A Study to Identify the Correlates of Pseudobulbar Affect in Patients with Parkinsonian Disorders and ALS

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BACKGROUND

- Pseudobulbar affect (PBA) is a frontal disinhibition syndrome associated with inappropriate laughter and crying to minor stimulus, independent of affective disturbance[1].
- PBA has been primarily studied in amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS)[2,3]. Recent studies have demonstrated PBA in other neurological conditions[4] such as Parkinson's disease (PD), and atypical parkinsonism (aP) such as corticobasal degeneration (CBD), progressive supranuclear palsy (PSP), multiple system atrophy (MSA)[5,6].
- We have observed that PBA is more common in parkinsonian patients with associated cognitive impairment. However PBA has been observed in ALS patients with or without cognitive impairment

OBJECTIVE

- Our objective is to determine whether cognitive and psychiatric co-morbidities correlate with PBA in patients with PD, atypical parkinsonism (aP) and ALS.

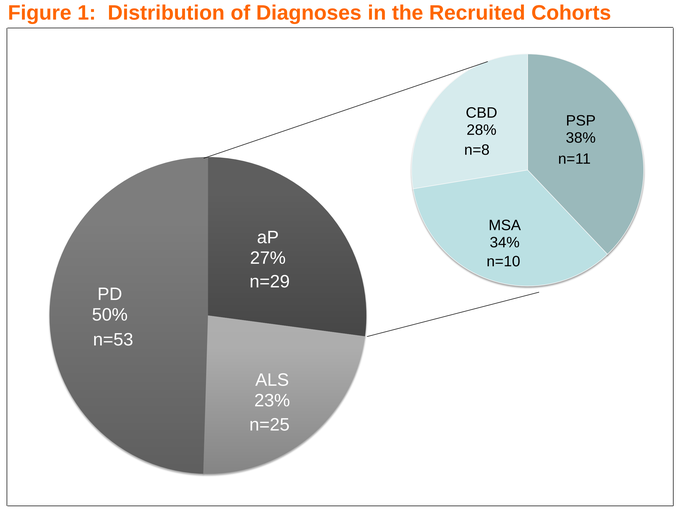
METHODS

We aimed to enroll 50 PD patients, 30 ALS patients and 30 aP (10 PSP, 10 MSA and 10 CBD). In this IRB approved study patients were recruited from the Parkinson's disease or ALS centers.

- Any person with a definite diagnosis of PD, aP or ALS identified through clinical practice was eligible to participate.
- Exclusion criteria:
  - >30% of all questionnaire was incomplete
  - Patients with advanced disease who are unable to communicate answers
  - Non-English speaking patients
- Participating subjects completed a series of self-report questionnaires:
  - Center for Neurological Study-Lability Scale for PBA (CNS-LS)
  - Beck Depression Inventory-II (BDI)
  - State-Trait Anxiety Inventory- Trait (STAI)
  - Self and Other Apathy Evaluation Scales (AES)
  - The Short Form-36 quality of life measure (SF36-QOL)

RESULTS

Figure 1: Distribution of Diagnoses in the Recruited Cohorts



- There are no intragroup differences between the 3 subgroups recruited on demographic and individual questionnaires.

RESULTS (continued…)

Table 1: Patient Demographics

		PD	ALS	aP	p-value
	Age (years)	63.4 ± 10.5	61.6 ± 8.7	68.8 ± 7.9	0.36
	Duration of Illness	5.0±4.8	2.4±1.6	3.9±2.3	0.54
Gender	Male	30	13	17	0.795
	Female	23	13	12	
Education	<12 years	2	2	2	0.675
	High School	10	6	4	
	Some college	23	9	11	
	>16 years	13	2	7	
Ethnicity	Caucasian	48	21	25	0.694
	Hispanic	2	3	2	
	African American	2	1	1	
	Other	1	0	1	

- There are no statistically significant differences in demographics between the aP subgroups measured through Chi-square/ t-tests and ANOVA.

Figure 2 and Table 2: Prevalence of PBA and Mean Questionnaire Scores By Cohorts

	PD	ALS	aP	p-value
MoCA	25.1±3.94	23.3± 3.30	21.4±5.07	0.001**
PBA	10.1±3.83	11.2±7.00	11.7±5.23	0.378
BDI	10.7±9.36	11.3±6.64	14.1±7.74	0.192
STAI	36.4±10.54	35.9±8.03	37.9±10.1	0.733
Self AE	54.6±6.67	53.9±7.66	50.2±10.2	0.058*
Other AE	53.9±8.32	49.8±9.92	47.6±12.4	0.38

**statistically significant
* trend towards statistical significance

- There were no statistically significant differences in degree of PBA as measured on the CNS-LS scores between groups
- There is increased cognitive impairment in the ALS and aP groups compared to the PD cohort.

