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Common causes in visual and cognitive decline in healthy aging: Silversight Cohort Study

MPH-2 Final Thesis

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ABSTRACT:

Background: Sensory perception and cognitive function are mutually linked, but it is not clear whether this link is due to age-related common causes for sensory and cognitive variables, or cognitive losses can result from progressive deterioration of sensory input in aging. Previous studies addressing this question rarely included auditory sense and used only standard acuity tests to assess vision. Here we used an extended battery of sensory tests, including auditory, visual and cognitive assessment, in order to study the presence of common causes of age-related decline in sensory perception and cognitive function in a population of healthy adult participants.

Methods: This study was performed in 186 subjects (51.07% females, 48.92% males) participating in the Silversight cohort study. In all participants (youngest: 22 years old, oldest: 86 years old) multiple measurements of visual sense, audiogram testing and cognitive abilities were performed. Univariate analyses of hearing and vision were performed to compare our data with previous studies. The associations between aging, sensory perception and cognitive function were assessed by multivariate analysis, including factor analysis and mediation analysis.

Results: 4.44% prevalence of visual impairment was found, 39.4% hearing impairment and 1.75% dual-sensory impairment in age group of greater than 51 years of age confirming the pattern of sensory processing impairment in older age groups. No presence of common cause due to age was detected in sensory processing. However, sensory processing was found to significantly mediate the effect of age on cognitive function in the population of older participants.

Conclusion:

The finding that sensory variables mediate age effect on cognitive function only in the old population, these results provide support for information degradation/sensory deprivation hypothesis, stating that progressive deterioration of sensory input is associated with lower cognitive processing scores. A more detailed characterisation of this phenomenon can be obtained by applying structural equation modelling methods to analyse these data.

Common causes in perceptual and cognitive decline in healthy aging: Silversight Cohort Study

1. Introduction (Background and Context)

1.1. Aging, Perception and Cognition

There is an increase in the population of people of age over 60-64 taking place all over the world (Owsley, 2011). Demographic studies from world population aging in the United Nations have mentioned that population of age 64 years have crossed the population of age 5-15 years in 2018 (United Nations., 2019). Therefore, geriatric population is comprising the larger section of the society, which consequently increases the incidence and prevalence of age-related eye diseases, visual impairments with underlying mechanisms and the way these factors affect cognitive functions, everyday activities and quality of life (Owsley, 2011).

In the early 1963, Robert Weale first summarized scientific information on how the process of aging affects the visual perception in his book *The Aging Eye* (Weale, 1963). This account has been extensively elaborated by research of the past 20 years, stating that vision declines with age through changes in peripheral and central processing due to pathological factors such as formation of cataract, glaucoma and age-related macular degeneration (Roberts & Allen, 2016b), but also in healthy population as a consequence of hardening and yellowing of the lens in presbyopia, changes in color perception, temporal resolution, visual acuity and a loss of fine detail pattern vision (Culham & Kline, 2002; Elliott & Lachman, 1988; Hutchinson et al., 2012; Kim & Mayer, 1994; Page & Crognale, 2005; Pardhan, 2004; Snowden et al., 2006; Spear, 1993; Wright et al., 1985).

In parallel to sensory changes, the process of aging brings about decline in cognitive abilities such as memory, attention and executive control (Hedden & Gabrieli, 2004; Hertzog & Schaie, 1988) resulting in slower processing speeds and in poor performance in tasks involving cognitive flexibility, manipulation of information and visuospatial processing (M. Hofer et al., 2012). Although the concept of cognitive aging has been only recently proposed (T. Salthouse, 2000), already in 1933 Miles discovered that there is a decline in perceptual, motor and cognitive abilities including learning abilities among people above the age of 30 years after evaluating 1600 people of age range 6 to 95 years (Andersen, 2012).

Epidemiological research has revealed that visual impairments are correlated with a decline in cognitive abilities (Ong et al., 2012) and described how sensory impairments may be linked with cognitive functions. Lindenberger & Baltes, 1994, explored the role and relationship of visual functioning in cognitive aging within the age range 70-100 years using data from the Berlin Aging Study (BASE) and proposed that age-related cognitive and perceptual changes may share a common underlying factor (Lindenberger & Baltes, 1994). Although visual impairment has repeatedly been associated with cognitive decline in geriatric population, it was difficult to characterize a causal link or an underlying common factor in the elderly with healthy vision (Spierer et al., 2016).

Visual, auditory and olfactory sense of perception have been explored in healthy aged population through various research studies to find their link to decline in cognitive function and corresponding hindrance to performance in daily living skills (Monge & Madden, 2016; Uhlmann et al., 1986; Valentijn et al., 2005). As a result, four main hypotheses have been formulated to describe this link and characterize the process of decline in visual perception and cognitive function throughout aging: sensory deficit hypothesis, the theory of cognitive load on perception, information degradation hypothesis and common-cause hypothesis (Monge & Madden, 2016; Roberts & Allen, 2016a).

The sensory deficit hypothesis states that deficits in sensory acuity (e.g. visual, auditory) leads to the decline in cognitive functioning and it was first proposed in studies by Lin et al. in 2004 (Lin et al., 2004),(Lindenberger & Ghisletta, 2009) and later supported in a study by (Gilmore et al., 2006). In this study subjects performed worse due to degraded sensory acuity directly affecting the performance on the tasks which examine cognitive facility (Wahl et al., 2013). The theory of cognitive load on perception was first proposed by Zwislocki et al. 1958 (Roberts & Allen, 2016b) when they observed that cognitive deficits affect audiogram measures and proposed that cognitive decline contributes to age-associated perception degradation. This theory was further tested by Schneider and Pichora-Fuller in 2000 (Schneider & Fuller, 2010) who established that age related impairment for some perceptual tasks, but not others, is due to poor cognition causing decline in perceptual measures. The information degradation hypothesis states that degraded perceptual signal, which may result from age-related degeneration or induced experimental manipulations, causes errors in processing of the perceptual information and this is turn leads to decline in the cognitive function. This theory was confirmed first by Schneider and Pichora-Fuller in 2000 and recently verified by Toner et al. in (2012) where the older and younger adults had better performance at their task in the higher contrast than the lower contrast conditions (Ebaid & Crewther, 2019).

1.2. Common-Cause Hypothesis

The common-cause hypothesis states that a common factor underlies the perceptual and cognitive decline throughout the lifelong aging process. The source of this cause is distinct from visual perception or other purely perceptual changes (Monge & Madden, 2016). Formulation of the common cause hypothesis dates back to 1973 when Lindenberger and Baltes discussed the question associated with the issue of the concept of "exploratory continuity against discontinuity" in cognitive aging at a press conference. Initially, age-related differences in the cognitive facility were summarized as cumulative outcome of socioeconomic, cultural, and environmental factors interacting with genetic factors which constitutes the 'exploratory life-span developmental continuity' perspective, whereas Baltes posed 'life-span developmental models of aging' in 1987. These models state that the process of aging is regulated by factors that emerge in the later stages of life explaining the concept of 'discontinuity' (Lindenberger & Baltes, 1994).

Developing this concept, Baltes in 1987 came up with the common cause hypothesis, which was born based on the idea that there is an increased correlation between the measures of sensory function and cognitive function in the older stage of life due to expression of physiological structure or dynamics of the aging brain and its integrity. With further transformation of this concept, as a result of cognitive aging and vision research involving the common cause hypothesis, a more modern formulation of this hypothesis states that the age associated impairments in the cognitive facility and sensory function have a common set of age-related alteration in the neuroanatomy and neurochemistry of the aging brain. The study of older adults of age 70-100 years with measures of visual acuity, auditory acuity and cognitive function tests (Lindenberger & Baltes, 1994) as well as Anstey et al in 1999 found that a latent variable of indicators of biological age like vision and hearing mediated the relationship between age and cognitive function (Anstey & Smith, 1999).

The theory of common cause was further supported in studies by Christensen et al., (2001), and Lindenberger & Ghisletta, (2009). They suggested that common cause could be physiological mechanism like reduced blood flow or 'sensory starvation' mechanism where cognition suffers from poor sensory quality but mentioned that nature of testing and conducted studies have an effect on the possible cause between sensory and cognitive facility. The research by Busey and Humes in 2010 (Humes et al., 2013) included a different theme as temporal order judgement variables were used for the study and degree of variability across various temporal order judgment tasks could be explained by two underlying latent factors which show performance on same and different locations. This variability could be predicted from other sensory and perceptual tasks. Humes et al (2013) has agreed with Salthouse (T. A. Salthouse, 2010) that long-standing observation of age-related changes in cognitive function is mediated by age-related changes in global sensory processing.

