Reduction of the Anticholinergic Burden Makes It Possible to Decrease Behavioral and Psychological Symptoms of Dementia

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Objective: *The aim of this study was to evaluate the impact of a reduction of the anticholinergic burden (AB) on the frequency and severity of behavioral and psychological symptoms of dementia (BPSD) and their repercussions on the care team (occupational disruptiveness).* **Methods:** *In this prospective, single-center study in an acute care unit for Alzheimer disease (AD) and related disorders, 125 elderly subjects (mean age: 84.4 years) with dementia presented with BPSD. The reduction of the AB was evaluated by the Anticholinergic Cognitive Burden Scale. BPSD were evaluated with the Neuropsychiatric Inventory–Nursing Home Version (NPI-NH). The effect of the reduction of the AB on the BPSD was studied using logistic regression adjusting for the variables of the comprehensive geriatric assessment.* **Results:** *Seventy-one subjects (56.8%) presenting with probable AD, 32 (25.6%) mixed dementia (AD and vascular), 17 (13.6%) vascular dementia, and 5 (4.0%) Lewy body dementia were included. Reducing the AB by at least 20% enabled a significant decrease in the frequency × severity scores of the NPI-NH (adjusted odds ratio: 3.5; 95% confidence interval: 1.6–7.9) and of the occupational disruptiveness score (adjusted odds ratio: 9.9; 95% confidence interval: 3.6–27.3).* **Conclusion:** *AB reduction in elderly subjects with dementia makes is possible to reduce BPSD and caregiver burden. Recourse to treatments involving an AB must be avoided as much as possible in these patients, and preferential use of nonpharmacologic treatment management plans is encouraged.* (Am J Geriatr Psychiatry 2018; 26:280–288)

Key Words: Behavioral disorders, cholinergic antagonist, drug effects, cognitive disorders, dementia

Highlights

- Reducing the anticholinergic burden makes it possible to decrease frequency and severity of BPSD among elderly people with dementia.

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- Reducing the anticholinergic burden in relatively autonomous subjects (ADL ≥ 3) brings about a reduction of the occupational disruptiveness of the BPSD on the caregivers.
- Anticholinergic burden could participate in the occurrence or the maintenance of the BPSD, and could thus constitute a potential avoidable cause.

INTRODUCTION

The behavioral and psychological symptoms of dementia (BPSD) affect more than 90% of subjects during the development of Alzheimer disease (AD) and are similarly frequent in other types of dementia.[1] BPSD are essentially noncognitive manifestations bringing about disorders that can affect mood, behavior, and perception.[2] Their nature varies as a function of the etiologic diagnosis of the dementia,[3] and they manifest at various stages of the neurodegenerative disease.[4]

The occurrence of BPSD is associated with poor prognosis because are associated with unfavorable health events, such as hospitalization,[5] more rapid progression of the causal neurodegenerative disease,[6] burnout of family carers[7] and caregivers,[8] poor quality of life,[9] and institutionalization.[10] For this reason, BPSD constitute a major challenge in the therapeutic management of patients with dementia and a subject of major preoccupation for patients and their caregivers. Consequently, the recommendations issued by the 2011 consensus of the National Institute on Aging–Alzheimer's Association have integrated BPSD into the diagnostic criteria for dementia.[11] BPSD can be evaluated in clinical practice by various instruments, including the Neuropsychiatric Inventory–Nursing Home Version (NPI-NH).[12]

Control of BPSD often requires symptomatic drug treatment.[13] Certain drugs are even more harmful when they have anticholinergic properties.[14] Such drugs are commonly used in elderly subjects[15] despite a mediocre safety profile.[16] Various classes of drugs are involved, including certain treatments for urinary incontinence, certain psychotropic drugs including neuroleptics, treatments for cardiovascular conditions, and antihistamines. Cholinergic antagonists block the postsynaptic nicotinic or muscarinic receptors and inhibit intracellular signaling.[17] These drugs bring about disturbances of the cholinergic system, which is involved in numerous functions of the central nervous system (cognitive, emotional, and behavioral),[18] and thus have iatrogenic potential known as the anticholinergic burden (AB).[19] Physiologic changes related to aging, such as greater permeability of the blood–brain barrier,[20] less linking to albumin, and relative hepatic insufficiency,[21] are responsible for the increased diffusion of cholinergic antagonists in the central nervous system, explaining the greater sensitivity to these treatments with age.

