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The Relationship Between Anticholinergic Medication Exposure, Daytime Functioning, and Self-Reported Memory Difficulties Among Older Adults

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ABSTRACT

Anticholinergics are commonly used in older populations to treat illnesses like overactive bladder, depression, allergic reactions, and sleep disorders. Given that acetylcholine is involved in the processes of attention, learning, and memory, it follows that drugs which inhibit its effects have the potential to impact both cognition and behavior. Due to age-related alterations in the rate of drug metabolism, reduced levels of cholinergic neurons, and polypharmacy in older individuals, the impact of anticholinergics is magnified in this population. However, the influence of anticholinergic medication exposure on day-to-day functioning and self-reported memory problems is rarely studied together. This paper is aimed at analyzing the association between anticholinergic exposure, daytime functioning, and self-reported memory problems among older community-dwelling adults 65 years and older. The study will employ a descriptive, cross-sectional approach in which anticholinergic burden will be determined by means of medication history using a burden measure, daytime functioning will be assessed in terms of activity and alertness measures, and difficulties in memory will be assessed by means of a self-report questionnaire. The study will point out the need to consider exposure, functioning, and memory difficulties as interrelated aspects rather than unrelated issues. The results of the study will provide justification for medication review, functional screening, and safer medication use.

***Keywords*:** Anticholinergic Burden, Older Adults, Daytime Functioning, Subjective Memory Difficulties, Polypharmacy, Medication Review, Cognitive Health.

1 INTRODUCTION

1.1 Background of Anticholinergic Medication Use in Later Life

Anticholinergics work by interfering with the action of muscarinic receptors, which react with the neurotransmitter acetylcholine in the peripheral and central nervous systems. These medications are prescribed for a vast number of disorders, including incontinence of urine, chronic obstructive pulmonary disease, depression, psychosis, Parkinson's disease, abdominal pain, and allergic reactions. There are many widely used drugs that have an anticholinergic effect in addition to their intended function, leading to accidental exposure of elderly patients. Such a phenomenon is known as anticholinergic burden, which is associated with many adverse health effects in the elderly population (Boustani et al., 2008).

Aging affects the metabolism of drugs and their effects on the brain. With aging, there is a decrease in liver and kidney functions, leading to an increase in drug half-life. Also, the blood-brain barrier becomes more permeable to drugs, and the cholinergic system itself loses its neurons and receptors due to age-related changes. Literature review revealed that these factors contribute to the sensitivity of older individuals to the central nervous system effects of anticholinergics such as confusion, reduced thought process, and memory problems (Campbell et al., 2009). In view of the fact that older individuals usually take multiple medications, the overall load can be significantly higher than the load from one medication alone.

1.2 Importance of Daytime Functioning and Memory in Older Adults

Independence in the later stages of life is contingent on the capacity to perform daily tasks such as dressing, meal preparation, money management, and correct medication administration. Alertness, concentration, and memory are key ingredients of performing these tasks. Hence, medications that have sedation and cognitive effects could impact not only tests but also everyday life by causing drowsiness, loss of energy, and inability to maintain daily routines. Studies focusing on the functional burden of medications have demonstrated a correlation between exposure to medications with anticholinergic and sedative effects and physical and functional impairment in the elderly population (Hilmer et al., 2007).

The importance of the outcome can be explained on the grounds that the effect is not only clinically relevant but also personally relevant. Older people often become aware of the changes in their memory well before the condition is revealed through clinical assessment; and such a self-reported effect has been suggested as an important measure which should be studied (Jessen et al., 2014). Studies based on the population data show that exposure to anticholinergic medication is linked to worse results on cognitive tests among older individuals and exposure over the time has also been linked to brain atrophy and lower cognitive test scores (Fox et al., 2011; Cai et al., 2013).

1.3 Research Problem, Objectives, and Significance of the Study

While the cognitive effects of anticholinergics have received wide attention, many older people keep being prescribed such medications in high numbers, and the everyday impact on their functioning is frequently neglected in regular practice. An individual may cope with the tasks but become exhausted, slower, and more forgetful than before. Such changes can be easily blamed on the natural aging process and not on any drugs taken. This way, the association of the prescribed medication, daily functioning, and self-assessment of one's memory is never studied in an integrated manner. The purpose of the current study is to assess the relationship between exposure to anticholinergics, daytime functioning, and memory complaints in older patients. The particular aims are to determine the anticholinergic load in study participants, to describe their daytime functioning, to assess their memory complaints, and to explore the association of the three variables. This research is important for identifying potential drug-induced problems and dealing with them before it is too late.

