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Neuropsychological Correlates of Capacity Determinations in Alzheimer's Disease: Implications for Assessment

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Abstract

Objectives—To explore the neuropsychological correlates of the capacity to consent to research and to appoint a research proxy among persons with Alzheimer's disease.

Design, Setting, and Participants—Interview study of 77 persons with Alzheimer's disease recruited through an Alzheimer's disease research center and a memory disorder clinic.

Measurements—The capacity to consent to two research scenarios (a drug randomized clinical trial and a neurosurgical clinical trial) and the capacity to appoint a research proxy were determined by five experienced consultation psychiatrists who rendered categorical judgments based on videotaped interviews of the MacArthur Competence Assessment Tool-Clinical

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Research (MacCAT-CR) and the Capacity to Appoint a Proxy Assessment (CAPA). Mattis Dementia Rating Scale-2 (DRS-2) was used to assess neuropsychological functioning.

Results—The capacity to appoint a proxy and to consent to the drug randomized clinical trial, as determined by a majority or greater opinion of the 5-psychiatrist panel, were predicted by Conceptualization and Initiation/Perseveration subscales whereas the capacity to consent to a neurosurgical randomized clinical trial was predicted by the Memory subscale. Furthermore, the more lenient individual psychiatrists' judgments were predicted by the Conceptualization subscale whereas the stricter psychiatrists' judgments were predicted by the Memory subscale.

Conclusions—How experienced psychiatrists view Alzheimer's patients' capacity for consenting to research and for appointing a proxy may be related to the patients' conceptualization and memory functioning. More explicit and standardized guidance on the role of short term memory in capacity determinations may be useful.

Keywords

decision-making capacity; neuropsychology; Alzheimer's disease

Alzheimer's disease (AD) is an incurable and devastating illness. The number of persons with AD worldwide is expected to reach 81.1 million by 2040.(1) Thus, clinical research with persons suffering from AD is a public health priority, but such research raises the problem of involving persons with impaired decision-making capacity. In response, the study of decision-making capacity in persons with dementia has grown steadily,(2) including the impact of Alzheimer's disease on decisional capacity, (3–6) the neuropsychological correlates of decisional abilities, (7–12) and the nature of capacity judgments made by expert evaluators.(13–17)

We recently conducted a study examining two types of decision-making capacity constructs involving AD patients, regarding three different situations of decision-making—the capacity to appoint a proxy and the capacity to consent to two different randomized controlled trials of varying risk profiles and demand characteristics.(16, 18) (For convenience, we refer to three specific 'capacities' although they exemplify two different *types* of capacity.) In this paper, we explore the relationship between neuropsychological domains and these three different specific decision-making capacities as determined by categorical judgments of expert clinicians to provide clues for future research into two issues. First, examining the neuropsychological predictors of incapacity should increase our understanding of the phenomena of incapacity and this could, for example, provide clues to whether and how remediation might be targeted. Thus, using the majority decisions of a 5-person expert judge panel as a provisional "gold standard" for capacity, we examine the neuropsychological predictors of the three decision-making capacities. Second, because there is considerable variability among even experienced psychiatrists' categorical judgments of capacity, we explore whether the neuropsychological correlates of individual capacity evaluator's judgments may help explain the variability. Marson and colleagues have shown, for example, that different neuropsychological predictors are associated with various rates of incompetency judgments made by physicians.(7, 14) Such knowledge could provide clues for future research to enhance reliability of capacity judgments.

METHODS

Subjects

The subjects were persons with possible or probable Alzheimer's disease by NINCDS criteria(19) recruited for a multi-site study comparing the capacity to appoint a proxy decision-maker for research consent and the capacity to give informed consent for two

hypothetical research studies of varying risks and benefit.(18) Seventy-seven of 84 subjects from two of the study sites were administered the Mattis Dementia Rating Scale-2 (DRS-2) (20) in addition to the capacity interviews (seven subjects were unable or unwilling to complete the DRS-2) and are the subjects of this paper. The study was reviewed and approved by the institutional review board at the University of Michigan. Given the minimal risk of this interview study, the subjects provided their own informed consent when determined to be capable by the interviewer; otherwise, a surrogate gave permission in addition to subject assent.

