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Drugs with anticholinergic properties and cognitive performance in the elderly: results from the PAQUID Study

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Objectives
To measure the association between the use of drugs with anticholinergic properties and cognitive performance in an elderly population, the PAQUID cohort.

Methods
The sample studied was composed of 1780 subjects aged 70 and older, living at home in South western France. Data on socio-demographic characteristics, medical history and drug use were collected using a standardized questionnaire. Cognitive performance was assessed using the following neuropsychological tests: the Mini-Mental State Examination (MMSE) which evaluates global cognitive functioning, the Benton Visual Retention Test (BVRT) which assesses immediate visual memory, and the Isaacs' Set Test (IST) which assesses verbal fluency. For each test, scores were dichotomized between low performance and normal to high performance using the score at the 10th percentile of the study sample as the cut-off point, according to age, gender and educational level. The association between the use of drugs with anticholinergic properties and cognitive performance was examined using logistic regression models, adjusting for several potential confounding factors.

Results
About 13.7% of the subjects used at least one drug with anticholinergic properties. In multivariate analyses, the use of these drugs was significantly associated with low performance in the BVRT [odds ratio (OR) = 1.6; 95% confidence interval (CI) 1.1, 2.3] and in the IST (OR = 1.9; 95% CI 1.3, 2.8). The association found with low performance in the MMSE (OR = 1.4; 95% CI 1.0, 2.1) was barely statistically significant.

Conclusion
These findings suggest that the use of drugs with anticholinergic properties is associated with low cognitive performance among community-dwelling elderly people.

Introduction

Because the ageing population grows regularly, cognitive impairment among the elderly is of concern. The concept of cognition refers to information processing and psychomotor functions that enable organisms to adapt to and manipulate the environment. Although the aetiology of cognitive disorders in elderly people is multifactorial, medication use is often suspected. Many drugs are cited as potential causes of cognitive impairment in vulnerable individuals. However, certain classes

of drugs are more commonly implicated, such as benzodiazepines, opioids, tricyclic antidepressants and anticholinergic drugs [1–4].

The neurotransmitter acetylcholine is widely distributed in the brain, occurring in all parts of the forebrain, midbrain and brainstem. It has mainly excitatory effects which are mediated by various subtypes of nicotinic or muscarinic receptors. Muscarinic receptors mediate the main cognitive effects attributed to cholinergic pathways, namely effects on attention, learning, and short-term memory [5]. It has been postulated that normal ageing is accompanied by a relative deterioration of the central cholinergic system. This cholinergic deficit may contribute to the cognitive decline that occurs with normal ageing [6, 7]. It may also explain the increased sensitivity of elderly subjects to drugs which block central muscarinic receptors [8, 9].

Anticholinergic drugs have been considered potentially inappropriate in elderly subjects [10, 11]. They are used therapeutically to block muscarinic receptors in a wide variety of clinical disorders such as Parkinson's disease and urinary incontinence. Other classes of drugs used for entirely different therapeutic reasons also have anticholinergic properties (e.g. antihistamines and classical antipsychotics) [7, 12]. Drugs with anticholinergic activity are frequently responsible for peripheral and central adverse effects, particularly in older adults. Also, common medical problems existing in the elderly (such as angina, congestive heart failure, diabetes mellitus, urinary dysfunction, constipation, glaucoma, sleep disturbance and dementia) may be worsened by their use [7].

Central nervous system side-effects may occur with usual doses of anticholinergic drugs. These include subtle neuropsychological deficits, especially involving memory and attention, as well as delirium [3, 12]. Whether a patient experiences adverse effects or not due to anticholinergic activity depends on several factors, including the degree to which the drug crosses the blood–brain barrier, the anticholinergic load resulting from the use of multiple drugs that block muscarinic receptors, baseline cognitive status, and individual pharmacokinetic and pharmacodynamic variability [2, 3, 7, 13].

The toxicity of drugs with anticholinergic properties is a well-known problem, but to our knowledge few epidemiological studies have investigated the effect of overall use of these drugs on cognition. The aim of this study was to assess the association between the use of drugs with anticholinergic properties and cognitive performance among community-dwelling elderly subjects.

