)
3	0 (0.0)	3 (7.5)

Dotted lines reflect cutoff for ≥ 1.5 standard deviation below mean performance of NC participants.

Table 5. Neuropsychological Correlates of Decisional Capacity Performance of People with Mild Cognitive Impairment

Variable	Understanding	Appreciation	Reasoning
	Pearson Correlation Coefficient		
Mini-Mental State Examination	0.42[§]	0.46[§]	0.44[§]
Wide Range Achievement Test-3 Reading	0.36	0.29	0.37
Boston Naming Test	0.25	0.40	0.17
Token Test	0.38	0.38	0.23
Controlled Oral Word Association	0.47[§]	0.38	0.39
Similarities	0.59[‡]	0.49[‡]	0.34
Matrix Reasoning	0.47[§]	0.37	0.32
Delis Kaplan Executive Function System Trail Making Test			
Part A	−0.63[‡]	−0.68[‡]	−0.52[‡]
Part B	−0.52[‡]	−0.20	−0.31
Judgment	0.41[§]	0.42[§]	0.31
California Verbal Learning Test II			
Trials 1–5	0.38	0.21	0.41[§]
Long-Delay Free Recall	0.14	0.20	0.24

$P <$ [‡] .001; [§] .01.

previous differences for Similarities ($F_{(1,37)} = 1.9$, $P = .17$) and Matrix Reasoning were no longer significant ($F_{(1,37)} = 4.3$, $P = .04$). Similar findings emerged when education was considered among each of the differences reported above, which did not reach statistical significance, including MMSE ($F_{(1,37)} = 2.3$, $P = .14$), WRAT-3 Reading ($F_{(1,37)} = 0.08$, $P = .78$), TMT-A ($F_{(1,37)} = 2.5$, $P = .12$), and Judgment ($F_{(1,37)} = 5.1$, $P = .03$).

DISCUSSION

The primary findings of the current study are that differences exist between the research capacity of NCs and people with MCI, and a comparison of the effect sizes suggests that the most robust difference is for understanding the nature of the research study and its procedures. Individual item analyses revealed between-group differences for understanding the nature of the project (the study's objective and salient procedural elements), how the study differs from ordinary treatment, and the risks and benefits of the study. In addition, expert review of the capacity interviews suggests that these impairments may have clinical significance in a reasonable proportion of persons with MCI (40% in this study). Recall and memory difficulties in the participants with MCI did not appear to be related to this difference, which might, in part, reflect that participants retained a copy of the consent statement throughout the decisional capacity interview and were encouraged to refer back to the statement as needed. Furthermore, among the participants with MCI, no significant correlations were observed between the MacCAT-CR Understanding dimension and learning and memory performances. Therefore, the hallmark memory impairment noted in the majority of this diagnostic group (80%) cannot wholly account for the findings. Rather, executive functioning and information processing are stronger correlates of performance on Understanding, which previous competency research in aging,[19] AD,[8–10] and MCI[7] supports. For example, a previous study[7] reported that, despite the characteristic memory impairment observed in MCI, measures of attention, executive function, and information processing were the most robust correlates of financial capacity in individuals with MCI.

More modest but significant differences were observed for the ability of participants with MCI to appreciate the effects of research participation on their situation and reason through the process of deciding to participate or not participate. Both of these abilities appear to be related most strongly to elements of executive function. Past research examining decisional capacity for treatment in patients with AD has found that executive functioning is related to appreciating consequences of one's decision.[8] Similarly, recent work examining decisional capacity for a noninvasive research protocol found that executive functioning is related to appreciation and reasoning.[19] Collectively, these prior studies support the current findings and suggest that future studies investigating interventional strategies for improving decisional capacity in persons with MCI may want to target problems with executive functioning or information processing speed.

The experienced clinicians judged 40% of the participants with MCI to be "incapable" of providing consent, which differs from prior work, in which 60% of patients with AD were judged "incapable."[17] It is likely that the risk of the research protocol implemented and the range of cognitive impairment severity for each sample influence the difference in competency rates between these groups.[20]

There may be several reasons why nearly half of the participants with MCI in the current study were judged "incapable." First, the "incapable" participants with MCI had lower education levels than their "capable" peers, which may have contributed to fundamental differences in understanding the procedures, appreciating the risks and benefits, and reasoning through the options of participating versus not participating. The hypothetical clinical trial used in the current study was intentionally designed to represent a complex, but ecologically valid, randomized, clinical trial with several procedures, some of which may have been more difficult to understand for less-educated participants. Second, the MacCAT-CR administration procedures implemented in the present study did not use any corrective feedback, so the transcripts reviewed by the expert clinicians were limited to participant responses based on the structured interview. As has been previously demonstrated, corrective feedback could have improved participants' decisional capacity performances.[21] Finally, these competency determinations were based on two raters instead of three, the latter of which is more common in the research literature.[10,17]

Taken together, the MacCAT-CR between-group differences and expert ratings suggest that people with MCI have more impairments in higher-level instrumental activities of daily living than NCs. This finding is consistent with previous literature examining global functional[22,23] and financial abilities.[7] The data suggest that, despite the predominantly amnestic MCI sample under investigation, the higher-order functional impairment noted in the present study is not associated with memory difficulties but rather with executive dysfunction. In particular, measures of verbal and nonverbal reasoning, judgment, and information processing were most prominently related to decisional capacity performance. Furthermore, the decisional capacity performance differences observed suggest that even thoroughly screened participants with MCI have clinically relevant higher-order functional difficulties. Although functional integrity is traditionally a key differentiating feature distinguishing persons with MCI from patients with dementia, functional skills deteriorate insidiously over time in neurodegenerative diseases, similar to the subtle, progressive declines seen in cognitive functioning. Therefore, the present findings emphasize the field's need to reevaluate current functional assessment tools and reconsider how functional impairment is characterized. In light of the fact that participants with MCI with early functional changes decline more rapidly[24] and convert to dementia faster[25] than their functionally intact peers with MCI, improving procedures for identifying participants with MCI with early functional changes is particularly important.

Collectively, these findings are among the first to characterize the decisional capacity for research participation of individuals with MCI and extend the decisional capacity literature to include preclinical AD. The findings suggest that additional research is warranted to determine whether persons with MCI are a vulnerable subject population that may require protections similar to those for other cognitively impaired populations.[26] However, the study has some limitations. First, the relevance of interventional strategies, such as corrective feedback or repetition of information, to decisional capacity performance of participants with MCI was not examined. The performance of participants with MCI may have improved if interventional strategies were implemented throughout the hypothetical consenting process. Second, the study implemented a rigorous hypothetical clinical trial with complicated procedures and a lengthy consent statement (9 pages, which is common within the principal investigator's institution). The data, therefore, reflect a stringent assessment of capacity for research consent in this cohort because of the greater amount of information required for understanding the clinical trial. However, an attempt was made to minimize the memory demands of this information by allowing participants to retain a copy of the consent form during the interview. Third, several differences that fell between a conventional alpha level of .05 and the a priori significance level of .01 were observed, which may have been statistically significant if the sample size had been larger. Finally, the cross-sectional nature of the study design precludes conclusions regarding the longitudinal effect of decisional capacity impairments on cognitive progression or conversion to dementia in this MCI cohort. Future work in this area will provide rich information about the relation between decisional capacity limitations and conversion.

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