Neuroepidemiology

Original Paper

Neuroepidemiology 2021;55:126–134
DOI: 10.1159/000513813

Received: October 7, 2020
Accepted: December 14, 2020
Published online: February 24, 2021

The Association of Cognitive and Visual Function in a Nationally Representative Study of Older Adults in India

Joshua R. Ehrlich[a, b] Tochukwu Ndukwe[c] Sandy Chien[d] Jinkook Lee[d, e, f]

[a]Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI, USA; [b]Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, MI, USA; [c]University of Michigan Medical School, Ann Arbor, MI, USA; [d]Center for Economic & Social Research, University of Southern California, Los Angeles, CA, USA; [e]Department of Economics, University of Southern California, Los Angeles, CA, USA; [f]RAND Corporation, Santa Monica, CA, USA

Keywords
Dementia · Cognitive impairment · Vision impairment · Blindness · Epidemiology

Abstract
Introduction: Due to population aging, India is poised to experience a large increase in the burden of both dementia and vision impairment (VI). Prior studies from other settings suggest that VI may be a modifiable risk factor for cognitive decline and dementia. However, to date, no studies have examined the association of impaired visual acuity and cognition in India. ***Methods:*** A total of 3,784 participants in wave 1 of the population-based Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India underwent visual acuity testing and a cognitive test battery. Multivariable linear regression was used to model the cross-sectional associations of mild (<6/12–6/16), moderate (<6/18–6/60), and severe visual acuity impairment/blindness (<6/60) with cognitive performance scores corresponding to total cognition, orientation, memory, language/fluency, executive function, and informant-reported cognitive status. Models were adjusted for demographic, socioeconomic, and health characteristics. ***Results:*** The weighted percentage of participants with any VI was 52.6%. VI was independently associated with lower cognitive scores across all domains, even after adjustment for known dementia risk factors. In fully adjusted models of total cognition (mean score: 130.7), mild, moderate, and severe VI/blindness were associated with a significant change of −3.5 (95% CI: −6.3, −0.6), −8.2 (95% CI −10.5, −5.6), and −16.8 (95% CI −22.3, −11.3) units, respectively. A dose-response association between level of VI and cognitive function was observed for all cognitive outcomes except for language/fluency domain scores. Associations were robust when cognitive tests dependent on visual function were excluded. Across each fully adjusted model of total, domain-specific, and informant-reported cognitive performance, moderate VI was equivalent to 5–9 years of cognitive aging. ***Discussion/Conclusion:*** This study illustrates that VI is cross-sectionally associated with lower cognitive performance, largely in a dose-response pattern, across various cognitive domains in the Indian population. These findings are important for informing future longitudinal and interventional studies.

karger@karger.com
www.karger.com/ned

Karger

Joshua R. Ehrlich
Ophthalmology and Visual Sciences, University of Michigan
1000 Wall Street
Ann Arbor, MI 48105 (USA)
joshre@med.umich.edu

Introduction

Dementia is a leading cause of disability and death globally [1]. In 2016, an estimated 43–47 million people were living with dementia with an expected increase to over 100 million by 2050. The largest increase is projected in low- and middle-income countries (LMICs) due to a large aging population and increased longevity [1, 2]. In India, the over age 60 population is projected to increase from 8% in 2015 to 19% in 2050, accounting for approximately 320 million people [3]. The number of adults with dementia in India is projected to increase concomitantly over this period [4].

Prior studies have reported that up to 41% of the global burden of dementia may be due to known, potentially modifiable risk factors [1, 5, 6]. Vision impairment (VI), which affects over 1 billion people globally [7], may be one such modifiable risk factor since up to 80% of VI and blindness is avoidable or treatable, often with low-cost interventions like cataract surgery and eyeglasses [8]. In various settings and populations, prior studies have demonstrated that VI is associated with cognitive decline and dementia [9–14]. However, several important gaps remain in understanding the nature of this association. For example, while various hypotheses have been proposed to account for the association between VI and cognitive decline and dementia, to date, little research has been done to test hypothesized pathways [15].

There is also a paucity of research on the association between visual and cognitive function in LMICs. Data from high-income countries may not be readily generalizable to LMICs due to the role of culture and geographic context in shaping health, disease, and the aging process [16]. Additionally, access to health services, ongoing epidemiologic transitions, and variation in the causes of vision loss and cognitive decline between settings may impact the vision-cognition relationship. A recently published systematic review identified only 8 published studies that have examined this association in LMICs globally and the only one from India relied on self-reported, rather than objectively measured, visual function [17]. Moreover, only one of these 8 studies reported associations with VI and specific domains of cognitive functioning. Thus, there remain critical gaps in understanding the relationships between visual and cognitive function in LMICs, including in India, which is home to the greatest number of individuals with blindness and VI in the world [7].

The Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD) is a population-based study that represents the entire Indian population aged 60 and older. Through its focus on late-life cognition, LASI-DAD provides novel opportunities to study the association of cognition with economic, demographic, and health characteristics of older Indian adults. In the current investigation, we examined the association of VI with overall and domain-specific cognitive function in LASI-DAD.

