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Association between toxocariasis seropositivity and serointensity and cognitive function in older U.S. adults

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Abstract: The nematodes *Toxocara canis* (Werner, 1782) and *Toxocara cati* (Schrank, 1788) have been associated with worse human cognitive function in children and middle-aged adults. In this study, we sought to determine the association between *Toxocara* seropositivity and serointensity determined by detection of IgG antibodies against the *Toxocara* antigen recombinant Tc-CTL-1 and cognitive function in older adults, including approximately 1,350 observations from the 2013–2014 National Health and Nutrition Examination Survey. Mean fluorescence intensity was used to quantify IgG antibodies against the *Toxocara* recombinant Tc-CTL-1 antigen, and respondents were considered positive at values greater than 23.1. In adjusted models from sample sizes ranging from 1,274 to 1,288 depending on the individual cognitive task, we found that *Toxocara* seropositivity was associated with worse performance on the animal-fluency task (b = -1.245, 95% CI: -2.392 to -0.099, P< 0.05) and the digit-symbol coding task (b = -5.159, 95% CI: -8.337 to -1.980, P< 0.001). *Toxocara* serointensity assessed using log-transformed mean fluorescence intensity as a continuous variable was associated with worse performance on the digit-symbol coding task (b = -1.880, 95% CI: -2.976 to -0.783, P < 0.001). There were no significant associations with tasks assessing memory. Further, age modified the association between *Toxocara* and cognitive function, although sex, educational attainment, and income did not. These findings suggest that *Toxocara* might be associated with deficits in executive function and processing speed in older U.S. adults, although additional research is required to better describe cognitive function in older adults who are seropositive for *Toxocara* spp.

Keywords: *Toxocara cati*, *Toxocara canis*, toxocariasis, cognition, National Health and Nutrition Examination Survey

Among the factors associated with cognitive decline and dementia are several different infectious diseases (Aiello et al. 2006, Kountouras et al. 2007, Maheshwari and Eslick 2015, Nimgaonkar et al. 2016). Neuroinvasive nematodes with a worldwide distribution *Toxocara canis* (Werner, 1782) and *Toxocara cati* (Schrank, 1788) have previously been associated with decreased cognitive function in both children and young adults (Gale and Hedges 2020).

The prevalence of infection with species of *Toxocara* Stiles, 1905 varies by region, ranging from less than one percent to 86 percent or more, including a prevalence of 5.1 percent in the United States (Berrett et al. 2017, Gale and Hedges 2020). The definitive hosts of *T. canis* and *T. cati* are dogs and cats, respectively (Gale and Hedges 2020), with humans functioning as paratenic hosts (Ma et al. 2018). *Toxocara canis* and *T. cati* can infect humans via embryonated eggs in the soil and contaminated food (Woodhall and Fiore 2014).

Although *T. canis* and *T. cati* are separate species, most assays do not distinguish between the two (Ma et al. 2018). In humans, third-stage *Toxocara* larvae can penetrate the brain, which can result in encephalitis, meningitis, and inflammation (Holland and Hamilton 2013). Risk factors for *Toxocara* infection include increasing age, male sex, lower income, and lower educational attainment (Berrett et al. 2017).

In animal models, *Toxocara* has been associated with decreased memory and decreased exploratory behaviour, although not all findings have been consistent (Gale and Hedges 2020). In a murine model, *T. canis* was associated with decreased learning (Hamilton et al. 2006). A systematic review of neurotoxocariasis in humans found associations with decreased cognitive function, confusion, and encephalitis (Deshayes et al. 2016). Further, *T. canis* has been associated with decreased cognitive function in preschool children (Nelson et al. 1996). In one pediatric sample, *Toxocara* was associated with decreased cognitive function (Marmor et al. 1987). In another pediatric sample, children seropositive for *Toxocara* scored lower on the Wechsler Intelligence Scale for Children – Revised and on the Wide Range Achievement Test – Revised (Walsh and Haseeb 2012). Likewise, in a large sample of young

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to middle-aged adults aged 20 to 59 years representative of the U.S. population, *Toxocara* seropositivity was associated with decreased function on the digit-symbol coding task, although there were no associations between *Toxocara* seropositivity and performance on a task of simple reaction time in adjusted models (Erickson et al. 2015).

