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Prevalence of Concurrent Vision and Hearing Impairment and Cognitive Dysfunction in an Old Population. The Ural Very Old Study

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Prevalence of Concurrent Vision and Hearing Impairment and Cognitive Dysfunction in an Old Population. The Ural Very Old Study.

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Short title: Vision and Hearing Impairment and Cognitive Dysfunction in a Very Old Population

Key words: Blindness; Hearing loss; Vision impairment; Cognitive dysfunction; Dementia; Ural Very Old Study

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Abstract

Objective: To assess the prevalence of vision impairment, hearing impairment and dual sensory impairment as combination of vison and hearing impairment, in association with cognitive dysfunction in a population aged 85+ years.

Methods: The population-based Ural-Very-Old-Study was conducted in rural and urban Bashkortostan/Russia and included a detailed ocular and systemic examination including assessment of moderate to severe vision impairment/blindness (MSVI) (best corrected visual acuity <6/18), moderate to severe hearing loss (MSHL), and cognitive function.

Setting: A rural and urban area in Bashkortostan/Russia.

Participants: Out of 1882 eligible individuals aged 85+ years, 1526 (81.1%) individuals participated.

Primary and secondary outcome measures: Prevalence of vision, hearing and dual sensory impairment and cognitive dysfunction.

Results: The study included 731 (47.9%) individuals (mean age:88.1±2.7 years (median:87 years;range:85-98years)) with measurements of MSVI/blindness, MSHL and cognitive function. The prevalence of MSVI/blindness, MSHL, DSI and dementia were 51.8% (95% confidence interval (CI):48.2,55.5), 33.1% (95%CI:29.7,36.5), 20.5% (95%CI:17.8,23.5), and 48.2% (95%CI:44.5,51.8), respectively. Lower cognitive function score was associated with lower visual acuity (*P*<0.001) and higher hearing loss score (*P*=0.03), after adjusting for older age (*P*=0.001), rural region of habitation (*P*=0.003), lower educational level (*P*<0.001), and higher depression score (*P*<0.001). Higher dementia prevalence was associated with higher MSHL prevalence (OR:2.18;95%CI:1.59,2.98;*P*<0.001), higher MSVI/blindness prevalence (OR: 2.09;95%CI:1.55,2.81;*P*<0.001), and higher DSI prevalence (OR:2.80;95%CI:1.92,4.07;*P*<0.001).

Conclusions: In this very old, multi-ethnic population from Russia, dual sensory impairment (prevalence:20.5%), as compared to hearing impairment (OR:2.18) and vision impairment alone (OR:2.09), had a stronger association (OR: 2.80) with dementia. The findings show the importance of hearing and vision impairment, in particular their combined occurrence, for dementia prevalence in an old population.

Strengths and limitations of this study

- In a very old, multi-ethnic population from Russia, dual sensory impairment (prevalence: 20.5%), as compared to hearing impairment (OR: 2.18) and vision impairment alone (OR: 2.09), had a stronger association (OR: 2.80) with dementia.
- The findings reveal a relatively high prevalence of sensory impairment in the very old population and show the importance of hearing and vision impairment, in particular their combined occurrence, for dementia prevalence in an old population.
- Future studies may explore the effect of vision improvement strategies such as providing adequate glasses for distance and near and cataract surgery, and the effect of hearing improvement measures such as providing hearing aids, on the prevention of the development or progression of dementia.

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- Limitations are that the participation rate was 47.9%, however, the relatively high age of 85+ years as inclusion criterion should be taken into account; and that hearing impairment was not phonometrically measured.

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Introduction

Due to growth and ageing of the population, the role of dementia as major cause of the global burden of disease has further gained importance during the past decades.[1,2] In view of estimations of further rising trends in the global prevalence of dementia, and taking into account the absence of any evidence-based therapy with a major impact on the course of the disease, detection of risk factors of dementia and the reduction of their influence is of thus major importance.[3,4] In the 2020 update to the Lancet Commission report on dementia, about 40% of dementia was attributed to 12 major modifiable risk factors.[3] These included hearing impairment among other factors such as lower level of education, arterial hypertension, obesity, smoking, depression, physical inactivity, social isolation, diabetes mellitus, alcohol consumption, head injury, and air pollution. Although vision impairment was associated with a higher risk of dementia in some investigations which showed an up to 8 times higher risk of dementia for visually impaired individuals, the association between vision impairment and dementia has remained unclear so far.[5-8] In particular, the effect of a combined occurrence of vision impairment with hearing impairment as dual sensory impairment has not fully been explored and recognized as risk factor for cognitive dysfunction. Using data from the US National Health and Aging Trends Study, a recent nationally representative cohort study of community-dwelling Medicare beneficiaries aged 65+ years revealed that self-reported functional vision impairment, self-reported functional hearing impairment and combined self-reported vision and hearing impairment had adjusted cross-sectional hazard ratios of dementia of 1.89, 1.14, and 2.00, respectively.[9] Similar results were obtained during a follow-up of 7 years for the incidence of dementia. These previous studies had limitations such as being based on self-reported impairment in vision and hearing and including Medicare beneficiaries as a subgroup of the total population in the case of Kuo´s study, and such as not being focused on the very old population, we conducted the present population-based study on individuals aged 85+ years and who underwent measurements of visual acuity and cognitive function. In addition, it was performed in Russia, i.e. in a world region for which only a scarcity of population-based data on dual sensory impairment and cognitive dysfunction have been available so far.

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Methods

The Ural Very Old Study (UVOS) is a population-based study performed in the rural region in the Karmaskalinsky District in a distance of 65 km from the capital Ufa, and in the urban region of Kirovskii in Ufa in the Republic of Bashkortostan / Russia. The study was approved by the Ethics Committee of the Academic Council of the Ufa Eye Research Institute and informed written consent was obtained from all participants. Inclusion criteria were an age of 85+ years and living in the study regions. The Republic of Bashkortostan has a population of about 4.07 million people and it is geographically located in the west of the southern Ural Mountains about 1300 km east of Moscow. Its capital Ufa is an economic, scientific and cultural center and has a population of 1.1 million inhabitants including Russians, Bashkirs, Tatars, Ukrainians and other ethnicities.

