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Demographic and neuropsychiatric factors associated with off-label medication use in frontotemporal dementia and Alzheimer's disease

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Abstract

Objectives—Off-label medication use for treating cognitive impairments and neuropsychiatric symptoms occurs in frontotemporal dementia (FTD) and Alzheimer's disease (AD). We compared use of cognitive and psychiatric medications in FTD and AD and evaluated the relationship between neuropsychiatric symptoms and medication use.

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CONTRIBUTION:
Dr. Tartaglia - study concept and design and analysis and interpretation, wrote manuscript.
Dr. Hu - acquisition of data, analysis.
Drs. Mehta and Neuhaus - analysis and interpretation.
Drs. Yaffe, Miller and Boxer - critical revision of the manuscript for important intellectual content.
Dr. Boxer - obtained funding, designed and supervised the study, and wrote the manuscript.

Methods—Cognitive and psychiatric medication use, demographic variables and Neuropsychiatric Inventory (NPI) subscale symptoms were obtained from the National Alzheimer's Coordinating Center Uniform Data Set (n=3958, 8.1% FTD). Bivariate statistics and logistic regressions were calculated to evaluate which demographic or NPI subscale symptoms predicted medication use.

Results—Although cognitive medication was used more commonly in AD (78%) it was also commonly used off-label in FTD (56%). Psychiatric medications were in greater use in FTD than AD (68 vs. 45%, respectively, $p<0.001$). In FTD, cognitive medication use was associated with elevated NPI elation scores and psychiatric medication use was associated with history of prior psychiatric disease. In AD, demographic variables (white, longer disease duration, higher education, more severe disease or being male) were most predictive of cognitive medication use while having psychiatric disease, being white, having longer disease duration, being younger, greater disease severity, being disinhibited or anxious were associated with psychiatric medication use. Off-label antipsychotics were used in 4.7% of patients with AD and 10% of patients with FTD.

Conclusions—Our results revealed significant off-label medication use in both FTD and AD. A notable finding from this study was the lack of consistent relationships between medication use and neuropsychiatric symptoms across the two illnesses.

Keywords

acetylcholinesterase inhibitors; antipsychotics; Alzheimer's disease; frontotemporal dementia

Introduction

Alzheimer's disease (AD) and frontotemporal dementia (FTD) are common causes of dementia that are associated with considerable morbidity and mortality as well as caregiver distress. FTD is the most common cause of dementia in patients under the age of 60 [1–3], however, there are no FDA approved medications for treatment of FTD [4, 5]. In contrast, modestly effective cognitive treatments including acetylcholinesterase inhibitors (AchI; donepezil, galantamine and rivastigmine) and the NMDA-receptor antagonist, memantine [6] are approved for the symptomatic treatment of AD [6].

Patients with AD and FTD usually display different symptoms with AD classically presenting with a slowly progressive episodic memory deficit. Deficits in cholinergic neurotransmission are believed to be central to the development of AD[7] and the efficacy of AChI for stabilizing cognitive function has been directly related to central effects on acetylcholinesterase function [8, 9]. However, patients with AD can also often develop behavioral impairments, such as agitation and irritability; often these are the most troublesome symptoms for the caregivers [10, 11]. There are no FDA approved drugs for behavioral and psychological symptoms in any dementias but there is often off-label use. There is some evidence that donepezil and Memantine have some benefit on behavioral and psychological symptoms in AD [11,12] but often psychiatric medications including antipsychotics, antidepressants, and anxiolytics are used off-label to treat behavioral symptoms at all levels of disease severity[13, 14].

In FTD syndromes, behavioral and neuropsychiatric symptoms feature prominently. In behavioral variant (bvFTD), the most common of the FTD syndromes, the earliest and most conspicuous symptoms involve behavioral abnormalities that cause significant impairment and caregiver burden [15–19]. There are no FDA approved drugs for these symptoms and physicians routinely prescribe off-label AChIs and memantine [20, 21] although now both AChI and Memantine have been reported to worsen behavior in bvFTD patients [22,23]. Selective serotonin reuptake inhibitors (SSRIs) and antipsychotic medications are also commonly used in bvFTD to target behavioral abnormalities, although RCT are scarce to support their efficacy [24].