The main objective of this study was to evaluate the effect of reducing the AB by at least 20% to have a clinically significant impact on the frequency and severity of BPSD measured by the NPI-NH. Secondary objectives were to evaluate the frequency of BPSD in our sample, to evaluate the impact of reducing AB by at least 20% on the repercussions of BPSD on the care team (evaluated by the NPI-NH), and to compare the characteristics of patients who were exposed or not exposed to an AB.

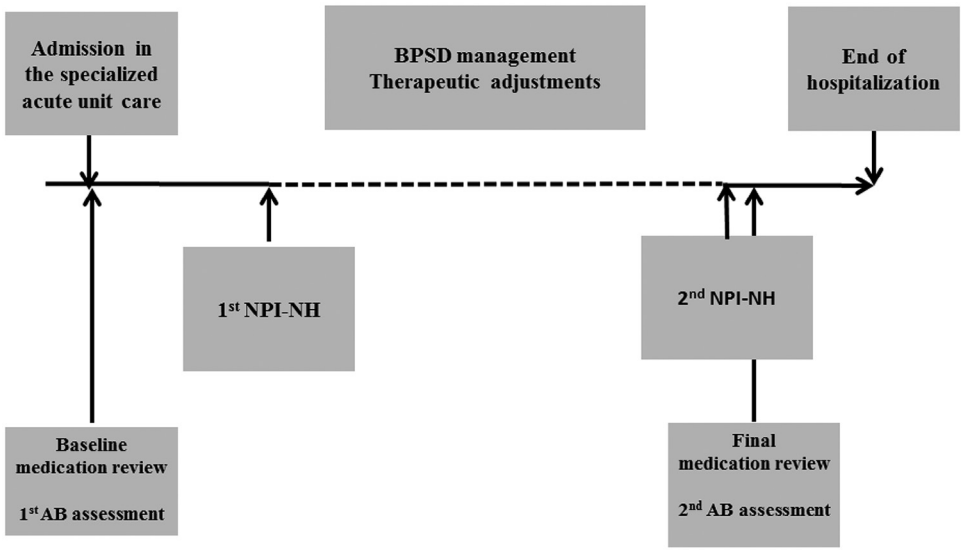
METHODS

Study Design

This was a prospective, single-center study carried out in a dedicated acute geriatric care unit specializing in the management of patients with dementia (AD or related disorders) at the University Hospital of Reims, France. This unit is dedicated to the therapeutic management of patients presenting with AD or related disorders associated with BPSD for which ambulatory therapeutic management is not appropriate. The functioning of the unit has been described elsewhere.[22] The dementia diagnosis was established by senior practitioners (neurologist or geriatrician) according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria.[23]

Starting from the patients' admission, medications that were potentially inappropriate in terms of the AB were substituted by other treatments with a lower or nonexistent AB where possible. Other treatments, such as oxybutynin, haloperidol, or loxapine, were stopped, and hydroxyzine was substituted by a benzodiazepine

FIGURE 1. Study design from admission to the end of hospitalization. Therapeutic adjustments were performed after the first AB assessment and the first BPSD assessment according to the NPI-NH.



with no AB, such as oxazepam. The study design is described in Figure 1.

Study Sample

Subjects were aged 65 years or older, suffering from AD or related disorders, admitted between July 15, 2015 and February 20, 2017 for therapeutic management of BPSD. Subjects who were protected by law and individuals with psychotic disorders as their main diagnosis were not included. Given that our work was more of an exploratory strategy, there was no calculation of the number of subjects necessary, in the absence of prior data of the literature.

