A Comparison of Depression Screening Tools in Parkinson's Disease and Normal Community Controls Using a Brain and Body Donation Database

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DEDICATION

To my family, who supported me unconditionally through all of the ups and downs and experiences of medical school, including the writing of this thesis.

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ABSTRACT

The purpose of this study was to review and compare a variety of depression inventories in Parkinson's disease (PD) and normal controls (NC) to look for patterns or trends to help with clinical management of these patients. The study population consisted of subjects enrolled in a brain and body donation program who were receiving annual neurological and neuropsychiatric assessments. Statistical models were applied to the data to compare trends between screening tools, medications, and demographics. The frequency of depression was greater in PD cases than NC across the inventories. The greatest frequency of positive screens came from the Neuropsychiatric Inventory (NPI). Because the NPI requires an informant to administer, and had the highest percent of positive screens in both PD and NC groups, this study suggests that a caregiver or partner may be a helpful addition in clinical practice during depression screening in elderly patients with and without PD.

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INTRODUCTION

The most common psychiatric complication in patients affected by Parkinson's Disease (PD) is depression. The prevalence of depression in PD is extremely variable between studies, ranging from 7-76%[12]. Depression is thought to be more prevalent in PD than the general elderly population. Screening accurately for depression in PD is clinically relevant as depression is associated with a reduced Health Related Quality of Life, a more rapid progression of motor deficits, and increased caregiver stress. Screening for depression clinically in a PD population may prove challenging as disease manifestations of PD often mimic depression, such as facial masking, change in appetite and insomnia.

Numerous screening scales are used clinically to assess depression in PD patients. Of these screening tools the validity of Beck Depression Inventory, Montgomery-Asberg Depression Scale, Geriatric Depression Scale, and Hamilton Rating Scale for Depression have been validated by previous studies for use in Parkinson's Disease[7,10]. Other published studies scrutinize screening tools individually or question the validity for use in the PD population but no studies were found that assess patterns of depression detection found between multiple

screening tools and compare patterns between PD patients and elderly controls. This study focuses on the patterns of depression found between various scales when comparing PD and NC subjects to gain knowledge to help with clinical management.

The scales in this study use a variety of informants. The Geriatric Depression Scale is self administered by the patient and is validated for screening purposes in normal elderly and PD patients[13]. The Hamilton Rating Scale for Depression is administered by the clinician, and is validated for use in PD and normal elderly[5]. The Unified Parkinson's Disease Rating Scale uses a combination of patient and clinician ratings. The Neuropsychiatric Inventory uses a caregiver informant[2].

The hypothesis of this study is that that there will be differences in the pattern of depression found between the various scales, considering that they ask about different symptoms and use different informants.

MATERIALS AND METHODS

Subjects in this study were drawn from the Banner Sun Health Research Institute Brain and Body Donation Program (BBDP), an IRB approved study of aging and neurodegenerative disease. Subjects met inclusion criteria if they were enrolled in the BBDP, had completed the necessary depression related assessments, carried the diagnosis of either clinically probable Parkinson's Disease (PD) or Normal Control (NC), and were included regardless of treatment for depression. Those with dementia, and other neurodegenerative disease were excluded. NC was defined as being free of neurodegenerative disease, including PD and Alzheimer's. The scales chosen for this study were the scales routinely administered as part of the Brain and Body Donation Program. The medications that the various groups were currently being prescribed were also analyzed.

Cut-off scores for the various scales were based on literature searches, with the most commonly used, or validated score, being the one used in this study. Depression in this study is defined as exceeding the pre-determined cutoff for each screening tool, but is not defined further because the scales are meant for screening not diagnosis. Scales that could be used for mixed purposes, without all

questions being relevant to depression, were only analyzed as to their relevance to depression.

The Geriatric Depression Scale (GDS) 30-item scale, with score range 0-30, was self administered by the patient, and was positive for depression with a score >9[6,7]. The Hamilton Rating Scale for Depression (HAMD), with range 0-50 , was administered by a clinician with a cutoff score >9[10]. Parts of the Unified Parkinson's Disease Rating Scale (UPDRS) were used based on their relevance to depression screening and included "motivation" and "depression". Answers were elicited through interview and clinical observation, with range 0-4, and a cutoff score of >1 was used[11]. Neuropsychiatric Inventory (NPI) categories relevant to depression were analyzed. An informant, usually the spouse, was interviewed separately from the subject for the NPI. Depression (NPI-D), Apathy (NPI-Apa), Appetite (NPI-App) and Irritability (NPI-I) were analyzed. For the NPI, depression was defined as any positive response[2], without further classification based on severity.

