Journal of the International Neuropsychological Society (2007), **13**, 1047–1059.

DOI: 10.1017/S1355617707071299

CRITICAL REVIEW

The association of specific neuropsychological deficits with capacity to consent to research or treatment

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(RECEIVED March 2, 2007; FINAL REVISION May 25, 2007; ACCEPTED May 25, 2007)

Abstract

Informed consent is key to ethical clinical research and treatment, but partially rests on the ability of individual patients or research participants to use disclosed information to make a meaningful choice. Although the construct of decisional capacity emerged from legal and philosophical traditions, several investigators have begun examining the relationship of specific neuropsychological abilities to decisional capacity. This line of research may foster development of better consent procedures, as well as aid in refining the construct of decisional capacity toward a form that better reflects the underlying neurocognitive processes. We conducted a systematic search of the published literature and thereby identified and reviewed 16 published reports of empirical studies that examined the relationship between specific neuropsychological abilities and capacity to consent to research or treatment. Significant relationships between neuropsychological scores and decisional capacity were present across all the reviewed studies. The degree to which specific neuropsychological abilities have particular relevance to decisional capacity remains uncertain, but the existing studies provide a solid basis for *a priori* hypotheses for future investigations. These ongoing efforts represent an important conceptual and empirical bridge between bioethical, legal, and neuropsychological approaches to understanding meaningful decision-making processes. (*JINS*, 2007, *13*, 1047–1059.)

Keywords: Bioethics, Mental competency, Activities of daily living, Cognition disorders, Schizophrenia, Dementia

INTRODUCTION

The importance of informed consent to ethical clinical practice and research is virtually axiomatic (Faden et al., 1986). Valid consent rests on (a) *voluntariness*—the choice must be made in the absence of coercion or undue influence, (b) *disclosure*—the potential patient or research participant must be provided with the information relevant to making an informed choice, and (c) *decisional capacity*—the patient or research participant must have the capacity to use the disclosed information to make a meaningful choice (Grisso & Appelbaum, 1998; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979).

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The decisional capacity component of valid informed consent clearly involves cognitive functions, yet the construct evolved primarily within legal and philosophical traditions related to competency (Appelbaum & Roth, 1982). As a part of growing efforts to bring empirical methods to the study of bioethical issues (Dunn et al., 2006a; Halpern, 2005; Kim, 2004), several investigators over the past 10 to 15 years have begun examining the relationship of specific neuropsychological abilities to decisional capacity. Greater clarity regarding the neurocognitive processes implicated among those with impairments in decisional capacity may facilitate efforts to develop more effective consent procedures (Dunn & Jeste, 2001; Eyler & Jeste, 2006; Flory & Emanuel, 2004; Palmer, 2006). Better understanding of the neuropsychological basis of capacity and incapacity may also help shape the ongoing evolution of the construct of decisional capacity to better reflect the neurocognitive processes requisite for making meaningful choices about treat-

ment or research participation (Moye & Marson, 2007; Northoff, 2006; Royall, 2002).

A wide range of studies, across several populations, have documented that overall cognitive test performance is correlated with level of decisional capacity (Bambara et al., 2007; Barton et al., 1996; Dunn et al., 2007a; Fisher et al., 2006; Fitten & Waite, 1990; Grisso & Appelbaum, 1995; Karlawish et al., 2005; Kim & Caine, 2002; Kovnick et al., 2003; Marson et al., 1995b; Palmer et al., 2005, 2007; Raymont et al., 2004; Resnick et al., 2007). Yet, if neuropsychological data are to inform development of improved consent procedures, as well as to contribute to the evolution of decisional capacity as a meaningful applied construct, it is important to go beyond establishing the presence of a general relationship, by taking into account the role of specific neurocognitive abilities in decisional capacity.

Below we provide a critical review of the empirical literature regarding the relationship of neuropsychological abilities to capacity to consent to research or treatment. We begin with an overview of the construct of decisional capacity, including its conceptual relationship to neuropsychological abilities, as well as describing instruments to measure decisional capacity. Next, we describe our literature search strategy and the resulting published empirical studies. We then discuss general conclusions that we believe can (and those that cannot yet) be supported by the extant empirical data, including a consideration of the methodological challenges inherent in this area of research. We also highlight some of the next logical and needed steps in empirical inquiry on this topic. We anticipate that consideration of the methodological challenges inherent in this line of research may also have relevance to other endeavors to clarify relationships between neuropsychological and everyday functioning (*cf.* Reynolds, 2007).

DEFINING DECISIONAL CAPACITY

The term "competency" is generally reserved to describe the outcome of a judicial proceeding, whereas the term "decisional capacity" is a broader descriptor of the ability to give meaningful consent for a particular choice in a given situation (Ganzini et al., 2005). Nonetheless, the concept of decisional capacity for consent developed from consideration of the abilities deemed relevant to competency by case law (Appelbaum & Grisso, 1988; Appelbaum & Roth, 1982; Marson & Ingram, 1996; Meisel et al., 1977; Roth et al., 1977).

Decisional capacity is not context free; it is generally conceptualized as a situation specific variable in that what is usually at issue is one's capacity to make a particular decision. As identified by Appelbaum and colleagues (Appelbaum & Grisso, 1988; Appelbaum & Roth, 1982), the term "decisional capacity," whether in regard to consent to treatment or research, is defined in terms of four functional tasks or abilities: (1) Understanding—the ability to comprehend the information being disclosed relevant to the choice presented, (2) Appreciation—the ability to apply the information to one's own situation or condition, (3) Reasoning—the ability to consider and compare potential consequences of the proposed treatment or research protocol relative to alternatives, and (4) Expression of a choice—the ability to communicate a stable choice. Although initially identified as different legal standards of varying levels of stringency for establishing competency, in contemporary use, these four abilities are usually described as components or dimensions (rather than criterion levels) of decisional capacity (Grisso & Appelbaum, 1998).