Materials and Methods

Data Source

The Longitudinal Aging Study in India (LASI) consists of over 72,000 community-dwelling adults age 45 and older and their spouses and is representative of the country, as well as each state and union territory in India. The study is harmonized with the Health and Retirement Study (HRS) in the United States and other HRS sister-studies worldwide. Several studies in the HRS network have launched separate in depth studies of late-life cognition and dementia using a harmonized cognitive assessment protocol (HCAP) that is comparable across geographic and cultural contexts [18]. The LASI-DAD, one of the HCAP studies, consists of 4,096 participants age 60 years and older from 18 states and union territories that are representative of the Indian population. Participants were recruited into LASI-DAD through a stratified random sampling process that ensured an approximately equivalent number of participants at high and low risk of cognitive impairment based on results of cognitive test results in LASI. The LASI-DAD study protocol has been described in detail elsewhere [18, 19].

Cognitive Performance Measures

The LASI-DAD cognitive test protocol was developed in consideration of illiteracy and innumeracy in the population. Cognitive function was measured using a summary total cognition variable, as well as domain-specific summary variables. The total cognition variable was developed to assess overall cognitive function and has been described previously [19]. A variant of this total cognition variable was constructed for this study that omitted cognitive tests that were largely dependent on vision. Domain-specific cognitive performance was assessed using summary variables based on the factor structure of the LASI-DAD cognitive battery described by Gross et al. [20]. The online suppl. Appendix (see www.karger.com/doi/10.1159/000513813for all online suppl. material) lists the individual cognitive tests that comprised each of these summary variables. Additionally, informant assessment of cognition was modeled using results of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) [21].

Vision Impairment

Vision was measured in the LASI survey using a tumbling E chart displayed on a laptop situated at 3 m distance from the participant. Each eye was tested separately using the participant's habitual refractive correction (e.g., eyeglasses and contact lenses) for distance vision, if available. Categorization of VI was based on World Health Organization definitions using measured visual acuity in the better-seeing eye [22]: mild VI (<6/12–6/18), moderate VI (<6/18–6/60), severe VI (<6/60–3/60), and blindness (<3/60). Due to the relatively small number of participants with severe VI and blindness, these were collapsed into a single category for analyses.

Table 1. Weighted sample characteristics by VI status

Characteristics	Total, *n*	Total, %[c]	Vision impairment status, %[a]				*p* value[b]
			normal ≥6/12	mild VI <6/12–6/18	moderate VI <6/18–6/60	severe VI/blind <6/60	
Total, % (*n* = 3,784)			47.4	16.5	32.4	3.7	
Age							
60–69	2,312	62.5	54.1	16.5	26.7	2.6	<0.001
70–79	1,090	27.7	39.5	18.0	38.3	4.1	
80+	382	9.8	27.1	11.8	51.6	9.5	
Gender							
Male	1,745	49.2	49.0	15.1	32.6	3.2	0.12
Female	2,039	50.8	45.9	17.8	32.1	4.3	
Education							
None	1,852	55.5	41.5	17.2	36.2	5.1	<0.001
Primary school	1,003	23.7	47.9	16.6	33.3	2.2	
≥Secondary school	929	20.8	62.8	14.4	21.0	1.8	
Marital status							
Married	2,491	65.7	49.9	17.2	30.1	2.8	<0.001
Widowed	1,224	32.7	43.6	15.1	36.0	5.4	
Other	69	1.7	24.9	16.3	51.0	7.9	
Urbanicity							
Urban	1,434	29.0	55.5	16.6	25.7	2.2	<0.001
Rural	2,350	71.0	44.1	16.4	35.1	4.4	
Consumption quartile							
1st	947	30.7	43.6	16.6	33.6	6.2	<0.001
2nd	946	24.9	46.2	16.4	34.8	2.6	
3rd	946	23.3	48.3	17.0	32.0	2.7	
4th	945	21.1	53.5	15.8	28.2	2.5	
BMI, kg/m^2							
<18.5	850	26.1	37.0	17.6	39.7	5.7	<0.001
18.5–24.9	1,837	49.9	49.7	15.7	31.2	3.4	
25.0–29.9	762	17.7	55.9	16.2	26.6	1.3	
≥30.0	287	6.3	51.6	19.5	25.8	3.1	
Diabetes							
No	3,115	86.2	46.2	16.7	33.4	3.6	0.01
Yes	669	13.8	54.9	14.8	25.8	4.5	
Heart disease							
No	3,526	94.7	46.9	16.5	32.7	3.8	0.29
Yes	258	5.3	55.9	16.5	25.6	2.0	
Hypertension							
No	2,298	66.1	47.1	16.4	32.8	3.8	0.49
Yes	1,486	34.0	48.1	16.6	31.5	3.7	
Stroke							
No	3,680	97.3	47.4	16.6	32.4	3.7	0.79
Yes	104	2.7	48.3	13.9	32.5	5.4	
Ever smoked							
No	2,949	78.7	47.3	16.6	32.1	4.0	0.61
Yes	835	21.3	47.9	16.0	33.3	2.8	

VI, vision impairment. [a] Based on visual acuity in the better-seeing eye. [b] Pearson χ^2 test. [c] Table contains raw counts and survey-weighted percentages, so percentages may not sum to 100%.

