Small Longitudinal Study of Serum Anticholinergic Activity and Cognitive Change in Community-Dwelling Older Adults

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Objective: *The discriminative ability of serum anticholinergic activity (SAA) to differentiate between older individuals with stable versus deteriorating cognition remains undetermined. We examined the relationship between SAA changes, the presence or absence of a mild neurocognitive disorder, age and anticholinergic medication over a one-year time period.* **Methods:** *SAA at baseline and one-year follow-up was measured for 121 older adults without dementia. Participants were classified at both timepoints as being cognitively intact or meeting the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for a mild neurocognitive disorder. Medications were assessed according to the Anticholinergic Cognitive Burden (ACB) scale.* **Results:** *SAA changes did not discriminate between individuals whose cognition remained stable versus those with improvement or decline (H[3] = 0.725, p = 0.867). SAA change did not vary between age groups, and could not reliably differentiate between individuals on ACB medication or not.* **Conclusion:** *While SAA does not appear to be a valid biomarker for cognitive decline, longitudinal studies with a larger sample size and longer duration are required to confirm this finding.* (Am J Geriatr Psychiatry 2015; 23:326–329)

Key Words: SAA, older adults, anticholinergic

INTRODUCTION

The validity of serum anticholinergic activity (SAA) as a biomarker of cognitive dysfunction in older adults is a subject of continuous debate.[1–3] Over the past three decades, the SAA assay has been used to quantify drugs that possess anticholinergic activity in vitro and to document elevated serum anticholinergic levels in community-dwelling and hospitalized patients with delirium and dementia.[1,4–6] Anticholinergic medication, plasma proteins, and endogenous anticholinergic hormones such as cortisol may all contribute to measurable SAA, which essentially measures serum displacement of radioactive [^{3}H]Quinuclidinyl benzilate binding to an in vitro suspension of rat brain muscarinic receptors.[1–3,7] Most published studies use cross-sectional rather than longitudinal designs and show significant interindividual variability in SAA, with no clear cut-off that predicts the presence of delirium or chronic neurocognitive dysfunction.[1,2]

To test the hypothesis that SAA is a biomarker of cognitive decline, we explored whether changes in SAA over time could be used to discriminate between community-dwelling older adults with stable versus deteriorating cognitive function. We also examined the relationship between SAA changes, age, and anticholinergic medication.

METHODS

Study Design and Participants

A prospective 1-year longitudinal cohort study of all new consecutive patients aged 65 years and older

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presenting for evaluation of urinary incontinence at an outpatient clinic was conducted from February 2009 to February 2011 in Quebec, Canada. Patients with existing dementia or depression were excluded. The study was approved by the Ethics Review Board of the Institut universitaire de gériatrie de Montréal. All participants provided written informed consent.

Measurement of SAA

SAA was measured at baseline and 1 year after inception into the cohort using the radioreceptor assay method developed by Tune and Coyle.[8] SAA is reported in picomoles of atropine equivalents per milliliter (pmol/mL), based on the amount of [^{3}H] QNB displacement that would have been caused by a standard amount of atropine in a 200-μL sample. The limit of detection for each batch of SAA in this study varied from 0.247 pmol/mL to 0.46 pmol/mL, with a standard linear curve ($r = 0.99$) from 0.50 to 25.00 pmol/mL and a coefficient of variation <12%. Undetectable SAA values were set at the lower limit of detection for each SAA assay ($N = 5$).

Measurement of Cognitive Change Over Time

We previously described how a geriatrician and an experienced neuropsychologist, blinded to each participant's SAA level, independently classified participants at baseline and again at 1-year follow-up as being cognitively intact or meeting the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,* criteria for a mild neurocognitive disorder.[9] Participants were categorized into one of four groups. The first group had persistent cognitive dysfunction, meeting criteria for a mild neurocognitive disorder both at baseline and 1-year follow-up. The second group met criteria for a mild neurocognitive disorder at baseline but not at the 1-year follow-up. The third group was deemed to have normal cognition at baseline but met criteria for a mild neurocognitive disorder at 1 year. The fourth group was cognitively normal both at baseline and follow-up.

Use of Anticholinergic Medications

Use of medication was self-reported by participants and validated against medication containers. The anticholinergic activity of each medication was assessed according to the Anticholinergic Cognitive Burden (ACB) scale and summed to yield an ACB score for each time point.[4] Higher scores indicate greater anticholinergic burden. Participants were subdivided into those that had an increase in ACB scores at the 1-year follow-up, those that had a decrease in ACB scores, those whose ACB score remained stable, and those not taking any anticholinergic medications at baseline and follow-up.

Analysis

Changes in SAA over 1 year were calculated by subtracting the baseline SAA from the SAA at the 1-year follow-up. Descriptive statistics were used to determine the distribution of SAA changes by cognitive status changes, change in ACB, and age. Age was divided into three groups based on the age of the participants at baseline: 60–69 years, 70–79 years, and 80 years and older. The distribution of SAA values were not normally distributed, and we found evidence of outliers. Thus, the Kruskal-Wallis one-way analysis of variance by ranks nonparametric test was used to assess statistical significance ($p < 0.05$) between groups. For the analysis comparing changes in SAA with changes in anticholinergic medication intake, two groups did not have sufficient sample size for comparison, so the nonparametric Mann-Whitney U test was used to compare participants whose ACB score increased with those who were not taking any anticholinergic medication at both time points.

RESULTS

One hundred twenty-one participants with complete data were analyzed. The mean age of the participants was 71 years (standard deviation [SD]: 7.2), and most were women ($N = 102$; 84.3%). The mean change in SAA over 1 year for the entire sample was 0.08 (SD: 1.20; range: −2.60 to 5.71); mean baseline values were 1.03 pmol/mL (SD: 0.75; range: 0.24–4.65) and mean 1-year follow-up values were 1.10 pmol/mL (SD: 1.30; range: 0.18–8.36). Half the cohort ($N = 60$) demonstrated a pattern of increase in SAA, whereas the other half ($N = 61$) showed a decrease at 1 year.