The concept of common cause has also met certain criticism. For example, the investigation of the presence of common cause was investigated in studies by Salthouse in 1993, 1994, 1997 and is summarized in the study published in 1998, which suggested that age-related variance across cognitive variables is shared similarly to variance across non-cognitive variables. This was consistent with findings of Lindenberger & Baltes in 1994. However, an analysis of the primary dataset from the study in 1998 suggested there is no independent age-related influence on the sensory and cognitive variables after investigating sample size of 380 adults of age 18 to 87 years (Fristoe et al., 1997; Hambrick, 1998; T. A. Salthouse, 1993, 1994). After accounting for the age-associated influence of what variables have in common, there was no evidence of age-associated effect on cognitive variables individually. Salthouse speculated that age difference can be a function of performance in cognitive tasks and explain the difference in cognitive facility but there are many factors that mediate the evident association between increase in age and lower scores on measures of working memory functioning by factors as slow speed of processing information (T. A. Salthouse, 1994). The factors were further explained as characteristics of the sample, variation across dataset with respect to specific variables (Hambrick, 1998).

A recent study carried out by Shaqiri et al in (2019) revealed weak correlations between visual tests in younger and older adults with absence of a common factor from the study sample of 92 older participants and 104 younger participants using a larger set of perceptual tests than the previous studies. There could be a possible overlap in the studies of common cause hypothesis with the investigation by Wahl & Heyl et al in (2013) revealing that sensory deficit of visual perception is associated to loss of “everyday functioning” to a greater degree than that of auditory perception. Their multidimensional analyses reveal a complex perspective of loss and maintenance to understand sensory impairment and psychosocial adaptation in old age and a paradox with common cause hypothesis.

Finally, while cross-sectional studies have indicated the link between sensory acuity and cognitive function, longitudinal studies found that although visual acuity decline was related to the cognitive one, the statistical association between sensory and cognitive aging is weaker (Lindenberger & Ghisletta, 2009). Researchers such as (Anstey et al., 2003) have suggested that statistical modelling techniques used in cross-sectional studies maybe partly responsible for developing the common cause theory in the first place. This trend in the literature indicates a requirement for more research to establish the presence of the link and its characteristics.

Thus, scientific literature to date is not consistent on the issue of the common cause hypothesis in cognitive aging and vision. Research studies have found evidence that cognitive decline is associated with healthy aging, but whether the same is equally true for decline in visual abilities of the healthy aging population is still unknown (Varin et al., 2019). Moreover, different dataset used and how were they tested for the purpose of the research in previous studies poses a question on the possible interpretations of the common cause hypothesis. Past studies have included a relatively small number of sensory and cognitive measures to reliably assess the presence of a common cause. More test measures for characterizing perceptual and cognitive ability with a required sample size can add more power to the study and its statistical analyses to better formulate the presence or absence of the underlying common causes. While recent study by Shaqiri et al in (2019) have used a larger set of perceptual tasks, a multivariate dataset including a range of visual perception tests and neuropsychological tests for cognitive variables shall be helpful to establish presence or absence of common causes through the motive of our project and additional findings can be expected to better characterize the relationship between the effect of aging on visual decline and cognitive decline in healthy adults.

Our study focuses on the investigation of presence of a common cause or a set of common causes in visual and cognitive decline by using a unique dataset from measures of variety of visual perception tests and neuropsychological tests which assess functional vision assessment and cognitive facility. While testing the common cause hypothesis is the primary objective of the project, since this hypothesis provides a direct conceptual link between neuroanatomical and functional correlates of brain aging, perception, and cognition, verifying other hypotheses can also be of interest. Due to the complexity of the multivariate dataset which will be used in the study, exploring a spectrum of suitable statistical analysis methods constitutes an important aspect of the project.

Existing methodology in the majority of past studies have used correlational analyses to explore the reason for cognitive and perceptual decline in aging, but the analyses were insufficient to test the hypotheses in this domain (Monge & Madden, 2016). Nevertheless, these correlational analyses were able to predict sizeable correlations of between-person differences in the rates of decline, both within and across cognitive facility and sensory function. Lindenberger and Baltes (1994) have used structural equation modelling (SEM) for testing their model to examine the relationship between sensory ability like visual and auditory acuity and the cognitive ability or intellectual functioning in the very old population, which led them to establish that sensory abilities are a strong predictor for individual differences in the cognitive ability for old and very old people in their study population. Study by Christensen et al. in (2001) have come up with an alternate model called the common cause factor (CCF) with the primary finding that aging is not only related to the common cause which is responsible for the decline in variables for perception and cognition with age but also responsible for affecting the individual variables.

Lindenberger and Ghisletta in their longitudinal study in (2009) have used random and fixed effects coefficient modelling (also termed “latent growth curve” or “underlying latent cause” modelling) while Humes et al. in (2013) have used principal component analysis (PCA). They obtained a single global sensory processing factor and a single global cognitive function factor, and performed correlation analysis to find that age, global cognitive function, and global sensory processing were significantly correlated. Results from SEM analysis were in accord with the correlation results, leading to conclusion that age-related changes in cognitive function might be mediated by age-related changes in global sensory processing. The most recent study (Shaqiri et al., 2019) used a larger dataset with variety of perceptual tests unlike the previous studies and performed correlational analyses and factor analysis to study differences between the younger and older populations, but found weak correlation between test measures in younger group as well as the older group.

One of the drawbacks of most of these studies involving evidence for detecting the common cause of visual perception and cognition is that they do not involve hearing or other sensory factors. In the study by Lindenberger and Ghisletta (2009) auditory acuity was investigated, but interindividual differences were not statistically reliable. However, the claim of having the presence of a common cause or not is required to be confirmed with different visual perceptual tests which represent comprehensive visual abilities and the methodology for our study is planned based on that. In our study, we have a unique dataset with data on various visual perception tests to test if the common cause is present or not among the older population. Furthermore, we have included auditory perception data into the dataset. From the data of our cohort, we have age range from younger to older adults who have been measured on various visual perception parameters signifying the functional vision in terms of visual acuity, colour vision, contrast sensitivity function, audiogram measures etc. and measurement on various parameters of neuropsychological tasks signifying the cognitive facility like mental state, attention, information processing facility etc. and self-assessment questionnaires.

SEM is a modelling framework that integrates a number of different multivariate techniques into a single framework and suitable for modelling a causal system. SEM includes exploratory factor analysis (EFA). It is favorable to answer our research question because we are looking at the psychological concept by factor analysis, which is the chosen technique for conducting the analysis from literature. Mediation analysis is suitable technique for biological and epidemiological aspect such as measures for sensory perception, cognitive function in our study. All the analyses shall be performed on R software and MATLAB. Data formatting, data cleaning, further requirement for data transformation and approaching the missing data was done prior data analysis.

In the context of this research, we aim to study the hypothesis that one or several common factors underlie decline in sensory perception or cognitive decline or both using our dataset to explain the possible relationship between aging, sensory perception, and cognition in healthy aging adults. The long-term research goal of this line of research is to associate physiological brain changes with potential common causes of age-associated impairment of the cognitive facility and sensory function. Although the link between perception and cognition has been indicated in multiple studies proposing four different hypotheses about age impact on task performance in aged individuals, a clear concept and methodology for identification of the underlying mechanisms is still debatable and not confirmed. This study will thus contribute to the current state-of-the-art in linking perceptual and cognitive changes both methodologically and by the analysis an extensive set of sensory and cognitive variables. Cohort studies such as the one addressed in this project are an important research tool to characterize age impact on society and to help the development of new approaches to provide better quality of life for the aging population.

2. Silversight Cohort Study: Methods and data description

2.1) Silversight Cohort Study

French cohort study Silversight evaluates anatomic and functional changes induced by healthy and pathological visual aging through cross-sectional and longitudinal studies. The aim of this research is to understand the relationship between aging and visual symptoms to identify functional biomarkers for normal and pathological aging (Lagrené et al., 2019).

2.2) Methods

All clinical and functional measures were conducted at the national eye hospital CHNO des Quinze-Vingt, Paris. The data from measurements of visual, auditory and cognitive parameters has been progressively collected over the last 5 years (Bécu et al., 2020). The following section describes quantitative variables extracted from these measurements for statistical analysis.

2.3) Data Description

Participants

One hundred eighty six subjects (95 female and 91 male) were included in this study: 92 young adults (range: 26-51 yrs.) and 94 older adults (range: 51-86 yrs.). The participants were part of the Silversight cohort population (~350 enrolled subjects) at the Vision Institute - Quinze-Vingt National Ophthalmology Centre, in Paris (Bécu et al., 2020). All participants were voluntary and gave informed consent (parents gave informed consent for their child). The procedures were performed in accordance with the tenets of the Declaration of Helsinki, and they were approved by the Ethical Committee CPP Ile de France V (ID_RCB 2015-A01094-45, No. CPP: 16122 MSB). Participants habitually wearing far-vision lenses kept their glasses on during visual acuity test. The dataset consists of **59** measurements which can be classified into three main categories: functional visual assessment, functional auditory assessment and neuropsychological examination.