Covariates

We considered conceptually relevant covariates based on existing literature on known risk factors for VI and for dementia [6, 8, 23, 24]. The following socioeconomic and demographic covariates were included: age, sex, highest education (illiterate, primary school, secondary school or more), marital status (married, widowed, and other), urbanicity (urban and rural), and per capita household consumption quartile. We also considered the following health-related variables: self-reported diagnosis of diabetes, heart disease, hypertension, and stroke; a history of having ever been a smoker; and BMI. BMI was calculated based on weight and height measured by the LASI-DAD research team.

Table 2. Summary statistics for outcome variables

Outcome	Overall (n = 3,784)			VI status			
	mean	SD	range	no VI, mean	mild VI	moderate VI	severe VI/blind
Total cognition 1[a]	130.7	46.0	7–282	136.8	124.9	114.2	93.3
Total cognition 2[b]	102.3	33.5	7–214	105.7	97.8	91.1	78.3
Orientation	9.7	2.8	0–13	10.1	9.4	9.0	8.0
Memory	58.2	21.8	1–147	60.1	54.7	51.1	43.9
Language/fluency	19.5	5.4	0–42	19.8	19.1	18.3	17.4
Executive function	17.0	9.3	0–32	17.8	16.5	14.6	10.5
IQCODE	3.4	0.5	1–5	3.3	3.4	3.5	3.7

IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; SD, standard deviation; VI, vision impairment. [a] Total cognition 1 includes all tests in the cognitive test battery. [b] Total cognition 2 excludes cognitive tests that were largely dependent on vision (see online suppl. Appendix).

Statistical Analyses

We first conducted descriptive analyses to report the prevalence of VI and to examine bivariate associations between VI and demographic variables, socioeconomic status, and health measures. We accounted for survey design features and applied survey weights. We formally tested the differences between VI status and covariates, using Pearson's χ^2 test. For all cognitive test variables, there were complete data for ≥85% of the sample. Thus, observations that were missing, including due to failure to complete a task because of illiteracy or innumeracy, were imputed, as is common in survey data analysis; the imputation method for cognitive test data in LASI-DAD has been previously described [20]. We then conducted multivariable ordinary least squares regression analyses to examine the association between cognitive measures and VI status, while adjusting for other covariates. For each cognitive outcome, we conducted 4 separate analyses. The first model only included VI status without adjusting any covariates; the second was adjusted for age and sex; the third added demographic and socioeconomic covariates (education, marital status, urbanicity, and consumption); and the fourth was fully adjusted and contained all aforementioned covariates in addition to health-related variables (BMI, smoking status, and self-reported diagnoses of diabetes, stroke, hypertension, and heart disease). Cognitive aging refers to changes in cognitive performance that occur as a part of the aging process [25]. To calculate the number of years of cognitive aging with which VI was equivalent, we assumed that the change in cognition from age 60–69 to age 70–79 represented 10 years of cognitive aging. All analyses were conducted using Stata version 14.2.

Results

The characteristics of the analytic sample (n = 3,784), stratified by VI status, are presented in Table 1. Overall, 52.6% had VI; specifically, 16.5, 32.4, and 3.7% had mild VI, moderate VI, and severe VI/blindness, respectively. Those with VI were more likely to be older, have lower educational attainment, be unmarried, live in a rural setting, belong to a lower consumption quartile, have a lower BMI, and be nondiabetic; they were no more likely to be female (p = 0.12), or have heart disease (p = 0.29), hypertension (p = 0.49), or a history of stroke (p = 0.79) or smoking (p = 0.61).

Table 2 presents summary statistics for each of the cognitive performance outcomes, both overall and stratified by VI status. These unadjusted scores were highest in respondents with no VI, and each shows a step-wise decrease across categories of worsening VI. The results from linear models of total cognition are presented in Table 3. Total cognition scores were significantly associated with VI in a step-wise pattern (Fig. 1), wherein worse VI was associated with lower cognitive performance scores. When cognitive tests that depended strongly on vision were removed from the total cognition variable, the association between VI and cognition was similar. In the fully adjusted total cognition models, moderate VI was equivalent to 7.0–8.5 years of cognitive aging.

Domain-specific cognitive performance was also modeled. Across all cognitive domains, VI was independently associated with lower cognitive performance scores (Table 4). There was a clear step-wise pattern between worse VI and worse cognitive performance in the orientation, memory, and executive function domains across all levels of model adjustment. Informant-reported cognitive function also followed this pattern. However, scores on the language/fluency domain, while significantly lower in those with VI compared to normal vision, did now follow a step-wise pattern after adjustment for demographic (model 3) and health factors (model 4). In fully adjusted models, moderate VI was equivalent to 9 years of cogni-

