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The Association of Psychological Well-being with Sensory and Cognitive Function and Neuronal Health in Aging Adults

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Abstract

Objectives—Psychological well-being (PWB) may be a potential modifiable risk factor of age-related diseases. We aimed to determine associations of PWB with sensorineural and cognitive function and neuronal health in middle-aged adults.

Methods—This study included 2039 Beaver Dam Offspring Study participants. We assessed PWB, hearing, visual acuity, contrast sensitivity impairment, olfactory impairment, cognition and retinal (macular ganglion cell inner-plexiform layer,mGCIPL) thickness. Age-sex-education-adjusted multivariable linear, logistic regression and generalized estimating equation models were used and then further adjusted for health-related confounders.

Results—Individuals with higher PWB had better hearing functions, visual acuity and thicker mGCIPL and reduced odds for hearing, contrast sensitivity and olfactory impairment in age-sex-education-adjusted models. Effects on mGCIPL and visual and olfactory measures decreased with adjustment. Higher PWB was associated with better cognition, better combined sensorineural-cognitive function and decreased cognitive impairment.

Discussion—PWB was associated with sensorineural-cognitive health indicating a potential of PWB interventions for healthy aging.

Keywords

Purpose in Life; Positive Relations; Cognition; Senses; Retinal Thickness

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Disclosure of Interest
The Authors declare that there is no conflict of interest.

Introduction

Age-related sensory losses and cognitive decline and dementia are common in older adults and public health challenges in aging populations. Sensory and cognitive declines might influence each other over the lifespan and are affected by neurodegeneration, sharing common risk factors (Albers et al., 2015; Merten, Fischer, et al., 2020; Pronk et al., 2019; Schubert et al., 2019). Recently, retinal nerve cells and, specifically, macular ganglion cell inner-plexiform layer thickness (mGCIPL) was found to be associated with sensorineural (hearing, vision and olfactory function) and cognitive function and has been discussed as a marker of neuronal health (Merten, Paulsen, et al., 2020; Ward et al., 2020). Neurodegenerative processes start in midlife, decades before clinical symptom onset, indicating a need for early intervention and prevention (Jack et al., 2013).

In the search for modifiable risk factors for age-related diseases, psychological well-being (PWB) has received growing interest. PWB is an overarching term for a multifaceted concept including eudaimonic (e.g., purpose, fulfillment) and hedonic (e.g., feeling good) components. Having a purpose in life and positive relations with others are two PWB key aspects that have been associated with mental and physical health (Ryff, 2014; Windsor et al., 2015). Purpose in life represents a self-organizing life aim that provides a sense of meaning, stimulates goals and manages behaviors (McKnight & Kashdan, 2009). Positive relations and social support through deep, trusting interpersonal relations are important for PWB (Ryff, 2014).