Assessment of AB

The AB was assessed using the Anticholinergic Cognitive Burden Scale (ACBS),[24] which made it possible to rate the anticholinergic power from 1 (mild) to 3 (high). The total ACBS score was calculated by adding the scores of each medication taken by the patient. In the absence of prior data in the literature regarding a threshold for reduction, a threshold of clinically significant reduction was set at a minimum of 20% reduction in the AB at baseline, judged on the last prescription preceding hospitalization. The medications taken into account by the ACBS are listed in Supplemental File 1. A first evaluation of the AB was carried out at admission to the unit on the last prescription preceding admission using the ACBS and again at 48 hours before discharge on the prescription delivered at the end of hospitalization.

Assessment of BPSD

BPSD were evaluated using the NPI-NH, which assess 12 domains (delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy, disinhibition, irritability/lability, aberrant motor behavior, sleep and nighttime behavior disorders, appetite and eating changes). The frequency score of each domain was rated from 1 (<1 per week) to 4 (once or more per day or continuously present). The severity score was rated from 1 (present but not distressing to the patient) to 3 (very stressful and upsetting; typically requires specific management). The occupational disruptiveness score that measures impact on the workload of the caregivers was rated from 0 (not at all) to 5 (very severely or extremely).

The scores of the NPI-NH were assessed by the care team during daily multidisciplinary meetings. A first

measurement of the NPI-NH by the paramedical team was carried out in the 48 hours after admission in the course of the daily multidisciplinary meeting; a second measurement was then performed 48 hours before discharge from the unit. Because the researchers were the prescribers, they did not participate in the scoring of the NPI-NH so as not to influence the possible therapeutic modifications.

Outcome Measured

The main endpoint was a reduction of the frequency × severity score on the NPI-NH. A clinically significant reduction was defined as a reduction of four points or 30%.[25] The secondary endpoint was the reduction in occupational disruptiveness score on the NPI-NH. A clinically significant reduction was defined as a reduction of four points.[26]

Covariates

Sociodemographic variables such as age, sex, and place of residence were recorded. Data were also extracted from the comprehensive geriatric assessment, such as one element of the cognitive assessment (Mini-Mental State Exam [MMSE][27]), the severity of dementia, mood evaluation (using the Mini-Geriatric Depression Scale[28] if the MMSE > 15 and the Cornell scale[29] if the MMSE < 15), comorbidities assessed using the Charlson Comorbidity Index,[30] a functional evaluation using activities of daily living (ADLs)[31] and instrumental ADLs[32] scales, and nutritional assessment using the Mini Nutritional Assessment.[33]

Because baseline correlation between the AB and the frequency × severity score of the NPI-NH may bias the result of the change correlation, AB × frequency × severity score at baseline was taken into account. The values of the AB and frequency × severity score at baseline were multiplied. This composite value was subsequently divided into quartiles. The first quartile was considered as the reference class. The same procedure was applied for the correlation between the AB and occupational disruptiveness score of the NPI-NH at baseline.

Statistical Analysis

In the descriptive analysis quantitative variables are described as mean ± standard deviation and qualitative variables as number and percentage. We compared demographic and clinical characteristics using Student t and χ^2 tests. Bivariate analyses were carried out to evaluate (1) the association between the reduction in frequency × severity score of the NPI-NH and (2) the reduction of the AB by at least 20%, with social-demographic variables, various clinical variables, and the correlation between AB × frequency × severity score at the baseline. Multivariate analysis by logistic regression was performed to identify variables independently associated with a reduction in the frequency × severity scores, with a forward selection, including in the model all variables with $p < 0.20$ on bivariate analysis.

Results are presented as odds ratios (ORs) with 95% confidence interval (95% CIs). The same analyses were also performed for the outcome "occupational disruptiveness." Goodness of fit of the final model was assessed using Nagelkerke's R^2 method. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). A $p = 0.05$ was considered to be statistically significant.

Ethical Considerations

This study was approved by the Institutional Review Board of the Reims University Hospitals (protocol number 2016-16). Before inclusion, all patients (or their main caregiver) gave oral consent to participate to the study, in accordance with French legislation. For statistical analyses, data were rendered anonymous.