Out of 1882 eligible inhabitants aged 85+ years and living in the study regions, the study consisted of 1526 (81.1%) participants including inhabitants of retirement homes. The urban group (1238 (81.3%) out of 1523 individuals) and the rural group (288 (80.2%) out of 359 individuals) did not differ significantly in the participation rate. Based on the census performed in Russia in 2010, age and gender distribution in the study population did not vary markedly from the Russian population age 85+ years, with a marked preponderance of females.[12]

The series of examinations the study participants underwent included a standardized interview by trained social workers with almost 300 questions on the socioeconomic background, diet, smoking, alcohol consumption, physical activity, quality of life and quality of vision, history of any type of injuries and inter-personal violence, and health assessment questions.[10] All questions were taken from standardized interviews published in the literature, such as the "Center for Epidemiologic Studies Depression Scale (CES-D) Scoresheet" and the Folstein test.[12-17] The physical examinations consisted of the measurement of the anthropomorphic parameters, arterial blood pressure and pulse rate. Using blood samples taken under fasting conditions, we measured the serum concentrations of transaminases, bilirubin, blood lipids, glucose, creatinine, hemoglobin, and others and performed a blood cell count. We applied the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER statement guidelines).[18] The Ural Very Old Study design was similar to the design of the Ural Eye and Medical Study (UEMS) which has been described in detail previously.[10]

Besides other ocular examinations, we measured best corrected visual acuity (BCVA), expressed in LogMAR (logarithm of the minimal angle of resolution) and determined the ocular axial length by sonography. Using the World Health Organization (WHO) criteria, we defined moderate to severe vision impairment (MSVI) as BCVA of <6/18 but ≥3/60 in the better eye or binocularly, and blindness as BCVA of <3/60 in the better eye or binocularly.

Hearing loss was assessed by a series of 11 standardized questions, ten of which were derived from the "Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S)".[19-22] The prevalence of self-reported hearing loss as a binary variable was assessed by the single question "Do you experience a hearing loss?". The questions could be answered by "no" (0 points), "sometimes" (2 points) and "yes (4 points). The total hearing loss score was the sum of all points and could range between 0 points and 44 points. The amount of hearing loss was assessed by the hearing loss score. The HHIE-S had been applied in previous investigations.[19-21] The diagnostic performance of the HHIE-S against five definitions of hearing loss as assessed by pure-tone audiometry had been explored in a previous study revealing sensitivities ranging between 53% and 72% and specificities from 70 to 84% with the different definitions.[23] Based on the WHO hearing impairment grading system, we defined mild hearing impairment ("No problems in quiet but may have real difficulty following conversation in noise") by a hearing loss score of 11 to 17; moderate hearing impairment ("May have difficulty in quiet hearing a normal voice and has difficulty with conversation in noise") by a hearing loss score of 18 to 24; moderately severe hearing impairment ("Needs loud speech to hear in quiet and has great difficulty in noise) by a hearing loss score of 25 to 31; severe hearing impairment ("In quiet, can hear loud speech directly in one's ear, and, in noise, has very great difficulty.") by a hearing loss score of 32-38; and profound hearing impairment ("Unable to hear and understand even a shouted voice whether in quiet or noise") by a hearing score of 39 to 44.[24] We defined dual sensory impairment as MSVI/blindness combined with moderately severe or more severe hearing impairment (grade 3+). Cognitive function was assessed using the Mini-Mental Status Examination scale.[14]

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Using a statistical software package (SPSS for Windows, version 25.0, SPSS, Chicago, IL), we determined the demographic characteristics of the study population (presented as mean ± standard deviation) and assessed the prevalence of MSVI/blindness, hearing impairment and dual sensory impairment (presented as mean and 95% confidence intervals (CIs)). We performed a regression analysis as univariate analysis with the cognitive function score as dependent variable, followed by a multivariable analysis that included as independent variables all those parameters which were significantly associated with the cognitive function score in the univariate analysis. Finally, we conducted a binary regression analysis of the relationships between the prevalences of cognitive dysfunction, vision impairment, hearing impairment and dual sensory impairment. We calculated the standardized regression coefficient beta, the non-standardized regression coefficient B, odds ratios (ORs) and the 95% CIs. All P-values were two-sided and considered statistically significant when the values were less than 0.05.

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Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Results

Out of 1526 individuals primarily participating in the Ural Very Old Study, the present investigation included 731 (47.9%) individuals (530 (72.5%) women; 201 (27.5%) men) for whom measurements and data of BCVA, hearing loss and cognitive function were available. The study population was composed of 251 (34.3%) individuals of Russian ethnicity, 334 (45.7%) Tatars, 83 (11.4%) Bashkirs, 25 (3.4%) Chuvash, 5 (0.7%) Mari, and 33 (4.5%) others. The mean age was 88.1 ± 2.7 years (median: 87 years; range: 85 – 98 years). The individuals with assessment of vision loss, hearing loss and cognitive function as compared with the individuals without these examinations did not vary significantly in age (88.1 ± 2.7 years versus 88.5 ± 3.0 years; *P*=0.10), level of education (4.6 ± 2.1 versus 4.4 ± 2.1; *P*=0.08) and sex (*P*=0.10).

Among the 731 participants, 23 (3.1%) individuals were illiterate, 133 (18.2%) had passed the 5th class, 159 (21.8%) had passed the 8th class, 29 (4.0%) had passed the 10th class, 15 (2.1%) had passed the 11th class, 172 (23.5%) had a specialized secondary education, 194 (26.5%) were graduates, and 4 (0.5%) were postgraduates. There were 124 individuals (17.0%) who were living in a joint family, 77 (10.5%) in a nuclear family, 266 (36.4%) were living alone, and 261 (35.7%) cohabited with another family member; 170 23.3%) participants were married, 16 (2.2%) were unmarried, 13 (1.8%) were divorced, and 531 (72.6%) were widowed. Almost all study participants (718 (98.2%) owned a house or apartment, while 13 (1.8%) had rented a house or flat; 18 (2.5%) individuals had a car, 49 (6.7%) had a laptop or computer, and 100 (13.7%) a mobile phone. Almost all study participants (1715, 97.8%) owned a television and a telephone (682, 93.3%). Mean body height was 158 ± 9 cm (median: 158 cm; range. 105-180 cm), mean body weight was 65.9±11.3 kg (median:66.0 kg; range:31.8-103 kg), and mean body mass index was 26.5±4.5 kg/m^2 (median: 25.8 kg/m^2; range: 14.7-59.0 kg/m^2). Mean systolic and diastolic blood pressure were 156.9 ± 26.4 mmHg and 79.6±13.9 mm Hg, respectively, the prevalence of arterial hypertension (stage 1+) was 87.0% (95%CI:84.5,89.4), and the prevalence of diabetes was 13.8% (95% CI: 11.3, 16.4).

Out of the 731 study participants, 342 (46.8%;95%CI:43.2,50.4) individuals fulfilled the definition of MSVI, and 37 individuals (5.1%;95%CI:3.5,6.7) fulfilled the definition of blindness in the better eye or under binocular conditions. The combined prevalence of MSVI and blindness was 51.8% (95%CI:48.2,55.5). The mean hearing loss score was 19.5±15.4 (median:22;range:0-44). Out of the 731 study participants, 291 (39.8%) had a normal hearing score, 55 (7.5%) had mild hearing impairment (grade 1), 143 (19.6%) individuals had moderate hearing impairment (grade 2), 66 (9.0%) persons had moderately severe hearing impairment (grade 3), 58 individuals (7.9%) had severe hearing impairment (grade 4), and 118 (16.1%) had profound hearing impairment (grade 5). Dual sensory impairment, defined as MSVI/blindness combined with moderately severe hearing impairment grade 3+ was present in 150 (20.5%;95%CI:17.8,23.5) individuals.