All statistical analyses were performed using SAS software Version 9.1. Means were compared by using the two-sample *t* test,

proportions were compared by using the Pearson chi-square test, and odds ratios were assessed by using logistic regression.

RESULTS

Subject demographics are shown in Table 1. The PD group was younger, and had more men than the NC group. There was not a statistical difference between MMSE scores, which differed by an average of 0.5. Medications used at the time of the examinations are shown in Table 2. There was no difference between groups in the percentage of patients treated with antidepressants.

A positive depression screen was defined as exceeding the pre-determined cut-off for each assessment which was individually determined by literature review. Positive depression screens were more common in the PD group than the NC, a pattern that was statistically significant in most scales (exceptions being NPI-Irritability and HAMD), and conserved between all scales. The GDS and the NPI had higher yield in the PD group than the HAMD or the UPDRS I. This is shown in Table 3.

Adjustment for age, MMSE and sex did not substantially alter the Odds Ratio (OR) for PD and GDS. However, adjustment for age, MMSE, and sex did reduce the OR for PD versus UPDRS I Depression, NPI-Q Apathy, and NPI-Q Irritability. This is shown in Table 4.

Table 1: Demographics			
	PD	Not PD	*P*
Age (y); mean (SD), N	75.2 (8.7), 92	81.6 (7.6), 518	<.001
MMSE; mean (SD), N	27.8 (2.3), 92	28.3 (1.8), 518	.02
Female	37/92 (40%)	328/518 (63%)	<.001
UPDRS III - Off; mean (SD), N	25 (15), 57	4.6 (6.7), 516	<.001
PD – Parkinson's Disease. MMSE – Mini Mental State Exam. *UPDRS III - Unified Parkinson's Disease Rating Scale part III*			

Table 2: Medications					
	PD	Not PD		PD	Not PD
Antidepressant	19/83 (23%)	106/482 (22%)	Dopaminergic Agent	82/83 (99%)	10/485 (2%)
SSRI	12/83 (14%)	54/483 (11%)	Cholinesterase Inhibitor	8/83 (10%)	26/485 (5%)
Other	12/83 (14%)	59/483 (12%)	Statin	24/83 (29%)	189/483 (39%)
Anxiolytic	10/83 (12%)	41/484 (8%)	Vitamin E	14/82 (17%)	73/475 (15%)
Sedative Hypnotic	10/83 (12%)	43/485 (9%)	NSAID	16/82 (20%)	86/483 (18%)
Typical Antipsychotic	1/83 (1%)	0/482 (0%)	Estrogen	2/82 (2%)	58/480 (12%)
Atypical Antipsychotic	2/83 (2%)	3/483 (1%)			
PD- Parkinson's Disease. SSRI – selective serotonin reuptake inhibitor. NSAID – Nonsteroidal anti-inflammatory drug					

Table 3: Depression Rating Scales			
	PD	Not PD	*P*
UPDRS I			
Depression; mean (SD), N	0.36 (0.62), 92	0.21 (0.49), 517	.01
Motivation; mean (SD), N	0.44 (0.76), 91	0.18 (0.48), 518	<.001
Hamilton Depression Scale; mean (SD), N	3.8 (3.2), 89	2.8 (3.3), 507	.02
Geriatric Depression Scale; mean (SD), N	6.9 (5.2), 86	4.5 (4.5), 504	<.001
UPDRS I			
Depression > 1	7/92 (8%)	16/501 (3%)	.04
Motivation > 1	6/91 (7%)	19/518 (4%)	.19
Hamilton Depression Scale > 9	5/89 (6%)	23/507 (5%)	.66
Geriatric Depression Scale > 9	29/86 (34%)	65/504 (13%)	<.001
NPI-Q			

Depression	32/92 (35%)	115/518 (22%)	.009
Apathy	21/92 (23%)	61/518 (12%)	.004
Irritability	25/92 (27%)	127/518 (25%)	.59
Appetite	21/92 (23%)	64/518 (12%)	.008

PD – Parkinson's disease. UPDRS I – Unified Parkinson's Disease Rating Scale part I. NPI-Q – Neuropsychiatric Inventory Questionnaire.