While the available findings to date show a potential association between *Toxocara* and worse cognitive function in children and young to middle-aged adults, few if any studies have investigated whether *Toxocara* is associated with cognitive function in older adults, although any such associations might be helpful in examining whether *Toxocara* might be involved with neurodegenerative diseases. To better understand the associations between *Toxocara* and cognitive function in older adults, we used data from the U.S. Center for Disease Control and Prevention's National Health and Nutrition Examination Survey to evaluate the association between *Toxocara* and cognitive function in older adults aged 60 to over 80 years.

MATERIALS AND METHODS

Study sample

Participant data for this study come from the U.S. Center for Disease Control and Prevention's 2013–2014 National Health and Nutrition Examination Survey (NHANES). Although more recent data are available, the 2013–2014 cycle is the most recent that contains data for both *Toxocara* antibodies and cognitive function to enable a determination of the association between *Toxocara* and cognitive function in older adults. The complete NHANES data include 10,175 individuals. Inclusion in our analytic sample was limited by the presence of data for *Toxocara* and cognitive functioning. *Toxocara* data are available for a subset of the Mobile Exam Center subsample (https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/SSTOCA_G.htm) that had surplus sera after initial lab work was completed—6,600 participants. We further limited the analytic sample to include participants aged 60 or over as they were the only participants asked to complete the cognitive functioning tasks. For various reasons, each of the cognitive functioning measures had small differences in the amount of data available. The cognitive functioning measure with the least missing had 1,477 valid observations. The final sample limitation was missing data on model covariates.

Item-level missing values for the covariates ranged from 0 to 7.24 percent (based on the cognitive functioning measure with the least amount of missing data) with a mean of 0.73 percent (standard deviation 1.59) and median of 0.07 percent.

NHANES provides variables representing the complex sampling design (i.e., weights, strata, primary sampling units) for different subsamples of the data that they recommend being employed in analyses to make the results representative of the U.S. population. However, the *Toxocara* data for the 2013–2014 data cycle present a unique challenge in this regard. Because the *Toxocara* data were derived from surplus sera, it is not a subsample that is characterised in terms of national representativeness. In other words, the valid data for *Toxocara* were not by design, and there are, therefore, no complex sampling characteristics to incorporate into analyses to make them nationally representative. Therefore, our treatment of the data is as a convenience sample in this application.

Assessment of *Toxocara* spp.

The NHANES tested for *Toxocara* by a Luminex assay to detect and quantify IgG antibodies against the *Toxocara* antigen recombinant Tc-CTL-1, an immunodominant *Toxocara* antigen that distinguishes between *Toxocara* and other parasitic infections in murine models (https://onlinelibrary.wiley.com/doi/full/10.1111/tmi.12607), although it does not distinguish between *Toxocara canis* and *Toxocara cati*. NHANES defined *Toxocara* seropositivity as mean fluorescent intensity values for recombinant Tc-CTL-1 greater than 23.1 (https://wwwn.cdc.gov/Nchs/Nhanes/2013–2014/SSTOCA_H.htm last accessed 5/2021). The assay is validated against reference serum and has a sensitivity of 90% and a specificity of 99% (Anderson et al. 2015). In our analyses, we used the seropositivity variable provided by NHANES and also used mean fluorescence intensity as a continuous variable (serointensity) after natural-log transformation because of its skewed distribution.