The mean cognitive function score obtained in the Mini Mental test was 22.2±6.4 (median:24;range:0-30). In univariate analysis, a higher cognitive score was associated with younger age (P<0.001), urban region of habitation (P<0.001), higher level of education (P<0.001), lower hearing loss score (P<0.001), higher body mass index (P=0.002), longer waist (P<0.001) and hip (P=0.003) circumference, higher prevalence of alcohol consumption (P=0.02), higher number of meals taken daily (P<0.001), higher number of days per week with fruit intake (P<0.001), higher serum concentration of triglycerides (P=0.02), urea (P=0.03), higher leucocytes blood cell count (P=0.02), lower diastolic blood pressure (P=0.005), lower depression score (P<0.001), and a lower State Trait anxiety score (P<0.001), and with the ocular parameters of better BCVA (P<0.001), longer ocular axial length (P=0.04) and lower prevalence of dry eye (P=0.02). It was not significantly associated with sex (P=0.15), Russian versus non-Russian ethnicity (P=0.20), body height (P=0.07), body weight (P=0.09), waist-hip circumference ratio (P=0.09), current smoking (P=0.56), systolic (P=0.75) and mean (P=0.15) blood pressure, prevalence of arterial hypertension (P=0.11), serum concentration of glucose (P=0.78), creatinine (P=0.48), hemoglobin (P=0.19), and erythrocyte count (P=0.22), and with the ocular parameter of refractive error (P=0.80).

In multivariable analysis, we first dropped due to collinearity the parameter of the anxiety score (variance inflation factor: 4.9). Due to lack of statistical significance, we then dropped the parameters of prevalence of alcohol consumption (P=0.96), number of days with fruit intake (P=0.77), dry eye prevalence (P=0.82), leucocytes blood cell count (P=0.78), waist circumference (P=0.80), diastolic blood pressure (P=0.65), ocular axial length (P=0.53), number of meals taken daily (P=0.15), hip circumference (P=0.42), serum concentration of triglycerides (P=0.05), and body mass index (P=0.05). In the final model, higher cognitive function score was associated with younger age (P=0.001), urban region of habitation (P=0.003), higher level of education (P<0.001), lower BCVA (P<0.001), higher hearing loss score (P=0.03), and higher depression score (P<0.001) (Table 1). If the BCVA and hearing loss score were replaced by the prevalence of dual sensory impairment, a lower prevalence of the latter was associated with a higher cognitive function score (beta: -0.11; B: -1.70; 95%CI: -2.66, -0.74; P=0.001).

In a reverse manner, a higher prevalence of MSVI was associated with a lower cognitive function score (OR: 0.92; 95%CI: 0.89, 0.94; P<0.001), as was a higher prevalence of moderately severe hearing loss (OR: 0.93; 95%CI: 0.90, 0.95; *P*<0.001) and a higher prevalence of dual sensory impairment (OR: 0.90; 95%CI: 0.88, 0.93; *P*<0.001). In multivariable analysis, a higher prevalence of dual sensory impairment was associated with a lower cognitive function score (OR:0.94;95%CI:0.91,0.98;*P*=0.001), after adjusting for older age (OR:1.16;95%CI:1.08,1.24;*P*<0.001), rural region of habitation (OR:2.32;95%CI:1.51,3.56, *P*<0.001), and higher depression score (OR:1.03;95%CI:1.01,1.06;*P*<0.002). In that model, the prevalence of dual sensory impairment was not significantly associated with sex (*P*=0.08). If the depression score was dropped, the association with a higher anxiety score became significant (OR: 1.03; 95CI: 1.01, 1.05; *P*=0.001).

If cognitive dysfunction was defined by Mini Mental test score of <24, 332 (45.4%;95%CI:41.8,49.0) study participants fulfilled the definition. A higher prevalence of cognitive dysfunction was associated (univariate analysis) with a higher hearing loss grade (OR:1.13;95%CI:1.08,1.27;*P*<0.001), with a higher prevalence of hearing loss grade 3+ (OR:2.18;95%CI:1.59,2.98), with a higher prevalence of MSVI / blindness (OR:2.09;95%CI:1.55,2.81;*P*<0.001), and with a higher prevalence of a dual sensory impairment (OR:2.80;95%CI:1.92,4.07;*P*<0.001).

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Discussion

In our ethnically mixed study population with an age of 85+ years from Bashkortostan/Russia, the prevalences of MSVI/blindness, moderately severe hearing loss and dual sensory impairment were 51.8%, 33.1% and 20.5%, respectively. In multivariable analysis, a higher prevalence of all three variables was associated with a lower cognitive function score and higher cognitive dysfunction prevalence. After adjusting for age, region of habitation, educational level and depression score, a lower cognitive function score was associated with worse BCVA and a higher hearing loss score. As a corollary, the risk for cognitive dysfunction increased by 2.18 for the presence of moderately severe or more advanced hearing loss, by 2.09 for the presence of MSVI/blindness, and by 2.80 for the presence of dual sensory impairment.

The findings made in our study on a population aged 85+ years cannot directly be compared with the observations made in many previous studies, since previous investigations usually did not include a sufficient number of participants in that age category, and since hearing impairment, vision impairment and cognitive dysfunction have rarely been assessed together. In their study on the prevalence of dual sensory impairment and its relationship with dementia in community-dwelling Medicare beneficiaries, Kuo and colleagues found an 1.9-fold, 1.1-fold, and 2.0-fold increase in the cross-sectional hazard of dementia for self-reported functional vision impairment, hearing impairment, and dual sensory impairment, respectively.[9] Despite differences in the assessment of sensory impairment (self-reported versus measurements), study design (nationally representative sample of Medicare beneficiaries aged 65+ years versus population-based recruitment of 85+ years olds) and study region (US versus urban and rural Russia), the figures reported by Kuo and associates are similar to those found in our study, with a higher cross-sectional risk of dementia for the presence of dual sensory impairment as compared to the presence of vision impairment or hearing impairment taken separately. Kuo and colleagues additionally observed that sensory impairment was associated with an increased incidence of dementia during over 7-years follow-up. The results of our study also agree with other investigations, such as a longitudinal study of older US adults from the Health and Retirement Study which reported higher hazards of incident dementia for individuals with self-reported visual impairment, hearing impairment and dual sensory impairment as compared to individuals without such impairments.[25-28] In the study conducted by Hwang and colleagues, functional dual sensory impairment as compared to vision impairment or hearing impairment alone was stronger associated with all-cause dementia during a follow-up of 8 years in a group of highly educated and mostly White elderly adults.[26] In the English Longitudinal Study of Aging, individuals with poor and moderate self-reported hearing were had a 57% and 39% higher hazard of incident dementia during a follow-up of 9 years, respectively.[27] The finding of a concurrence of vision impairment and cognitive impairment concurs also with the results of precent meta-analyses.[29,30]