Table 2: Cognitive and Psychiatric correlates of PBA between groups

	PD		ALS		aP	
	PBA	p-value	PBA	p-value	PBA	p-value
MoCA	-0.193	0.166	-0.288	0.163	0.062	0.751
BDI	0.349	0.011**	0.090	0.670	0.337	0.074*
STAI	0.456	0.001**	0.253	0.222	0.456	0.013**
Self AES	0.033	0.816	0.050	0.812	0.002	0.993
Other AES	-0.79	0.630	0.386	0.084	0.052	0.798
SF36 PCS	-0.157	0.267	0.110	0.602	0.231	0.228
SF36 MCS	-0.286	0.038**	-0.129	0.540	-0.314	0.097*

SF36 PCS = SF36- QOL physical component score; SF 36- QOL mental component score
**statistically significant; * trend towards statistical significance

Poster available for download.

RESULTS (continued…)

- There was a positive correlation with PBA and anxiety scores in PD and aP groups, this association was not found in the ALS group.
- Depression scores and Mental Health QOL impairments positively correlate with PBA scores only in the PD group.
- MoCA scores did not correlate with PBA for any of groups; however there are observed differences between the groups.

DISCUSSION

- This study demonstrates that, despite its definition, PBA correlates with affective disturbance in PD and aP patients but not in ALS patients.
- The results suggest that individuals with parkinsonian disorders and PBA symptoms should be evaluated and/or treated for co-morbid mood problems.
- Previous studies have reported increased burden of illness[7] associated with PBA and an association between depression and PBA in a movement disorders population[5]. In addition to these observations our study also demonstrates an association between PBA and anxiety in parkinsonian patients.
- Limitations of this study include:
  - Small sample size
  - Exclusion of patients with advanced disease due to impaired language and communication in all groups
  - MoCA scores may be artificially reduced to disease specific symptoms affecting writing

CONCLUSION

- The proposed mechanism of PBA is disruption of inhibitory signals descending from the cerebral cortex to motor regions of the brainstem implicated in the regulation of emotional output[8].
- Our findings suggest that an alternate pathophysiological mechanism for PBA may be present in ALS compared to parkinsonian patients.
- Future studies should be directed toward evaluation of the pathophysiologic mechanism of PBA in each neurological conditions.
- Additional testing of mood effects of dextromethorphan-quinidine (an FDA-approved treatment for PBA[9]), or effect of antidepressants on PBA should be considered in in patients with parkinsonian conditions.

REFERENCES

1. Moore, S.R., Gresham, L.S., Bromberg, M.B., Kasarkis, E.J., Smith, R.A., 1997. A self report measure of affective lability. J Neurol Neurosurg Psychiatry. 63, 89-93.
2. Pioro EP, Brooks BR, Cummings J, et al. Dextromethorphan Plus Ultra Low-Dose Quinidine Reduces Pseudobulbar Affect. Annals of neurology 2010;68:693-70
3. Garnock-Jones KP. Dextromethorphan/quinidine: in pseudobulbar affect. CNS drugs 2011;25:435-445.
4. Work SS, Colamonico JA, Bradley WG, Kaye RE. Pseudobulbar affect: an under-recognized and under-treated neurological disorder. Advances in therapy 2011;28:586-601.
5. Strowd R, Cartwright M, Okun M, Haq I, Siddiqui M. Pseudobulbar affect: prevalence and quality of life impact in movement disorders. Journal of Neurology 2010;257:1382-1387.
6. Alvarez-Gonzalez E, Maragoto-Rizo C, Arteche-Prior M, Perez-Parra S, Carballo M, Alvarez-Gonzalez L. [A clinical and epidemiological description of a series of patients diagnosed as suffering from progressive supranuclear palsy]. Revista de neurologia 2004;39:1006-1010.
7. Colamonico J, Formella A, Bradley W. Pseudobulbar affect: burden of illness in the USA. Advances in therapy 2012;29:775-798.
8. Parvizi J, Coburn KL, Shillcutt SD, Coffey CE, Lauterbach EC, Mendez MF. Neuroanatomy of Pathological Laughing and Crying: A Report of the American Neuropsychiatric Association Committee on Research. J Neuropsychiatry Clin Neurosci 2009;21:75-87
9. Garnock-Jones KP. Dextromethorphan/quinidine: in pseudobulbar affect. CNS drugs 2011;25:435-445.