2 REVIEW OF LITERATURE

2.1 Anticholinergic Burden and Its Measurement

Since anticholinergic burden is not directly measurable, several clinical scales have been devised for classifying the degree of anticholinergic effect of individual drugs and determining the combined score for all the medications taken by an individual. Such scales include, but are not limited to, the Anticholinergic Risk Scale, the Anticholinergic Drug Scale, and the Anticholinergic Cognitive Burden scale (Rudolph et al., 2008; Carnahan et al., 2006). The drugs are assessed for their anticholinergic effects on a scale and then combined to provide a total burden score. It has been validated that higher burden scores on such scales correlate with serum anticholinergic activity and unwanted effects.

There is not always consistency among the scales. Systematic reviews have reported discrepancies among the measures of classifying the same drugs and their inconsistency in predicting the outcome in different clinical situations (Welsh et al., 2018). Likewise, the review on the accuracy of measures used to quantify anticholinergic burden in the central nervous system highlighted the fact that all available scales are just proxy measurements for the actual anticholinergic burden in the central nervous system (Kersten & Wyller, 2014). Despite such shortcomings, the burden scale still remains the most convenient way to measure the exposure in observational studies, and a systematic review identified the relation between risk scale scores and outcomes in older patients (Salahudeen et al., 2015).

2.2 Anticholinergic Exposure and Cognitive Outcomes

There is evidence that anticholinergic use may impact cognition in large studies. In one of the Medical Research Council Cognitive Function and Aging Study, there was cognitive impairment amongst older individuals using anticholinergics with definite actions, with stronger effects observed among those on multiple anticholinergics (Fox et al., 2011). Anticholinergic drugs have been shown to cause cognitive impairment, falls, and death in meta-analyses of anticholinergic drugs' impact (Ruxton et al., 2015). A study conducted on a large prospective cohort found that high cumulative exposure to anticholinergics was linked to increased incidence of dementia, and a subsequent nested case-control study in the United Kingdom found that anticholinergics had a significant impact on antidepressant, bladder, antipsychotic, and antiepileptic outcomes (Gray et al., 2015; Dening & Morriss, 2019).

There is also some evidence that the risk builds up with long-term usage. People who had taken these drugs for many years performed poorly on cognitive tests and had abnormal structural changes and metabolism in their brain (Cai et al., 2013). While there is no proof of causality between the medicines and the development of dementia because the underlying diseases might affect cognition, this still means that anticholinergic drug usage needs to be considered as a modifiable risk factor.

2.3 Daytime Functioning and the Functional Burden of Medication

Daytime function is defined as the capability to be awake and complete everyday activities without being excessively fatigued or assisted. In older people, it is typically assessed using everyday activities

of daily living, instrumental activities like managing medicines and money, and sleep-related wakefulness. The Drug Burden Index was created to quantify the functional burden of anticholinergic and sedative medicines, and elevated scores were linked to decreased physical and cognitive performance in community-living older people (Hilmer et al., 2007). Literature has also suggested that falls, confusion, and immobility are frequently seen effects of excessive anticholinergic load (Boustani et al., 2008; Salahudeen et al., 2015). However, very few studies have considered the impact of the individual's self-reported memory along with their actual performance. Studies have used formal cognitive tests and cases of dementia as endpoints, meaning that more common problems may be overlooked. Clinical reviews have indicated that anticholinergic drugs can affect attention, processing speed, and short-term memory in small ways and that their effects might first become noticeable through complaints in daily activities (Campbell et al., 2009).

2.4 Self-Reported Memory Difficulties, Prescribing Guidance

Subjective cognitive decline is a subjective perception of reduced ability that cannot be measured using conventional instruments. An internationally recognized group proposed a conceptual model suggesting that subjective complaints reflect an initial cognitive alteration and should be examined in detail (Jessen et al., 2014). The value of self-report lies in its relevance to the patient, simplicity of measurement, and possibility of being conducted outside medical facilities where conventional assessments are unfeasible. In turn, self-reported memory is sensitive to mood state, sleep disturbances, and personality traits, which calls for interpretation in context with other factors. The prescription guidelines have increasingly incorporated these worries into their guidance. The Beers Criteria by the American Geriatrics Society advises against the use of potent anticholinergic drugs among older adults and the combination of two or more anticholinergics. These guidelines rely on the awareness of the practical implications of exposure, which in turn relies on evidence of such linkages between medical data and real-life events.

