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Neuropsychological Findings in Clinically Atypical Autopsy Confirmed Corticobasal Degeneration and Progressive Supranuclear Palsy

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Corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) are distinct neurodegenerative disorders with tau pathology [1] that are classified within the group of atypical parkinsonisms. Typical clinical features of CBD (ie, the corticobasal syndrome or CBS) include asymmetric Parkinsonism, dystonia, myoclonus, alien limb phenomenon, and apraxia [2] whereas postural instability, early falls, relatively symmetric Parkinsonism, and vertical supranuclear gaze palsy are typically associated with PSP pathology (ie, the progressive supranuclear palsy syndrome or PSPS) [2]. However, overlapping and atypical clinical features of these diseases can lead to clinical diagnoses that do not always concur with the ultimate pathological diagnosis.

While neuropsychological studies in PSPS and CBS to date provide us with a starting point to understand cognitive status in these groups, the degree of heterogeneity and the overlap in neurologic findings, which can lead to autopsy diagnoses that vary from clinical diagnoses, calls into question the accuracy of existing reports on cognitive findings in CBS and PSPS. The purpose of the current study was to address this limitation by investigating the neurocognitive profiles of clinically atypical, histopathologically confirmed, cases of CBD and PSP.

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We identified all cases pathologically evaluated between January 1st 1998 to December 31st 2006 that (1) had a brain autopsy examination and received a histopathological diagnosis of CBD or PSP (N=57); (2) had completed an antemortem 4-hr neuropsychometric test; (3) was evaluated by a specialist in Movement Disorders or Behavioral Neurology at our institution, (4) did not receive a definitive diagnosis of CBS or PSPS at the time of neuropsychological testing and (5) does not meet current published criteria for PSP if the pathological diagnosis was PSP [2] or does not meet published criteria for CBS if the pathological diagnosis was CBD [2].

Nine histopathologically confirmed cases of CBD and eight cases of PSP were identified that met our inclusion criteria. Demographic information, clinical diagnoses at the time of neuropsychological testing, and neuropsychological test data were obtained by review of medical charts. For cases that had multiple neuropsychological evaluations, only the test results associated with the patient's initial presentation to the clinic was used in the present analyses. Neuropsychological measures [3] were administered by trained psychometrists under the supervision of a senior neuropsychologist. Global cognitive status was assessed using the Kokmen Short Test of Mental Status [4]. Published age corrected normative data was used when available to convert raw scores to standard scores. Hoehn and Yahr stage [5] was determined at the time of the initial neuropsychological evaluation to provide a gross estimate of motor functioning. The pathological protocol and diagnoses was standard and based on accepted and published criteria. Nonparametric tests (Mann Whitney U tests) were conducted using the SPSS statistical package with the significance level for all analyses set to $p < .05$

Table 1 provides the demographic characteristics for the CBD and PSP groups. The CBD group was significantly younger than the PSP group, $t(15) = 2.78$, $p = .014$.

None of the 17 cases received a specific isolated clinical diagnosis of CBS or PSPS at the time of neuropsychological testing. Of those with CBD pathology, three were diagnosed with frontotemporal dementia (FTD), while the other six were diagnosed as FTD with Parkinsonism, apraxia of speech, posterior cortical atrophy, asymmetric chorea with cognitive impairment and two with the non-specific diagnosis of cognitive impairment. By the time of the last clinical evaluation prior to death, only two of the nine CBD cases were diagnosed as CBS. Of those with PSP pathology, two were diagnosed as apraxia of speech, while the other six were diagnosed as atypical Parkinsonism, FTD, Alzheimer's disease, CBS vs. PSPS vs. Pick disease, and two with progressive dementia. By the time of the last clinical evaluation prior to death, only three of the eight PSP cases were diagnosed as PSPS; one case was diagnosed as CBS and another case as PSPS vs. CBS.