We previously compared the use of FDA-approved medications for AD as well as other psychiatric medications in AD and FTD in the State of California Alzheimer's Disease Centers as well as a handful of other research centers involved in a longitudinal natural history study of FTD [20]. We found frequent off-label use of both AD and psychiatric medications in both AD and bvFTD, however the study was limited by the heterogeneous nature of the data sources, precluding the identification of potential factors accounting for such medication use. The aim of the current study was therefore to compare use of cognitive and psychiatric medication and to identify demographic and neuropsychiatric factors associated with use of each type of medication in two patient groups that can have overlapping signs and symptoms: bvFTD and AD. We sought to test the hypothesis that use of both cognitive (donepezil, rivastigmine, galantamine and memantine) and psychiatric medications (antidepressants, antipsychotics, anxiolytics, and mood stabilizers) would be associated with specific neuropsychiatric symptoms for which the medications were initially approved, regardless of the associated dementia syndrome.

Methods

Data consisted of variables from a Uniform Data Set (UDS) collected from more than 30 Alzheimer's disease centers (ADC) throughout the United States and catalogued at the National Alzheimer's Coordinating Center (NACC). A full description of the NACC dataset has been previously provided [25, 26]. ADCs are National Institute on Aging (NIA)–funded centers that enroll patients via self-referral or referral from a community health care provider. Many are university-affiliated memory disorders clinics in urban settings. These centers have been collecting data on their patients from 1984 to 2010 and the NACC has been a central repository since 1999.

Patients

The study cohort consisted of 3958 (3638 AD (79%) and 320 FTD (6%)) participants who had a diagnosis of probable AD according to the National Institute of Neurological Diseases and Stroke–Alzheimer's Disease and Related Disorders Association criteria or its equivalent [27], or probable bvFTD according to Neary criteria[28] at the initial visit. The data was collected between Sept. 2005 and Dec. 2009. In addition to a diagnosis of probable AD or bvFTD, case were included only if they had medication use data, a Neuropsychiatric Inventory (NPI) score[29], as well as all the following data (vascular disease, race, disease

duration, education, age, sex, psychiatric disease, and Clinical Dementia Rating sum of boxes score). Patients with a history of stroke or traumatic brain injury were also excluded.

Variables Analyzed

The main predictor variables analyzed were the presence or absence of each of the following NPI symptoms: delusions, hallucinations, agitation, dysphoria, anxiety, apathy, irritability, euphoria, disinhibition, aberrant motor behavior, night-time behavior disturbances, and appetite and eating abnormalities[29].

The following variables were also included as predictors: presence or absence of history of psychiatric disease and vascular disease. Psychiatric disease included past or recent: anxiety disorder, depression, obsessive compulsive disorder (OCD), Post-traumatic stress disorder (PTSD), psychosis/schizophrenia/ hallucination, bipolar, attention deficit hyperactivity disorder (ADHD), and substance abuse. Vascular disease included past and/or recent: heart attack or cardiac arrest, atrial fibrillation, angio/endarectomy/stent, bypass, pacemaker, congestive heart failure, transient ischemic attack, smoker, hypertension, hypercholesterolemia, Vitamin B12 deficiency, and diabetes. The original Clinical Dementia Rating sum of boxes (CDR-SB) [30] assesses overall level of disease severity and CDR-SB scores are useful for comparing disease severity between AD and FTD [31]. Additional predictor variables included: age, gender, race, education level, and disease duration. Age was calculated using the patients' date of birth and the date of the visit. Race was coded as white (Caucasian) or non-white (African-American, Asian/Pacific Islander, Native American, Hispanic/Latino, other and unknown) for the baseline characteristics analysis.

The outcome variables analyzed included cognitive medications and 15 other psychoactive medications (either over-the-counter or prescription) being used at the initial visit. These were recorded based on Multum drug codes. The cognitive medications analyzed were: memantine and acetylcholinesterase inhibitor (AChI) donepezil separately and then as a group with rivastigmine, galantamine and memantine.