RESULTS

Study Sample

During the study period 125 patients were included. Average age was 84.4 ± 5.3 years. Most subjects were women (64.8%). Among the subjects included, 54 (43.2%) came from their own home, 57 (45.6%) from a nursing home, and 14 (11.2%) from senior housing. Seventy-one subjects (56.8%) had AD, 32 (25.6%) mixed dementia (AD and vascular), 17 (13.6%) vascular dementia, and 5 (4.0%) Lewy body Dementia.

The average MMSE score was 13.2 ± 5.2. Fourteen (11.3%) patients were at the mild stage, 35 (28.2%) at the moderate stage, 39 (31.5%) at the moderately severe stage, and 36 (29.0%) at the severe stage (one missing data). According to their cognitive decline as evaluated

by the MMSE, 70 subjects (56.0%) were likely to present with depression after evaluation with the Mini-Geriatric Depression Scale (score ≥ 1) or by the Cornell scale (score ≥ 10). At the functional level, 94 (75.2%) had an ADL score ≥ 3. According to the Mini Nutritional Assessment, 45 subjects (38.5.0%) were at risk of undernutrition or malnourished (Mini Nutritional Assessment score ≤ 23.5). According to the Charlson Comorbidity Index, 68.8% of subjects presented with moderate to severe comorbidities. The characteristics of the sample are summarized in Table 1.

Frequency of the BPSD in the Sample

According to the NPI-NH, 31 (24.8%) patients had delusions, 21 (16.8%) hallucinations, 49 (39.2%) agitation/aggression, 45 (36%) depression/dysphoria, 57 (45.6%) anxiety, 25 (20%) apathy/indifference, 5 (4%) disinhibition, 47 (37.6%) aberrant motor behavior, 53 (42.4%) irritability/lability, 42 (33.6%) sleep and nighttime behavior disorders, and 33 (26.4%) experienced appetite and eating changes. None had elation/euphoria. These data are presented in Table 1.

Reduction in the Frequency × Severity Score

By multivariate analysis a reduction of at least 20% in the AB, as estimated by the ACBS, was significantly associated with a reduction in the frequency × severity score, as assessed by the NPI-NH ($OR_{adjusted}$: 3.5; 95% CI: 1.6–7.9; Wald $\chi^2 = 9.32$, df = 1, p = 0.002). The reduction of the frequency × severity score was also associated with high probability of depression ($OR_{adjusted}$: 3.6; 95% CI: 1.6–8.0; Wald $\chi^2 = 9.61$, df = 1, p = 0.002). These results are presented in Table 2.

Reduction in the Occupational Disruptiveness Score

By multivariate analysis a reduction of at least 20% in the AB was significantly associated with a reduction in the occupational disruptiveness score ($OR_{adjusted}$: 9.9; 95% CI: 3.6–27.3; Wald $\chi^2 = 19.94$, df = 1, p < 0.0001). Patient autonomy (ADL ≥ 3) was also associated with a reduction in the occupational disruptiveness score ($OR_{adjusted}$: 3.0; 95% CI: 1.1–8.1; Wald $\chi^2 = 4.83$, df = 1, p = 0.03). These results are presented in Table 2.

TABLE 1. Characteristics of the Sample (N = 125)