2.3.1) Measures for sensory assessment:

i) Functional visual assessment

A. National Eye Institute – Visual Function Questionnaire (NEI-VFQ). General questionnaire designed by the National Eye Institute about the health and vision. Questions on difficulty with activities like reading newspaper or using cell phones, pursuing cooking, sewing, repairing using hand tools around house which are a part of activities of daily living skills. It is a measure of vision-targeted health status.

B. Pelli-Robson contrast sensitivity test (PR). Pelli-Robson chart consists of several horizontal lines of capital letters and the contrast of the letters decreases with each line. It is widely used to test contrast sensitivity.

C. Lanthony 15-hue desaturated test (HUE15) In this test, there are 15 disks which are desaturated, and the subject is asked to arrange the disks in the correct colour order. It enables us to see if the subject is capable of distinguishing subtle colour variations. The results are evaluated according to Moment of Inertia Method proposed by Vingrys and King-Smith (1988) and the confusion index is used.

D. Binocular visual field (BINO) It is assessed by means of Goldmann perimetry test with Octopus 900 machine. This device will measure the right and left monocular visual fields and provide us the intersection of the area of two isopters. In addition, the reaction time is considered and the result is corrected accordingly.

E. Contrast sensitivity function (CSF) Contrast sensitivity varies along with the spatial frequency (cycle per degree ~ cpd) and is measured by using a free computer program, Freiburg Vision Test (FrACT) developed by Michael Bach. The measure is a fundamental aspect of vision providing useful information in relation to subject's visual function which may not be revealed by visual acuity measure. It is measured at 6 spatial frequencies (0.5, 1, 2, 4, 8, 16 cpd).

F. Brightness acuity test (BAT) The device simulates three light conditions:
    1) direct overhead sunlight (high)
    2) partly cloudy day (medium)
    3) bright overhead commercial lighting (low).

   It is used to assess glare sensitivity and the subject is asked to use the dominant eye and look at the ETDRS chart through the BAT instrument under high light setting. It helps in assessing functional outdoor visual acuity by simulating the outdoor lighting conditions. The experiments consist of six testing conditions:
    1) 100% contrast ETDRS chart with light on
    2) 100% contrast ETDRS chart with light off
    3) 10% contrast ETDRS chart with light on
    4) 10% contrast ETDRS chart with light off
    5) 5% contrast ETDRS chart with light on
    6) 5% contrast ETDRS chart with light off.

G. Useful field of view (UFOV). It evaluates three aspects of functional vision and visual attention:
   1) processing speed
   2) divided attention
   3) selective attention

In the first subtest (processing speed), the subject needs to identify the target presented inside the central box. In the divided attention test, the subject not only identify the presented target but also localize where it is displayed. In the third subtest, it is similar to the second test but with several triangles surrounded as distractors. The results are recorded in seconds.

H. C-Quant (CQUANT) The OCULUS C-Quant is used to measure the amount of straylight at the retina. The test is conducted monocularly and the results are presented in absolute straylight value as a log(s). The measured variables are CQUANT_OD_log (for the right eye) and CQUANT_OG_log (for the left eye).

I. ETDRS (VA_OD, VA_OG, VA_BINO). Visual acuity measured by ETDRS chart. The score corresponds to the last line of letters that the subject can read. Visual acuity is measured in log MAR.

ii) Functional hearing assessment

Audiometry was performed and audiogram was obtained of the participants. Audiogram is a graph that display audible thresholds for standardised frequencies. Audiogram provides measurement of air conduction and bone conduction. All subjects pass an audiometric test, in which a subject listen with either his left or right ear to various sounds or words at different frequencies (in Hz: 125, 250, 500, 1000, 2000, 3000, 4000, 6000, 8000). For each ear and each frequency, the medical doctor notes the hearing threshold in dB. For purpose of our research, we have only included the data from air conduction audiogram as it is used in previous literature on studies of ageing and hearing impairment.

2.3.2) Neuropsychological examination for cognitive assessment

The objective for the neuropsychological assessment is to determine the presence or absence of a general neuropsychological disorder which may have repercussion on the visual cognitive functions.

A. Vienna test system (VTS). This battery of tests includes several computerized psychological assessments of which only five cognitive and neuropsychological assessments are chosen for the study: 3D mental rotation test (D3), trail making test (TMT), figural memory test (FGT), Corsi block-tapping test (CORSI), go/no go test (INHIB).

    i. 3D mental rotation test (D3): The subject is asked to imagine how the brick should look like from the perspective indicated. The number of correct answers in 3 minutes is recorded and analysed

    ii. Trail making test (TMT): It consists of two parts and assesses psychomotor rapidity (part A) and mental flexibility (part B). In part A, numbers 1 to 25 are displayed on the screen and the subject have to click on them in ascending order. In part B, there are numbers 1 to 13 and letters A to L and they should be arranged in ascending order, i.e., 1, A, 2, B, etc. The working time in part A and B are recorded, and difference B-A (DSCORE) and quotient B/A (QSCORE) are analysed. The measured variables are TMTS2DSCOREDif (for DSCORE) and TMTS2QSCOREQuo (for QSCORE).

    iii. Figural memory test (FGT) consists of three phases and allows us to evaluate long-term figural episodic memory. There are several figures displayed one by one and the subject is required to reproduce the figure after it is presented either immediately (phase 1), after a short break (phase 2), or after a 30-minute break (phase 3). Thus, three variables are scored: the numbers of figures reproduced correctly in phase 1 (FGTS11LSsommed; sum of learning), 2 (FGTS11RKVArest; short term retention), and 3 (FGTS11RLVArest; long term retention).

    iv. Corsi block-tapping test (CORSI): It measures the spatial memory span by showing the subject a sequence of cubes which needs to be repeated either forwards or backwards. The task becomes more difficult as the number of displayed cubes increases. The immediate block span forwards (CORSIS1UBSEmpa; short term span) and the immediate block span backwards (CORSIS5UBSEmpa; working memory span) is scored.

v. Go/no-go test (INHIB) A sequence of triangles and circles is shown on the screen and the subject is asked to react only to triangles by pressing a button. The number of commission errors is recorded, and sensitivity index, i.e., z (hits) – z (false alarm) is computed and analysed. The measured variable is INHIBS3DWIndic.

B. Perspective taking/spatial orientation test (Persp). In this test the subject is presented with a picture including seven objects at various locations on the screen and is asked to indicate the location of the target from a specific perspective. For instance, by imagining standing at the stop sign and facing the house, point out where the traffic light is located. The score is recorded as the absolute directional error in degrees (column Persp.)

2.3.3) Data Pre-Processing

In the multivariate dataset, different combination of variables of sensory and cognitive measurements were used for univariate and multivariate analyses. In case of multivariate analyses, recoding of the variables was done after plotting correlation matrices to assess the positive correlation with age variable which was important for further statistical analyses. Imputation of missing values in the dataset was done using the 'MICE' package on R as a pre-requisite before performing factory analyses. Averaging of variables were done on MS-Excel to remove noise during the data analysis (Shaqiri et al., 2019).

2.3.4) Statistical Methods:

As an initial step number of subjects as a function of test was plotted to get an overview as descriptive analysis.

i) Univariate Analysis: Univariate analyses were performed on at the initial step to summarize and look for patterns within the dataset for description of the data. The analyses were performed on finding pattern on different combinations like prevalence of auditory impairment across age groups, prevalence visual impairment across age groups, prevalence of dual sensory (audio-visual) impairment across age groups. A comparison was performed with similar analyses conducted in different countries to find similar patterns. Prior to proceeding with multivariate analysis, age distribution was plotted which showed bimodal distribution. Therefore, Age was further divided into young and old categories and multivariate analyses were performed on each group following this to find the relationship between sensory perception and cognitive function by testing common cause hypothesis. A comparison was done to compare the pattern between young and the old population. Correlation matrices were plotted for the sensory and cognitive variables using Corrplot package to check the correlation of each with age. For variables which showed negative correlation which age were recoded and plot to obtain positive correlation with age.

ii) Principal component analysis (PCA): assists in summarizing and visualizing information in our multivariate dataset with individuals/observations in multiple inter-correlated quantitative variables. PCA was performed on the sensory and cognitive variables by Factoextra and Factomine R packages to obtain principal components by reduction from multivariate dataset. Following this, exploratory factor analysis was performed using the Psych package with number of factors obtained from the PCA on sensory and cognitive variables to test common cause hypothesis.

iii) Exploratory Factor Analysis (EFA): is a statistical technique within factor analysis which was used to discover underlying latent variables of our large multivariate dataset and uncover the relationship between measured variables. To determine optimal number of factors for our group of measurement, EFA was run where we extracted F factors with 'varimax' rotation using R function 'Principal' from the 'Psych' package on R. Final step in the analyses was mediation analyses for young and old population which revealed the role of sensory perception as a mediator between the relationship of age and cognitive function with similar Psych package.

iv) Mediation analysis: was run by extracting the values of sensory perception and cognitive function across dimension 1 of the PCA analyses. The statistical analyses were performed using R software Version 1.1.463 – © 2009-2018 RStudio, Inc.

