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Research Consent Capacity Varies with Executive Function and Memory in Parkinson's Disease

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Abstract

Background—We examined the association between cognitive domains and research consent capacity in PD. Our hypothesis was that research consent capacity is best predicted by executive function.

Methods—A cohort of 90 PD patients and 30 normal older adults were administered the MacArthur Competence Assessment Tool for Clinical Research, Dementia Rating Scale-2, and the Montreal Cognitive Assessment. Experts classified patients as either “capable” or “not capable” of providing informed consent to participate in two clinical trials.

Results—MacArthur Competence Assessment Tool for Clinical Research Reasoning scores for both clinical trial types were most associated with executive functions and delayed recall. As scores on these domains improved, the odds of an expert rating of “capable of consent” increased.

Conclusions—These results extend our previous findings by demonstrating that memory and executive abilities appear closely associated with capacity when evaluated using either a structured interview or expert judgment of that interview.

Keywords

Parkinson's disease; decision-making; capacity; cognitive impairment; informed consent

Non-motor symptoms of Parkinson's disease (PD),[1] in particular cognitive changes,[2] may have significant impact on patient quality of life and daily function, including the ability to make decisions.[3] Using two research scenarios to examine the capacity to consent to research, we found that PD patients with normal cognition generally show preserved decisional abilities while patients with borderline range cognitive impairment had clinically significant deficits in their decisional abilities.[4] Although such associations between global cognition and capacity are informative, the cognitive domains that underpin these decision-making impairments remain not well understood.

Given their relevance for goal-directed behaviors, executive functions (i.e., attention, planning, organizing, working memory, and inhibitory control) have been linked to a number of everyday life contexts in PD, including motor control, multitasking, medication management, and driving (see [5] for review). Thus, the goal of the current study was to build on our previous study [4] by examining relationships between cognitive domain performances and research consent capacity. The hypothesis for the current investigation was that research consent capacity in PD is best predicted by executive function. We used the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR), a well-validated measure of decisional capacity[6], and two well known measures of cognitive performance in PD - the Dementia Rating Scale 2 (DRS-2)[7] and Montreal Cognitive Assessment (MoCA) [8].

Methods

Participants

We used non-proportional stratified sampling to enroll 90 patients with PD separated into three groups of 30 patients each using cut-points based on DRS-2 performance. Thirty

neurologically normal older adults served as a reference for all three patient groups' capacity scores. Eligible PD participants had: (1) a diagnosis of idiopathic PD by a movement disorder neurologist at the Udall Center for Parkinson's Research at the University of Pennsylvania and (2) performance on the DRS-2 total age- and education-corrected scaled score in one of the following three categories: “normal” DRS-2 ≥9, “borderline” DRS-2 of 6 to 8, and “impaired” DRS-2 ≤5. All patients were interviewed “on” medication.

Procedure

Two trained research assistants collected data over two days to limit fatigue and assure that the capacity interviewer was blinded to cognitive data. Subjects underwent two MacCAT-CR interviews, one describing an early phase, double-blind, placebo-controlled study to test the safety and tolerability of a PD medication,[9, 10] and the other describing a double-blind, sham-surgery controlled, randomized trial to test the safety and tolerability of injecting a growth factor gene into the brains of PD patients. Administration of the two MacCAT-CR interviews was counterbalanced to rule out order effects. Three physicians, each with at least five years of expertise in capacity assessment, viewed independently each capacity interview and rated whether the subject was capable of providing his or her own informed consent. [11, 12] A full description of our procedure, including descriptions of the MacCAT-CR, DRS-2, and MoCA domains is documented in the Supplementary Material.

Data Analyses

All analyses were performed using IBM SPSS v20.0. Our statistical approach is also documented in the Supplementary Material.

Results

Subject Characteristics—Demographic and clinical characteristics are documented in the Supplementary Material and Table S1. Because our normal controls showed nearly uniform research consent capacity and MoCA and DRS-2 scores at or near ceiling levels of performance, statistical analyses included only our patient sample (n=90).

DRS-2 Predictors of Capacity to Consent

MacCAT-CR and DRS-2—Spearman correlations between the DRS-2 subscales and patient scores on the MacCAT-CR drug and surgical trial capacity interviews (Table 1) suggest that the *Understanding* ability was consistently, and positively, related to all five DRS-2 subscale performances. Consistent with our expectations, however, the *Initiation-Perseveration* and *Memory* subscales were uniquely associated with the ability to *Reason* about the drug or surgical trials. *Initiation-Perseveration* and *Memory* subscales were also uniquely associated with *Appreciation*, but only on the drug trial.

Expert Ratings of Capacity and DRS-2 Subscale Performance—Overall, 60% (54/90) of PD patients were judged to be capable of giving informed consent for the drug trial by the expert raters. Direct logistic regression tested which of the five DRS-2 subscales were most associated with the expert evaluation of adequate decision-making capacity. A test of the full model with all five predictors was statistically significant, χ^2 (5) = 51.94,

p<0.001, indicating that the predictors, as a set, reliably distinguished between patients that the experts rated as capable or not capable. Overall classification accuracy by the DRS-2 subtests was moderate, with 75% and 83% of the patients correctly predicted as not capable or capable, respectively. Table 2 shows that only the DRS-2 *Initiation-Perseveration* and *Memory* subscales were significant predictors of expert rated capacity; the odds of being judged capable of consent by the expert raters increased 1.4× with each unit increase in the *Initiation-Perseveration* and or *Memory* subscales (DRS-2 Scaled Scores with Mean = 10, SD=3).