A reason for the association between impairment in vision and hearing and cognitive dysfunction may be a sensory impairment-related reduction in external stimuli for cognitive activities, in addition to an increased risk of social isolation, depression, and reduced physical activity.[31-33] All these factors have been known to increase the risk for cognitive dysfunction and dementia.[3] Another reason may be an increase in cognitive load in individuals with sensory impairments since more cognitive resources may be needed for the support of the visual and hearing function. It may lead to a lack of remaining resources for cognitive tasks.[33-35] One of the reasons for a higher risk of cognitive dysfunction for dual sensory impairment as compared to vision impairment or hearing impairment alone could be that individuals with hearing impairment tend to perform lip reading what depends on sufficient vision. In addition, individuals with dual sensory impairment have a limited ability to compensate for a single sensory impairment by employing functioning of an unimpaired sensory system. Besides these causal relationships, other factors leading to the co-occurrence of sensory impairment and cognitive dysfunction could be a common mechanism, such as microvascular changes, leading to sensory impairment and cognitive dysfunction, and the possibility of a sensory impairment as a sequel of cognitive dysfunction, such as in the situation of patients with cognitive dysfunction and cataract, who may not have the means, support or willingness for cataract surgery to be performed.

Assuming an at least partially causative relationship between sensory impairment and cognitive dysfunction, any improvement in vision or hearing impairment by providing correcting glasses and hearing aids and performing cataract surgery could be meaningful.[36-38] To cite an example, the pilot study of the Aging and Cognitive Health Evaluation in Elders trial suggested a slowing of memory decline by treatment of hearing impairment.[37] Another example may be providing simple reading glasses. In the population-based Beijing Eye Study, higher cognitive function was associated with a lower amount of undercorrection of refractive error after adjusting for younger age, rural region of habitation, educational level, occupation, depression score, BCVA and history of cardiovascular disorder.[40] Correspondingly, individuals wearing glasses for correction of their refractive error as compared to subjects without glasses showed a significantly higher cognitive score. These results also fit with observations made in a study by Rogers and Langa, who reported that in an 8.5 years follow-up study poor vision at baseline was associated with incident dementia.[41] Simple,

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cheap treatment of refractive errors by providing adequate eyeglasses may not only increase the quality of life, but may potentially also provide cost-effective prophylaxis of cognitive dysfunction and dementia

The limitations of our study have to be considered. First, we did not measure presenting visual acuity, so that we could not assess the prevalence of undercorrection of refractive error. Second, the participation rate in our study was 47.9%, a figure considerably lower than those for other population-based studies. In view of the relatively high age of 85+ years as inclusion criterion, the study may give, however, some information about the prevalence of vision and hearing impairment and their combined occurrence in that age group. In addition, the main goal of our study was not to examine the prevalences of vision and hearing impairment but their relationship with cognitive function. Third, we did not phonometrically measure hearing impairment, but the study participants underwent an interview with standardized questions about their subjective hearing capacity. The validity of these questions of the Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S) had been assessed in previous investigations.[19-21] Fourth, our study had a cross-sectional design so that cross-sectional associations could, however, longitudinal cause-effect relationships could not be explored. Strengths of our study were that it was the first population-based study on the prevalence of dual sensory impairment as well as their relationship with cognitive function in the age group of 85+ years with a relatively large study sample size, and the inclusion of a multitude of systemic parameters.

In conclusion, in this very old multi-ethnic population from Bashkortostan/Russia, vision impairment, hearing impairment and dual sensory impairment as combination of both were relatively common and were associated with cognitive dysfunction. Assuming a causal relationship, providing hearing aids, and providing glasses for distant and reading vision and cataract surgery, may potentially be measures to reduce the impact of cognitive dysfunction by reducing some of its risk factors.

a. Contributorship statement: Design of the study: MMK, GMK, JBJ; Examination of participants: MMB, GMK, EMR, IAR, AAF, AMT, NIB, KRS, AVG, IPP, DFY, NEB, NAN; Examination of clinical images and data collection: MMB, GMK, EMR, IAR, AAF, AMT, SPJ, NIB, KRS, AVG, IPP, DFY, NEB, NAN, JBJ; Statistical analysis: SPJ, JBJ; Funding: MMK, JBJ; Writing the first draft: SPJ, JBJ, Approval of final draft: MMB, GMK, EMR, IAR, AAF, AMT, SPJ, NIB, KRS, AVG, IPP, DFY, NEB, NAN, JBJ.

b. Competing interests: None

c. Funding: None

d. Data sharing statement: The data will be shared upon reasonable request.

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Table 1

Associations (multivariable analysis) between the cognitive function score assessed in the mini-mental test and other parameters

	Standardized regression coefficient	Non-standardized regression coefficient B	95% Confidence Interval of B	*P*-Value	Variation inflation factor
Age (years)	-0.11	-0.25	-0.39, -0.11	0.001	1.13
Region of habitation (rural / urban)	0.10	1.42	0.47, 2.37	0.003	1.28
Level of education (0-5)	0.24	0.71	0.51, 0.90	<0.001	1.25
Depression score	-0.38	-0.22	-0.26, -0.19	<0.001	1.05
Best corrected visual acuity (LogMAR)	-0.15	-1.55	-2.22, -0.88	<0.001	1.17
Hearing loss score	-0.07	-0.03	-0.05, -0.002	0.03	1.10

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Concurrent Vision and Hearing Impairment Associated with Cognitive Dysfunction in a Population Aged 85+ Years: The Ural Very Old Study

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Concurrent Vision and Hearing Impairment Associated with Cognitive Dysfunction in a Population Aged 85+ Years: The Ural Very Old Study

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Abstract

Objective: To assess the prevalence of vision impairment, hearing impairment and dual sensory impairment (DSI) as combination of vison and hearing impairment, in association with cognitive dysfunction in a population aged 85+ years.

Methods: The cross-sectional population-based Ural-Very-Old-Study, conducted in rural and urban Bashkortostan/Russia between 2017 and 2020, included a detailed ocular and systemic examination with assessment of moderate to severe vision impairment/blindness (MSVI) (best corrected visual acuity <6/18), moderate to severe hearing loss (MSHL), and cognitive function.

Setting: A rural and urban area in Bashkortostan/Russia.

Participants: Out of 1882 eligible individuals aged 85+ years, 1526 (81.1%) individuals participated.

Primary and secondary outcome measures: Prevalence of vision, hearing and dual sensory impairment and cognitive dysfunction.