While in previous research reduced PWB has often been considered a result of reduced physical health, growing research operationalizes PWB as a determinant of various health outcomes in order to investigate its protective utility for human health (Ryff, 2014). PWB has been associated with reduced mortality (Cohen et al., 2016; Diener & Chan, 2011; Laugesen et al., 2018; Pantell et al., 2013) and better physical health (Ryff, 2014; Windsor et al., 2015; Yoo & Ryff, 2019), including vascular, metabolic and inflammation factors (Boylan & Ryff, 2015; Brooks et al., 2014; Cohen et al., 2016; Kiecolt-Glaser et al., 2010; Kim et al., 2013; Radler et al., 2018; Smith & Ruiz, 2002; Yang et al., 2016; Yu et al., 2015; Zilioli et al., 2015). Multiple pathways that may explain how PWB might positively affect human health have been suggested (Ryff & Kim, 2020). One pathway might be through better lifestyle and health behaviors. Higher purpose in life has been associated with better physical function (Kim et al., 2017) and more health-protective behaviors, i.e. physical activity and vegetable intake (Hill et al., 2018; Hooker & Masters, 2016), preventive health care, medical check-ups and cancer screenings (Chen et al., 2019; Kim et al., 2014). Another mechanism might be through the contribution of enriched and stimulating environments, i.e., social activities (Lu et al., 2003) that could improve brain reserve (Stern, 2009). Finally, psychological and social resources could be protective against negative emotional effects and stress; and effects of PWB on physiological processes of immune function and stress hormones are plausible (Berkman et al., 2013). Vascular, metabolic and inflammation factors have been shown to be important risk factors for sensory and cognitive decline (Schubert et al., 2019; Whitson et al., 2018) and system-wide neurodegenerative processes may play a role in declining sensory and cognitive function (Albers et al., 2015). Therefore, potential better lifestyles and more brain reserve in individuals with higher PWB could also contribute to better sensory and cognitive function. However, few cohort studies on sensory function and PWB exist (Boesveldt et al., 2017; Kramer et al., 2002; Mick et al., 2018; Mick & Pichora-Fuller, 2016; Strawbridge et al., 2000). Limitations of such previous studies are self-reported sensory assessments and/or a focus on social functions, while other aspects of PWB, such as purpose in life, and more complex constructs remain unstudied. Some epidemiological studies have been investigating PWB and cognition and found that PWB was associated with better cognitive function, less decline (Barnes et al., 2004; James et al., 2011; Kim et al., 2019; Lewis et al., 2017; Seeman et al., 2001; Windsor et al., 2015), and reduced risk for mild cognitive impairment and dementia in older adults (Boyle et al., 2010; Kuiper et al., 2015; Scarmeas et al., 2001; Xu et al., 2019). However, previous work often relied on verbal-only cognitive assessments, which can be confounded e.g. by hearing loss, and few studies in midlife exist (Kats et al., 2016; Lewis et al., 2017; Nakanishi et al., 2019). Furthermore, existing research on PWB and sensory and cognitive functions largely featured self-reported measures of confounding risk factors for sensory and cognitive decline. Studies with a thorough characterization of participants' health are lacking. To our knowledge, studies on the association between PWB and multiple measures of sensorineural functioning and measures of neuronal health, such as mGCIPL, have not been conducted.

Importantly, PWB can be modified by group interventions and environmental changes (Chan et al., 2017; Friedman et al., 2019; Ryff, 2014). Purpose in life can be renewed through career counseling, higher education or volunteer activities. Regular group exercises can improve social support satisfaction (Chan et al., 2017). PWB interventions might, therefore, promote healthy brain aging. With neuropathologic changes occurring decades prior to clinically manifested symptoms, interventions to prevent sensory and cognitive decline and neurodegenerative diseases may be most beneficial in midlife.

The aim of this study was to determine the association of PWB with sensorineural and cognitive function and mGCIPL thickness as a marker of neuronal health in midlife.

Materials and Methods

Study Population

This cross-sectional study is based on participants of the 10-year follow-up of the Beaver Dam Offspring Study (BOSS), a prospective cohort study of aging (Nash et al., 2011). The adult offspring of the population-based Epidemiology of Hearing Loss Study (EHLS) participants were eligible for the baseline BOSS examination (2005-2008) and have been followed every 5 years. PWB was assessed for the first time at the 10-year follow-up (2015-2017). We included all BOSS 10-year follow-up participants in this study who had a measure of PWB and at least one of the sensory or cognitive outcomes or mGCIPL. The study was approved by the University of Wisconsin Health Sciences Institutional Review Board (2014-1337, Beaver Dam Offspring Study) with written informed consent from all participants before each examination.

Measurements

With the exception of long-term inflammation, all measures included in this study were based on the assessment at the 10-year follow-up.