Neuropsychological tests

For the 2013–2014 cycle, the NHANES assessed memory function with the word-list memory test from the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) (Welsh et al. 1994). This test is a 10-item list of words that is read to participants after which they are asked to recall as many as possible. Specifically, we analysed performance on trial 1 (immediate recall of the 10-item word list), total (total number of words recalled from all three trials), and delayed recall (5-minute delayed recall of the list). A measure of executive function, the verbal fluency test, was also part of the CERAD battery. On this measure, participants are tasked to generate as many names of animals as possible in sixty seconds. Finally, the digit-symbol coding test from the Wechsler Adult Intelligence Scale-III edition (1997) was also administered to NHANES participants. This measure can be broadly thought of as evaluating processing speed as participants are required to look at a key with digits paired with symbols and then quickly fill in a portion where the numbers are present, but their paired symbols are missing. In addition to processing speed, this measure taps into attention, working memory, and even motor function since the participants must efficiently write in the correct symbols. The total score for this measure is the number of correct matches made within the 120-second time limit. While the name of this measure is technically the digit-symbol coding test, the NHANES website refers to this test as digit symbol as well as the digit-symbol substitution test (DSST). See: https://wwwn.cdc.gov/Nchs/Nhanes/2013–2014/CFQ_H.htm

Covariates

We selected several covariates to be included to control for possible confounding in the statistical models based on plausible associations with either *Toxocara* exposure or cognitive function. As such, in all statistical models, we adjusted for age in years (respondents older than 80 were coded as 80 by NHANES to protect respondents from deductive disclosure), sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Other), marital status, immigration status, education, poverty-to-income ratio (PIR), self-rated health, body-mass index, smoking status, and alcoholic drinks consumed in a week. The PIR is the ratio of total family income to the U.S. poverty threshold; as such, a PIR of greater than one indicates an income above the poverty thresh-

Table 1. Descriptive statistics of study variables.

	Mean	SD	Minimum	Maximum
Cognition				
CERAD W-L				
Trial 1	4.88	1.71	0	10
Total	19.60	4.64	0	30
Delay	6.22	2.30	0	10
Animal fluency	16.66	5.60	0	36
Digit-symbol coding	45.55	18.56	0	105
Toxocara				
Seropositive	0.08	0.27	0	1
ln(MFI) (Serointensity)	2.43	0.83	-2	9
Controls				
Age	69.98	6.79	60	80
Female	0.52	0.50	0	1
Race-ethnicity				
Non-Hispanic white	0.55	0.50	0	1
Non-Hispanic black	0.19	0.39	0	1
Mexican-American	0.09	0.29	0	1
Other	0.17	0.37	0	1
Marital Status				
Married	0.56	0.50	0	1
Cohabiting	0.02	0.15	0	1
Divorced or separated	0.17	0.38	0	1
Widowed	0.20	0.40	0	1
Never married	0.05	0.21	0	1
Immigrant	0.22	0.41	0	1
College degree or more	0.24	0.43	0	1
Poverty-to-income ratio	2.64	1.58	0	5
Self-rated health	3.05	0.98	1	5
Body-mass index	28.09	5.79	16	63
Non-smoker	0.87	0.33	0	1
Some days	0.03	0.16	0	1
Everyday	0.10	0.30	0	1
Alcoholic drinks/week	2.11	5.17	0	60

Note. Trial 1 N = 1,288, Total N = 1,286, Delay N = 1,286, Animal fluency N = 1,282, Digit-symbol coding N = 1,274. *Abbreviations*: CERAD W-L = Consortium to Establish a Registry for Alzheimer's disease Word Learning subtest, ln = natural log, MFI = mean fluorescent intensity. Source: National Health and Examination Study, 2013–2014.

old. The combination of PIR and educational attainment provides an estimate of socioeconomic status (Suresh et al. 2011), which is the reason we included both variables in our statistical models.

Statistical analysis

We calculated means and standard deviations or frequencies for covariates and performance on the neuropsychological tests. In that the outcome variables were continuous, we used linear regression to model the associations between *Toxocara* and cognitive function. The focal independent variables were *Toxocara* seropositivity and *Toxocara* serointensity. The dependent variables were performance on each of the tests of cognitive function. We used separate models for each of the two focal independent variables and for each dependent variable.