Table 4: Depression adjusted for age, MMSE, and sex.				
	Crude OR	**Adjusted OR**	**95% CI**	***P***
UPDRS I				
Depression > 1	2.6	1.65	0.57 to 4.8	.35
Motivation > 1	1.85	1.60	0.56 to 4.6	.38
Hamilton Depression Scale > 9	1.25	1.54	0.53 to 4.5	.43
Geriatric Depression Scale > 9	3.4	3.3	1.88 to 5.9	<.001
NPI-Q				
Depression	1.87	1.53	0.90 to 2.6	.11
Apathy	2.2	1.61	0.86 to 3.0	.14
Irritability	1.15	0.80	0.46 to 1.40	.44
Appetite	2.1	1.77	0.97 to 3.2	.06
Abbreviations in table 4: MMSE – Mini Mental State Exam. OR – Odds ratio. CI – Confidence Interval.				

DISCUSSION

The purpose of this study was to review and compare patterns of depression findings between scales in NC and PD, which has not been done previously, to gain knowledge that can be applied clinically. The scales used in this study are intended for screening purposes only, not for diagnosis, or classification of depression. The overall trends in the data were consistent between the four scales with the PD group showing more positive screens than NC. This differed from the hypothesis in that it was expected that different patterns would be found between screening tools as they ask about different symptoms, and use different informants.

This conserved pattern suggests that PD patients suffer from depression with greater frequency than NC, which is consistent with previous literature. It also suggests that depressive symptoms are similar among PD versus NC, considering individual scales ask about different depressive symptoms, but the overall pattern was conserved. Age, gender, and cognitive status seem to play a role in the pattern seen because of the decrease in odds ratio when these were controlled for in all scales but the GDS, the only scale that was self administered by the patient.

The NPI, an informant based scale, and GDS, a patient reported scale, had the highest rates of positive screens in both PD and NC. The GDS has been validated for use in PD in previous studies, while the NPI has not. This high number of positive screens using the NPI suggests that it may be beneficial to the clinician to involve a caregiver in the assessment of the patient, in both PD patients or in a general primary care setting where more healthy adults without neurological disease are seen. With high numbers of NCs exceeding the cutoff for depression across multiple scales, there are also implications for the primary care setting where the majority of patients come alone to doctor visits. It may be best to not only rely on one screening modality for every patient, but make use of strengths and weaknesses of the different methods.

It is notable that equal percentages of PD and NC were being treated for depression, despite the higher rate of positive depression screens across all inventories in the PD group. This may suggest that depression is undertreated in PD compared to the general elderly population. Overall it may be beneficial to consider lowering the threshold for treatment of depression taking into account clinician suspicion, caregiver concern or patient disclosure.

Limitations to the study include not having a gold standard comparison to determine the validity of the scales. The HAMD and GDS have been validated for use in depression and serve as a rough estimate for the actual prevalence of depression in this population. However, the goal of the study was to compare patterns and trends to make recommendations to the use of screening scales in initial evaluation of depression, not determine accuracy of the scales. A positive screening test should prompt further clinical evaluation, and is not a substitute for DSMIV criteria. The statistical differences in demographics of the groups reflect the demographics of this Brain Bank Population and follow the expected trend in a cohort of PD and elderly controls.

FUTURE DIRECTIONS

This thesis showed similar patterns of depression across multiple inventories, meaning the PD group consistently had higher rates of positive screens than the NC. It showed that the presence of an informant in both Parkinson's Disease and healthy controls is a valuable addition to the screening process. This leads to further inquiry regarding patterns of depression screening in other disease states such as Alzheimer's disease, and how the presence of an informant might also impact the number of positive screens in that population.

It would be interesting to repeat this study using a gold standard of diagnosis of depressions, such as the involvement of clinical psychiatrist and DSM-IV criteria, to compare the patterns of depression screening with the actual prevalence of depression in this population.

Despite depression being more prevalent in Parkinson's Disease than healthy elderly individuals, the treatment between the groups is similar. It would be beneficial to find ways to increase the treatment of depression in Parkinson's Disease, which would likely start with more screening modalities in this population.

CONCLUSIONS

The pattern of depression identification between Parkinson's Disease patients and Normal Control is similar across the scales analyzed in this study, meaning the PD group had higher percentages of positive screens using all screening modalities. Informant information seems particularly useful for screening, particularly for elderly controls, based on the high prevalence using the NPI. Self-administered tools for the office seem to be a good starting point for patients or controls which could be followed by a clinician driven semi-structured interview. Caregiver/informant driven information should be explored further as to relevance for clinical practice.

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