Methods

Study population

PAQUID (Personnes, âgées *quid*?) is an ongoing prospective epidemiological study of cerebral and functional ageing processes designed in 1988–1989. It is conducted among French elderly subjects aged ≥65 years, living in the community in two administrative areas in South western France (Gironde and Dordogne). To be included, subjects had to meet the following criteria: (i) be at least 65 years old on 31 December 1987, (ii) live at home at the time of inclusion in the study, and (iii) be registered on the electoral rolls of 75 randomly selected districts. A random sample of 5555 subjects was drawn from the electoral rolls of each district, after stratification by age and gender. Among them, 3777 subjects (68.8%) agreed to participate in the study. This sample was representative in terms of age and gender of the population of Gironde and Dordogne aged 65 and older. Participants were interviewed at home by trained psychologists at inclusion in the study (1988–1990) and again after a lapse of 1 year (in Gironde only), 3 years, 5 years, 8 years, 10 years and 13 years. The protocol of the PAQUID Study was approved by the ethics committee of the University of Bordeaux 2 (Bordeaux, France) and written informed consent was obtained from each participant. The methodology of the PAQUID Study and the main characteristics of the sample have been described in detail elsewhere [14].

The present cross-sectional study was conducted using data collected at the 5-year point. The 5-year follow-up allowed us to take into account the evolution of diagnosis of dementia and have a sample of normal subjects aged ≥70 years. Also, the 5-year questionnaire included the most complete information on health status. Among the 2084 subjects present at this follow-up, 304 subjects who had at least one condition which could interfere with cognitive performance or its assessment were excluded: dementia ($n = 154$), blindness ($n = 26$), significant hearing impairment ($n = 79$), living in an institution ($n = 117$) and being confined to bed ($n = 24$). The following analyses were thus conducted on a sample of 1780 subjects. Based on the frequency of use of drugs with anticholinergic properties observed in the PAQUID Study, it was estimated that 1780 subjects would allow the demonstration of at least a 1.8-fold increased risk of poor cognitive performance in subjects using drugs with anticholinergic properties compared with non-users, with a 90% statistical power and a 0.05 two-sided significance level.

Data collected

Data on demographic characteristics (age, gender, educational level) were collected using a standardized questionnaire. Health status was recorded by individual reports of past and present diseases (myocardial infarction, angina pectoris, stroke and hypertension). Subjects were asked to report all drugs used over the 2 weeks preceding the interview, including both prescriptions and over-the-counter drugs. The drugs used were gathered and confirmed by inspection of drug packages in personal pharmacies. Drugs with anticholinergic properties from seven therapeutic classes were examined: H_1-antihistamines, gastrointestinal and urinary antispasmodics, antiemetics, bronchodilators, antiparkinsonian drugs, antidepressants and antipsychotics. Many drugs in each of these groups have moderate or strong anticholinergic activity and have been reported to potentially induce delirium in elderly people.

Depressive symptoms were assessed using a French version of the Center for Epidemiologic Studies-Depression Scale (CES-D). The CES-D consists of 20 self-reported items rated from 0 to 3 according to the frequency of symptoms and feelings experienced over 1 week. The score ranges from 0 (no depressive symptoms) to 60. According to a previous validation study for the French population, women were considered to have depressive symptoms if they scored >22 and men if they scored >16 [15].

Cognitive functioning was assessed through a battery of neuropsychological tests including the Mini-Mental State Examination (MMSE) [16] which provides a measure of global cognitive functioning, the Benton Visual Retention Test (BVRT) [17] which assesses immediate visual memory, and the Isaacs' Set Test (IST) [18] which assesses verbal fluency. The MMSE is composed of 30 items evaluating several cognitive functions: orientation in time and place, memorizing three words, calculation, recall of three words, language and visual construction. Each correct answer receives 1 point. The total score ranges from 0 to 30. The multiple-choice form of the BVRT consists of 15 stimulus cards representing one, two or three geometric figures and 15 multiple-choice cards. After the presentation of the stimulus card for 10 s, subjects are asked to recognize the initial figure from an array of four possibilities. Each correct answer receives 1 point. The total score ranges from 0 to 15. The test involves visual spatial perception, visual conceptualization and immediate memory span. It also requires a form of selective attention since the memorized stimulus has to be selected from three similar distracters. The IST measures the ability to generate in 60 s lists of words from four semantic categories (colours, animals, fruits and cities). According to Isaacs and Kennie's initial rules, the maximum number of words to be generated in each category was limited to 10. As this rule led to a major ceiling effect on the total score at 60 s, we used the total number of words given by the subjects during the first 15 s. Scores depend on the integrity of semantic memory networks and the patient's ability to initiate systematic search and retrieval strategies. Working memory is also required to keep track of which words have already been mentioned.