We also evaluated whether different levels of age, educational attainment, or PIR, or differences in sex were associated with increased vulnerability to *Toxocara*. In separate models, therefore, we interacted either *Toxocara* seropositivity or serointensity with age, sex, educational attainment, and PIR.

To address potential problems associated with false positives due to multiple testing, we used a multivariate test of the null hypothesis that *Toxocara* was not associated with cognitive function considered within the joint covariance of the dependent variables (i.e., the cognitive functioning measures). To do this, we joined all of the multivariable models for each focal predictor (*Toxocara* seropositivity or serointensity) into a single parameter vector that accounted for the covariance of the dependent variables. If the P value of the multivariate model was greater than 0.05, we disregarded any significant individual findings from the multivariable models (Rencher and Scott 1990). We used Stata 16.1 (StataCorp, Stata Statistical Software, release 16, College Station, Texas) for all statistical computations.

Table 2. Adjusted models of cognitive functioning on *Toxocara*: unstandardised coefficients and 95% confidence intervals from linear regression.

	Seropositivity	ln(MFI) (Serointensity)
CERAD W-L		
Trial 1	-0.224	-0.042
	[-0.573, 0.126]	[-0.161, 0.077]
Total	-0.411	-0.050
	[-1.341, 0.519]	[-0.334, 0.235]
Delay	0.162	0.030
	[-0.280, 0.605]	[-0.108, 0.168]
Animal fluency	-1.245*	-0.276
	[-2.392, -0.099]	[-0.619, 0.067]
Digit-symbol coding	-5.159**	-1.880***
	[-8.337,-1.980]	[-2.976, -0.783]
Multivariate p[a]	0.001	0.004

Note. Each cell in the table represents the results from a separate model. The main independent variable is listed in the column headers and the dependent variable is listed in the row labels. Each model is adjusted for age, sex, race, marital status, immigration status, education, poverty-to-income ratio, self-rated health, body-mass index, smoking status, and alcoholic drinks consumed in a week. [a] The multivariate test is a test of the null hypothesis considered within the joint covariance of the dependent variables (i.e., cognitive functioning measures) that the measure of *Toxocara* (i.e., seropositive for *Toxocara* and ln(MFI) (serointensity)) is related to cognitive functioning. It is applied here to address potential problems of reporting false positives because of the number of statistical tests performed. Trial 1 N = 1,383. Total N 1,381. Delay N = 1,381. Animal fluency N = 1,378. Digit-symbol coding N = 1,371. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. *Abbreviations*: Consortium to Establish a Registry for Alzheimer's Disease, Word Learning; ln(MFT) = natural log of the mean fluorescent intensity. Source: National Health and Nutrition Examination Survey, 2013–2014.

RESULTS

Table 1 shows sample clinical and demographic characteristics. Eight percent of the sample was seropositive for *Toxocara*, although this seroprevalence is not representative of the U.S. population. The average age was 69.98 years (standard deviation: 6.79 years), and 52 percent of the sample were women. Twenty-four percent had obtained a college degree (Table 1).

While there were no associations between either *Toxocara* seropositivity or serointensity on Trial 1, total, or delay CERAD W-L scores (Table 2), *Toxocara* seropositivity was associated with worse performance on the animal fluency task (b = -1.245, 95% confidence interval, -2.392 to -0.099, $P < 0.05$), which withstood multivariate correction for alpha inflation due to multiple testing ($P = 0.001$). *Toxocara* serointensity was not associated with performance on the animal fluency test (b = -0.276, 95% confidence interval, -0.619 to 0.067). Both *Toxocara* seropositivity (b = -5.159, 95% confidence interval, -8.337 to -1.980, $p < 0.001$) and serointensity (b = -1.880, 95% confidence interval, -2.976 to -0.783, $p < 0.001$) were associated with

Table 3. Adjusted models of cognitive functioning on the interaction of *Toxocara* and age: unstandardised coefficients from linear regression.