Results: The study included 731 (47.9%) individuals (mean age:88.1±2.7 years (median:87 years;range:85-98years)) with measurements of MSVI/blindness, MSHL and cognitive function. The prevalence of MSVI/blindness, MSHL, DSI and dementia were 51.8% (95% confidence interval (CI):48.2,55.5), 33.1% (95%CI:29.7,36.5), 20.5% (95%CI:17.8,23.5), and 48.2% (95%CI:44.5,51.8), respectively. Lower cognitive function score was associated with lower visual acuity (*P*<0.001) and higher hearing loss score (*P*=0.03), after adjusting for older age (*P*=0.001), rural region of habitation (*P*=0.003), lower educational level (*P*<0.001), and higher depression score (*P*<0.001). Higher dementia prevalence was associated with higher MSHL prevalence (OR:2.18;95%CI:1.59,2.98;*P*<0.001), higher MSVI/blindness prevalence (OR: 2.09;95%CI:1.55,2.81;*P*<0.001), and higher DSI prevalence (OR:2.80;95%CI:1.92,4.07;*P*<0.001).

Conclusions: In this very old, multi-ethnic population from Russia, dual sensory impairment (prevalence:20.5%), as compared to hearing impairment (OR:2.18) and vision impairment alone (OR:2.09), had a stronger association (OR: 2.80) with dementia. The findings show the importance of hearing and vision impairment, in particular their combined occurrence, for dementia prevalence in an old population.

Strengths and limitations of this study

- A population-based recruited multi-ethnic study sample of individuals aged 85+ years and living in rural and urban region in Bashkortostan / Russia was ophthalmologically and systemically examined.
- Vision was tested as best corrected visual acuity, hearing loss was assessed with the help of a standardized questionnaire, and cognitive function was examined applying the Mini Mental test.
- Limitations of the study include a relatively low participation rate of 47.9%, and that hearing impairment was not phonometrically measured.
- Strengths of the study are the high age of the study participants, the combination of a multitude of examinations in the area of ophthalmology, hearing loss and internal medicine,

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and performance in Russia for which public health information has been relatively scarce so far.

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Introduction

Due to growth and ageing of the population, the role of dementia as major cause of the global burden of disease has further gained importance during the past decades.[1,2] In view of estimations of further rising trends in the global prevalence of dementia, and taking into account the absence of any evidence-based therapy with a major impact on the course of the disease, detection of risk factors of dementia and the reduction of their influence is of thus major importance.[3,4] In the 2020 update to the Lancet Commission report on dementia, about 40% of dementia was attributed to 12 major modifiable risk factors.[3] These included hearing impairment among other factors such as lower level of education, arterial hypertension, obesity, smoking, depression, physical inactivity, social isolation, diabetes mellitus, alcohol consumption, head injury, and air pollution. Although vision impairment was associated with a higher risk of dementia in some investigations which showed an up to 8 times higher risk of dementia for visually impaired individuals, the association between vision impairment and dementia has remained unclear so far.[5-8] In particular, the effect of a combined occurrence of vision impairment with hearing impairment as dual sensory impairment has not fully been explored and recognized as risk factor for cognitive dysfunction yet. Using data from the US National Health and Aging Trends Study, a recent nationally representative cohort study of community-dwelling Medicare beneficiaries aged 65+ years revealed that self-reported functional vision impairment, self-reported functional hearing impairment and combined self-reported vision and hearing impairment had adjusted cross-sectional hazard ratios of dementia of 1.89, 1.14, and 2.00, respectively.[9] Similar results were obtained during a follow-up of 7 years for the incidence of dementia.

The strengths of some of previous studies were that they addressed sensory impairment and cognitive function and their association by using objective measures of sensory functions, and that they analyzed nationally representative and longitudinal data with a relatively long follow-up.[9-11] Some of the previous investigations however had limitations such as being based on self-reported impairment in vision and hearing, including Medicare beneficiaries as a subgroup of the total population in the case of Kuo´s study, and not being focused on the very old population.[12] We therefore conducted the present population-based study on individuals aged 85+ years and who underwent measurements of visual acuity and cognitive function and assessment of hearing loss. In addition, we performed the study in Russia, a world region for which population-based data on dual sensory impairment and cognitive dysfunction have only scarcely been available so far, and which is one of the world regions with a relatively fast ageing of the population.[13,14]

Methods

The Ural Very Old Study (UVOS) is a population-based study performed in the rural region in the Karmaskalinsky District in a distance of 65 km from the capital Ufa, and in the urban region of Kirovskii in Ufa in the Republic of Bashkortostan / Russia.[15,16] The study, conducted between November 2017 and December 2020, was approved by the Ethics Committee of the Academic Council of the Ufa Eye Research Institute and informed written consent was obtained from all participants. In the situation of individuals who were not able to understand the meaning of the consent, the closest relative was informed and consented. Inclusion criteria were an age of 85+ years and living in the study regions.

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The Republic of Bashkortostan has a population of about 4.07 million people and it is geographically located in the west of the southern Ural Mountains about 1300 km east of Moscow. Its capital Ufa is an economic, scientific and cultural center and has a population of 1.1 million inhabitants including Russians, Bashkirs, Tatars, Ukrainians and other ethnicities.

Out of 1882 eligible inhabitants aged 85+ years and living in the study regions, the study consisted of 1526 (81.1%) participants including inhabitants of retirement or nursing homes. The urban group (1238 (81.3%) out of 1523 individuals) and the rural group (288 (80.2%) out of 359 individuals) did not differ significantly in the participation rate. Based on the census performed in Russia in 2010, age and gender distribution in the study population did not vary markedly from the Russian population age 85+ years, with a marked preponderance of females.[17]

Using a bus, the study participants were brought from their homes to the Ufa Eye Institute where a team of about 20 trained technicians and ophthalmologists performed all examinations. Those individuals which were unable to come to the hospital, underwent the interview and all examinations, which could be performed outside of the hospital, in their homes. The series of examinations included a standardized interview by trained social workers with almost 300 questions on the socioeconomic background, diet, smoking, alcohol consumption, physical activity, quality of life and quality of vision, history of any type of injuries and inter-personal violence, and health assessment questions.[15] All questions were taken from standardized interviews published in the literature, such as the “Center for Epidemiologic Studies Depression Scale (CES-D) Scoresheet” and the Folstein test.[17-22] The physical examinations consisted of the measurement of the anthropomorphic parameters, arterial blood pressure and pulse rate. Using blood samples taken under fasting conditions, we measured the serum concentrations of transaminases, bilirubin, blood lipids, glucose, creatinine, hemoglobin, and others and performed a blood cell count. We applied the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER statement guidelines).[23] The Ural Very Old Study design was similar to the design of the Ural Eye and Medical Study (UEMS) which has been described in detail previously.[15]

Besides other ocular examinations, we measured best corrected visual acuity (BCVA), expressed in LogMAR (logarithm of the minimal angle of resolution) and determined the ocular axial length by sonography. Using the World Health Organization (WHO) criteria, we defined moderate to severe vision impairment (MSVI) as BCVA of <6/18 but ≥3/60 in the better eye or binocularly, and blindness as BCVA of <3/60 in the better eye or binocularly.