3. Results:

3.1) Descriptive analysis:

The first plot as shown in Figure 1 was plotted on number of subjects as a function of performed tests with the purpose of choosing number of subjects from the sample for further analyses. A threshold of more than equal to 40 tests performed was determined and 107 subjects were chosen from the sample for further analyses.

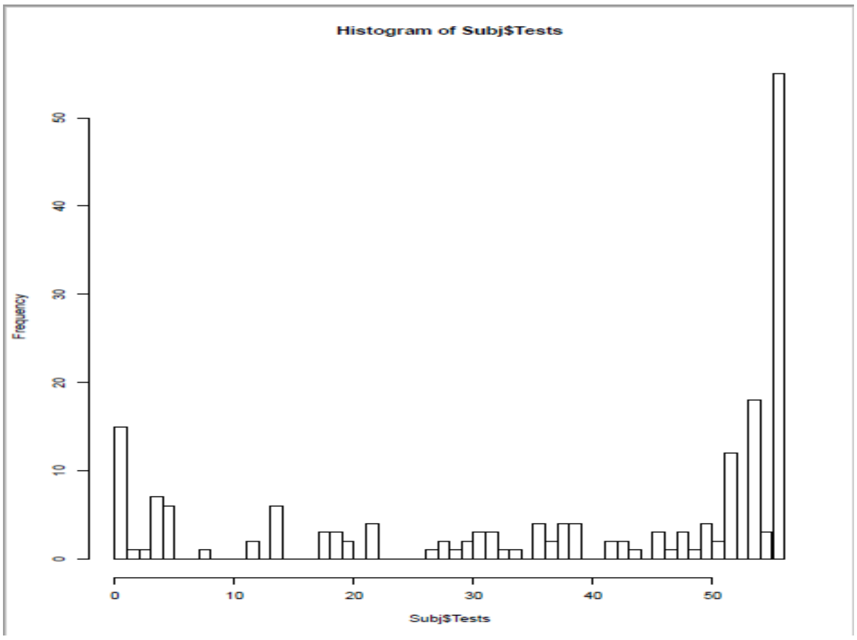

Figure 1: Histogram for number of subjects as a function of tests performed

Variables	Mean	S. D	n
Age	51.63	22.27	186
PR_OD	1.70	0.13	131
PR_OG	1.68	0.16	131
PR_Bino	1.88	0.15	131
HUE15_OD_ConfusionIndex	129	1.40	0.48
HUE15_OG_ConfusionIndex	129	1.38	0.44
BINO_VF_RT	135	16879.72	1540.98
BINO_VF_SSRT	135	16104.81	1598.77
CSF_BINO_16cpd	78	0.11	0.13
CSF_MONO_16cpd	78	0.22	0.34
BAT_WithoutGlare100	109	-0.10	0.12
BAT_WithGlare100	109	-0.03	0.15
BAT_WithoutGlare10	109	0.27	0.14
BAT_WithGlare10	109	20.29	9.54
BAT_WithoutGlare5	109	0.43	0.17
BAT_WithGlare5	108	20.92	10.87
UFOV Processing_Speed	136	0.01	0.00
UFOV Divided_Attention	136	0.04	0.07
UFOV Selective_Attention	136	0.11	0.10
CQUANT OD_Log	99	1.11	0.26

CQUANT OG_Log	99	1.10	0.26
Persp	129	35.19	23.59
D3S1CAReponses	135	14.28	5.29
TMTS2DSCOREDif	124	12.08	10.39
TMTS2QSCOREQuo	124	1.58	0.42
FGTS11LSsommed	124	27.68	10.25
FGTS11RKVArest	124	6.60	2.27
FGTS11RLVArest	123	6.39	2.68
CORSIS1UBSEmpa	135	5.47	1.60
CORSIS5UBSEmpa	135	5.15	1.32
INHIBS3DWIndic	124	3.33	0.73
R125	138	-17.93	5..97
R250	138	-17.54	5.77
R500	138	-18.48	8.58
R1000	138	-13.99	10.69
R2000	138	-18.95	14.77
R3000	138	-20.40	17.22
R4000	138	-24.42	20.37
R6000	138	-27.21	23.42
R8000	138	-32.32	28.38
L125	137	-16.13	7.97
L250	137	-18.91	9.33
L500	137	-17.12	11.45
L1000	137	-13.47	12.32
L2000	137	-17.37	14.79
L3000	137	-19.60	17.81
L4000	137	-21.57	20.25
L6000	137	-31.06	23.73
L8000	137	-31.82	28.19
logmar_od	90	-.0.06	0.12
logmar og	90	-.0.04	0.13
logmar bino	90	-0.11	0.10

Table 1: Descriptive analysis of multivariate dataset denoting mean, standard deviation and number of subjects with data in each variable

3.2) Sensory decline with Age:

i) Hearing decline with Age

Assessment of auditory impairment was conducted within the sample to compare the results with previous literature. The mean hearing threshold was plotted as a function of frequency for all Males and Females from calculation of the mean and standard deviation of each subject.

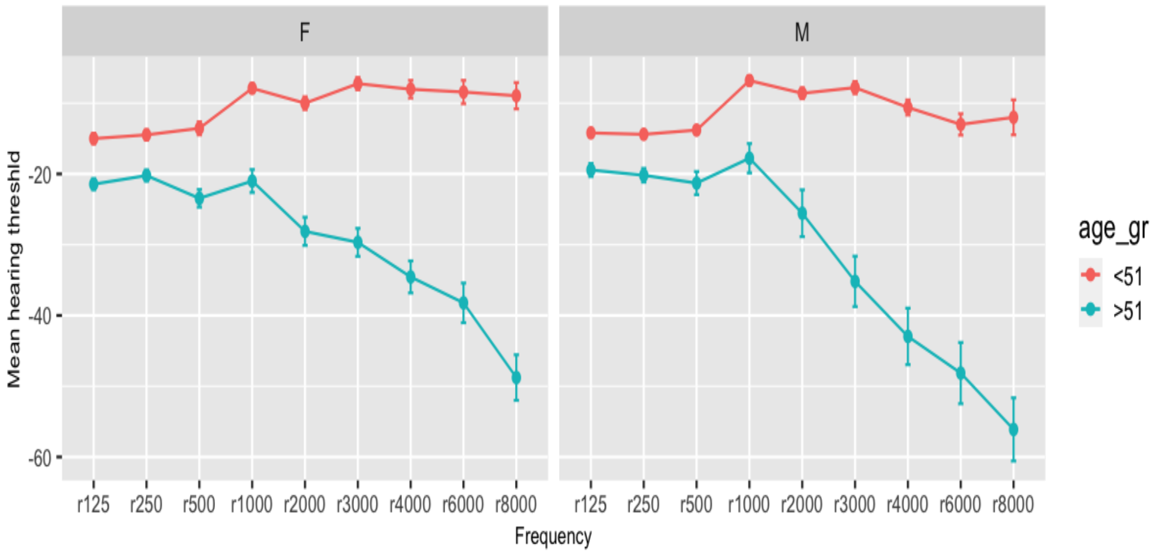

Figure 2: Plot of mean hearing threshold as a function of frequency for females and males

The above graph depicts the mean hearing threshold as function of frequency within males and females. It also depicts the pattern in young (< 51 years) and old (> 51 years), which states that with ageing the hearing threshold decreases across the frequencies. Mean hearing threshold below 25 dB is considered as hearing impairment. In previous literature, similar analyses were done where the subjects with hearing impairment were plotted as a function of age categories: 15-50, 51-60, 61-70 and 71+ years. In an epidemiological study by Wilson et al. ((Wilson et al., 1999) data on similar analysis on population from Australia and United Kingdom was retrieved and compared with our results on population from France. The results were in accordance with the previous literature which confirms that ageing is associated with hearing impairment. Similar analysis on the population of Australia as done in the study by (Wilson et al., 1999) and (Cruickshanks et al., 1998). Number of subjects were classified within mild (25-35 dB), moderate (35-45 dB) and severe (45-65 dB) hearing impairment. Comparison with previous results revealed that mild hearing impairment has the maximum prevalence than moderate and severe within the sample. Prevalence percentage of hearing impairment was higher in older population than younger population.