Psychiatric medications were categorized as antipsychotic, mood stabilizer, antidepressant and anxiolytic medications. Use of the following antipsychotic agents was recorded: promethazine, risperidone, olanzapine, quetiapine, haloperidol, clozapine, prochlorperazine, aripiprazole, perphenazine. Mood stabilizers included: carbamazepine, valproic acid, lithium or lamotrigine. Antidepressants included: citalopram, sertraline, mirtazapine, trazodone, paroxetine, venlafaxine, maprotiline, amitriptyline, fluoxetine, dulozetine, nortriptyline, doxepin, clomipramine, fluvoxamine, escitalopram, and bupropion. Anxiolytic medications consisted of lorazepam, clonazepam, alprazolam, temazepam, zolpidem, eszopiclone, doxylamine, flurazepam, midazolam, phenobarbital, triazolam, chlordiazepoxide, oxazepam, buspirone, diphenhydramine, hydroxyzine, meprobamate, and ramelteon.

Statistical Analysis

The objective of the study was to compare neuropsychiatric symptoms and medication usage in AD and FTD and determine any interaction between the symptoms and medication. A two sample Student t-tests were used to compare demographic variables (age, disease

duration, years of education) between AD and FTD patients. Chi-square tests were used to compare the categorical variables (gender, race, comorbities (psychiatric and vascular), cognitive and psychiatric medication use, and NPI variables) between AD and FTD patients.

We fit binary logistic regression models separately for AD and FTD patients to evaluate the relationship between medication usage and NPI correcting for vascular disease, race, disease duration, education, age, sex, psychiatric disease, and CDR sum of boxes.

We included random center effects in the logistic regression models to accommodate potential correlation of responses within centers. Analyses were conducted using SPSS (version 17.0).

Results

Demographics and other descriptive variables for the FTD group as compared to the AD group are shown in Table 1. The FTD patients were younger, had a higher proportion of whites and were more highly educated ($p < 0.001$) than the AD patients. The FTD group had higher CDR sum of boxes as well as CDR global scores, indicating greater disease severity. The AD group had a higher proportion of females than the FTD group ($p<0.001$) and although vascular risk factors were slightly more prevalent in the AD group, this may not be clinically significantly different (86 vs. 81%, $p=0.04$).

Consistent with the early predominance of behavioral symptoms in this disorder, history of psychiatric disease was more common in the FTD group (56 vs. 46%, $p= 0.002$). In addition, neuropsychiatric abnormalities including agitation, anxiety, elation, apathy, disinhibition, irritability, motor disturbances, nighttime behaviors and appetite changes assessed using the NPI were more prevalent in FTD than AD (Table 1). There was no difference in prevalence of delusions, hallucinations or depression between the two groups.

Medication use

Use of cognitive medications approved by the FDA for treatment of AD was more common in the AD than FTD group (Table 2). The opposite was true for psychiatric medications, as there was greater use in the FTD group (Table 2). In the AD group, the most frequently used cognitive medication was donepezil followed by memantine, whereas the opposite was observed in FTD with greater usage of memantine than donepezil. 56% of AD subjects as compared to 26% of FTD subjects took donepezil, whereas 43% of AD subjects vs. 33% of FTD subjects took memantine. Use of each class of psychiatric medication (antidepressants, antipsychotics, anxiolytics or mood stabilizers) was more common in the FTD than the AD group.

In the multivariate model controlling for vascular disease, race, disease duration, education, age, sex, history of psychiatric disease and disease severity (CDR-SB) variables, type of dementia predicted use of cognitive medications (as a group), as well as donepezil and memantine individually. When controlled for these variables the model indicated that cognitive medications were more commonly used by AD patients than FTD patients ($p < 0.001$) and the probability of FTD patients being on cognitive medications was less than AD

patients (Table 2). Patients with FTD had a higher probability of being on psychiatric medications as a group, as well as antidepressants, antipsychotics, anxiolytics and mood stabilizers individually compared to patients with AD (Table 2).