NEUROPSYCHOLOGICAL ABILITIES AND DECISIONAL CAPACITY

In the early to mid-1990s, Marson and colleagues published a series of groundbreaking conceptual and empirical reports relating neuropsychological abilities to legal competency standards (e.g., Marson et al., 1993, 1995b, 1996). The initial reports were focused on the capacity of patients with Alzheimer's disease to consent to treatment, but the concepts and methods have wider relevance to treatment and research consent. For example, Marson (2001) noted that:

> ". . . impaired learning and short-term recall will limit the amount of encoded information available for further processing . . . receptive language measures are relevant to capacity to consent because of their sensitivity to reduced comprehension of [the disclosed information] . . . conceptualization and executive function measures are important . . . because of their relevance to organized processing of [disclosed information]. Measures of judgment and reasoning are equally important as they make possible a patient's rational weighing of all this information, and his/her internal determination of a treatment choice" (p. 273).

STRUCTURED INSTRUMENTS FOR OPERATIONALIZING DECISIONAL CAPACITY

Over 20 different instruments have been published for assessing one or more dimensions of decisional capacity (Dunn et al., 2006b). Below we describe three of the most commonly used instruments, to illustrate how decisional capacity constructs are commonly operationalized in this area of research. These three instruments are the MacArthur Competence Assessment Tool for Treatment (MacCAT-T; Grisso et al., 1997; Grisso & Appelbaum, 1998) or Clinical Research (MacCAT-CR; Appelbaum & Grisso, 2001), and the Capacity to Consent to Treatment Instrument (CCTI; Marson et al., 1995b).

The MacCAT-T and MacCAT-CR are administered and scored through a semistructured interview. Each was initially developed for applied evaluations of decisional capacity (Appelbaum & Grisso, 2001; Grisso et al., 1997), and the specific content of the disclosures (and specifically

https://doi.org/10.1017/S1355617707071299 Published online by Cambridge University Press

acceptable responses) are tailored to the specific decision at hand. This tailoring of content increases the ecological validity of the instruments, but complicates comparison of results from different settings or contexts (Dunn et al., 2006b). The MacCAT-T and MacCAT-CR each yield four subscale scores corresponding to the four dimensions of decisional capacity. The Understanding subscale on both instruments has 13 items, but is differentially weighted so that the MacCAT-T version has a range of 0 to 6 points, whereas the MacCAT-CR version has a range of 0 to 26 points. The MacCAT-T Appreciation subscale has two items (range, 0 to 4 points), whereas the MacCAT-CR version consists of three items (range, 0 to 6 points). The Reasoning subscale on both the MacCAT-CR and MacCAT-T consists of four items (range, 0 to 8 points), and Expression of a Choice on both scales consists of a single item (range, 0 to 2 points).

The CCTI (Marson et al., 1995b) is also administered by means of an interview format. Decisional capacity is evaluated in the context of two standardized (hypothetical) treatment scenarios. The CCTI items and scores are organized in reference to five "legal standard" (LS) subscales, including LS1 (expression of a choice; potential range, 0 to 4 points), LS3 (appreciation; potential range, 0–10 points), LS4 (reasoning; potential range, 0–12 points), and LS5 (understanding of the situation and choices; potential range, 0 to 70 points). There is also an LS2 ("reasonable choice") subscale, but it was only included for exploratory purposes as it does not correspond to generally accepted definitions of decisional capacity or competence.

Using the above or similar measures of specific components of decisional capacity, several published empirical studies have emerged in the past two decades which have evaluated the relationships between specific neuropsychological abilities to decisional capacity. Our review of this research follows below.

METHODS

Data Sources

The primary literature search for the present review was conducted in September 2006 with updates through April 2007. The first step was to list published reports that we knew, through our prior work on this topic, were relevant to focus of this review (such as Carpenter et al., 2000; Marson et al., 1996; Moser et al., 2002; Palmer et al., 2004; Palmer & Jeste, 2006; Stroup et al., 2005). We used these published reports to identify potential common keywords, index terms, PubMed and Medical Subject Headings (MESH), and PsycINFO descriptors that would facilitate computerized search of the literature using the PsycINFO and PubMed databases. The list of potential search terms was quite large, and we tried a variety of combinations, but these generally took a form similar to the following: ["capacity to consent" or "decisional capacity" or "competenc*"] AND ["cogniti*" or "neurocogniti*" or "neuropsycholog*"]. (The asterisk represents a "wild card" that searches for all words that include the stem.) These searches returned an enormous number of citations, the vast majority of which were found upon further inspection to be "false positives." We examined the title, article type, and abstract (when available) to determine whether the article appeared to be an empirical study of decisional capacity and whether neuropsychological abilities (or a synonym) were described. As we were unable to identify a set of search parameters that was simultaneously sensitive and specific, the search was necessarily an iterative one of identifying relevant reports, examining the bibliographies of identified references, as well as using the "Related Articles" function in PubMed to identify any additional potentially relevant articles.

Inclusion Criteria

The criteria for inclusion in the present review were the following: (a) report of empirical data published in a peer-reviewed English-language journal (we are not aware of any otherwise eligible reports that were excluded on the basis of language), (b) decisional capacity evaluated in reference to consent to treatment or research using a formal capacity rating scale, and (c) neuropsychological scores from multiple cognitive domains considered as potential predictors of decisional capacity. We excluded studies focused on a single aspect of decisional capacity such as understanding of placebo control procedures.

Review Process/Data Extraction

We carefully read each identified article and recorded the following information for presentation in the present review: target population and sample characteristics, decisional capacity measure, neuropsychological tests and scores analyzed, and relevant data analyses and results.