Table 3. Association of VI and total cognition

Domain	Model 1[a] β (95% CI)	Model 2[b] β (95% CI)	Model 3[c] β (95% CI)	Model 4[d] β (95% CI)
Total cognition 1[e]				
No VI	Reference	Reference	Reference	Reference
Mild VI	−11.9 (−15.8, −8.0)**	−9.3 (−13.1, −5.6)**	−4.1 (−6.9, −1.2)**	−3.5 (−6.3, −0.6)*
Moderate VI	−22.6 (−25.7, −19.5)**	−18.0 (−21.0, −15.0)**	−8.9 (−11.3, −6.5)**	−8.2 (−10.5, −5.8)**
Severe VI/blind	−43.5 (−50.8, −36.1)**	−34.9 (−41.9, −27.9)**	−20.0 (−25.5, −14.5)**	−16.8 (−22.3, −11.3)**
Total cognition 2[f]				
No VI	Reference	Reference	Reference	Reference
Mild VI	−7.9 (−10.8, −5.1)**	−6.2 (−9.0, −3.5)**	−2.7 (−5.0, −0.5)*	−2.1 (−4.4, 0.1)
Moderate VI	−14.6 (−16.9, −12.3)**	−11.4 (−13.6, −9.2)**	−5.4 (−7.2, −3.5)**	−4.7 (−6.6, −2.9)**
Severe VI/blind	−27.4 (−32.8, −22.1)**	−21.6 (−26.8, −16.4)**	−11.5 (−15.9, −7.2)**	−9.0 (−13.3, −4.7)**

CI, confidence interval; VI, vision impairment; CI, confidence interval. [a] Model 1: unadjusted. [b] Model 2: age and sex adjusted. [c] Model 3: Model 2 and education, marital status, urbanicity, and consumption quartile. [d] Model 4: Model 3 and BMI, diabetes, heart disease, hypertension, stroke, and smoking status. [e] Total cognition 1 includes all cognitive tests. [f] Total cognition 2 excludes any cognitive tests that largely dependent on vision. * $p < 0.05$. ** $p < 0.01$.

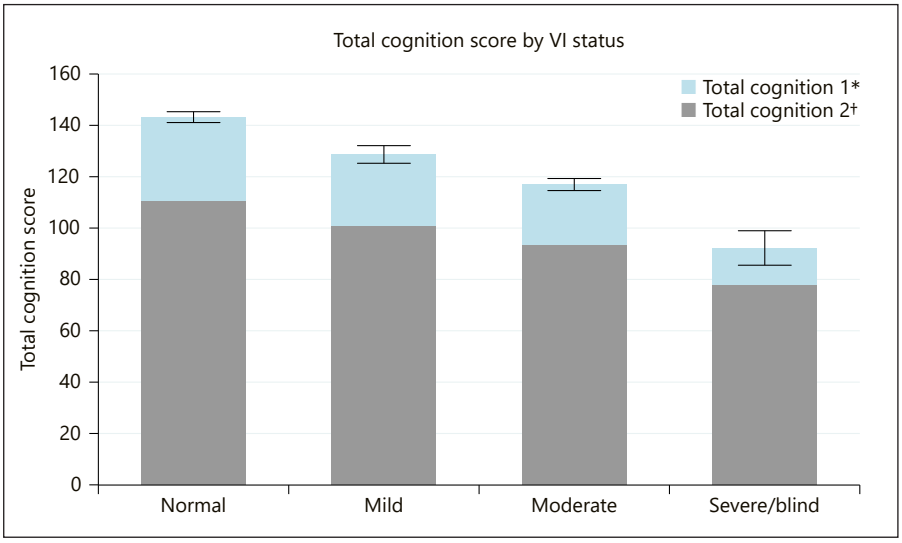

Fig. 1. Association between severity of VI and total cognition scores. The figure illustrates that worse categories on VI were associated with lower total cognition scores. VI, vision impairment. *Total cognition 1 includes all tests in the cognitive test battery. †Total cognition 2 excludes any cognitive tests that were strongly dependent on vision.

Color version available online

tive aging in the orientation domain, 7 years in memory, 9 years in language/fluency, 5 years in executive function, and 7 years in informant-reported cognitive function.

Discussion/Conclusion

In a nationally representative cohort of older Indian adults, this study found that VI was strongly and independently associated with poorer cognitive performance, largely in a dose-response pattern. To our knowledge, this is the first study to investigate the association of objectively measured VI with cognitive outcomes in the Indian population. Moreover, this study provides novel evidence for the association of VI with specific domains of cognitive function, including orientation, memory, language/fluency, and executive function.

There is an urgent need to understand more fully the associations between visual and cognitive function in India. Due to ongoing demographic transitions, nearly 1 in 5 Indians is projected to be age 60 years or older by 2050, compared to just 1 in 12 in 2015 [3], representing a mas-

Table 4. Association of VI and domain-specific cognitive function[a]