Measures

The DRS-2 is a widely used assessment of cognitive abilities in individuals with mild to severe brain dysfunction.(20) In addition to the overall total score (with a potential range of 0 to 144 points; lower scores indicating worse cognitive functioning), the DRS-2 has five subscales: Attention (0 to 37 points) measures the ability to perform auditory-visual and verbal-nonverbal attention tasks; Initiation/Perseveration (0 to 37 points) measures verbal initiation and articulation, and oral-verbal and graphomotor skills; Construction (0 to 6 points) measures the ability to reproduce basic visual designs and to write one's own name; Conceptualization (0 to 39 points) measures the ability to identify visual and verbal similarities and differences; Memory (0 to 25 points) measures environmental and time orientation, short-term verbal recall, and verbal and visual recognition memory.

The MacArthur Competence Assessment Tool-Clinical Research (MacCAT-CR) is the most widely used instrument for assessing the abilities relevant to capacity for informed consent to research, and has been adapted and validated for use in persons with depression, schizophrenia, and dementia, among other disorders.(3, 21, 22) It has excellent content validity, inter-rater reliability, and good test-retest reliability.(3, 23, 24) It assesses the range of abilities relevant to capacity for giving informed consent to research according to the four-abilities model of decision-making capacity: understanding, appreciation, reasoning, and expressing a choice.(23) Two versions of the instrument were used based on different research scenarios of varying complexity and risk/benefit ratios(18): a randomized clinical trial of a medication for AD ("drug RCT") and a randomized placebo-controlled (sham surgery) neurosurgical trial of cell transplantation for AD ("neurosurgical RCT").

The Capacity to Appoint a Proxy Assessment (CAPA), an instrument specifically developed by our team, assesses the capacity to appoint a proxy decision-maker regarding participation in research. The CAPA also follows the 4 abilities model,(25) and has high internal consistency (Cronbach's alpha of 0.87) and excellent inter-rater reliability (intraclass correlation coefficients of 0.93 to 0.99), as described elsewhere.(18)

Procedures

Subjects were administered three capacity interviews: the CAPA, the MacCAT-CR (Drug RCT), and the MacCAT-CR (Neurosurgery RCT) during two in-home visits approximately two weeks apart. During the first visit, the CAPA and one of the MacCAT-CR interviews (randomly chosen) were conducted; the second MacCAT-CR and the DRS-2 were administered during the second visit. Each capacity interview was video-recorded. The DRS-2 administration was not video-recorded.

The MacCAT-CR and CAPA yield subscale scores but do not by themselves yield categorizations of capacity or incapacity; a capacity evaluator must exercise judgment in applying the data for the given context to yield a capacity status for each subject.(26) In this study, five consultation psychiatrists, recruited from the membership of the Academy of Psychosomatic Medicine (APM), were asked to make capacity judgments based on the

video-recorded capacity interviews. Consultation psychiatrists frequently perform capacity evaluations in the hospital setting.(2) The psychiatrist judges rated all three capacity interviews for each subject (reviews of the interviews of a given subject were separated by several months). Each judge's capacity determination was made on a 4-point scale regarding the subject's decisional capacity (definitely capable, probably capable, probably not capable, definitely not capable). Details of the expert judge evaluation procedures are extensively discussed elsewhere.(16, 18)

Analyses

Analyses were conducted using STATA 10.1. The subjects' capacity status was dichotomized by combining "probably" and "definitely" judgments of the expert judges(26) and used as the dependent variable for all models. For each of the three decision-making capacities (i.e., the capacity to appoint a research proxy, to consent to the drug RCT, and to consent to the neurosurgery RCT), multiple logistic regression models were used to examine the neuropsychological predictors of the capacity status. We constructed six models for each decision-making capacity. The first model used the capacity judgments of the majority of the five expert judges as the dependent variable. Five additional models were constructed with each of the five individual judge's capacity determinations as the dependent variable, for each type of decision-making capacity. For all of the models, the DRS-2 subscale scores (Attention, Initiation/Perseveration, Construction, Conceptualization, and Memory) were the independent variables and age and gender were added as covariates, with all independent variables added simultaneously. The DRS-2 subscale scores had correlation coefficients ranging from 0.21 between Construction and Memory subscales to 0.63 between Conceptualization and Initiation/Preservation. Education years and MMSE level were not used as covariates to avoid removing the variance that was the focus of the analysis. Significance was defined as $p < 0.05$ (two-tailed) for all analyses. In all of the logistic models, we standardized each of the five DRS subscales by the observed standard deviation to ensure that the meaning of the estimated odds ratios was comparable across the five DRS subscales, i.e., as the odds ratio associated with one standard deviation increase in each subscale rather than as the odds ratio associated with one point increase in each subscale. This was done because the DRS-2 subscales have different ranges of possible scores so that the interpretation of effect sizes based on change in scores could be misleading.