Characteristic	Value
Age, yr, mean ± standard deviation	84.4 ± 5.3
Female sex	81 (64.8)
Place of residence	
Home	54 (43.2)
Nursing home	57 (45.6)
Senior housing	14 (11.2)
Charlson Comorbidity Index	
Mild (1–2)	39 (31.2)
Moderate to severe (≥3)	86 (68.8)
ADL ≥ 3	94 (75.2)
MMSE, mean ± standard deviation	13.2 ± 5.2
Diagnosis of dementia	
AD	71 (56.8)
Vascular	17 (13.6)
Lewy body dementia	5 (4.0)
Mixed	32 (25.6)
At risk of depression (Mini-GDS ≥ 1; Cornell ≥ 10)	70 (56.5)
At risk of undernutrition and malnourished	45 (38.5)
Duration of hospitalization, days mean ± standard deviation	11.18 ± 3.1
BPSD prevalence according to NPI-NH	
Delusions	31 (24.8)
Hallucinations	21 (16.8%)
Agitation/aggression	49 (39.2%)
Depression/dysphoria	45 (36.0%)
Anxiety	57 (45.6%)
Elation/euphoria	0 (0%)
Apathy/indifference	25 (20.0%)
Disinhibition	5 (4.0%)
Irritability/lability	53 (42.4%)
Aberrant motor behavior	47 (37.6%)
Sleep and nighttime behavior disorders	42 (33.6%)
Appetite and eating changes	33 (26.4%)
Baseline AB × (frequency × severity) score	
Quartile 1 (0–48)	90 (72.0%)
Quartile 2 (49–96)	30 (24.0%)
Quartile 3 (97–144)	4 (3.2%)
Quartile 4 (145–192)	1 (0.8%)
Baseline AB × OD score	
Quartile 1 (0–17)	75 (60.0%)
Quartile 2 (18–35)	32 (25.6%)
Quartile 3 (36–52)	13 (10.4%)
Quartile 4 (53–70)	5 (4.0%)

Notes: Values are total number of cases with percents in parentheses, unless otherwise defined. Data were missing for nutritional status (N = 8) and probability of depression (N = 1). Mini-GDS: Mini Geriatric Depression Scale; OD: occupational disruptiveness.

Comparison of Characteristics of Subjects Exposed and Not Exposed to an AB

There were no significant differences in the characteristics between patients exposed to an AB and those not exposed. The detailed results are presented in Table 3.

TABLE 2. Reduction of the Frequency × Severity Score and Occupational Disruptiveness on the NPI-NH

	(Model 1) Frequency × Severity of BPSD[a]								(Model 2) Occupational Disruptiveness of BPSD[b]							
	Not Adjusted				Adjusted				Not Adjusted				Adjusted			
Variables	Wald χ^{2c}	OR	95% CI	p	Wald χ^{2c}	OR	95% CI	p	Wald χ^{2c}	OR	95% CI	p	Wald χ^{2c}	OR	95% CI	p
Age																
<75 yr		1.0								1.0						
75–85 yr	0.05	0.8	0.06–9.1	0.83					1.45	4.6	0.4–55.5	0.23				
>85 yr	0.0009	1.0	0.08–11.1	0.98					2.16	6.3	0.5–73.6	0.14				
Men		1.0								1.0						
Women	1.5	1.6	0.8–3.4	0.22					0.19	1.2	0.5–2.7	0.66				
Mild dementia		1.0								1.0						
Moderate dementia	1.43	0.4	0.07–1.9	0.23					0.22	0.7	0.1–3.7	0.64				
Moderately severe dementia	2.96	0.2	0.05–1.2	0.09					1.37	0.4	0.1–2.0	0.24				
Severe dementia	3.54	0.2	0.04–1.1	0.06					2.12	0.3	0.1–1.5	0.15				
ADL < 3		1.0								1.0				1.0		
ADL ≥ 3	0.63	1.4	0.6–3.2	0.43					6.4	3.0	1.3–7.2	0.01	4.83	3.0	1.1–8.1	0.03
Living at home		1.0								1.0						
Other	0.34	1.2	0.6–2.6	0.56					0.28	1.2	0.6–2.7	0.59				
Comorbidities																
Mild		1.0								1.0						
Moderate to severe	0.67	0.7	0.3–1.6	0.41					1.26	0.6	0.2–1.5	0.26				
Low probability of depression		1.0				1.0				1.0						
High probability of depression	9.66	3.4	1.6–7.2	0.002	9.61	3.6	1.6–8.0	0.002	1.67	1.7	0.8–3.7	0.20				
Not at risk of undernutrition		1.0								1.0						
At risk of undernutrition	0.53	0.8	0.3–1.6	0.47					4.64	0.4	0.2–0.9	0.03				
Baseline AB × (frequency × severity) score[d]																
Increasing risk for each quartile	4.45	2.4	1.1–5.3	0.03												
Baseline AB × OD score[e]																
Increasing risk for each quartile									10.17	4.4	1.8–11.1	0.001				
Reduction of the AB	9.69	3.4	1.6–7.2	0.002	9.32	3.5	1.6–7.9	0.002	20.9	10.0	3.7–26.7	<0.0001	19.94	9.9	3.6–27.3	<0.0001

Notes: Data were missing for nutritional status (N = 8) and probability of depression (N = 1). OD: occupational disruptiveness.

