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Substance Use History in Behavioral-Variant Frontotemporal Dementia versus Primary Progressive Aphasia

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Abstract

Background—As older adults are prone to cognitive disorders, the interaction of the fields of substance use and misuse and cognitive neuroscience is an emerging area of research. Substance use has been reported in some subtypes of frontotemporal dementia (FTD), such as behavioral variant frontotemporal dementia (bvFTD). However, characterization of substance use in other subtypes of FTD, such as primary progressive aphasia (PPAPH), is unknown.

Objective—The objective of this baseline analysis was to explore whether any measures of substance use history differed significantly among bvFTD (n = 842) and PPAPH (n = 526) in a large national dataset.

Design/Methods—The National Alzheimer's Coordinating Center's (NACC) Uniform Data Set (UDS) study is a national dataset that collects data on patients with various cognitive disorders and includes some questions on substance use. We used each substance use variable as the outcome and the FTD subtype as the predictor.

Results—Total years smoked cigarettes, age when last smoked cigarettes, and average # of packs/day smoked when participants smoked, and any recent, remote, or combined recent/remote history of alcohol abuse or drug abuse did not significantly differ between the bvFTD and PPAPH subtypes (all p-values > 0.001). A significantly greater percentage of participants smoked in the

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last 30 days in the bvFTD subtype (10.4%, *n* = 834) compared to the PPAPH subtype (3.3%, *n* = 517) ($p < 0.001$).

Discussion—Clinical providers in both the dementia and substance use fields are encouraged to screen for and monitor substance use in all FTD subtypes.

Keywords

frontotemporal; dementia; cigarette smoking; alcohol; substance use; drug

INTRODUCTION

Substance use disorders are a growing area of concern in the older adult population [1–6]. Previous literature in older adults shows that these disorders range from prescription misuse disorders to illicit substance use. As older adults are also prone to cognitive disorders, the interaction of the fields of substance use and misuse and cognitive neuroscience is an emerging area of research [7–16]. One particular cognitive disorder that is increasingly becoming recognized is frontotemporal dementia [FTD] [17–23]. A characteristic feature of FTD is behavioral disinhibition, which can be manifested by substance use. Substance use has been reported in some FTD subtypes [24] such as the behavioral variant (bvFTD) subtype. For example, there are several reports of alcohol and other drug use in those with bvFTD [25–29].

However, characterization of substance use in other subtypes of FTD, such as primary progressive aphasia (PPAPH), is unknown. Patients with PPAPH initially present with changes in expressive and receptive language, and later on, some patients may develop behavioral abnormalities more typical of frontal lobe dementias[17]. Disinhibition, impulsivity and executive dysfunction, which are constructs highly relevant to substance use disorders [14, 30–32], can be a part of PPAPH [33–36]. Since disinhibition, impulsivity and executive dysfunction are some common features of substance use disorders and FTD, it is reasonable to theoretically consider that patients with other subtypes of FTD might be prone to substance use disorders. But, to our knowledge, there is no previous literature comparing substance use history among the FTD subtypes. Substance use disorders could precede, follow, or occur concomitantly with FTD, and causal factors could play or not play a role in the relationship between substance use disorders and FTD.

The National Alzheimer's Coordinating Center's (NACC) Uniform Data Set (UDS) study is a national dataset [37] that collects data on patients with various cognitive disorders, such as Alzheimer's dementia and FTD, and includes some questions on substance use. Thus, the NACC UDS dataset can be used to characterize substance use history in the various subtypes of FTD. The aim of this baseline analysis was to explore whether any measures of substance use history differed significantly among 2 subtypes of frontotemporal dementia in the NACC UDS dataset: behavioral variant frontotemporal dementia (bvFTD) and primary progressive aphasia (PPAPH). Since behavioral disinhibition, impulsivity and executive dysfunction are some common features between substance use disorders and FTD subtypes, we hypothesized that participants diagnosed with bvFTD would have a similar substance use history as participants diagnosed with PPAPH.