RESULTS

Reports Identified

By means of the above search procedures, we identified 16 empirical reports (from 15 studies) evaluating the associations between specific neuropsychological scores and decisional capacity. The targeted diagnostic groups generally fell into one of three categories (schizophrenia, dementia, or other medical conditions). Studies of capacity to consent to research generally used the subscale scores from the MacCAT-CR, whereas those of capacity to consent to treatment generally used the subscale scores from the MacCAT-T or CCTI. In two of the reports (Earnst et al., 2000; Marson et al., 1997), the analyzed scores were based on physician ratings of decisional capacity, but even these physician ratings were based on impressions formed while viewing videotapes of each participant being interviewed with the CCTI. In one additional study by Dymek et al. (1999), the relationship of neuropsychological scores to decisional capacity was evaluated in terms of factor loadings with decisional

capacity composite scores (the latter themselves derived from factor analysis of the CCTI).

The reports included five studies of capacity to consent to research (Carpenter et al., 2000; Moser et al., 2002; Palmer & Jeste, 2006; Stroup et al., 2005) or treatment (Palmer et al., 2004) among patients with schizophrenia or schizoaffective disorder, and eight reports on the capacity to consent to treatment (Dymek et al., 1999; Earnst et al., 2000; Gurrera et al., 2006; Marson et al., 1995a, 1996, 1997; Moye et al., 2006) or research (Pucci et al., 2001) among patients with mild-to-moderate Alzheimer's disease or related dementias. [Two of the reports for patients with Alzheimer's disease were based on the same patient sample, but one focused on predictors of decisional capacity under a Reasoning standard (Marson et al., 1995a), and the other focused on Understanding, Appreciation, and Expression of a Choice (Marson et al., 1996).] The remainder of identified studies focused on capacity to consent to treatment among patients with cognitive complaints (not necessarily dementia) secondary to Parkinson's disease (Dymek et al., 2001), ambulatory oncology patients (Casarett et al., 2003), or nondemented Veterans Hospital nursing home residents (Moye & Karel, 1999). Several of the studies included a healthy or other nonimpaired comparison, but due to constricted variance, there were few significant correlates of decisional capacity in these groups. Thus, the study findings reviewed and summarized below are from the analyses within the targeted patient samples of each study.

Bivariate Relationships Between Neuropsychological and Decisional Capacity Scores

Impairment in the Expression of a Choice was rare among patients with schizophrenia, as well as among the oncology patients, so information on the bivariate correlates of this dimension of decisional capacity were frequently omitted from the published reports. As shown in Table 1, bivariate correlations between neuropsychological scores and Understanding, Appreciation, and Reasoning were evaluated and reported in all five of the studies of schizophrenia patients, and as shown in Table 2 within several of the studies of other patient populations. (Some of the latter studies also considered bivariate correlates of Expression of a Choice, so these are also provided in Table 2.)

There was considerable variability between studies in terms of the overall magnitude of correlations between neuropsychological scores and decisional capacity scores. For example, in the study from Stroup et al. (2005), the correlations between specific neuropsychological scores (other than the composite score) and MacCAT-CR Understanding for schizophrenia patients ranged from r = .06, for a reading recognition test, to r = .22, for working memory (both ps $< .001$). The parallel values for the MacCAT-CR Understanding in Moser et al.'s (2002) study of schizophrenia patients ranged from r = .41, $p < .05$, for the Delayed Memory Index score from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998), to r = .71, $p < .001$ for Matrix Reasoning (Wechsler, 1997). Similar variability between studies was observed in terms of the magnitude of correlations with Appreciation and Reasoning.

Because of the substantial variability between studies, it may be more appropriate to consider the pattern of highest and lowest bivariate correlations within each study. There is a triad of correlations between each neuropsychological score and Understanding, Appreciation, and Reasoning, respectively. Among the five schizophrenia studies the highest correlation within each triad occurred with Understanding for 17 triads, with Reasoning for 13 triads, and with Appreciation for 12 triads. The lowest correlation in each triad occurred with Understanding for 4 triads, Appreciation for 12 of the triads, and 20 occurred with Reasoning. [The terms "highest" and lowest" refer only to relative comparisons of the absolute value of the correlation magnitudes. Assertions of statistically significant differences between such correlations would require testing null hypotheses of the form $r_{xy} - r_{xz} = 0$ (see Cohen & Cohen, 1983). None of the reports tested such null hypotheses.] The highest correlations between specific neuropsychological and decisional capacity scores in other populations, as listed in Table 2, also tended to occur most frequently with the Understanding dimension. An exception was the study of nondemented nursing home residents by Moye & Karel (1999), wherein the correlations with Understanding subscale were often lower than those for the other capacity dimensions.

Relative to neuropsychological tests of other cognitive abilities, working memory scores had the highest bivariate correlations with Appreciation in three of the five schizophrenia studies (Carpenter et al., 2000; Palmer et al., 2004; Stroup et al., 2005), and the highest bivariate correlations with Reasoning in two of the five schizophrenia studies (Palmer et al., 2004; Stroup et al., 2005). Among the nonschizophrenia studies, measures sensitive to executive functions were frequently among the strongest correlates of Understanding, Appreciation, or Reasoning. Across studies, however, the difference in the proportion of variance explained by working memory or executive functions relative to the next strongest neuropsychological correlate from a different neuropsychological ability area tended to be negligible.