[a]Model 1 (multivariate): Nagelkerke $R^2 = 0.28$. In multivariate analysis using logistic regression, variables included in the model were stage of dementia, high probability of depression, baseline anticholinergic burden × (frequency × severity score), and reduction of the AB. Variables retained in the final model were high probability of depression and reduction of the AB.

[b]Model 2 (multivariate): Nagelkerke $R^2 = 0.32$. In the multivariate analysis using logistic regression, variables included in the model were level of ADL ≥ 3, high probability of depression, risk of undernutrition, baseline anticholinergic burden × OD, and reduction of the AB. Variables retained in the final model were level of ADL ≥ 3 and reduction of the AB.

[c]ORs were tested with Wald χ^2 tests with 1 degree of freedom.

[d]Baseline AB × (frequency × severity) score: assessment of the correlation between AB (according to the ACBS) and frequency × severity of BPSD (assessed by the NPI-NH) at baseline.

[e]Baseline AB × OD score: assessment of the correlation between AB (according to the ACBS) and OD of BPSD (assessed by the NPI-NH) at baseline.

TABLE 3. Comparison of Characteristics of Patients Exposed and Not Exposed to an AB

Variables	ACBS = 0 (N = 21)	ACBS ≥ 1 (N = 104)	p
Age, mean ± standard deviation[a]	83.14 ± 7.05	84.71 ± 4.87	0.34
Female sex[b]	13 (61.90)	68 (65.38)	0.76
Duration of hospitalization, mean ± standard deviation[c]	10.20 ± 2.48	11.38 ± 3.20	0.11
Place of residence[d]			
Home	10 (47.62)	44 (42.31)	0.65
Comorbidity score, mean ± standard deviation[e]	7.14 ± 2.10	7.49 ± 1.77	0.43
Presence of depression[f]	13 (61.90)	57 (55.34)	0.58
Presence of undernutrition[g]	11 (52.38)	34 (35.42)	0.15
ADL, mean ± standard deviation[h]	3.50 ± 1.67	3.54 ± 1.38	0.88
MMSE , mean ± standard deviation[i]	13.19 ± 6.78	13.22 ± 4.85	0.98

Notes: Values are total number of cases with percents in parentheses, unless otherwise defined. Data were missing for nutritional status (N = 8) and probability of depression (N = 1). Test statistics are t values for differences in means and χ^2 values for differences in proportions.

[a]t test: 24 df; t = –0.97.
[b]χ^2 test: 1 df; χ^2 = 0.09.
[c]t test: 123 df; t = –1.61.
[d]χ^2 test: 1 df; χ^2 = 0.20.
[e]t test: 123 df; t = –0.79.
[f]χ^2 test: 1 df; χ^2 = 0.31.
[g]χ^2 test: 1 df; χ^2 = 2.10.
[h]t test: 123 df; t = –0.14.
[i]t test: 24 df; t = –0.02.

Description of Prescription of Drugs with AB

One hundred four patients were exposed to drugs with AB. The average AB at admission in exposed patients was 3.7 ± 1.6 according to the ACBS. We succeeded in reducing the AB by at least 20% in 78 patients (62.4%). Supplemental File 2 gives the details for the 10 most frequently prescribed drugs in our sample, their AB according to the ACBS, and the strategy adopted (pursuit, discontinuation, or substitution).