Psychological Well-being—Assessment of PWB was based on participants' responses to the two subscales Positive Relations with Others and Purpose in Life of the Ryff Psychological Well-Being inventory (Ryff, 2014). Each subscale had 7 items. Scores could vary between 7-49 (from low to high). PWB was defined as the sum of both scales' score (14-98 points) and z-standardized. Internal validity alphas for Purpose in Life and Positive Relations with Others and for the combined PWB scale were acceptable and good (0.73, 0.77 and 0.83, respectively).

Sensorineural Measures

Hearing Measures: Hearing thresholds for both ears were obtained at 0.5,1,2,3,4,6 and 8kHz (air-conduction) and 0.5 and 2kHz (bone-conduction) using clinical audiometers with TDH-50P earphones and ER-3A insert earphones (in cases of probable ear-canal collapse). Testing followed American National Standards Institute standards for equipment and American Speech-Language-Hearing Association guidelines (American National Standards Institute, 1999, 2010; American Speech-Language-Hearing Association (ASHA), 1978) and was conducted in a sound-treated booth. In the very few instances when testing was outside a booth, the insert earphones were used. When necessary, masking was done. The pure-tone average (PTA) of air-conduction thresholds at 0.5,1,2 and 4kHz in decibel hearing level (dB HL) for each ear was used to measure hearing sensitivity, with impairment defined as PTA>25dB HL (Merten, Paulsen, et al., 2020). Higher-order auditory function was assessed with two additional hearing tests. The dichotic digits test (DDT) was administered binaurally with 25 sets of triple-digit pairs. 3 digits were presented to each ear simultaneously at 70dB HL. The participant's task was to repeat as many of the 6 digits as possible. The Word Recognition in Competing Message (WRCM) with the Northwestern University Auditory Test Number 6 was administered to the better ear. In the WRCM, 25 words were presented by a single female speaker to the better hearing ear at 36dB HL above the individual's hearing threshold at 2kHz. If thresholds at 2kHz were equal, the right ear was tested. The competing message (single male speaker) was added at a level 8dB HL below the female speaker's level in that same ear (Wiley et al., 1998; Wilson et al., 1990). The percentage of correctly repeated digits from both ears in the free recall condition was the DDT outcome and the percentage of correctly repeated words was the WRCM outcome (Merten, Paulsen, et al., 2020).

Vision Measures: Contrast sensitivity (CS) was measured in each eye separately using a Pelli-Robson letter chart (Pelli et al., 1988). Participants were instructed to read as many letters as possible until 2 letters in a triplet were missed. We used the last triplet in which a participant correctly identified at least 2 of the 3 letters to assign a log CS score. Impairment was defined as log CS score≤1.55 (Paulsen et al., 2018). We measured best-corrected monocular visual acuity (VA) in each eye with the Early Treatment Diabetic Retinopathy Study chart R modified for a 2-m distance (ETDRS Coordinating Center Department of Epidemiology and Preventive Medicine University of Maryland School of Medicine, 1980;

Paulsen et al., 2018). We asked participants to read the letters from the 2-m chart until they could no longer correctly identify at least 3 of 5 letters on a line (scores 0 – 70). For those unable to read any letters at 2-m, a 1-m chart was used (scores − 30 – −1). People, who could not read any letter on the 1-m chart were assigned values of −40. The number of correctly identified letters was the VA outcome.

Olfaction Measure: To test olfaction, the San Diego Odor Identification Test (SDOIT) was used. Eight common odorants were randomly presented with a 45s interstimulus interval. A picture board including the 8 odorants and additional 12 distractor items was used to aid identification (verbal response or pointing on item on picture board). The number of correctly identified odors were summed and impairment defined as <6 out of 8 correct (Merten, Paulsen, et al., 2020).

Cognitive Measures: We conducted a neurocognitive test battery consisting of: Trail-Making Tests A and B (TMTA, TMTB), modified Rey Auditory Verbal Learning Test (AVLT), Digit Symbol Substitution Test (DSST), and Verbal Fluency Test (VFT) measuring the cognitive domains of attention, speed, executive function, memory and verbal fluency (Merten, Paulsen, et al., 2020). Participants were allowed to use assistive devices when performing cognitive tasks (their own glasses and/or hearing aids and we provided reading glasses and/or a Pocket Talker (Pocket Talker Pro™, Williams Sound, Eden Prairie, MN) if they needed them).