2.5 Research Gap

Previous studies have focused on anticholinergic exposure and objective cognitive function or dementia. Daytime function and memory complaints have been studied in isolation, or not at all, even though they are the domains that older people tend to be most aware of. Medication burden has been discussed without any consideration of the individual's daytime function, and memory complaints have been discussed without any consideration of medication use. Anticholinergic exposure does not mean that each individual will experience the same degree of difficulty, and memory complaints can result from tiredness or lack of functioning and not memory. It is thus important to look at the relationship between these three constructs simultaneously, as they paint a more complete picture of the effects of anticholinergics on older people. The current study aims to fill this void by studying the three constructs in one sample of older individuals.

3 METHODOLOGY

3.1 Research Design and Exposure–Outcome Investigation Framework

In the current study, a descriptive cross-sectional research design has been used to explore the link between anticholinergic medication exposure, daytime functioning, and perceived memory problems among the elderly population within a specified period. The choice of the cross-sectional study design is appropriate since it helps evaluate medication exposure, functional status, and perceived memory simultaneously in a community setting without following up on individuals for an extended period of time. In developing an investigation framework, three dimensions were considered. The exposure dimension refers to the anticholinergic burden measured based on all medications taken by participants on a regular basis. The dimension of daytime functioning refers to the ability to perform daily tasks independently and to be alert during the day. The dimension of memory involves the frequency and severity of memory problems experienced during daily routines by the participant.

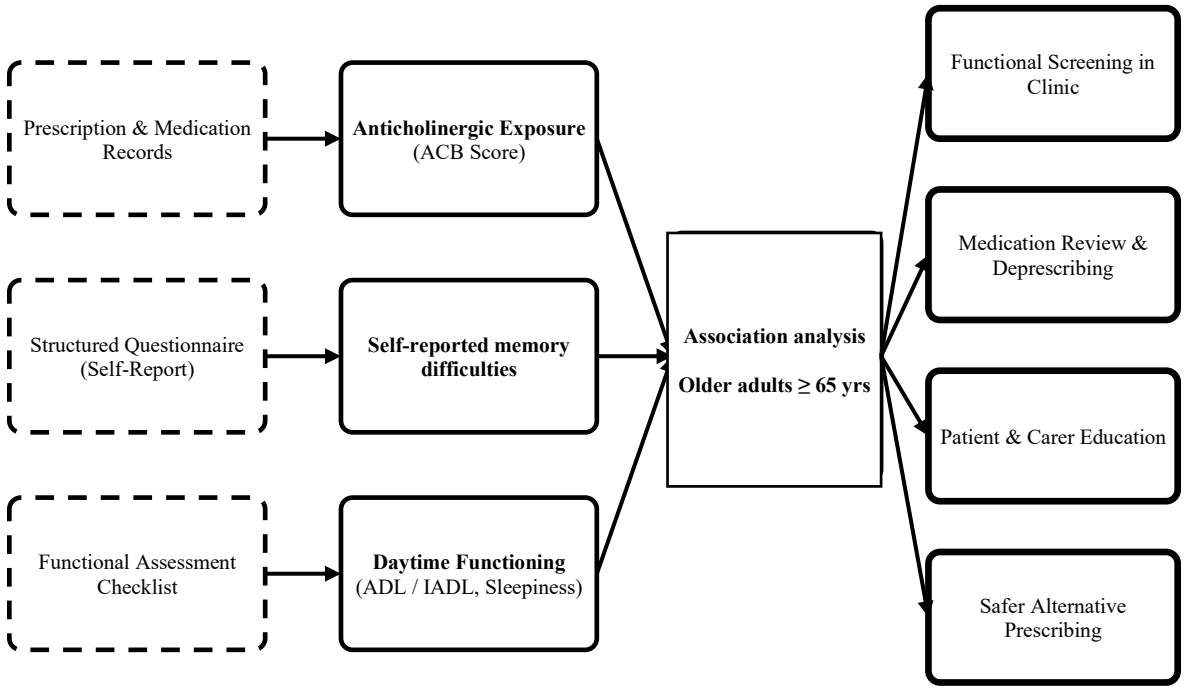


Figure 1. Integrated Medication Risk Assessment and Functional Care Pathway for Older Adults

Figure 1 above shows a composite model linking anticholinergic exposure, reported memory problems, and daytime functioning through association modeling of adults who are 65 years or older. The importance of drug record keeping, questionnaires, and functional testing in enhancing clinical screening, drug assessment, safe prescribing practices, and patient education is emphasized.

