

Ziad A, Olekhnovitch R, Ruiz F, Berr C, Bégaud B, Goldberg M, Zins M, Mura T

**Anticholinergic drug use and cognitive performances in middle age: findings from the CONSTANCES cohort**

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**ABSTRACT**

**BACKGROUND** - Previous studies have shown associations between the use of anticholinergics (AC) and cognitive performance in the elderly, considering AC as a homogeneous set of drugs. The present study aims to assess the relationship between exposure to AC drugs and cognitive performance in middle-aged adults according to AC potency and drug class. **METHODS** - Our cross-sectional study used baseline data of 34 267 participants aged 45–70 from the Consultants des centres d'examen de santé de la sécurité sociale (CONSTANCES) cohort. The cumulative exposure to AC was measured using national reimbursement databases over the 3-year period preceding assessment of cognitive performance. Eight classes of AC drugs were differentiated. Episodic verbal memory, language abilities and executive functions were evaluated by validated neuropsychological tests. Analyses were controlled on lifestyle and health status variables. **RESULTS** - This study showed a negative association between overall cumulative AC exposure and cognitive performances after adjustment. The use of drugs with possible AC effect according to the Anticholinergic Cognitive Burden scale (ACB-1 score) was only associated with executive functions. Analyses of AC exposure across drug classes showed a negative association between the use of AC antipsychotics and all cognitive functions assessed. Heterogeneous associations were found for the use of AC anxiolytics, AC opioids and AC drugs targeting the gastrointestinal tract or metabolism. We did not find significant associations between the use of antihistamines, antidepressants, cardiovascular system or other AC medications and cognitive function. **CONCLUSION** - Association between AC drugs and cognitive performance was highly heterogeneous across drug classes; this heterogeneity will have to be considered by future studies.

**KEYWORDS:** Cognitive impairment; Ageing; Anticholinergic; Constances cohort; Middle-age; Pharmacoepidemiology

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