Most of the neuropsychological studies of decisional capacity among dementia patients focused on capacity to consent to treatment, but Pucci et al. (2001) evaluated the correlations between neuropsychological scores and an overall rating of capacity to consent to research among 70 patients with mild to moderate Alzheimer's disease. Significant neuropsychological correlates of decisional capacity scores included the total score on the Alzheimer's Disease Assessment Scale–Cognitive (ADAS-COG) r = −.66 (higher ADAS-COG scores indicate worse performance), $p < .001$, Mini-Mental State Examination r = .60, Token Test r = .40, verbal fluency r = .36, Ravens Colored Matrices r = .34, verbal span r = .26, constructional praxis r = .25, and visual

https://doi.org/10.1017/S1355617707071299 Published online by Cambridge University Press

Table 1. Correlations between neuropsychological scores and Understanding, Appreciation, and Reasoning scores (schizophrenia samples)

	Understanding					Appreciation					Reasoning				
Study no.	I	II	III[a]	IV	V	I	II	III[a]	IV	V	I	II	III[a]	IV	V
Population	SC/SA	SC/SA	SC	SC	SC	SC/SA	SC/SA	SC	SC	SC	SC/SA	SC/SA	SC	SC	SC
Sample size	49–59	30	25	70	1,447	49–59	30	25	70	1,447	49–59	30	25	70	1,447
Capacity scale	Mac CAT-T	Mac CAT-CR	Mac CAT-CR	Mac CAT-CR[b]	Mac CAT-CR	Mac CAT-T	Mac CAT-CR	Mac CAT-CR	Mac CAT-CR	Mac CAT-CR	Mac CAT-T	Mac CAT-CR	Mac CAT-CR	Mac CAT-CR	Mac CAT-CR
Severity of psychopathology															
General	−.17	−.34	−.48*	−.37*	−.06*	−.02	−.27	−.47*	−.16	−.06*	−.12	−.47*	NS	−.10	−.01
Negative symptoms	−.23		−.50*	−.31*	−.14**	−.19		−.40	−.19	−.12**	−.26		−.55	−.06	−.09**
Positive/psychotic symptoms	−.22	−.38*	−.25	−.18	−.01	−.04	−.37*	−.28	−.08	−.01	−.11	−.52*	−.14	.01	−.02
Neuropsychological scores															
General															
DRS Total	.49**					.27^					.44**				
RBANS Total		.82**	.55*				NS	.60*				.76*	.18		
Neuropsychological Battery Composite				.44*	.23**				.30*	.24**				−.001	.26**
Receptive Language & Semantic Knowledge															
GORT Reading Comprehension		.30*					NS					NS			
PIAT Reading Comprehension				.45**					.56**					.06	
Token Test				.39*					.36*					−.02	
WAIS-III Vocabulary			.57*					.56*					.27		
WRAT-III Reading Recognition		NS	.54*		.06		NS	.58*		.02		NS	.29		.02
Verbal Composite	.35^			.52**		.08			.35*		.45*			.15	
RBANS Language		NS	.51*				NS	.54*				NS	.34		
Attention/Working Memory															
Continuous Performance Test					.15**					.15**					.12**
DRS Attention	.25					.15					.33^				
RBANS Attention		NS	.44*				NS	.51*				NS	.22		
WAIS-III Letter Number Sequencing		NS	.56*				.81*	.59*				NS	.16		
Working Memory Composite	.38*			.40*	.22**	.37*			.32*	.23**	.54**			.04	.26**
Processing Speed (Composite)	.30*			.30*	.19**	.11			.24	.19**	.43*			−.02	.21**
Visuospatial/Constructional															
DRS Construction	−.02					−.03					.16				
Matrix Reasoning			.71*					.64*					.45*		
RBANS Visuospatial/Constructional		NS	.44*				.24*	.54*				NS	.08		
Perceptual Organization Composite	.31^			.16		.22			.22		.47**			.02	
Executive functioning															
DRS Conceptualization	.30^					.17					.45**				
DRS Initiation/Perseveration	.35*					.14					.16				
Executive Composite	.41*			.30*	.15**	.24			.35*	.16**	.39*			−.01	.19**
Episodic Learning/Memory															
DRS Memory	.54**					.27^					.46**				
Hopkins Verbal Learning Test					.16**					.20**					.24**
RBANS Immediate Memory		NS	.63*				NS	.57*				.30*	.23		
RBANS Delayed Memory		NS	.41*				NS	.47*				NS	.13		
Auditory Learning Composite				.50**					.29*					.05	
Visual Learning Composite				.40*					.22					.11	
Learning Composite	.47*					.34*					.45*				

Note. Key to Study Numbers: I = Palmer et al. (2004); II = Carpenter et al. (2000); III = Moser et al. (2002); IV = Palmer & Jeste (2006); V = Stroup et al. (2005). NS reported as nonsignificant, but precise magnitude of the correlation not provided. DRS = Mattis Dementia Rating Scale; GORT = Grey Oral Reading Test; MacCAT-CR = MacArthur Competence Assessment Tool for Clinical Research; MacCAT-T = MacArthur Competence Assessment Tool for Treatment; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; SA = schizoaffective disorder; SC = schizophrenia; WAIS-III =Wechsler Adult Intelligence Scale–Third Edition; WRAT-III = Wide Range Achievement Test–Third Edition.

[a]Correlations reported by Moser et al. (2002) were corrected for age.

[b]Palmer & Jeste (2006) reported multiple trials for the MacCAT-CR Understanding subscale; correlations summarized in this table are those for Trial 2, which corresponds to the standard administration and scoring for this subscale.

*$p < .05$ [$p < .01$ for Palmer et al. (2004)]; **$p < .001$; ^Palmer et al. (2004) used a nontraditional alpha of ($p < .01$), the correlations indicated with the ^mark had $p < .05$ but $p > .01$.