	Model 1[b] β (95% CI)	Model 2[c] β (95% CI)	Model 3[d] β (95% CI)	Model 4[e] β (95% CI)
Orientation				
No VI	Reference	Reference	Reference	Reference
Mild VI	−0.7 (−0.9, −0.4)**	−0.5 (−0.7, −0.3)**	−0.2 (−0.4, −0.0)*	−0.2 (−0.4, −0.0)*
Moderate VI	−1.1 (−1.3, −0.9)**	−0.9 (−1.0, −0.7)**	−0.4 (−0.6, −0.3)**	−0.4 (−0.5, −0.2)**
Severe VI/blind	−2.0 (−2.5, −1.6)**	−1.6 (−2.0, −1.1)**	−0.7 (−1.1, −0.4)**	−0.7 (−1.1, −0.3)**
Memory				
No VI	Reference	Reference	Reference	Reference
Mild VI	−5.3 (−7.2, −3.5)**	−4.5 (−6.3, −2.7)**	−2.5 (−4.1, −0.9)**	−2.2 (−3.8, −0.6)**
Moderate VI	−9.0 (−10.5, −7.5)**	−7.1 (−8.5, −5.6)**	−3.6 (−4.9, −2.3)**	−3.2 (−4.5, −2.0)**
Severe VI/Blind	−16.2 (−19.6, −12.7)**	−12.8 (−16.2, −9.4)**	−7.2 (−10.2, −4.2)**	−5.7 (−8.7, −2.6)**
Language/fluency				
No VI	Reference	Reference	Reference	Reference
Mild VI	−0.7 (−1.2, −0.2)**	−0.5 (−1.0, −0.1)*	−0.1 (−0.6, 0.3)	−0.1 (−0.6, 0.3)
Moderate VI	−1.5 (−1.9, −1.1)**	−1.2 (−1.5, −0.8)**	−0.5 (−0.9, −0.2)**	−0.5 (−0.8, −0.1)*
Severe VI/blind	−2.4 (−3.3, −1.5)**	−1.8 (−2.7, −0.9)**	−0.8 (−1.7, 0.0)	−0.5 (−1.3, 0.3)
Executive function				
No VI	Reference	Reference	Reference	Reference
Mild VI	−1.4 (−2.2, −0.5)**	−0.8 (−1.6, −0.1)*	0.1 (−0.5, 0.8)	0.3 (−0.3, 0.9)
Moderate VI	−3.3 (−3.9, −2.6)**	−2.5 (−3.1, −1.9)**	−0.9 (−1.4, −0.4)**	−0.7 (−1.3, −0.2)**
Severe VI/blind	−7.3 (−8.8, −5.8)**	−5.8 (−7.2, −4.3)**	−3.0 (−4.2, −1.8)**	−2.3 (−3.6, −1.1)**
IQCODE				
No VI	Reference	Reference	Reference	Reference
Mild VI	0.1 (0.1, 0.1)**	0.1 (0.0, 0.1)**	0.1 (0.0, 0.1)*	0.1 (0.0, 0.1)*
Moderate VI	0.2 (0.1, 0.2)**	0.1 (0.1, 0.2)**	0.1 (0.0, 0.1)**	0.1 (0.0, 0.1)**
Severe VI/blind	0.3 (0.2, 0.4)**	0.3 (0.2, 0.4)**	0.2 (0.1, 0.3)**	0.2 (0.1, 0.2)**

CI, confidence interval; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; VI, vision impairment. [a] For all outcomes, lower scores represent worse cognitive function, except for the IQCODE, where high scores represent greater cognitive decline. [b] Model 1: unadjusted. [c] Model 2: age and sex adjusted. [d] Model 3: Model 2 and education, marital status, urbanicity, and consumption quartile. [e] Model 4: Model 3 and BMI, diabetes, heart disease, hypertension, stroke, and smoking status. * $p < 0.05$. ** $p < 0.01$.

sive increase in the population at highest risk for cognitive impairment and dementia. Additionally, India is home to nearly one-quarter of the blind and visually impaired people in the world, approximately 80% of whom are 50 years or older [7]. Since age is a strong common risk factor for both vision and cognitive impairments, these data suggest that India is likely poised to experience a large increase in the number of older adults with co-occurring visual and cognitive pathology over the coming decades.

Blindness and VI could represent a key modifiable risk factor for cognitive impairment and dementia in India and elsewhere. An estimated 80% of VI and blindness is preventable or curable [8] and more than half of cases are attributable to cataract or uncorrected refractive error [26], both of which can be cured with highly cost-effective interventions. However, ultimately, large-scale randomized trials are needed to determine whether intervening to improve visual function can delay or slow cognitive decline and the risk of incident dementia. First, however, population-based data like those presented herein are vital for characterizing this association. While wave 1 of LASI-DAD provides nationally representative data on the cross-sectional association, future waves will contribute to a longitudinal understanding.

Prior studies, largely from high-income countries, have reported a consistent association between vision and cognitive outcomes [9–13]. In a forthcoming systematic review, we identified 110 studies on the association of VI and cognitive outcomes, 91 (83%) of which reported a positive association. One study from the United States showed that while VI strongly predicted future cognitive

decline, cognitive performance was not a strong predictor of visual outcomes [9]. In a study from Singapore in which 31% of participants were of Indian ancestry, baseline vision and visual decline over 6 years were both strongly predictive of accelerated cognitive decline compared to those with better vision and slower visual decline [13].

A recent systematic review identified only 8 published studies on the association of vision with cognition or dementia in LMICs [17]. Of these, 5 employed objective measures of visual function (e.g., a vision chart), 2 relied on self-reported visual difficulty, and 1 did not report its methodology. The only study from India, by the 10/66 Dementia Research Group, found that self-reported visual difficulty was not consistently associated with dementia or with cognition among those who had dementia in adjusted models [27]. However, among the 5 studies from a diverse group of Asian and African LMICs that analyzed objectively measured visual function, there was a consistent significant association between worse visual and cognitive function after adjustment for likely confounders [28–32]. To date, no similar studies have been conducted in India.