In TMTA, consecutive numbers were to be connected and in TMTB, consecutive numbers and letters were to be connected in an alternating fashion. Completion time in seconds was the outcome with longer durations indicating poorer performance. Inability to complete each subtest in 5min resulted in a score of 301s (Reitan, 1992). In DSST, participants convert numbers to symbols based on a key. The number of correctly converted numbers in 90s served as outcome score. For the AVLT, subjects were asked to recall as many words as they could from a list of 15 verbally presented words. Three trials with the same 15-word list were administered followed by a new 15 words distractor list. Immediately after recalling words from the distractor list, the participant was asked to recall as many words as they could from the first word list. The number of words correctly recalled from the first list in the final trial was our measure of memory function (González et al., 2015; Ivnik et al., 1992a; Zhong et al., 2014). In the VFT, the task is to produce as many words as possible starting with the letters F,A and S, within 60s for each letter. Total numbers of words provided for the three letters were summed as test outcome (Strauss et al., 2006).

The Mini-Mental-State Examination (MMSE) was completed by participants aged >50 years. Memory concerns were ascertained by two questions. Cognitive impairment was defined as memory concerns and impairment in at least one cognitive domain (executive function, memory, verbal function), self- or surrogate report of physician diagnosis of Alzheimer's disease or dementia, or a MMSE score<24 (Merten, Paulsen, et al., 2020). We used cut-offs of 1.5 standard deviations (*SD*) below the mean; or roughly equivalent, 3rd-5th percentile of published age-specific norm distributions of the tests to determine impairments on the cognitive tests (Ivnik et al., 1992b, 1992a, 1996; Tombaugh, 1999).

Measure of Neuronal Health: Optical coherence tomography (OCT) utilizing automated segmentation techniques was used to measure the thickness of the retinal nerve cell layers. We conducted a Macular Cube 512x128 scan on each eye, centered on the fovea, using the Cirrus 5000 HD-OCT (Carl Zeiss Meditec, Inc). The mGCIPL represents a combination of neuronal cell bodies and dendrites in the macula. Average mGCIPL thicknesses (in μm) from each eye were used in analyses (Merten, Paulsen, et al., 2020).

Other Variables: We assessed participants' age, sex, education, smoking status, history of heavy alcohol consumption (ever been drinking more than four alcoholic beverages per day), diabetes (history of diabetes diagnosis and/or glycated hemoglobin≥6.5%), history of cardiovascular disease (stroke, myocardial infarction, angina, congestive heart failure, transient ischemic attack, peripheral vascular disease, thrombosis, angioplasty or a stent operation, coronary bypass, and/or carotid arteries surgery), waist circumference (in cm), regular exercise (at least once a week long enough to work up a sweat) and long-term inflammatory status. We measured high-sensitivity c-reactive protein, interleukin-6, vascular cell adhesion protein 1 and intercellular adhesion molecule 1 from stored blood samples and defined long-term elevated inflammation as being repeatedly in the highest group for at least one inflammation marker at baseline and 5-year follow-up (Nash et al., 2011; Paulsen et al., 2018). For high-sensitivity c-reactive protein, participants were divided into three risk groups (<1, 1–3, and >3mg/L) according to established cut-points and we compared the highest risk group (>3mg/L) to the rest (Pearson et al., 2003). For the other three markers, we compared the highest tertile against the rest.