Table 2. Correlations between neuropsychological scores and Understanding, Appreciation, Reasoning, and Expression of a Choice (non-schizophrenia samples)

	Understanding				Appreciation				Reasoning				Expression of a Choice		
Study no.	VIa	VII	VIII	IX	VIa	VII	VIII	IX	VIb	VII	VIII	IX	VIa	VII	VIII
Population	AD	PD	Nursing home	Cancer	AD	PD	Nursing home	Cancer	AD	PD	Nursing home	Cancer	AD	PD	Nursing home
Sample size	29	20	16	45	29	20	16	45	29	20	16	45	29	20	16
Capacity scale	CCTI	CCTI	MacCAT-T	MacCAT-CR	CCTI	CCTI	MacCAT-T	MacCAT-CR	CCTI	CCTI	MacCAT-T	MacCAT-CR	CCTI	CCTI	MacCAT-T
General (MMSE total)	.62**				.49*				.55*				NS		
Receptive Language & Semantic Knowledge															
Auditory Comprehension Screen	.63**	NR			.45*	NS			NS	NR			.66**	NR	
Geriatric Evaluation of Mental Status															
Command Comprehension			−.03				.11				.30				−.03
Rapid Estimate of Adult Literature in Medicine				.45*				.34*				.17			
Reading Comprehension Screen	NS				NS										
Token Test	.61**	NR			.44*	NS			.48*	NR			NS	NR	
WAIS-R Comprehension	.72**	.70**			.56*	NS			NS	NR			NS	.67*	
Expressive Language															
Animal Fluency	NS	NR		.42*	NS	NS		.34*	.44*	NR		.21	NS	NR	
Letter Fluency	NS	NR			.48*	NS			.57*	NR			NS	NR	
Boston Naming Test	.72**	NR			.43*	NS			NS	NR			.62**	NR	
Geriatric Evaluation of Mental Status									NS						
Sentence Repetition			−.14				−.18				−.03				−.08
Confrontation Naming			.25				.31				.18				.49*
Generative Naming			.24				.34				.37				.25
Attention/Working Memory															
DRS Attention	NS	NR			NS	NS			.46*	.58*			NS	.58*	
Geriatric Evaluation of Mental Status															
Digits Forward			−.11				49*				.25				.09
Digits Backward			−.11				.55*				.48*				.14
MMSE "W-O-R-L-D Backward" task				.37*				.30				.29			
MMSE 3-item delayed recall				.27				.14				.01			
WAIS-R Digit Span	NS	NR			NS	NS			.44*	NR			NS	NR	
WMS-R Information/Orientation		NR				NS				NR				NR	
WMS-R Mental Control		NR				NS				NR				NR	
Processing Speed															
Trial Making Test Part A	−.56*	NR			−.58**	NS			−.45*	NR			NS	NR	
Visuospatial/Constructional															
DRS Construction	NS	NR			NS	NS			NS	NR			NS	NR	
Executive Functioning															
DRS Conceptualization	.81**	NR			.50*	NS			NS	NR			NS	NR	
DRS Initiation/Perseveration	.64**	NR			NS	NS			.60**	NR			NS	NR	
Executive Interview (EXIT25)		−.75**				NS				−.67*				.53*	
Trail Making Test Part B	NS	NR		−.52**	NS	NS		−.31	NS	−.60*		−.42**	NS	NR	
WAIS-R Similarities	.67**	NR			NS	NS			NS	NR			.54*	NR	
Episodic Learning/Memory															
DRS Memory	.60**	.71**			NS	NS			NS	NR				.73**	
Geriatric Evaluation of Mental Status															
Immediate Verbal Memory (list learning)			.09				.16				−.13				.17
Recent Verbal (list recall)			−.15				.37				.32				.22
Wechsler Memory Scale–Revised															
Logical Memory I	.55*	NR			NS	NS			NS	NR			NS	NR	
Logical Memory II	NS	.65*			NS	NS			NS	.48**			NS	NR	
Verbal Paired Associates I	NS				NS				NS				NS		
Verbal Paired Associates II	NS				NS				NS				NS		

Note. Key to Study Numbers: VIa = Marson et al. (1996), VIb = Marson et al. (1995a), VII = Dymek et al. (2001), VIII = Moye & Karel (1999), IX = Casarett et al. (2003). NS = nonsignificant (precise magnitude of the correlation not provided); NR = not reported (Dymek et al. 2001, provided the four strongest correlates for each decisional capacity dimension except for those with Appreciation, for which there were no significant neuropsychological correlates). AD = Alzheimer's disease; CCTI = Capacity to Consent to Treatment Instrument; DRS = Mattis Dementia Rating Scale; MacCAT-T = MacArthur Competence Assessment Tool for Treatment; MMSE= Mini Mental Status Examination; PD = Parkinson's disease; WAIS-R Wechsler Adult Intelligence Scale–Revised.

*$p < .05$; **$p < .001$.

search r = .24, all *p*s < .05; nonsignificant correlates of decisional capacity were Corsi Blocks r = .21, a story recall task, r = .20, and an ideomotor praxis score r = .03.

Bivariate Correlations With Severity of Psychopathology

The association between severity of psychopathology and decisional capacity was considered in all five of the schizophrenia studies. As shown in Table 1, these bivariate correlations tended to be lower than those between overall cognitive performance and decisional capacity. It might be noted, however, the correlations between negative symptoms (e.g., apathy, social withdrawal) and decisional capacity tended to be stronger than those between positive symptoms (e.g., hallucinations, delusions, and thought disorder) and decisional capacity.

Multivariate Models of Decisional Capacity Scores

Multivariate models of decisional capacity were considered in several of the identified studies, including two of the schizophrenia studies (Palmer et al., 2004; Stroup et al., 2005), the study of patients with Parkinson's disease (Dymek et al., 2001), Marson and colleagues studies of Reasoning (Marson et al., 1995a) and other decisional capacity components (Marson et al., 1996) among patients with Alzheimer's disease, and several other studies of patients with Alzheimer's disease or related dementias (Earnst et al., 2000; Gurrera et al., 2006; Marson et al., 1997; Moye et al., 2006). The method of entry of independent variables was sometimes unclear; however, in most of the studies it appears that the investigators used forward stepwise entry, with the order of entry determined by statistical criteria (ordered by the highest partial correlations among variables not yet in the model) rather than as tests of *a priori* hypotheses.

Selected key findings from the multivariate analyses from each study are described in Table 3. The component independent variables differed across studies, but neuropsychological scores that frequently emerged as significant independent variables in the multivariate models included tests of episodic memory, a variety of "executive functions," working memory, confrontational naming, fluency, auditory comprehension, and psychomotor speed. As expected when using automated entry criterion, the first neuropsychological variable to enter the model was generally that with the strongest bivariate correlation. Once one cognitive variable was in the model, either no or at most one additional neuropsychological score would account for significant additional variance in the dependent variable.