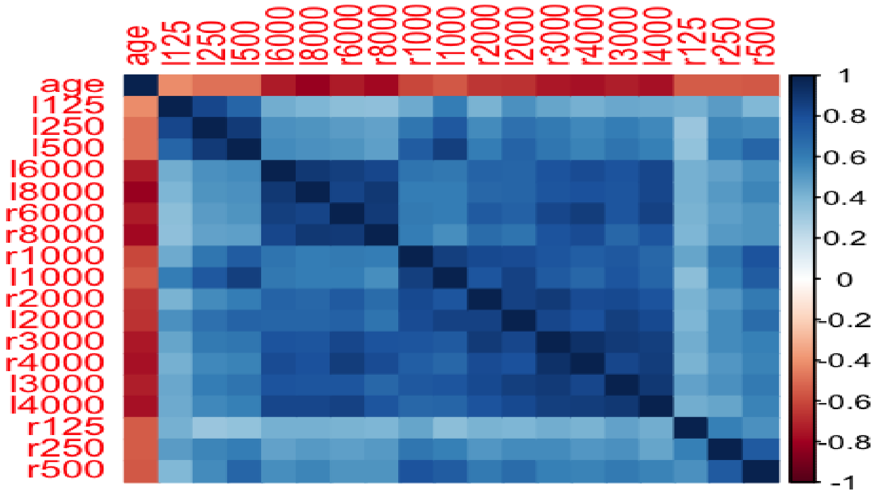

Figure 3: Correlation matrix of age and auditory variables in right and left ear

The above correlation matrix was plotted with the CORRPLOT function on R, has been plotted with age and hearing threshold across frequencies (0.125, 0.25, 0.5, 1, 2, 3, 4, 6 and 8 KHz) for right and left ears. The variables show negative correlation with Age variable with recoding. The variables show positive correlation within themselves.

ii) Visual decline with Age

We conducted analyses to chart out the visual impairment in our sample using the visual acuity (Log MAR) variable, across age groups 20-40, 41-60, 61-80 and 81+ years. We had the data on visual acuity for 90 subjects out of the 186 subjects. The older age group (61-80) revealed highest visually impaired prevalence of 4.44%. The prevalence of impairment within our sample was studied and compared with previous literature. In the study by (Dawes et al., 2014), similar findings were noted with 14% prevalence of visual impairment among a total sample size of 503325 subjects recruited for the study.

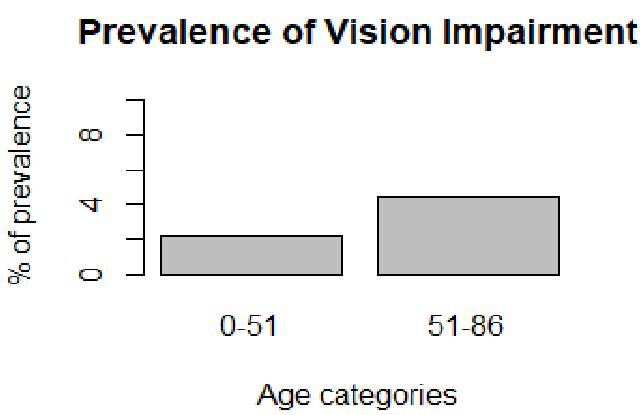

Figure 4: Bar plot showing prevalence of visual impairment in the dataset

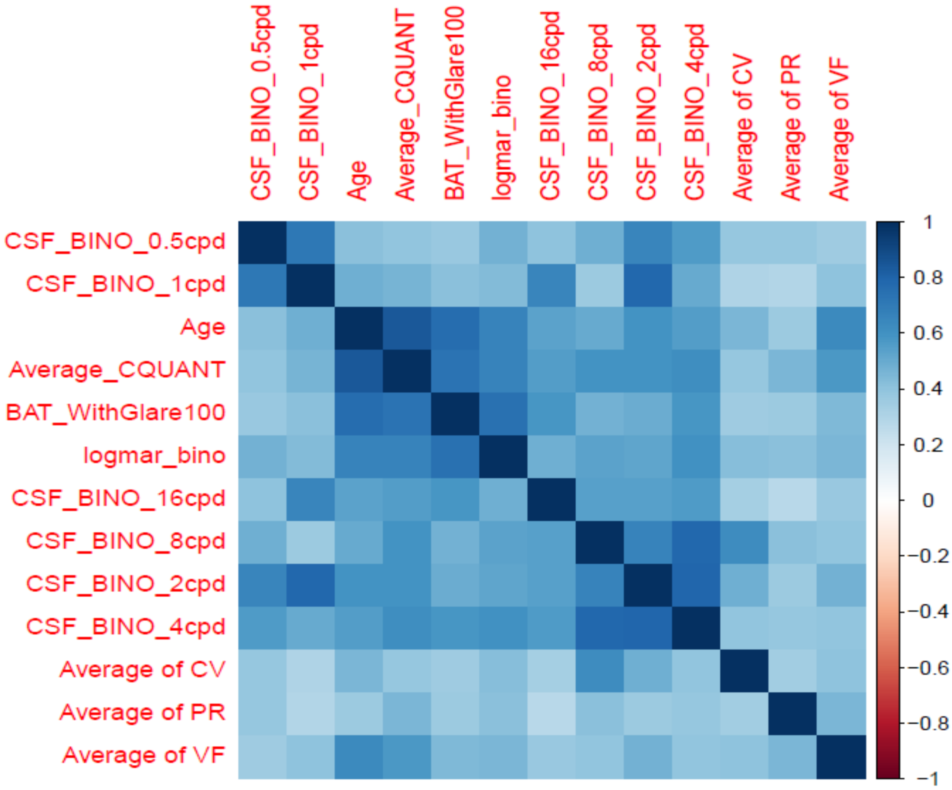

Figure 5: Correlation matrix of age and visual variables

Correlation matrix was plotted for checking correlation for all visual variables with age variable. Averaging of few visual variables was done to remove noise before conducting the analysis. Contrast sensitivity quantified by Pelli-Robson, colour vision quantified by Hue-15 test, visual field quantified by perimetry and straylight measurement on retina quantified by CQUANT test were averaged. Binocular visual acuity, brightness acuity test to measure glare at 100% contrast on ETDRS chart with lights and contrast sensitivity function at 0.5, 1, 2, 4, 8, 16 cycle per degree spatial frequencies were extracted from main dataset and included in the analysis. While, checking the correlation of each variable with age some showed negative correlation and was further recoded to make all variables be positively correlated with age. In the figure above, we can see the Corrplot for all visual variables positively correlated with Age which is pre-requisite for performing multivariate analysis further. We repeated the similar analysis for plotting the correlation for younger and older population within our sample for mediation analysis further, which was done in study conducted by (Shaqiri et al., 2019), have divided their correlation between young and old group with N=196, finding weak correlations between visual tests across the young and old groups.

iii) Dual-Sensory decline with Age

In the study by (Dawes et al.) published in 2014, stated that impairment of vision and hearing (dual-sensory impairment) commenced from the middle age and was prevalent in older population than the younger population. 3.1% prevalence rate for dual-sensory impairment was observed in their large sample size of 503325 subjects. Similar analysis to find prevalence in our dataset was done and 1.75% prevalence % was found in our dataset in 61-80 years age group.

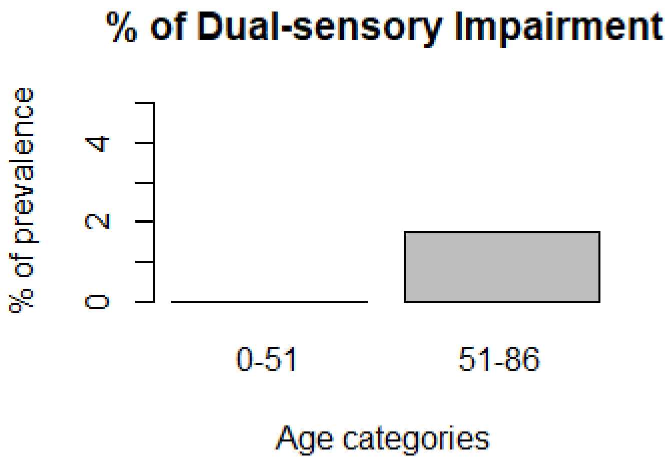

Figure 6: Prevalence of dual-sensory impairment across the dataset

The figure above depicts the presence of dual-sensory impairment in our sample similar to analysis in the study by (Dawes et al., 2014) and confirms the finding that hearing and vision impairment goes hand in hand through the process of ageing.

vi) Factor Analysis:

PCA was done on all visual variables after plotting correlation matrix and recoding for variables which showed negative correlations with age. The PCA revealed the principal components from the multivariate dataset of visual variables which has been shown in the figure below. We derived two principal components here with 43.99% variance across Dimension 1 and 12.62% variance across Dimension 2.