DISCUSSION

In our study reducing the AB by at least 20% made it possible to significantly reduce the frequency and severity of BPSD. Furthermore, subjects with a high probability of depression were more likely to have a reduction of the frequency and severity of BPSD. This could be related to the nonpharmacologic management of BSPD in the specialized acute unit for patients with AD and related disorders. Indeed, they could experience fewer depressive symptoms at discharge through psychotherapeutic interventions carried out by a clinical psychologist. To the best of our knowledge this is the first study to establish a link between a reduction in the AB and a reduction in BPSD as evaluated by the NPI-NH. Other works have established a link between the use of treatments with AB and the occurrence of BPSD, such as hallucinations and delusional ideas.[34] Thus, cholinergic antagonists could aggravate the pre-existing cholinergic deficit that favors the occurrence of BPSD in patients with dementia.[35–37] In addition, it has been established that in patients presenting with AD, there is overexpression of muscarinic M2 and M4 receptors to acetylcholine,[38] involved in the occurrence of BPSD, constituting even more sites of blockage for cholinergic antagonists. The effect of reducing the AB on the BPSD in our sample, who mostly suffered from AD and mixed dementia, seems to strengthen these prior results.

In our study subjects presented a majority of disruptive BPSD. In fact, subjects who presented with such BPSD needed hospital-based therapeutic management. This has previously been described in other countries[39] and is also coherent with the goals of the acute care unit for AD and related disorders.[40]

We also found that reducing the AB by at least 20% made it possible to significantly reduce caregiver burden. The significant reduction in the occupational disruptiveness score as assessed by the NPI-NH mainly concerned patients whose autonomy was relatively preserved (ADL ≥ 3). In fact, a reduction in the AB among these relatively autonomous subjects brings about a reduction in the occupational disruptiveness of the BPSD on the caregivers, arising from the mitigation of both the frequency and severity of some of the more frequent BPSD in subjects with conserved functional autonomy, such as disruptive BPSD.[41] This is in agreement with previous data from the literature reporting that disruptive BPSD such as agitation/aggression, anxiety, and irritability/lability increase caregiver burden.[42] Nevertheless, data concerning the causality between BPSD and loss of autonomy (or functional limitation) remain controversial.[43,44]

The physiopathologic mechanisms of BPSD are subject to controversy because they are considered to

be multifactorial, relating namely to the etiology of the neurodegenerative disease,[3] an imbalance of certain neurotransmitters,[35] the severity of the cognitive lesion,[45] or the involvement of neurovascular factors.[46] In the elderly subject several causes are often confounded. Thus, the iatrogenic effect of medications with AB could contribute to the occurrence or maintenance of BPSD and could thus constitute a potentially avoidable cause.

Our study has several limits. First, it was a single-center study. Second, our sample was of modest size (125 subjects). Finally, the evaluation of the AB by the ACBS precluded taking into account the dosage regimen of the drugs or the duration of exposure.

Our study also has several strong points. It was carried out in a prospective manner to ensure temporality and potential causality between the reduction in the AB and its disruptiveness on the BPSD evaluated by the NPI-NH, both for the patient and for the caregiving staff. Furthermore, the fact that all patients received the same pharmacologic and nonpharmacologic management other than a reduction in the AB limits the potential for confusion bias. In addition, the decrease in BPSD was independent of the baseline correlation between AB and frequency × severity score (and occupational disruptiveness score) of the NPI-NH, thus making it possible to avoid the bias related to the baseline correlation. Finally, the subjects in our sample mostly presented disruptive BPSD, which have the greatest negative impact on the patients and their family carers.

In conclusion, reducing the AB made it possible to significantly decrease the frequency, severity, and occupational disruptiveness of BPSD in patients with dementia hospitalized in an acute care unit for patients with AD and related disorders. A strategy of reducing AB in these subjects made it possible to improve their behavioral and psychological symptomatology as well as the quality of the care dispensed by reducing the burden on the caregivers. The use of treatments with anticholinergic potential must be avoided as far as possible in elderly subjects with dementia. Other, larger scale prospective studies are nevertheless warranted to support these results. Finally, it would be interesting to study the effect of a reduction in the AB on BPSD among subjects with dementia living in an institution, because these subjects are more exposed to an AB because of their severe comorbidities.[47]

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APPENDIX: SUPPLEMENTARY MATERIAL

Supplementary data to this article can be found online at doi:10.1016/j.jagp.2017.08.005.

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