In the course of the interviews, the psychologists applied the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) criteria for the diagnosis of dementia [19]. Subjects who met these criteria were seen by a neurologist to confirm or reject the diagnosis of dementia and to determine its aetiology according to the National Institute of Neurologic and Communicative Diseases and Stroke-Alzheimer Disease and Related Disorders Association (NINCDS-ADRDA) criteria [20].

Statistical analyses

Descriptive statistics were compiled in the sample according to age, gender, educational level, cardiovascular risk factors and diseases, number of drugs used, depressive symptomatology, results attained on neuropsychological tests and use of drugs with anticholinergic properties.

Because the neuropsychological tests scores were not normally distributed in this sample, they were treated as categorical variables rather than continuous variables. For each test, scores were dichotomized between low performance and normal to high performance using the 10th percentile of the sample as the cut-off point, according to age, gender and educational level [21, 22]. Age was categorized as follows: 70–74, 75–79, 80–84, ≥85. The educational level was categorized according to the level of schooling: no degree (0–5 years of schooling), primary school level (6–9 years), high school level and above (10 years and more).

For each neuropsychological test, the performance of users of drugs with anticholinergic properties was compared with that of non-users using the χ^2 test. When this association was statistically significant at a level of $P < 0.2$, logistic regression models were used in order to adjust for potential confounding factors. The dependent variable was the test performance (low *vs.* normal to high, as defined above). The independent variables were the use of at least one drug with anticholinergic properties, depressive symptomatology, the report of at least one cardiovascular disease or risk factor, the use of at least one psychotropic drug with no anticholinergic

properties and the number of non-psychotropic drugs with no anticholinergic properties (0–3 *vs.* 4 and more). Age, gender and educational level were not included in these models since they were considered in the classification of scores on neuropsychological tests. Goodness of fit for the logistic regression models was examined using Hosmer and Lemeshow goodness-of-fit statistics.

Tricyclic antidepressants and antipsychotics could have been prescribed for disorders which can be accompanied by cognitive impairment. In order to dissociate the effects of these drugs on cognitive performance from the effects of the other drugs with anticholinergic properties, the same analyses were conducted, excluding (i) users of tricyclic antidepressants and antipsychotics with anticholinergic properties, and (ii) users of drugs with anticholinergic properties other than tricyclic antidepressants and antipsychotics.

Complementary analyses of missing data were performed to measure the quality of the results. For each neuropsychological test, when the proportion of missing data was at least 5%, subjects who completed the test were compared with subjects who did not complete the test for the following characteristics: age, gender, educational level, cardiovascular risk factors and diseases, number of drugs used and depressive symptomatology. The χ^2 test and Student's *t*-test were used in these comparisons. Missing data were then replaced by low performance (at or below the 10th percentile of the sample) and were introduced in the statistics described above. A previous study conducted in the PAQUID cohort showed that missing values in the BVRT or in the IST were strongly related to the risk of incident dementia or Alzheimer's disease 3 years after the neuropsychological evaluation [23]. Thus, to refuse a test would seem to have almost the same meaning as to perform poorly in it.

All statistical analyses were performed using SAS statistical software release 8.02 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Characteristics of the sample studied are summarized in Table 1. The median age was 77.3 years (minimum 67.3; maximum 102.5); the sex ratio was 0.7. The median number of drugs used was 4 (minimum 0; maximum 16), 9.2% of the subjects had depressive symptomatology, 59.2% had a history of at least one cardiovascular disease or risk factor.

Cognitive performance is summarized in Table 2. The MMSE was completed by 99.2% of the subjects, the BVRT by 88.7% and the IST by 89.7%.

The use of at least one drug with anticholinergic properties was reported by 13.7% of the subjects ($n = 244$). Antipsychotics with anticholinergic properties were the most often reported (Table 3). Use of multiple drugs with anticholinergic properties occurred for 6.6% of users.