Hearing loss was assessed by a series of 11 standardized questions, ten of which were derived from the “Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S)”.[24-27] The prevalence of self-reported hearing loss as a binary variable was assessed by the single question “Do you experience a hearing loss?”. The questions could be answered by “no” (0 points), “sometimes” (2 points) and “yes (4 points). The total hearing loss score was the sum of the points of all questions of the questionnaire and could range between 0 points and 44 points. The amount of hearing loss was assessed by the hearing loss score. The HHIE-S had been applied in previous investigations.[24-26] The diagnostic performance of the HHIE-S against five definitions of hearing loss as assessed by pure-tone audiometry had been explored in a previous study revealing sensitivities ranging between 53% and 72% and specificities from 70 to 84%, depending on the definition of hearing loss.[28] Based on the WHO hearing impairment grading system, we defined mild hearing impairment ("No problems in quiet but may have real difficulty following conversation in noise") by a hearing loss score of 11 to 17; moderate hearing impairment ("May have difficulty in quiet hearing a normal voice and has difficulty with conversation in noise") by a hearing loss score of 18 to 24; moderately severe hearing impairment ("Needs loud speech to hear in quiet and has great difficulty in noise) by a hearing loss score of 25 to 31; severe hearing impairment ("In quiet, can hear loud speech directly in one's ear, and, in noise, has very great difficulty.") by a hearing loss score of 32-38; and profound hearing impairment ("Unable to hear and understand even a shouted voice whether in quiet or noise") by a hearing score of 39 to 44.[28,29] We defined dual sensory impairment as MSVI/blindness combined with moderately severe or more severe hearing impairment (grade 3+). Cognitive function was assessed using the Mini-Mental Status Examination scale.[19]

Using a statistical software package (SPSS for Windows, version 25.0, SPSS, Chicago, IL), we determined the demographic characteristics of the study population (presented as mean ± standard deviation) and assessed the prevalence of MSVI/blindness, hearing impairment and dual sensory impairment (presented as mean and 95% confidence intervals (CIs)). We performed a regression analysis as univariate analysis with the cognitive function score as dependent variable, followed by a multivariable analysis that included as independent variables all those parameters which were significantly associated with the cognitive function score in the univariate analysis. Finally, we conducted a binary regression analysis of the relationships between the prevalence of cognitive dysfunction, vision impairment, hearing impairment and dual sensory impairment. We calculated the standardized regression coefficient beta, the non-standardized regression coefficient B, odds ratios (ORs) and the 95% CIs. All P-values were two-sided and considered statistically significant when the values were less than 0.05.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Results

Out of 1526 individuals primarily participating in the Ural Very Old Study, the present investigation included 731 (47.9%) individuals (530 (72.5%) women; 201 (27.5%) men) for whom measurements and data of BCVA, hearing loss and cognitive function were available (Table 1, 2). The individuals with assessment of vision loss, hearing loss and cognitive function as compared with the individuals without these examinations did not vary significantly in age (88.1 ± 2.7 years versus 88.5 ± 3.0 years; P=0.10), level of education (4.6 ± 2.1 versus 4.4 ± 2.1; P=0.08), sex (P=0.10) and ethnic background (Russian versus non-Russian) (P=0.06).

Out of the 731 study participants, 342 (46.8%;95%CI:43.2,50.4) individuals fulfilled the definition of MSVI, and 37 individuals (5.1%;95%CI:3.5,6.7) fulfilled the definition of blindness in the better eye or under binocular conditions. The combined prevalence of MSVI and blindness was 51.8% (95%CI:48.2,55.5). The mean hearing loss score was 19.5±15.4 (median:22;range:0-44). Out

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of the 731 study participants, 291 (39.8%) had a normal hearing score, 55 (7.5%) had mild hearing impairment (grade 1), 143 (19.6%) individuals had moderate hearing impairment (grade 2), 66 (9.0%) persons had moderately severe hearing impairment (grade 3), 58 individuals (7.9%) had severe hearing impairment (grade 4), and 118 (16.1%) had profound hearing impairment (grade 5). Dual sensory impairment, defined as MSVI/blindness combined with moderately severe hearing impairment grade 3+ was present in 150 (20.5%;95%CI:17.8,23.5) individuals.

The mean cognitive function score obtained in the Mini Mental test was 22.2±6.4 (median: 24;range: 0-30). Stratified by the category of cognitive dysfunction, 399 individuals had a cognitive ranging between 24 to 30, 162 participants had a score ranging between 19 and 23, for 137 individuals the score ranged between 10, and 18and 33 participants had a score of less than 10 (Table 3). In univariate analysis, a higher cognitive score was associated with younger age (P<0.001), urban region of habitation (P<0.001), higher level of education (P<0.001), lower hearing loss score (P<0.001), higher body mass index (P=0.002), longer waist (P<0.001) and hip (P=0.003) circumference, higher prevalence of alcohol consumption (P=0.02), higher number of meals taken daily (P<0.001), higher number of days per week with fruit intake (P<0.001), higher serum concentration of triglycerides (P=0.02), urea (P=0.03), higher leucocytes blood cell count (P=0.02), lower diastolic blood pressure (P=0.005), lower depression score (P<0.001), and a lower State Trait anxiety score (P<0.001), and with the ocular parameters of better BCVA (P<0.001), longer ocular axial length (P=0.04) and lower prevalence of dry eye (P=0.02). It was not significantly associated with sex (P=0.15), Russian versus non-Russian ethnicity (P=0.20), body height (P=0.07), body weight (P=0.09), waist-hip circumference ratio (P=0.09), current smoking (P=0.56), systolic (P=0.75) and mean (P=0.15) blood pressure, prevalence of arterial hypertension (P=0.11), serum concentration of glucose (P=0.78), creatinine (P=0.48), hemoglobin (P=0.19), and erythrocyte count (P=0.22), and with the ocular parameter of refractive error (P=0.80).

In multivariable analysis, we first dropped due to collinearity the parameter of the anxiety score (variance inflation factor: 4.9). Due to lack of statistical significance, we then dropped the parameters of prevalence of alcohol consumption (P=0.96), number of days with fruit intake (P=0.77), dry eye prevalence (P=0.82), leucocytes blood cell count (P=0.78), waist circumference (P=0.80), diastolic blood pressure (P=0.65), ocular axial length (P=0.53), number of meals taken daily (P=0.15), hip circumference (P=0.42), serum concentration of triglycerides (P=0.05), and body mass index (P=0.05). In the final model, higher cognitive function score was associated with younger age (P=0.001), urban region of habitation (P=0.003), higher level of education (P<0.001), lower BCVA (P<0.001), higher hearing loss score (P=0.03), and higher depression score (P<0.001) (Table 4). If the BCVA and hearing loss score were replaced by the prevalence of dual sensory impairment, a lower prevalence of the latter was associated with a higher cognitive function score (beta: -0.11; B: -1.70; 95%CI: -2.66, -0.74; P=0.001).