Subjects from both the CBD and PSP groups tended to have the most difficulty on tasks of learning and word fluency (Table 2). Outside of these domains, the PSP group tended to display low average, or better, performance. The CBD group also performed lower relative to the normative group on verbal comprehension, perceptual organization, and cognitive flexibility. Comparisons of neuropsychological performance across groups revealed no significant differences in this relatively small sample size.

In the current study we demonstrate no significant differences in the neurocognitive profiles of pathologic confirmed cases of CBD and PSP with atypical clinical presentations.

Neuropsychometric testing showed that the PSP and CBD groups scored lower than the normative sample on learning, and letter and category fluency. The CBD group also performed lower relative to the normative group on verbal comprehension, perceptual organization, and cognitive flexibility. These findings are not surprising since in both CBD and PSP there is underlying regional anatomic destruction by the pathological processes. The frontal subcortical

regions are affected in both CBD and PSP which may account for worse performance on tests of learning, processing speed, and executive function.

There were no statistically significant differences observed comparing CBD and PSP. The lack of differences between the two groups may have been due to the relatively small sample size, although it is more likely that neuropsychological tests are not different between clinically atypical CBD and PSP. Therefore, refined diagnosis of CBD and PSP with atypical presenting clinical features is unlikely to be aided with neuropsychological tests alone, but will require the use of multiple indicators including clinical features, neuropsychological tests, and structural and functional neuroimaging.

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Table 1

Sample Characteristics

	PSP	CBD	Total
Age*	75.38 (6.69)	63.78 (9.90)	69.24 (10.21)
Education	13.63 (2.72)	13.56 (3.71)	13.59 (3.18)
Mental Status (STMS)	30.60 (4.66)	27.50 (4.47)	28.69 (4.62)
Gender			
Female	62.5 %	66.7 %	64.7 %
Male	37.5 %	33.3 %	35.3 %
Dominantly affected limb side			
Right	40.0 %	57.1 %	50.0 %
Left	40.0 %	28.6 %	33.3 %
Both	20.0 %	14.3 %	16.7 %
Symptom onset to 1st testing	2.89 (2.10)	1.69 (1.10)	2.25 (1.70)
Symptom onset to death	7.00 (2.36)	5.55 (2.38)	6.23 (2.41)

Note: Mean (SD) or percentages are presented. PSP = Progressive Supranuclear Palsy, CBD = Corticobasal Degeneration. Age and education are reported as the mean (standard deviation). Gender and affected limb side are reported as percentages (# of patients). STMS = Short Test of Mental Status. Time to 1st testing = mean time in years (SD) from symptom onset to first neuropsychological evaluation. Symptom onset to death = mean time in years (SD) from onset of symptoms to death.

* = significant difference between groups.

Table 2

Neurocognitive Performance by Group

	PSP		CBD	
Domain	**Mean**	**SD**	**Mean**	**SD**
Verbal Comprehension	95.17	12.79	84.86	13.54
Perceptual Organization	89.50	9.42	81.50	17.52
Immediate Memory				
Story Learning	5.88	2.64	6.50	4.46
Design Learning	6.57	3.55	5.67	2.73
Word List Learning	7.63	1.99	6.13	2.94
Delayed Memory				
Story Recall	5.63	2.87	7.67	3.20
Design Recall	6.71	3.68	5.00	2.19
Word List Recall	8.75	3.69	7.00	2.00
Word list recognition	8.00	2.77	8.38	2.66
Language				
Confrontation Naming	9.00	2.51	8.57	4.35
Category Fluency	5.57	2.76	3.71	2.36
Letter fluency	6.43	2.50	4.43	2.57
Auditory Comprehension	9.00	4.24	8.71	2.43
Attention/Concentration	9.00	1.41	3.75	2.06
Visuospatial Ability				
Block Design	8.00	2.09	6.80	.837
Processing Speed	82.50	2.12	64.33	11.06
Executive Functioning				
Cognitive Flexibility	9.00	1.41	6.50	.70

Note: Most values are reported as scaled scores (Mean = 10, SD = 3). Verbal comprehension, perceptual organization, and processing speed are standard scores (Mean = 100, SD =15)