In the current study, we found that VI and cognitive performance were associated in a dose-response pattern in the LASI-DAD sample, which is weighted to be representative of the entire over 60 Indian population. Specifically, worse categories of VI were associated with progressively lower total cognition, orientation, memory, executive function, and informant-reported cognition, even after adjustment for known demographic and socioeconomic associations with cognitive impairment, dementia, and VI [6, 23]. This pattern was not observed in fully-adjusted models of language/fluency. The reasons for differential domain-specific effects are not clear, but possibilities include the specific effects of VI on brain structure and function or the effect of dual-tasking on specific cognitive processes.

Recently published studies from the Women's Health Initiative (WHI) in the United States [12] and from a large cohort of older adults in China [14] reported a similar dose-response relationship between worse categories of VI and incident dementia. In the WHI, over a mean 3.8 years of follow-up, the hazard ratio for incident dementia among participants with baseline visual acuity <6/12, <6/24, and <6/30 was 2.1, 5.2, and 5.7, respectively, with similar findings in models of incident mild cognitive impairment [12]. In the Chinese study, over 15,000 older adults were followed up for 6 years and mild, moderate, and severe VI at baseline were associated with a hazard ratio for incident dementia of 1.2, 2.1, and 8.7, respectively. The consistent dose-response relationship in these studies and in LASI-DAD contributes to our understanding of the association between visual and cognitive function, though considerable additional work is needed, particularly in LMICs like India.

Findings from the current study may have implications for future epidemiological and interventional research in India. Few prior studies have examined the association between vision and cognitive function across multiple domains [33, 34]. In a cohort from the U.S., Dearborn et al. [34] reported that VI was associated with future declines in visuospatial, verbal episodic memory, and executive function domains but not working memory or scanning and tracking. While that study reported associations over 5 years of follow-up, data were not analyzed to determine whether associations varied based on VI severity. Future research in India is needed to characterize longitudinal domain-specific associations, which may help to inform the choice of outcome measures and interventions in future trials that aim to slow cognitive decline through optimizing vision.

There were several unexpected findings in this study. First, those with diabetes were less likely to have VI, though diabetes is an important cause of VI and blindness in India and globally [35]. This may have been the case if those who self-reported a diagnosis of diabetes were also more likely to have received routine medical care, including eye exams and vision enhancing interventions like eyeglasses and cataract surgery. Additionally, low BMI (<18.5 kg/m^2) was associated with both VI and lower cognitive performance, while high BMI (>25.0 kg/m^2) was associated with better cognitive performance. Previous studies in India have shown that obesity is more common among those with higher education and socioeconomic status [36], which may help to account for this phenomenon. Moreover, undernutrition is associated with a diverse set of adverse health outcomes (including VI that can be caused by vitamin deficiencies) and may contribute to this finding [37]. Compared to current data from the Global Burden of Disease (GBD) project, data from LASI-DAD estimate a higher prevalence of mild and moderate VI and a similar prevalence of blindness in India. Of note, however, there are no up-to-date national-level data from India included in the GBD models, so data from LASI and LASI-DAD may make an important contribution to understanding the current epidemiology of VI and blindness at the state and national level in India [7].

This study had several limitations. First, data were cross-sectional so it was not possible to assess the direc-

tionality of associations or to prospectively assess the association between changes in vision and cognition. Second, it is possible that participants with VI had difficulty seeing to complete vision-dependent cognitive tests, which could have affected performance, though our findings were robust in a model that excluded cognitive tests that depended strongly on vision. Likewise, it is plausible that cognitive impairment could impact visual perception, resulting in a cross-sectional association due to reverse causality. Duration and cause of vision loss could impact cognitive function, though these data were not available in LASI or LASI-DAD. Due to the nature of observational data, there is also a possibility of residual confounding and that cognitive effects attributable to vision may be reflective of differences in demographics, though we sought to control for key demographic and socioeconomic variables. This study also had a number of strengths. As a population-based study, findings from LASI-DAD are nationally representative. Future waves of LASI-DAD will provide longitudinal data that will be used to build on this study's findings in order to describe the longitudinal association of vision and vision changes with cognitive trajectories and incident dementia. Findings from the IQCODE, a validated informant-reported measure of cognitive status, corroborate the results of performance tests, which may be particularly relevant given the high-degree of demographic heterogeneity in the sample. Additionally, LASI and LASI-DAD are part of the HRS and HCAP families of studies, which facilitates cross-national comparisons of risk factors for late-life cognitive decline and dementia.

This study used novel data from LASI-DAD to describe the association of VI with cognitive performance across multiple cognitive domains in the Indian population. As in other geographic contexts, VI appears to be strongly and independently associated with worse cognitive outcomes in India. Given the large and growing population of older adults in India, there is a pressing need to characterize potentially modifiable risk factors for cognitive decline and dementia in this population. The current study provides foundational epidemiologic data for future longitudinal and interventional studies with the overarching goal of characterizing and decreasing the population burden of cognitive decline and dementia in India.