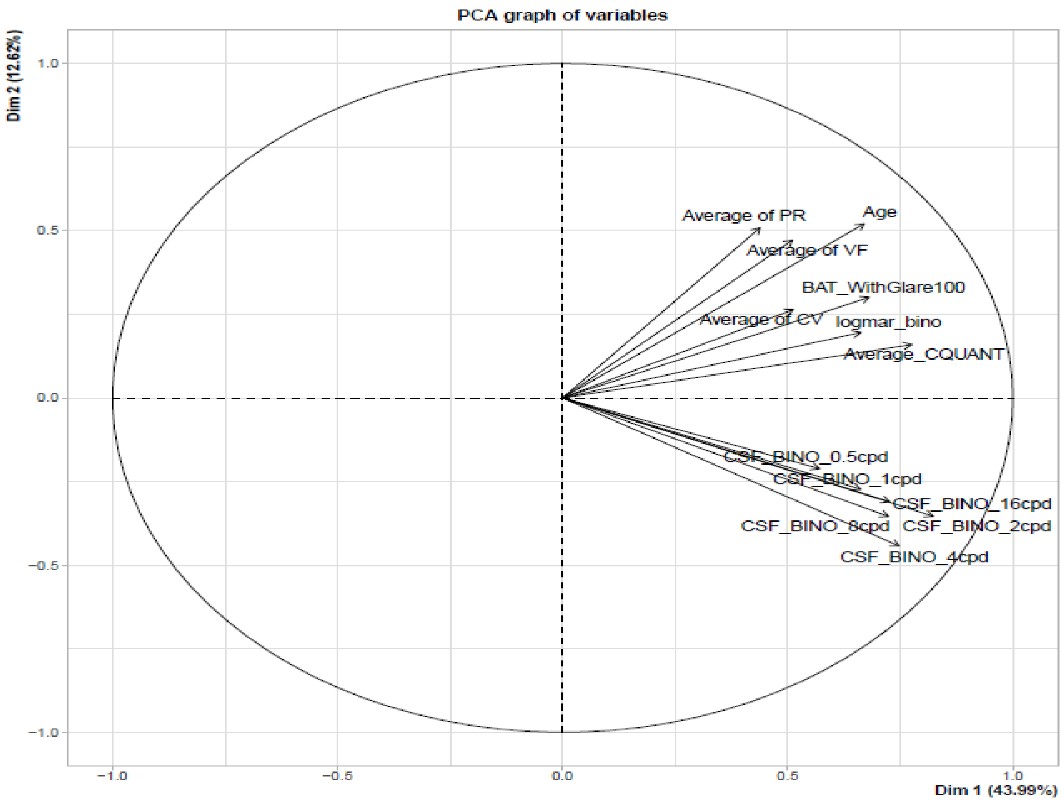

Figure 7: PCA plot of visual variables

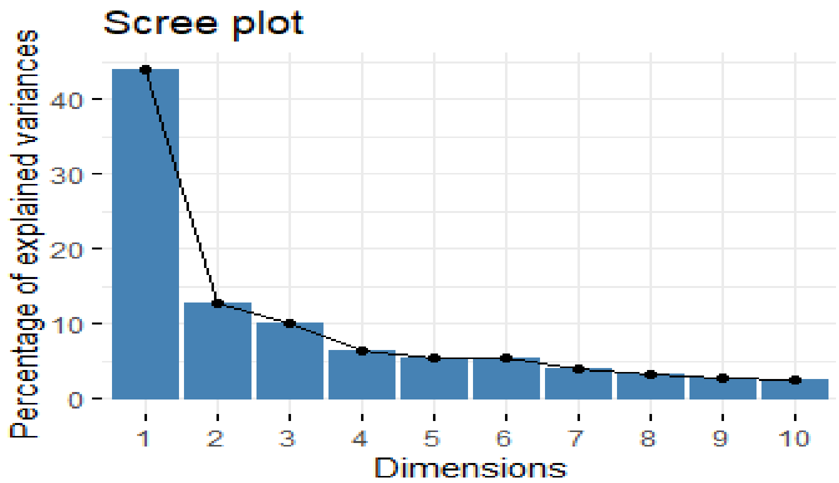

Figure 8: Scree plot showing eigenvalues in principal components for visual variables

The scree plot above from the PCA on visual variables show the eigenvalues across the dimensions. The first two dimension display the highest variance across 1 and 2. This indicated the number of factors for running EFA. The missing values were imputed by MICE package before running EFA using the Psych package. Given to the factor analysis done in previous literature in the study by (Shaqiri et al., 2019), we computed exploratory factor analysis taking number of 2 factors from the PCA and scree plot results, which further reveals the factor structure showing how single factors load on specific visual variables.

Visual Variables	PA1	PA2
Average_PR	0.44	0.07
Average_CV	0.59	0.18
Average_VF	0.61	0.15
BAT_WithGlare100	0.74	0.14
Average_CQUANT	0.83	0.24
logmar_bino	0.72	0.22
CSF_BINO_0.5cpd	0.12	0.45
CSF_BINO_1cpd	0.14	0.63
CSF_BINO_2cpd	0.17	0.95
CSF_BINO_4cpd	0.25	0.62
CSF_BINO_8cpd	0.54	0.37
CSF_BINO_16cpd	0.50	0.35

Table 2: Standardized loadings (pattern matrix) based upon correlation matrix for visual variables

The table 2 above shows the result from conducting EFA on the visual variables. We derived 2 factors from the modelling based on 2 number of factors, 'varimax' rotation and specifying 'pa' principal axis on R function on the 'Psych' package with purpose of simplifying the factor structure done in the similar manner in the study by (Shaqiri et al., 2019). It shows two underlying latent factors which has the loadings from each variable on these factors. We can see that variables Average_CQUANT has highest loading of 0.83 on factor 1 along with BAT_WithGlare100 and logmar_bino. On the other hand, variables like CSF_BINO_2cpd has highest loading of 0.95 on Factor 2 along with CSF_BINO_1cpd and CSF_BINO_4cpd.

3.3) Cognitive decline with Age:

In this section, we discuss the similar analysis conducted on cognitive variables as done for the visual variables in the previous section. We conducted correlations on each cognitive variable with Age to check their relationship. While some variables showed positive correlations, negative correlations with age was noticed for variables like D3S1CAReponses denoting mental rotation, FGTS11LSsomed, FGTS11RKVArest, FGTS11RLVArest which denote figural memory, CORSIS1UBSEmpa, CORSIS5UBSEmpa denote corsi block tapping test for spatial memory span and working memory span, INHIBS3DWIndic denote the saccadic inhibition. They were recoded, after which correlations were done and the figure below was obtained to have all cognitive variables be positively correlated with age for further factor analyses.

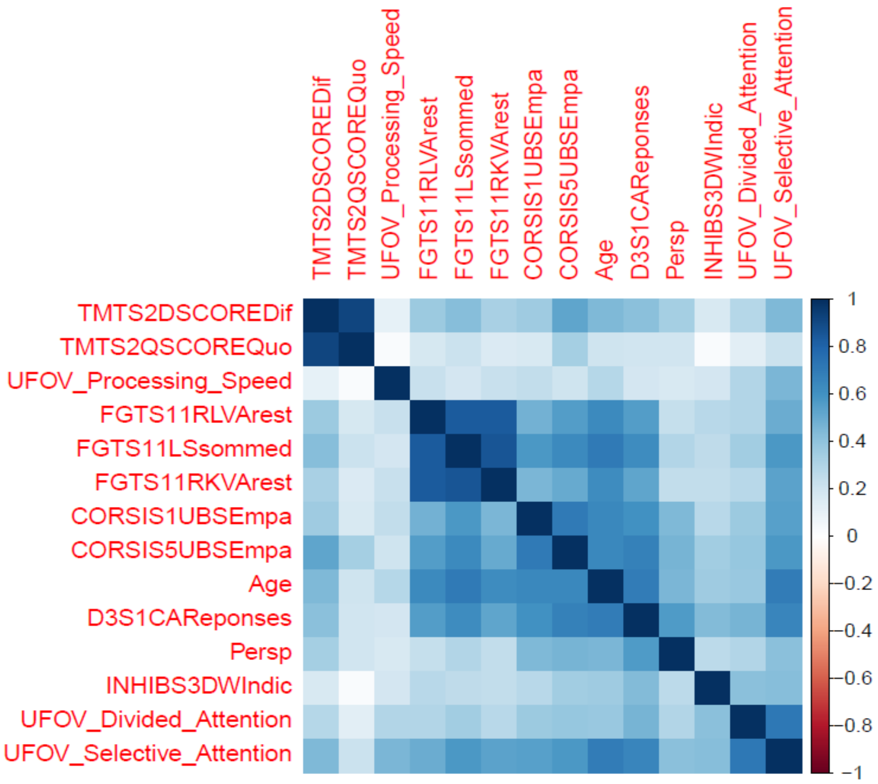

Figure 9: Correlation matrix for Age and cognitive variables

PCA was done after positive correlation noted in the correlation matrix plotted. The PCA resulted in the principal components with 46.84% variance across dimension 1 and 11.93% variance across dimension 2 derived from multivariate dataset of the cognitive variables, shown in the figure below. Furthermore, scree plot shows the eigenvalues on the principal components which help us determine the number of factors to be used for EFA.