Other Results

In a factor analytic study of CCTI scores from patients with Alzheimer's disease, Dymek et al. (1999) examined the degree to which specific neuropsychological scores, from the same test battery listed in Table 2 for other studies from this research group (Dymek et al., 2001; Marson et al., 1995a), loaded with either of two CCTI factor scores that had been identified in an earlier stage of analysis. Most of the neuropsychological scores loaded with the first CCTI factor score that was composed of items involving stating rational reasons for one's choice, generation and description of potential consequences of one's choice, and memory of disclosed information. However, the episodic memory test scores loaded more strongly with a second CCTI factor score that consisted solely of items related to memory of disclosed information.

DISCUSSION

We identified and reviewed 16 published reports of empirical studies that examined the relationship between specific neuropsychological abilities with capacity to consent to treatment or research. The magnitude of correlations between neuropsychological and decisional capacity scores varied widely between studies, but significant relationships among these scores were present across all the studies in this review. No particular cognitive abilities or tests stood out as consistently unique predictors of overall decisional capacity, and there were no clear patterns of differential relationships between specific neuropsychological abilities and specific components of decisional capacity.

Although the association is not sufficiently strong that cognitive impairment may be viewed as functionally equivalent to impaired decisional capacity (Etchells et al., 1997; Kim & Caine, 2002), the presence of the general association between cognition and decisional capacity appears undeniable. In the case of schizophrenia, findings across studies suggest that cognitive deficits have a more deleterious effect on decisional capacity than do the primary psychiatric symptoms. The general strength of these relationships between neuropsychological tests and decisional capacity scores is particularly notable given the variety of potential influences on manifest decisional capacity, but parallels the pattern seen in terms of predictors of other dimensions of independent functioning among people with schizophrenia (Bowie et al., 2006; Green et al., 2000).

Methodological limitations common among the reviewed studies include relatively small sample sizes (only 7 of the studies had patient samples larger than 30), and the fact that 13 of the 16 reports were focused on people with schizophrenia or dementia. Schizophrenia is characterized by diffuse and heterogeneous cognitive impairment (Fioravanti et al., 2005; Heinrichs & Zakzanis, 1998; Savla et al., in press), and even among those with mild to moderate Alzheimer's disease, there may be nonfocal deficits, together with wide between-patient variation in the level and pattern of cognitive impairment (Salmon & Bondi, 1999; Salthouse & Becker, 1998). Specific cognitive-decisional capacity relationships might be more apparent in patient populations with less diffuse patterns of impairment. Also