Table 1
Characteristics of subjects included in the study ($n = 1780$)

Characteristics	n (%)
Gender	
Female	1039 (58.4)
Male	741 (41.6)
Age (years)	
< 75	683 (38.4)
75–80	444 (24.9)
80–85	402 (22.6)
≥ 85	251 (14.1)
Educational level	
No degree	488 (27.4)
Primary school level	822 (46.2)
High school level and above	470 (26.4)
Depressive symptomatology (CES-D)	
No	1562 (90.8)
Yes	158 (9.2)
Number of drugs used	
0	106 (6.0)
1–3	561 (31.5)
At least 4	1110 (62.5)
Use of at least one psychotropic drug	
No	1078 (60.7)
Yes	699 (39.3)
At least one cardiovascular disease or risk factor*	
No	703 (40.8)
Yes	1020 (59.2)

**At least one of the following cardiovascular diseases or risk factors: myocardial infarction, angina pectoris, stroke, hypertension, use of at least one antidiabetic drug.*

In univariate analyses, the use of drugs with anticholinergic properties was more frequent among subjects having a score at or below the 10th percentile in the MMSE, in the BVRT or in the IST (Table 4). In multivariate logistic regression models, the use of drugs with anticholinergic properties was barely significantly associated with low results in the MMSE at the 0.05 level (Table 5). The association with low results in the BVRT (Table 6) or in the IST (Table 7) was statistically significant.

In order to assess the effects of a potential inverse causality bias, users of tricyclic antidepressants or

Table 2
Cognitive performance of subjects included in the study (n = 1780)

Neuropsychological tests	10th percentile	25th percentile	Median	75th percentile	Range
Mini-Mental State Examination (n = 1766)	23	26	28	29	(14–30)
Benton Visual Retention Test (n = 1579)	8	10	11	13	(0–15)
Isaacs' Set Test of verbal fluency (n = 1596)	20	23	27	31	(2–52)

antipsychotics with anticholinergic properties were excluded from the analyses. After adjusting for potential confounding factors, we found a statistically significant association between the use of drugs with anticholinergic properties and low results in the MMSE [odds ratio (OR) = 1.7; 95% confidence interval (CI) 1.1, 2.8; $P = 0.03$]. The association found with low results in the BVRT (OR = 1.5; 95% CI 0.9, 2.6; $P = 0.1$) or in the IST (OR = 1.6; 95% CI 0.9, 2.8; $P = 0.1$) did not reach statistical significance at the 0.05 level.

When users of drugs with anticholinergic properties other than tricyclic antidepressants and antipsychotics were excluded from the analyses, we found that the use of tricyclic antidepressants or antipsychotics with anticholinergic properties was significantly associated with low performance in the IST (OR = 2.3; 95% CI 1.4, 3.8; $P = 0.001$). The association found with low performance in the BVRT (OR = 1.5; 95% CI 0.9, 2.6) did not reach statistical significance at the 0.05 level ($P = 0.1$). No association was found with low performance in the MMSE (OR = 1.0; 95% CI 0.6, 1.8; $P = 0.9$).

Complementary analyses of missing data were conducted for the BVRT and the IST. Subjects who did not complete these tests were more often women, were older and had a lower educational level than subjects who completed them. They more often showed depressive symptomatology, they more often reported the use of psychotropic drugs and they had higher drug consumption.

When missing data were replaced by low performance (at or below the 10th percentile point), the use of drugs with anticholinergic properties was significantly more frequent among subjects who scored poorly in the BVRT (20.0% *vs.* 11.6%, $P < 0.0001$) or in the IST (20.7% *vs.* 11.8%, $P < 0.0001$). These associations remained statistically significant after adjusting for potential confounding factors (BVRT: OR = 1.7; 95% CI 1.3, 2.3; $P = 0.0005$; IST: OR = 1.9; 95% CI 1.4, 2.6; $P = 0.0001$).

Discussion

The results of this study showed that the current use of drugs with anticholinergic properties was significantly associated with low cognitive performance among community-dwelling elderly people.

The use of drugs with anticholinergic activity is a biologically plausible and potentially modifiable risk factor for cognitive impairment, as suggested by the cholinergic hypothesis of geriatric memory dysfunction [6]. The anticholinergic drug scopolamine has been used to model some aspects of the cognitive changes that occur with ageing. When administered to young and healthy subjects, the drug produced a pattern of reversible memory and cognitive deficits that mimic those occurring with normal ageing [24–26]. In older subjects, the impairment produced was consistent with the fact that elderly people are more sensitive than younger people to side-effects of drugs which block muscarinic receptors, including cognitive impairment [8, 9].