There are three assumptions underlying the model above. Firstly, anticholinergic exposure is assumed to be a continuous variable rather than a binary one since the risk that comes from being exposed to a single but weak drug cannot be the same as that from a number of strong drugs. Secondly, daytime functioning is assumed to be a mediating experience that carries forward the effect of medication to day-to-day experiences such as feeling drowsy and having reduced attention, which

affects memory ability negatively. Finally, reported memory is assumed to be an important outcome in its own right despite not being formally impaired, as it reflects the older patient's concerns.

3.2 Participant Selection and Medication Profile

The selected sample comprises adults residing in the community above the age of 65 years who were regularly taking at least one prescription drug and who could respond to questions about their memory and activities of daily living. The selection of the sample was carried out using purposive sampling, whereby participants were recruited via outpatient clinics, community health centres, and senior citizens' groups. Individuals suffering from dementia or cognitive impairment, individuals with an acute disease or hospitalization within the previous month, individuals with severe visual and hearing impairment such that participation in the study was not possible, and individuals who were unable to give informed consent were excluded. This process was aimed at ensuring that the self-reporting of memory could be considered a valid report and not a symptom of existing dementia. The demographic and clinical information obtained included age, sex, education, type of residence, number of co-morbidities, number of regularly used drugs, and the clinical reason for prescribing anticholinergic drugs.

3.3 Data Collection Procedure and Instruments

The data were obtained by means of a structured interview supplemented with the examination of patients' medications. Data on the medications were collected from their current prescriptions, pharmacy logs, and the medications patients were carrying to the appointment. Participants were questioned regarding non-prescription medications, including sleeping pills and anti-allergy tablets. The anticholinergic score of each medicine was calculated based on the established burden scale, and the total burden score was obtained by adding all individual scores. Daytime function was assessed using the activities of daily living and instrumental activities checklist together with a short test for daytime sleepiness. Memory problems were evaluated using a structured memory test assessing how often patients forget people's names, appointments, conversations, and the placement of things, and how troubling this is for them. Depression symptoms were tested using a brief depression test to control for the influence of low mood during the analysis. The interviews were performed by trained researchers in a quiet place and lasted about thirty minutes. Prior to conducting the study proper, the questionnaires and checklists were assessed for relevance and understandability among older people by a geriatrician and a clinical pharmacist, and a pilot study was also conducted among a small number of older people to verify that the questions could be properly answered and that the duration of the interview was reasonable. The information about the medications of each participant was entered twice in order to ensure accuracy, and the calculation of the scores was done according to a standardized protocol for all drugs.

3.4 Measurement System, Statistics, and Ethics

Anticholinergic drug exposure was categorized into three levels: none (burden score = 0), low (burden score = 1 to 2), and high (burden score ≥ 3). The measure of daytime functioning was the number of tasks completed per day, along with the sleepiness score, while memory difficulty was defined as the total score on the questionnaire, with higher scores reflecting increased difficulties. Descriptive statistics were used to summarize the characteristics of participants and the distribution of drug exposure. Comparisons among different levels of drug exposure were done using chi-square test or analysis of variance /non-parametric equivalents based on data distribution. Correlation analysis was applied to determine any association between functioning and memory scores. Multiple regression was further proposed to evaluate the association between anticholinergic burden and functioning and memory after controlling for age, education, medication load, mood, and sleep. The ethical aspects involved in the study included obtaining informed consent in writing from all participants, voluntary participation in the study, record confidentiality, proper data management, and obtaining clearance from the appropriate institutional review board before collecting data. It was ensured that participation in the study would not influence the medical care of the subjects in any way. Additionally, the study team did not alter any medication of the subjects.

4 RESULTS AND DISCUSSION

4.1 Participant Characteristics and Exposure–Outcome Patterns

Describing the characteristics of the participants is the first step in interpreting how anticholinergic exposure relates to daily life. Age, sex, education, number of chronic conditions, and number of regular medicines all influence both the likelihood of exposure and the likelihood of functional or memory difficulty. Older participants and those with several conditions are more likely to take multiple drugs, and they are also more likely to report tiredness and forgetfulness for reasons unrelated to medication. The comparison of exposure groups therefore focuses on whether difficulty in functioning and memory rises step by step across the no exposure, low exposure, and high exposure groups, and whether this pattern remains after the background factors have been taken into account.