Predictors of specific medication use in Frontotemporal Dementia

To identify neuropsychiatric symptoms and other factors associated with the use of cognitive and psychiatric medications in FTD, we used binary logistic regression analysis in the AD and FTD groups separately with models that included disease severity (CDR sum of boxes), NPI, the presence of vascular disease, disease duration as well as demographic variables. Figure 1a and 1b; Table 3.

Cognitive medications—In FTD, cognitive medication use was most strongly associated with the presence of elevated elation scores on the NPI (OR 2.38, [95% CI: 1.21, 4.70] p=0.012).

Donepezil—There were no statistically significant associations with donepezil use.

Memantine—Memantine use was associated with higher levels of education (OR 1.14 [95% CI: 1.04, 1.25] p=0.004) and greater disease severity (higher CDR-SB; OR 1.07, [95% CI: 1.02, 1.14] p=0.011). FTD patients were less likely to be on memantine if they were female, (OR 0.56, [95% CI: 0.32, 0.95] p=0.031), or had some NPI Disinhibition (OR 0.53, [95% CI: 0.30, 0.95] p=0.032).

Psychiatric medication—Having a history of psychiatric disease was associated with higher probability of any psychiatric medication use, (OR 4.47, [95% CI: 2.49, 8.05] p<0.001), whereas psychiatric medication use was lower in patients with elevated irritability on the NPI, (OR 0.53, [95% CI: 0.29, 0.97] p=0.039).

Antidepressants—Use of the most commonly prescribed type of psychiatric medication, antidepressants, was also associated with a history of psychiatric disease (OR 4.14, [95% CI: 2.41, 7.12] p<0.001). The odds of taking an antidepressant were lower if irritability was present on the NPI, (OR 0.51, [95% CI: 0.29, 0.91] p=0.022).

Antipsychotic medications—Antipsychotic medication use was associated with greater disease severity as indicated by higher CDR-SB scores (OR 1.21, [95% CI: 1.1, 1.3] p<0.001), but was less common in individuals with elevated elation (OR 0.22, [95% CI: 0.05, 0.99] p=0.048) or apathy scores on the NPI (OR 0.23, [95% CI: 0.10, 0.77] p=0.014).

Mood stabilizers—Mood stabilizer use was associated with FTD patients' age; younger patients were less likely to be on mood stabilizers, (OR 0.89, [95% CI:0.81, 0.97] p=0.01). The odds of mood stabilizer use were higher if they had appetite changes (OR 5.37, [95% CI:1.03, 27.9] p=0.046) but lower with nighttime behaviors on the NPI (0.145, [95% CI: 0.02, 0.90] p=0.038).

Anxiolytics—There were no statistically significant associations with anxiolytic use.

Prediction of medication use in Alzheimer's Disease

Cognitive medications—In AD, we found that demographic variables were most predictive of medication use. The odds of taking any cognitive medication were higher if the patients were white (OR 1.78, [95% CI: 1.44, 2.20] p<0.001), had a longer disease duration (OR 1.08, [95% CI: 1.05, 1.11] p<0.001), were more educated (OR 1.04, [95% CI: 1.01, 1.07] p<0.001), had more severe disease (higher CDR-SB; OR 1.07, [95% CI: 1.04, 1.10] p<0.001) or were male (OR 1.23, [95% CI: 1.034, 1.46] p=0.019). The odds of being on cognitive medication were lower if they displayed elevated depression on the NPI (OR 0.90, [95% CI: 0.66, 0.98] p=0.027) or were older (0.97, [95% CI: 0.96, 0.98] p<0.001).

Donepezil—Donepezil use was associated with the presence of disinhibition (OR 1.24, [95% CI: 1.03, 1.49] p=0.024) and irritability on the NPI (OR 1.18, [95% CI: 1.00, 1.38] p=0.044). AD patients were less likely to take donepezil if they had vascular risk factors (OR 0.82, [95% CI: 0.67, 0.99] p=0.043), were younger (OR 0.98, [95% CI: 0.97, 0.99] p<0.001), or had evidence of depression on the NPI (OR 0.76, [95% CI: 0.65, 0.89] p=0.001).