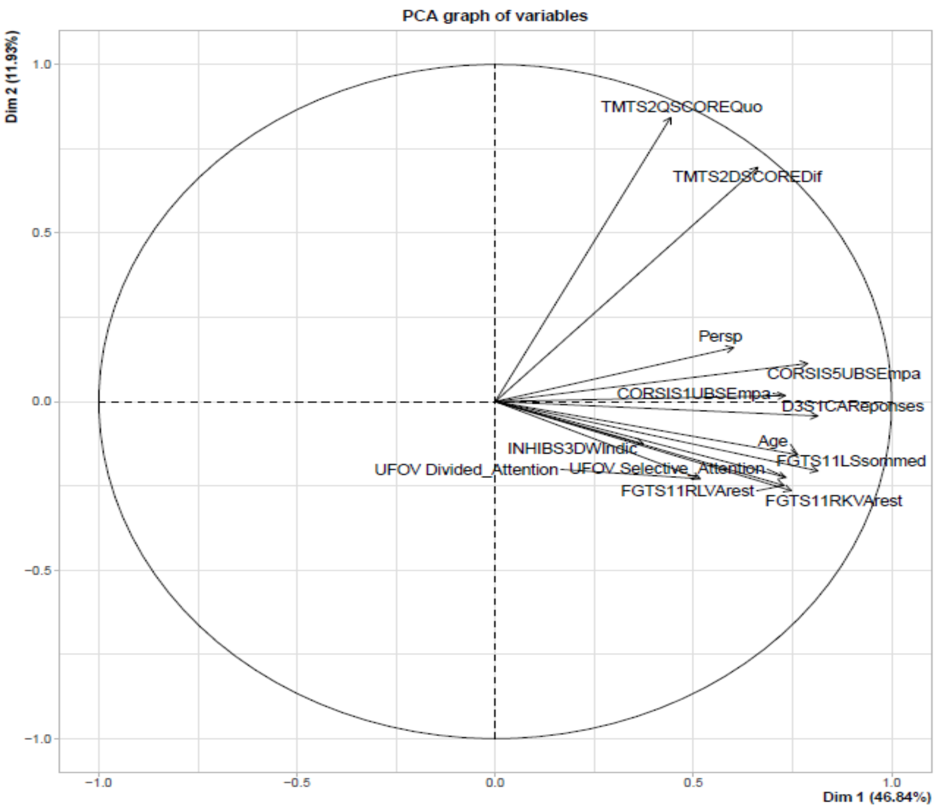

Figure 10: PCA plot of cognitive variables

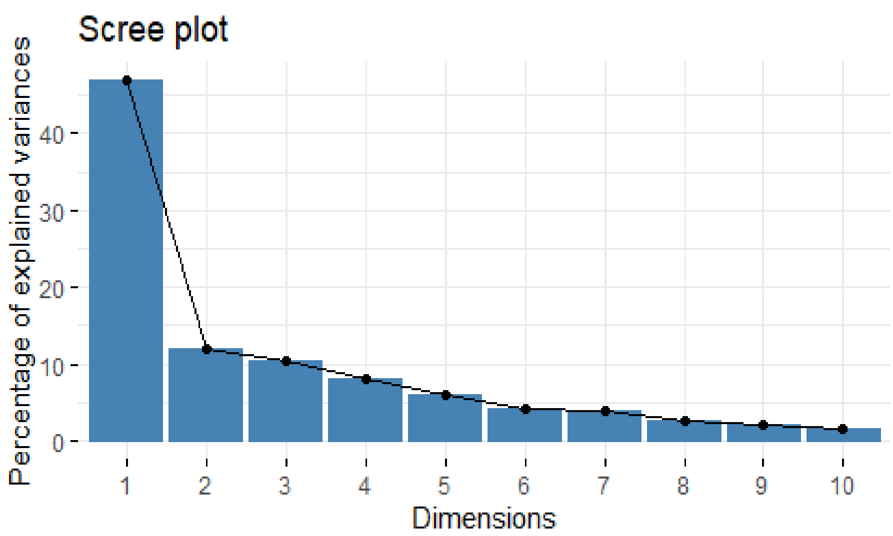

Figure 11: Scree plot showing eigenvalues across principal components for cognitive variables

EFA results have been shown in the table 3 below where, we can see two latent underlying f actors with loadings on each cognitive variable on factor 1 and factor 2. FGTS11LSsommed, D3S1CAReponses, FGTS11RKVArest and UFOV_Selective_Attention having highest loadin g on 0.85, 0.79, 0.78 and 0.77 on Factor 1, whereas, TMTS2DSCOREDif and TMTS2QSCO REQuo have highest loading on Factor 2 with 0.90 and 0.94 scores respectively. This is simil ar to finding on the graphical representation of the PCA from direction of the variables in the across Dim1 and Dim 2.

Cognitive Variables	PA1	PA2
UFOV_Processing_Speed	0.10	-0.09
UFOV_Divided_Attention	0.61	0.09
UFOV_Selective_Attention	0.77	0.11
Persp	0.56	0.11
D3S1CAReponses	0.79	0.08
TMTS2DSCOREDif	0.43	0.90
TMTS2QSCOREQuo	0.12	0.94
FGTS11LSsommed	0.85	0.08
FGTS11RKVArest	0.78	0.05
FGTS11RLVArest	0.72	0.06
CORSIS1UBSEmpa	0.70	0.13
CORSIS5UBSEmpa	0.73	0.21
INHIBS3DWIndic	0.36	0.02

Table 3: Standardized loadings (pattern matrix) based upon correlation matrix for visual variables

3.4) Testing Common-Cause Hypothesis:

The mediation analysis was conducted in the final step of the statistical analysis, where the sample was divided into two groups: young and old. This was done in the study by (Shaqiri et al., 2019) where comparison between findings of the two groups were done. The age distribution for our dataset showed bimodal distribution, therefore, we decided to divide the sample into two age groups: young (<52 years) and old (> 52 years) from determining median age as 52 years across the age of 186 subjects. The age distribution was once again checked across the two groups which revealed a normal distribution. Multivariate analyses were done after this on the two groups by performing correlations, PCA, EFA and mediation analysis across the factor derived from sensory processing and cognitive function with age variable. The mediation analysis was conducted using the 'Psych' package on R. The primary aim to perform mediation analysis was to determine if 'Sensory processing' mediates the relationship between 'Age' and 'Cognitive function' across young and old population. We extracted the score of each individual on Dim 1 from PCA performed on young population for sensory processing and cognitive function. The mediation was conducted using the scores for both parameters and age. Hence in the analysis, dependent variable was cognitive function, independent variable was age and mediating variable was sensory processing. Based on the variance across Dim 1 in PCA plot and eigenvalues in the scree plot we see that only one dimension is sufficient to describe sensory and cognitive variables. In the older population, the mediation analysis resulted for total effect of age on cognition with 0.06, the direct effect of age on cognitive without sensory with 0.05 and indirect effect of age on cognitive through sensory with 0.01 as depicted in the Figure 12. Findings were recorded with p-value= 0.0257 (C. I= 0.01-0.01). Figure 13 show mediation in younger population show that total effect of age on cognitive function is 0.1 and direct effect of age on cognitive without sensory variable is 0.1. Indirect effect of age on cognitive through sensory is 0. Findings were recorded with p-value= 0.0000742 (C. I= 0.01-0.01).