Interpreting these comparisons requires care. A higher burden in people who report more forgetfulness could reflect the effect of the drugs, but it could equally reflect the fact that people with conditions such as depression, urinary problems, or chronic pain are both more likely to be prescribed these medicines and more likely to feel tired or forgetful. The adjusted analysis is intended to reduce, but cannot remove, this confounding by indication.

This is schematically illustrated by figure 2 above, where it was hypothesized that as the anticholinergic burden rises, difficulty with daily functioning and memory recall would rise in proportion. This is a diagrammatic representation only and does not illustrate actual values.

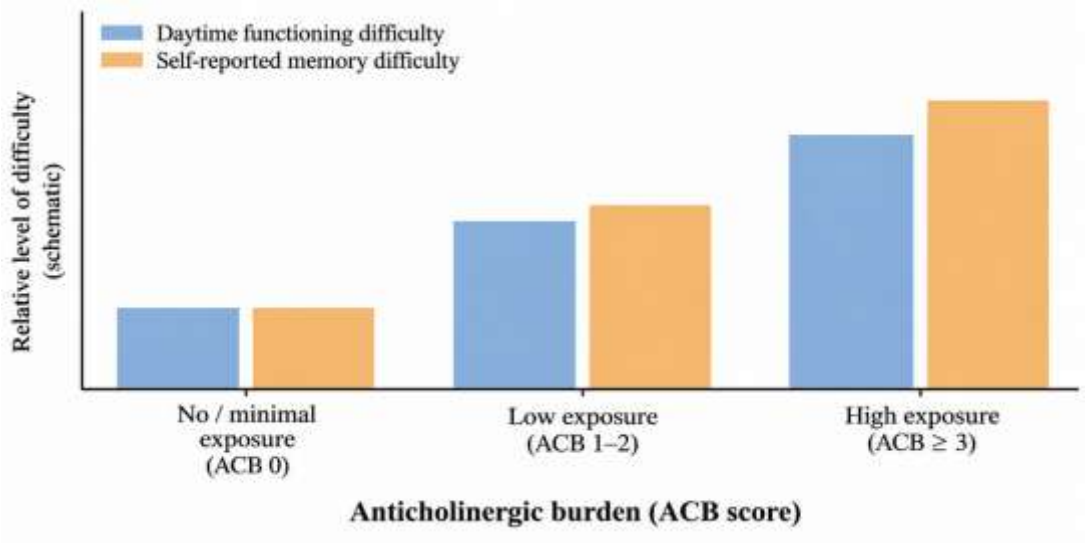


Figure 2: Expected Pattern of Daytime Functioning and Memory Difficulty Across Anticholinergic Exposure Levels

4.2 Exposure, Daytime Functioning, and Memory Difficulty Relationships

Functioning and memory problems are distinct dimensions of health that go hand in hand with each other. Functioning refers to what the individual can do and how awake and alert he or she is, while self-rated memory refers to how well the individual thinks he or she can remember things.

Table 1. Summary of Key Indicators for Assessing Anticholinergic Exposure, Daytime Functioning, and Memory Difficulties

Study dimension	Key indicators	Assessment method
Anticholinergic Exposure	Number of Anticholinergic Drugs, Total Burden Score, Exposure Category	Medication Records and Burden Scale
Daytime Functioning	Independence in Daily and Instrumental Activities, Daytime Sleepiness, Fatigue	Activities Checklist and Sleepiness Scale
Self-Reported Memory Difficulty	Forgetting Names, Appointments, Conversations, and Objects; Distress Caused	Structured Memory Questionnaire
Covariates	Age, Sex, Education, Chronic Conditions, Mood, Sleep Quality	Interview and Brief Screening Scales

One participant can have a high level of exposure but experience no impairments in terms of activities and yet experience forgetfulness; another can experience fatigue and lack of independence but rate his or her memory as good. There is thus a need to study each of the two aspects on its own and to look at the relationship between them.

Table 1 describes the indicators employed in the assessment of each of the dimensions of the study. This table indicates how measurements were carried out and the methods used, hence enabling comparison between exposure, functioning, and memory.