METHODS

Study Setting and Measures

Data were extracted from NACC's UDS [37–40]. Data were contributed by 29 Alzheimer Disease Centers (ADCs) from across the United States. The data collection used for this analysis began in September 2005 and had a freeze date of March 2014.

The variables in this analysis were from the baseline initial visit packet form [41] when a participant was enrolled in the UDS study and the derived variables packet [42]. All UDS forms are freely accessible on the NACC website [43]. Demographic data were from form A1. Clinical and substance use data were from form A5, form B2 and form B6. Medication data were from form A4, and neurocognitive data were from form C1.

As of the March 2014 data freeze, the number of participants in the entire NACC UDS was 29,913. For this analysis, we selected those participants with one of the following two final primary diagnoses (form D1): behavioral variant frontotemporal dementia (n = 842) and primary progressive aphasia (n = 526).

Statistical Analysis

We estimated and tested all statistical models using Stata/SE version 13 (College Station, TX). We considered p values < 0.001 as statistically significant due to the number of analyses conducted. Parametric and non-parametric analyses were used as appropriate. To increase the sample size for the analyses, we combined recent and remote histories of medical disorders, alcohol and drug abuse, and we collapsed the packs per day of cigarette smoking from 5 categories to 3 categories. We also individually analyzed "recent/active history of alcohol abuse," "remote/inactive history of alcohol abuse," "recent/active history of drug abuse," and "remote/inactive history of drug abuse." Because there is the potential of missing data when data are being collecting from 29 different ADCs, we present the varying sample size on which every analysis is based.

For the main substance use analyses that had continuous variables, we estimated and tested an ANCOVA model. For the main substance use analyses that had categorical variables, we used either logistic regression or multinomial regression. We used each substance use variable as the outcome and the FTD subtype as the predictor. For all analyses, we adjusted for demographic (age, education, sex), clinical (Parkinsonian features), medication (antidepressant use, antipsychotic use), and site (Alzheimer Disease Center) variables.

RESULTS

Table 1 presents demographic differences. The bvFTD subtype had a significantly lower mean age and years of education compared to the PPAPH subtype. A significantly lower percentage of females were in the bvFTD subtype compared to the PPAPH subtype. Compared to the PPAPH subtype, a significantly greater percentage in the bvFTD subtype lived in some type of assisted home and a significantly lower percentage in the bvFTD subtype lived independently.

Table 2 presents clinical differences. Compared to the PPAPH subtype, a significantly greater percentage in the bvFTD subtype had Parkinsonian features and used an antidepressant or an antipsychotic. The bvFTD subtype had a significantly greater Mini-Mental State Examination raw score compared to the PPAPH subtype.

Table 3 presents substance use differences. After adjusting for demographic, clinical and medication variables, the two FTD subtypes were similar on most measures of substance use history. The bvFTD group does have higher percentages than the PPAPH subgroup across most measures of substance use history, but the sizes of these effects are not consistently large. A significantly greater percentage of participants smoked in the last 30 days in the bvFTD subtype compared to the PPAPH subtype ($p < 0.001$).

DISCUSSION

In this analysis of substance use history among two subtypes of FTD in a national dataset, we found that participants with the bvFTD and PPAPH subtypes were similar on most measures of substance use history. A significantly greater percentage of participants smoked in the last 30 days in the bvFTD subtype compared to the PPAPH subtype ($p < 0.001$).

These results suggest that substance use may need to be screened more carefully in patients diagnosed with the PPAPH subtype of FTD, not just bvFTD which has received more attention in the literature. Clinical treatment providers working with patients diagnosed with either FTD subtype may need to continue screening for and monitoring substance use patterns even after a FTD diagnosis is made – not assuming that substance use will remit with increased age and risk underdiagnosing a substance use disorder in an older adult [2, 44–48]. The one significant finding of a greater percentage of participants smoked in the last 30 days in the bvFTD subtype compared to the PPAPH subtype is consistent with the characteristic behavioral disinhibition of the bvFTD subtype. Future research should more formally explore cigarette smoking patterns among the various FTD subtypes.