	Seropositivity	ln(MFI) (Serointensity)
CERAD W-L		
Trial 1		
Toxocara	-0.306	0.361
Age	-0.066***	-0.052*
Toxocara × Age	0.001	-0.006
Total		
Toxocara	-9.075	-2.767
Age	-0.219***	-0.304***
Toxocara × Age	0.126	0.039
Delay		
Toxocara	-2.079	-0.840
Age	-0.114***	-0.142***
Toxocara × Age	0.032	0.013
Animal fluency		
Toxocara	-6.338	-1.489
Age	-0.246***	-0.283***
Toxocara × Age	0.074	0.018
Digit-symbol coding		
Toxocara	-41.826*	-11.662*
Age	-1.151***	-1.451***
Toxocara × Age	0.533*	0.142
Multivariate p[a]	0.028	0.002

Note. Each set of three coefficient in the table represents the results from a separate model. The cognitive functioning dependent variable is listed in the rows followed by the main and interaction effects. Each model is adjusted for sex, race, marital status, immigration status, education, poverty-to-income ratio, self-rated health, body-mass index, smoking status, and alcoholic drinks consumed in a week. a The multivariate test is a test of the null hypothesis considered within the joint covariance of the dependent variables (i.e., cognitive functioning measures) that the measure of *Toxocara* (i.e., seropositive for *Toxocara* and ln(MFI) (serointensity)) is related to cognitive functioning. It is applied here to address potential problems of reporting false positives because of the number of statistical tests performed. Trial 1 N = 1,288, Total N = 1,286, Delay N = 1,286, Animal fluency N = 1,282, Digit-symbol coding N = 1,274. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. *Abbreviations*: CERAD W-L = Consortium to Establish a Registry for Alzheimer's disease Word Learning subtest, ln = natural log; MFI = mean fluorescent intensity. Source: National Health and Nutrition Examination Survey, 2013–2014.

Table 4. Adjusted models of cognitive functioning on the interaction of *Toxocara* and sex: unstandardised coefficients from linear regression.

	Seropositivity	ln(MFI) (Serointensity)
CERAD W-L		
Trial 1		
Toxocara	-0.123	-0.029
Female	0.497***	0.575
Toxocara × Female	-0.301	-0.041
Total		
Toxocara	-0.142	-0.026
Female	1.722***	1.845*
Toxocara × Female	-0.803	-0.071
Delay		
Toxocara	0.405	0.059
Female	0.735***	0.887*
Toxocara × Female	-0.725	-0.086
Animal fluency		
Toxocara	-0.949	-0.213
Female	-0.269	0.120
Toxocara × Female	-0.875	-0.186
Digit-symbol coding		
Toxocara	-3.000	-1.574*
Female	5.328***	6.928*
Toxocara × Female	-6.590*	-0.920
Multivariate p[a]	0.535	0.960

Note. See Note in Table 3

worse performance on the digit-symbol coding task (Table 2). Both the *Toxocara* seropositivity and serointensity findings withstood multivariate correction for alpha inflation due to multiple testing (seropositivity p = 0.001; serointensity p = 0.004) (Table 2).

Overall, there were few interactions between either *Toxocara* seropositivity or serointensity and age, sex, educational attainment, and PIR. However, age interacted with *Toxocara* seropositivity in predicting performance on the digit-symbol coding task. The associated multivariate test was also significant (P = 0.028). To facilitate an interpretation of the interaction between *Toxocara* seropositivity and age, their relationship with the digit-symbol coding task is depicted in Fig. 1. Predictions are presented for positive and negative seropositivity at ages 60, 70, and 80 and over. At age 60, seronegative participants had 10 more correct matches than the seropositive participants. By age 70, the difference shrinks to about four, and by 80 and over, there is no difference. In other words, the dampening relationship of seropositivity on digit-symbol coding performance goes away with age in this sample. The multivariate test was also significant (P = 0.002) for age interacting with *Toxocara* serointensity, although in this case there were no significant interactions on the univariate tests for cognitive tasks (Table 3).