Statistical Analyses

Statistical analyses were conducted using SAS software v.9.4 (SAS Institute, Inc, Cary, NC). The composite cognitive function score (in *SD*) was created using a principal component analysis on neurocognitive test data (TMTA, TMTB, DSST, AVLT, VFT) (Merten, Paulsen, et al., 2020). Moreover, using principal component analysis, we calculated a combined sensorineural-cognitive function (brain aging) score in order to represent the integrity of the entire sensorineural system by combining sensorineural (PTA, CS, SDOIT) and neurocognitive (TMTA, TMTB, DSST, AVLT, VFT) test performances (Schubert et al., 2019).

We used multivariable linear regression, logistic regression and generalized estimating equation (GEE) models to assess the strength of associations of the determinant PWB with sensorineural and cognitive function, mGCIPL thickness and the combined measure of the brain aging as outcomes. Secondary analyses with individual cognitive tests are shown in Appendix 1. The GEE approach was used for paired measures (hearing sensitivity, hearing impairment, CS, VA, mGCIPL) to include both measures in a single model adjusting for the correlation between paired measures. There was insufficient variation in CS and olfactory test performance to support continuous analyses in this middle-aged cohort. Models were adjusted for age, sex and education and repeated additionally adjusting for chronic health conditions and behaviors (smoking, history of heavy alcohol consumption, diabetes, cardiovascular disease, long-term inflammation, waist circumference and exercise). We tested for sex interactions. Regression diagnostic plots were used to evaluate the fit and whether data satisfied the assumptions of linear regression. In order to visualize our results, we generated forest plots of the associations of psychological well-being (per 1SD Increase) and the odds for impairment in sensory and cognitive function (Appendix 2).

Results

This study included 2039 participants (mean age=58 years; *SD*=10, range=27-89; 55% women; Table 1). There were no significant sex interactions.

Higher PWB was associated with better hearing sensitivity (−0.91dB HL decrease per 1*SD* increase in PWB*;* 95*%* confidence interval (CI) −1.64,−0.18; p=.01) and dichotic digits performance (0.91*%* increase per 1*SD* increase in PWB*;* 95*%* CI 0.35,1.48; p=.002) in fully-adjusted models. Effect sizes were comparable to 1.5 years and 3.5 years of less aging, respectively. Individuals with higher PWB had reduced odds of hearing impairment (odds ratio OR=0.88 per 1*SD* increase in PWB*;* 95*%* CI 0.77,0.99; p=.04) in fully-adjusted models (Table 2, Appendix 2). In fully-adjusted models, PWB did not show associations with WRCM, VA, or risk for CS or olfactory impairment (Appendix 2).

Higher PWB was strongly associated with better cognitive function (0.07*SD* increase per 1*SD* increase in PWB; 95% CI 0.03,0.11; p=.0006), which compared to an effect of 2 years of less aging and decreased odds for cognitive impairment (OR=0.60 per 1*SD* increase in PWB; 95% CI 0.47,0.76; p<.0001) in fully-adjusted models (Table 3, Appendix 2). PWB was also associated with better cognitive test scores on the TMTA, TMTB and DSST (Appendix 1).

Individuals with higher PWB had thicker mGCIPL in age-sex-education-adjusted models, which was comparable to an effect of 1.5 years of less aging, but the effect size slightly decreased and was no longer statistically significant in the fully-adjusted model (0.33µm increase per 1SD increase in PWB; 95% CI −0.05,0.71; p=.08; Table 3).

Moreover, higher PWB was associated with higher scores on our combined sensorineural-cognitive measure of brain aging (0.08*SD* increase per 1*SD* increase in PWB; 95% CI 0.04,0.12; p<.0001; Table 3), comparable to 2 years of less aging.

Discussion

We found that higher PWB was associated with better sensorineural and cognitive function in middle-aged adults. These associations remained after adjusting for education, chronic health conditions and health behaviors. Notably, with every 1 SD increase in PWB participants showed benefits in sensorineural-cognitive function that were comparable to a difference of around 2 years of less aging.