The logistic regression results for the surgical setting, in comparison to the drug trial, indicated that the expert raters were more conservative in assigning adequate capacity in this scenario. Across all PD patients, only 48% were judged capable to consent (43/90). The overall model was again significant, χ^2 (5) = 54.86, p< 0.001, indicating a significant effect of the 5 independent variables on the expert ratings of capacity (Table 2). Compared to the drug trial results, the DRS-2 subtests were slightly better at detecting patients that the experts judged to be not capable on the surgical trial, as the model identified 85% of patients judged to not have capacity. DRS-2 subtest prediction of capacity to consent was comparable to the drug trial at 79%. The *Initiation-Perseveration* and *Memory* subscales on the DRS-2 continued to predict expert capacity ratings. Overall, the odds of being judged capable of consent increased by 1.4× with each unit increase in the DRS-2 subscale scaled score (SS, Mean = 10, SD=3) for the *Initiation-Perseveration* or *Memory* subscales.

MoCA Predictors of Capacity to Consent

To test and validate our findings with the DRS-2 we conducted comparable analyses with the MoCA. Correlations between the MacCAT-CR abilities and MoCA subscales for PD participants (n=90) are reported in the Supplementary Material and Table S2. Spearman correlations between the MoCA subscales and patient scores on the MacCAT-CR capacity interview for both scenarios showed a pattern similar to the surgical trial results for the DRS-2 subscales. We subsequently confirmed with logistic regression that the MoCA *Visuospatial/Executive* subscale was a significant predictor of expert rated capacity. Overall, the odds of being judged capable of consent increased by 1.9× or 2.8× with each unit increase in *Visuospatial/Executive* score for the drug and surgical trial, respectively.

We then tested how well each of the MoCA subscales predicted expert rated capacity decisions with receiver operator characteristic (ROC) curves and area under the curve (AUC). We found that MoCA *Visuospatial/Executive* scores ≤ 3 (score range 0-5) showed sensitivity/specificity values of .86/.72 and .79/.79 for detecting the absence of expert-rated capacity for the drug and surgical trials, respectively. These results are further documented in the Supplementary Material.

Discussion

As noted in a meta-analytic review of executive function impairment in PD by Kudlicka and colleagues in this journal [13] such impairments are often observed in PD, yet anticipated empirical associations between those deficits and decision making in naturalistic contexts are “urgently needed”. Our research addresses this need by revealing associations between

cognitive domains that are often disrupted in early PD and a real world context of critical importance to patients, families, and clinical researchers – research consent capacity. The results are also in accord with findings of reduced medical treatment decision abilities in PD patients with mild cognitive impairment[14].

The DRS-2 Initiation and Perseveration and Memory subscales require acquisition and encoding of visual and verbal material, retrieval, organization, and cognitive flexibility[7]. These cognitive processes appear to overlap substantially with research decision-making abilities that include appraising study risks and benefits against the option to participate and consequences of participation. As such, the associations reported in the current study extend our previous results by showing that although overall cognitive total scores appear associated primarily with MaCAT-CR *Understanding*, executive functions and memory show more specific relationships with other demanding decision making abilities and predicted expert-rated capacity to consent to research. We subsequently validated our DRS-2 results using logistic regression and ROC curve analyses to show that the MoCA *Visuospatial/Executive* subscale was most predictive of expert capacity judgment. This suggests that this subscale may assess cognitive abilities deemed important by experts performing research consent capacity evaluation.

The value and relevance of our findings should be weighed against the following limitations. Data were gathered at an in-home interview in the context of two hypothetical clinical trials from participants who were familiar with research conducted in an academic medical center environment and who had approximately 15-16 years of education. In addition, we allowed subjects to retain the informed consent form during the capacity assessment. Other capacity assessment methods, such as giving persons a card with the relevant disclosure and then taking it away prior to assessing understanding, could yield different proportions of persons capable of consent and the degree to which memory or executive ability determines capacity performance.