In a reverse manner, a higher prevalence of MSVI was associated with a lower cognitive function score (OR: 0.93; 95%CI: 0.90, 0.97; P=0.001), after adjusting for older age (OR: 1.20; 95%CI: 1.10, 1.30; P<0.001), higher mean arterial blood pressure (OR: 1.02; 95%CI: 1.001, 1.03; P=0.04), longer axial length (OR: 1.27; 95%CI: 1.04, 1.55; P=0.02), and lower prevalence of previous cataract surgery (OR: 0.46; 95%CI: 0.30, 0.70; P<0.001). A higher prevalence of hearing loss (grade 3+)

correlated with lower cognitive function score (OR: 0.95; 95%CI: 0.92, 0.97; *P*<0.001) after adjusting for older age (OR: 1.08; 95%CI: 1.01, 1.14; *P*00.02) and higher depression score (OR: 1.02; 95%CI: 1.01, 1.04; *P*=0.01). In multivariable analysis, a higher prevalence of dual sensory impairment was associated with a lower cognitive function score (OR:0.94;95%CI:0.91,0.98;*P*=0.001), after adjusting for older age (OR:1.16;95%CI:1.08,1.24;*P*<0.001), rural region of habitation (OR:2.32;95%CI:1.51,3.56, *P*<0.001), and higher depression score (OR:1.03;95%CI:1.01,1.06;*P*<0.002). In that model, the prevalence of dual sensory impairment was not significantly associated with sex (*P*=0.08). If the depression score was dropped, the association with a higher anxiety score became significant (OR: 1.03; 95CI: 1.01, 1.05; *P*=0.001).

If cognitive dysfunction was defined by Mini Mental test score of <24, 332 (45.4%;95%CI:41.8,49.0) study participants fulfilled the definition. A higher prevalence of cognitive dysfunction was associated (univariate analysis) with a higher hearing loss grade (OR:1.13;95%CI:1.08,1.27;*P*<0.001), with a higher prevalence of hearing loss grade 3+ (OR:2.18;95%CI:1.59,2.98), with a higher prevalence of MSVI / blindness (OR:2.09;95%CI:1.55,2.81;*P*<0.001), and with a higher prevalence of a dual sensory impairment (OR:2.80;95%CI:1.92,4.07;*P*<0.001).

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Discussion

In our ethnically mixed study population with an age of 85+ years from Bashkortostan/Russia, the prevalence of MSVI/blindness, moderately severe hearing loss and dual sensory impairment were 51.8%, 33.1% and 20.5%, respectively. In multivariable analysis, a higher prevalence of all three variables was associated with a lower cognitive function score and higher cognitive dysfunction prevalence. After adjusting for age, region of habitation, educational level and depression score, a lower cognitive function score was associated with worse BCVA and a higher hearing loss score. As a corollary, the risk for cognitive dysfunction increased by 2.18 for the presence of moderately severe or more advanced hearing loss, by 2.09 for the presence of MSVI/blindness, and by 2.80 for the presence of dual sensory impairment.

The findings made in our study on a population aged 85+ years cannot directly be compared with the observations made in many previous studies, since previous investigations usually did not include a sufficient number of participants in that age category, and since hearing impairment, vision impairment and cognitive dysfunction have rarely been assessed together. In their study on the prevalence of dual sensory impairment and its relationship with dementia in community-dwelling Medicare beneficiaries, Kuo and colleagues found an 1.9-fold, 1.1-fold, and 2.0-fold increase in the cross-sectional hazard of dementia for self-reported functional vision impairment, hearing impairment, and dual sensory impairment, respectively.[12] Despite differences in the assessment of sensory impairment (self-reported versus measurements), study design (nationally representative sample of Medicare beneficiaries aged 65+ years versus population-based recruitment of 85+ years old) and study region (US versus urban and rural Russia), the figures reported by Kuo and associates are similar to those found in our study, with a higher cross-sectional risk of dementia for the presence of dual sensory impairment as compared to the presence of vision impairment or hearing impairment taken separately. Kuo and colleagues additionally observed that sensory impairment was associated with an increased incidence of dementia during over 7-years follow-up. The results of our study also agree with other investigations, such as a longitudinal study of older US adults from the Health and Retirement Study which reported higher hazards of incident dementia for individuals with self-reported visual impairment, hearing impairment and dual sensory impairment as compared to individuals without such impairments.[30-33] In the study conducted by Hwang and colleagues, functional dual sensory impairment as compared to vision impairment or hearing impairment alone was stronger associated with all-cause dementia during a follow-up of 8 years in a group of highly educated and mostly White elderly adults.[31] In the English Longitudinal Study of Aging, individuals with poor and moderate self-reported hearing were had a 57% and 39% higher hazard of incident dementia during a follow-up of 9 years, respectively.[32] The finding of a concurrence of vision impairment and cognitive impairment concurs also with the results of precent meta-analyses.[34,35]

A reason for the association between impairment in vision and hearing and cognitive dysfunction may be a sensory impairment-related reduction in external stimuli for cognitive activities, in addition to an increased risk of social isolation, depression, and reduced physical activity.[36-38] All these factors have been known to increase the risk for cognitive dysfunction and dementia.[3] Another reason may be an increase in cognitive load in individuals with sensory impairments since more cognitive resources may be needed for the support of the visual and hearing function. It may lead to a lack of remaining resources for cognitive tasks.[38-40] One of the reasons for a higher risk of cognitive dysfunction for dual sensory impairment as compared to vision impairment or hearing impairment alone could be that individuals with hearing impairment tend to perform lip reading what depends on sufficient vision. In addition, individuals with dual sensory impairment have a limited ability to compensate for a single sensory impairment by employing functioning of an unimpaired sensory system. Besides these causal relationships, other factors leading to the co-occurrence of sensory impairment and cognitive dysfunction could be a common mechanism, such as microvascular changes, leading to sensory impairment and cognitive dysfunction, and the possibility of a sensory impairment as a sequel of cognitive dysfunction, such as in the situation of patients with cognitive dysfunction and cataract, who may not have the means, support or willingness for cataract surgery to be performed.

Assuming an at least partially causative relationship between sensory impairment and cognitive dysfunction, any improvement in vision or hearing impairment by providing correcting glasses and hearing aids and performing cataract surgery could be meaningful.[41-44] To cite an example, the pilot study of the Aging and Cognitive Health Evaluation in Elders trial suggested a slowing of memory decline by treatment of hearing impairment.[42] Another example may be providing simple reading glasses. In the population-based Beijing Eye Study, higher cognitive function was associated with a lower amount of undercorrection of refractive error after adjusting for younger age, rural region of habitation, educational level, occupation, depression score, BCVA and history of cardiovascular disorder.[45] Correspondingly, individuals wearing glasses for correction of their refractive error as compared to subjects without glasses showed a significantly higher cognitive score. These results also fit with observations made in a study by Rogers and Langa, who reported that in an 8.5 years follow-up study poor vision at baseline was associated with incident dementia.[46] Simple,

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cheap treatment of refractive errors by providing adequate eyeglasses may not only increase the quality of life, but may potentially also provide cost-effective prophylaxis of cognitive dysfunction and dementia

The reason for the association between a higher cognitive function score and urban region of habitation may be the higher level of education in the cities and other lifestyle-associated parameters. Policy implications of our findings may be, among others, to further increase the frequency of cataract surgeries in Russia, to provide best correcting glasses to correct refractive errors including presbyopic refractive error, to provide hearing aids to address hearing loss, and to prevent hearing loss by adequate protective measures at the working place and in daily life.