Table 3. Multivariate models of decisional capacity

Authors (year)	Samples Composition	Summary of key results from multivariate analyses
Marson et al. (1995a)	29 mild or moderate AD	DV: CCTI Reasoning IV: DRS Initiation/Perseveration subscale entered 1st, $R^2 = 0.36$**, after which no other neuropsychological variable accounted for significant additional variance.
Marson et al. (1996)	29 mild or moderate AD	DV: CCTI Understanding; IVs: DRS Conceptualization subscale** and BNT ** entered 1st and 2nd, cumulative $R^2 = 0.81$**, then nothing else. DV: Expression of a Choice; IV: Auditory Comprehension Screen entered 1st, $R^2 = 0.44$**, then nothing else.
Marson et al. (1997)	Combined sample of 16 NC 29 mild AD	DVs: Five physicians independently categorized each participant based on videotapes of CCTI interviews. (Stepwise DFAs were conducted to separately predict each physicians categorizations) IVs: Physician 1 (90% rated incompetent) LM II ** and WAIS Similarities*, cumulative $R^2 = 0.79$ Physician 2 (52% rated incompetent), LM I, $R^2 = 0.43$** Physician 3 (24% rated incompetent) Letter fluency** and Cognitive Competency Test*, cumulative $R^2 = 0.38$ Physician 4 (14% rated incompetent) Trails A** and WAIS-R Comprehension*, cumulative $R^2 = 0.46$ Physician 5 (0% rated as incompetent) No multivariate model computed. The overall correct classification rates based on the DFA models were generally good, ranging from 79% to 100%.
Earnst et al. (2000)	Combined sample of 10 NC 21 mild or moderate AD	Five trained physicians independently categorized each participant under each of four legal standards as well as an overall judgment of competency (PJ) based on videotapes of CCTI interviews. (Stepwise DFAs were conducted to separately predict each physicians categorizations) The 1st significant NP variable to enter as an IV in a stepwise regression model for each legal standard and PJ rating by the physicians were: DV: Understanding; 1st IV to enter was DRS Conceptualization (2 physicians' models), LM I (1 physician's model), DRS Memory (1 physician's model), BNT (1 physician's model) DV: Appreciation: 1st IV to enter was BNT (3 physicians' models), Trails B (1 physician's model), DRS Conceptualization (1 physician's model) DV: Reasoning: 1st IV to enter was BNT (2 physicians' models), DRS Memory (2 physicians' models), LM I (1 physician's model) DV: Expression of a Choice; 1st IV to enter was BNT (2 physicians' models), ACS (1 physician's model), WAIS-R Similarities (1 physician's model) DV: PJ; 1st IV to enter was DRS Conceptualization (2 physicians' models), BNT (2 physicians' models), DRS Memory (1 physician's model)
Dymek et al. (2001)	20 cognitively impaired PD patients	DV: CCTI Understanding; IVs: EXIT25** and DRS Memory** entered 1st and 2nd, cumulative $R^2 = 0.68$, then nothing else. DV: CCTI Reasoning; IV: EXIT25 entered 1st, $R^2 = 0.45$*, then nothing else. DV: CCTI Expression of a Choice; DRS Memory** entered 1st, $R^2 = 0.55$, then nothing else
Gurrera et al. (2006)	88 mild to moderate dementia	The investigators used PCA with individual items from the MacCAT-T, CCTI, and Hopemont Capacity Assessment Interview, and derived five components, four of which were used as dependent variables in subsequent analyses, i.e., Understanding (eigenvalue 2.40), Appreciation (eigenvalue 1.35), Reasoning (eigenvalue 1.67), Choice (eigenvalue 1.34). They also used PCA to identify three cognitive components from a 10 test neuropsychological battery: Component 1 (LM I and II, BNT; eigenvalue 4.59), Component 2 (Trails A & B, Mazes, Visual Search and Attention Test; eigenvalue 1.40), Component 3 (Digit Span and Vocabulary subtests from the WAIS-III, and letter fluency; eigenvalue 1.17) Stepwise linear regression modeling used with capacity components as the DVs and neuropsychological factors as the potential IVs: DV: Understanding; significant IVs (in order of entry) NP components 1**, 3**, 2**, cumulative $R^2 = 0.78$** DV Appreciation; significant IVs (in order of entry) NP components 1**, 2*, 3*, cumulative $R^2 = 0.25$** DV: Reasoning; significant IVs (in order of entry) NP components 1**, 2**, 3**, cumulative $R^2 = 0.40$** DV Choice; significant IVs (in order of entry) NP components: 1*, 3*, cumulative $R^2 = 0.10$*
Moye et al. (2006)	53 NC 53 mild to moderate dementia	DV: MacCAT-T dichotomized as impaired or unimpaired (MacCAT-T subscale score < 2.5 *SD*s from the Mean of NCs constituted "impaired") at baseline and 9-month follow-up visits. Results for the stepwise DFAs were described as follows: "*Baseline delayed Logical Memory successfully classified participants into impaired and unimpaired overall capacity groups at the initial time period by stepwise [DFA]. Baseline Boston Naming, delayed Logical Memory, and Trails B together successfully classified participants into impaired and unimpaired capacity groups at the 9-month time period by stepwise [DFA]. Performance on these cognitive tasks correctly classified 94.3% of participants as decisionally impaired or within normal lists at both the initial and 9-month time periods. Demographic variables were not predictive of group membership*." (p. 81)
Palmer et al. (2004)	59 SC/SA	DV: MacCAT-T Understanding; IV: DRS Memory entered 1st, $R^2 = 0.27$** DV: MacCAT-T Reasoning; IV: DRS Conceptualization entered 1st, $R^2 = 0.22$**, then nothing else. DV: Expression of a Choice; IV: Abstraction/Cognitive Flexibility composite entered 1st, $R^2 = .14$*, then nothing else
Stroup et al. (2005)	1,447 SC	DV: MacCAT-CR Understanding; IVs: Working Memory Composite**, Processing Speed Composite*, and PANSS negative symptoms* entered 1st, 2nd, and 3rd, respectively, cumulative $R^2 = 0.08$, then nothing else DV: MacCAT-CR Appreciation; IVs: Working Memory Composite** and PANSS negative symptoms* entered 1st and 2nd respectively, $R^2 = 0.04$, then nothing else. DV: MacCAT-CR Reasoning; IVs: Working Memory Composite*, Verbal Memory Composite*, Executive Functioning Composite*, Education (years)* entered 1s through 4th, respectively, $R^2 = 0.04$, then nothing else.

Note. AD = Alzheimer's disease; BNT = Boston Naming Test; DFA = discriminant function analysis; CCTI = Capacity to Consent to Treatment Instrument; DRS = Mattis Dementia Rating Scale; DV = Dependent Variable; EXIT25 = Executive Interview; IV = Independent Variable; LM = Logical Memory; MacCAT-T = MacArthur Competence Assessment Tool for Treatment; NC = normal comparison subject; NP = neuropsychological; PANSS = Positive and Negative Syndrome Scale; PCA = Principal Components Analysis; PD = Parkinson's disease; PJ = Overall (physician) judgment of competency; SC = schizophrenia; SA = schizoaffective disorder; WAIS/WAIS-R/WAIS-III = Wechsler Adult Intelligence Scale (1951, 1981, or 1997, versions, respectively).
*$p < .05$; **$p < .001$.

https://doi.org/10.1017/S1355617707071299 Published online by Cambridge University Press

note that the majority of authors for 11 of the 16 reports were from one of three research groups (Harvard Medical School, University of Alabama at Birmingham, or our own group at the University of California, San Diego). In short, the pattern of results described here may not generalize to other populations or to clinical or research settings markedly distinct from those in which many of these studies were conducted.

Interpretation of any observed differential relationships between specific neuropsychological abilities and specific aspects of decisional capacity is also hampered by instrumentation issues, particularly the multifactorial nature of neuropsychological tests (Gladsjo et al., 2004; The Psychological Corporation, 1997), and the lack of psychometric equivalence among neuropsychological tests as well as among within-instrument decisional capacity subscales (Chapman & Chapman, 1978; Dunn et al., 2006b). For instance, the highest correlations between neuropsychological and decisional capacity scores occurred most frequently with the Understanding dimension; however, the MacCAT-CR Understanding subscale has substantially more items and a much wider range relative to the other MacCAT-CR subscales, and similar subscale differences are also present within the MacCAT-T and CCTI.

The Understanding and Expression of a Choice subscales may not require equivalent complexity because the underlying constructs are not equivalently complex. The Appreciation and/or Reasoning components may warrant more comprehensive assessment than is provided by the commonly used decisional capacity scales, but there remains a lack of full consensus regarding specifically what type and range of item content is necessary and sufficient for Appreciation or Reasoning. Although the Understanding and Expression of a Choice subscales are generally comparable across a variety of decisional capacity instruments, it is not clear whether the underlying constructs for Appreciation and Reasoning subscales from various instruments actually measure fully parallel constructs across instruments (Gurrera et al., 2007; Moye et al., 2004a,b).