Table 2: Analytical Comparison Framework for Anticholinergic Exposure Groups

Exposure group	**Daytime Functioning Outcome Examined**	**Memory Outcome Examined**	**Statistical Approach**
No Exposure (score 0)	Reference Level of Independence and Alertness	Reference Level of Memory Complaints	Descriptive Statistics
Low Exposure (score 1–2)	Differences in Activity Independence and Sleepiness Compared with Reference	Differences in Questionnaire Score Compared with Reference	Chi-Square Test and ANOVA
High Exposure (score ≥ 3)	Greater Limitation and Sleepiness Expected	Higher Frequency and Distress of Memory Complaints Expected	ANOVA and Correlation
All Groups, Adjusted	Association after Controlling for Age, Mood, Sleep, and Number of Medicines	Association after controlling for the same factors	Multiple Regression

Table 2 presents the way in which each measure will be used for comparisons between exposure groups. It demonstrates that the analysis process involves a transition from comparing groups to more complex models, making sure that the results do not depend merely on raw comparisons. The hypotheses indicated in table 2 are to be tested using the collected data.

In addition, the type of drug taken needs to be considered when discussing the findings since bladder antimuscarinics, tricyclic antidepressants, first-generation antihistamines, and certain antipsychotics have different degrees of passage through the blood-brain barrier, and thus a person taking one potent drug will be more affected than one taking several weaker ones. For this reason, the various types of anticholinergics are outlined for each exposure category, and the contribution of individual drugs is considered wherever possible. It is possible that the relationship between the participants' exposure to anticholinergic drugs and memory complaints will be found to be mediated by their daytime functioning.

4.3 Clinical Implications and Strategies for Reducing Anticholinergic Burden

Analysis of the results will have value when it comes to the safe prescription of medications for elderly individuals. Those who have been identified as being exposed to a higher degree but who function poorly or have impaired memories may help the clinician determine those individuals who should receive priority in medication review. When an anticholinergic agent that is not necessary can be removed from a patient's regimen, it can be done slowly, the dosage can be reduced, or it can be replaced with a different agent that will have less impact on the brain. Pharmacists can assist by

checking the anticholinergic burden of the medicines prescribed, as well as making recommendations for suitable alternatives. Functional screening can be performed easily during routine visits at minimal cost, including screening for tiredness, problems with performing daily activities, and memory loss. Patients should be aware that any new episodes of confusion or impairment in their memory can be due to the medication they have been taking.

The last thing is that the results should be communicated to the patients and their doctors in a comprehensible manner, and in case there is a need to discontinue the use of one medication, this decision should be taken collectively by the physician and the patient. A sudden stoppage of anticholinergics can result in withdrawal symptoms or recurrence of the initial problem; thus, a slow discontinuation is required. The development of policies that would encourage medication review would be useful.

5 CONCLUSION

5.1 Summary of Findings and Overall Conclusion

The research has revealed the correlation between anticholinergic drug use, daytime performance, and subjective problems with memory among the elderly. It has been shown that all three aspects are interconnected and must be studied together, rather than individually. The model that was developed for the research is based on the combination of information about the use of medications, performance, and subjective complaints regarding the problems with memory, and makes it possible to isolate the influence of exposure from the impact of age, mood, sleep, and number of drugs. It should be pointed out that the safety of using medications at old age is not only the treatment of the disease but also the protection of alertness and self-confidence.

5.2 Clinical Implications, Limitations, and Future Research Directions

According to the study, there is a need to regularly assess the medications taken by older adults with respect to anticholinergic burden, as well as to include functional assessment and memory queries in that process. Pharmacists, doctors, and caregivers can cooperate in finding high-risk drug combinations, as well as in evaluating the possibility of switching to alternative treatments. Several limitations must be noted. Firstly, the cross-sectional nature of the study does not allow conclusions about cause-and-effect relationships and the direction of associations, as people who suffer from memory or functional impairment are likely to receive certain drugs. Secondly, self-reports of memory and daytime functioning are subject to recall bias and to the effect of the current mood and individual characteristics. Thirdly, anticholinergic burden rating scales vary among themselves, and those are just approximations of receptor blockade, and therefore the findings of the study cannot be extrapolated to all older people. Further research can employ longitudinal designs, larger samples of different kinds, objective cognitive measures, and activity/sleep monitoring through wearable devices.

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