The limitations of our study have to be considered. First, we did not measure presenting visual acuity, so that we could not assess the prevalence of undercorrection of refractive error. Second, the participation rate in our study was 47.9%, a figure considerably lower than those for other population-based studies. It may have introduced a selection bias, in particular since individuals with marked dementia could not participate in the study. In view of the relatively high age of 85+ years as inclusion criterion, the study may give, however, some information about the prevalence of vision and hearing impairment and their combined occurrence in that age group. In addition, the main goal of our study was not to examine the prevalence of vision and hearing impairment but their relationship with cognitive function. Third, we did not phonometrically measure hearing impairment, but the study participants underwent an interview with standardized questions about their subjective hearing capacity. The validity of these questions of the Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S) had been assessed in previous investigations.[19-21] Fourth, our study had a cross-sectional design so that cross-sectional associations could, however, longitudinal cause-effect relationships could not be explored. Fifth, the study could not include those individuals with an advanced stage of dementia which did not allow taking part in the interview and in the examinations. Strengths of our study were that it was the first population-based study on the prevalence of dual sensory impairment as well as their relationship with cognitive function in the age group of 85+ years with a relatively large study sample size, and the inclusion of a multitude of systemic parameters.

In conclusion, in this very old multi-ethnic population from Bashkortostan/Russia, vision impairment, hearing impairment and dual sensory impairment as combination of both were relatively common and were associated with cognitive dysfunction. Assuming a causal relationship, providing hearing aids, and providing glasses for distant and reading vision and cataract surgery, may potentially be measures to reduce the impact of cognitive dysfunction by reducing some of its risk factors.

a. Contributorship statement: Design of the study: MMK, GMK, JBJ; Examination of participants: MMB, GMK, EMR, IAR, AAF, AMT, NIB, KRS, AVG, IPP, DFY, NEB, NAN; Examination of clinical images and data collection: MMB, GMK, EMR, IAR, AAF, AMT, SPJ, NIB, KRS, AVG, IPP, DFY, NEB, NAN, JBJ; Statistical analysis: SPJ, JBJ; Funding: MMK, JBJ; Writing the first draft: SPJ, JBJ, Approval of final draft: MMB, GMK, EMR, IAR, AAF, AMT, SPJ, NIB, KRS, AVG, IPP, DFY, NEB, NAN, JBJ.

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b. Competing interests: None
c. Funding: None
d. Data sharing statement: The data will be shared upon reasonable request.

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Table 1

Characteristics of the participants of the Ural Very Old Study

	Mean ± standard deviation
Age (years)	88.1 ± 2.7 (median: 87; range: 85-98)
Men / women	201 (27.5%) / 530 (72.5%)
Ethnicity	
Russian	251 (34.3%)
Tartars	334 (45.7%)
Bashkirs	83 (11.4%)
Chuvash,	25 (3.4%)
Mari	5 (0.7%)
Others	33 (4.5%)
Level of education	
Illiterate	23 (3.1%)
Passed the 5th class	133 (18.2%)
Passed the 8th class	159 (21.8%)
Passed the 10th class	29 (4.0%)
Passed the 11th class	15 (2.1%)
Specialized secondary education	172 (23.5%)
Graduates	194 (26.5%)
Postgraduates	4 (0.5%)
Family type	
Living in a joint family	124 (17.0%)
Living in a nuclear family	77 (10.5%)
Living alone	266 (36.4%)
Living together with another family member	261 (35.7%)
Family status	
Married	170 (23.3%)
Unmarried	16 (2.2%)
Divorced	13 (1.8%)
Widowed	531 (72.6%)

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Table 2

Anthropometric data (mean ± standard deviation; median, range; 95% confidence intervals (CI)) of the participants of the Ural Very Old Study

	Total study population	Men	Women
n	731	201	530
Body height (cm)	158 ± 9 (158; 105-180)	166 ± 7 (167; 140-180)	154 ± 8 (154; 105, 177)
Body weight (kg)	65.9 ± 11.3; 66.0: 31.8-103	70.6 ± 9.2 (70.4; 43.8-92.7)	64.0 ± 11.6 (63.4; 31.8-103.0)
Body mass index (kg/m^2)	26.5 ± 4.5; 25.8; 14.7-59.0	25.6 ± 2.9 (25.6; 17.1-35.0)	26.9 ± 5.0 (26.0; 14.7-59.0)
Systolic blood pressure	156.9 ± 26.4 (155; 91-237)	149.6 ± 23.9 (150; 04, 213)	159.6 ± 26.8 (159; 921, 237)
Diastolic blood pressure	79.6 ± 13.9 (79; 25-177)	76.0 ± 12.6 (76; 44-119)	80.9 ± 14.2 (80; 25-177)
Arterial hypertension (stage 1+), prevalence	87.0%; 95%CI:84.5,89.4	79.4% (95%CI: 73.7, 85.1)	89.8% (95%CI: 87.3, 92.5)
Diabetes mellitus, prevalence	13.8%; 95% CI: 11.3, 16.4	12.5% (95%CI: 7.8, 17.2)	14.3% (95%CI: 11.3, 17.4)

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Table 3

Demographic data of the study population stratified by the category of cognitive dysfunction

Cognitive function score	n	Age (years)	Men / women	Urban / rural region of habitation	Level of education
24-30	399	87.7 ± 2.6	120/379	335 / 64	5.3 ± 1.9
19-23	162	87.9 ±2.3	40 / 122	119 / 43	4.2 ± 2.0
10-18	137	89.1± 3.1	34 / 103	84 / 53	3.6 ± 1.9
<10	33	89.8 ± 3.1	7 / 26	17 / 16	3.4 ± 1.8

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Table 4

Associations (multivariable analysis) between the cognitive function score assessed in the mini-mental test and other parameters

	Standardized regression coefficient	Non-standardized regression coefficient B	95% Confidence Interval of B	*P*-Value	Variation inflation factor
Age (years)	-0.11	-0.25	-0.39, -0.11	0.001	1.13
Region of habitation (rural / urban) (reference: rural region)	0.10	1.42	0.47, 2.37	0.003	1.28
Level of education (0-5)	0.24	0.71	0.51, 0.90	<0.001	1.25
Depression score	-0.38	-0.22	-0.26, -0.19	<0.001	1.05
Best corrected visual acuity (LogMAR)	-0.15	-1.55	-2.22, -0.88	<0.001	1.17
Hearing loss score	-0.07	-0.03	-0.05, -0.002	0.03	1.10

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4,5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, 5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4,5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	4,5
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5, 6
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

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Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	--
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	6
		Cross-sectional study—Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6, 7
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9, 10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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