Despite the above limitations, the consistency of findings of significant cognitive–decisional capacity relationship in terms of consent to treatment as well as consent to research has clear pragmatic implications. Most notably, across neuropsychiatric and other medical populations, clinicians and researchers should be alert to the presence of cognitive deficits when providing informed consent. Although the majority of neuropsychological consent research has focused on patients with schizophrenia or dementia, the need to be mindful of the potential influence of cognitive dysfunction may be even more relevant when consenting people with conditions that may affect cognitive functioning but for which the neurocognitive deficits are not as salient (Awad et al., 2004; Bishop et al., 2003; Collie, 2005; Newman et al., 2001; Waldstein et al., 1991).

As is true for most functional tasks, the capacity to consent to research or treatment likely draws on a wide variety of cognitive functions (Marson, 2001); as cognitive impairment of any form might affect decisional capacity, researchers and clinicians should be alert to the possibility of impaired decisional capacity among cognitively impaired individuals, regardless of the specific form of that cognitive impairment. However, several authors have suggested that *specific* cognitive abilities, such as episodic memory, executive functions, or working memory, may be differentially important to specific dimensions of decisional capacity, or even to all four dimensions of decisional capacity (Dunn et al., 2007b; Marson & Harrell, 1999). Clarification of causal relationships between specific cognitive deficits and specific impairments in decisional capacity dimensions would foster efforts to develop compensatory consent procedures (Dunn & Jeste, 2001; Eyler & Jeste, 2006; Flory & Emanuel, 2004; Palmer, 2006).

The overall pattern seen in the bivariate correlations reviewed above were not strongly suggestive of differential affects of specific cognitive abilities on decisional capacity. From a conceptual standpoint, the Reasoning and Appreciation components of decisional capacity seem particularly likely to tap executive functions, but (perhaps for reasons related to the instrumentation issues described above), in several of the studies, tests of executive functions tended to have higher correlations with Understanding than with Appreciation or Reasoning (Casarett et al., 2003; Dymek et al., 2001; Marson et al., 1995a, 1996; Palmer et al., 2004).

Among studies that included multivariate models, many of the final significant models included scores from tests of episodic memory, confrontational naming, a variety of "executive functions," working memory, and psychomotor speed. However, across virtually all of the available studies, the multivariate analyses were exploratory in nature. The lack of *a priori* hypothesis-driven analyses likely reflects the relatively early stage of this line of research, as well as the fact that the neuropsychological data were often collected and presented in the context of examining other, more primary goals (such as establishing the level, frequency, and specific forms of impaired decisional capacity). Nonetheless, although atheoretical or statistically derived multivariate models may have predictive value and lay the groundwork for hypothesis generation, their explanatory value in terms of identifying the relative importance of potential independent variables tends to be very limited (Tabachnick & Fidell, 1996; Thompson, 1995). The potential unique roles of executive functions, working or episodic memory, or other specific cognitive abilities suggested by the frequent emergence of such variables in the reported multivariate models may be most appropriately viewed as the basis for *a priori* hypotheses for future research (cf. Hey et al., 2006)

One direction for potentially fruitful follow-up research would be to consider neuropsychological abilities in terms of more homogeneous constructs. For instance, as noted above, from a conceptual standpoint (as well as some of the patterns seen in the data reviewed above), it seems at least possible that impairment in "executive functions" could have a particularly deleterious influence on decisional capacity

(Dunn et al., 2007b; Marson & Harrell, 1999; Schillerstrom et al., 2007). But the term "executive functions" covers a wide array of more specific and only loosely related processes (Palmer & Heaton, 2000). It might therefore be helpful to deconstruct "executive functions" by examining and comparing the relative influence among specific types of executive abilities on decisional capacity. To the degree possible, these different executive skills should be measured with measures of comparable psychometric quality (cf. Delis et al., 2001; Jefferson et al., 2006). It may also be helpful to examine the pattern of errors on both the neuropsychological tests and decisional capacity scales on an individual level to identify specific processes underlying deficient performance (cf. Kaplan, 1988; Knight & Silverstein, 2001; Marson et al., 1999).

In addition to research addressing the above methodological considerations, there may be value in trying to more directly bridge empirical bioethics, cognitive psychology, and cognitive neuroscience (Northoff, 2006). There is a burgeoning literature on the effects of cognitive heuristics and biases (Tversky & Kahneman, 1974) on the choices and preferences of patients and physicians (Brewer et al., 2007; Fagerlin et al., 2005; Sedlmeier & Jaeger, 2007; Smith et al., 2006). Also, in a recent study from our research center, Eyler et al. (2007) examined the relationship of MacCAT-CR scores to (functional magnetic resonance imaging measured) brain activation patterns (Understanding scores were significantly correlated with hippocampal activation, but, contrary to the *a priori* hypotheses, not with activation in the inferior prefrontal cortex). Bringing together such lines of research with hypothesis driven neuropsychological studies of decisional capacity in a wider range of neurocognitive populations would be helpful in clarifying how patients actually make decisions in the consent process, what cognitive and contextual factors influence those decisions, and what neurological factors support (or impede) valid decision making.

In summary, over the past decade and a half, there has been rapid growth in the volume of empirical bioethics research, with particular emphasis on issues of informed consent and decisional capacity among neuropsychiatric and other medical populations at risk for impaired capacity. Further clarification of the role of specific neuropsychological abilities or deficits, contextual influences, and the underlying neurological processes or systems, in the informed consent process may foster consent as a meaningful dialogue rather than as a legalistic ritual.

ACKNOWLEDGMENTS

This work was supported, in part, by NIH grants AG028827 and MH64722. The authors express their appreciation to Nancy Stimson, Outreach Services Librarian at the University of California, San Diego Biomedical Library, for her assistance in conducting the literature search, and to Laura Dunn, M.D., for her thoughtful input, and comments on an earlier version of this manuscript.

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