Clinician Ratings of Cognition Predict Trajectory of Cognitive Decline in Newly Diagnosed Individuals with Parkinson's disease

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Abstract

Objective: The overall goal of this study was to learn whether clinician ratings of cognition would predict trajectory of changes in memory performance over a 5-year period in newly diagnosed individuals with Parkinson's disease (PD).

Background: Current methods for defining PD-mild cognitive impairment require self-reported cognitive concerns, in ideal situations, verified by a secondary source. The bulk of the existing literature has focused on the relationship between self-reported subjective and objective cognitive performance and yielded mixed findings. To date, the prognostic utility of clinician-rated subjective and objective cognitive decline using a well-validated measure remains elusive.

Methods: A secondary data analysis of the Parkinson's Progression Markers Initiative (PPMI) included 430 newly diagnosed patients with PD who were followed for up to five years. Memory was assessed using the Hopkins-Verbal Learning Test Retention Index (HVLT-R). Clinician rating for cognitive status was assessed using item 1 from the Unified Parkinson's disease Rating Scale (UPDRS) Part I. Clinician ratings were dichotomized as CC+ (range = 1 to 2) or CC- (score of 0). Motor severity was assessed using the UPDRS Part III, depression using the Geriatric Depression Scale-15, and working memory using Letter-Number-Sequencing. Multilevel models (MLM) examined the longitudinal relationship between clinician ratings of cognition and memory performance.

Results: Clinician ratings of cognition at baseline were associated with worse scores on an objective HVLT-R memory index (b=-4.60, p<.01). Moreover, those with worse working memory performance had worse average memory ability (b=-1.40, p<.001) and declined at a faster rate from occasion-to-occasion (b=-0.46, p<.01). Mood and motor severity did not explain individual differences or trajectories of change in memory performance.

Conclusions: Clinician ratings of cognition, as measured by the UPDRS Part I, are sensitive to declines in cognitive performance in de novo patients with PD. Future work should examine the diagnostic power of the UPDRS Part I in the evaluation of Parkinson's disease mild cognitive impairment and/or dementia.

Background

Current methods for defining PD-mild cognitive impairment require self-reported cognitive concerns, in ideal situations, verified by a secondary source (Litvan et al., 2012). The bulk of the existing literature has focused on the relationship between self-reported subjective and objective cognitive performance and yielded mixed findings. Some have found evidence for the existence of such a relationship (Hong et al., 2014) while others contend that the relationship is weak (Dujardin et al., 2010) and possibly confounded by mood (Santangelo et al., 2014). To date, the prognostic utility of clinician-rated subjective and objective cognitive decline using a well-validated measure in PD remains elusive. Thus, the overall goal of this study was to learn whether clinician ratings of cognition would predict trajectory of changes in memory performance over a 5-year period in newly diagnosed individuals with Parkinson's disease (PD).

Aims

1. Describe the pattern of five-year change in a memory performance.
2. Examine whether demographic factors explained individual differences in level of memory performance and individual differences in rates of change.
3. Examine whether clinician ratings of cognition explained individual differences in level of and rates of change in memory performance.
4. Examine whether motor severity, mood, and working memory performance explained individual differences in level of and rates of change in memory performance. In addition, since motor severity, mood, and working memory performance were assessed repeatedly, an additional question was whether occasion-to-occasion fluctuations in motor severity, mood, and working memory performance might predict occasion-to-occasion fluctuations in memory performance.

Subtle, cognitive decline informs individual differences in ***rate of change*** in memory performance.

Referral for more detailed neuropsychological testing, in the presence of cognitive concerns verified by a secondary source, is critical to monitor trajectories of cognitive change in PD.