RESULTS

Table 1 summarizes subjects' demographic and cognitive characteristics.

Five-Psychiatrist Panel's Capacity Determinations and Neuropsychological Performance

Per the determinations of the majority opinion in the 5-judge panel, 60% of participants had capacity to appoint a proxy, 43% had capacity to consent to a randomized drug trial, and 16% had capacity to consent to a randomized neurosurgery trial. Table 2 displays the neuropsychological predictors of each of the three decision-making capacities as determined by the 5-judge panel.

The 5-judge panel's determinations of capacity to appoint a research proxy and capacity to consent to the lower risk research scenario (Drug RCT) are predicted by the Conceptualization and Initiation/Perseveration subscales, with particularly high odds ratios associated with the Conceptualization subscale. For the capacity to consent to the neurosurgery trial, although the Conceptualization subscale showed the highest odds ratio (OR=5.49), it was not statistically significant [95% CI=0.64–46.94; Wald $\chi^2(1)=2.42$; $p=0.12$], whereas the odds ratio associated with Memory subscale was significant.

Individual Psychiatrist's Judgments and Neuropsychological Performance

As shown in Table 3, the proportion of subjects judged to have capacity varied considerably among the expert judges, with a range of 49–83% (depending on the expert) of subjects being judged capable of appointing a research proxy, 18–70% judged capable of consenting to the drug RCT, and 8–39% judged capable of consenting to the neurosurgery RCT. Table 3 summarizes the relationship between significant neuropsychological domains of the DRS-2 subscales and individual expert's capacity judgments, for the three capacities. For the capacity to appoint a research proxy, performance on the Conceptualization subscale was a significant predictor for all of the judges' determinations, whereas Memory and Initiation/Perseveration subscales were predictors for two judges and Construction for one expert's judgment.

For the capacity to consent to the drug RCT, the capacity judgments of the strictest judge (Judge C with only 18% judged to have capacity) were significantly predicted by the Memory subscale. However, the other four judges' capacity judgments were predicted by the Conceptualization subscale. For the capacity to consent to the neurosurgery RCT, the Memory subscale significantly predicted the judgments of the three strictest judges, and Conceptualization predicted the two most lenient judges.

DISCUSSION

In this study, we examined the relationship between AD patient-subjects' performance on various neuropsychological domains and categorical determinations of capacity as given by expert clinicians (taken individually and as a group), for three different situations of decision-making capacity in the research context. The main findings are as follows.

First, across the three different capacities, individual capacity evaluators who are inclined to be "strict" and demand higher level of functioning for the subjects to be deemed capable may be especially affected by the dense short term memory deficits characteristic of AD. Since memory impairment tends to occur early in AD, this would translate into a high proportion of subjects being deemed incapable. In contrast, the more lenient judges' determinations are significantly predicted by performance on the Conceptualization subscale. Although a comparison is difficult due to differing methodologies, our results appear consistent with previous findings of Marson and colleagues who found that delayed verbal recall (a component of verbal memory) predicted the strictest capacity judgments and simple executive function predicted more lenient capacity judgments.(27)

Second, the expert panel's judgments of capacity are predicted by the Memory subscale for capacity to consent to the higher risk scenario and by Conceptualization and Initiation/Perseveration for the lower risk scenario and for the scenario of appointing a research proxy. This seems consistent with the above finding that when a higher threshold of capacity is applied to persons with AD, the area of early, severe impairment such as memory may predict incapacity judgments of experts.(18)

Third, unlike the capacity to consent to the two research scenarios, individual psychiatrist's judgments of capacity to appoint a proxy were predicted by neuropsychological subscales but not in any consistent manner relative to "strictness" of judgments. This may reflect the fact that capacity to appoint a proxy is a relatively unexplored concept both conceptually and empirically, and the experts' individual judgments may show considerable variability as a result. At least one judge in our study commented that his categorical judgments regarding this capacity evolved over the course of the 36 months of the study.(16)