These results extend previous findings to a study of multiple objectively and comprehensively assessed sensory and cognitive functions and associations in midlife, a time when interventions should be more efficacious (Boesveldt et al., 2017; Boyle et al., 2010; Kim et al., 2019; Kramer et al., 2002; Kuiper et al., 2015; Lewis et al., 2017; Mick et al., 2018; Mick & Pichora-Fuller, 2016; Nakanishi et al., 2019; Strawbridge et al., 2000; Windsor et al., 2015). Importantly, we were able to show that associations were independent of confounding of multiple physiologically assessed health factors such as inflammation and vascular risks, exceeding studies based on self-report. Moreover, we could compare associations across different sensorineural functions and found that among the senses, associations with hearing measures were strongest.

Our results are in line with research on the connection between PWB and various health functions. Since PWB is not simply the reverse of psychological distress its associations with physical and neuronal health are likely complicated and bi-directional (Ryff, 2014). Most previous studies have shown that PWB is often compromised in those with chronic health conditions or illness. However, growing research has also investigated its protective utility for human health (Boylan & Ryff, 2015; Brooks et al., 2014; Cohen et al., 2016; Kiecolt-Glaser et al., 2010; Kim et al., 2013; Radler et al., 2018; Ryff, 2014; Ryff & Kim, 2020; Smith & Ruiz, 2002; Windsor et al., 2015; Yoo & Ryff, 2019; Yu et al., 2015; Zilioli et al., 2015). A better lifestyle and health behaviors (Hooker & Masters, 2016; Kim et al., 2014) and enriched and stimulating environments, i.e., social activities (Lu et al., 2003) could improve brain reserve (Stern, 2009) and are considered to contribute to these effects. Moreover, psychological and social resources could be protective against negative emotional effects and stress(Berkman et al., 2013). Importantly, PWB is considered modifiable (Chan et al., 2017; Friedman et al., 2019; Ryff, 2014), emphasizing a potential of PWB interventions to slow or stabilize sensory and cognitive decline. Strategies to maintain PWB might be most beneficial when applied early in the process of declining sensory and cognitive functions. However, future longitudinal studies are needed to assess the direction of effects between PWB and sensory and cognitive health. Moreover, future research needs to determine the efficacy of PWB intervention for improvement in neuronal health (Ryff, 2014).

We found associations of PWB with hearing and cognitive impairment that remained when adjusting for health-related confounders, suggesting an association independent of potential confounding through better health. This is consistent with three cohort studies showing associations between self-reported hearing impairment and reduced social functioning (Kramer et al., 2002; Mick et al., 2018; Strawbridge et al., 2000). We extend this research to objectively assessed hearing and confounder variables and we used a more multifaceted measure of PWB, which incorporated positive relations and purpose in life. Our results are also in line with existing epidemiological research primarily in older adults that shows associations of PWB with better cognition, less decline and reduced risk for impairment (Barnes et al., 2004; Boyle et al., 2010; James et al., 2011; Kats et al., 2016; Kim et al., 2019; Kuiper et al., 2015; Lewis et al., 2017; Nakanishi et al., 2019; Scarmeas et al., 2001; Seeman et al., 2001; Windsor et al., 2015; Xu et al., 2019). This study expands upon the limited research on midlife and extends findings to associations of the multifaceted PWB construct with performance on a verbal and visual cognitive test battery while adjusting for well-characterized potential health confounders.

There is always some task-impurity when assessing sensory and cognitive function using behavioral tests. To minimize measurement error due to sensory problems, participants used assistive devices when performing cognitive tasks (their own glasses and/or hearing aids and we provided reading glasses and/or a Pocket Talker (Pocket Talker Pro™, Williams Sound, Eden Prairie, MN) if they needed them). Longitudinal research has shown associations between sensory and cognitive decline and system-wide neurodegeneration can be considered a source of these co-occurring losses (Albers et al., 2015; Merten, Fischer, et al., 2020; Pronk et al., 2019; Schubert et al., 2019). It is difficult to disentangle the task-impurity problem from the co-occurring age-related declines in these systems with cross-sectional data. We did not include sensory measures in the analyses on cognitive function to avoid overcontrolling. Our results on an association of PWB with brain aging, which includes multiple dimensions of sensorineural and cognitive function even after confounder adjustment reflect this idea of system-wide neurodegeneration.