Since substance use history has not been reported in these two subtypes of FTD, we wondered if the results in Table 3 were or were not comparable to those with an Alzheimer's dementia diagnosis. Since the NACC UDS dataset includes participants with an Alzheimer's diagnosis, we briefly report the substance use history in those with a probable Alzheimer's diagnosis: total years smoked (mean 25.1, $n = 2,894$), age when last smoked (mean 45.6, $n = 2,650$), any history of alcohol abuse (5.9%, n = 7,416), any history of drug abuse (0.8%, $n = 7,425$). Though a formal comparison of FTD with Alzheimer's dementia is beyond the scope of this manuscript, the history of alcohol abuse and drug abuse in those with probable Alzheimer's dementia is at least comparable to those with either subtype of FTD. Future research should more formally explore substance use patterns in FTD versus Alzheimer's dementia.

This analysis has several strengths. First, we were able to analyze a large number of participants with these two subtypes of FTD from a national dataset, which has not been done before to our knowledge. Second, we controlled for demographic, clinical, medication and site covariates in the main substance use analyses, due to having access to such data

from a national dataset. Finally, we had a significant percentage of women represented in the sample, which allowed us to control for sex in the main analyses.

Inevitably, this analysis has several limitations. First, this analysis was a post-hoc analysis, and the original UDS study was not designed to analyze substance use history in cognitively impaired populations. Second, there are no details on quantity or pattern of alcohol and drug use, as the questions in the original UDS study were categorical in nature. The assessments of alcohol and drug abuse and co-occurring psychiatric disorders were relatively crude. For example, detailed questions such as “alcohol abuse within the past 30 days” or “drug abuse within the past 30 days” were not included, which would be important in assessing whether the disinhibition of FTD is more likely to result in new onset substance use or relapse. Third, the substance use history was captured by retrospective recall, and analyses based on retrospective recall have their own design limitations [49–52]. Fourth, since we analyzed data at one time point, we cannot comment on causality or reverse causality between substance use and the FTD diagnosis. The baseline assessment could have been administered prior to, following, or concomitantly with the emergence of the first of FTD. Finally, most of the participants were Caucasian, and these results cannot be generalized to other ethnicities.

CONCLUSIONS

In summary, we found that participants with the bvFTD and PPAPH subtypes were similar on most measures of substance use history. Substance use disorders are a growing area of concern in the older adult population, and clinical treatment providers in both the dementia and substance use fields are encouraged to screen for and monitor substance use patterns in all various FTD subtypes. Future directions including further studies confirming or refuting these results, using standardized substance use interviews/scales to more accurately capture substance use history, and recruiting a more ethnically diverse sample.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic differences between bvFTD and PPAPH at the baseline visit.

	bvFTD[a]	PPAPH[b]	Wilcoxon rank-sum or Pearson Chi-Square
	Mean (S.D.[c]) or %		
Age (years)	63.1 (10) *n* = 842	66.9 (8.6) *n* = 526	*p* < 0.001
Years of education	15.0 (3.2) *n* = 820	15.6 (2.8) *n* = 511	p = 0.004
Female	35.4% *n* = 842	49.4% *n* = 526	*p* < 0.001
Caucasian	93.6% *n* = 829	95.8% *n* = 518	*p* = 0.095
Hispanic	3.5% *n* = 833	2.3% *n* = 519	*p* = 0.22
Married	78.7% *n* = 840	80.2% *n* = 521	*p* = 0.50
Live in a retirement community, assisted living, skilled nursing, or other home	12.7% *n* = 841	6.3% *n* = 524	*p* < 0.001
Able to live independently	19% *n* = 832	38.6% *n* = 524	*p* < 0.001
Lives alone	9.4% *n* = 840	13.9% *n* = 526	*p* = 0.011