Memantine—The odds of taking memantine were greater if subjects were white (OR 2.17, [95% CI: 1.76, 2.68] p<0.001), had a longer disease duration (OR 1.03, [95% CI: 1.00, 1.05] p=0.017), were more educated (OR 1.05, [95% CI: 1.03, 1.07] p<0.001) or had more severe disease (CDR-SB; OR 1.12, [95% CI: 1.09, 1.14] p<0.001). The odds of taking memantine were lower with higher NPI irritability scores (OR 0.84, [95% CI: 0.71, 0.99] p=0.041) and increasing age (OR 0.98, [95% CI: 0.97, 0.98] p<0.001).

Psychiatric medications—The model also predicted psychiatric medication use in AD. The odds of taking a psychiatric medication were greater if patients had psychiatric disease, (OR 9.71, [95% CI: 8.17, 11.5] p<0.001), were white (OR 1.53, [95% CI: 1.22, 1.91] p<0.001), had longer disease duration (OR 1.04, [95% CI: 1.01, 1.07] p=0.002), were younger (OR 0.98, [95% CI: 0.98, 0.99] p<0.001), had greater disease severity (OR 1.05, [95% CI: 1.03, 1.07] p<0.001), were disinhibited (OR 1.33, [95% CI: 1.07, 1.64] p=0.009) or anxious (OR 1.24, [95% CI: 1.04, 1.48] p=0.016).

Psychiatric medications were used in 21% of patients with AD without a psychiatric diagnosis while 28% of patients with a psychiatric diagnosis were not treated with a psychiatric medication.

Antidepressants—The odds of being on an antidepressant were greatest if AD patients had a history of psychiatric disease, (OR 11.50, [95% CI: 9.61, 13.75] p<0.001), and were also higher if they were white (OR 1.84, [95% CI: 1.45, 2.33] p<0.001), had vascular risk factors (OR 1.32, [95% CI: 1.04, 1.67] p<0.001), had longer disease duration (OR 1.03, [95% CI: 1.01, 1.06] p=0.009), were younger (OR 0.98, [95% CI: 0.97, 0.99] p<0.001), had greater disease severity (CDR-SB; OR 1.03, [95% CI: 1.01, 1.06] p=0.004), or displayed disinhibition on the NPI (OR 1.38, [95% CI: 1.11, 1.72] p=0.004).

Antipsychotics medications—Antipsychotic medication use was associated with greater disease severity (higher CDR-SB; OR 1.19, [95% CI: 1.15, 1.24] p<0.001),

psychiatric disease, (OR 1.56, [95% CI: 1.08, 2.26] p=0.019), hallucinations (OR 1.58, [95% CI: 1.03, 2.42] p=0.035) or apathy on the NPI (OR 1.48, [95% CI: 1.03, 2.12] p=0.035). Antipsychotic use was less common in individuals with elevated disinhibition on the NPI (OR 0.64, [95% CI: 0.42, 0.97] p=0.036).

Mood stabilizer—The odds of being on a mood stabilizer were higher with greater disease severity (CDR-SB; OR 1.19 [95% CI: 1.00, 1.24] p= 0.039), or the presence of delusions (OR 3.86, [95% CI: 1.24, 12.0] p=0.020) and lower if subjects were white (OR 0.33, [95% CI: 0.11, 0.99] p<0.047).

Anxiolytics—The odds of being on an anxiolytic were higher if a patient had a history of psychiatric disease, (OR 2.47, [95% CI: 1.87, 3.27] p<0.001), was anxious (OR 1.52, [95% CI: 1.16, 1.98] p=0.002), or displayed abnormal nighttime behaviors, (OR 1.34, [95% CI: 1.02, 1.76] p=0.039). The odds of anxiolytic use were lower in individuals who were apathetic (OR 0.62, [95% CI: 0.47, 0.81] p<0.001).