We did not find associations between PWB and visual function (VA or CS impairment) or olfactory impairment, which were objectively assessed in our study. One study reported associations of self-reported vision loss with lower social network diversity (among men only), and reduced social participation and support (Mick et al., 2018). Another cohort study found an association of social network size and socializing frequency and odor identification performance (Boesveldt et al., 2017). Our measure of PWB was not restricted to a social dimension but also entails purpose in life and these earlier studies incorporated potential confounder variables based on self-report. We found associations in the age-sex-education-adjusted models, which diminished in fully-adjusted models. This might mean that associations between PWB and vision and olfaction might primarily be confounded by healthier lifestyles and health status, or we might be over-adjusting for pathways through which PWB would promote sensory and cognitive. Similarly, associations of PWB with mGCIPL were shown in age-sex-education-adjusted models and decreased to a trend level when adding health variables, which could be due to confounding or over-adjustment.

Limitations and Strengths

We used inflammation markers from earlier BOSS waves, as these were not measured at the 10-year follow-up. Due to the cross-sectional design, we were not able to investigate the temporality of effects of PWB and our functional outcomes. The BOSS cohort is primarily non-Hispanic White, which may limit the generalizability of results to other populations. Strengths of this study include the large middle-aged sample with a variety of objectively assessed sensorineural and cognitive functions and the mGCIPL. Furthermore, we were able to address numerous potential confounders assessed with physical examination data.

Conclusion

Higher PWB was associated with better function in multiple sensorineural and cognitive functions in midlife, a time when prevention and intervention methods should be more efficacious. The remaining associations after adjusting for various potential confounders emphasizes its potential for healthy aging interventions. However, future studies will be needed to determine the temporality of effects and the efficacy of midlife PWB interventions for healthy sensory and cognitive aging and neurodegeneration.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement

The datasets for this manuscript are not publicly available because of data protection regulations. Requests to access the datasets though data sharing agreements should be directed to Dr. Karen J. Cruickshanks.

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Table 1.

Characteristics of the Analytic Sample of the Beaver Dam Offspring Study (N=2039)

	n(%)			
Sex				
Women	1118(54.8)			
Men	921(45.2)			
Education				
0-12 years	552(27.1)			
13-15 years	707(34.7)			
16 years and more	780(38.3)			
Smoking				
Never	1172(57.9)			
Former	637(31.4)			
Current	217(10.7)			
History of heavy alcohol	374(19.0)			
Cardiovascular Disease	232(11.5)			
Diabetes	252(12.4)			
Long-term elevated inflammation	765(46.8)			
Exercise at least once a week	1369(67.7)			
Visual Acuity, letters correct, better eye	59.2(5.8)			
Hearing impairment	533(27.4)			
Contrast Sensitivity impairment	137(7.0)			
Olfactory impairment	110(5.7)			
Cognitive impairment	83(4.1)			
	M(SD)	**Range**	**Skewness**	**Kurtosis**
Age, yrs	57.9(9.6)	27–89	0.13	−0.17
Waist circumference, cm	103.2(16.5)	64–179.5	0.46	0.40
Hearing sensitivity, PTA worse ear, dB HL	21.0(15.0)	−3.8–125	2.08	7.56
DDT score, % correct	78.8(11.4)	35.3–100	−0.31	−0.27
WRCM score, % correct	54.5(17.2)	0–92	−0.88	0.66
Cognitive function	0(1)	−6.4–3.5	−1.24	4.45
Brain aging	0(1)	−6.2–3.2	−1.29	4.19
mGCIPL, worse eye, µm	77.1(9.0)	23–98	−1.57	5.58
Psychological well-being	81.1(12.5)	24–98	−0.94	0.54