[a] bvFTD = behavioral variant frontotemporal dementia

[b] PPAPH = primary progressive aphasia

[c] S.D. = standard deviation

Table 2

Clinical differences between bvFTD and PPAPH at the baseline visit.

	bvFTD	PPAPH	Wilcoxon rank-sum or Pearson Chi-Square
	Mean (S.D.) or %		
Heart attack/cardiac arrest	3.7% *n* = 841	3.4% *n* = 526	*p* = 0.798
Hypertension	42.2% *n* = 839	41.4% *n* = 524	*p* = 0.776
Parkinsonian features	7.1% *n* = 837	1.9% *n* = 525	*p* < 0.001
Seizures	3.2% *n* = 836	3.6% *n* = 522	*p* = 0.664
Diabetes	10% *n* = 838	6.5% *n* = 523	*p* = 0.025
Thyroid disease	12.2% *n* = 837	15.9% *n* = 516	*p* = 0.053
Hachinski Ischemic total score	0.92 (1.3) *n* = 831	1.0 (1.4) *n* = 525	*p* = 0.995
Geriatric Depression Scale total score	3.4 (3.3) *n* = 637	3.3 (2.8) *n* = 407	*p* = 0.428
Antidepressant	52.8% *n* = 839	40.9% *n* = 521	*p* < 0.001
Antipsychotic	19.5% *n* = 839	4% *n* = 521	*p* < 0.001
Mini-Mental State Examination raw total score	21.4 (7.8) *n* = 748	20.2 (8.0) *n* = 474	*p* = 0.004

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Table 3

Substance use differences between bvFTD and PPAPH at the baseline visit.

		bvFTD	PPAPH	ANCOVA[a], Logistic Regression[a], or Multinomial Regression[a]
		Mean (S.D.) or %		
Total years smoked cigarettes		24.4 (15.0) *n* = 328	20.9 (13.9) *n* = 167	$F(1,446) = 4.29$, $p = 0.0388$
Age when last smoked cigarettes (i.e., quit)		42.2 (12.7) *n* = 251	40.7 (13.8) *n* = 159	$F(1,365) = 0.89$, $p = 0.345$
Smoked cigarettes in the last 30 days		10.4% *n* = 834	3.3% *n* = 517	odds ratio = 0.35, 95% CI (0.20, 0.63), $p < 0.001$
Average # of packs/day smoked when participants smoked	1 cigarette – <½ pack	26.9% *n* = 324	28.5% *n* = 165	all coefficients with $p > 0.05$
	½ – < 1 pack	32.4% *n* = 324	34.5% *n* = 165	
	>1 pack	40.7% *n* = 324	37% *n* = 165	
Any history of alcohol abuse		12.4% *n* = 839	7.5% *n* = 522	odds ratio = 0.75, 95% CI (0.48, 1.16), $p = 0.199$
Recent/active history of alcohol abuse		2.2% *n* = 839	1.2% *n* = 522	odds ratio = 0.63, 95% CI (0.23, 1.74), $p = 0.371$
Remote/inactive history of alcohol abuse		10.3% *n* = 839	6.3% *n* = 522	odds ratio = 0.80, 95% CI (0.49, 1.28), $p = 0.347$
Any history of drug abuse		3.7% *n* = 836	1.7% *n* = 519	odds ratio = 1.03, 95% CI (0.42, 2.56), $p = 0.941$
Recent/active history of drug abuse		0.7% *n* = 836	0.4% *n* = 519	odds ratio = 1.30, 95% CI (0.19, 8.71), $p = 0.787$
Remote/inactive history of drug abuse		3.0% *n* = 836	1.4% *n* = 519	odds ratio = 0.95, 95% CI (0.34, 2.67), $p = 0.924$

[a] All analyses adjusted for: age, education, sex, Parkinsonian features, antidepressant use, antipsychotic use, site