Discussion

We found that more than half of all FTD patients at specialized NIH-designated dementia research centers take cognitive medications approved for the treatment of AD, despite no evidence of efficacy from randomized placebo-controlled clinical trials. The only double-blind, placebo-controlled clinical trial of a cholinesterase inhibitor in FTD showed no clear benefit[32]. An open-label study of donepezil in 12 patients with FTD found that caregivers of the treated patients endorsed a higher level of disinhibition and compulsiveness that reversed upon discontinuation of donepezil [22]. Recently, Memantine too has been shown to be of no benefit in FTD [23].

As expected, a higher percentage of AD patients took cognitive medications. Although none of the demographic or neuropsychiatric variables examined were associated with cognitive medication use in FTD, in AD race, years of education and disease severity were strongly associated with cognitive medication use.

Psychiatric medication, both antipsychotics and antidepressants were more common used in FTD than in AD despite delusions, hallucinations and depression being similarly prevalent in the two groups. In both disorders, the recent or past history of psychiatric disease was the strongest predictor of psychiatric medication as a group and antidepressant use, whereas greater disease severity was associated with antipsychotic medication use. It is unclear whether psychiatric symptoms were the presenting feature of the dementia and so misdiagnosed and treated with psychiatric medications or alternatively, psychiatric medications were prescribed to target psychiatric and behavioral symptoms that arise later in the course of dementia. Given the presence of these psychiatric and behavioral symptoms despite taking psychiatric medications indicates the ineffectiveness of the medications and warrants further investigation.

Consistent with previous studies, we found that neuropsychiatric abnormalities as measured by the NPI were more common in FTD than AD [33–35]. However, AD patients also displayed

frequent neuropsychiatric abnormalities including agitation in 35%, apathy in 44%, disinhibition in 20%, and irritability in 39%, yet such symptoms were less frequently associated with psychiatric medication use than in FTD. Because neuropsychiatric symptom severity was not included in our analyses, it is possible that the more frequent use of psychiatric medications in FTD reflected greater severity of symptoms.

A notable finding from this study was the lack of consistent relationships between medication use and neuropsychiatric symptoms across the two illnesses. For example, the presence of apathy was associated with a higher probability of being on an antipsychotic in AD, but a lower probability of antipsychotic use in FTD. Disinhibition was associated with increased odds of taking donepezil or an antidepressant in AD, but decreased probability of taking an antipsychotic. However, in FTD, the presence of disinhibition was associated with decreased odds of memantine use. These findings suggest that our analyses identified neuropsychiatric variables that: 1) may have provided a rationale for prescription of different medications, 2) were symptoms possibly attributable to medication use, or 3) were possibly disease-associated symptoms present in individuals who were treated with such medications. An analysis of longitudinal changes in medication use, cognitive and neuropsychiatric status could help to distinguish between these possibilities.

The most significant limitation of this study was our inability to determine causality between neuropsychiatric symptoms and medication use due to the cross-sectional nature of the analysis. Future study of the longitudinal data available for a subset of this cohort will be necessary to determine the reasons for medication use.

In conclusion, psychiatric medications are commonly used off label in FTD and AD but despite their frequent use many distressing behaviors persist in both disorders. In FTD, cognitive medications are also frequently used off-label with no clear benefit. It is clear that more effective pharmacologic and non-pharmacologic interventions are needed to manage the neuropsychiatric symptoms in dementia, particularly FTD.