These findings raise some intriguing possibilities for interpretation. In a previous report,(16) we noted that there were two recurring questions raised by the expert judges in their written comments accompanying their capacity determinations and during a post-study meeting. One question was: How long must the person retain the information to be deemed to have intact capacity? We noted that the lack of a widely accepted answer to this question may have contributed to variability in judgment. Another recurring theme among the judges was: Do the subjects show that they grasp “the big picture?” As one judge put it, “if you don’t understand the concept, the details won’t save you.” Although all of the judges felt that this was an important issue, what constitutes “grasping the big picture” may have varied among the judges since there are currently no uniform guidelines on how to use such a criterion. It is possible therefore that our findings regarding the neuropsychological predictors of capacity judgments reflect the variability among the judges regarding these two issues. Since many (albeit not all) of the items on the DRS-2 Memory subscale relate to the ability to retain information, it is plausible that the judgments of those who felt that subjects ought to “retain information” for a relatively longer period would be best predicted by the Memory subscale. As “rapid forgetting” is one of the hallmarks of AD,(28) one might also expect that those judges placing emphasis on information retention would tend to rate a relatively high proportion of AD patients as having impaired capacity. In contrast, other judges may have instead focused on the “getting the big picture” issue which may be more related to abilities associated with abstract thinking and executive function, such as assessed in the DRS-2 Conceptualization subscale. Although executive functions are also commonly affected in AD, those deficits may be less salient than those in memory, at least in the early/milder-stages of the illness, and thus judges who emphasize “the big picture” over memory may appear more lenient when evaluating capacity of AD patients.

Our findings may also have implications for improving the decision-making abilities of persons with dementia. For example, if one accepts the view that long-term retention of information is not a necessity for capacity—a view that is explicitly adopted in the laws of some nations(29)—then decision aids that accommodate more limited memory may be useful in assessing the decisional capacity of AD patients. A recent study by Rubright and colleagues found that a memory and organizational aid may in fact improve the performance of AD patients on capacity measures related to an early phase drug trial.(30)

There are, however, important limitations to our conclusions. First, this was a small, exploratory study intended to generate hypotheses rather than to test them, and we allowed increased potential for type I errors involved in multiple statistical tests when examining results of individual expert judges. Thus, the positive findings should be seen as provisional and suggestive (since there is a greater chance of a false positive finding), requiring further investigation, rather than definitive. Second, the capacity judgments studied were for the research context, which is still a relatively new area of practice. Thus, generalizing to the treatment context should be done cautiously. Third, our judges made their decisions under somewhat artificial conditions, since they did not follow the usual procedure of capacity determination, which would have involved actual interviews with individualized probing of unclear areas (rather than just viewing videos) and the availability of more background clinical information.

Finally, the DRS-2 may have limitations in identifying differential influence of specific cognitive domains. For instance, the Construction subscale has a potential range of only 7 points (0 to 6 points), whereas the Conceptualization subscale has a potential 40-point range (0 to 39 points). Although effect sizes can be standardized for interpretation, the differential subscale length may affect the reliability of each subscale, potentially limiting the magnitude of association due to psychometric reasons.(31) The subscales may also have differential sensitivity to impairment in their respective targeted constructs so that conclusions about

differential associations must be provisional.(32) A more comprehensive neuropsychological battery that is designed to be more sensitive to differences in the normal range of cognitive functioning might be used in the future to investigate more definitively the possibility of specific neuropsychological findings. On the other hand, the presently observed pattern of findings seems at least conceptually coherent in that they match what might be expected given what is known about the cognitive deficits associated with AD, as well as the cognitive operations likely to be most critical for competent decision-making. (11, 33) These are clearly issues warranting further research.

CONCLUSIONS

The assessment of decision-making capacity is currently guided by broad principles and standards.(2) In applying these standards, capacity evaluators exercise considerable clinical judgment and may do so in varying ways.(16) One important issue in evaluating persons with Alzheimer's disease is the role that different degrees of memory impairment ought to play in determining the patient's capacity status. Sometimes it may be sufficient for a person to retain information long enough to make an informed decision, whereas in other situations, it may be ethically more relevant for the person to be able to store and retrieve that information. The amount of risk at issue, as well as the nature of the participation in research (e.g., one-time procedure versus a long term longitudinal commitment) may need to be taken into account in weighing the importance of memory. It appears that clinicians will likely incorporate such considerations on their own, although to a varying degree. Making the practice more uniform by providing more specific normative guidance—for example, making more specific the importance of retention of information for some types of research scenarios—may be an important way of increasing the reliability of capacity judgments.