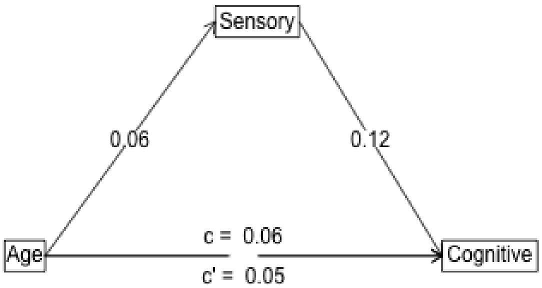

Figure 12: DAG for mediation in old subjects

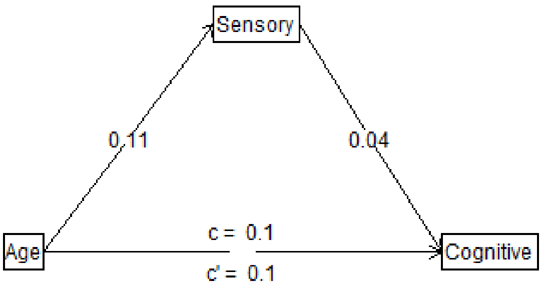

Figure 13: DAG for mediation in young subjects

4. Discussion:

The focus of research in cognitive aging primarily on description and explanation of age-related changes in cognitive functioning. Previous literature has reported that a large proportion of age-related variance in cognitive functioning is accounted by age-related impact in sensory and motor processing. Common cause hypothesis suggests that a common factor is influenced by aging, and this factor in turn influences both aging, sensory processing and cognition. Information degradation hypothesis suggests that perceptual decline influences performance in cognitive tasks, in that impoverished sensory processing is compensated by cognitive resources, thereby taking up those resources from being used for cognitive tasks. Sensory deprivation hypothesis suggests further that constant strain on cognitive resources due to impaired sensory processing progressively leads to a cognitive decline.

Therefore, testing of the age-factor affecting sensory and cognitive factors separately against age factor affecting cognitive decline through sensory decline by mediation implying the test of common cause against information/sensory degradation hypotheses. The mediation analysis has been able to depict the role of sensory processing as a mediator between age effect on cognitive abilities across young and old population. In young population the results are consistent with the hypothesis that sensory variables to not mediate age effect on cognition (as c=c'), but in the old population there is more pronounced mediation effect of sensory variables. This gives support for sensory deprivation hypothesis.

From results section, we could see that sensory decline mediates the effect of aging on cognitive function which confirms the Information degradation/ sensory deprivation hypothesis in the old population with statistically significant p-value. The similar was not noted for younger population where we saw sensory processing does not mediate the effect between aging on cognitive functioning with not statistically significant p-value.

Similar analyses have been conducted by (S. M. Hofer et al., 2003) in their study, which included sensory processing (visual abilities, auditory acuity), cognitive functioning and motor abilities for 1041 subjects. Absence of common cause factor was reported from the research with further indication that effect of the process of aging on sensory processing and cognitive abilities is relatively independent, multidimensional and complex in nature. The common cause theory of cognitive decline has been studied by analysing the performance in intellectual and sensory domain, but in the terms of visual functioning or perception, only a small set of tests has been evaluated and the previous results have shown the common cause does not exist.

In this study, a lager battery of measurements was used to represent comprehensive visual functioning ability and drew conclusions by comparing the younger and older populations (cross-sectional analysis). We found in general the older population performed worse than the young group. This finding is similar to previous studies where motion detection and other visual perception tests were used. Besides, we also found that the variation within the old group was larger than that within the young group and this implied that participants in the old group have different degrees of age-related degeneration. According to the PCA and EFA results, we did not find a common cause that can explain either the processing through sensory perception decline and cognitive decline.

The results from sensory perception variables supported the finding stating that there is no evidence for a common factor underlying visual abilities or auditory abilities in the older population, although our measurements were different from those had been used in previous studies. For example, (Shaqiri et al., 2019) tested vernier discrimination and backward masking, Freiburg Visual Acuity Test, orientation discrimination, contrast sensitivity, motion direction discrimination, biological motion perception, simple reaction time, visual search test, and Simon test. Furthermore, we classified some variables as cognitive functioning abilities but, in previous studies, tests from intellectual domain were used which might be the reason we did not see strong correlations among our cognitive variables.

However, we found there is stronger correlations from Corrplot matrices for perceptual variable in our population. If we looked into the PCA variable correlation, we could find intercorrelations between BAT, C-Quant, PR, VF, visual acuity log MAR which are in line with the results from

Corrplot correlation tests and the simple structure model from EFA. We agree that this is due to decreased contrast sensitivity and increased sensitivity to glare in the elderly population and it has been established that visual function decreased linearly with age for the acuity, contrast sensitivity, glare, and visual field tests. Although we do not find a single common cause to explain visual perceptual decline, we still have stronger categorization by combination of perceptual variables in the old group compared to the young group.

There is relatively stronger link seen between different tests in the old group than in the young, especially in relation to BAT, CSF, CQUANT, and PR (perceptual variables) and in relation to CORSI, D3 and TMT (cognitive variables). Thus, even though no single common cause seems to exist, it is possible that with a larger sample a common cause maybe existing in decline of sensory processing and cognitive functioning through aging of subjects and several important factors related to age can potentially be formulated.

In this preliminary study, we applied cross-sectional design and only had 186 participants (92 young and 94 old adults) where sections of them did not complete all tests. It should be noted that we require to be cautious while interpreting findings from cross-sectional studies. Strengths for our analysis is a multivariate dataset with large battery of data on vision, audition, cognition on the subjects from the Silversight cohort study on french population. Limitation can be noted as small sample size and requirement for stronger predictors of cognitive functioning rather using the ones we used for our analysis.

Therefore, a longitudinal study with more subjects would be suggested to study the age effect on visual and auditory functioning decline in lifespan. The choice of perceptual and cognitive measures may be another limitation of this study. Since we would like to examine the relations among all variables which were not widely used in testing the common cause theory for cognitive or visual perceptual decline, we computed PCA and EFA to explore our multivariate data set. Based on our EFA results, it seemed that the intercorrelations between variables are more complicated than the simple structure model. Thus, for the future study, confirmation factor analysis or structural equation modelling (Kline, 2011) methods can be used to confirm the information degradation without first extracting principal factors and would be recommended to fit a complex model with hypothesized latent factors.

5. Conclusion:

This study is the first cross sectional research from Silversight Cohort study exploring the presence of common cause due to aging on decline in sensory processing and cognitive function and mediation of sensory perception between effect of age on cognitive function confirming information degradation and sensory deprivation hypothesis. The current study demonstrates statistically significant mediation of sensory variable between age effect on cognitive functioning in healthy adults. We report a mediation present in older population than younger population. This shift has been linked to the development of information degradation and sensory perception hypotheses where aging effects the ability to see or deteriorates the quality of vision and audition which in turn causes cognitive function to be declined.

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Résumé en Français

Contexte: La perception sensorielle et la fonction cognitive sont mutuellement liées, mais il n'est pas clair si ce lien est dû à des causes communes liées à l'âge pour les variables sensorielles et cognitives, ou si les pertes cognitives peuvent résulter d'une détérioration progressive de l'apport sensoriel au cours du vieillissement. Les études précédentes portant sur cette question incluaient rarement le sens auditif et utilisaient uniquement des tests d'acuité standard pour évaluer la vision. Ici, nous avons utilisé une batterie étendue de tests sensoriels, y compris une évaluation auditive, visuelle et cognitive, afin d'étudier la présence de causes courantes de déclin lié à l'âge de la perception sensorielle et de la fonction cognitive dans une population de participants adultes en bonne santé.

Méthodes: Cette étude a été réalisée chez 186 sujets (51,07% de femmes, 48,92% d'hommes) participant à l'étude de cohorte Silversight. Chez tous les participants (le plus jeune: 22 ans, le plus âgé: 86 ans), de multiples mesures du sens visuel, des tests d'audiogramme et des capacités cognitives ont été effectuées. Des analyses univariées de l'audition et de la vision ont été effectuées pour comparer nos données avec des études antérieures. Les associations entre le vieillissement, la perception sensorielle et la fonction cognitive ont été évaluées par analyse multivariée, y compris l'analyse factorielle et l'analyse de médiation.

Résultats: une prévalence de 4,44% de déficience visuelle a été trouvée, 39,4% de déficience auditive et 1,75% de déficience sensorielle double dans le groupe d'âge de plus de 51 ans confirmant le modèle de déficience du traitement sensoriel dans les groupes plus âgés. Aucune présence de cause commune due à l'âge n'a été détectée dans le traitement sensoriel. Cependant, le traitement sensoriel s'est avéré un médiateur significatif de l'effet de l'âge sur la fonction cognitive dans la population de participants plus âgés.

Conclusion : La découverte que les variables sensorielles médiatisent l'effet de l'âge sur la fonction cognitive uniquement dans la population âgée, ces résultats soutiennent l'hypothèse de dégradation de l'information / privation sensorielle, indiquant que la détérioration progressive de l'apport sensoriel est associée à des scores de traitement cognitif plus faibles. Une caractérisation plus détaillée de ce phénomène peut être obtenue en appliquant des méthodes de modélisation d'équations structurelles pour analyser ces données.