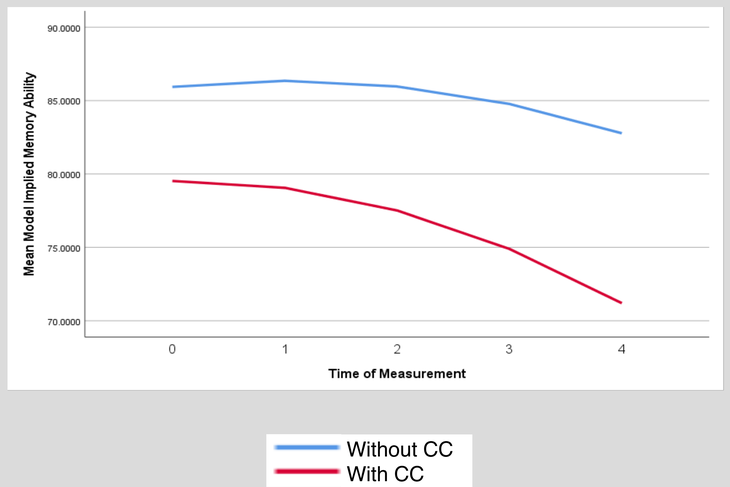
Table 1. Summary of Results

	Model 1	Model 2	Model 3	Model 4	Model 5
Fixed Effects					
Initial Status					
Intercept	83.63***	84.16***	105.18***	106.79***	89.96***
Age			-0.61***	-0.56***	-0.36***
Education			0.87**	0.72**	0.49*
Sex			5.55***	5.46**	4.59**
CC				-6.91***	-4.60**
Mean Motor					-0.16*
Time-Varying Motor					-0.09
Mean Mood					-0.77*
Time-Varying Mood					-0.58*
Mean WM					1.40***
Time-Varying WM					0.72**
Rate of Change					
Time		-1.01**	5.87*	6.12*	-0.43
Time-Squared+		-0.33	-0.42	-0.43	-0.22
Time X Age			-0.10**	-0.08**	-0.02
Time X Education			-0.08	-0.12	-0.19
Time X Sex			0.66	0.65	0.27
Time X CC				-1.19	-0.29
Time X Mean Motor					-0.03
Time X Mean Mood					-0.13
Time X Mean WM					0.46**
Random Effects					
Level 1					
Within Person	270.76***	250.10**	253.38***	253.035***	241.27***
Time-Varying WM					5.25*
Level 2					
In Initial Status	178.21***	184.33**	148.10***	141.17***	127.59**
In Rate of Change		6.86*	7.45**	7.24**	3.60
Fit Statistics					
Deviance	16377.66	16354.50	15313.14	15294.07	15192.60
AIC	16383.66	16366.50	15337.14	15322.07	15240.60
BIC	16400.27	16399.71	15402.80	15398.68	15371.87
η^2 Within	–	0.00	0.20	0.26	0.28
η^2 Between	–	0.08	0.08	0.08	0.11
η^2 Time Slope	–		0.00	0.03	0.52
R^2 Total	0.53	0.61	0.60	0.60	0.62

Notes: CC = Cognitive Complaints Group; WM = Working Memory; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; η^2, R^2 = Variance Explained. + Interactions with quadratic time could not be estimated as it had no reliable random variance. Model 1 = Unconditional Means Model; Model 2 = Unconditional Growth Model; Model 3 = Conditional Growth Model I with added Age, Education, Sex, Time X Age, Time X Education, and Time X Sex; Model 4 = Conditional Growth Model II with added SCI and SCI X Time; Model 5 = Conditional Growth Model III with added Person mean Motor Severity, Person mean Mood, Person mean WM, Time X Person mean Motor Severity, Time X Person mean Mood, Time X Person mean WM, time-varying Person centered motor severity, time-varying Person centered mood, and time-varying Person centered WM. All models estimated homogeneous variance and no covariance in repeated measures ("scaled identity"). Random effects were uncorrelated ("variance components").

***p < .001; **p < .01; *p < .05

Figure 1. Model implied individual differences in five-year change in memory ability for participants with and without subjective cognitive impairment (CC).



Discussion

After controlling for the effects of demographic factors on individual differences (i.e., older age, fewer years of formal education, female sex) and rates of change (i.e., older age), the presence of clinician ratings of cognition predicted poorer average memory performance over the study duration.

While motor severity and self-reported depressive symptoms slightly contributed to the prediction of worse average memory performance, only working memory contributed to both the prediction of worse average memory performance and increased rate of decline over the study duration.

In addition, slight occasion-to-occasion above-average improvements in self-reported depressive symptoms and working memory were associated with slight above-average improvements in working memory performance.

Notably, the final model explained more than half of the reliable individual differences in the rates of change in memory performance.

Limitations include memory performance was limited to a single list-learning task, and the exploration of the impact of clinician ratings on cognitive status in PD.

Findings suggest that clinician ratings of cognition, as measured by the UPDRS Part I, may inform future changes in level of memory performance.

Further, concurrent objective, albeit subtle, cognitive decline not only informs changes in level of memory performance but also informs individual differences in rate of decline in memory performance, highlighting the importance of referral for more detailed neuropsychological testing in the presence of cognitive concerns verified by a secondary source.