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Table 1

Participant characteristics, n=77

Demographics	n (%) or Mean±SD	
Female	38 (49.4%)	
White	76 (98.7%)	
Age (years)	74.8±9.8	
Education (years)	15.2±3.2	
MMSE score (potential range)	n (%) or Mean±SD	
MMSE score (0–30)	20.5±5.1	
<12	6 (7.8%)	
12–17	11 (14.3%)	
18–23	37 (48.1%)	
24+	23 (29.9%)	
DRS (potential range)	Mean±SD	Median (25th, 75th percentile)
DRS Total (0–144)	106.5±17.7	109 (95,119)
DRS Attention (0–37)	33.6±3.0	35 (32,36)
DRS Initiation/Perseveration (0–37)	22.0±8.1	22 (16,27)
DRS Construction (0–6)	5.1±1.6	6 (5,6)
DRS Conceptualization (0–39)	33.4±4.9	35 (31,37)
DRS Memory (0–25)	12.4±4.5	13 (10,15)

Table 2
 Relationship between Performance on DRS-2 Subscales and 5-Judge Panel Categorical Capacity Judgments, (n=77)^a

DRS Domains	Capacity to Appoint a Proxy, 60% Judged to have capacity	Capacity to Consent to Drug RCT, 43% Judged to have capacity	Capacity to Consent to Neurosurgery RCT, 16% Judged to have capacity
	OR (95% CI; Wald ²)	OR (95% CI; Wald ²)	OR (95% CI; Wald ²)
Attention	1.28 (0.38–4.27; 0.16)	0.49 (0.15–1.59; 1.41)	0.38 (0.08–1.82; 1.46)
Initiation/Perseveration	3.43 (1.05–11.18; 4.18, p=0.04)^b	2.85 (1.09–7.44; 4.57, p=0.03)	3.08 (0.70–13.47; 2.23)
Construction	0.57 (0.19–1.75; 0.96)	0.53 (0.20–1.41; 1.64)	1.08 (0.36–3.21; 0.17)
Conceptualization	19.58 (3.14–122.31; 10.13, p=0.001)	14.91 (2.73–81.34; 9.75, p=0.002)	5.49 (0.64–46.94; 2.42)
Memory	2.71 (0.78–9.42; 2.47)	1.43 (0.58–3.49; 0.60)	4.52 (1.24–16.44; 5.23, p=0.02)

^aStandardized multiple logistic regression model. All Wald ² tests with df = 1. Covariates included: Age, gender.

^bSignificant ORs are bolded (p<0.05)

Table 3

DRS-2 Predictors^a of Categorical Capacity Determinations of Individual Judges, (n=77)^b

Capacity to Appoint a Proxy (CAP)			Consent Capacity for Drug RCT			Consent Capacity for Neurosurgery RCT		
Judge (A-E)-% Judged to have Capacity	Predictors	OR (95% CI; Wald 2; p-value)	Judge (A-E)-% Judged to have Capacity	Predictors	OR (95% CI; Wald 2; p-value)	Judge (A-E)-% Judged to have Capacity	Predictors	OR (95% CI; Wald 2; p-value)
A--83%	Conceptualization	3.04 (1.05--8.83; 4.19; p=0.04)	A--70%	Conceptualization	2.84 (1.14--7.07; 5.05; p=0.03)	A--39%	Conceptualization	11.61 (2.38--56.58; 9.21; p=0.002)
	Memory	4.18 (1.13--15.46; 4.59; p=0.03)						
B--57%	Initiation/Perseveration	3.10 (1.07--9.01; 4.32; p=0.04)	D--51%	Conceptualization	5.24 (1.54--17.84; 7.02; p=0.01)	B--26%	Conceptualization	4.30 (1.06--17.47; 4.15; p=0.04)
	Conceptualization	4.64 (1.39--15.54; 6.21; p=0.01)						
C--55%	Initiation/Perseveration	3.20 (1.27--8.09; 6.08; p=0.01)	B--44%	Conceptualization	9.65 (2.31--40.28; 9.68; p=0.002)	D--21%	Memory	3.60 (1.28--10.15; 5.86; p=0.02)
	Conceptualization	3.59 (1.23--10.50; 5.44; p=0.02)						
D--49%	Construction	0.22 (0.07--0.70; 6.55; p=0.01)	E--33%	Conceptualization	4.33 (1.06--17.71; 4.16; p=0.04)	E--14%	Memory	4.30 (1.21--15.29; 5.08; p=0.02)
	Conceptualization	12.83 (2.62--62.88; 9.91; p=0.002)						
E--49%	Conceptualization	4.53 (1.38--14.85; 6.21; p=0.01)	C--18%	Memory	6.02 (1.56--23.20; 6.79; p=0.01)	C--8%	Memory	22.04 (1.54--315.96; 5.18; p=0.02)
	Memory	3.76 (1.32--10.76; 6.12; p=0.01)						

^a Only significant (p<0.05) DRS predictors listed.

^b Standardized multiple logistic regression model. All Wald chi-square tests with df = 1. Covariates included: Age, gender