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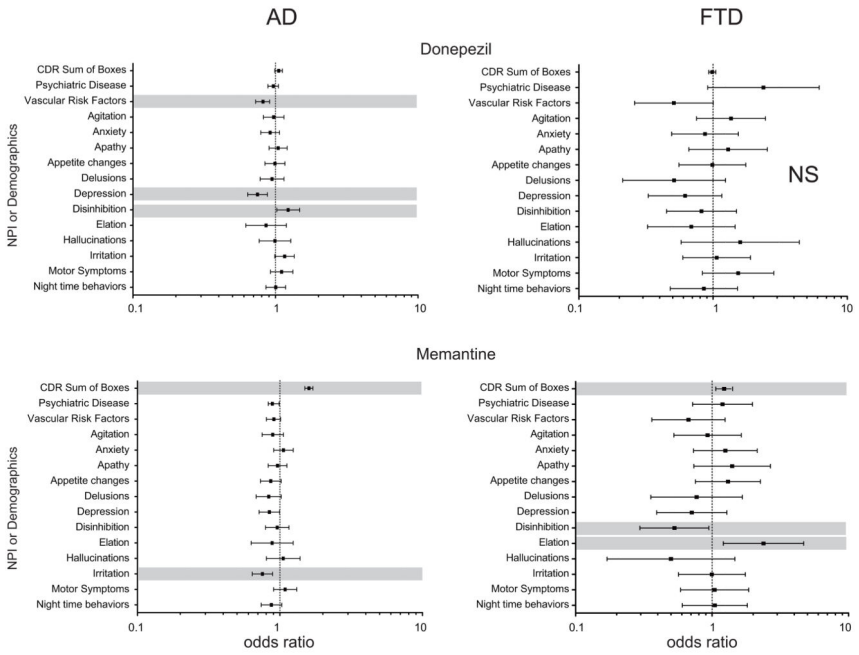

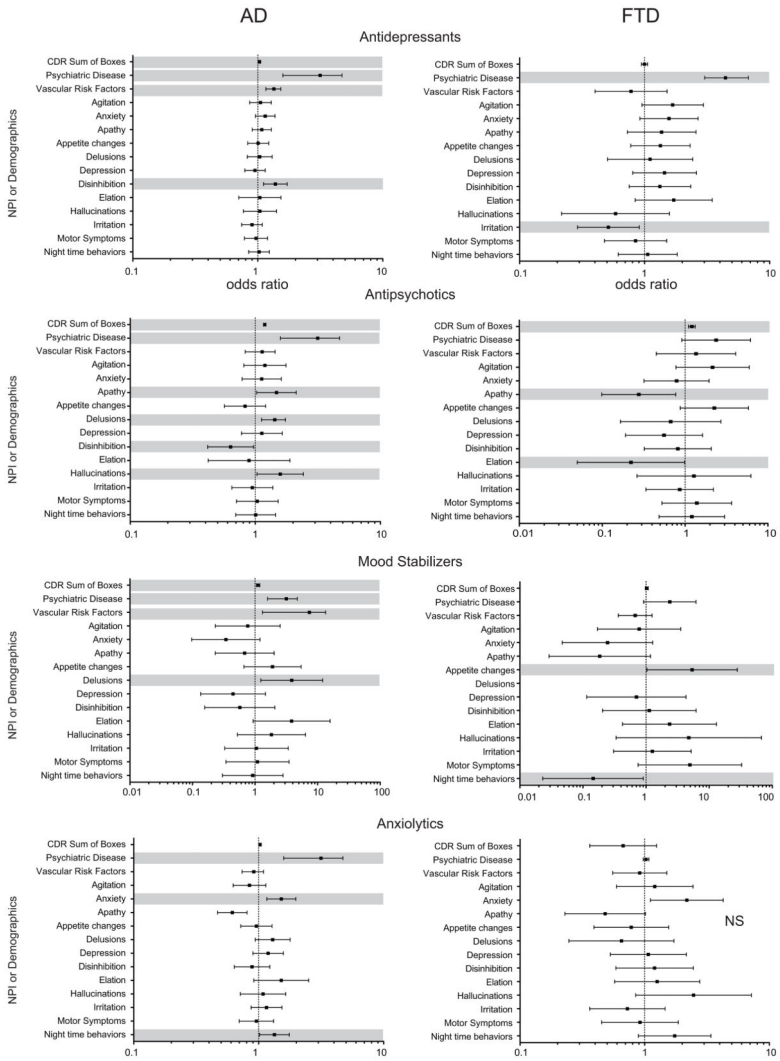

Fig 1.