Because elderly people often have multiple illnesses which are generally treated with different types of medication [27], there is a risk that more than one drug with anticholinergic properties will be given. This could lead to cumulative anticholinergic toxicity and increase the risk of adverse effects. In our study, only 6.6% of users took more than one drug with anticholinergic activity.

Our findings are consistent with previous experimental and epidemiological studies showing that the use of certain drugs with anticholinergic activity such as tricyclic antidepressants, antiparkinsonian drugs, diphenhydramine, scopolamine and oxybutynin was associated with cognitive impairment [4, 8, 28–31]. Several studies have also found that medication use in general, and use of anticholinergic drugs in particular, was a common risk factor for delirium [32–34]. Previous studies conducted among clinical samples (i.e. elderly presurgical, medical, nursing home or gerontopsychiatric patients) have shown an association between serum anticholinergic activity (SAA) which quantifies a person's overall anticholinergic charge caused by all drugs taken and

Table 3
Frequency of use of drugs with anticholinergic properties (n = 1777)*

Drugs	n (%)
Antipsychotics	**80 (4.5)**
Acepromazine	39 (2.2)
Aceprometazine	71 (4.0)
Fluphenazine	1 (0.1)
Levomepromazine	5 (0.3)
Periciazine	1 (0.1)
Thioproperazine	1 (0.1)
Thioridazine	2 (0.1)
H_1-antihistamines	**57 (3.2)**
Chlorpheniramine	18 (1.0)
Clocinizine	2 (0.1)
Cyproheptadine	2 (0.1)
Dexchlorpheniramine	3 (0.2)
Diphenhydramine	1 (0.1)
Doxylamine	1 (0.1)
Hydroxyzine	17 (1.0)
Meclozine	4 (0.2)
Mequitazine	1 (0.1)
Oxomemazine	3 (0.2)
Phenyltoloxamine	4 (0.2)
Pizotifene	1 (0.1)
Tricyclic antidepressants	**53 (3.0)**
Amitriptyline–single and combination products	17 (1.0)
Amoxapine	3 (0.2)
Clomipramine	16 (0.9)
Desipramine	1 (0.1)
Dosulepin	3 (0.2)
Imipramine	3 (0.2)
Maprotiline	5 (0.3)
Nortriptyline	1 (0.1)
Opipramol	1 (0.1)
Trimipramine	4 (0.2)
Gastrointestinal/urinary antispasmodics	**52 (2.9)**
Aconite	1 (0.1)
Belladonna alkaloids	11 (0.6)
Buzepide metiodide	6 (0.3)
Clidinium bromide	1 (0.1)
Homatropine methylbromide	1 (0.1)
Hyoscyamus	1 (0.1)
Isopropamide iodide	3 (0.2)
Oxybutynin	22 (1.2)
Prozapine	1 (0.1)
Tiemonium	6 (0.3)
Bronchodilators	**13 (0.7)**
Ipratropium bromide	11 (0.6)
Oxitropium bromide	2 (0.1)
Antiemetics	**4 (0.2)**
Metopimazine	4 (0.2)
Antiparkinsonian anticholinergics	**3 (0.2)**
Orphenadrine	1 (0.1)
Trihexyphenidyl	2 (0.1)

Information on drug use was missing for three subjects.

Table 4
Use of drugs with anticholinergic properties according to cognitive performance

Neuropsychological tests	At least one drug with anticholinergic properties, n (%)	P-value
Mini-Mental State Examination*		
10th percentile (n = 261)	50 (19.2)	0.006
>10th percentile (n = 1503)	190 (12.6)	
Benton Visual Retention Test*		
10th percentile (n = 256)	46 (18.0)	0.007
>10th percentile (n = 1321)	153 (11.6)	
Isaacs' Set Test of verbal fluency*		
10th percentile (n = 199)	41 (20.6)	0.001
>10th percentile (n = 1396)	165 (11.8)	

The Mini-Mental State examination was completed by 1766 subjects, the Benton Visual Retention Test by 1579 and the Isaacs' Set Test by 1596.

their metabolites [35, 36] and cognitive impairment or delirium [37–43]. Recently, Mulsant *et al.* measured serum anticholinergic activity in a sample of 201 subjects living in the community and examined the association between SAA and cognitive performance. They found that subjects with SAA at or above the sample's 90th percentile point were significantly more likely than subjects with undetectable SAA to show a low MMSE score [22].