Nevertheless, these results are important for research that recruits PD patients with borderline or mild cognitive impairment. They suggest the need to attend to deficits in memory and executive function, as subtle disruption in these areas increases the likelihood that a patient is not capable of giving consent. Indeed, people with PD MCI may also have reduced awareness of executive function impairment, potentially compromising safety and judgment in naturalistic settings [15]. In such cases, study precautions should be considered, including a structured assessment of capacity and asking the patient to designate a study partner. We remind readers and investigators that a brief measure of executive function such as the DRS-2 *Initiation-Perseveration* subscale, *Visuospatial/Executive* subscale of the MoCA, or even a brief screening instrument such as the MoCA is not a sufficient measure of capacity. Low performance on these scales, however, may serve as a prompt to consider additional protections to guard against the possibility of mistakenly judging a patient who is not capable as capable.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. Weintraub D, Doshi J, Koka D, et al. Neurodegeneration across stages of cognitive decline in Parkinson disease. Archives of neurology. 2011; 68:1562–1568. [PubMed: 22159053]
2. Troster AI, Troster AI. Neuropsychological characteristics of dementia with Lewy bodies and Parkinson's disease with dementia: differentiation, early detection, and implications for “mild cognitive impairment” and biomarkers. Neuropsychology Review. 2008; 18:103–119. [PubMed: 18322801]
3. Litvan I, Aarsland D, Adler CH, et al. MDS Task Force on mild cognitive impairment in Parkinson's disease: critical review of PD-MCI. Mov Disord. 2011; 26:1814–1824. [PubMed: 21661055]
4. Karlawish J, Cary M, Moelter ST, et al. Cognitive impairment and PD patients' capacity to consent to research. Neurology. 2013; 81:801–807. [PubMed: 23892706]
5. Dirnberger G, Jahanshahi M. Executive dysfunction in Parkinson's disease. Journal of neuropsychology. 2013; 7:193–224. [PubMed: 24007368]
6. Appelbaum, PS.; Grisso, T. The MacArthur Competence Assessment Tool - Clinical Research. Sarasota, FL: Professional Resource Press; 2000.
7. Jurica, PJ.; Leitten, CL.; Mattis, S. Dementia Rating Scale - 2 (DRS-2) Professional Manual. Lutz, FL USA: Psychological Assessment Resources, Inc.; 2001.
8. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society. 2005; 53:695–699. [PubMed: 15817019]
9. Karlawish JH, Casarett DJ, James BD. Alzheimer's disease patients' and caregivers' capacity, competency, and reasons to enroll in an early-phase Alzheimer's disease clinical trial. Journal of the American Geriatrics Society. 2002; 50:2019–2024. [PubMed: 12473015]
10. Rubright J, Sankar P, Casarett DJ, Gur R, Xie SX, Karlawish J. A memory and organizational aid improves Alzheimer disease research consent capacity: results of a randomized, controlled trial. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry. 2010; 18:1124–1132. [PubMed: 20808101]
11. Karlawish J, Kim SY, Knopman D, et al. Interpreting the clinical significance of capacity scores for informed consent in Alzheimer disease clinical trials. American Journal of Geriatric Psychiatry. 2008; 16:568–574. [PubMed: 18556397]
12. Kim SY, Appelbaum PS, Kim HM, et al. Variability of judgments of capacity: experience of capacity evaluators in a study of research consent capacity. Psychosomatics. 2011; 52:346–353. [PubMed: 21777717]
13. Kudlicka A, Clare L, Hindle JV. Executive functions in Parkinson's disease: systematic review and meta-analysis. Movement disorders : official journal of the Movement Disorder Society. 2011; 26:2305–2315. [PubMed: 21971697]
14. Martin RC, Okonkwo OC, Hill J, et al. Medical decision-making capacity in cognitively impaired Parkinson's disease patients without dementia. Movement disorders : official journal of the Movement Disorder Society. 2008; 23:1867–1874. [PubMed: 18759361]
15. Kudlicka A, Clare L, Hindle JV. Awareness of executive deficits in people with Parkinson's disease. Journal of the International Neuropsychological Society : JINS. 2013; 19:559–570. [PubMed: 23410890]

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Table 1

Correlations between the MacCAT-CR abilities and DRS-2 subscales for PD participants (n=90).

Scenario	Drug Study			Surgical Study		
	MacCAT-CR Ability			MacCAT-CR Ability		
DRS-2 Subscale	Understanding	Appreciation	Reasoning	Understanding	Appreciation	Reasoning
Attention	.30**	.13	.19	.32**	.24*	.20
Initiation & Perseveration	.54**	.44**	.37**	.55**	.34**	.33**
Construction	.22*	.11	.14	.25*	.33**	.04
Conceptualization	.29**	.26*	-.02	.41**	.17	.16
Memory	.58**	.57**	.29**	.51**	.39**	.36**

* $p<.05$,

** $p<.01$ (Spearman Correlations)

Table 2

Logistic regression of DRS-2 subscales predicting expert ratings of PD participants' (n=90) capacity to consent research involving a drug or surgical trial.

	B	*p*-value	Odds Ratio	95% CI %
Drug Study				
Attention	.23	.12	1.26	0.94-1.69
Initiation & Perseveration	.35	.001	1.41	1.15-1.74
Construction	-.03	.80	.97	.75-1.26
Conceptualization	.19	.15	1.20	.93-1.56
Memory	.31	.002	1.36	1.12-1.66
Surgical Study				
Attention	.27	.10	1.31	.95-1.80
Initiation & Perseveration	.31	.003	1.37	1.11-1.68
Construction	.07	.62	1.07	.82-1.40
Conceptualization	.22	.11	1.24	.95-1.62
Memory	.31	.002	1.36	1.12-1.66