Brief Report

Serum Anticholinergic Activity and Motor Performance in Elderly Persons

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Background. Medications prescribed to elderly persons often have an anticholinergic effect, as do many commonly used over-the-counter drugs. Anticholinergic medications are known to produce psychomotor slowing, especially in older persons.

Methods. The present study examined whether the cumulative anticholinergic load present in the serum of community volunteers was associated with decrements on tests of psychomotor performance (gait speed and simple manual response time) known to predict falls in elderly persons.

Results. Serum anticholinergic activity (SAA) was relatively low in this group; however, an elevated SAA was associated with a significant slowing in both gait speed and simple response time.

Conclusion. Cumulative anticholinergic burden may be one of the factors contributing to an increased risk of falls in the older population.

Methods

Participants

Participants (Table 1) came from an ongoing study examining the relationship of SAA to cognitive performance in elderly persons. Participants did not have a history of major neurological or psychiatric disease, nor were they taking any sedative-hypnotics, antidepressants, or antipsychotics (the major types of medications associated with falls in the elderly population). All participants received a physical examination by a nurse practitioner. To exclude cognitively-impaired individuals, potential participants were given the Repeatable Battery for the Assessment of Neuro-psychological Status (8). Of 90 individuals tested, two had an age-adjusted scaled score on this battery more than 1.5 standard deviations below the mean and so were excluded.

Procedure

Prior to testing, 10 cc of blood were drawn to measure SAA using a radioreceptor competitive binding assay (6). Anticholinergic medications in the serum competitively inhibit binding of tritiated quinuclidinyl benzilate (which binds with high affinity to all muscarinic receptor subtypes). Displacement of quinuclidinyl benzilate bound to a homogenate of rat forebrain was used to quantify SAA, reflecting the cumulative anticholinergic effect of all exogenous substances (and their metabolites) taken by the participant. Atropine was used to develop a standard curve, and results are expressed in picomoles of atropine equivalents per milliliter (pmol/mL).
Participants were given a simple response-time task (SRT) in which they pressed a button with the index finger of their dominant hand as soon as a 1-centimeter dot appeared in the center of a computer screen. The interstimulus intervals between the participant’s response and the appearance of the next dot varied randomly between 1.5 and 3 seconds. Simple manual response time is a strong predictor of falls in elderly individuals (9).

Participants walked a 15-foot course along a carpeted corridor. They began from a full stop and were told to walk at their usual pace until they crossed the marked finish line. Walking time was measured with a stopwatch to the nearest 1/10th of a second from the signal to begin until the participant’s foot crossed the 15-foot mark. Participants walked the course twice, and the two times were averaged. Walking speed has been shown to predict falls in the elderly population, and is a marker for mobility and risk for falls (10). The participants performed the 15-foot walk and the SRT within 20 minutes of the blood draw.

RESULTS

The distribution of SAA values was skewed, with the majority of participants having lower SAA values. Thus, participants were categorized into three groups at natural breaks in the distribution: 29 persons with low SAA (0–0.8 pmol/mL), 33 with moderate SAA (0.81–1.89 pmol/mL), and 26 with high SAA (> 1.9 pmol/mL).

Univariate analyses of variance were run between the three SAA groups on participant characteristics and performance measures (Table 1). The SAA groups did not differ in age, education, or sex ratio, but did differ significantly in the time they took to walk 15 feet and in their simple manual response time. Tukey post hoc comparisons (HSD) were performed with the error rate held to .05. These comparisons showed that, on the 15-foot walk, the High-SAA group was significantly slower than the Low-SAA group, whereas on the SRT, both the Medium- and the High-SAA groups were slower than the Low-SAA group. No other comparisons were significant.

Because (i) the SAA groups did not differ in age or sex, (ii) older women have more falls than do older men (3), and (iii) increased age is strongly related to a slowing in both response time and gait speed (11), we performed a multivariate analysis of covariance (MANCOVA) on the 15-foot walk and SRT results. Even after controlling for age and sex, SAA group still had a significant effect on the two performance tasks (F = 3.43, df = 4,164; p = .01).

Another potential confounder is participant health. In particular, individuals with cerebrovascular disease often have psychomotor deficits and may coincidently be taking many medications, including anticholinergics (e.g., digoxin). Thus, it could be a difference in neurological status and not SAA that produced the performance differences between groups. To estimate the severity of cerebrovascular disease in our participants, we created a Framingham Stroke Risk Profile for each participant (12). This profile uses a variety of risk factors (e.g., hypertension, diabetes) to calculate the probability that an individual will have a stroke within the next 10 years. Table 1 shows that there was no significant difference in stroke risk between the groups, making it unlikely that variability in the severity of cerebrovascular disease in the three SAA groups confounded the effect that SAA had on motor performance.

DISCUSSION

In this study, an elevation in SAA was associated with a psychomotor slowing on two tasks (gait speed and simple manual response time) that have been shown to predict balance problems and falls in elderly persons. The gait speed found here is similar to that reported in the literature (11) for community-dwelling persons in their 70s who typically walk at a rate of 1.1–1.2 m/s. If we transform the 15-foot walk times for the SAA groups into a similar metric, the Low-SAA group had a mean gait speed of approximately 1.1 m/s, whereas the High-SAA group had a mean speed of about 0.9 m/s. The degree of slowing found within the High-SAA group is certainly not in the range (e.g., 0.5 m/s) associated with a high risk of falling (10). However, if even high-functioning, cognitively intact individuals show motor performance slowing with the relatively low SAA levels found here, then given the amount of anticholinergic drugs taken by elderly persons (4,13), an elevation in an individual’s cumulative anticholinergic burden could increase the risk of falls, particularly in frail or institutionalized older individuals. That is, anticholinergic burden may be one of the factors associated with a heightened risk of
falls in the older population. This may be especially true of patients with Alzheimer’s disease who are known to be hypersensitive to anticholinergic medications.

There are several limitations to this study. SAA reflects anticholinergic activity in participants’ blood, not in their brains. Medications that do not cross the blood–brain barrier will contribute to SAA without having a corresponding central effect, thus weakening any relationship between SAA and performance. The possible existence of nonpharmaceutical contributions to SAA associated with endogenous physiological sources (14) may also complicate the present results as it is not clear that such physiological sources affect brain function. Finally, it is not presently possible to determine which of the wide variety of medications taken by the participants led to an increased SAA, because relatively few medications have been specifically examined for their anticholinergic activity (4), and those that have were not examined at therapeutic concentrations. However, there were a number of medications taken by individuals in this study that are known to produce moderate-to-high SAA including oxybutynin, diphenhydramine, digoxin, cimetidine, ranitidine, and prednisone. The above factors limit the present clinical utility of the SAA measure for predicting the risk that anticholinergic medications have for balance in a particular individual. However, the results do suggest that an older individual’s existing anticholinergic burden should be considered prior to prescribing an anticholinergic medication or when evaluating possible causes of falls, especially in the case of frail, demented, or balance-impaired individuals (13).

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