Our results were obtained from a large community-based sample of normal elderly subjects, using very simple neuropsychological tests known to be strong predictors of dementia [21, 23]. Also, low cognitive performance was defined after taking into account the gender, age and educational level of subjects. Analyses were adjusted for a number of potentially confounding factors, such as depressive symptomatology and health status. However, it was not possible to assess whether there was a duration–response or a dose–response relationship between the use of drugs with anticholinergic properties and cognitive performance since no data on doses, duration and frequency of use were collected.

There were relatively few missing data for the neuropsychological tests. This is probably due to the fact that subjects were not volunteers but randomly selected from electoral rolls and tested at home rather than in clinic. In complementary analyses, the potential biases which might be induced by these missing data were

Table 5
Association between use of at least one drug with anticholinergic properties and low score at the Mini-Mental Status Examination (≤10th percentile) — multivariate logistic regression model

Variables	OR (95% CI)	*P*-value
At least one drug with anticholinergic properties		
No	1	
Yes	1.4 (1.0, 2.1)	0.05
Depressive symptomatology (CES-D)		
No	1	
Yes	1.4 (0.9, 2.3)	0.1
At least one non-anticholinergic psychotropic drug		
No	1	
Yes	1.2 (0.9, 1.6)	0.2
At least one cardiovascular disease or risk factor		
No	1	
Yes	1.1 (0.8, 1.5)	0.4
Number of non-psychotropic and non-anticholinergic drugs		
<4	1	
≥4	0.9 (0.7, 1.2)	0.5

Table 6
Association between use of at least one drug with anticholinergic properties and low score at the Benton Visual Retention Test (≤10th percentile) — multivariate logistic regression model

Variables	OR (95% CI)	*P*-value
At least one drug with anticholinergic properties		
No	1	
Yes	1.6 (1.1, 2.3)	0.015
Depressive symptomatology (CES-D)		
No	1	
Yes	1.6 (1.0, 2.5)	0.05
At least one non-anticholinergic psychotropic drug		
No	1	
Yes	1.0 (0.7, 1.3)	0.8
At least one cardiovascular disease or risk factor		
No	1	
Yes	1.1 (0.8, 1.5)	0.5
Number of non-psychotropic and non-anticholinergic drugs		
<4	1	
≥4	1.2 (0.9, 1.7)	0.2

minimized by keeping all subjects in the analysis and replacing missing data by low performance. Since we found similar results to those reported in the principal analyses, it could be assumed that selection biases caused by missing data did not affect the quality of the results.

Additional analyses were conducted to determine whether a reverse causality bias might have altered the results. Indeed, tricyclic antidepressants and antipsychotics could have been prescribed for disorders which can be accompanied by cognitive impairment. Therefore, the association found between the use of drugs with anticholinergic properties and low cognitive performance might have been falsely increased. However, when users of tricyclic antidepressants and antipsychotics with anticholinergic properties were excluded from the analyses, the results found, although not statistically significant, perhaps due in part to a lack of power, were consistent with those reported in the main analyses.

These results show that potential adverse effects of drugs with anticholinergic properties on cognition should be considered when these drugs are prescribed

Variables	OR (95% CI)	*P*-value
At least one drug with anticholinergic properties		
No	1	
Yes	1.9 (1.3, 2.8)	0.0015
Depressive symptomatology (CES-D)		
No	1	
Yes	2.0 (1.2, 3.2)	0.007
At least one non-anticholinergic psychotropic drug		
No	1	
Yes	1.0 (0.7, 1.4)	0.9
At least one cardiovascular disease or risk factor		
No	1	
Yes	0.9 (0.6, 1.2)	0.4
Number of non-psychotropic and non-anticholinergic drugs		
<4	1	
≥4	1.4 (1.0, 2.0)	0.04

Table 7
Association between use of at least one drug with anticholinergic properties and low score at the Isaacs' Set Test of verbal fluency (≤10th percentile) — multivariate logistic regression model

to elderly patients. Several of these drugs are known for their influence on cognitive impairment, particularly antipsychotic drugs, but others are less well known. Thus, in patients presenting cognitive impairment and using drugs with anticholinergic activity, serious consideration should be given to switching to a drug without such activity.

Lastly, this study was cross-sectional and did not allow determination of the direction of the association reported here. Further studies are needed to confirm our results and to investigate the effect of chronic and long-term use of drugs with anticholinergic properties on cognitive performance in the elderly.

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