Statement of Ethics

Ethics approval for this study was obtained from the Indian Council of Medical Research and all collaborating institutions, including the University of Southern California; University of Michigan; the All India Institute of Medical Sciences, New Delhi; the International Institute of Population Sciences, Mumbai; All India Institute of Medical Sciences, Bhubaneshwar; Dr. S.N. Medical College, Jodhpur; Government Medical College, Thiruvananthapuram; Grant Medical College & J.J. Hospital, Mumbai; Guwahati Medical College, Guwahati; Institute of Medical Sciences, BHU, Varanasi; Madras Medical College, Chennai; Medical College, Kolkata; National Institute of Mental Health and Neurosciences, Bengaluru; Nizam's Institute of Medical Sciences, Hyderabad; and Sher-e-Kashmir Institute of Medical Sciences, Srinagar; Indra Gandhi Institute of Medical Sciences, Patna; Gwailor Medical College, Madhya Pradesh; All India Institute of Medical Sciences, Rishkesh; and Government Medical College, Chandigarh. Informed consent was obtained from all study participants.

Conflict of Interest Statement

All authors disclose no conflict of interest.

Funding Sources

This work was supported by grants from the National Institutes of Health (K23EY027848 to JRE, R01AG051125, RF1AG055273 and U01AG064948 to JL) and by an unrestricted grant from Research to Prevent Blindness to the University of Michigan Department of Ophthalmology and Visual Sciences. Sponsors had no direct role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Author Contributions

J.R.E.: conceptualization and design of study, planning of analyses, interpretation of results, and drafting of manuscript. T.N.: interpretation of results and drafting of manuscript. S.C.: data analysis and critical revision of manuscript. J.L.: conceptualization and design of study, planning of analyses, interpretation of results, oversight of study team, and critical revision of manuscript.

References

1 GBD 2016 Dementia Collaborators. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan; 18(1):88–106.
2 Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. Alzheimers Dement. 2013 Jan;9(1):63–e2.
3 United Nations Population Fund. Caring for our elders: early responses. India ageing report-2017. New Delhi, India: UNFPA; 2017.
4 Prince M, Wimo A, Guerchet M, Ali G, Wu Y, Prina M. World Alzheimer Report 2015, the global impact of dementia: an analysis of prevalence, incidence, cost and trends [Internet]. 2015 [cited 2020 Apr 13];87.