Toxocara seropositivity interacted with sex to predict performance on the digit-symbol coding task, but the associated multivariate test was not significant (Table 4), and although the interaction between *Toxocara* seropositivity and educational attainment predicted performance on the digit-symbol coding task, the multivariate test was not significant (Table 5). There were no significant interactions between either *Toxocara* seropositivity and serointensity and PIR (Table 6).

DISCUSSION

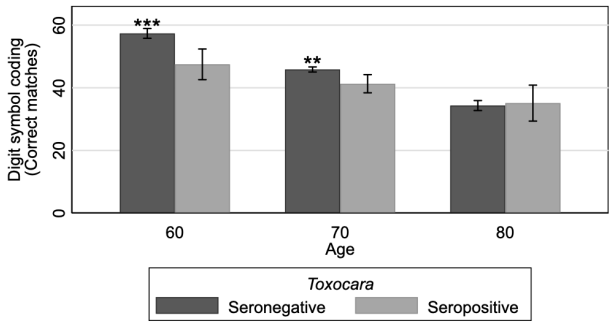
Previous findings have shown adverse associations between *Toxocara* and cognitive function in an animal model (Hamilton et al. 2006), in children (Marmor et al. 1987, Nelson et al. 1996, Walsh and Haseeb 2012), and in young to middle-aged adults (Erickson et al. 2015). Consistent with these findings, we found adverse associations between *Toxocara* and cognitive function in older adults in statistical models adjusted for age, sex, race-ethnicity, marital status, immigration status, education, PIR, self-rated health, body-mass index, smoking status, and the weekly number of alcoholic drinks.

In this sample of older adults, we found that *Toxocara* was associated with worse performance on the animal fluency test and on the digit-symbol coding test, both of which assess aspects of executive function. In addition, the digit-symbol coding test also assesses processing speed. In contrast, there were no significant differences in memory function between *Toxocara* seropositive or seronegative groups, and there were no associations between memory function and serointensity. However, our analyses includ-

Table 5. Adjusted models of cognitive functioning on the interaction of *Toxocara* and educational attainment: unstandardised coefficients from linear regression.

	Seropositivity	ln(MFI) (Serointensity)
CERAD W-L		
Trial 1		
Toxocara	-0.281	-0.048
College degree	0.319**	0.269
Toxocara × College degree	0.293	0.029
Total		
Toxocara	-0.646	-0.130
College degree	0.828**	0.015
Toxocara × College degree	1.205	0.379
Delay		
Toxocara	0.071	0.004
College degree	0.424**	0.165
Toxocara × College degree	0.467	0.123
Animal fluency		
Toxocara	-1.283	-0.362
College degree	2.069***	1.128
Toxocara × College degree	0.193	0.406
Digit-symbol coding		
Toxocara	-6.690***	-2.475***
College degree	5.908***	-0.204
Toxocara × College degree	7.768*	2.814**
Multivariate p[a]	0.221	0.082

Note. See Note in Table 3



Note: [a] Model adjusted for sex, race-ethnicity, marital status, immigrant status, educational attainment, poverty-to-income, self-rated health, body-mass index, smoking status, and alcohol consumption.
** $p < .01$, *** $p < .001$ for age-specific seropositive vs. seronegative comparisons. N = 1,274.
Source: *National Health and Nutrition Examination Survey*, 2013-2014

Fig. 1. The relationship of *Toxocara* seropositivity and digit-symbol coding by age: Adjusted predictions from linear regression

ed only five neuropsychological tests. Additional tests of memory and executive function, as well as tasks assessing other cognitive domains, would provide a more complete evaluation of the deficits in cognitive functioning associated with *Toxocara*.