Note. Sample sizes differ slightly due to missing data; If not stated otherwise measure was collected at the 10-year follow-up; Long-term elevated inflammation was based on measures from stored blood samples from the baseline and 5-year follow-up, where we measured high-sensitivity c-reactive protein, interleukin-6, vascular cell adhesion protein 1 and intercellular adhesion molecule 1. Long-term elevated inflammation was defined as being repeatedly in the highest group for at least one inflammation marker at baseline and 5-year follow-up. For high-sensitivity c-reactive protein, participants were divided into three risk groups (<1, 1–3, and >3mg/L) according to established cut-points and we compared the highest risk group to the rest. For the other three markers, we compared the highest tertile against the rest.

DDT, dichotic digits test; M, mean; mGCIPL, macular ganglion cell-inner plexiform layer; *SD*, standard deviation; PTA, pure-tone average 0.5-4 kHz; WRCM, word recognition in competing message test.

Table 2.

Associations Between Psychological Well-Being (per 1SD Increase) and Hearing, Vision and Olfaction

	Model 1 [a]	Model 2 [b]
	B (95% CI)	**B (95% CI)**
Hearing sensitivity score, in dB HL [c]	−1.00 (−1.61,−0.40) **	−0.91 (−1.64,−0.18) *
Dichotic digits test score, in % [d]	1.02 (0.52,1.53) ***	0.91 (0.35,1.48) **
Word recognition score, in % [d]	0.48 (−0.22,1.18)	0.56 (−0.26,1.37)
Visual acuity score, in letters correct [c]	0.31 (0.02,0.60) *	0.20 (−0.14,0.54)
	OR (95% CI)	**OR (95% CI)**
Hearing sensitivity impairment [c]	0.88 (0.79,0.98) *	0.88 (0.77,0.99) *
Contrast sensitivity impairment [c]	0.87 (0.77,0.97) *	0.92 (0.81,1.05)
Olfactory impairment [e]	0.82 (0.68,1.00) †	0.88 (0.69,1.11)

† $p < .10$;

* $p < .05$;

** $p < .01$;

*** $p < .001$.

Note: CI, confidence interval; dB HL, decibel hearing level; OR, odds ratio.

[a] Model adjusted for age, sex and education

[b] Model adjusted for age, sex, education, chronic health conditions and health behaviors (smoking, history of heavy alcohol consumption, diabetes, cardiovascular disease, long-term elevated inflammation, exercise and waist circumference)

[c] Generalized estimating equation model

[d] Multivariable linear regression model

[e] Multivariable logistic regression model

Table 3.

Associations Between Psychological Well-Being (per 1SD Increase) and Cognition, MGCIPL and Brain Aging

	Model 1 [a]	Model 2 [b]
	OR (95% CI)	**OR (95% CI)**
Cognitive impairment [c]	0.56 (0.46, 0.69) ***	0.60 (0.47, 0.76) ***
	B (95% CI)	**B (95% CI)**
Cognitive score, in SD [d]	0.09 (0.06,0.13) ***	0.07 (0.03, 0.11) ***
MGCIPL thickness, in μm [e]	0.36 (0.03,0.70) *	0.33 (−0.05,0.71) †
Brain aging score, in SD [d]	0.11 (0.07,0.14) ***	0.08 (0.04,0.12) ***

† $p < .10$;

* $p < .05$;

** $p < .01$;

*** $p < .001$.

Note: SD, standard deviation; OR, odds ratio; mGCIPL, macular ganglion cell-inner plexiform layer

[a] Model adjusted for age, sex and education

[b] Model adjusted for age, sex, education, chronic health conditions and health behaviors (smoking, history of heavy alcohol consumption, diabetes, cardiovascular disease, long-term elevated inflammation, exercise and waist circumference)

[c] Multivariable logistic regression model

[d] Multivariable linear regression model

[e] Generalized estimating equation model