5 Mukadam N, Sommerlad A, Huntley J, Livingston G. Population attributable fractions for risk factors for dementia in low-income and middle-income countries: an analysis using cross-sectional survey data. Lancet Glob Health. 2019 May;7(5):e596–603.
6 Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020 Jul 30; 396(10248):413–46.
7 GBD 2019 Blindness and Vision Impairment Collaborators, Vision Loss Expert Group of the Global Burden of Disease Study. Trends in prevalence of blindness and distance and near vision impairment over 30 years: an analysis for the global burden of disease study. Lancet Glob Health. 2020 Dec 1.
8 World Health Organization. World report on vision. Geneva, Switzerland: World Health Organization; 2019.
9 Zheng DD, Swenor BK, Christ SL, West SK, Lam BL, Lee DJ. Longitudinal associations between visual impairment and cognitive functioning: the Salisbury Eye Evaluation Study. JAMA Ophthalmol. 2018 Sep 1;136(9):989–95.
10 Naël V, Pérès K, Pérès K, Dartigues J-F, Letenneur L, Amieva H, et al. Vision loss and 12-year risk of dementia in older adults: the 3C cohort study. Eur J Epidemiol. 2019 Feb; 34(2):141–52.
11 Fischer ME, Cruickshanks KJ, Schubert CR, Pinto AA, Carlsson CM, Klein BE, et al. Age-related sensory impairments and risk of cognitive impairment. J Am Geriatr Soc. 2016; 64(10):1981–7.
12 Tran EM, Stefanick ML, Henderson VW, Rapp SR, Chen JC, Armstrong NM, et al. Association of visual impairment with risk of incident dementia in a women's health initiative population. JAMA Ophthalmol. 2020 Apr 16; 138(6):624–633.
13 Lim ZW, Chee ML, Soh ZD, Cheung N, Dai W, Sahil T, et al. Association between visual impairment and decline in cognitive function in a multiethnic Asian population. JAMA Netw Open. 2020 Apr 1;3(4):e203560.
14 Lee ATC, Richards M, Chan WC, Chiu HFK, Lee RSY, Lam LCW. Higher dementia incidence in older adults with poor visual acuity. J Gerontol A Biol Sci Med Sci. 2020 Nov; 75(11):2162–8.
15 Whitson HE, Cronin-Golomb A, Cruickshanks KJ, Gilmore GC, Owsley C, Peelle JE, et al. American Geriatrics Society and National Institute on aging bench-to-bedside conference: sensory impairment and cognitive decline in older adults. J Am Geriatr Soc. 2018 Sep 24;66(11):2052–8.
16 Leibing A, Cohen L. Thinking about dementia: culture, loss, and the anthropology of senility [Internet]. New Brunswick, NJ: Rutgers University Press; 2006
17 Gbessemehlan A, Guerchet M, Helmer C, Delcourt C, Houinato D, Preux PM. Association between visual impairment and cognitive disorders in low-and-middle income countries: a systematic review. Aging Ment Health. 2020 Sep 8;1–10.
18 Banerjee J, Jain U, Khobragade P, Weerman B, Hu P, Chien S, et al. Methodological considerations in designing and implementing the harmonized diagnostic assessment of dementia for longitudinal aging study in India (LASI-DAD). Biodemography Soc Biol. 2020 Jul–Sep;65(3):189–213.
19 Lee J, Banerjee J, Khobragade PY, Angrisani M, Dey AB. LASI-DAD study: a protocol for a prospective cohort study of late-life cognition and dementia in India. BMJ Open. 2019 Jul 1;9(7):e030300.
20 Gross AL, Khobragade PY, Meijer E, Saxton JA. Measurement and structure of cognition in the Longitudinal Aging Study in India-Diagnostic Assessment of Dementia. J Am Geriatr Soc. 2020 Aug;68(Suppl 3):S11–9.
21 Jorm AF. A short form of the informant questionnaire on cognitive decline in the elderly (IQCODE): development and cross-validation. Psychol Med. 1994;24(1):145–53.
22 World Health Organization. ICD-11 for mortality and morbidity statistics (version: 04/2019). 9D90 vision impairment including blindness. Geneva, Switzerland: World Health Organization; 2019.
23 National Academies of Sciences, Engineering, and Medicine. Making eye health a population health imperative: vision for tomorrow. Washington D.C.: The National Academies Press; 2016.
24 Thulasiraj RD, Nirmalan PK, Ramakrishnan R, Krishnadas R, Manimekalai TK, Baburajan NP, et al. Blindness and vision impairment in a rural south Indian population: the Aravind comprehensive eye survey. Ophthalmology. 2003 Aug;110(8):1491–8.
25 Harada CN, Natelson Love MC, Triebel KL. Normal cognitive aging. Clin Geriatr Med. 2013 Nov;29(4):737–52.
26 GBD 2019 Blindness and Vision Impairment Collaborators, Vision Loss Expert Group of the Global Burden of Disease Study. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the right to sight: an analysis for the Global Burden of Disease Study. Lancet Glob Health. 2020 Dec 1.
27 Prince M, Acosta D, Ferri CP, Guerra M, Huang Y, Jacob KS, et al. The association between common physical impairments and dementia in low and middle income countries, and, among people with dementia, their association with cognitive function and disability. A 10/66 Dementia Research Group population-based study. Int J Geriatr Psychiatry. 2011 May;26(5):511–9.
28 Luo Y, He P, Guo C, Chen G, Li N, Zheng X. Association between sensory impairment and dementia in older adults: evidence from China. J Am Geriatr Soc. 2018 Mar;66(3):480–6.
29 Ong SY, Cheung CY, Li X, Lamoureux EL, Ikram MK, Ding J, et al. Visual impairment, age-related eye diseases, and cognitive function: the Singapore Malay Eye study. Arch Ophthalmol. 2012 Jul;130(7):895–900.
30 Jonas JB, Wei WB, Zhu LP, Xu L, Wang YX. Cognitive function and ophthalmological diseases: the Beijing Eye Study. Sci Rep. 2018; 8(1):1–11.
31 Heward J, Stone L, Paddick S-M, Mkenda S, Gray WK, Dotchin CL, et al. A longitudinal study of cognitive decline in rural Tanzania: rates and potentially modifiable risk factors. Int Psychogeriatr. 2018;30(9):1333–43.
32 Ferdous T, Cederholm T, Kabir ZN, Hamadani JD, Wahlin A. Nutritional status and cognitive function in community-living rural Bangladeshi older adults: data from the poverty and health in ageing project. J Am Geriatr Soc. 2010 May;58(5):919–24.
33 Hämäläinen A, Phillips N, Wittich W, Pichora-Fuller MK, Mick P. Sensory-cognitive associations are only weakly mediated or moderated by social factors in the Canadian Longitudinal Study on aging. Sci Rep. 2019 Dec 23;9(1):19660–8.
34 Dearborn PJ, Elias MF, Sullivan KJ, Sullivan CE, Robbins MA. Poorer visual acuity is associated with declines in cognitive performance across multiple cognitive domains: the Maine-Syracuse Longitudinal Study. J Int Neuropsychol Soc. 2018;24(7):746–54.
35 Gadkari SS, Maskati QB, Nayak BK. Prevalence of diabetic retinopathy in India: the All India Ophthalmological Society Diabetic Retinopathy Eye Screening Study 2014. Indian J Ophthalmol. 2016 Jan;64(1):38–44.
36 Hu P, Lee J, Beaumaster S, Kim JK, Dey S, Weir D, et al. Cognitive function and cardiometabolic-inflammatory risk factors among older Indians and Americans. J Am Geriatr Soc. 2020;68(S3):S36–44.
37 Martins VJ, Toledo Florêncio TM, Grillo LP, do Carmo P Franco M, Martins PA, Clemente AP, et al. Long-lasting effects of undernutrition. Int J Environ Res Public Health. 2011 Jun;8(6):1817–46.