While we did not find interactions that withstood multivariate correction for multiple testing (Rencher and Scott 1990) between either *Toxocara* seropositivity or serointensity and sex, educational attainment, and PIR, there was evidence supporting an interaction between both *Toxocara* seropositivity and serointensity and age. Predictions from the model presented in Fig. 1 show that the relationship between *Toxocara* seropositivity and digit-symbol coding performance is relatively large around age 60 but is null by

Table 6. Adjusted models of cognitive functioning on the interaction of *Toxocara* and poverty-to-income ratio: unstandardised coefficients from linear regression

	Seropositivity	ln(MFI) (Serointensity)
CERAD W-L		
Trial 1		
Toxocara	0.117	0.010
PIR	0.104**	0.148
Toxocara × PIR	-0.152	-0.022
Total		
Toxocara	0.114	0.072
PIR	0.254**	0.365
Toxocara × PIR	-0.234	-0.053
Delay		
Toxocara	0.446	0.089
PIR	0.080	0.131
Toxocara × PIR	-0.127	-0.025
Animal fluency		
Toxocara	-1.555	-0.357
PIR	0.232*	0.159
Toxocara × PIR	0.138	0.035
Digit-symbol coding		
Toxocara	-7.397**	-2.763*
PIR	1.910***	1.039
Toxocara × PIR	0.994	0.382
Multivariate p[a]	0.453	0.775

Note. See Note in Table 3

age 80. While we did not design our study to identify why this relationship might go away with age, it is possible that age-related factors that contribute to the kinds of cognitive decline captured by the digit-symbol coding task begin to set in after age 60, diminishing the relative contribution of the *Toxocara* seropositivity to digit-symbol coding performance.

Regardless of the mechanism, however, it appears that *Toxocara* does not help to differentiate cognitive functioning among the older old as it does among the younger old, a finding suggesting that although *Toxocara* is associated with worse cognitive function in older adults it might not contribute to ongoing neurodegeneration after age 80 years. Additional research, however, is required to fully determine the contribution of *Toxocara* to neurodegeneration in later life. However, the loss of the dampening effect of age on the association between *Toxocara* seropositivity and performance on the digit-symbol coding task further suggests that *Toxocara* seropositivity might not contribute to cognitive decline after age 80 years.

Also, although we did not have data available to examine *Toxocara*'s relationship with cognitive functioning in younger adults, it seems unlikely that the pattern we observed would extend to younger individuals. For instance, if the pattern did extend to younger adults, the difference in performance on the digit-symbol coding exercise would be quite large at about 20 matches among people aged 40 years. It seems more likely that a smaller difference between seropositive and seronegative groups would be more constant through midlife until age-related cognitive declines begins.

Strengths of this study include its large sample size, objective measures of the dependent and independent variables, statistical adjustment for multiple variables that could affect associations between *Toxocara* and cognitive func-

tion, and multivariate correction for alpha inflation due to multiple testing. A limitation is the study's cross-sectional design, which prevents us from making conclusions about the causes of the associations we found. Similarly, because it is a cross-sectional study, we do not know when the initial *Toxocara* infection occurred. Other potentially confounding variables for which we did not control could have resulted in residual confounding. The limited number of neuropsychological tests is an additional limitation. Other tasks assessing executive function, memory, and other cognitive domains would provide a more complete assessment of the association between *Toxocara* and cognitive function.

In conclusion, in adjusted models, *Toxocara* was associated with worse performance on animal-fluency and digit-symbol coding cognitive tasks in this sample of older adults with a mean age of 69.98 years, findings that suggest that *Toxocara* could be associated with deficits in executive function and processing speed in older U.S. adults. Given previous estimates of the high seroprevalence of *Toxocara* in many world regions including 5.1 percent in a sample representative of the U.S. population (Berrett et al. 2017) and the possible association with worse executive function, *Toxocara* seropositivity and serointensity could be important factors in cognitive deficit in older adults, as well as a significant personal and public-health problem. Additional research is required to determine whether *Toxocara* infection is associated with dementia.

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