Fig 1a. Odds ratio graphs of possible predictors of Donepezil and Memantine use in AD and FTD. Gray line indicates significant positive or negative association between possible predictor and medication use.

Fig 1b. Odds ratio graphs of possible predictors of psychiatric medication use in AD and FTD. Gray line indicates significant positive or negative association between possible predictor and medication use.

Table 1

Comparison of demographic, risk factors, medication use and NPI variables between AD and bvFTD

Demographics	AD (3638)	FTD (320)	p
Age *	75.9+/− 8.8	64.8 +/− 9.8	<0.001
Gender χ^2	1604/2034 (56%)	110/210 (34%)	<0.001
Disease duration *	5.63 +/− 3.6	6.00+/− 4.9	0.185
Education level *	14.0 +/− 3.7	14.9 +/− 3.2	<0.001
RACE χ^2 (white)	83%	95%	<0.001
CDR Sum of Boxes *	6.88 +/− 4.4	7.89 +/− 4.9	<0.001
CDR Global *	1.22+/− 0.7	1.41+/− 0.9	<0.001
0	0.10%	0.60%	
0.5	26.30%	22.80%	
1	46.60%	38.80%	
2	18.90%	22.20%	
3	8.20%	15.60%	
Vascular Risk Factor	86%	81%	0.04
Psychiatric Disease	46%	56%	0.002
Neuropsychiatric Symptoms as			
Delusions	18%	16%	0.541
Hallucinations	9%	9%	0.606
Agitation	35%	50%	<0.001
Depression	37%	41%	0.165
Anxiety	36%	49%	<0.001
Elation	5%	19%	<0.001
Apathy	44%	73%	<0.001
Disinhibition	20%	58%	<0.001
Irritability	39%	52%	<0.001
Motor	22%	49%	<0.001
Night Behaviors	26%	41%	<0.001
Appetite/Eating changes	24%	50%	<0.001

*Welch, Brown-Forsyth because Levene's test of homogeneity <0.05)

Table 2

Comparison of medication use between AD and bvFTD and OR for medication use in FTD compared with AD

Medication Use	AD (3638)	FTD (320)	p	OR	95% CI
Donepezil	56%	26%	<0.001	0.22	0.17–0.29
Memantine	43%	33%	0.001	0.38	0.29–0.50
Antidepressant	39%	57%	<0.001	1.56	1.16–2.08
Antipsychotic	4.7%	10%	<0.001	2.00	1.26–3.18
Anxiolytic	8.1%	18%	<0.001	2.25	1.58–3.19
Mood stabilizer	0.5%	3.8%	<0.001	4.94	2.03–12.04
Use of any medication approved by the FDA for treatment of cognition	78%	56%	<0.001	0.20	0.15–0.27
Use of any medication used to treat psychiatric symptoms	45%	68%	<0.001	2.12	0.58–2.86

Table 3

Significant positive and negative predictors of medication use in FTD and AD.

Medication class	Medication	FTD	AD
Cognitive	All cognitive medication	NA	(+) white, educated, male, disease severity, disease duration (−) depression, older
	Donepezil	NA	(+) disinhibition, irritability (−) vascular, younger, depressed
	Memantine	(+) elation, education, disease severity (−) female, disinhibited	(+) white, disease severity, educated, disease duration (−) irritability, older
Psychiatric	All psychiatric	(+) psychiatric hx (−) irritability	(+) psychiatric hx, white, disinhibited, disease severity, disease duration, younger, anxious
	Antidepressant	(+) psychiatric hx (−) irritability	(+) psychiatric hx, white, vascular risk, disease severity, disease duration younger, disinhibition
	Antipsychotic	(+) disease severity (−) elation or apathy	(+) disease severity, psychiatric disease, hallucinations, apathy (−) disinhibition
	Mood stabilizer	(+) appetite (−) younger, nighttime behaviors	(+) disease severity, delusions (−) white
	Anxiolytic	NA	(+) psychiatric disease, anxiety, nighttime (−) apathetic

NA= no variables associated with medication use

(+) higher probability of being on medications

(−) less probability of being on medication